# HYGENE and Vladimír Bencko et al. EPIDENIOLOGY Selected Chapters

**SECOND REVISED EDITION** 

#### Hygiene ad Epidemiology

Selected Chapters

#### Vladimír Bencko et al.

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In Prague, September 2019 Vladimír Bencko

## INTRODUCTORY NOTE

Hygiene and epidemiology we conceive classically as tightly connected, partially overlapping disciplines without any fashionable attributes or transient labels making the orientation in basic disciplines of the preventive efforts in medicine just more difficult or confusing. The goal of hygiene and epidemiology in our present situation is to positively influence the **quality of human life**.

**Hygiene**, together with **epidemiology**, represent the integral, **biomedical fundaments** of **public health** or **community medicine** representing a more recent concept. Unlike the social medicine, which is the third indispensable component of public health, that strongly accentuates moral, ethical, and organizational aspects of health care, hygiene and epidemiology since ancient times, have been **developing out of empiricism**, and over a hundred years, these two disciplines have shared the same rules as other sciences. For example from the thousand year of empirical experience, some correct anti-epidemic measures were deduced even times of. The **threat of vast epidemics** depopulating countryside and towns and paralysing the fighting armies, compelled medicine to develop a new medical discipline. Hygiene bears the name of the **Goddess of Health** – the Greek **Hygieia** together with Asclepias worshipped in Epidaurus of the Peloponnesian Peninsula. She is presented as beautiful woman, whose symbol is a snake drinking water from a bowl the goddess holds in her hand.

Hygiene is science of **health preservation**. Originally, it deals with all factors affecting the physical health and psychic well-being of man. Relating to man's health it includes the **quality of water and** other **drinks**, **food and nutrition**, **clothing**, **working conditions and physical strain** as such, **sleep**, **cleanliness of the body**, **bad habits** like **tobacco**, **alcohol** and the other **drug abuse**, and **mental health**. As to the public aspects, it covers **climate**, **soil**, sorts of building materials and **housing** arrangements, **heating**, **ventilation**, **waste disposal**, medical knowledge of **disease incidence and prevention**, down to burial of the dead.

The firm link of hygienic theories and practice with health status of the population remained preserved in the original form only in infectious diseases, later on in the self-contained epidemiology the remarkable course of which to present day epidemiology of non-communicable diseases is sufficiently well known.

Since the Enlightenment era, the efforts for disease prevention in our country have traditionally enjoyed a good standard. The important drive was the charitable attitude of many physicians and health personnel and straining create organizational, and educational conditions enabling **primary prevention principles** to be introduced into practice. The Institute of Hygiene at Czech Faculty of Medicine at Charles University of Prague (the present Institute of Hygiene and Epidemiology, First Faculty of Medicine, Charles University) was founded in the school year 1897/1898. An analogical Institute at the German Faculty of Medicine in Prague was founded in 1884. However, it ceased to exist along with the German section of Charles University in the turbulent post-war time when the Czech sector, after Nazi close down was re-opened.

The current institutional integration of hygiene and epidemiology at the First Faculty of Medicine in the school year 1992/1993, including teaching programme and final state examinations reflect the rational integrative efforts in the past decades in the field of education and training of medical youth at the break of millenniums.

Here follow some examples of various successful **practical applications** of our **preventive medicine**, more specifically, in epidemiology branch. The post-war activities against **venereal diseases** and the starting campaign resulting in a significant drop of the incidence of **tuberculosis** and then **brucellosis**, requiring a close cooperation with the veterinary service, deserve, by extent and organization, as well as by achieved positive results, and despite a fairly long time lapse, the highest appreciation.

The former Czechoslovakia was the first country in the world that started anti-polio mass vaccination already in beginning of the sixties, thus being an example for other countries. Our physicians shared in the first and until today unique eradication action of another infectious disease – **smallpox**. Neither of the two praiseworthy deeds has ever been fairly appreciated on the international scene, though, e.g. smallpox eradication surely was a big success of the preventive medicine on a global scale, and deserved the highest esteem by awarding a prize equivalent to the Nobel prize. John Snow is often recognized as the founder of epidemiology. He, a practicing physician, conducted what is regarded today as a classic study of the transmission of cholera in London in the mid – 1800s. For the development of epidemiology in our country became important establishment of the National Institute of Public Health founded in 1925 in Prague. The Institute's collaborators had been acquiring experience mostly in the USA. Thus a modern school of epidemiology was born, of its representatives at least Karel Raška should be remembered. He was head of the contagious diseases division at WHO headquarters in Geneva, and was one of the authors and managers of the smallpox eradication programme. In the post-war time our top specialists passed the training courses in epidemiology at the London School of Hygiene and Tropical Medicine with which some of our health research and educational institutions have been keeping up busy working contacts ever since. Concerning the noncommunicable diseases, we must remember the extensive epidemiological study on endemic goitre performed by our clinical endocrinologists in the late forties and early fifties, which can still stand the current, relatively strict qualitative criteria for epidemiological studies, resulting in the systematic iodination of salt. Again, we were among the first to introduce fluoridation of drinking water for caries prevention. This campaign was, as well preceded by thorough epidemiological study.

The frequent socio-political changes, occurring in our country in the last century unfortunately too often, used to disrupt the balanced system of prevention. Today we have to adapt the primary prevention system to the extensive social and economic changes we are now undergoing. Much has already been done but a backup to **complexly structured primary prevention activities** are still urgently needed.

Our school of hygiene rooted from the traditional German school of bacteriology-based hygiene founded by **Max von Pettenkofer** who implemented a **sand filtration** into production of a **safe drinking water** and **Robert Koch**. Founder of our school of hygiene, **Gustáv Kabrhel**, pupil of Max von Pettenkofer enriched the process with an experimental aspects e.g. by providing study of effectiveness of the sand filtration (**Kabrhel-index**), later on with pathophysiological factors to be demonstrated in the works of **Jaroslav Teissinger**, who already in the mid/thirties laid the foundations of the present day **biological exposure tests or biomarkers of exposure to environmental toxicants**. A few years following the last London smog episode when the most reliable health indicator was recorded mortality, **Ladislav Kapalin** and **Karel Symon** tried to demonstrate the adverse environmental effects on the changes of **growth** and **haematological parameters** in exposed children, and in this way, they contributed to the application of rather sophisticated and more sensitive indicators of the health status of children.

The **network of hygienic stations** according to the Soviet model set up in the late fifties, together with the establishment of the Medical Faculty of Hygiene, the present 3<sup>rd</sup> Faculty of Medicine at Charles University in fact was a progressive undertake though fraught with inherent faults usual in any kind of systems designed for a rather different setting, and probably optimal elsewhere. Nowadays what we still miss most is the expert, critical analysis of successes, failures or errors of our previous hygienic service. There are two circumstances likely to make this problem still very difficult. The first: the effectivity of hygienic service activities can be rated by success in preventing health threatening factors. This brings us, in the first place, to skating on a thin ice of any kind of conditionals. The other serious issue, was the advanced public health legislation, which, owing to profuse numbers of exceptions became less effective than expected. Then the famous Parkinson-laws relentlessly operated on either side of the iron curtain. From the relatively modest beginnings, the hygienic stations became inflated to the "maxi" size in the late eighties, frequently criticized by the Western experts on the problems of preventive medicine of our public health system. However, it is necessary to underline that these critics envy us the institutionalised structure of public health engaged in primary prevention, i.e. disease prevention by influencing life style, living conditions, resistance of the human organism, etc., and warned against total disruption of this structure while trying to square up with the totalitarian legacy.

The trends in **integrating primary prevention** into the current activities of every physician and paramedical personnel have been implemented but slowly and with **many obstacles** in all social systems in global scale. This is evident in the problems related to implementation such global WHO programs, like the decade dedicated to the "Drinking water for all", or "Health for all by 2000" anchored in national programmes adapted to the local conditions. Intentionally, primary prevention tries to **suppress the causes of the diseases, reduce their incidence, and improve life expectancy and quality of life**. The constituents of **primary prevention** are **protection** and **promotion** of health.

**Health protection** strives to safeguard humans against any **unacceptable health risks** produced by the activities of man. In the Health Protection Programme the government and industry invest tens of thousand millions crowns yearly. There is no need to glorify or condemn this fact, as it is a must. But for that the present day industrial sphere would collapse because of incompatibility of harmful living conditions with human existence.

The purpose of the preparatory studies of the students for your final state examination in hygiene and epidemiology is **to understand the fundamental principles and importance of the primary prevention in context with medical practice**. This also covers timely notifications of infections, their flexible surveillance thereof, reports on incident malignancies enabling administration of the national cancer register, and chiefly, the necessity of your **personal engagement** as physicians in primary prevention programmes and last but not least in the early diagnosis and a rational treatment of your patients, that is, the **secondary prevention**. The qualified advice on life style, occupational risks and health risks from bad habits considering the social and health situation in the family at your patient may significantly help to create your profile of a desired, competent family doctor.

Here are some closing notes: By the old proverb "Cut your coat according to your cloth" we naturally try to introduce the up to date style of teaching and research work of our Institute, as you can see from the quotations on important projects and publications by the staff of the Institute published during the past decades. It consists of **biological monitoring** and **health risk assessment of human exposure to environmental toxicants**, mostly **toxic metals** and **polyhalogenated hydrocarbons**, and health aspects of increasing risks from **traffic emissions**. Our interest involves the selected issues of **hospital hygiene**, before all **antibiotics resistance** and **waste disposal** from health care facilities. Presently, the Institute is dealing with **indoor environment** problems including the permanent urgent problems of smoking being one of the important **risk factors of life style**.

Currently, we participate in international multicentre studies organized by International Agency for Research on Cancer (IARC), WHO/Lyon and National Cancer Institute (NCI) Bethesda, concerning **epidemiology of cancer** and **ethical aspects of environmental epidemiology** and **quality of life**.

Like other institutes engaged in the field of primary prevention we also try to continue meaningful cooperation on the international scene with WHO, IPCS, CCMS/NATO, etc.

A certain hope open to us in the future is the **steadily rising cost of patients' treatment** that will urge responsible political bodies to recognize the **importance of primary preven-tion** from cost/benefit aspects and introduce its principles in the health care practice policy.

These questions are related to the key issues of philosophy, and hopefully as well to the future practice of **sustainable survival philosophy** – or in a more euphemistic term – the sustainable development principle. Apart from the expected progress of noncommunicable diseases epidemiology there exist a number of potential risks arising from **gene manipula-tions** in microbiology, pharmaceutical microbiology and, e. g. **bio transformation of per-sistent xenobiotics** – all of them involved in the solution of **waste disposal** problems. The described future tasks require, under consideration of some hygienic and epidemiological specifics, **unrestrained mutual cooperation** of the both medical branches. As documented

by experience of some other fields of sciences the fastest progress is expected when the individual disciplines overlap, e.g. in methodical applications of **molecular toxicology** in **environmental epidemiology**. A wider range of applied epidemiological methods in clinical studies is awaiting us as well.

The focus of interest of both disciplines remains the **primary prevention** of most widespread diseases and subsequent efforts to positively influence the **quality of human life**.

In medicine, until our days, the Hippocrates' statement still holds: Life is short, and Art is long; the occasion is fleeting, experience fallacious, and judgment difficult. The physician must not only be prepared to do what is right himself, but must also motivate the patient, the attendants, and externals cooperate. If we honour this in curative medicine, we should do so in preventive medicine twice as much.

In Prague September 2019 Vladimír Bencko

## PART - ENVIRONMENT AND HUMAN HEALTH

### CHAPTER 1.1 BIOLOGICAL MONITORING AND HUMAN EXPOSURE TO XENOBIOTICS

In the background of the growing interest of public health authorities in biomarkers of human exposure to environmental pollutants is the simple fact that the **total extent** of **environmental pollution** is often **difficult** to **assess**, both qualitatively and quantitatively. Analyses of non-systematically collected air and surface water samples yield virtually worthless data in this respect, for the actual degree of environmental contamination may vary across a relatively wide range. Concentrations of **air pollutants** are influenced by actual **weather conditions**, local air movement or by **inversions** that may be the cause of the critical accumulation of emissions in the given areas. The quality of **surface waters**, especially in streams, is generally dependent on **flow rate**, i.e., the degree to which the incoming discharges are diluted by the stream flow. In particular, fluctuation in the quality of surface water is influenced by the discharge of industrial effluents that vary considerably both in amount and composition, depending on the actual industrial production technology used.

Ideally, a continuous measurement of environmental pollution can be effected through the use of a **network** of **automated monitoring systems**, e.g., a **hexagonal scheme** of **air** pollution monitoring networks; or **line systems** for the monitoring of **traffic** or **water stream** pollution, preferably those capable of automatic sampling, analysis, registration and evaluation of data.

The **automated monitoring systems** are not easily accessible at present, both technically and economically, and their use in the near future is expected to remain **limited to highly populated localities having the greatest degree of environmental pollution**.

As an alternative to the technical approach to this problem, **biological indicators** could be used to monitor pollution of the environment. This method appears to be particularly well suited to demonstrating environmental pollution by **potentially toxic organic and inorganic xenobiotic** and **toxic elements**, including toxic metals.

The efforts to use animals in monitoring of noxious substances present in a working environment have a long tradition, starting from **canaries** or **mice** in **coalmines**, used as indicators of presence of, e.g., carbon mono- or dioxide, up to the recent form of a wide range of biological exposure tests. As example of impacts on animal species, it may serve to count losses or even extinction of **honeybee** populations to indicate environmental pollution in the areas affected by the emissions containing **arsenic** and **fluorides**. This was described in the first half of the last century.

The examination of animals is able to complete the information obtained by the examination of inhabitants. It may be even assumed that the changes of body burdens of environmental pollutants start earlier than those in man, because the **animals** are **exposed** to the **impact of contamination more directly**, by all routes including **local food chains**. Thus, **free-living** as well as **domestic animals might signal in advance the danger threatening the human inhabitants**.

In Minamata, **death of cats** in fishermen's families was an early indication. This **warning signal** was, unfortunately, **disregarded** because of the clinical resemblance of poisoning symptoms due to alkylated mercury to a kind of virosis affecting the cat's central nervous system.

Interestingly, **haematological changes** found in **hares** living in the area polluted by industrial emissions were **comparable** with those encountered in **local children**. Similarly, we found virtually identical concentrations of arsenic in the hair of children and hairs of rabbits living in the same locality.

The advantages of investigations of environmental pollution effects on animals are not limited to the above-mentioned toxic metals and non-metal inorganic pollutants. In the course of the **Seveso** accident it was, besides cutaneous affections in children (chloracne), first of all a **mass dying of small animals**, which **drew attention to dioxin leakage**. In the same way **cattle and domestic animals** were dying in **Bhopal** following an inhalation of **methylisocyanate**, which is also an organic poison.

#### 1.1.1 Human exposure assessment

The assessment of human exposure to xenobiotics can be performed by the examination of a **suitable human tissue** and **fluid** that appears to be more appropriate than the analysis of plant or animal materials currently used in ecological studies to demonstrate environmental pollution.

The human materials that are accessible for sampling include **blood** and **urine**, but also **hair** and **nails**, the derivatives of the ectoderm, **saliva** and **breast milk**.

Basic immunity status indicators like secretory IgA and lysozyme can be detected in saliva (as like as in tears and vaginal smear) when there is no chance to collect blood samples in specific field studies.

Successful attempts have also been made to measure **lead** and non-metal pollutants such as **fluorine** accumulation in **deciduous teeth** to demonstrate non-occupational **exposure** to lead or **saturation** by fluorides in children.

Fat extracted from breast milk samples is quite frequently analysed for polyhalogenated hydrocarbons and other lipophylic xenobiotics (dioxins, dibenzofurans, PCBs, hexachlorobenzene, DDT and its metabolites) to assess a potential **exposure of breast-fed children** to this family of xenobiotics.

The method of **hair analysis** appears to be ideally suited for use in **pilot prospective studies**. If an excessive exposure is detected it is recommendable that the examination be completed by analyses of other biological materials, most often **blood and urine**, in order to obtain a **closer specification of the degree of exposure in the respective population**. Attempts at the use of hair analyses in clinical diagnostics are perhaps one of the further prospects of this technique of investigation. In this context, the method of **multi-elemental analysis** enabling mutual comparison of the content of **various trace elements** holds promise for being more useful than isolated monitoring of just one microelement content in hair. This approach, based on the knowledge of the selected spectrum of toxic trace metals and their mutual proportion in hair, is also of course of advantage if biological markers of exposure in the general environment are taken into account.

Major advantages and limitations of the use of human hair analysis as a biomarker of excessive exposure to trace metals can be summed up as follows:

- The extent of exposure in the general environment does not as a rule reach the level of exposure in occupational settings, and varies greatly from individual to individual, leading thus to relatively great intra-group differences in values. The only rational approach that might help to overcome this problem is to use the method of group approach when assessing the risk of environmental exposure. Our experiences to date suggest that there should be at least 20 individuals per population group to be sampled to ensure that the differences in element content of hair samples in these groups can be quantified statistically.
- When comparing the trace element content of human hair in "exposed" and "control" groups it is preferable, according to our experience, to use the geometric mean and standard error of the mean of the values found. In the case of great inter-group differences, the use of non-parametric tests, e.g., the Wilcoxon test, is commonly advisable. Where only a smaller difference in inter-group values exists, the use of the t-test to compare the means (for two groups), or the F-test to compare the variances (for more groups than two) is of advantage for assessing the significance of inter-group differences.
- Because the frequency distribution pattern for the intra-group values of hair element content is as a rule asymmetrical, a logarithmic transformation should precede the employment of comparative tests.
- Just for illustrating the inter-group differences it is, as a rule, preferable to use the median and range, especially for ease of calculation. The median, however it may differ in its absolute value from the respective geometric mean, still constitutes the tool of choice for the orientation assessment of inter-group differences.
- The accumulation of trace elements in hair might be at least partially dependent on age and sex. To overcome this problem we use groups of 10-year old boys as the most suited representatives of non-occupationally exposed populations under surveillance.
- To date no totally reliable data have been gathered, allowing the establishment of generally applicable limits for normal content of individual trace elements in human hair. The element content of hair tends to vary from one geographical region to another, depending on the natural background conditions, including composition of soil, element concentration in water and food, and local eating habits. From this, it follows that all find-

ings obtained in the area under surveillance be compared against the values in **suitable control groups** of "unexposed" human populations.

With the exception of mercury and selenium, no biological limit values (or exposure indexes) (i.e., concentrations which, if surpassed, would indicate overexposure and a potential public health concern), have been established as yet for exposures to toxic trace elements in the general and occupational settings. Consequently, their determinations in hair can hardly be interpreted as representing exposure tests in the classic sense, but may substantially help in monitoring excessive exposure or, in other words, can help to monitor rate of exposure due to environmental pollution in general environment or in occupational settings.

Hair samples are far simpler to collect, transport and store than samples of blood and urine, and so is their processing prior to analysis, with the exception of problems with removal of external contamination which can be neglected when exposure comes from food basket or drinking water. Parts of human hair samples are also very easy to preserve for later control reanalyses. While blood and urine concentrations well reflect recent exposure, but usually vary within a relatively wide range, hair as well as nails reflects a long time or past exposure averaging their extent during the period of their growth. Detection of toxic metals in the sampled human materials could help to overcome problems with detection/ demonstration of multimedia integrative exposure to toxic metals and metalloids.

The data provided by human hair analysis techniques may well serve as a basis for **identifying the population groups at specific risk and excessively contaminated areas, including their geographical delimitation**.

One of the essential conditions for ensuring the realistic evaluation of population excessive exposure in occupational and environmental settings is the examination of **sufficiently large population groups** and the use of a **group diagnostics approach**.

This principle needs to be observed as well when we are interested to prove human exposure to **genotoxic xenobiotics**. One of the advanced methods for this purpose is FISH.

Fluorescence in situ hybridization (FISH) technique is a method for **detecting** problematic types of stabile **chromosomal aberrations** such as **translocations**, **inversions**, **inclusions** and **aneuploidy**, and the possibility of digitizing the image record. Stabile chromosomal aberrations do not cause the loss of genetic material and can be transmitted to next generation of cells, accumulate in the genetic material and **account for a long-term exposure to genotoxic substances**.

Detection of gene segments and individual genes is used in both clinical and tumor **cytogenetics**, as well as in **molecular epidemiology**.

Human biomonitoring (HBM) has a long tradition both in health care and public health with wide range of applications. Its **advantage is the integration of all exposure routes and sources**. Since HBM information demonstrates an integrated exposure, it offers the opportunity to trace and mimic a realistic exposure scenario. It reduces the number of assumptions that need to be done when estimating exposure rate of selected populations in environment and occupational settings, and thus helps to reduce the uncertainties in health risk assessment. In spite of some challenges, such as further harmonization in the area of HBM, necessity to derive equivalents of markers of external exposure, but also an addressing the ethical and political aspects of its application, HBM is an efficient and cost-effective way to measure the level of exposure of the human body to xenobiotics.

## CHAPTER 1.2 OUTDOOR AIR POLLUTION

Air pollution – both indoor and outdoor – is a major environment-related health threat, causing a range of respiratory and cardiovascular ailments.

Where and when people are exposed:

- Primarily indoors we spend the most of our life indoors.
- Exposure to pollutants from both outdoor and indoor sources, but the population dose/ exposure commitment from indoor sources is 100–1 000 times higher than from outdoor sources.
- In indoor environment exposure to outdoor air O<sub>3</sub>, NO<sub>2</sub> is lower, also sometimes (air conditioning buildings, filtered ventilation systems) fine PM exposure is indoors lower.
- Level of some VOCs are much more higher indoors than outdoors (in that case outdoor contribution to this exposure could be ignored).
- Indoor CO levels are similar or higher than outdoors (lethal CO poisonings occurs only indoors).
- The most important single source of air pollution exposure is tobacco smoke the dominant source of almost all indoor air pollutants, but it is only marginal outdoor air pollution.

Outdoor air pollution is a particularly serious threat to the swelling populations of the world's cities. With the increased combustion of fossil fuels, industrial processes and growing car use, urban populations are exposed to a long list of pollutants that include sulphur dioxide, nitrogen oxide, nitrogen dioxide, carbon monoxide, ozone, dioxins, suspended particulate matter and a host of volatile organic compounds. Open burning of urban waste with high components of plastics like polyvinyl chloride (PVC) is also a significant source of dioxins, furans and heavy metals in many communities. People who are poor often live close to these sites or work in them.

Depending on season, meteorological factors and source strengths, different components are dominant in particular episodes: **ozone** is important in episodes occurring in hot sunny weather in summer; **sulphur dioxide** and acid aerosols feature more in episodes occurring in calm cold conditions in the winter (particularly in coal-burning communities); while episodes involving **nitrogen dioxide** and **particles** are liable to arise in any season. In each type of episode, however, several pollutants may be increased and the population is exposed to a complex pollutant mixture.

The source of air pollutants have changed greatly over the past few decades in most, especially European countries as the coal for domestic heating has diminished and virtually disappeared in major towns; at the same time greatly increased number of motor vehicles, and the consequent greater congestion on the roads, has led to increased emissions from that source. The net result has been substantial reduction in many pollutants but an increase in complexity of the pollution mixture.

Cities in developing countries have much higher average pollutant concentrations than cities in industrialized countries. In the late 1990s, the average annual concentration of PM10 (small particles with diameters less than 10 microns) in North American, Western European

and Japanese cities ranged from 30 to 45  $\mu$ g/m<sup>3</sup>. Chinese and Indian cities, on the other hand, had averages of nearly 200  $\mu$ g/m<sup>3</sup> of PM10.

In addition, forest fires, whether accidental or started to clear forestland for agricultural purposes, have been the cause of severe smoke haze pollution in Asia, Latin America and North America – causing serious health concerns for children and the elderly. Moreover, dust storms in many regions of the world (especially in Central Asia), the magnitude of which aggravates by desertification and deforestation, represent another significant source of outdoor air pollution.

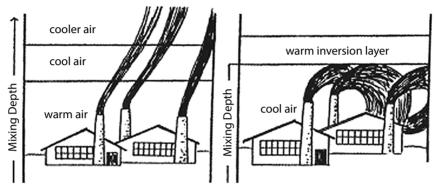


Figure 1.2.1 Atmospheric condition - inversion

The first interests in outdoor pollution are coming from the first half of the 20th century and all these disasters have the common conditions: inversion with fog and, as a result of these conditions a high concentration of the  $SO_2$  and so called black smoke (Tab. 1.2.1). This type of smog have got the name from London (London – type smog), in fact it is reduction smog, in our country is often used the name "winter smog".

After the London (Tab. 1.2.1) disaster (1952) the first decision to improve the outdoor environment became more realistic and the British government started some changes. Nowadays this type of smog in London does not exist, at least the "literary" type of it. As other big

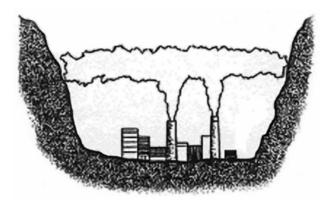


Figure 1.2.2 Atmospheric condition – inversion in valley