Air pollution and cancer

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Diploma Work

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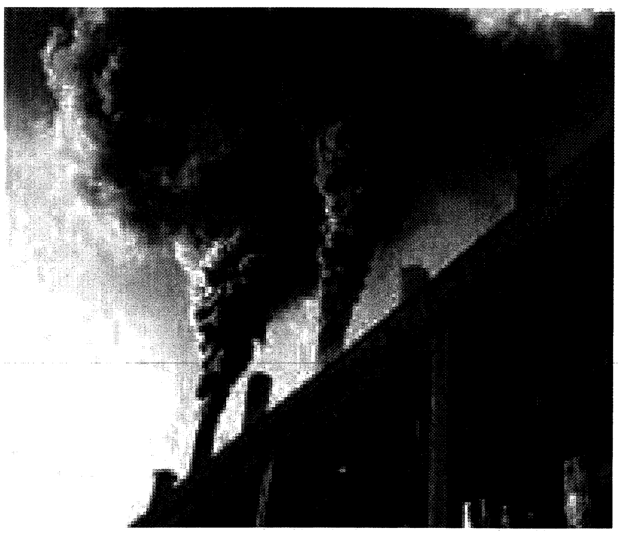
29 March 2006



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Abstract:

This review article tries to follow the main issue relevant in the discussion of air pollution in a broad perspective as possible. It should include the foundation of this topic as well as some of the latest studies. A technical presentation of some details regarding origin, types and measurements of the typical urban air pollutants is then follow by a more focus medical-oriented description of health aspects.
Elaboration is given on malignant disease recently claimed to be associated with air pollution exposure and this is presented as summery of few studies conducted over exposed population all over the world.

Introduction:

What is air pollution? What dose it consist of? And most important, what dose it do? These issues will most probably very much concern the people of the 21^{st} century as man kind and environmental factors are in a never ending intimate contact with a bidirectional relationship. Developmental effect on global and local air pollution are apparent both on the developed world and the developing world, more over, different types of air pollution affect primarily the very poor rural population of the developing countries. Therefore, exposure to air pollution crosses all boundaries of social and economic levels and has a major effect and national, human and natural resources.
Air pollution is one type of environmental pollution which its sources may be of natural origin or as most common encountered, a man made added substance to the atmosphere, it is important to mention that soil and water are also being polluted especially near industrialized areas and big urban complexes.
Preventive aspects of air pollution regarding cancer are presented last as for this topic is relatively new and is not as conclusive as a risk factor compared to other risk factors such as smoking. How ever, even small modification in the incidence of lung

cancer are considered highly desirable as for this cancer is the number one cause of death due to cancer diseases and presents a huge burden on the person and the society. Many countries establish a set of standards (based upon the WHO guidelines and standards) of air quality and limitation of air pollution produced by industries and vehicles, these values where obtained by certain types of studies and quantify or qualify the exposure limits. Then follow the establishment of a net work of monitoring systems in different location which could monitor and track the air composition continuously.

Understanding of the basic building blocks of environmental science and its health risk are fundamentals for proper implantation of better controlled standards of our ambient air.

This review starts with brief historical notes followed by a presentation of the very basic sources of air pollution we meet in our every day life; from transportation methods to the production facilities of the modern society needs and even our own contribution to air pollution by home base sources. This issue is followed by the different types of air pollution we breathe every day, these are divided artificially to gaseous and particulate pollutants, majority of which produced by the one single most common chemical reaction in this context - combustion.

Monitoring of air pollution is then reviewed in some technical details as for this is the foundation of assessment of the risk related to air pollution and standards in this highly specialized topic contribute much to world wide acceptance of local measurements mainly on health aspects.

Air pollution and its main effect on biological systems with few examples of typical pollutant cycles in the environment are then presented and this is followed by air pollution behavior in the respiratory system which is a crucial step in understanding the mechanisms by which the effect is produced by particulate or gaseous pollutants. Systemic review of specific types of pollution and there health affect with detailed body systems responses like respiratory system and the specific diseases thought to origin due to air pollution.

The last part is dedicated to cancer and; the pathogenesis by which air pollution act on tissues, the biomarkers which are thought to predict air pollution exposure and the risk to develop cancer. Few recently publicized articles are summarized at the end of this diploma work which should help to conclude this issue in the summary.

Historical notes:

The history of air pollution did not start in the 20th century and is as old as the usage of one of its main sources - coal. Already in the 14th century in London there where protests against the usage of special type, smoky or sea coal, producing big amount of smoke. In the 16th century the parliament of Great Britain already made legislation regarding the usage of coal. It was only in the mid 20th century that air pollution as a whole, not only the smoke, was regarded as a health hazard. The end of the 2nd World War marked the beginning of a new area where world wide acceptance of the need for monitoring and limitation of pollutant production was established (1, 15).

Sources of air pollution:

In the discussion of air pollution and preventive strategies it is wise to be aware of the many different sources responsible for air pollution for they have a major implication on exposure risk and of course on preventive measures. The sources may be roughly divided into natural and manmade of which stationary, mobile and indoor sources are the different types.

Natural sources are defined as any kind of pollution which was not generated by human activity. Here we can mention for instance, volcano eruption or natural occurring fires. Natural pollution as such is not preventable and therefore not commonly dealt with although exposure may still be reduced by certain measures.

Manmade pollution may be divided into three types: industrial sources, power stations and personal sources (1, 15).

1. Industrial Sources

Our modern society relies on industry for the production of our basic needs which once where made in our dwelling areas. This resulted in the transfer of the polluting sources from our residential area to the places where the factories are located.

For example: a soap factory's emission of pollutant is much lower then the total amount of pollution produced by home made production of the same soap however this factory will be subjected to many accusations about its polluting effects and at the same time will be more efficient in finding ways of controlling its polluting by products.

Raw materials are the main reason factories produce pollution and the typical ones are lumber from trees, gasoline from crude oil and iron from ore. In this process the raw material which change into the desirable product is left as an unwanted material or as commonly addressed, a "by product", some of it however can be changed and used as material for other products.

Industrial systems producing pollution are stationary and produce usually constant types and amounts of polluting substance. This fact is very important in the controlling and monitoring of these systems as the technology of how to reduce the pollution exists and can be applied to this factory, then the monitoring and the reduction of pollution can be monitored regularly (1, 15).

2, power stations

Power stations play an important role in supporting our every day activities and needs; we are more and more dependent on their energy supply in each part of our modern household and daily life. It is difficult to imagine life without them. The energetically efficiency of these systems is much higher in comparison to individual home based systems that supplied our need many years ago. For example: if the cumulative pollution of heating, food storage and light was measured it would have been far more then the power station located 200km from our homes which supplies electricity to 1.5 million people.

Our modern society consumes even greater amount of energy compared to old civilization in almost any aspect of our lives so the advantages of these power stations is even greater and as mention above the methods of how to monitor and control these pollutants is easier to apply.

Power stations are about converting energy from one form to another and transporting that energy. "When a large power plant, producing 3000 MW, uses a million kilograms per hour of 4% ash coal, it must somehow dispose of 40,000 kg of ash per hour. Some will be removed from the furnaces by the ash-handling systems, but some will go up the stack with the flue gases. If 50% of the ash enters the stack and the fly ash collection system is 99% efficient, 200 kg of ash per hour will be emitted to the atmosphere. For a typical generating plant, the gaseous emissions would include

341,000 kg of oxides of sulfur per day and 185,000 kg of oxides of nitrogen per day". (Fundamentals of Air Pollution 3rd Edition, pages 145-161)

The management can use lower ash or sulfur coal which is more expensive, buy a better system which collects the ash and other by products or install better equipment which controls the pollution (1, 15).

3, Personal Sources

Modern society which moved to centralized power stations and industries still possesses many different sources of pollution for example: cars, home furnaces and fire places etc'.

"The energy release and air pollution emissions from personal sources in the United States are greater than those from industry and utilities combined" (Fundamentals of Air Pollution 3rd Edition, pages 161-165)

In urban areas of the developed world the personal use of cars cause more than half of the total national air pollution and this trend forces the automobile industry to search for systems which will limit the emission from cars as also developing nations increase dramatically the number of cars per capita (1).

Controlling the air pollution from personal sources pose grate challenge concerning public opinion and most citizens will find it difficult to realize that their cars produce more pollution than the big power station 200km from their houses produce or that the employees of the factory produce more pollution by going to work in their private cars than the factory itself (1, 15).

Types of air pollution:

Combustion:

When substance react with oxygen with accompanied heat and light it is called combustion, this reaction is used in the utilization of substance with high potential energy to produce thermal energy.

We use it in power planets utilization of fossil fuel, at home or in automobile engine.

This reaction is also used in the elimination process of unwanted waste product as means of reducing the waste volume i.e. Incinerators.

The problems with the combustion reaction occur because the process also produces many other products, most of which are termed *air pollutants.*

Types of pollutants are the following: carbon monoxide, carbon dioxide, oxides of sulfur, oxides of Nitrogen, smoke, fly ash, metals, metal oxides, metal salts, aldehydes, ketones, acids, polycyclic aromatic hydrocarbons, and many others.

These relatively small quantities of materials emitted from the combustion process.

Many factors effect the process of combustion, time temperature and turbulence have crucial effect on the process and its effectiveness which in tern effect the pollutant production in each cycle. An appropriate temperature in an automobile engine will result in complete combustion and emission of gasoline particles into the atmosphere. Turbulence is necessary for the complete reaction of fuel molecule with oxygen which unless sufficient will also result the loss of fuel particles into the air.

Fuel may be in the form of gaseous liquid or in solid state with each having the proper system which can utilize it efficiently. Some system like car engines need to evaporate the fuel and then heat it for proper reaction to occur all of this in 2500 RPM which mean 5000 separate combustion process in each minute.

With a solid fuel, such as coal or wood, a series of steps are involved in combustion. These steps occur in a definite order, and the combustion device must be designed with these steps in mind (1, 15).

The cycle of operation of the combustion source is very important as far as emissions are concerned. A steady process, such as a large steam boiler, operates with a fairly uniform load and a continuous fuel flow. The effluent gases, along with any air pollutants, are discharged steadily and continually from the stack.

Particles emitted from combustion process can be predicted up to certain level and as long as the parameters are fully defined. This table shows some typical products of combustion:

Comparison of Combustion Pollutants[a]

Contaminant	Power plant emission (gm/kg fuel)			Refuse burning emission (gm/kg refuse)		Uncontrolled automotive emis: on (gm/kg fuel)	
	Coal	Oil	Gas	Open burning	Multiple chamber	Gasoline	Diesel
Carbon monoxide	Nil	Nil	Nil	50.0	Nil	165.0	Nil
Oxides of sulfur (SO_2)	(20)*x*	(20)*x*	(16)*x*	1.5	1.0	0.8	7
Oxides of nitrogen (NO_2)	0.43	0.68	0.16	2.0	1.0	16.5	16
Aldehydes and ketones	Nil	0.003	0.001	[illegible]	0.5	0.8	1.6
Total hydrocarbons	0.43	0.05	0.005	[illegible]	0.5	33.0	.0
Total particulate	(75)*y*	(2.8)*y*	Nil	11	11	0.05	18.0

(15)

Measurement and Monitoring of air pollution:

A. analysis and measurement of gaseous pollutants:

The goals of testing the air are to identify and quantify the air pollutants.

"First stage is the qualitative identification stage. This is followed by separate collection and quantification stages. The last stage is the concurrent collection and quantification of a given pollutant" (Fundamentals of Air Pollution 3rd Edition, pages 254-257).

Gaseous SO2 is an example. By certain reaction of ambient SO2 with lead peroxide stick the presence of sulfur is detected but in this method no quantification is possible. Following the detection the quantification process is preformed by passing certain amount of air through absorbing material in the area of concerned and then taking it to laboratory for further measurements which yield the SO2 amount.

The final step is concerning the concurrent measurements of quantity of SO2 in the environment which is done by flame photometric SO2 analyzer for example. Here the air containing SO2 is fed into H2 flame and light due to combustion excitation is detected by photometer (1, 11, 15).

Many different substances are in our atmosphere and the most commonly measured are CO, 03, N02, SO2, and non methane volatile organic compounds. Some of these substances are being routinely measured in Europe including the recently new members of the EU such as the Czech Republic mainly because they are yet a potential toxic health risk and because the need for monitoring and control urban air pollution by these substances (13).

1. Carbon Monoxide

Most commonly used method for measurement of CO is the non dispersive infrared photometry. This technique involve the absorption of infrared beam by the CO, the machine calibration is done with a non absorbing gas and a mixture with known amount of CO. the different amount of CO in the atmosphere is pushing a container membrane and thus changing the conductivity of the circuit and this is expressed in numbers (1, 15).

2. Ozone

This measuring is based on reaction between the O3 and ethylene generating light and therefore called a chemo luminescence reaction. The apparatus consist of constant ethylene source, ambient air inlet, reaction chamber and photometric system. When the ethylene concentration is much higher then the ozone the reaction speed is dependent only on the ozone ambient air amount (1, 15).

3. Nitrogen Dioxide

This method is similar to O3 measuring system and involve the chemo luminescence reaction emitting light, NO2 concentrations are determined indirectly from the difference between the NO and NOX (NO + NO2) concentrations in the atmosphere. Unlike the ozone system here the ozone is in high concentration like the ethylene before and the NO react with it according its own concentration in the ambient atmosphere. The light produced by the reaction between ozone and the NO is measured by the photomultiplier tube and converted to an NO concentration (1, 15).

4, Sulfur Dioxide

As discussed above here we can find few technique to measure the SO2, this involve first the collection of the sample and then measurement inside liquid device which accumulate the SO2, after collection the sample is transferred the laboratories which analyze the SO2 by colorimetric system after a certain reaction occur and producing measurable dye in the liquid, absorption of light of 548nm is linear to SO2 concentration. Continuous analyzers are no available which utilize the same principle.

B. analysis and measurement of particulate pollutants:

Chemical composition, mass concentration and size distribution are the common characteristic for particulate mater air pollution.

All over the world and in Europe //and the Czech republic the size of the particulate mater is set to 10 micrometer and 2.5 micrometer which is a newer standard now accepted widely, this size are qualities of air particles which have anatomic correlation to human health which may be affected by inhalation of air containing these particles size, transport in the atmospheric air may be estimated accordingly and the deposition in the respiratory system is determined along with other factors also by the size.

Chemical composition may have specific effect on the biologic system and therefore on the population being exposed health state.

Chemical composition of particulate pollutants is important in determining the source of the air born pollutant and the fate of it in the environment (1, 15).

Monitoring network:

Air quality standards are being employed all over the developed world mostly following the standards defined by The U.S. Environmental Protection Agency. These standards are defined in terms of concentration and time span for a specific pollutant; for example: CO limits are 9 ppm/volume (part per million) for 8 hr, not to be exceeded more than once a year. When this is exceeded mostly in periods of very severe weather conditions such as occur in Prague during the summer. The agency may issue some recommendation for the authorities in order to reduce the possibility of recurrence (1, 11, 15).

In order to receive this information on air quality a stationary monitoring network was established which monitor any violation of air quality standard.

"Long-term trends are measured by stationary air quality monitoring networks. The trends in other atmospheric trace gases such as methane, NO, NO2, and CO are similarly measured in rural as well as urban locations. Atmospheric budgets of various gases are developed to allow estimation of whether sources are man made or natural".

Stationary monitoring system will give information regarding the following: background concentration levels of the pollutant's levels, the highest levels reached, representative concentration levels, impact of local sources and impact of remote sources.

Prior to situating the location of each stationary sampling system the following measurements must be done: proper assessment of the size and distance of the area monitored from the source and defining the rezones for collecting this Intel.

A mobile monitoring system is carried on a movable platform such as airplanes or vehicles. This has the advantage of being able to locate the monitoring system in special hot spots which are suspected of exciding the standard limits. This system may also measure the distance dependent distribution of pollutants from its source and to define the border of this distribution patterns. The main disadvantage in this mobile monitoring system is that most types of measuring equipment are very sensitive to non stable condition of the environment where they operate, all of which are complicated to achieve on mobile platforms.

Remote sensing systems are the ones that are capable of measuring or estimating the amount of pollutant while being located in distant places. Satellites are being used for this purpose such as monitoring volcanic activity or even local condition by CO2 laser beam and its reflection measurement (1, 15).

Quality assurance:

Historically many different organization started to measure and monitor the air quality and were doing so under different conditions, different equipment and under different set of standards which resulted in a questionable data and conflicting information, which hamper very much the possible implication of this data. New regulation and standard systems are now being forced to guarantee non questionable reproducible data flow which can be used as recommendation for operational strategies and monitoring whether air quality is improving or worsening in a given region over an extended period (1, 15).

Air pollution effect on biological systems:

For many years the harmful effects of air pollution are being investigated and the worrying picture of increasing mortality rate and morbidity have resulted in an increased effort to reduce this pollutant. It is essential to consider, in this respect, the effect of these pollutants on the biologic systems as a complex including plants, animals and humans. And from this to continue further with investigation regarding the effect on people. I will describe three elements of air pollution which interact with environment's ecosystems in general: Carbon cycle as a global scale, sulfur cycle on regional scale and fluoride cycle on local scale.

A. The Carbon Cycle: Global Scale

The amount of CO_2 in the atmosphere was constant for thousands of years due to constant production and utilization by plants (photosynthesis). Human interaction with the global cycle is most evident since the beginning of the industrialized revolution which was followed by a steady increase in global CO_2 levels until today. This interaction may have a crucial effect on global warming with implications on ocean depth and agricultural regions. The common causes of the increasing CO_2 concentration are obvious and were discussed earlier; the differences are estimated to be from 200ppm before the industrialized revolution up to 600ppm today.

B. The Sulfur Cycle: Regional Scale

Fossil fuel and ore smelting are the main sources for sulfur production and the transporting process occur in a specific layer of the atmosphere which carrying it to distant location. This effect aquatic systems and lowers the acidity, SO is also a known as carcinogen in humans.

C. The Fluoride Cycle: Local Scale

Fluoride is released into the food chain from fertilizing substances and some typical industries, it accumulate in plants and may damage bone and teeth of consumers (1, 15).

<u>Total body burden:</u>

"The presence of air pollutants in the surrounding ambient air is only one aspect of determining the impact on human beings. An air pollution instrument can measure the ambient concentration of a pollutant gas, which may or may not be related to its interaction with individuals. More detailed information about where and for how long we are breathing an air pollutant provides additional information about our actual exposure. Finally, how an air pollutant interacts with the human body provides the most useful information about the dose to a target organ or bodily system" (Fundamentals of Air Pollution 3rd Edition, pages 349-350)

Humans have many systems which can deal with pollutants and eliminate them, this capacity is very much depended on the time and amount of exposure, today even a very low concentration of pollutants can be observed in different body systems giving us a clue of past exposure to this pollutants.

Some of these chemicals enter the body by respiration and other by eating polluted food. "The concept of *total body burden* refers to the way a trace material accumulates in the human system" (Fundamentals of Air Pollution 3rd Edition, pages 349-350), this mean presence of pollutants and other chemicals in blood, urine, adipose tissue, bones, hairs and teeth. Blood and urine play part in excretion of this substance as they may hold it for shorter periods; fat tissue may accumulate it for years and bones or teeth for the all life of the individual.

A. Lead and the Human Body

Lead exposure can follow many activates and occupations but most common exposure are due to inhalation of contaminated air from using of leaded gasoline, waste incinerators and some manufacturing process or exposure by ingestion.

The most vulnerable population is children and newborns with CNS not yet fully developed. Neurobehavioral impairments include intellectual impairment, developmental regression, ataxia, seizures and coma, adult population may manifest lead exposure with deteriorating renal function and some behavioral changes accompanied with GIT symptoms.

Inhalation of lead-containing air results in absorption of the lead into the blood from where it is mobilized to liver and other soft tissue organs, some may be cleared instantly by urine and some accumulate in bone which store up to 95% of total body burden of lead. Liver and kidney represent the soft tissue which can affect the total body lead (1, 10, 15).

B. Carbon Monoxide and the Human Body

Another example of air pollution totally affecting the body burden is carbon monoxide (CO), every individual has base line levels of CO resulting from hemoglobin break-down and other normal metabolic processes. CO is directly absorbed in the lungs by the blood stream and smokers have higher levels than non smokers. Types of air pollution associated with high levels of CO exposure are as follows: automobile emission, and indoor pollution of home usage of coal and wood for heating and cooking. In this respect, which will be discussed later on, the problem is extremely severe in poor population such as in China, India, and Africa.

During normal respiration the different affinity of O_2 and CO_2 in different parts of the body allow the O_2 to be delivered to tissue and the CO_2 to be carried to the lungs for elimination. CO, however, has much higher affinity to hemoglobin and therefore displace the O_2 and result in suffocation.

Base line levels of CO are 0.5%, but smoking and urban exposure may lead to an elevation of this level. Measuring the human CO level may serve very well as an indicator for the environmental levels, and can give clue to general population exposure risks (1, 10, 15).

The human respiratory system:

Lungs play a major role in two function of our body, the first function is to deliver O2 from the inhaled air into the demanding tissue while simultaneously to excrete the CO2 produced by tissue metabolism, air containing O2 is entering to upper air ways and transported to the alveoli where the O2 diffuse into the blood which deliver it to the tissues. In the same level of the alveoli the CO2 diffuse from the blood stream into the inhaled air which contain lower amount of it and then by exhalation the CO2 is excreted from the body. Any changes in the ambient air concentration may affect the efficiency of this process. Higher levels of CO2 may interfere with the excretion process of CO2 while lower levels of O2 may interfere with the utilization of ambient air O2.

The respiratory system as well as GIT or skin are the main part of our body which interact with the surrounding environment and therefore any trace substances such as air pollution will inter our system through this port of entry.

Because of the very different flows in the various sections of the respiratory region, which means that high flow will be present in the upper bronchus and trachea while very little flow is present in the lower part due to increase total size of the many small bronchiole, particles suspended in air and gaseous air pollutants are treated differently in the lung (1, 6, 10).

A. Particle and Gas Behavior in the Lung

The major characteristic effecting particles movement in the lung is their size and aerodynamic behavior, while gasses contents of the air are influence mainly by their solubility and absorption in the mucosa of the different respiratory regions.

Particle deposition is size dependable, therefore bigger particles may be cleaned by nasal hairs or upper respiratory mucus secretion and smaller parts may get into the alveoli.

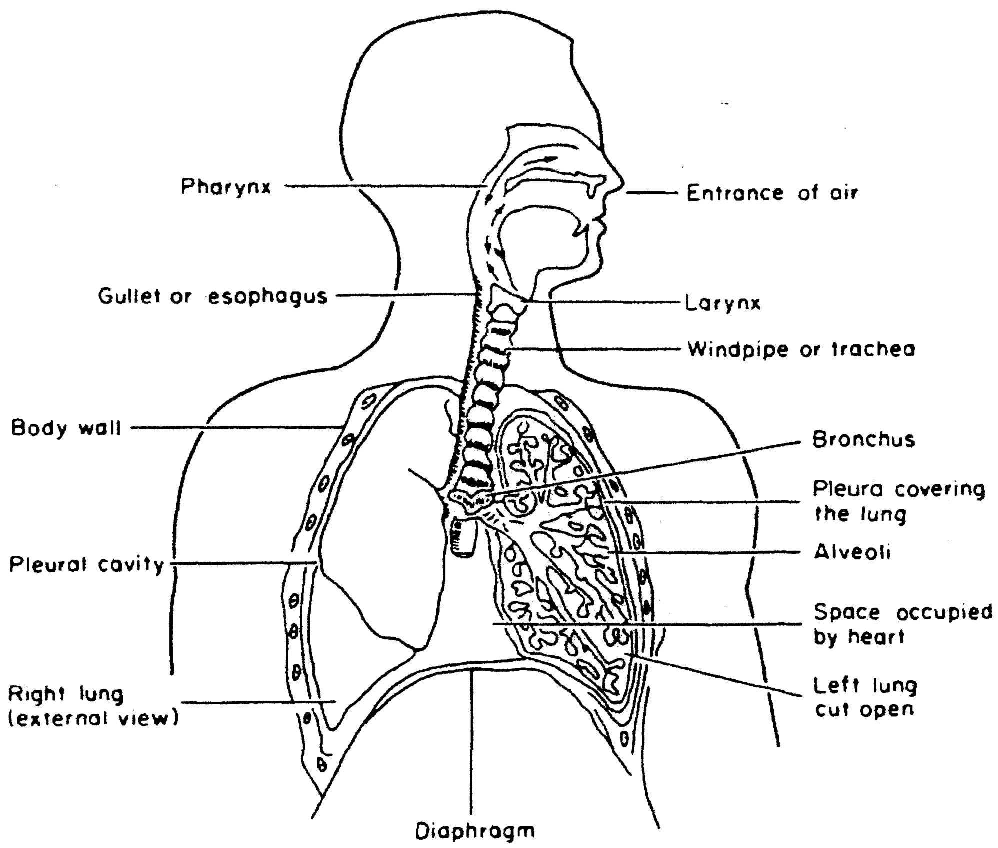
B. Removal of Deposited Particles from the Respiratory System:

Few systems play a role in the removal of particles from the respiratory system, the upper part is protected by nose blowing, sneezing, coughing, and swallowing and when these fail the mucus covering the respiratory mucosa is continually cleared by ciliary movement which strokes upward the mucus film with the particles into the GIT.

In the pulmonary region particles may do translocation into the lymph system or blood system or they may be engulfed by alveolar macrophage which can then migrate to the ciliary region and removed into the GIT.

Regarding gases, solubility controls removal from the air stream. Some highly soluble gases such as SO2 are absorbed in the upper airways, whereas less soluble gases such as NO2 and O3 may penetrate to the pulmonary region. Irritant gases are thought to stimulate neuroreceptors in the respiratory walls and cause a variety of responses, including sneezing, coughing, bronchoconstriction and inflammation or irritation (1, 6, 10).

Schema of human respiratory system:



(1)

Air pollution effect on human health:

World health organization produced recently the epidemiological data claming that 3 million people die worldwide annually from air pollution diseases; three times more than the death due to car accidents, it is twice the amount of breast cancer death or prostate cancer death (WHO epidemiological database).

The adverse effect of air pollution on our health is the major motivating power to try and control it, not all air pollutant can be controlled, not all are manmade and finally not every one of us can chose if to be or not to be exposed to air pollution. As mention above exposure to air pollution cross all borders of continents, races and economics because Chinese women working in some poor rural areas are being expose to very high levels of indoor pollution which increase her risk to get some chronic diseases just like western urban population exposed to high traffic pollutants during day time. Some populations are at high risk of developing adverse effect even from low ambient pollution, this includes children, elderly and people with cardiovascular and respiratory diseases (6, 10).

Air pollution principally affects the respiratory and circulatory systems. The respiratory system is the principal route of entry for air pollutants, some of which may alter the function of the lungs.

Data regarding health effect come from few types of studies: clinical, epidemiological, and toxicological. Toxicological studies are conducted on animals or simpler cellular systems such as bacteria and clinical and epidemiological studies focus on human subjects.

Generally speaking, clinical studies provide evidence on the effects of air pollutants under reproducible laboratory conditions. Exposure level may be measured, the physiological effect may be quantified, and the health state of the subject known.

The fact that the subjects are exposed to the actual pollutants existing in their community is both the greatest strength and the greatest weakness of epidemiological studies. The strength is the real-world condition of the exposure and the subjects; the weakness is the difficulty in quantifying the relationship between exposure and subsequent effects.

In the future, the development of biomarkers may provide a better indication of target dose.

Health effects from air pollutants range from mild eye irritation to mortality.

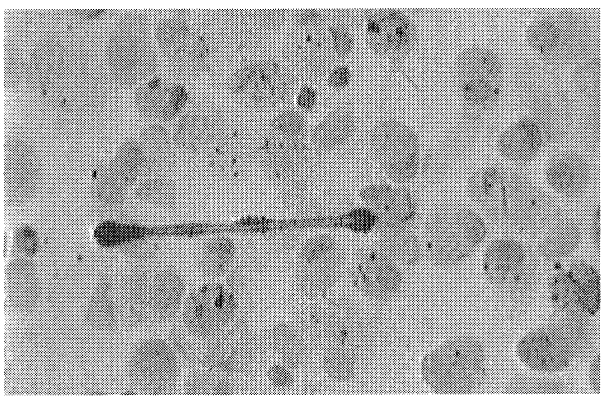
In most cases, the effect is to aggravate preexisting diseases or to degrade the health status, making persons more susceptible to infection or development of a chronic respiratory disease (7).

Types of air pollutants and their effect on human:

Particulate matter and effect on human health:

Conventionally this type of air pollution is divided into categories of size as for this is their major health implication. The mechanism by which the health effect is done is damage to mucociliary system which result in reduce clearance of the respiratory system. Mononuclear system inside the lung is also being affected by access particulate pollution and the measured activities of these cells are weaker under highly polluted environment. This effect reduces the lung capacity to fight infection. Local irritation is yet another mechanism by which air pollution act on lung and this may contribute to inflammatory process and local reaction by fibrotic changes. Implicated pathologies by these mechanisms are straightforward therefore and to number some of them it include chronic obstructive pulmonary disease initiation and exacerbation of existing ones, recurrent lung infection due to reduce immunity and clearance, increase incidence of asthma and exacerbation of existing asthma in patients (3, 10).

Particle matter residing in human lung:



(3)

Carbon monoxide:

The reactivity of this molecule is maybe the most important factor contributing to its biological effect, carbon monoxide react strongly with hemoglobin to produce highly stable complex which occupy the hemoglobin as an oxygen carrier and reduce to total blood capacity to deliver oxygen to the tissue.

Maternity effects are prominent and result in low birth weight infants which are further at increase risk for other infant morbidities and increase total mortality in the prenatal period (3).

Sulfur dioxide:

The effect of the substance is divided into acute and chronic exposures. The acute effect is associated with increased lung reactivity and bronchial constriction, while the chronic exposure is difficult to differentiate from particles effect and is probably quite similar. Health hazards are implicating the exacerbation of asthma and chronic bronchitis with a very serious effect on cardiovascular diseases (3).

Polycyclic aromatic hydrocarbons:

These groups of molecules are the major component in air pollution which contributes to the development of cell aberration and carcinogenicity. It is thought to result from direct carcinogenic effect on respiratory tissue that may lead to development of different cancerous diseases such as lung cancer and upper part of respiratory system cancers such as cancer of larynx, nasopharynx and oral cavity (3).

Cancer and air pollution:

The estimation regarding the contribution of air pollution to cancers and especially to lung cancer claims that maybe only small percentage is related to air pollution. Few researches presented in the following tables demonstrate some correlation between urban dwelling as a polluted environment and the increase incidence of lung cancer. Most of these studies were conducted upon a smoking population as in this type of population the increase in the incidence of the lung cancer is more apparent (5).

Table 1. Summary of cohort studies on lung cancer in urban areas.

Study population	Area	Summary of findings on lung cancer	Standardization variables (other than age)	References
187,783 white males followed 1952 to 1955	United States (9 states)	Relative death rate = 1.33 in cities with over 50,000 population in comparison with rural areas.	Smoking	Hammond and Horn, 1958 (25)
69,868 men followed 1958 to 1962	California, United States	Relative death rate = 1.30 in urban counties (Los Angeles, San Francisco Bay area, and San Diego) in comparison with other California counties.	Smoking	Buell et al., 1967 (9)
About 500,000 men followed 1959 to 1965	United States (25 states)	Relative death rates of 1.23, 1.14, and 0.98 in metropolitan areas with more than one million inhabitants, less than 1 million, and nonmetropolitan areas, respectively, among men with occupational exposure to dust, fumes, gases, or X-rays. Corresponding rates for men without such occupational exposures were 0.98, 0.97, and 0.92.	Smoking	Hammond, 1972 (26)
25,444 men and 26,467 women followed 1963 to 1972	Sweden	Relative death rate about 1.6 and 1.2 in male smokers of cities and towns, respectively, in comparison with smokers in rural areas. Similar trend in women (based on small numbers).[a]	Smoking	Cederlöf et al., 1975 (27)
34,440 doctors followed 1951 to 1971	United Kingdom	No increase in relative death rate in "conturbations, large towns, or small towns" in comparison with rural areas.	Smoking	Doll and Peto, 1981 (28)
About 7.5 million men and women followed 1961 to 1973	Sweden	About 40 and 20% of male and lung cancer incidence explainable by urban factors other than smoking.	Diagnostic intensity, smoking (only available for about 1 % of cohort)	Ehrenberg et al., 1985 (12)
4475 men followed 1964 to 1980	Finland (3 urban and 3 rural areas)	Increased incidence in urbanized (relative risk ≈ 1.2) but not in urban married smokers in relations to married smokers in rural areas.	Marital status, smoking	Tenkanen and Teppo, 1987 (29)

[a] An extended follow-up of the male part of the cohort through 1979 showed smoking standardized death rates of 1.4 and 1.1 in cities and towns, respectively (J Carstensen, personal communication).

(5)

Cancer markers in high risk population:

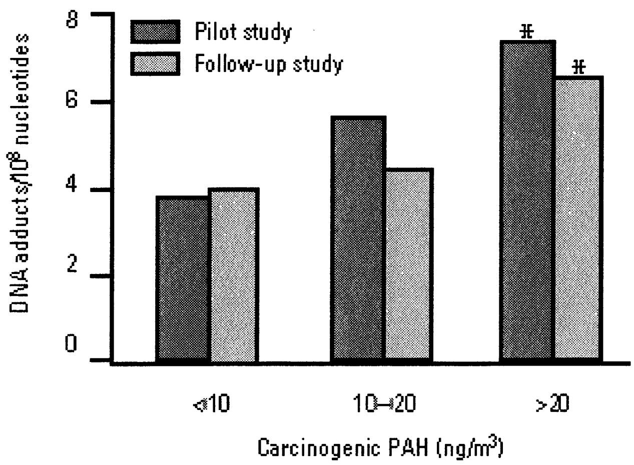
Many researches are trying to find and develop a marker for air pollution exposure, this marker should originate in the biological system of human being so to reduce any extrapolation from animal models. The biomarker should give us some indication of the exposure both qualitative and quantitative, it was proposed to use DNA adducts and other oxidative products of DNA as biomarkers of personal exposure in polluted areas (16).

As mention above the topic of cancer, in this aspect, is relatively new and only recently was starting to be investigated, it is estimated that the relative contribution of air pollution to cancer in general and lung carcinoma specifically is minor (10). However, in this respect of cancer mainly regarding lung cancer and its very high mortality, there is no debate regarding the profit that should come out of its prevention.

Biomarkers of air pollution:

Few researches used biologic material as a marker of personal exposure to ambient air pollution, they where preformed in places where the result could be compared. Places such as: rural and urban population or residential areas which are highly polluted by stationery sources such as: power station or industrial area. These markers are designed to reflect the exposure of much different kind of pollutants some of which are known as carcinogen and others are suspected as ones. These include polycyclic aromatic hydrocarbons and its metabolite, nitrous oxides and other compounds that induce the generation of reactive oxygen species and many others.
Poly cyclic aromatic hydrocarbons are a good example as they have long been studied. They react with macromolecules to form DNA adducts, albumin adducts, urinary metabolites as 1-hydroxypyrene, oxidized proteins. They may be assessed as mutagens through the usage of the suspected carcinogenic material such as the urinary metabolite of poly cyclic aromatic hydrocarbons as inducer of mutation on cell culture of bacteria (*Salmonella typhimurium*) (16). Teplice program is a good example of using biomarkers as sign of exposure in non-smoking population residing in polluted area of the Czech Republic, the measured ambient pollutants of polycyclic aromatic hydrocarbons correlated positively to the measured DNA adducts (13).

DNA adduct levels in nonsmoking women from Teplice district with personal exposure to carcinogenic PAH



(13)

Brain cancer:

In 2003 a new research team was established to investigate the possible connection between air pollution and brain cancer, the research team was focused on animal models of air pollution exposure compare to human cadavers died due to brain cancer.

This issue gained some attention due to increase incidence in some urban population and especially in youngsters where brain cancer is the main cause of death due to neoplasm's (9).

Lung cancer:

Lungs are the primary and main portal of entry to many types of air pollutions, we are being expose during our life to many types of air pollutions such as particulate mater (PM10, PM2.5) or inorganic molecules such as nitrous and sulfur compounds, of which some are being absorbed from the epithelium into our body and some lodge in the alveoli and cause irritation and chronic inflammation (1, 6, 10, 15). Epidemiologic studies analyzing data from different places estimate the relative risk of exposure to various types of air pollution especially due to incomplete combustion as shown in table 6 (5).

Table 6. Summary of epidemiologic evidence of relative risks of various types of exposure to combustion-source pollutants.

Exposed groups	Primary combustion sources	Exposure indicators or indexes	Rate ratio
Cigarette smokers	Tobacco	Smoking status and history, cigarettes/day	7.0–22.0
Coke-oven workers	Coal	Job classifications	2.5–10.0
Railroad workers, truck drivers, diesel mechanics	Diesel	Job classifications	1.2–2.6
Residents of areas with high ambient air pollution	Complex mix from coal, wood, diesel, gasoline	Respirable, fine, or sulfate particle concentrations	1.0–1.6
Nonsmokers exposed to environmental tobacco smoke	Tobacco	Smoking status of family members and co-workers	1.0–1.5

(5)

Table 7 presents the work of a few research teams who were trying to calculate the attributed risk of air pollution to lung cancer; the data was obtained from extrapolation of animal studies and from specific occupational exposure. The results as presented here showed a discrepancy between each other but otherwise all the researchers estimate that the real risk may be higher and reach 10% of lung cancer as a result of air pollution exposure (5).

Table 7. Estimates of the population attributable risk (PAR%) of lung cancer due to air pollution in the U.S. population.

Source	Method	Estimated attributable risk
Doll and Peto (*19*)	Extrapolation from occupationally exposed groups using past and then-current levels of B[*a*]P	0 to 2% overall (10% of current lung cancer in urban areas) 1% of future lung cancer
Karch and Schneiderman (*47*)	Relative risk of urban vs rural residents from Hammond and Garfinkel (1978) and proportion of 1980 population residing in urban areas	12% of 1980 lung cancer 10 to 19% of future lung cancer based on 1980 levels of TSP
U.S. EPA (*46*)	Summation of numbers of cancers attributable to >20 individual pollutants from toxicologic and other data	<1% given current levels of pollution

(5)

<u>Environmental tobacco smoke and passive smoking</u>

The exposure to pollutant from the environment are not limited to the out door activities but also to the indoor part of the day as noted above. In passive smoking however the source is one of the family members or any smoking person sharing the building with non smokers. Many studies showed that the high percentage of non smoking population are being exposed to environmental tobacco smoke (ETS) in there homes or working places. The estimation of ETS exposure may be assessed by several ways and in the following studies volatile organic compounds (VOC) such as benzene, 1,3-butadiene, and 2,5-dimethylfuran were measured in a breath measurement technology.

Result as presented in the following table showed increase concentration of all VOC in the breath tests of non-smokers. This evidence supports the idea regarding the possible adverse effects due to ETS exposure in non-smoking population (8).

Table 3. Average increase in breath concentrations of benzene, 1,3-butadiene, and 2,5-dimethylfuran ($\mu g/m^3$)[a] experienced by smokers and nonsmokers during smoking sessions.

Compound	Nonsmokers (n = 4)[b]	Smokers (n = 5)
Benzene	25.7 ± 12.9[c]	478 ± 144
1,3-Butadiene	14.4 ± 5.3[d]	353 ± 24
2,5-Dimethylfuran	27.1 ± 18.1[e]	340 ± 71

[a]Mean ± SD. [b]n = 3 for benzene. [c]Includes one preexposure and one postexposure measurement below limit of quantitation (LOQ). [d]Includes two preexposure measurements below limit of detection (LOD), and two pre- and one postexposure measurement below LOQ. One-half the detection limit was used for measurements below the LOD. [e]Includes two pre- and one postexposure measurement below LOQ.

(8)

Other method for estimating exposure to ETS is by urine analysis of specific types of metabolite originating in the tobacco smoking. These include the total urinary cotinine as a marker for nicotine uptake and urinary specific metabolite from the group of

methylnitrosamine which in the parental structure is a known tobacco-specific lung carcinogen (14).
Over all it is not clearly define what are the trash hold levels of exposure for a specific diseases initiation and the age related aspect of this risk, some studies showed increase incidence of lung cancer in children exposed to ETS and even source specific characters such as paternal smoking with increase incidence of childhood brain tumors and maternal smoking without significant increase of any malignant diseases (4, 17).

Norwegian cohort study of lung cancer:
A study which included over 16,000 men (over 30 years) was conducted in Norway and estimated the exposure level of the group during this time and the percentage of lung cancer diagnosed in this follow-up. Where levels of nitrogen dioxide are high, men have a greater chance of developing the disease. (Smoking is still, by far, the biggest factor).
This large-scale study has provided clear signs that there is a definite correlation between the levels of pollution and lung cancer in men. During the study more than 400 men developed lung cancer and in order to calculate in the research smoking habits the result were modified but even so the correlation between air pollution and lung cancer was demonstrated.
The investigators were using two large databases. One contained information each individual cancer cases in Norway; the other contained information on the average annual concentration of air pollutants at each of the participants' home addresses. This enabled the investigators to produce lung cancer risk estimates for each individual.
All participants in this study agreed already in 1972 to take place in the long term follow-up of cardiovascular diseases. At the beginning the age group was 40 to 49; about 56% were current smokers and anther 25% were former smokers. During the 27-year follow-up, 2,802 of the men developed cancer; in 418 cases, it was lung cancer.
As expected smoking habits still played a major role in lung cancer development, the relative risk for lung cancer ranged from 4.58 in former smokers to 36.47 in heavy smokers (the comparison was with those who had never smoked).

The research was focusing on two typical pollutants currently measured all over the studies area:

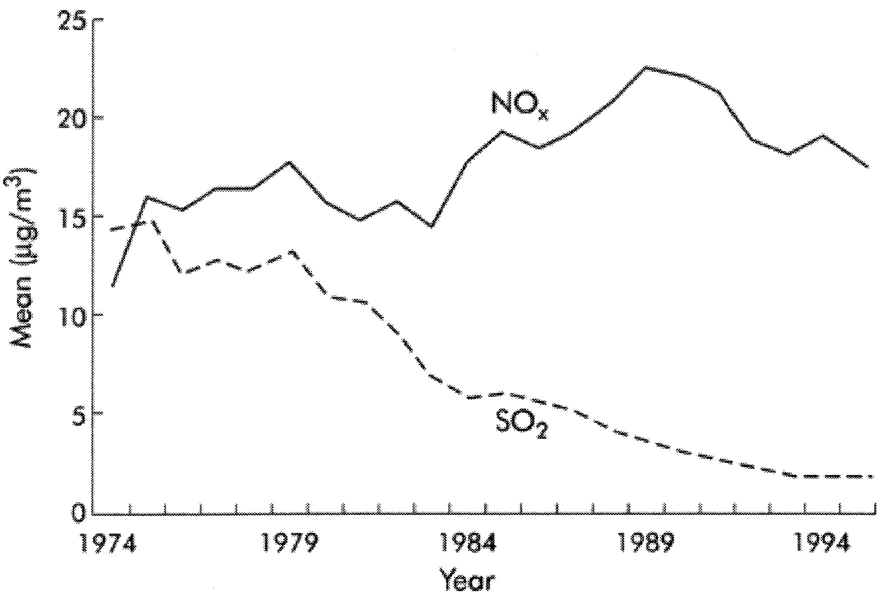
-Nitrogen oxides, the main source of which is vehicular emissions.

-Sulfur dioxide, which is released primarily from heating fuels.

These pollutants were estimated for each participant in the study and any changes of air pollution due to changes of living places in side Norway were also incorporated into the data and calculated according the new levels.

Due to the fact that long time may pass between exposure and lung cancer development, statistical analysis focused mainly on the effect of air pollution exposure during the first five years of follow-up. During that time, the median levels of nitrogen oxides and sulfur dioxide at the men's homes were 10.7 and 9.4 µg/m3, respectively. During the remainder of the study, the nitrogen oxide levels tended to increase, whereas the sulfur dioxide concentrations decreased.

Mean yearly estimated concentration of sulphur dioxide (SO_2) and nitrogen oxides (NO_x) at the home address of the members of the cohort (13)



(12)

A small, but nonetheless significant, increase in lung cancer risk was seen with high nitrogen oxide levels but not with sulfur dioxide levels. In comparison to the men whose average annual exposure to nitrogen oxides was less than 10 µg/m3 during the first five years of the study, those whose average annual exposure surpassed 30 µg/m3 had a 36% increase in risk. Furthermore, a dose-response relationship was found: Lung cancer risk rose by 8% for every 10-µg/m3 rise in the nitrogen oxide level.

The association between nitrogen oxide concentrations and lung cancer risk could not be explained by other variables. In fact, levels of this pollutant were quite evenly distributed during the first five years of follow-up, regardless of the participants' smoking status, occupation, or education level.

Because there were so few cases of lung cancer among never smokers, the investigators could not quantify the extent to which air pollution increased their lung cancer risk. Among smokers, air pollution appeared to have a weaker effect on heavy smokers than on light smokers; however, this difference did not reach significance. In the non-smoking group the umber of lung cancer was comparatively so small that statistical results could not be obtained while in the smoking group light smoker where affected more dramatically by air pollution than did the heavy smoker. However both groups had significantly higher rate of lung cancer in the highly polluted areas (12).

<u>Lung cancer and indoor air pollution in China</u>:

In county of Xuan Wei population of around 1 million people who are mainly farmers. Smoking is very common in men and reach about 40% while in women is less than 0.1%. This population traditionally uses three types of fuel for domestic usages such as cooking and heating, smoky coal, smokeless coal and wood. Cooking is done inside the house in shallow, un-vented pits, which is responsible for very high air pollution levels.

Traditionally, women are more occupied with cooking and house managing, while men spend most of their time outside in the open air.

Between the years of 1973 and 1979 the Annual age-adjusted lung cancer rates in this county were 27.7 in males (which is one of the highest in China), and 25.3 in females (which is the highest in China). It is very unusual to find such a similarity between the rates of men and women. In this region the survey concluded that this is the only case where cancer mortality exceeded the national average.

Annual lung cancer mortality rates vary greatly among the regional communities, but were found to be highest in places where smoky coal is burned. Therefore, lung cancer mortality in Xuan Wei is thought to be associated with the domestic usage of smoky coal and especially in women who smoke very rarely in that region.

Due to the great variation in mortality between different regions that use the Smokey coal, the presence of other factors can not be ruled out.

Comparison between two communities:

Comparison was made to evaluate the association between smoky coal and lung cancer in two populations. The first group's mortality was high and smoky coal was used predominately as the fuel source while in the second group mortality was low and other non smoky fuel was used as an energy source. The Concentrations of particles of air pollution inside homes using smoky coal were very high and were considerably lower in homes which used smokeless coal. Mutagenicity was also measured and was found out to be very high where smoky coal was used and this was consistent with epidemiologic studies, which means that highest mutagenic sample came from area of highest lung cancer while low mutagenicity samples were obtained from smoke less energy usage. In one district which was highest in pollution and lung cancer it was estimated those residents were exposed to 100 times the allowance 24 hours exposures in the US.

The particles from smoky coal combustion are mainly of a size that remains longer in the air and which can be effectively deposited in the lung after inhalation. Carcinogenic polycyclic aromatic hydrocarbons were in very high levels and especially the benzopyrene was a component of this indoor pollution and reached levels comparable with some occupational risk such as coke oven plants.

Different cooking habits were responsible for the differences in PAH concentrations and mutagenicity in the two high-mortality communities. In one community the cooking habits consisted of two meals only that meant less frequencies of the fire being lit. Whereas in the two other communities three meals were prepared every day with shorter duration of stabile fire (which produces less smoke), but involving a longer starting process of the fires which is thought to produce the highest amount of pollutants.

The presence of several chemical compounds known to be carcinogenic in the smoky coal samples may contribute to the high lung cancer rates in the two communities where smoky coal consumption is the highest.

In this study they did not find any association between domestic open-fire wood smoke and lung cancer. It is believed that both the less efficient lung deposition of the large particles from wood combustion, with lower concentrations of biologically active compounds may contribute to the low rate of lung cancer in the communities using predominantly wood for fuel. Unlike smoky coal, 90% of the particles from smokeless coal were soot and unburned fuel, which may explain the lower lung cancer rates in the commune where it is widely used.

These findings presented in the study of physical, chemical, toxicological combined with epidemiologic correlation suggest a rather strong association between indoor pollution by a specific type of coal and lung cancer (3, 13).

Air pollution study in California:

Cohort's study was conducted which included 6,338 nonsmoking adults from California ages 27 to 95 between the years 1977 to 1992, this group was follow for any cases of cancer which was newly diagnosed. Monthly ambient air pollution data were interpolated according the home and working location, cumulated and then an average of daily exposure was obtain. Increased relative risk of incident of lung cancer in males with levels of 100 ppb and with ozone 3.56 was observed as well as increased incident of lung cancer in males associated with increase concentrations of particulate matter <10 μm and SO_2. Increased risks lung cancer incidents were associated with elevated long-term ambient concentrations of PM_{10} and SO_2 in both genders and with O_3 in males (2).

Prevention of air pollution induced diseases:

The preventive measures which can be taken in order to reduce mortality and morbidity can be divided principally in to pre-exposure stages which means measures taken while the population is still under environmental condition which do not possess any health risk. Pre-exposure prevention is divided into several levels: personal level, community level and national level, all of which can be enforced by legislative processes. Some of these levels of prevention are easily achieved such as following occupational standards in the working place or using different types of fuels, while others are more difficult and involve economical and emotional investments, here we can mention the enforcement of different types of energy source utilization.

Post exposure levels of preventive measures regarding air pollution may be divided as new adopted standards of air pollution which are more strict, such as introduction of smaller size of particulate matter air pollution which was PM10 (10um),but was then accompanied by PM2.5 (2.5um) standards. Post exposure may be of clinical aspect and include screening and follow-up of exposed population, in this part newly designed biological markers or even basic physical examination can serve the target of early diagnosed cancer diseases which, in the case of lung cancer, is highly desirable (1, 6, 15).

Conclusion

This issue of air pollution is very probable to gain increased public attention due to the geographic distribution of this problem, which practically affects almost every one of us. Air pollutant may travel long distances in the air, incorporated in biological systems and carried by food and water. In addition, the frame of pollutant is increased almost daily and new substances and their metabolite are pointed as carcinogens, which means that the relative contribution of air pollution to diseases such as lung cancer will most probably increase. This relative contribution was traditionally suppressed by the devastating effect of smoking as a risk of lung cancer but recent studies showed additive effect of both these factors on the mention disease. Last but not least the potentially preventable aspects of air pollution will most probably reflect in public opinion in most Western societies and will force governments to find a solution to this public health risk.

As mention earlier WHO posted figures claiming there have been over 3 million deaths world wide due to air pollution which is much higher than car accidents' death rate and even high compared to common malignant diseases. This huge number should be the strongest force and motivating factor in the war over controlling the exposure of the population to air pollution.

As a future member of the health care system, I believe that this system may participate in the preventive measures of air pollution exposure in a few levels as follows: occupational medicine may focus on the employee's environment such as industry or office and assess the exposure risk due to production process or the office exposure to indoor smoking.

A General Practitioner and community base medicine may act in many different ways for preventing lung cancer and other health risks. This could be achieved by screening patients for pollution associated diseases such as asthma or measuring children's exposure to parental smoking while maintaining high index of suspicion in specific patient populations which may be highly exposed.

Educational measures may be employed by branches of the health care system in order to reduce exposure and increase awareness to air pollution at home and in the working place.

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