1. INTRODUCTION

1.1. The Environment:

Environment means those external conditions which surround, act upon, and influence an organism or its parts (Kerr and Cool, 1956). This definition is a very broad one allowing for a multitude of factors that may affect the organism, whether the organism is an unicellular plant, an insect, or man himself.

Early sources of natural contamination were due to earthquakes, erupting volcanoes, plant pollen, and forest fires, which ravaged many acres of land as far back as the history of men (Opik, 1971).

Environmental pollution, an undesired spin-off human activity, was relatively insignificant until urbanization. People dug coal from the ground, used it to heat homes, and thus created an atmosphere of sulfurous smoke above the cities. From the thirteenth century onward, people have accepted a polluted atmosphere as a part of urban life. Power plants burn fossil fuels to generate electricity, steel mills have grown along river banks and lake shores; oil refineries have risen near ports and oil fields; smelters roast and refine metals near great mineral deposits; the automobile is all present. All these pollute the air, water, and soil around them.
When synthetic materials came of age, factories were built to produce them, little thought was given to the toxicity of chemicals not intended for use to man. Only a few of the three million known chemicals have been tested for toxic effects; many have been indiscriminately disseminated throughout the environment (Klaassen, 1980). Mankind is increasingly exposed to overcrowding, noise, and an atmosphere polluted by smoke and exhaust fumes in towns and cities, to chemical and physical hazards at work, to food that may contain residues of insecticides, fungicides, hormones, antibiotics and a host of other undesirable chemicals, and to polluted water in many rivers and lakes and even in the sea. In the developing countries, human health and life are continually jeopardized by biological pollution resulting from inadequate environmental sanitation, in particular the absence of safe water supplies. The consequences of these and other forms of environmental pollution are of direct and immediate concern to all of us.

1.2. Air Pollution;

When we think of the air pollution problem, however, we associate its source with some activity of man, whether it be farming, manufacturing, or just moving about in this world of ours. Practically all air is contaminated to some extent, or other, so some reasonable definition of the term "air pollution" is prerequisite to an orderly discussion (Faith, 1959).
Basically, air pollution is the presence of foreign substances in the air. Mazik (1971) has defined air pollution as a mixture of one or more contaminants of dust, fumes, gas, mist, odor, smoke, or vapor discharged into the air by nature and by man in such quantities and of such duration which tend to be injurious to human, animal, or plant life and property and interfere with the comforts of life itself.

Air contaminants may be dispersed rapidly in large quantities into the air or may accumulate in various concentrations, depending upon topography of the geographical area and the existing meteorological conditions at the time of dispersal.

Air pollution affects the health and well-being of all citizens of the globe. The extent to which polluted air causes ill health is difficult to measure. The problems confronting the scientist and the general public in air pollution concern the economic and social relationships which appear to be the most difficult to control. Many areas of academic discipline are being utilized in the physical and biological sciences to help understand the technical complexities of air pollution (Mazik, 1971).

1.3 Sources of Air Pollutants:

Five major sources account for 90% of the tons of pollutants that are emitted annually (Amdur, 1980):
Fig. 1: Major Air Pollutants and Principal Sources. Box Indicates Solid Particles; "Cloud" Indicates Gases.
Fig. 1: Major Air Pollutants and Principal Sources. Box indicates solid particles; "Cloud" indicates gases.
(i) Transportation (particularly automobiles) (60%)
(ii) Industry (19%)
(iii) Electric power generation (13%)
(iv) Space heating (6%) and
(v) Refuse disposal (3%)

1.4. Types of Air Pollutants:

According to Amour (1980) five pollutants account for nearly 98% of air pollution. These are carbon monoxide (52%), sulfur oxides (18%), hydrocarbons (12%) and nitrogen oxides (6%). A distinction is often made between two kinds of pollution:

1) The first is characterized by sulfur dioxide and smoke from incomplete combustion of coal and by conditions of fog and cool temperature. Because of its chemical nature, it is termed a reducing type of pollution.

2) The second is characterized by hydrocarbons, oxides of nitrogen, and photochemical oxidants. It is caused by automobile exhaust and occurs especially in areas such as the Los Angeles basin, where intense sunlight causes photochemical reactions in polluted air masses that are trapped by meteorological inversion layer. Because of its nature, it is described as an oxidizing type of pollution or photochemical air pollution.
The solution of many air pollution problems requires considerable knowledge of the chemistry both of the natural atmosphere and of contaminated atmospheres (Cadle and Magill, 1950).

New potential air pollutants are continually introduced through the use of new substances, combination of chemicals, and process changes. Classification schemes have been devised covering a variety of pollutants that may be present in the atmosphere.

On the basis of origin, air pollutants are classified as primary and secondary in quality. Primary pollutants are those which are emitted into the atmosphere as a consequence of a process. Secondary pollutants are formed as products of some reaction; generally, an existing pollutant reacts with some other substance in the atmosphere (Zusik, 1971).

On the basis of the state of matter, air pollutants are classified as gaseous or particulate type. Gaseous pollutants are present in the atmosphere as contaminants which behave similar to air itself.

Particle pollutants include dust of any type, fumes, mist, and sprays and are classified as solids or liquids. These pollutants are generally finely divided and dispersed in the atmosphere (Zusik, 1971).
1.5.1. Pollutant Concentration:

The amount of gaseous pollutants contained in air mass is given by the concentration in parts per million \( (C_{\text{ppm}}) \) as the ratio of the partial volume \( (C_v) \) of pollutant gas to the partial volume of the air. The other most valuable parameter is the particle-loading \( (C_{\text{mv}}) \) of the air, which is defined by Crawford (1980) as the total mass of suspended particle-material per unit volume of mixture. He has correlated \( C_v \) to \( C_{\text{ppm}} \) in the following equation:

\[
C_v = \frac{C_{\text{ppm}}}{10^6 + C_{\text{ppm}}} \approx 10^{-6} \frac{C_{\text{ppm}}}{C_{\text{ppm}}} \quad (1-1)
\]

The density of air is given by the perfect gas law:

\[
P_a = \frac{P}{\text{Rt}} \quad (1-2)
\]

in which \( R \) has the value of \( 287 \text{ J/kg} \cdot \text{K} \) for air. Here \( P \) is the pressure of the mixture. For gaseous and vapor pollutants at small concentrations, the perfect gas law holds quite well also:

\[
P_p = \frac{P_m \rho}{287 \mu \text{K}} \quad (1-3)
\]

where \( \mu \) is the molecular weight of the pollutant substance and \( P \) is the pressure of the mixture.
For particulate pollutants, the concentrations can be written in terms of the number distribution function \( n(d) \), where \( n(d) \) is now modified to represent number of particles per unit volume of mixture:

\[
C_v = \frac{\pi}{6} \int_0^\infty n(d) d \quad d \quad d \quad \cdots \quad (1 - 4)
\]

where \( d \) is the mean diameter based on mass; in any case, if \( \mu_p \) is the particle mass based on diameter \( d \), any diameter may be used in the integration.

The mass-volume concentration \( C_{mv} \) can be shown by the equation (1.5):

\[
C_{mv} = \int_0^\infty n(d) \mu_p(d) d = \frac{\pi}{6} \mu_p \int_0^\infty n(d) d \quad d \quad d \quad \cdots \quad (1 - 5)
\]

when a pollutant air mixture is flowing through a duct, the volumetric flow rate of mixture is denoted by \( \dot{Q} \), which represents the volume of mixture that crosses any fixed section of the duct in unit time.

The number of particles flowing past a section per unit time is given as:

\[
N = NQ \quad \cdots \quad \cdots \quad \cdots \quad \cdots \quad (1 - 6)
\]

in which \( N \) is the total number of particles per unit volume of mixture.
1.5.2. Gaseous Pollutants:

Gaseous pollutants in the atmosphere arise from two general sources: Combustion of fuels and the handling and processing of chemicals. The latter category includes not only chemical manufacture but related activities, such as petroleum refining, smelting of ores, and various solvent-handling activities (Faith, 1959).

Almost every gaseous material known escapes into the air at one time or another, but by far the most common are sulfur dioxide, hydrogen sulfide, carbon dioxide, nitrogen oxides, hydrocarbons and their derivatives (chiefly chlorine, bromine, hydrogen fluoride, and chlorinated solvents). Table-1 shows source and effects of some gaseous pollutants on living beings. The proper maximum allowable concentrations (M.A.C.) of various gases in air is subject to debate, and allowable limits have been promulgated for the protection of people living and working in various environments. These limits have been modified over the years, usually downward, to reflect increased knowledge of long range toxic effects of such substances.

For workers in industrial environments, standards have been published by the American Conference of Govermental Industrial Hygienists (1973), and their recommendations are given in Table-2.
<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Major Sources</th>
<th>Principal Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfur dioxide</td>
<td>Fuel combustion (coal, oil, cellulose material), industrial processes.</td>
<td>Sensory and respiratory irritant, plant damage, corrosion, possible adverse effects on health.</td>
</tr>
<tr>
<td>Hydrogen sulfide</td>
<td>Coke, distillation of tar, petroleum and natural gas refining, manufacture of rayon, and in certain chemical processes.</td>
<td>Odor nuisance, caused deaths in Costa Rica, Mexico, when large quantity escaped from units of a natural gas refining plant.</td>
</tr>
<tr>
<td>Carbon dioxide</td>
<td>Combustion processes.</td>
<td>Used as an index of pollution from combustion operations.</td>
</tr>
<tr>
<td>Nitrogen oxides (nitric oxide and nitrogen dioxide)</td>
<td>Fuel combustion, industrial processes.</td>
<td>Visibility reduction, plant damage, and sensory irritation are produced. In photochemical reactions involving nitrogen oxides, these gases may also cause adverse health effects, and nitrogen dioxide can cause decreased visibility.</td>
</tr>
<tr>
<td>Oxidants</td>
<td>Atmospheric photochemical reactions involving nitrogen oxides, organic gases, vapors, and solar radiation.</td>
<td>Sensory and respiratory irritation, plant damage, Provides and index of visibility reduction due to aerosols. Possible effects on health.</td>
</tr>
<tr>
<td>Substance</td>
<td>$C_{ppm}$</td>
<td>$C_{nv}$</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
<td>---------</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>100</td>
<td>120</td>
</tr>
<tr>
<td>Acetic Acid</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>Benzene</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Carbon disulfide</td>
<td>20</td>
<td>60</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>50</td>
<td>55</td>
</tr>
<tr>
<td>Carbon tetrachloride</td>
<td>10</td>
<td>65</td>
</tr>
<tr>
<td>Chloroform</td>
<td>25</td>
<td>120</td>
</tr>
<tr>
<td>Ethyl Alcohol</td>
<td>1000</td>
<td>1900</td>
</tr>
<tr>
<td>Hydrogen cyanide</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Hydrogen sulfide</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Nitric Oxide</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>Ozone</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Sulfur dioxide</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>Sulfuric Acid</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>
1.6. Chemical Reactions in Contaminated Atmospheres:

A variety of chemical reactions occur in the contaminated atmospheres of cities. The products of such reactions have been blamed for many of the unpleasant properties of polluted atmospheres.

The substances which can react chemically in the atmosphere fall into two groups: major natural constituents of the atmosphere, which are present in high concentrations, and contaminants, usually present at low concentrations. These groups differ in concentration by a factor of $10^6$ to $10^9$. This large difference in concentration is convenient for purposes of classification of reactions and calls for careful interpretation of the kinetic and photochemical data of the literature (Cadle and Magill, 1956).

The half-life for a first-order reaction does not change with concentration of the reactant. The velocity constant $K$ for a reaction is usually a function of the temperature. The relationship between velocity constant and temperature can generally be indicated by an equation:

$$K = Ae^{-E/RT}$$  

(1 - 7)

Where $A = a$ constant having the same dimension as $K$

$E = activation$  

energy$ $ for$ $the$ $reaction$

$R = gas$ $constant$

$T = absolute$ $temperature.$

The changes in heat content accompanying a number of reactions which might produce oxygen atoms are shown in Table-3.
<table>
<thead>
<tr>
<th>Reaction</th>
<th>$H_a$ (kcal)</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>$O_2 \rightarrow 0 + 0$</td>
<td>+118.2</td>
<td>2,420</td>
</tr>
<tr>
<td>$O + O_2 + H \rightarrow O_3 + H$</td>
<td>-3.6</td>
<td>Dark</td>
</tr>
<tr>
<td>$SO_2 + O_2 \rightarrow SO_3 + O$</td>
<td>+46.1</td>
<td>6,197</td>
</tr>
<tr>
<td>$H_2O + O_2 \rightarrow H_2O_2 + O + O$</td>
<td>+72.4</td>
<td>3,919</td>
</tr>
<tr>
<td>$NO + O_2 \rightarrow NO_2 + O$</td>
<td>+45.5</td>
<td>6,279</td>
</tr>
<tr>
<td>$NO_2 + O_2 \rightarrow NO + O_3$</td>
<td>+46.1</td>
<td>5,940</td>
</tr>
<tr>
<td>$CH_4 + O_2 \rightarrow CH_3OH + O$</td>
<td>+29.9</td>
<td>9,895</td>
</tr>
<tr>
<td>$CO + O_2 \rightarrow CO_2 + O$</td>
<td>-8.5</td>
<td>Dark</td>
</tr>
</tbody>
</table>
Almost no Indian city today can be said to be free from one kind of pollution or another. Delhi is known for its winter smog, Bombay for its noise menace, and Calcutta for its foul air, choked as this is with smoke from its several chimney stacks.

In India on an ordinary land, about 19 tonnes of dust settles down per square kilometre area, whereas in areas of heavy industries the settlement of dust is as high as 3.6 tonnes. In such areas of air pollution, people mostly suffer from diseases of the lungs, nose, ear, throat and eye (Behura, 1984).

Environmental pollution has produced facts that are scarier than fiction; Bombay, by releasing 1000 tonnes of pollutants in the air every day, has earned the title of 'The Gas Chamber'. In Delhi, a normal person's blood stream contains more DDT than in most part of the world. Calcutta releases 1100 tonnes of dust and injurious gases into the air every day. In fact, Calcutta has reached the pollution level of Los Angeles - one of the world's most polluted cities - though its economic development is less than 1% of Los Angeles.

It is heartening to find that, despite the compulsions of a developing economy, there is a lively awareness in India of the urgency of dealing with the latent problem of environmental decay and degradation. In our country, this growing
concern has taken the shape of two legislations: 'The Water Act' and 'The Air Act'. Soon to be passed and implemented. Acts will make it binding on all industries to take immediate measures to control pollution. Failure to do so will lead to substantial penalties and fines.

1.7.1. \( \text{SO}_2 \) Emission in India:

While it is agreed that sulfur oxides and nitrogen oxides make the largest contribution to acid precipitation, it is also accepted that 70% of the acidity is due to sulfur oxides and the reminder to oxides of nitrogen (Ahmed and Sharma, 1981). Major sources of sulfur oxide are coal, petroleum and metal smelters. In addition, \( \text{H}_2\text{SO}_4 \) plants and paper industries contribute 15% to the total sulfur emissions (Table-4). Cities like Bombay, Calcutta and Delhi have fairly high levels of \( \text{SO}_2 \); while other industrial cities like Ahmedabad, Nagpur and Hyderabad are also reaching critical levels. According to a survey conducted by National Environmental Engineering Research Institute (NEERI), Nagpur, Bombay leads over other cities in \( \text{SO}_2 \) concentration (Table-5) (Sampat and Sharma, 1981).

Apart from these sources, smaller industrial units and household activities also emit sulfur oxides, nitrogen oxides and other gases into the atmosphere.
<table>
<thead>
<tr>
<th>S. No.</th>
<th>Cities</th>
<th>Mean Value of SO₂ (Microgram/cubic meter)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Bombay</td>
<td>47.11</td>
</tr>
<tr>
<td>2.</td>
<td>New Delhi</td>
<td>41.43</td>
</tr>
<tr>
<td>3.</td>
<td>Calcutta</td>
<td>32.99</td>
</tr>
<tr>
<td>4.</td>
<td>Kanpur</td>
<td>15.97</td>
</tr>
<tr>
<td>5.</td>
<td>Ahmedabad</td>
<td>10.96</td>
</tr>
<tr>
<td>6.</td>
<td>Madras</td>
<td>8.39</td>
</tr>
<tr>
<td>7.</td>
<td>Nagpur</td>
<td>7.71</td>
</tr>
<tr>
<td>8.</td>
<td>Hyderabad</td>
<td>5.06</td>
</tr>
<tr>
<td>9.</td>
<td>Jaipur</td>
<td>4.15</td>
</tr>
</tbody>
</table>

Source: ISRL (Nagpur)
Table 5

Sulfur Dioxide Emissions in India (1978) (Petroleum not included)
(Sampat and Sharna, 1981)

<table>
<thead>
<tr>
<th>Source</th>
<th>$SO_2$ (Million lb)</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Combustion of coal</td>
<td>3040</td>
<td>9.75</td>
</tr>
<tr>
<td>2. Copper smelters</td>
<td>20.58</td>
<td>0.64</td>
</tr>
<tr>
<td>3. Zinc smelters</td>
<td>41.42</td>
<td>1.29</td>
</tr>
<tr>
<td>4. Sulfuric Acid Manufacturing</td>
<td>98.21</td>
<td>3.06</td>
</tr>
<tr>
<td>5. Pulp and Paper Industries</td>
<td>8.12</td>
<td>0.25</td>
</tr>
<tr>
<td>Total</td>
<td>3208.33</td>
<td>100.00</td>
</tr>
</tbody>
</table>
Recently, the Archaeological survey of India (ASI) has demanded a re-examination of the possibility of adverse effect of Mathura refinery on Taj Mahal. The $SO_2$ emitted by the chimneys of the refinery is converted into $H_2SO_4$ by the atmospheric oxidation, which is dissolving the calcium carbonate of the marble to calcium sulfate. It is estimated that the oil refinery would release 3 tonnes of $SO_2$ per day. Concentration of $SO_2$ would be 100 micrograms per cubic metre in Agra, which would play havoc with the monuments. The lake at Bharatpur Bird Sanctuary is getting acidified. It is also reported that redstone of Lal Quila at Delhi is being decolourised due to emissions from nearby railway yards. How many more monuments and lakes are being affected is yet to be found out.

1.7.2. Monitoring of Health Effects of Air Pollution in India

The paucity of data on health related studies in India led to a cross-sectional study being carried out at various traffic junctions of Ahmedabad city in order to elucidate the health hazards of autoexhaust pollution on occupationally exposed high risk population groups like traffic policemen and shopkeepers stationed at the traffic corners (Nedapa, 1979). Observations of this study confirm the view that the low ambient exposure to carbon monoxide in heavy smokers is not additive to the rise of carboxyhaemoglobin (COHb) in blood. A significant variation of lung function test was noted in a group heavily exposed to oxides of nitrogen.
1.2. The Epidemiology of Air Pollution:

In the search for adequate proof of correlation of human disease with air pollution, according to Phair (1959), three avenues have been most accessible. The first is the broad field of industrial toxicology. The second is the group of careful studies of the "epidemic" incidents when, for a variety of causes, large numbers of people are subjected to an extraordinary exposure. The third is the comparison of morbidity and mortality records collected routinely by health departments and other official agencies.

The several effects of air pollution have been classified by Benjamin Linsky (1955), air pollution control officer for the Bay Area (San Francisco, California) Air Pollution Control District:

(i) annoyance to senses of people
(ii) damage to health
(iii) interference with production and services
(iv) property damage
(v) vegetation damage
(vi) scaling of surfaces
(vii) sky-darkening, and
(viii) limited visibility.

The most important of these is the damage to human health. It is very well known that diseases of unknown
Fig. 2: Environmental pollution threat to man's survival.
etiology are produced by air pollution. In human beings, reactions such as local irritation of the respiratory tract, or if the pollutants are absorbed into the blood, tissue changes in the brain, liver, kidneys, and other tissues (Phair, 1959).

1.8.1. Annoyance to the Senses of People;

This category of air pollution effects includes a multitude of reactions that can be generally divided into two classes (Faith, 1959).

(i) Eye, Nose and Throat Irritation;

A case where an atmospherically produced eye irritant was known was reported in 1952 (Adams and Schneider, 1952).

In surveys carried out in Los Angeles in 1954, 1955, and 1956 (Faith et al., 1957), 10 to 15 panels of volunteer subjects (5 to 23 persons each) reported eye irritation at regular intervals during the smog season.

(ii) Odor;

Other problems are the extreme sensitivity of the sense of smell, tremendous variations among individuals, and desensitization of the olfactory nerve by some substances. Common descriptions of odors include sulfurous (hydrogen sulfide and mercaptans), nitrogeous (decaying plant and
animal life), oxidizing (ozone and chlorine), nauseating (methylene), aldehydic, sweet, and aromatic (coffee roasters) (Feith, 1959).

1.8.2. Damage to Health:

The health effects of air pollution must clearly differentiate between the hazard of industrial atmospheres inside manufacturing or processing plants and those of the "outside" atmosphere. Health effects in the first-mentioned environment are classified as occupational diseases and belong to the general field of industrial toxicology. Safe concentrations for a 8 hour exposure of healthy persons to toxic gases and dusts have been established (Feith, 1959).

In contrast to the effect of toxic compounds on small groups of healthy workers in industrial environments, the health problem of air pollution deals with the exposure of a larger segment of population. It may deal with extraordinary concentrations of pollutants for several days, such as in the Donora disaster, or with such lower levels almost continually.

There is no doubt that air pollution can cause widespread illness and sometimes death. This has been proved, unfortunately, in the several London disasters, as well as those at Donora and in the Heusv Valley.
The extent of damage to health from air pollutants in lower concentrations or for shorter times than those experienced in disasters is still a matter for speculation.

Since 1950, considerable research on the health effects of air pollutants has been carried out, but no definite conclusions have been reached. Nevertheless, many physicians report that patients with asthma, hay fever, and chronic respiratory diseases suffer especially during smog periods.

The suspicion of damage to health has been an important factor in developing air pollution control laws and in arousing public sentiment for clean air. In Los Angeles County an "alert" system has been established whereby a state of emergency may be called when the concentration of any one of four air pollutants reaches a prescribed value. The values chosen (ozone, 1.5 ppm; carbon monoxide, 125 ppm; sulfur dioxide, 10 ppm; nitrogen dioxide, 6 ppm) were recommended by a committee of physicians and other scientists on the basis of danger to human health.

Damage to the health of animals is related both to the damage to human health and damage to vegetation. Normally, though, animal deaths are related to ingestion of forage on which toxic dusts have accumulated. The more important pollutants of this type are fluorides, arsenic-containing compounds, certain lead compounds, and chlorine-containing insecticides (Phillips, 1956).
<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>33.1</td>
</tr>
<tr>
<td>Non-productive</td>
<td>20.2</td>
</tr>
<tr>
<td>Productive</td>
<td>12.9</td>
</tr>
<tr>
<td>Sore throat</td>
<td>23.1</td>
</tr>
<tr>
<td>Constriction of chest</td>
<td>24.5</td>
</tr>
<tr>
<td>Headache</td>
<td>17.0</td>
</tr>
<tr>
<td>Dyspnoea without orthopnea</td>
<td>12.9</td>
</tr>
<tr>
<td>Moistening of the eyes</td>
<td>12.3</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>8.4</td>
</tr>
<tr>
<td>Inflammation</td>
<td>8.0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7.4</td>
</tr>
<tr>
<td>Nausea without vomiting</td>
<td>7.1</td>
</tr>
<tr>
<td>Nasal discharge</td>
<td>6.6</td>
</tr>
<tr>
<td>Fever</td>
<td>2.6</td>
</tr>
<tr>
<td>Choking</td>
<td>2.3</td>
</tr>
<tr>
<td>Asthes and pains</td>
<td>1.9</td>
</tr>
<tr>
<td>Weakness</td>
<td>1.8</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>1.0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0.1</td>
</tr>
</tbody>
</table>
Klaassen (1980) has pointed out that acute episodes of high pollution cause mortality and morbidity. There are three classical examples: 65 people died in the Meuse valley, Belgium in 1930; 20 people died in Donora, Pennsylvania in 1948; 4000 people died in London in 1952. Each of these incidents occurred during an atmospheric temperature inversion that lasted for 3 to 4 days. During this time the concentration of pollutants surpassed the normal levels for these already heavily polluted areas, where coal was the main fuel; the pollution was of the reducing kind. Most of the people who fell ill or died were elderly; some had either cardiac or respiratory diseases or both; none could cope with the added stress of breathing heavily polluted air.

Acute effects on health are thus clearly associated with the reducing type of pollution. While there is less evidence to associate photochemical oxidant pollution with such effects on human health, there are significant correlations between levels of oxidants in the air and hospital admissions for allergic disorders, inflammatory disease of the eye, acute upper respiratory infections, influenza and bronchitis.

1.9. Absorption and Deposition of Toxicants by the Lungs:

The site of deposition of aerosols in the respiratory tract depends on the size of the particle. Particles of 5 μm, or larger in diameter, are usually deposited in the upper airway. Those deposited in the non-ciliated anterior portion of the nose remain there until removed by wiping, blowing, or
sneezing. In the posterior portion of the nose, a mucous blanket propelled by cilia carries insoluble particles to the pharynx in minutes. These particles are swallowed and pass to the gastrointestinal tract. Soluble particles dissolved in mucus may be carried to the pharynx or absorbed through the epithelium into the blood. Particles less than 2 μm in diameter remain suspended in the inhaled air and reach the alveolar zone of the lung, where they may be readily absorbed. The surface area is large (50 to 100 sq.m); the rate of blood flow is high; and the blood is in close proximity to the alveolar air (10 μm). The alveoli are often sites for absorption of liquid aerosols and particles, as well as gases. Liquid aerosols pass the alveolar cell membranes by passive diffusion in proportion to their lipid solubility. Particles can remain in lymphatic tissue for long periods of time, and, for this reason, the tissue has been called the dust store of the lungs (Maassen, 1980).

1.10. Choice of Air Pollutants, Sulfur Dioxide (SO₂) and Hydrogen Sulfide (H₂S) at Threshold Limit Values, as a Model for Toxicological Investigation;

For the present study, out of the several gaseous pollutants, SO₂ and H₂S have been selected for toxicological investigation of the brain. Interaction of SO₂ and H₂S with the lipid contents of the nervous tissue as the main target of experimental toxicosis, was studied because of the following reasons:
(1) The increasing pollution due to the massive industrial and automobile exhaust of sulfur compounds into the atmosphere, and its biological effects demand attention.

(2) Sulfur compounds in the air are suspected to cause deaths by respiratory ailments as well as by affecting the heart (Minsky, 1971).

(3) In Donora, Honea Valley and London, sulfur containing gases have caused a large number of fatalities in several air pollution disasters (McCabe and Clayton, 1952).

(iv) (a) Effects of H₂S on the central nervous system have been recognised for some time (Nacculo, 1969).

(b) Westermann et al. (1975) have shown that inhaled H₂S in animals, is rapidly circulated into blood via lungs, its toxic action blocks copper and iron containing enzymes, resulting in the damage to oxygen transport, in the liver. Even action on the CNS is a possibility (Westermann et al., 1975).

(c) Neurotoxic effect of H₂S is due to anoxia; as H₂S blocks the respiratory enzyme cytochrome oxidase and thus damages the brain (Klumon et al., 1979).

(d) H₂S exposure has revealed extensive necrosis of the parietal and occipital cortex of the brain, a reduction of Purkinje cells of cerebellar cortex and isolated accumulation of glia cells (Iund and Weiland, 1966).
(v) (a) Balchum (1960) has shown moderate activity of labelled $\text{SO}_2$ in brain.

(b) $\text{SO}_2$ poisoning altered the senses of taste and smell (Ferris et al., 1967).

(vi) Since brain is rich in lipids (Friede, 1960) and liquid aerosols pass the alveolar cell membranes by passive diffusion in proportion to their lipid solubility, it stands to reason that brain can be its most vulnerable target (Klassen, 1980). Further, the oxygen consumption of brain is very high (49 ml/min) (Canong, 1977). Therefore, it would be of interest to investigate the effects of sulfur containing gases on brain.

(vii) According to Medlars-II citation (March, 1981), no attempt has been made to update to evaluate the effect of sulfur containing gases on the lipid contents of the brain.

(viii) Because information on the toxic effects of long-term exposure to $\text{H}_2\text{S}$ and $\text{SO}_2$ at low concentrations is currently lacking, controlled epidemiologic studies which report individual exposure data need emphasis in future research (NIOSH, 1977).

1.11. Sulfur Dioxide ($\text{SO}_2$):

In the words of Kinney (1971) "at present the whipping boy in air pollution is sulfur".
The maximum allowable concentration (M.A.C.) in air for 8 hours of exposure is 10 ppm. Atmospheric S\textsubscript{O}\textsubscript{2} concentration is one of the measurements used by the County of Los Angeles in establishing an air pollution emergency action alert system. The concentration level of S\textsubscript{O}\textsubscript{2} for a second-stage alert, at which level general industrial operations may be curtailed, is 5 ppm.

S\textsubscript{O}\textsubscript{2} has been suspected in several air pollution disasters—notably Donora, the Haze Valley, and the several episodes in London (Faith, 1959). As far as health is concerned, S\textsubscript{O}\textsubscript{2} and its derivatives are still suspect but not 'convicted'.

1.12. Historical Reports of S\textsubscript{O}\textsubscript{2} Poisoning:

The first report of lasting harmful effects due to S\textsubscript{O}\textsubscript{2} alone came from France in 1921. Zeller (1953) reported that gas causes pneumonia, gastritis, entritis and even vaginitis.

In 1923, the first measurements of occupational environmental concentrations of S\textsubscript{O}\textsubscript{2} and its effects were reported by Lehmann from Germany.

1.13. Effects of S\textsubscript{O}\textsubscript{2} on Humans:

Yokoyama et al. (1971) observed that S\textsubscript{O}\textsubscript{2} is most likely absorbed as sulfuric acid or one of its ionization products and may undergo further biotransformation reactions in the body.
The ultimate fate of practically all absorbed \( \text{SO}_2 \) is apparently oxidation to sulfate ion, to be excreted principally as inorganic sulfate in urine.

It is well documented that persons engaged in occupations involving significant exposures to \( \text{SO}_2 \) consistently demonstrate injury associated with damage to respiratory tract (Rehoe et al., 1932; Bozotski, 1930; Greenwald, 1934; and Ferris et al., 1937). Exposure to unknown but probably high concentrations of \( \text{SO}_2 \) have caused death by asphyxia or bronchopneumonia with permanent damage (Salen, 1964); asthma-like attacks have also been reported (Romanoff, 1939). Single or repeated exposures are irritant to the nose and throat producing choking sensations, rhinorrhea, and cough (Greenwald, 1934).

Rehoe et al. (1932) has studied on workers in the refrigeration industry, where environmental concentrations of \( \text{SO}_2 \) averaging 20-30 ppm (range 5-70 ppm) obtained at the time of the study were associated with higher incidence of nasopharyngitis, alteration in the sense of taste and smell, and increased fatigue or dyspnea on exertion. Anderson's study (1950) considered changes in body weight, systolic blood pressure, or chest roentgenographic findings.

1.1a. Toxicity of \( \text{SO}_2 \) in Animals:

The effect of \( \text{SO}_2 \) on mammals is qualitatively the same that of respiratory and mucous membrane irritation and reflex...
bromchocoonstricttion with increased air way resistance.

1.15. Absorption, Distribution, Fate and Excretion of \( \text{SO}_2 \) in Animals;

Systrova (1957) working with inhaled \( ^{35} \text{S} \)-labeled \( \text{SO}_2 \) and also intravenously injected labeled sodium sulfite in cats, demonstrated that \( ^{35} \text{S} \) from either source was incorporated into the protein fractions of the blood and other organs. Balchum et al. (1960) found that in dogs exposed experimentally to \( ^{35} \text{SO}_2 \), the majority of the \( ^{35} \text{S} \) was concentrated in the trachea, bronchi, lungs, kidneys and esophagus. The ovaries, stomach, and brain were intermediate and substantially lower in activity and the liver, spleen, and heart muscle were least, apparently having a \( ^{35} \text{S} \) content as a result of diffusion from the blood or perhaps due to the blood they contained.

1.16. Mechanical Investigation of \( \text{SO}_2 \) Toxicosis;

Lee and Danner (1959) showed that exposure of guinea pigs to \( \text{SO}_2 \) (7-310 ppm) for 2 hr 30 min. among other changes, \( \text{SO}_2 \) increased the hemoglobin concentrations approximately 10% immediately after the exposure.

Recently, Gunnison et al. (1979) demonstrated that exposure of rabbits continuously to 10 ppm \( \text{SO}_2 \) for periods ranging from 3 hours to 3 days lead to sulfhydrolysis of disulfide bonds of proteins and cystine resulting in the formation of \( \text{S} - \text{SO}_3^2^- \) bonds in the lungs, trachea and plasma.
1.17. Hydrogen Sulfide ($H_2S$):

Of the various sulfur-bearing gases, $H_2S$ ranks second to sulfur dioxide as an air pollutant. It is an extremely toxic and evil-smelling gas. The maximum allowable concentration for an 8 hour exposure in working areas is 20 ppm, a value far above that found in the atmosphere.

The only air pollution disaster ascribed to $H_2S$ is the Poza Rica, Mexico, incident in 1950 (McCabe and Clayton, 1952). This was an industrial accident in which large quantities of $H_2S$ were released into the still early morning air.

1.18. Historical Reports of $H_2S$ Poisoning:

Hoppe-Seyler, in 1873, observed that the passage of $H_2S$ through the blood resulted in the formation of "Sulfomethemoglobin" (Mitchell and Davenport, 1932). Eisele and Poley (1930) demonstrated that exposure of rabbits to $H_2S$ induced crying, convulsions, trembling, respiratory disturbances, and increased salivation (Milby, 1952). Legge (1934) reported that workers in the spinning department and of an artificial silk factory in the Netherlands complained of burning and smarting of eyes, headache, dizziness, loss of appetite and weight loss.

1.19. Effects of $H_2S$ on Humans:

Persistent effect on human subjects after long term
exposure to $\text{H}_2\text{F}$ have not been conclusively demonstrated, but results of numerous studies (Foda, 1966; Ahlborg, 1951; McCabe and Clayton, 1952; and Michal, 1950) suggest that there are subacute effects.

McCabe and Clayton (1952) investigated that exposure of persons to $\text{H}_2\text{F}$ (1000-2000 ppm) in the air produced clinical changes viz.; loss of the sense of smell, burning eyes, cough, dyspnea, pulmonary edema, nausea, vomiting, unconsciousness, severe headache, vertigo, partial paralysis, neuritis of the acoustic nerve, and aggravation of pre-existent case of epilepsy. Effects of $\text{H}_2\text{F}$ on humans are summarized in Table-7.

1.20. Effects of $\text{H}_2\text{F}$ on the Central Nervous System;

Ahlborg (1951) stated that 70% of workers exposed to $\text{H}_2\text{F}$ in their daily work, often at 20 ppm or more, complained of fatigue, somnolence, lack of initiative, decreased libido, loss of appetite, headache, irritability, poor memory, anxiety and dizziness. Acute exposures to $\text{H}_2\text{F}$ at higher concentrations were associated with abnormal reflexes at both cranial and spinal nerve levels, poor memory for recent events, depression, either timidity or fierceness, and epilepsy like seizure.

A number of studies suggest that $\text{H}_2\text{F}$ produces subacute effects, particularly with the signs and symptoms of brain damage like rigidity, abnormal reflexes, and sleep disturbance (Foda, 1966; Ahlborg, 1951; McCabe and Clayton, 1952 and Michal, 1950).
The main systemic effects of \( \text{H}_2\text{S} \) poisoning are due to the action of the gas upon central nervous system. Higher concentrations of \( \text{H}_2\text{S} \) first stimulate and then depress the central nervous system (Goodman and Gilman, 1960). Grollman and Grollman (1965) stated that smaller quantities of \( \text{H}_2\text{S} \) (1 to 1000 of air), cause immediate unconsciousness lasting for several hours and then passing into fatal coma. In both of these forms the symptoms are due to direct action of sulfaides on the brain, particularly medulla oblongata. Often headaches, dizziness, giddiness, and loss of memory are complained of; the symptoms frequently appear only some time after the exposure to the toxic gas.

1.21. Toxicity of \( \text{H}_2\text{S} \) in Animals:

The effects of \( \text{H}_2\text{S} \) on humans and animals are similar. These studies have finer data on environmental conditions than do the human case studies and describe results that could not ethically be obtained with human subjects.

Land and Niland (1960) demonstrated the effects of \( \text{H}_2\text{S} \) on Rhesus monkeys in a chamber having \( \text{H}_2\text{S} \) concentration of 5000 ppm. The monkey showed necrosis of the occipital cortex of the brain, necrosis, hyperemia, and gliosis of the basal ganglia, a decrease in the neurons of the cerebellar cortex, moderate hyperemia of the liver; but normal heart, kidneys, and adrenals. The results indicated that the brain, particularly the motor cells of the cerebellum, was the principal target of
### Table 7: Effects of Hydrogen Sulfide Inhalation on Humans.

<table>
<thead>
<tr>
<th>No. of subjects</th>
<th>Concentration (mg/cum)</th>
<th>Duration of Exposure</th>
<th>Effects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17,000</td>
<td>-</td>
<td>Death</td>
<td>Mason &amp; Mason (1971)</td>
</tr>
<tr>
<td>1</td>
<td>2,800</td>
<td>≤ 20 min.</td>
<td>Death</td>
<td>Braynea (1951)</td>
</tr>
<tr>
<td>10</td>
<td>1,400</td>
<td>≤ 1 min.</td>
<td>Death, 1/10, Unconsciousness, abnormal ECG.</td>
<td>Frouza (1970)</td>
</tr>
<tr>
<td>342</td>
<td>1,400</td>
<td>≤ 20 min.</td>
<td>Hospitalization of 320, death of 22, residual nervous system damage in 4.</td>
<td>McCabe &amp; Clayton (1952)</td>
</tr>
<tr>
<td>1</td>
<td>1,400</td>
<td>≤ 25 min.</td>
<td>Unconsciousness, low blood pressure, pulmonary edema, convulsions, hematuria.</td>
<td>Reper (1956)</td>
</tr>
<tr>
<td>4</td>
<td>400-700</td>
<td>-</td>
<td>Unconsciousness.</td>
<td>Occup. Health (1952)</td>
</tr>
<tr>
<td>78</td>
<td>20-30</td>
<td>-</td>
<td>Burning eyes, headache, loss of appetite, weight loss, dizziness.</td>
<td>Legge (1938)</td>
</tr>
<tr>
<td><em>City of Terre Haute</em></td>
<td><em>0.003-11</em></td>
<td><em>Intermittent Air Pollution episodes over a two month period.</em></td>
<td>Numerous complaints of nausea, headache, shortness of breath, sleep disturbance, throat and eye irritation.</td>
<td>National Tech. Information Service (1961)</td>
</tr>
</tbody>
</table>
H₂S. This finding is supported by the work of Evans (1967), who noted that "the most conspicuous actions of sulfides are on the nerve centres, which were first stimulated, then paralysed. Effects of exposure to H₂S on various animals have been shown in Table-6.

1.22. Biological Investigation of H₂S Toxicosis:

Bosniak et al. (1967) exposed rabbits to H₂S at a concentration of 72 ppm for 1 hr 30 min. The activity of the enzymes ATP-phosphohydrolase and NADPH₂ oxidoreductase in heart muscles and in the lining of blood vessels was reduced in exposed animals. The authors cited this in support of the contention that H₂S inhibits intracellular respiration.

Bosniak et al. (1971) also investigated "subacute" H₂S poisoning in rabbits; exposed to H₂S in air at a concentration of 72 ppm for one hour per day for 16 days. A drop in serum albumin level and a rise in serum beta globulins was observed. The Ca⁺⁺ concentration in the rabbit serum was unchanged after the animal was exposed to H₂S, but there were lower serum concentrations of iron, copper, carbon dioxide, alkaline buffers, and magnesium, and a lower pH, last two observations being statistically significant. Thymol turbidity and glutamic-oxaloacetic transaminase activity were significantly increased in exposed rabbits, so were serum and heart alkaline phosphatase and ceruloplasmin activity in serum, heart, and brain.
<table>
<thead>
<tr>
<th>Route of Exposure</th>
<th>Species</th>
<th>Exposure Concentration (mg/cum)</th>
<th>Exposure duration</th>
<th>Effects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalation</td>
<td>Monkey</td>
<td>700</td>
<td>25 min; 17 min 3 days later.</td>
<td>Extensive changes in gray matter, moderate liver hyperemia.</td>
<td>Lund &amp; Mieland (1966)</td>
</tr>
<tr>
<td>Inhalation</td>
<td>Monkey</td>
<td>700</td>
<td>22 min.</td>
<td>Ataxia, areflexia, parenchymal necrosis in brain.</td>
<td>Lund &amp; Mieland (1966)</td>
</tr>
<tr>
<td>Inhalation</td>
<td>Rat</td>
<td>0.018</td>
<td>12 hr/day 3 months.</td>
<td>Motor chronic abnormalities.</td>
<td>Dana (1959)</td>
</tr>
<tr>
<td>Inhalation</td>
<td>Rabbit</td>
<td>100</td>
<td>1 hr/day - 14 days.</td>
<td>Disturbed metabolism in liver, brain, and kidneys; blood serum mineral, protein, and enzyme activity changes; depletion of buffers, lowered blood pH.</td>
<td>Bender et al. (1957)</td>
</tr>
<tr>
<td>Dermal</td>
<td>Rabbit</td>
<td>2 mg/liter</td>
<td>-</td>
<td>Decrease in carbonic-anhydrase activity - anhydrase index, blood-hemoglobin content, erythrocyte respiration, and cholinesterase activity.</td>
<td>Petrun (1955)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 mg/liter</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The studies of human serum in vitro (Besider et al., 1971) showed a decrease of alkaline phosphatase and ceruloplasmin activity on exposure to \( H_2F \). The authors concluded that \( H_2F \) produces protein, mineral, and consequently, acid disturbances. Disturbances of brain, liver, and kidney metabolism were also reported by the authors. One mechanism of action of \( H_2F \), they suggested, is based on its ability to bind alkali metals and thus decrease the activities of enzymes that require activation by these metals. The results of this study are consistent with the effects on cellular respiratory enzymes that have been attributed to \( H_2F \) and with the observations of unconsciousness and other signs of adverse effects on the brain that have been produced by \( H_2F \).

Waterman et al. (1975) found that \( H_2F \), when inhaled by animals, is rapidly introduced into the blood circulation via lungs. Its toxic action may depend upon blockage of enzymes, particularly those containing copper and iron, resulting in the damage to oxygen transport in the liver. "Even action on Central Nervous System is a possibility".

Since oxygen demand in the brain is very high (49 ml/min) (Canong, 1977), it is possible that \( H_2F \) poisoning might lead to damage to oxygen transport in the brain as well.

1.23 Mode of Action of \( O_{2} \) and \( H_2F \):

The mode of action of \( H_2F \) is of considerable interest both chemically and biologically because of its similarity
Recently, it has been postulated (Downie, 1978) that the toxicity of \( \text{H}_2\text{S} \) seems to be due to inhibition of cytochrome oxidase, and thus it resembles cyanide. Earlier, Rosider et al. (1974) suggested that \( \text{H}_2\text{S} \) binds alkali metals and thus decreases the activities of enzymes that require activation by these metals, thereby producing adverse effects on brain.

The toxicity of \( \text{H}_2\text{S} \) in animals has been thought to be due to its toxic action upon blockage of enzymes, particularly those containing copper and iron, resulting in the damage to oxygen transport, in the brain (Westermann et al., 1975). Authors have stated that "even action on the Central Nervous System is a possibility". Since consumption of oxygen in brain is 49 ml/min (Cannong, 1977), therefore it is a possibility that \( \text{H}_2\text{S} \) might also block oxygen transport in the brain.

On the other hand, the toxicity of \( \text{SO}_2 \) is of great significance due to the formation of sulfur-sulfonate metabolites by the sulfitolysis of disulfide bonds. Gunnison et al. (1979) have postulated that, quantitatively, sulfitolysis represents only a minor metabolic pathway of \( \text{SO}_2 \) toxicity; the major metabolic route is enzymatically catalyzed oxidation to sulfate. This latter reaction is presumably detoxifying in nature, while the sulfitolysis reaction is potentially toxic since it may alter the structure and thus the function of resulting proteins. The quantitative importance of sulfitolysis is inversely related to the activity of sulfite oxidase. It is apparent that sulfite oxidase activity is
critical for protection from sulfite toxicity. The deficiency of sulfite oxidase cause genetic disorder, severe mental retardation and neuromuscular problems.

Incuye et al. (1978) have studied the effect of sulfur oxides on living organisms. They reported that sulfite oxidation is remarkably accelerated by superoxide anion radical ($O_2^-$) and $Mn^{2+}$, suggesting sulfite radical formation in oxidation process. Lipid peroxidation has been given attention in connection with various metabolic disorders or symptoms of senility (Strahler et al., 1959; and Ceria, 1969). Since neurochemical studies of alterations in the brain lipids after exposure to $SO_2$ and $H_2S$ have not been reported in the literature. The explanation of the manifold signs and symptoms of sulfur toxicity remains to be analyzed.

1.2. The lipids:

Some time ago lipids were considered for the most part as a good source of energy. Through active research, lipids have now gained recognition as essential components of all cells and are involved in numerous biological processes. They are major component of all cell membranes, essential components of several crucial enzyme systems, include a potent class of hormones, and have been implicated in the cellular transport of some compounds, all of which make it clear that an error in lipid metabolism could have far reaching effect on the cell’s ability to carry out numerous essential processes (Spectator and
Brenneman, 1973). Some investigators working in the area of cancer research were quick to recognize the possible direct or indirect involvement of lipids in the neoplastic process and began to work to determine if lipids were involved. Tumors required enough lipids so that membrane synthesis can proceed at a sufficient rate to permit rapid growth. Tumor growth undoubtedly would be slow if the availability of lipids could be sufficiently reduced (Spectator and Brenneman, 1973). In the animal tissues, the largest amount of lipids occur in the brain, followed by liver, pancreas, heart, muscle, kidney, lung, jaw muscles, diaphragm and neck muscles (Bloor, 1943). Lipids are the most concentrated source of energy to the organism, yielding per gram over twice as many calories as do carbohydrates or proteins and in addition, they are stored in a relatively water free state in the tissues, in contrast to carbohydrates, which is heavily hydrated. The lipid depots serve as a reservoir of energy, available in times of restricted nutrition for the operation of the numerous endogenic processes necessary for maintenance of life. Much of the lipid of mammals is located subcutaneously, where it serves as an insulator against excessive heat loss to the environment. The subcutaneous lipid depots also insulate against mechanical trauma (White et al., 1978). The depot lipid consists chiefly of triacylglycerol. More than 99% of the lipid of human adipose tissue is triacylglycerol.

When an animal is excessively nourished, the quantity of body lipid increases, and conversely, during periods of prolonged fasting the amount of body lipid decreases. The low respira-
tory quotient of the body during fasting has for many years been taken as evidence that under these conditions fatty acids are used by the body tissues as their prime energy source (Fritz, 1961) and direct evidence for the uptake and utilization of fatty acids from the circulating blood by individual organs and tissues in the fasting state has been obtained (Skipp et al., 1964; and Cousios et al., 1963). Depot lipid is continuously being mobilized, new lipid is continuously being deposited, and the constancy of the quantity of depot lipid is the result of a relatively precise adjustment of the rates of these two processes. In the steady state the half-life of depot lipid in the mouse is about 5 days; in the rat, about 8 days. This means that in the rat almost 10% of the fatty acids in the depot lipid is replaced daily by new fatty acid. In the liver of the rat, the fatty acids have a half-life of about 2 days; in the brain, 10 to 15 days.

1.25. Interrelationships of Lipid Metabolism:

The central roles of acetyl CoA and 3-hydroxy-3-methylglutaryl CoA in lipid metabolism are depicted in Fig. 3 (White et al., 1973). In circumstances of limited utilization of carbohydrate and/or excessive mobilization of fatty acids to the liver, there is markedly diminished rate of operation of two of the three pathways for metabolizing acetyl CoA, viz., the citric acid cycle and fatty acid synthesis. The former effect is apparently based on the stimulatory action of
Fig. 3: A schematic representation of major interrelationships of the metabolism of fatty acids, cholesterol, and ketone bodies.
carbohydrate intermediates on citrate lyase; depressed activity of the latter enzyme could retard operation of the citric acid cycle. The limitation of fatty acid synthesis under circumstances of diminished formation of intermediates of the citric acid cycle and excess fatty acid accumulation is localized at the level of acetyl CoA carboxylase activity. The result is a channeling of acetyl CoA into its third metabolic fate; 3-hydroxy-3-methylglutaryl CoA formation and of products derived therefrom, viz., cholesterol and acetoacetate. Increased formation of latter, and of the associated 3-hydroxybutyrate and acetone, elevates their concentration in the blood above normal, resulting in ketonemia. If the blood level exceeds the renal threshold and appreciable amounts of ketone bodies appear in the urine, ketouria results.

Any circumstance associated with diminished availability of carbohydrate will accentuate utilization of fatty acids. In starvation, glycogen stores are rapidly depleted, and survival depends largely on energy derived from depot lipid. Mobilization of this lipid is reflected in lipemia. Degradation of fatty acids in the liver proceeds more rapidly than usual, with augmented production of acetoacetyl CoA and acetyl CoA and their products. In addition there is a deficit of oxaloacetate and thus a decrease in formation of citrate. The low level of oxaloacetate is further accentuated because it is being utilized for gluconeogenesis. This further impairs operation of the citric acid cycle.
Lipids are essential components of all cellular structures in the brain, surrounding nerve axons and dendrites in the peripheral nervous system, the cell bodies of sensory ganglion cells, and the nerves of the white matter of the central nervous system is a sheath of myelin, formed by the neurilemmal or schwann cells. Lipid constitutes 70 to 80% and protein 20 to 30% of the myelin dry matter. Lipid structure of myelin is depicted in Fig. 4 (White et al., 1978).

Myelin lipids are about 65% of the lipids of whole white matter. In mature myelin, the mole ratio of cholesterol to phosphoglycerides to galactolipids is 4:3:2. In adult myelin, cholesterol is found only in unesterified form. The ratio of cerebrosides to sulfatides in myelin is higher than in corresponding white matter. The sphingomyelin content is low in brain myelin although it is considerably higher in peripheral nerve myelin and increases with age in brain myelin. Phospholipids, mainly phosphatidylethanolamine, constitute about one-fourth of the total myelin phosphoglycerides. Diphospho- and triphosphoinositides appear to be concentrated in myelin fractions but may, in fact, be constituents of included axonal membranes. The phosphoinositides manifest the highest turnover rate of any of the lipids in the brain, bind Ca^{2+} as well as myelin basic protein in vitro, and may be important structural components of the myelin sheaths. Monoasialoganglioside is present in limited quantity in myelin fractions (White et al., 1978).
<table>
<thead>
<tr>
<th></th>
<th>Myelina</th>
<th>White Matter</th>
<th>Gray Matter</th>
<th>Peripheral Nerve Myelin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water, % fresh weight</td>
<td>46.0</td>
<td>71.6</td>
<td>81.9</td>
<td>-</td>
</tr>
<tr>
<td>Soluble in chloroform-methanol</td>
<td>3.0</td>
<td>30.6</td>
<td>52.6</td>
<td>-</td>
</tr>
<tr>
<td>Total lipids, % dry weight</td>
<td>70.0</td>
<td>72.9</td>
<td>32.7</td>
<td>69.5</td>
</tr>
</tbody>
</table>

**WEIGHT IN PERCENT OF TOTAL LIPID**

- **Cholesterol**: 27.7
- **Glycerolipids**: 27.5
- **Cerebrosides**: 22.7
- **Sulfatides**: 3.6
- **Phosphoglycerides**: 43.1
- **Phosphatidylyethanolamine**: 15.6
- **Phosphatidylethanolamine**: 22.7
- **Phosphatidylcholine**: 11.2
- **Phosphatidylserine**: 11.0
- **Phosphatidylinositol**: 0.3
- **Unidentified**: 1.1
- **Phospholipids**: 12.3
- **Sphingomyelin**: 7.9

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Fig. 4: Lipid structure of myelin. This section, 3 by 3 nm, contains 6 molecules of cholesterol, 5 molecules of phosphoglycerides of three different types, and 4 molecules of sphingolipid of two different types (Chapman, 1975).
Table - 9

Lipid Distribution in Human Nervous Tissues (*Norton*, 1956 and Harrocks et al., 1967)

<table>
<thead>
<tr>
<th></th>
<th>Myelina</th>
<th>White Matter</th>
<th>Gray Matter</th>
<th>Peripheral Nerve Myelin</th>
</tr>
</thead>
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<td>30.6</td>
<td>52.6</td>
<td>-</td>
</tr>
<tr>
<td>Total lipids, % dry weight</td>
<td>70.0</td>
<td>24.9</td>
<td>24.7</td>
<td>69.5</td>
</tr>
</tbody>
</table>

**Weight in Percent of Total Lipid**

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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Free fatty acids occur only in trace amounts in central nervous tissue, mainly as long chain fatty acids ($C_{10}$ to $C_{20}$) they constitute a large portion of the major lipids of the brain and spinal cord. Fatty acids of the human fetal brain were investigated by Hanson and Clausen (1958). The predominant acids were palmitic, stearic, and oleic in brain as a whole, and in fetal brain lecithin, phosphatidyl-ethanolamine, and phosphatidylserine. In adult brain oleic was dominant in all of these phospholipid fractions. Linoleic acid was practically absent in fetal brain but represented 1.5% of the total fatty acids present in adult brain. It is reported that free fatty acids are the respiratory fuels in cancer (Winhouse et al., 1973).

Brain has also capability of oxidizing free fatty acids (Little et al., 1959). On a specific activity basis liver was most active, testes and serum least active and brain was somewhere in between. Since long chain fatty acids are needed continuously for the integrity of membrane structure, Demade (1970) has indicated that fatty acids in the central nervous system can arise by synthesis in situ and by transport from the blood stream. A number of studies have again indicated that both possibilities exist (Dhepswarker and Mend, 1970; Dhepswarker et al., 1971; Sun and Horrocks, 1959).

Among the genetic defects that may lead to failure of myelination, deficiency in the fatty acid hydroxylase may limit
synthesis of \( L \)-hydroxy fatty acids found in various myelin lipids. In their absence, the myelin structure is imperfect, leading to behavioral and physical defects such as jumping and quaking, which occur in mutant strains of mice (White et al., 1978).

At present, no attempt has been made to evaluate the effect of air pollutants, \( SO_2 \) and \( H_2S \) at M.A.C. Levels in the various areas of the guinea pig brain. Therefore, it would be of interest to estimate the levels of fatty acids quantitatively after exposure of guinea pigs to sulfur-containing gases.

### 1.25.2 Phospholipids in the Brain:

Phospholipids occur in substantial amounts in both white and gray matter. Total amounts of phospholipids are higher in white matter than in gray matter, and the reported amounts range from 3.1 to 4.6 gm per 100 gm fresh tissue for gray matter and 6.2 to 9.3 gm for white matter (Kasuda, 1937; Randall, 1938; Brante, 1949; Johnson et al., 1949).

Isotope studies indicate that both lipid fatty acids and phospholipids, respectively, are metabolically more active than cholesterol, both in adult and in young brains (Welsh et al., 1940; Dawson, 1955). Labelled phosphorus, once incorporated into phospholipids, decreases only slowly in brain tissue, suggesting that there are compartments of phospholipid metabolism - as well as cholesterol metabolism - that are relatively inaccessible metabolically (Dawson and Dobbing, 1959).
The importance of phosphorus-containing lipids of the central nervous system, presumably dependent upon their role as membrane constituents.

Phosphatidyl glycerol is considered only a minor component of cerebral lipids. Stanishev et al. (1963) and Roesmayer et al. (1968) confirmed that the compound is biosynthesized in brain by the following reactions:

1. GDP-diacylglycerol + sn-glycero-3-phosphoric acid →
   3-sn-phosphatidyl-1'-glycerol-3'-phosphate + GMP .......... (1 - 8)

2. 3-sn-phosphatidyl-1'-glycerol-3'-phosphate →
   phosphatidylglycerol + P₄ .................. (1 - 9)

The stereospecificity of the reactions reported by two groups was emphasized by the observation that the natural phospholipid precursor has the 3-sn-phosphatidyl-1'-sn-glycero configuration (Raverkate and Van Deenen, 1965).

Neurochemical studies of regional phospholipid changes of the guinea pig and rat brain following exposure to SO₂ and H₂S (N.A.C.) levels have not been reported in the literature and present investigation provides information on the effects of SO₂ on brain phospholipids.

1.25.3 Cholesterol in the Brain:

Unesterified cholesterol has been suggested as a lipid that is characteristic of myelin sheaths, because it occurs in
white matter in amount greatly exceeding those in gray matter (Yasuda, 1937; Randall, 1939; Johnson et al., 1949 and Frants, 1949). The ranges of cholesterol per 100 gm fresh tissue for human and bovine brain are approximately 0.6 to 1.4 gm for gray matter, and 2.6 to 5.0 gm for white matter.

Studies in the cell layers of monkey cortex show that the cholesterol is almost a mirror image of that of the protein, cholesterol increases, and protein decreases, with increasing cortical depth (Robins et al., 1956). Further studies of incorporation of labelled cholesterol or labelled acetate into brain tissue indicate that the cholesterol of adult brain is relatively inert (Bloch et al., 1943; Heisch et al., 1940; Forn et al., 1950 and Van Bruggen et al., 1953). After intracerebral injection of labelled acetate in rats, however, some label is incorporated into cholesterol and appears to remain there indefinitely (Nicholas and Thomas, 1959). Passetti (1971) has substantiated the observation that microsomes are the subcellular site of brain cholesterol biosynthesis. To date, no report is available on the cholesterol levels in the guinea pig and rat brain following SO₂ and H₂S intoxication.

1.25.4. Gangliosides in the Brain:

Blank and Langerbeins (1941) demonstrated that gangliosides were present only in the gray matter of brain. More recent work has established that indeed the bulk of central nervous system gangliosides are concentrated in this tissue. The types and amounts of individual gangliosides present also
change with the age of the animal. Small amount of gangliosides in white matter (1/4 to 1/6 of the amount in cerebral cortex) suggest localization of gangliosides in axons.

The elucidation of the biosynthetic pathways, both major and minor, of ganglioside formation is still incomplete. Most of the work thus far has indicated that the synaptosomal fraction of brain contains the bulk of the biosynthetic activity. Much of the effort with regard to the individual enzymes involved in ganglioside degradation has been carried out in relation to certain genetic lipidoses in which several of these enzymes are partially or completely absent. While it appears that only one neuraminidase enzyme is necessary to cleave the various neuraminic residues from gangliosides, Gatt (1957) demonstrated that two separate enzymes, β-glycosidase and β-galactosidase fractions hydrolyse both glucose and galactose and are involved in the cleavage of these carbohydrates from gangliosides.

It is of interest that gangliosides can act as receptor substances for neurotoxins (Van Heyningen, 1959; North et al., 1961; North and Doary, 1961). Because gangliosides are specially abundant in nerve endings, it has been suggested that they function in the transmission of nerve impulse across synapses. They are also believed to be present at receptor sites for acetylcholine and other neurotransmitter substances (Lehninger, 1979). It has been demonstrated that the distribution of gangliosides resembles that of γ-aminobutyric acid (Lowden and Wolfe, 1961). Irwin and Sarnon (1971) also
indicated that behavioral stimulation, viz., stress, exercise, sensory stimulation, learning seem to be accompanied by ganglioside metabolism, compared to corresponding control animals. These complex lipids are also involved in tissue immunity and in cell-cell recognition sites fundamental to the development and structure of tissue (Lehninger, 1979). No information is available thus far, on the ganglioside levels in the guinea pig and rat brain following exposure to SO₂ and HF.

1.27. Lipid Peroxidation:

The individual and concentrated influences of nutrients, oxidants, and antioxidants on lipid peroxidation in vivo and in vitro have been studied for many years. These interacting compounds in lipid peroxidation involve cytochrome P-450 systems in some normal and pathological reactions in vivo. It is important that lipid peroxidation is a basic deteriorative reaction that is involved in many disease processes and chemical toxicities (Tappel and Billard, 1961). Recent interest in lipid peroxidation has probably resulted from the realization that oxygen radicals and other organic radicals do indeed exist in biological tissues for an appreciable time (Tien et al., 1961).

The chemical process of lipid peroxidation (Neal, 1976 and Pryor, 1976) is defined as the reaction of an oxidant initiator with a polyunsaturated fat (LE) to form a lipid-free radical intermediate (L); a peroxo free radical (LOO⁻) then forms when forms when oxygen reacts with this free radical intermediate.
A relatively nonspecific hydrogen abstraction reaction is initiated when the unpaired electrons of the peroxyl free radical react with another lipid molecule:

\[ L + O_2 \rightarrow L O O' \]  \hspace{1cm} (1 - 10)

\[ L O O' + H \rightarrow L O O H + L' \]  \hspace{1cm} (1 - 11)

The peroxyl free radical can also react with an antioxidant to terminate the reaction chain:

\[ L O O' + \text{Vitamin E} \rightarrow L O O H + \text{Vitamin E oxidized} \]  \hspace{1cm} (1 - 12)

Autocatalysis or branching reactions can be initiated when metals in their lower oxidation state catalyze homolytic decomposition of hydroperoxides. In the above series of reactions in vivo, biological membranes can react with hydroperoxides and carbonyl products and with free radicals, including peroxyl radicals, alkoxyl radicals, and hydroxy radicals. The ground state of polyunsaturated fatty acids (PUFA) is of singlet multiplicity. The reaction of PUFA with oxygen to form lipid hydroperoxides (LOOH) must therefore, involve a reaction to remove spin barrier.

1.27.1 Parameters of Lipid Free Radical Damage;

Danopoulos et al. (1979) summarized the possible parameters for following pathologic free radical reactions among membrane lipids, as a result of rationales given for polyunsaturated fatty acids and cholesterol.
1. Early or moderate free radical damage to membrane phospholipids:

(i) Meso conjugation in fatty acids.
(ii) cis → trans isomerization in fatty acids.
(iii) hindered rotation of nitrooxide spin probes placed within liposome membranes that are composed of lipids from the damaged membrane system.
(iv) minor losses in polyunsaturated acids such as arachidonic acid, 20:4.
(v) prevention of the above with lipophilic or amphipathic antioxidants.

2. Late or severe free radical damage to membrane phospholipids:

(i) malonaldehyde production.
(ii) lipid-soluble fluorescence due to malonaldehyde additions.
(iii) production of short-chain, and some times branched chain fatty acids.
(iv) decreased hindrance of rotation of nitrooxide spin probes within liposome membranes systems.
(v) major losses in polyunsaturated fatty acids.
(vi) prevention of the above with lipophilic or amphipathic antioxidants.

3. Free radical damage to cholesterol:

(i) decrease in extractable cholesterol.
(ii) appearance of several cholesterol oxidation products.

4. Consumption of tissue oxidants:

(i) ascorbic acid (reduced)
(i) ascorbic acid
(ii) glutathione
(iii) cysteine

5. Alterations in protective enzymes:
   (i) Superoxide dismutases
   (ii) Glutathione peroxidase

6. Liposomes: from central nervous system lipid extract from different animal models:
   (i) rate of free radical damage under conditions of auto-oxidation.
   (ii) Spin probe analysis of fluidity by n.p.r. spectrometry.
   (iii) Permeability rates of solutes in aqueous channels.

Lipid peroxidation occurs in animal tissues when antioxidant protective systems lacking. Among the protective systems in animals are the biological antioxidant vitamin E and selenium-glutathione peroxidase, a decomposer of peroxides. The occurrence of lipid peroxidation in biological tissues has been investigated by measurement of the major peroxidation products, lipid hydroperoxides and conjugated dienes, and the minor products, malonaldehyde, hexanal, fluorescent carbonylamine products, and volatile hydrocarbons. Conjugated dienes are formed in direct proportion to the formation of lipid hydroperoxides. The lipid hydroperoxides may be metabolized by selenium-glutathione peroxidase, or precission of alkoxy radicals can lead to the production of small amounts of volatile
hydrocarbons. The decomposition of $\omega_3$- and $\omega_6$-unsaturated fatty acid hydroperoxides leads to the formation of ethane and pentane respectively (Donovan and Mensel, 1970; and Dunarin and Tappel, 1977). The following reactions indicate the mechanism for pentane formation:

\[
\begin{align*}
\text{CH}_3\text{(CH}_2)_4\text{C - R + Fe}^{2+} & \rightarrow \text{CH}_3\text{(CH}_2)_4\text{C - R + Fe}^{3+} + \text{OH}^- \\
\text{OH}^- & \rightarrow \text{CH}_3\text{(CH}_2)_4\text{C - R + Fe}^{3+} + \text{OH}^- \\
& \hspace{1cm} \text{E-SCission} \\
\text{CH}_3\text{(CH}_2)_4\text{C - R} & \rightarrow \text{CH}_3\text{(CH}_2)_3\text{CH}_2 + \text{CR} \\
& \hspace{1cm} \text{E-SCission} \\
\text{CH}_3\text{(CH}_2)_3\text{CH}_2 & \rightarrow \text{CH}_3\text{(CH}_2)_3\text{CH}_3 \\
& \hspace{1cm} \text{ABSTRACTION}
\end{align*}
\]

The five-carbon free radical abstracts a hydrogen to form pentane. Hydroperoxides formed during lipid peroxidation can be decomposed by lower oxidation state metals. Since the in vivo concentrations of iron, hematina, and copper are high, it is assumed that they catalyse E-scission of alkoxy radicals.

It is important to point out that lipid peroxidation must be thought of as a two-step process. The first involves a mechanism for the formation of lipid hydroperoxides starting with PUFA and molecular oxygen. The second is the reactions of lipid hydroperoxides with substances like base to carry out what we now term lipid hydroperoxide-dependent lipid peroxidation. In the latter case, cytochrome P-450 reacts with the hydroperoxides to promote the peroxidation of microsomal lipid.
Considering that unsaturated fatty acids which undergo peroxidation are important constituents of biological membranes, structural and functional deterioration of biological membranes may follow. Mitochondrial swelling and decrease in oxidative phosphorylation (Utsumi et al., 1965), release of hydrolytic enzymes from lysosomes (Mills and Wilkinson, 1966), and change in endoplasmic reticulum (Sidlask and Tappel, 1974) have all been described as biochemical distortions, following lipid peroxidation.

Lipid peroxidation has been given attention in connection with various metabolic disorders or symptoms of senility (Strehler et al., 1959; Geriù, 1959). On the other hand lipid peroxidation in vivo has been claimed to be of basic importance in aging, damage to cells by air pollution and in oxygen toxicity (Tappel, 1973). On the other hand, studies suggest that radiation hazards (Incuye et al., 1979) or influence of various environmental pollutants (Hudd and Freeman, 1977) are closely related to lipid peroxidation.

Although direct uptake of oxygen will give a true nature of lipid peroxidation, the more commonly employed techniques is by estimating the production of malondialdehyde (one of the end product of fat peroxidation) pink pigment formed with 2 thiobarbituric acid (TBA) (Bartha and Bhishamurthy, 1979). The most recently developed technique for measurement of lipid peroxidation in vivo is the analysis of expired air for volatile hydrocarbon products of lipid hydroperoxide decomposition (Tappel and Millard, 1981).
It was reported that tissues most susceptible to lipid peroxidation appear to be those with low mitotic rate such as brain (Barber and Wilbur, 1959). Martha and Krishnamurthy (1973) showed that, of the different tissues from normal rat, the brain showed a considerably high degree of peroxidation, while liver, kidney, spleen and heart homogenates showed comparatively low peroxidation.

The effects of sulfur oxides on living organisms in an experimental model have shown that sulfite oxidation is remarkably accelerated by superoxide anion radical (O$_2^-$) and Mn$^{2+}$, suggesting sulfite radical formation in oxidation process (Inouye et al., 1978). It is already known that the sulfite accelerates lipid peroxidation in vitro. Tyler (1975) also observed the acceleration of mitochondrial lipid peroxidation by sulfite. Detailed mechanism of the sulfite-induced malonaldehyde formation is not clear. However, as indicated by Arada and Sato (1973), malonaldehyde formation seems dependent on sulfite radical formed by catalysis of metal ion, and O$_2^-$ or ·OH formed in the processes of sulfite oxidation. To my knowledge, the effects of air pollutants, SO$_2$ and H$_2$S, at M.A.C. levels on lipid peroxidation is not known, therefore, it would be of particular interest to investigate the amount of malonaldehyde formed in different regions of the guinea pig and rat brain following exposure to SO$_2$ and H$_2$S.

1.2. Action of Phospholipases:

Several phospholipases have been described with specifi-
city for hydrolysis of one or more of the bonds of the phosphoglycerides. These enzymes have been useful in study of the structure of phosphoglycerides as well as indicating routes of their degradation. The susceptible bonds in phosphatidylcholine are indicated by the Fig. 5 below (White et al., 1978).

\[ \text{Phospholipase A}_1 \rightarrow H_2CO \]  
\[ \text{Phospholipase A}_2 \rightarrow R_2 \]  
\[ \text{Phospholipase C} \rightarrow C \]  
\[ \text{Phospholipase D} \rightarrow H_2CO \]  
\[ OCH \]  
\[ CH_2CH_2 \]  
\[ (CH_3)_3 \]  

Fig. 5: Action of Phospholipases.
Phospholipase A₁ specifically removes the fatty acid from the 1 position and phospholipase A₂ from the 2 position. Removal of one fatty acid molecule from a phosphoglyceride yields a lysophosphoglyceride, e.g., lysophosphatidyl-ethanolamine. Lysophosphoglycerides are intermediates in phosphoglyceride metabolism but are found in cells or tissues in only very small amounts; in high concentrations they are toxic and injurious to membranes. Phospholipase B, a mixture of phospholipases A₁ and A₂, can bring about successive removal of the two fatty acids of phosphoglycerides. Phospholipase C hydrolyzes the bond between phosphoric acid and glycerol, while phospholipase D removes the polar head group to leave a phosphatidic acid (Lehninger, 1979). Phospholipase A₂, found as the proenzyme in pancreas, yields lysophosphatidylcholine, a strong detergent and a potent hemolytic agent, \(\text{Ca}^{2+}\). The requiring enzymes action of phospholipase A₂ provides either arachidonic or homo-\(\alpha\)-linolenic acids, the initial substrates for prostaglandin synthesis.

Lysophospholipase of pancreas and other tissues catalyzes hydrolysis of the single fatty acid ester bond (A) in lysophosphatidylcholine choline or lysophosphatidylethanolamine:

\[
\text{Lysophosphatidylcholine} + \text{H}_2\text{O} \xrightarrow{\text{Ca}^{2+}} \text{glycerylphosphocholine} + \text{fatty acid} \quad (1 - 10)
\]

Phospholipase B hydrolyzes both bonds A and B. Also, a widely distributed mammalian enzyme has been described which catalyzes resynthesis of phosphatidylcholine from the lyso compound and a fatty acyl CoA.
Lysophosphatidylcholine + RCOC=O → Phosphatidylcholine + COA ................... (1 - 17)

Phospholipase C, which cleaves bond C, is found in the toxin of clostridium volhpii and other strains of clostridia and bacilli.

Phosphoglyceride + H₂O → 1,2-diacylglycerol + Phosphorylated nitrogenuous base ..................... (1 - 18)

Phospholipase D, which has been found only in plant tissues, catalyzes transphosphatidylation reactions as well as hydrolytic cleavage of the terminal diester bond (at D) of glycerophosphatides containing choline, ethanolamine, serine, or glycerol, with the formation of phosphatic acid.

Phosphatidylcholine + H₂O → Phosphatidic acid + choline ....................... (1 - 19)

Phosphatidylcholine + ROH → Phosphatidyl-OR + choline ....................... (1 - 20)

Both reactions are activated by Ca²⁺. Reaction (1-20), a transphosphatidylation, could provide a mechanism for synthesis and turnover of phosphoglycerides (White et al., 1978).

To date, no previous report is available on the action of phospholipases in the different regions of the guinea pig and rat brains following exposure to air pollutants, SO₂ and H₂S at M.A.C. levels. It is therefore, appropriate to estimate the activity of lipase in cerebral hemisphere, cerebellum, brain stem and spinal cord in the sulfur-induced toxicosis in guinea pigs and rats.
1.29. Metabolic Disorders due to the Alterations in the Brain

Lipid Content:

There are number of inherited diseases which cause the deposition of abnormal lipid in central and/or peripheral nervous system and sometimes in other tissues or organs. A clinical classification of these disorders, towards one based upon the nature of the material which is stored in abnormal amount and of upon the nature of the enzymatic defect which is responsible. All, however, are characterized by a progressive course of cerebral and often visual deterioration but varying considerably in tempo in different varieties (Walton, 1977).

The changes in neutral lipids which are not the primary lipid abnormalities in the central nervous system can be divided into two groups, sterol and fatty acid changes. The first of these involve sterol changes in the central nervous system. Demosterol has been shown to be a constituent of glioblastomas and the presence of demosterol accumulation has been postulated as an efficient method for the diagnosis of brain tumors (Grossi-Pasolletti et al., 1971). A patient with Pelizaeus-Merzbacher disease was shown to have a 50% decrease in cholesterol when compared with control brains (Schneck et al., 1971). This reduction along with reduction of other lipids was diagnosed as a congenital defect in myelinization. Niemann-Pick disease is characterized by the accumulation of sphingomyelin and cholesterol in the central nervous system (Philippart et al., 1959).
Cerebral lipidoses in which the primary abnormality is in the disproportionate distribution of gangliosides GM$_1$ or GM$_2$. The onset of symptoms begins in early infancy before the age of 6 months with clinical and radiological skeletal changes, abnormal facies, and visceromegaly (Suzuki et al., 1971). Ganglioside GM$_2$ accumulates in the brain in Tay-Sachs disease, due to genetic lack of the enzyme required for its degradation. This disease is characterized by abnormally high content of GM$_2$ in brain. Retardation of development, paralysis, dementia, and blindness are symptoms; death occurs by the age of two to four years (Isenhager, 1979).

1.30. Intoxication of Sulfur Containing Cases Produce Disturbances in the Serum Lipid Metabolism:

Recent citations (Mediators II, 1991) by the World Health Organization and the U.S. National Library of Medicine are unable to report the biochemical effects of SO$_2$ and H$_2$S exposure on the lipid profiles in animals. However, there are reports concerning the effects of carbon disulfide (CS$_2$) on serum lipids.

Wronska-Sofer (1976) measured the specific activity of $^{32}$P phospholipids in plasma and aortic wall after CS$_2$ intoxication. Intoxication by CS$_2$ brought about elevation of the phospholipids in the blood due to de novo synthesis. Rudkowska et al. (1978) reported that occupational exposure to CS$_2$ raises the rate of serum lipid metabolism. The results of the studies carried out by Wronska-Sofer (1979) indicated that exposure of
rats to CF₂ disturbed the cholesterol metabolism of body resulting into the rise of cholesterol metabolism in the blood. The alterations aggravated the atherosclerotic changes in the vascular wall. Balabasova and Tabakova (1979) studied the inhalatory influence of CF₂ on some parameters of lipid metabolism in pregnant albino rats throughout the whole gestation period. A distinct rise in free fatty acid levels associated with a mild decrease in the triglyceride and phospholipid content was observed. Wroska (1979) reported that prolonged exposure of rabbits to CF₂ increased the lipid phosphorus in serum, aorta, and cardiac muscle at lower concentrations of CF₂, but a decrease in lipid phosphorus content was noted in the serum of rabbits during a high concentration of CF₂ intoxication. Further, studies carried out by Wronski-Mozer et al., (1980) found that long term exposure to CF₂ increased the concentration of total and free cholesterol, cholesterol esters, triglycerides and phospholipids in blood serum and a significant rise in the levels of cholesterol esters in the aorta wall. Lurman (1980) found that chronic intoxication with CF₂ in rabbits brought about an increase in total and free cholesterol, cholesterol esters, triglycerides and phospholipids contents in serum.

Recently, a clinic-experimental study (Aleksandrov et al., 198) revealed that thiol-disulfide and ascorbate systems in the acute period of brain concussion developed the vegetative disturbances, specifically hypoxia and increased vascular permeability.

1.3.1 Specific objectives of this Study;

The present study was undertaken with the following main
nine:

(i) To evaluate the normal concentration of various lipid components in the different regions of the guinea pig and rat brain.

(ii) Quantitative evaluation of the effect of SO₂ and H₂S intoxication on lipid levels in various regions of the guinea pig and rat brain.

(iii) Quantitative estimation of total lipids.

(iv) Quantitative estimation of phospholipids.

(v) Quantitative estimation of cholesterol.

(vi) Quantitative estimation of free fatty acids.

(vii) Quantitative estimation of esterified fatty acids.

(viii) Quantitative estimation of gangliosides.

(ix) Quantitative evaluation of the lipid peroxidation.

(x) Quantitative evaluation of lipase activity.