AICE* SURVEY OF USSR AIR POLLUTION LITERATURE

Volume XI

A SECOND COMPILATION OF TECHNICAL REPORTS ON THE BIOLOGICAL EFFECTS AND THE PUBLIC HEALTH ASPECTS OF ATMOSPHERIC POLLUTANTS

Edited By

M. Y. Nuttonson

The material presented here is part of a survey of
USSR literature on air pollution
conducted by the Air Pollution Section
AMERICAN INSTITUTE OF CROP ECOLOGY

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1972

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17. Key Words and Document Analysis. 17a. Descriptors

Air pollution	Acetic acid	Alcohols	Health
Hydrogen fluoride	Hydrocarbons	Ammonia	
Sulfur dioxide	Phthalic acids	Ethyl alcohol	

17b. Identifiers/Open-Ended Terms

Translations

17c. COSATI Field/Group 13B

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PREFACE

The present volume constitutes the second* compilation of technical reports resulting from a number of investigations of the biological effects of specific air pollutants which have been conducted at various public health institutes and in departments of public health of some of the universities of the USSR.

The great strides in the development of industrial chemistry in the country have stimulated studies of the biological effects of chemical air pollutants as well as studies dealing with public health implications of these pollutants. Such studies assume an ever-increasing importance in the Soviet Union.

Professor Ryazanov, in his comprehensive survey "The Basic Problems of Sanitary Protection of Atmospheric Air", which is presented in this volume, points out that industrial emissions and the automobile exhausts have become the primary problem of atmospheric pollution. He suggests that studies of the biological and toxicological effects of the newly produced chemical compounds as well as the establishment of their maximum permissible concentration must be intensified and accelerated as much as possible.

The material included in this volume deals with the biological effect of low concentrations of chemical toxic substances

(1) emitted from oil refineries,

(2) contained in the discharges of aluminum and superphosphate plants,

(3) contained in the discharges of the industries involved in the hydrolytic cleavage of wood, and

(4) contained in the emissions from a number of new substances which are either already employed in the current industrial use or are still under tests for use in industry.

The results of the above studies provide in the USSR a basis for the establishment of a series of new maximum permissible concentrations for new toxic substances in the atmospheric air and constitute the scientific criteria for assessing the degree of pollution of the air medium. They also form the foundation for a number of ameliorative sanitation measures to be undertaken.

Some background information on the distribution of the Soviet industry's production machine may be of interest in connection with that country's present

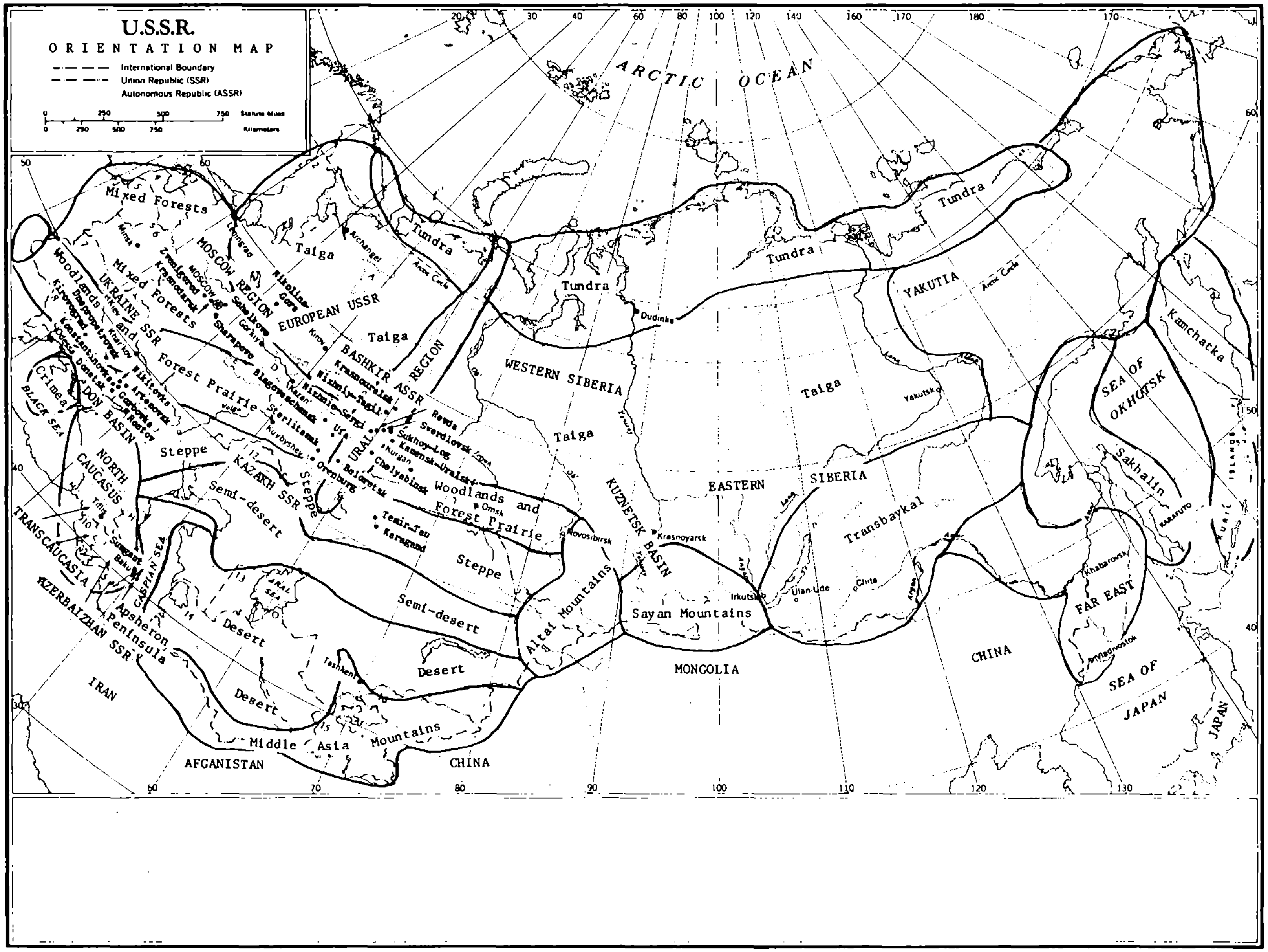
* The first compilation of this nature has been published in Volume VIII of the AICE Survey of USSR Air Pollution Literature.

and potential pollution problems and investigations. The planned distribution of production in the Soviet Union favors effective exploitation of the natural resources of the USSR, especially in its eastern areas where enormous natural resources are concentrated, and has led to the creation of large industrial centers and complexes of heavy industry in many of the country's economic areas (see page ix). The many diverse climatic conditions of the country and its major economic areas as well as the geographical distribution of the Soviet Union's principal industrial and mining centers and of its principal electric power stations and power systems can be seen from the various maps presented as background material in this volume.

It is hoped that the papers selected for presentation in this volume will be conducive to a better appreciation of some of the air pollution investigations conducted in the USSR. As the editor of this volume I wish to thank my co-workers in the Air Pollution Section of the Institute for their valuable assistance.

M. Y. Nuttonson

January 1972



ADMINISTRATIVE DIVISIONS

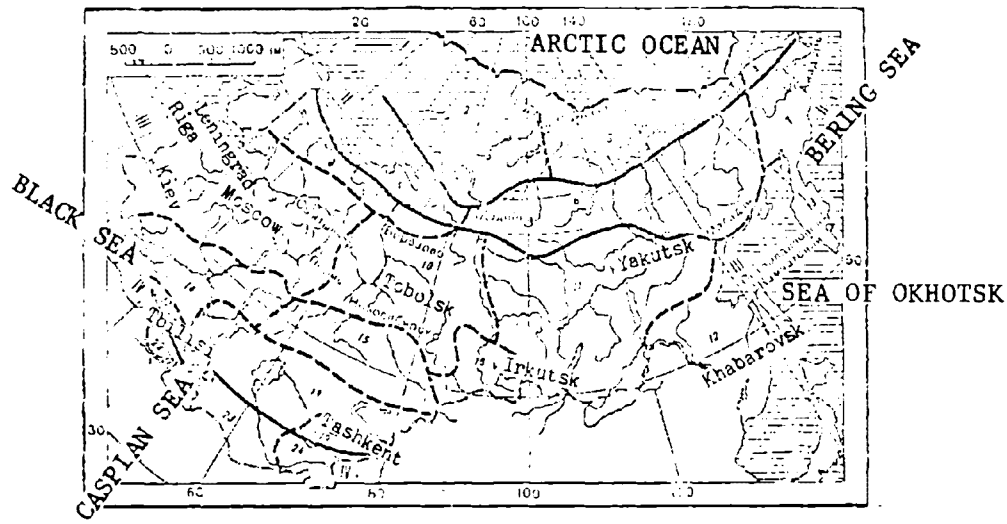
S.S.R.

1. R.S.F.S.R.
2. Karelo-Finnish S.S.R.
3. Estonian S.S.R.
4. Latvian S.S.R.
5. Lithuanian S.S.R.
6. White Russian S.S.R.
7. Ukrainian S.S.R.
8. Moldavian S.S.R.
9. Georgian S.S.R.
10. Armenian S.S.R.
11. Azerbaydzhan S.S.R.
12. Kazakh S.S.R.
13. Uzbek S.S.R.
14. Turkmen S.S.R.
15. Tadzhik S.S.R.
16. Kirgiz S.S.R.

A.S.S.R.

A. Komi ASSR
B. Udmurtskaya ASSR
C. Mariyskaya ASSR
D. Chuvashskaya ASSR
E. Mordovskaya ASSR
F. Tatarskaya ASSR
G. Bashkirskaya ASSR
H. Dagestanskaya ASSR
J. Severo-Osetinskaya ASSR
K. Kabardinskaya ASSR
L. Abkhazskaya ASSR
M. Adzharskaya ASSR
N. Nakhichevanskaya ASSR
O. Kara Kalpakskaya ASSR
P. Buryat-Mongol'skaya ASSR
Q. Yakutskaya ASSR

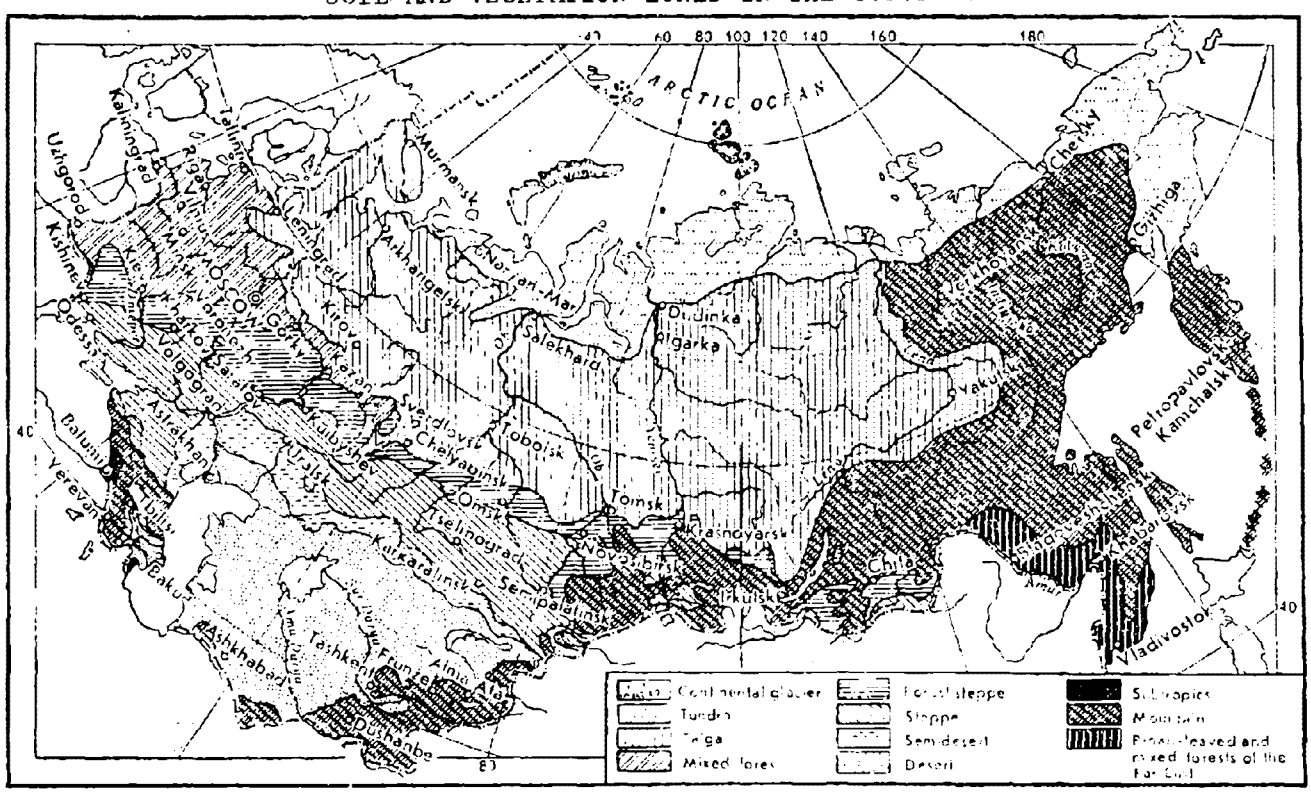
CLIMATIC ZONES AND REGIONS* OF THE USSR



Zones: I-arctic, II-subarctic, III-temperate, IV-subtropical
Regions: 1-polar, 2-Atlantic, 3-East Siberian, 4-Pacific, 5-Atlantic, 6-Siberian, 7-Pacific, 8-Atlantic-arctic, 9-Atlantic-continental forests, 10-continental forests West Siberian, 11-continental forests East Siberian, 12-monsoon forests, 13-Pacific forests, 14-Atlantic-continental steppe, 15-continental steppe West Siberian, 16-mountainous Altay and Sayan, 17-mountainous Northern Caucasus, 18-continental desert Central Asian, 19-mountainous Tyan-Shan, 20-western Transcaucasian, 21-eastern Transcaucasian, 22-mountainous Transcaucasian highlands, 23-desert south-Turanian, 24-mountainous Pamir-Alay

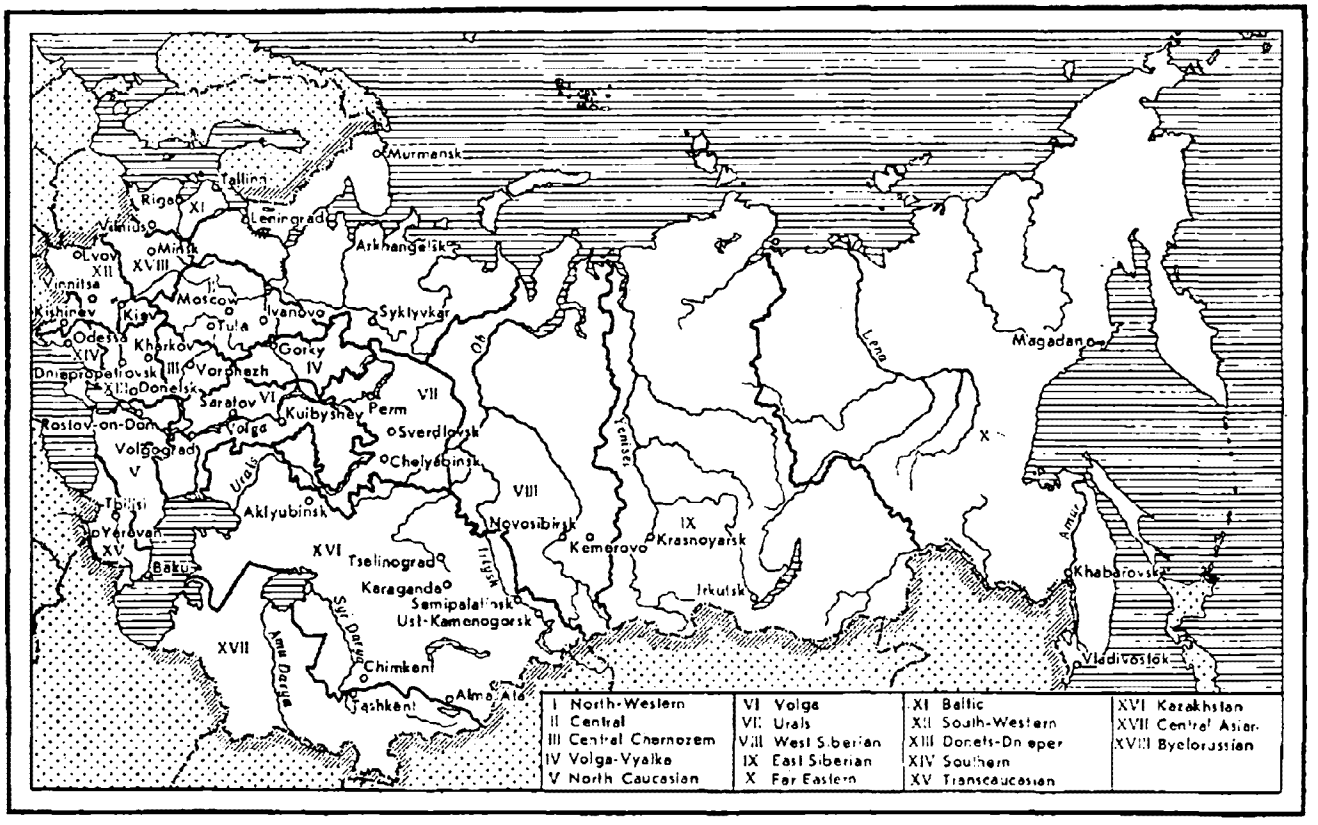
(After B. P. Alisov, "Climate of The USSR", Moscow 1956)

SOIL AND VEGETATION ZONES IN THE U.S.S.R.



(After A. Lavrishchev, "Economic Geography of the U.S.S.R.", Moscow 1963)

MAJOR ECONOMIC AREAS OF THE U.S.S.R.



PLANNED DISTRIBUTION OF INDUSTRIAL PRODUCTION IN ORDER TO BRING IT CLOSER TO RAW MATERIAL AND FUEL SOURCES

An example of the planned distribution of industrial production in the USSR is the creation of large industrial centers and complexes of heavy industry in many of the country's economic areas: the North-West (Kirovsk, Kandalaksha, Vorkuta), the Urals (Magnitogorsk, Chelyabinsk, Nizhny Tagil), Western and Eastern Siberia (Novosibirsk, Novokuznetsk, Kemerovo, Krasnoyarsk, Irkutsk, Bratsk), Kazakhstan (Karaganda, Rudny, Balkhash, Dzhezkazgan).

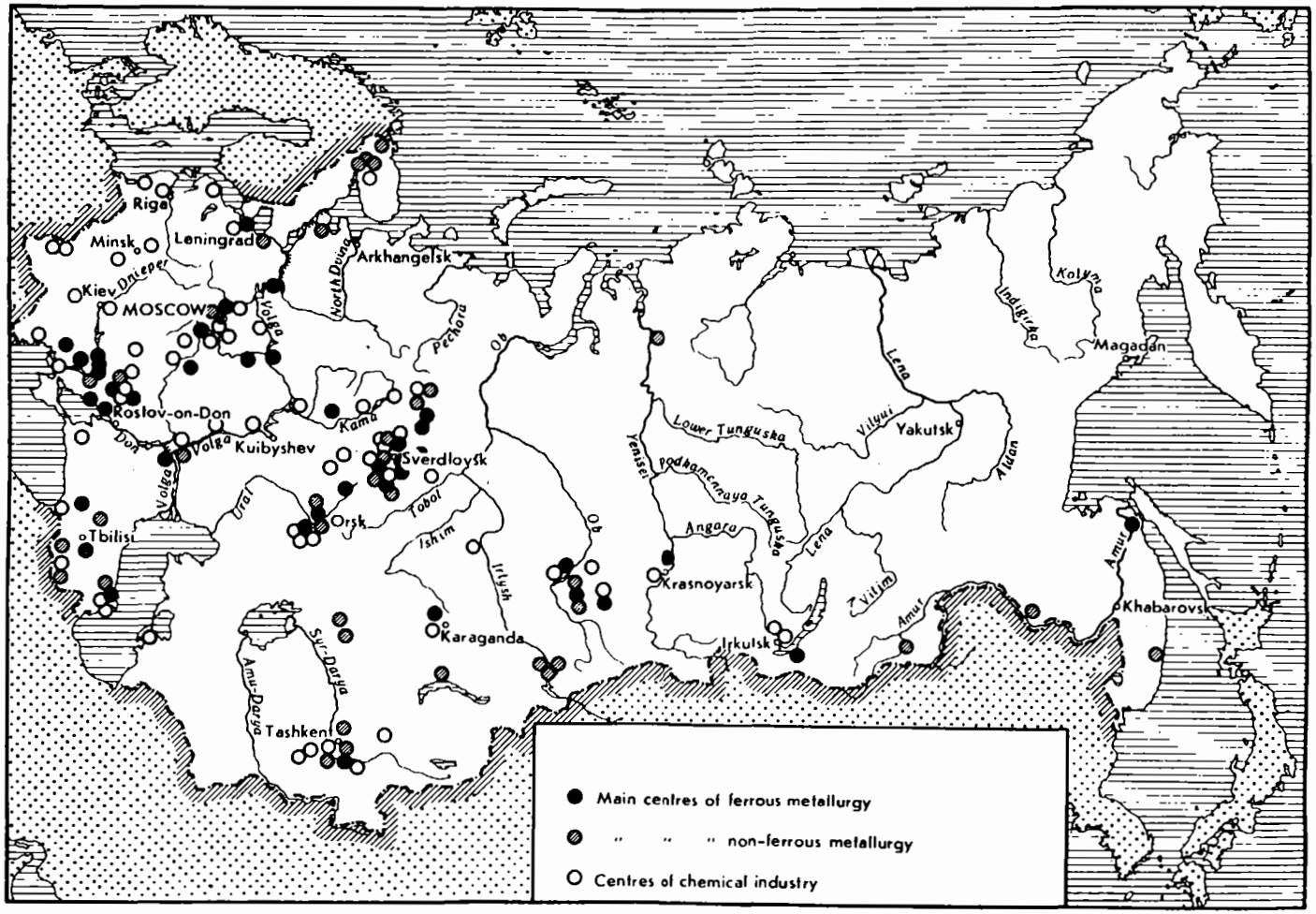
Large industrial systems are being created - Kustanai, Pavlodar-Ekibastuz, Achinsk-Krasnoyarsk, Bratsk-Taisnet and a number of others. Ferrous and non-ferrous metallurgy, pulp and paper, hydrolysis and saw-milling industries are being established in the Bratsk-Taishet industrial system. The Achinsk-Krasnoyarsk industrial system is becoming one of the largest centers of aluminum and chemical industries, and production of ferrous metals, cellulose, paper, and oil products.

Construction of the third metallurgical base has been launched in Siberia, and a new base of ferrous metallurgy, using the enormous local iron and coal resources, has been created in Kazakhstan. A high-capacity power system is being organized in the same areas. Non-ferrous metallurgy is being further developed in Kazakhstan, Central Asia and in Transbaikal areas. The pulp and paper, as well as the timber, industries are being developed at a fast rate in the forest areas of Siberia and the Far East.

Ferrous metallurgy is also developing in the European part of the country by utilizing the enormous iron ore resources of the Kursk Magnetic Anomaly and the Ukrainian deposits. Large new production systems are under construction in the North-West, along the Volga, in the Northern Caucasus and the Ukraine.

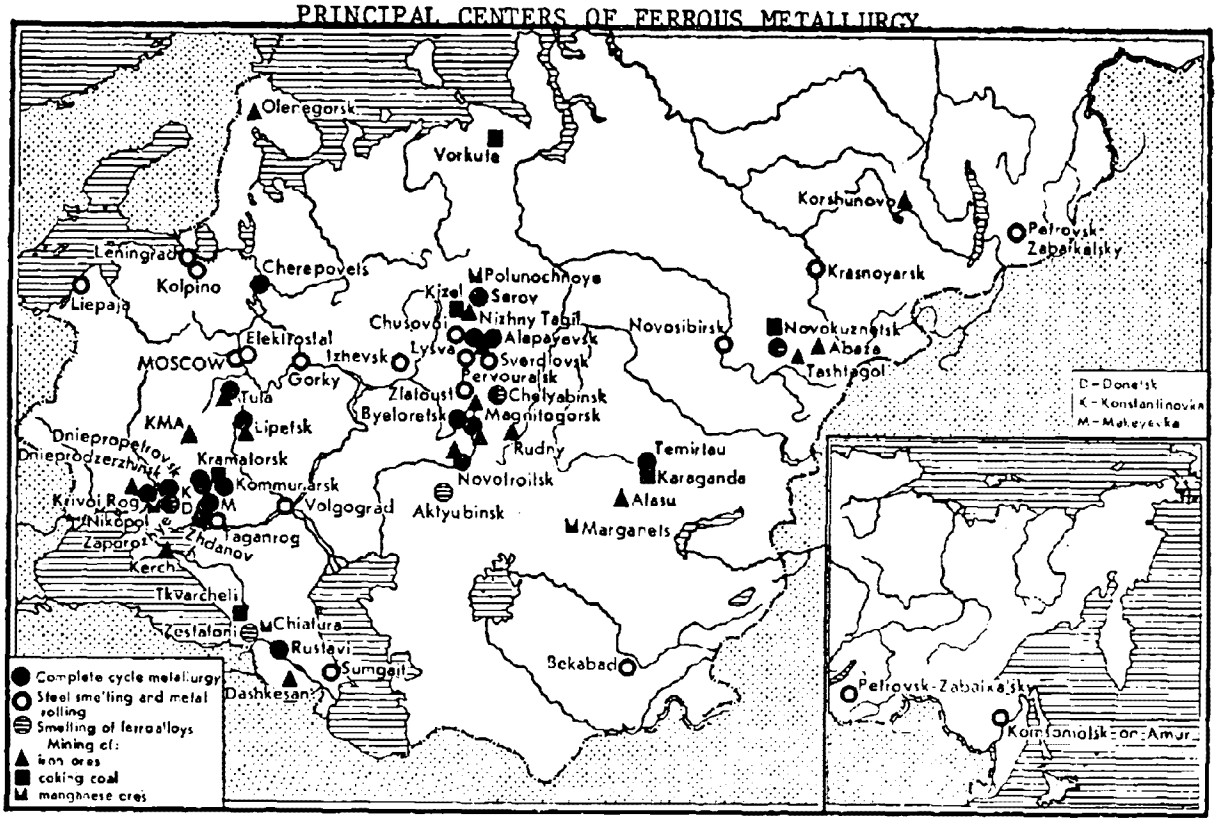
(After A. Lavrishchev, "Economic Geography of the U.S.S.R.", Moscow 1969)

THE MAJOR INDUSTRIAL CENTERS OF THE USSR

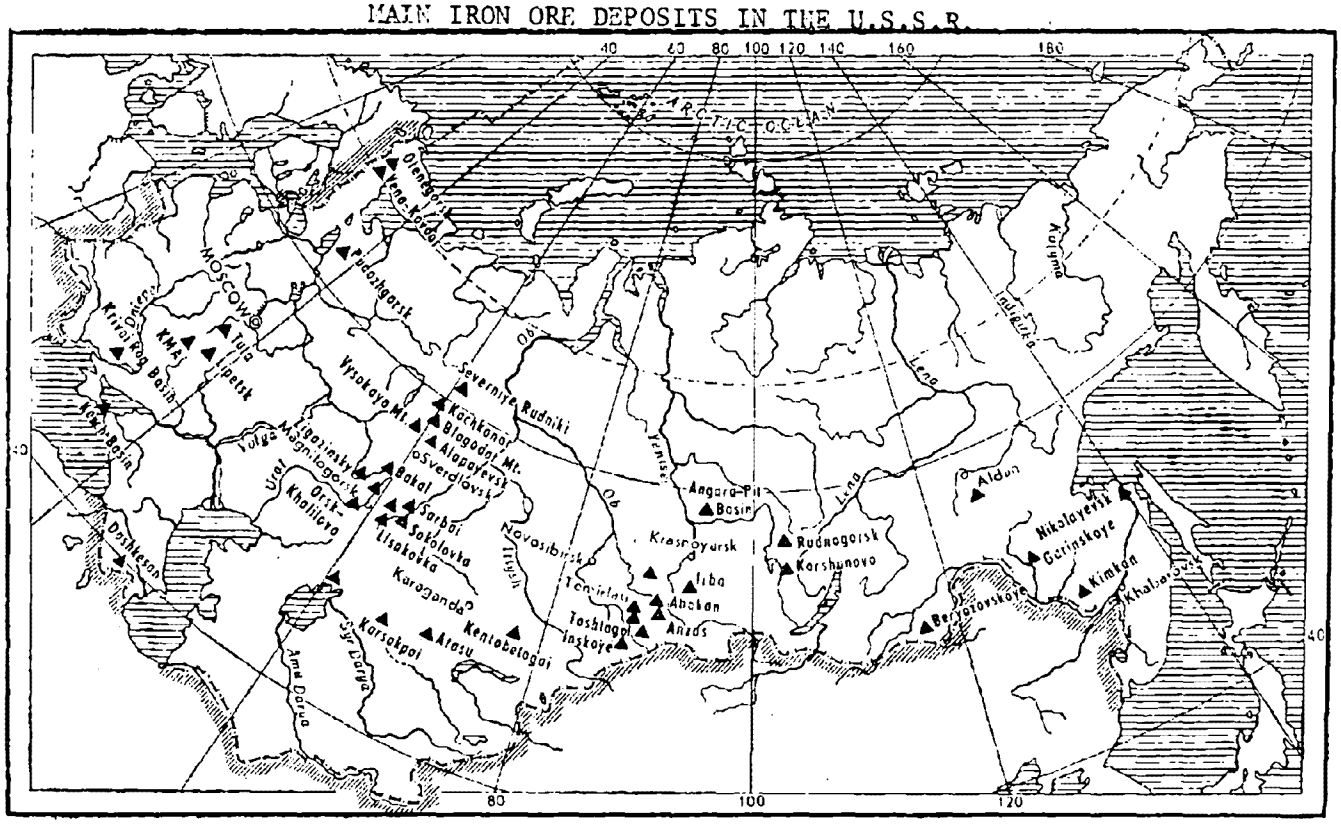


(After A. Efimov, "Soviet Industry", Moscow 1968)

PRINCIPAL CENTERS OF FERROUS METALLURGY

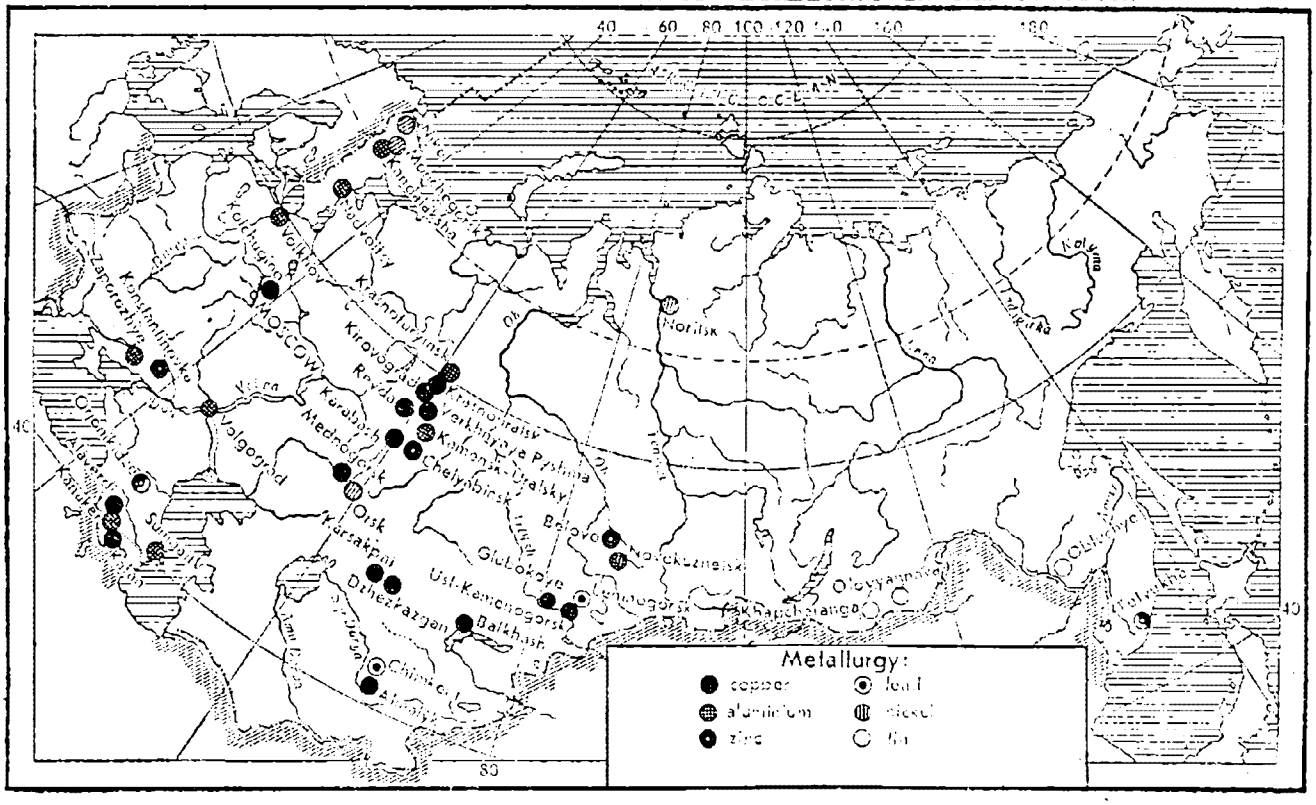


MAIN IRON ORE DEPOSITS IN THE U.S.S.R.

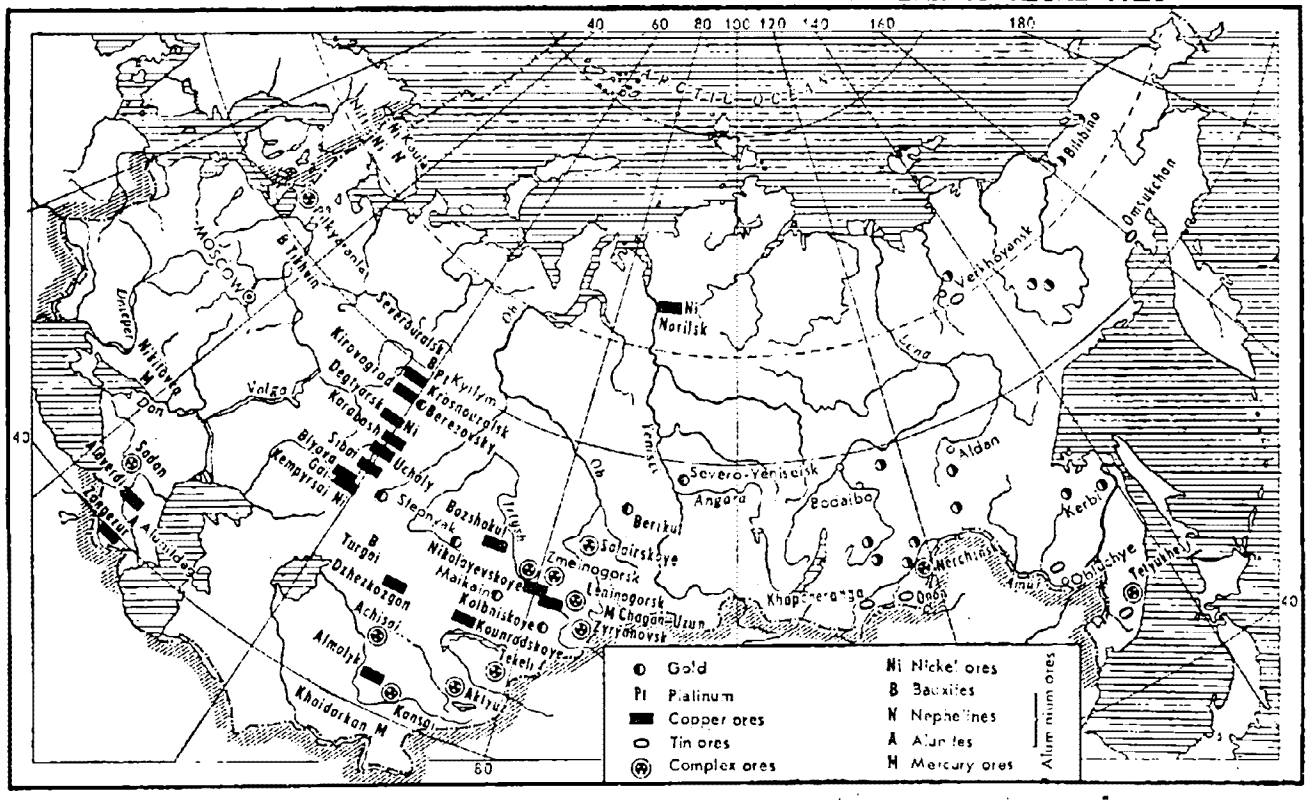


(After A. Lavrishchev, "Economic Geography of the U.S.S.R.", Moscow 1969)

PRINCIPAL CENTERS OF NON-FERROUS METALLURGY IN THE U.S.S.R.

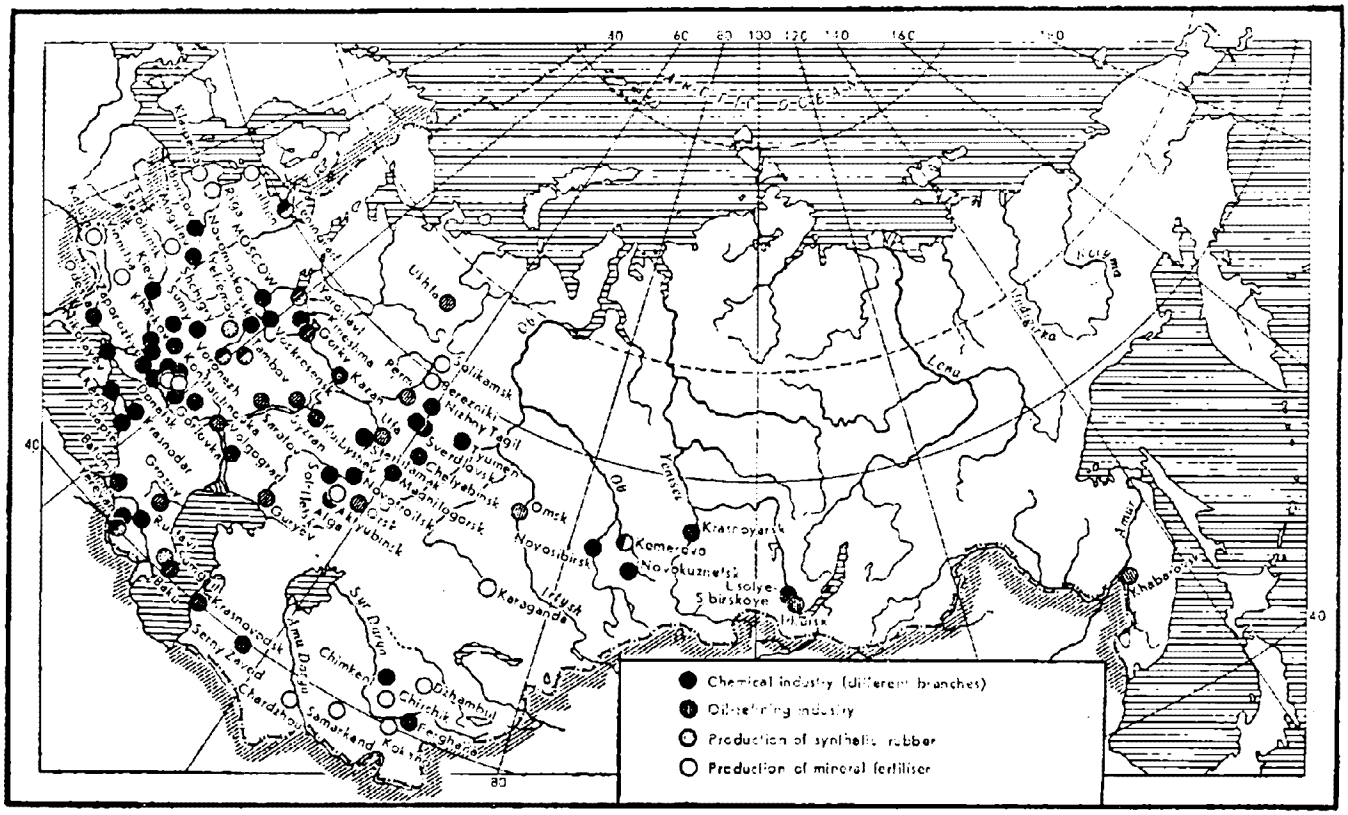


DISTRIBUTION OF MOST IMPORTANT DEPOSITS OF NON-FERROUS METAL ORES

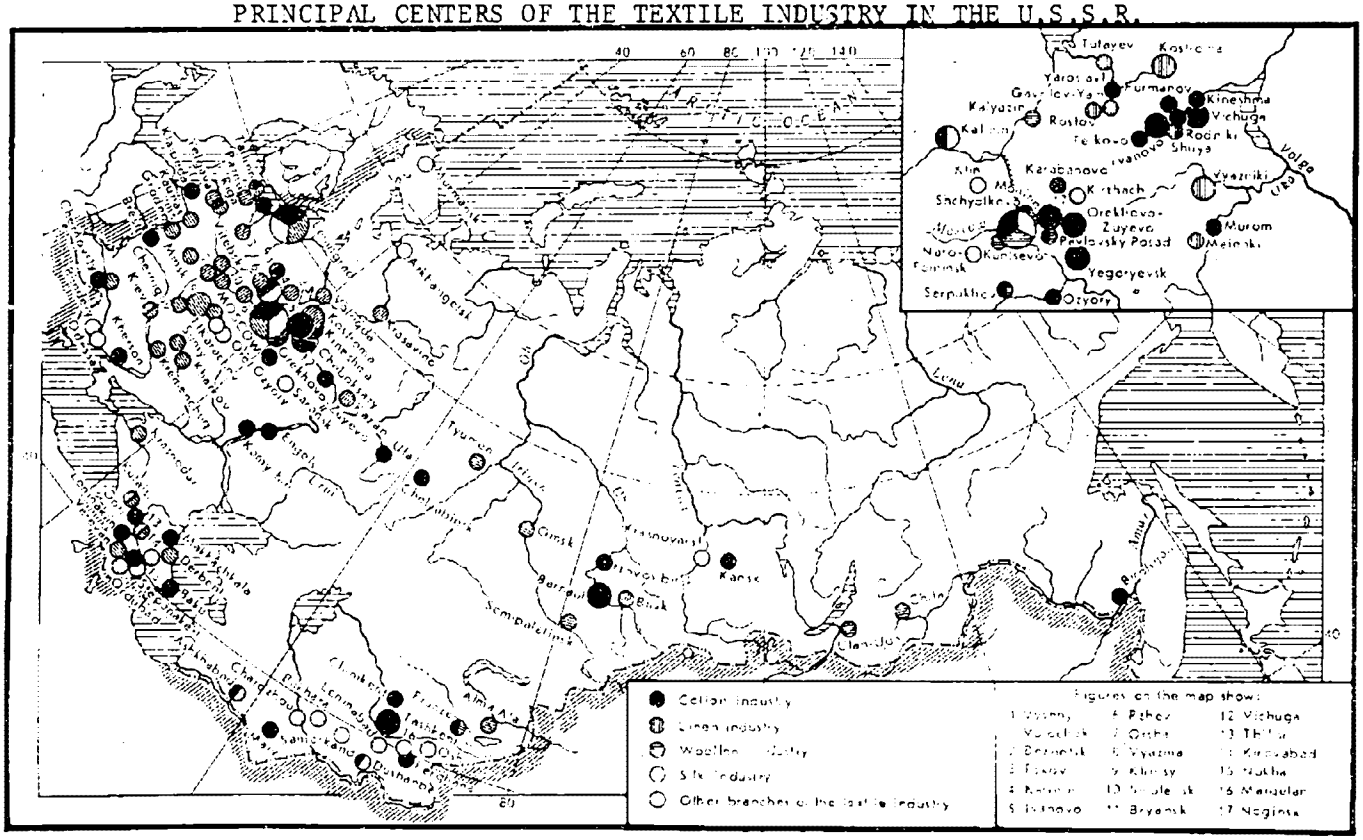


(After A. Lavrishchev, "Economic Geography of the U.S.S.R.", Moscow 1969)

PRINCIPAL CENTERS OF THE CHEMICAL INDUSTRY IN THE U.S.S.R.

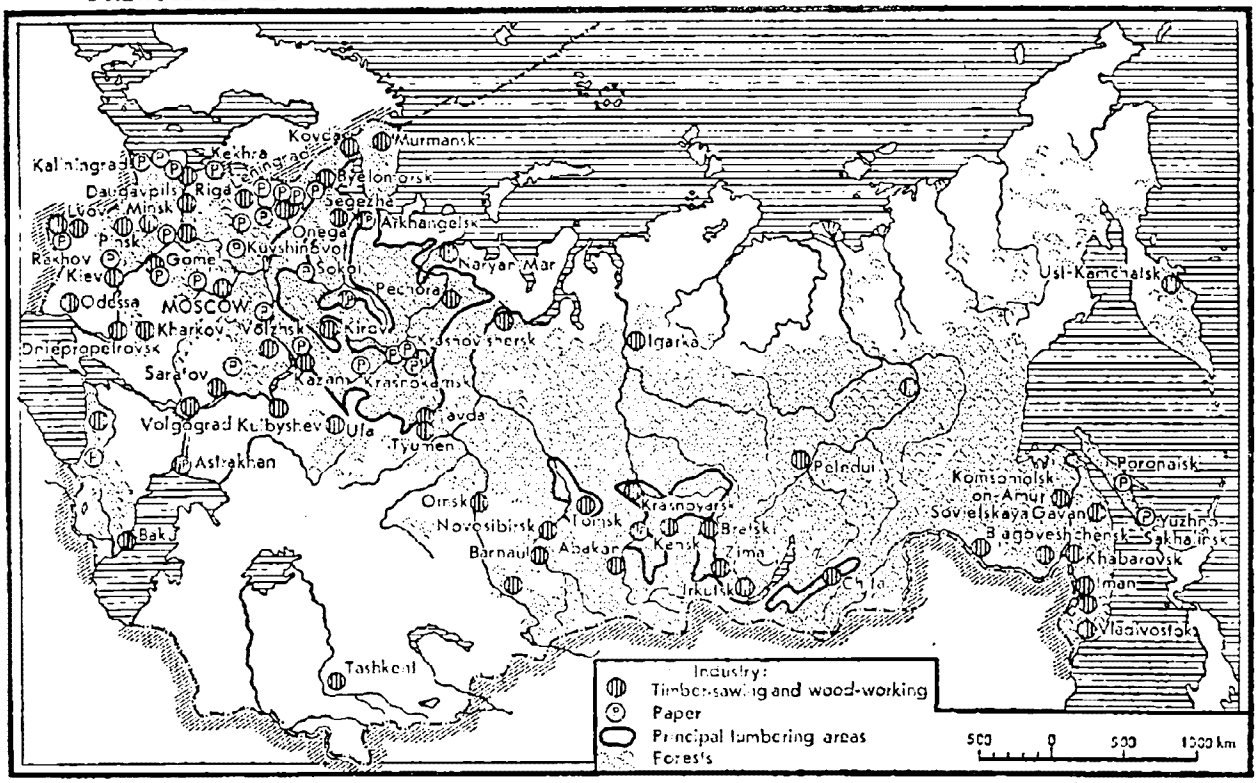


PRINCIPAL CENTERS OF THE TEXTILE INDUSTRY IN THE U.S.S.R.

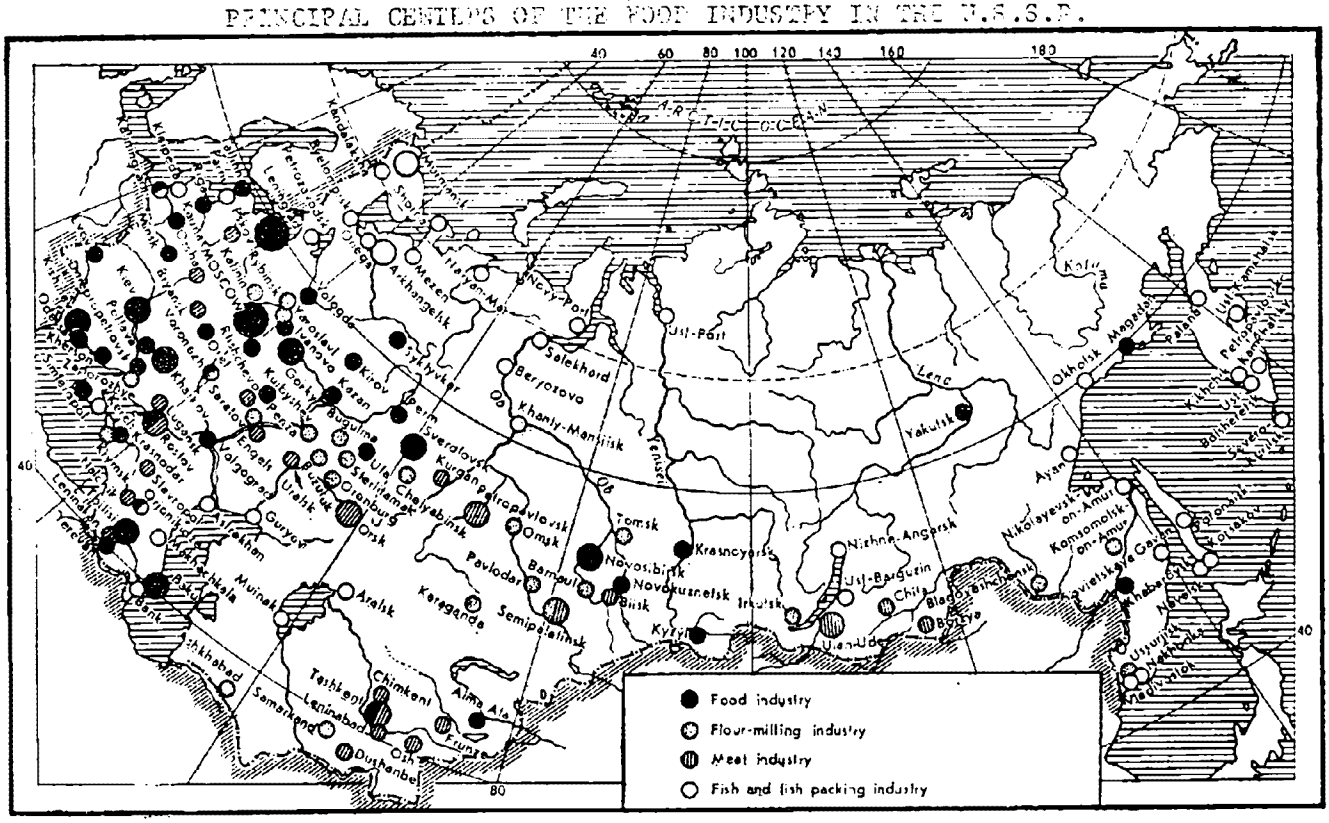


(After A. Lavrishchev, "Economic Geography of the U.S.S.R.", Moscow 1969)

PRINCIPAL CENTERS OF WOOD-WORKING AND PAPER INDUSTRIES IN THE U.S.S.R.

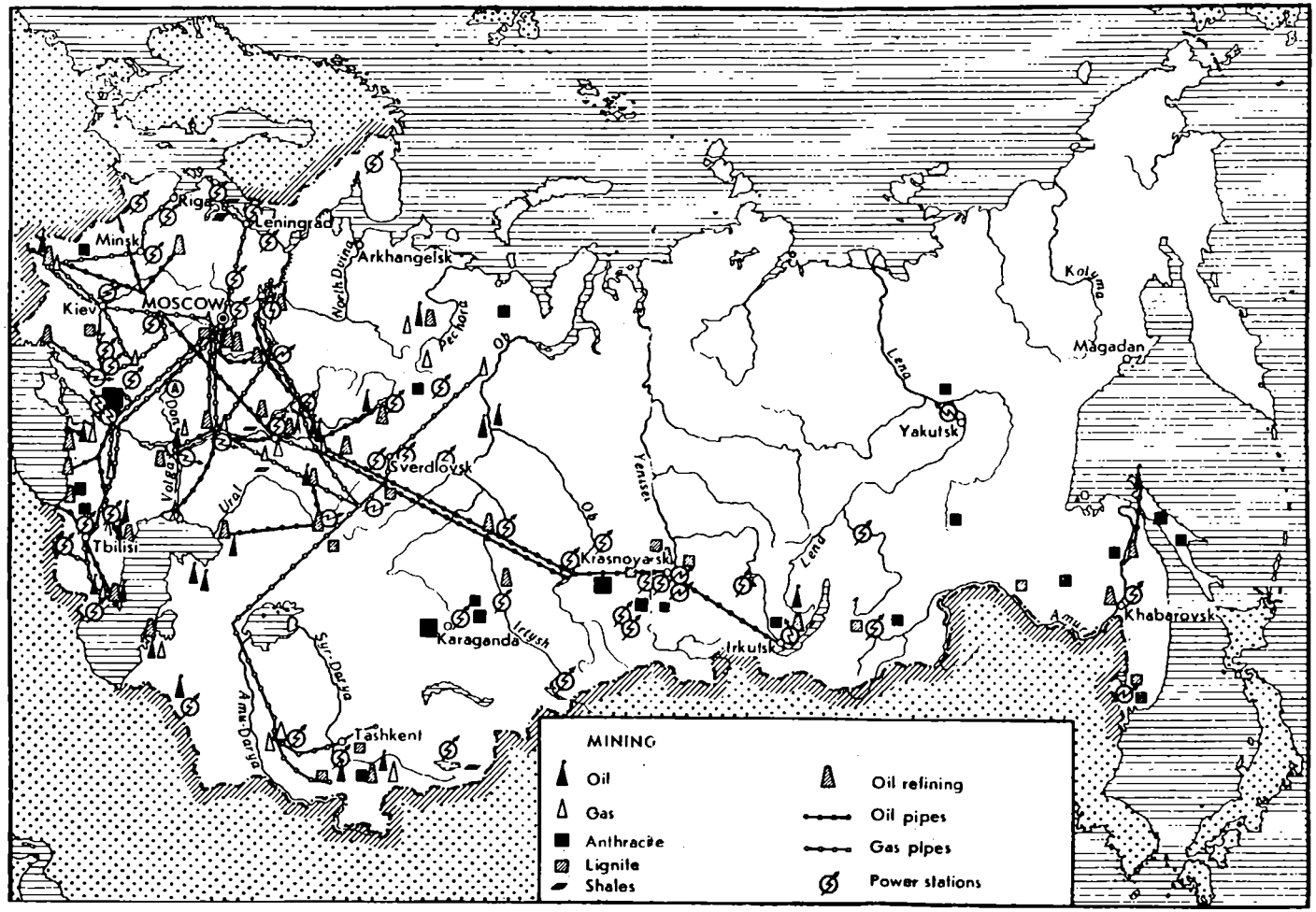


PRINCIPAL CENTERS OF THE FOOD INDUSTRY IN THE U.S.S.R.



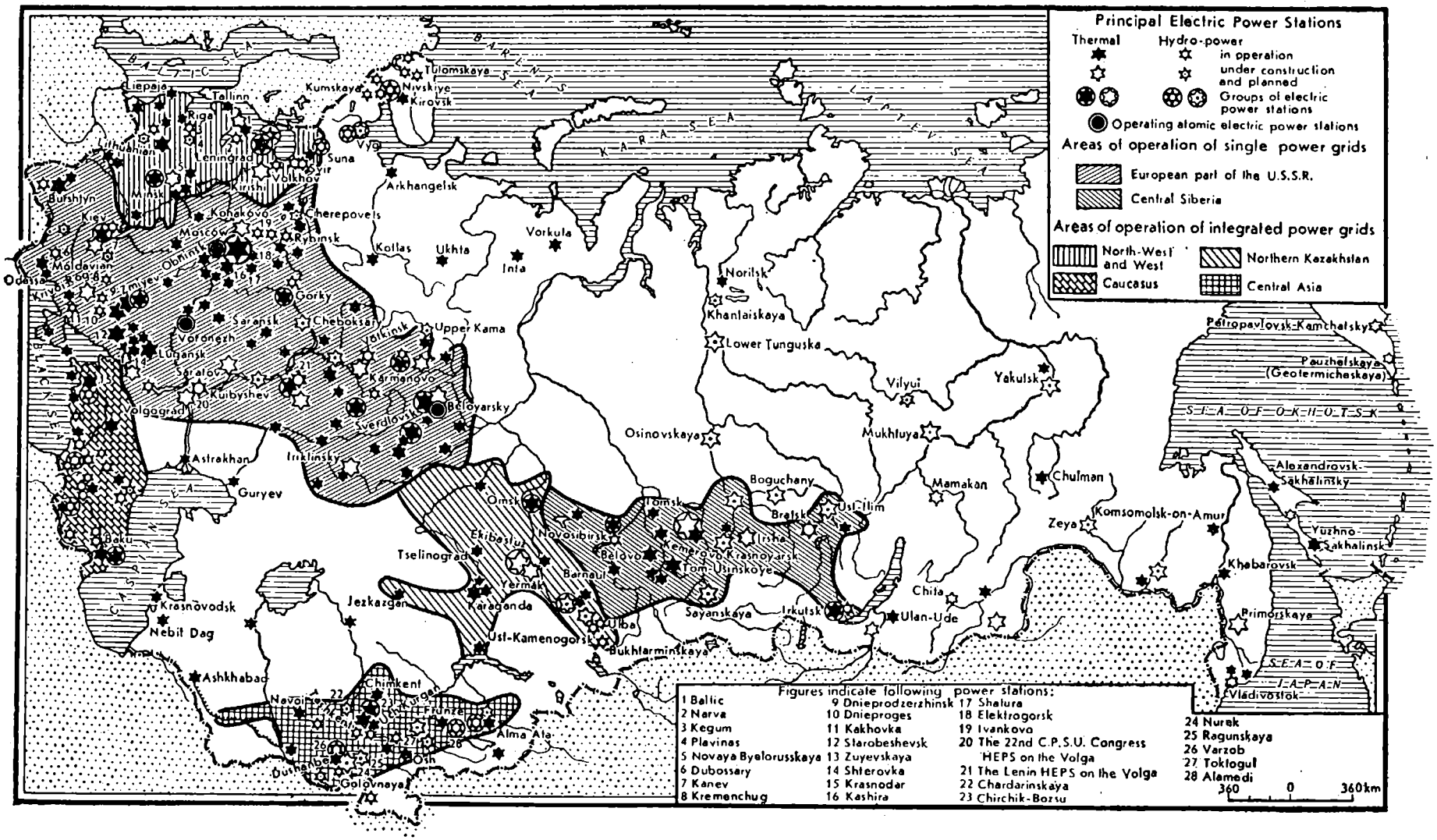
(After A. Lavrishchev, "Economic Geography of the U.S.S.R.", Moscow 1969)

THE MAIN MINING CENTERS OF THE USSR



(After A. Efimov, "Soviet Industry", Moscow 1968)

PRINCIPAL ELECTRIC POWER STATIONS AND POWER SYSTEMS IN THE U.S.S.R.



(After A. Lavrishchev, "Economic Geography of the U.S.S.R.", Moscow 1969)

MAXIMUM PERMISSIBLE CONCENTRATIONS OF NOXIOUS SUBSTANCES IN THE ATMOSPHERIC AIR OF POPULATED AREAS*

(V. A. Ryazanov)

From Akademiya Meditsinakikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 11, Izdatel'stvo "Meditsina" Moskva, p. 201-204, (1968).

Pollutant	Concentration, mg/m^3	
	Maximum single	Mean daily
1	2	3
1. Nitrogen dioxide	0.085	0,085
2. Nitric acid (based on HNO_3 molecule	0.4	0.4
(based on hydrogen ion)	0,006	0.006
3. Acrolein	0,30	0.10
4. Alpha-methylstyrene	0.04	0.04
5. Alpha-naphthoquinone	0.005	0.005
6. Amyl acetate	0.10	0,10
7. Amylene	1.5	1.5
8. Ammonia	0.20	0.20
9. Aniline	0,05	0.03
10. Acetaldehyde	0.01	—
11. Acetone	0,35	0.35
12. Acetophenone	0.003	0,003
13. Benzene	1.5	0.8
14. Gasoline (low-sulfur petroleum gasoline in terms of "C")	5,0	1,5
15. Shale gasoline (in terms of "C")	0,05	0,05
16. Butane	200.0	—
17. Butyl acetate	0.10	0.10
18. Butylene	3,0	3.0
19. Butyl alcohol	0.3	—
20. Butyl phosphate	0.01	—
21. Valeric acid	0.03	0,01
22. Vanadium pentoxide	—	0,002

* Approved by the Assistant Chief Public Health Physician of the USSR on 12 September 1967, No. 692-67.

1	2	3
23. Vinyl acetate	0.20	0.20
24. Hexamethylenediamine	0.001	0.001
25. Bivinyl	3.0	1.0
26. Diketene	0.007	—
27. Dimethylaniline	0.0055	—
28. Dimethyl sulfide	0.08	—
29. Dimethyl disulfide	0.7	—
30. Dimethylformamide	0.03	0.03
31. Dowtherm	0.01	0.01
32. Dichloroethane	3.0	1.0
33. 2,3-Dichloro-1,4-naphthoquinone	0.05	0.05
34. Diethylamine	0.05	0.05
35. Isopropylbenzene	0.014	0.014
36. Isopropylbenzene hydroperoxide	0.007	0.007
37. Caprolactam (vapors, aerosol)	0.06	0.06
38. Caproic acid	0.01	0.005
39. Malathion	0.015	—
40. Xylene	0.2	0.2
41. Maleic anhydride (vapors, aerosol)	0.2	0.05
42. Manganese and its compounds (in terms of MnO_2)	—	0.01
43. Butyric acid	0.015	0.01
44. Mesidine	0.003	—
45. Methanol	1.0	0.5
46. Metaphos	0.008	—
47. Metachlorophenyl isocyanate	0.005	0.005
48. Methyl acrylate	0.01	—
49. Methyl acetate	0.07	0.07
50. Methyl mercaptan	$9 \cdot 10^{-6}$	—
51. Methyl methracylate	0.1	0.1
52. Monomethylaniline	0.04	—
53. Arsenic (inorganic compounds other than arsine, in terms of AS)	—	0.003
54. Nitrobenzene	0.008	0.008
55. Parachloroaniline	0.04	—
56. Parachlorophenyl isocyanate	0.0015	0.0015
57. Pentane	100.0	25.0
58. Pyridine	0.08	0.08
59. Propylene	3.0	3.0
60. Propyl alcohol	0.3	—
61. Nontoxic dust	0.5	0.15
62. Metallic mercury	—	0.0003

1		2	3
63.	Soot (carbon black)	0.15	0.05
64.	Lead and its compounds (other than tetraethyl lead) in terms of Pb	——	0.0007
65.	Lead sulfide	——	0.0017
66.	Sulfuric acid (based on H_2SO_4 molecule)	0.3	0.3
	(based on hydrogen ion)	0.006	0.006
67.	Sulfur dioxide	0.5	0.05
68.	Hydrogen sulfide	0.008	0.008
69.	Carbon disulfide	0.03	0.01
70.	Hydrochloric acid (based on HCl molecule)	0.2	0.2
	(based on hydrogen ion)	0.006	0.006
71.	Styrene	0.003	0.003
72.	Thiophene	0.6	——
73.	Toluylene diisocyanate	0.05	0.02
74.	Toluene	0.6	0.6
75.	Trichloroethylene	4.0	1.0
76.	Carbon monoxide	3.0	1.0
77.	Acetic acid	0.2	——
78.	Acetic anhydride	0.1	——
79.	Phenol	0.01	0.01
80.	Formaldehyde	0.035	0.012
81.	Phosphoric anhydride	0.15	0.05
82.	Phthalic anhydride (vapors, aerosol)	0.10	
83.	Fluorine compounds (in terms F)		
	Gaseous compounds (HF, SiF_4)	0.02	0.005
	Soluble inorganic fluorides (NaF, Na_2SiF_6)	0.03	0.01
	Sparingly soluble inorganic fluorides (AlF_3, Na_3AlF_3, CaF_2)	0.2	0,03
	In the combined presence of gaseous fluorine and fluorine salts	0.03	0,01
84.	Furfural	0.05	0.05
85.	Chlorine	0.10	0,03
86.	Chlorobenzene	0.10	0.10
87.	Chloropropene	0.10	0.10
88.	Hexavalent chromium (in terms of CrO_3)	0.0015	0.0015
89.	Cyclohexanol	0.06	0.06
90.	Cyclohexanone	0.04	0.04
91.	Carbon tetrachloride	4.0	——
92.	Epichlorhydrin	0.2	0,2
93.	Ethanol	5.0	5.0
94.	Ethyl acetate	0.1	0.1

1	2	3
95. Ethylene	3.0	3.0
96. Ethylene oxide	0.3	0.03

REMARKS

1. In the combined presence in atmospheric air of several substances possessing a summation effect, the sum of their concentrations as calculated by the formula below (§ 2) should not exceed 1 for:

a) acetone and phenol
b) sulfur dioxide and phenol
c) sulfur dioxide and nitrogen dioxide
d) sulfur dioxide and hydrogen fluoride
e) sulfur dioxide and sulfuric acid aerosol
f) hydrogen sulfide and dowtherm
g) isopropylbenzene and isopropylbenzene hydroperoxide
h) furfural, methanol and ethanol
i) strong mineral acids (sulfuric, hydrochloric and nitric) in terms of the hydrogen ion concentration (H)
j) ethylene, propylene, butylene and amylene

should not exceed 1.3 for:

a) acetic acid and acetic anhydride

should not exceed 1.5 for:

a) acetone and acetophenone
b) benzene and acetophenone
c) phenol and acetophenone

2. Formula for the calculation:

$$X = \frac{a}{m_1} + \frac{b}{m_2} + \frac{c}{m_3} \ldots,$$

where X is the unknown total concentration:

$\frac{a}{m_1} + \frac{b}{m_2} + \frac{c}{m_3} -$ is the concentration of the substance being determined, divided by the corresponding maximum permissible concentration for isolated action.

3. In the combined presence in atmospheric air of:

a) hydrogen sulfide and carbon disulfide
b) carbon monoxide and sulfur dioxide
c) phthalic and maleic anhydrides and alpha-naphthoquinone, the maximum permissible concentrations for each of them individually are retained.

4. In the combined presence in atmospheric air of parachlorophenyl isocyanate and metachlorophenyl isocyanate, temporarily, until a method of their isolated determination is developed, the standardization should be made on the more toxic substance, i. e., parachlorophenyl isocyanate.

5. The maximum permissible concentrations of noxious substances in the atmospheric air of populated areas as formulated in December 1966 (No. 655-66), should be considered obsolete.

BASIC PROBLEMS OF SANITARY PROTECTION OF ATMOSPHERIC AIR

Prof. V. A. Ryazanov

From Akademiya Meditsinskikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 10, Izdatel'stvo "Meditsina" Moskva, p. 5-15. (1967).

The problem of atmospheric air pollution, which became very acute about 100 years ago, went through its major historic phase in the last century. At the present time, the state of the atmosphere has changed so much, and the sources of its pollution have become so complex, that the very problems that must be dealt with have become completely different and immeasurably more complex.

We cannot subscribe to the point of view of our foreign colleagues who consider the problem of purity of urban air with great pessimism and point to the inevitability of an increasing atmospheric pollution and the necessity for mankind to "get used to" or "adapt" to this "disease of civilization," since in their opinion nothing else can be done.

Many years of observations and reflection on this problem lead to the opposite conclusion. However, the striking changes which have occurred in this problem as a whole should be taken into consideration in order to arrive at a correct evaluation of the prospects and lines of its development.

Whereas the last century and the first half of the 20th century were typically characterized by atmospheric pollution caused by the use of mineral fuel in home heating stoves, fireplaces, chimneys, boilers, and electric power plants, and the chief components of this pollution - sulfur oxides, soot, and ash - were the most widely distributed and dangerous, this situation began to change in the middle of the 20th century. In many countries, particularly in the USSR, radical steps were initiated to eliminate the smoke pollution of the atmosphere: home heating stoves and small boilers were replaced by central heat supplied by heat and electric power plants, the process of coal combustion was improved so as to raise the efficiency of the furnaces and decrease the unburned component, ash collectors with a high degree of purification were constructed, the sulfur content of the fuel was restricted, and finally, the mineral fuel was replaced by natural gas at the major heat and electric power plants as well as in consumer use. In addition, technological and utility processes were electrified with substitution of smoking fuel by electric power. The problem of "smoke" properly speaking had been solved theoretically by the middle of the 20th century and also in practical applications in many cities of economically advanced countries.

There is no doubt that for young developing countries, no other means of solving the problem of "smoke" can be invented than the one that has been successful in economically more developed countries (introduction of a district heating system, installation of gas, electrification). We are skipping a number of secondary measures whose introduction plays an auxiliary part in the solution of this problem.

In addition to the fuel combustion process, other processes had a definite but more limited significance in air pollution. For example, the metallurgical industry contains major sources of polluted air, but their influence is confined to certain areas. Atmospheric air is frequently polluted in a given metallurgical district, but outside the limits of the latter pollution is absent. Dangerous concentrations of atmospheric pollution were produced by nonferrous metallurgical plants. When toward the end of the 19th century the oxide deposits were exhausted, the industry had to switch to poor polysulfide ores. This led to a very heavy pollution of atmospheric air with sulfur dioxide, causing the destruction of green vegetation extending many miles outward from the nonferrous metallurgical plants. Polysulfide ores produced a dust of very complex composition: it included numerous metallurgical compounds, many of which had a high toxicity. The pyrometallurgical process involved the conversion of all these extraneous metallic elements into fumes, which in turn increased the dispersity and hence the danger of the dust, and the oxidation of these elements with the formation of oxides was usually accompanied by an increase in their toxicity.

The development of metallurgy of light metals (aluminum, magnesium, beryllium) was associated with the emission of specific pollutants such as fluoride compounds, which resulted in the appearance of fluorosis among the juvenile population, and with the formation of tars containing enormous amounts of 3,4-benzpyrene and beryllium, which produced an extremely dangerous disease, berylliosis, among the surrounding population.

However, all these grave calamities suffered by the population as a result of the development of the metallurgical industry continued to remain a local phenomenon of regional importance, whereas the smoke produced by the combustion of fuel constituted a national calamity.

It is completely understandable, therefore, that although the solution to the control of smoke is still largely theoretical, it is nevertheless of major and fundamental importance.

In a scientific-theoretical sense, the enterprises of the metallurgical industry as sources of atmospheric pollution also constitute a practical area that is slowly yielding to the pressure of science. Theoretically, this problem has been largely solved. The solution found in this case consists in the complex utilization of the raw material. Instead of the emission into the atmosphere of enormous amounts of sulfur dioxide formed in the course of smelt-

ing of metals, these concentrated gases, completely suitable for production of sulfuric acid, should be regarded as the raw material for sulfuric acid plants, which should be built with nonferrous metallurgy as their base. Instead of using polymetallic ore, the latter should first be subjected to a fine selective separation by flotation, and each fraction should be sintered and melted in separate metallurgical furnaces. The dust residue should be trapped in modern cloth and fiberglass filters. A metallurgical center should consist of a complex of plants or shops producing dozens of different products and utilizing without residue everything of value contained in the ore.

Moreover, it should be noted that nonferrous metallurgy now has a powerful competitor in the form of plastics, which are rapidly displacing nonferrous metallurgical products from the consumer market because of their low cost, ease of fabrication, strength, anticorrosive properties, and a number of other qualities which make plastics irreplaceable, even though many of them are initially made as substitutes. The age of nonferrous metals is being superseded before our eyes by the age of plastics, to which the future belongs.

By the end of the first half of the 20th century, in addition to the fumes resulting from fuel combustion, an increasingly important role in the smoke pollution of urban atmospheric air had begun to be assumed by the exhaust gases of motor vehicles. For example in the U.S.A., during the period from 1920 to 1950, i.e., in only 30 years, the number of automobiles increased fivefold, from 10 to more than 50 million. Motor transport is one of the sources of urban pollution of atmospheric air with various noxious and offensive fumes, carbon monoxide, hydrocarbons, aldehydes, and tar compounds, including carcinogens, products of decomposition of antiknock agents containing a finely divided smoke of lead oxides, etc. However, the middle of the 20th century is best characterized by the appearance of the photochemical fog, an entirely new factor in man's environment.

The photochemical fog, which was incorrectly named "smog", was first noticed in Los Angeles in 1940. By 1945, the Los Angeles smog had become a serious problem.

A characteristic feature of the photochemical fog is its formation as a result of photochemical reactions taking place in the open air in the presence of sunlight. These photochemical reactions involve organic substances emitted with the exhaust gases of automobile engines. The most important role in these processes is thought to be played by olefins, particularly pentene and hexene. An important part is also attributed to nitrogen oxides, emitted from the exhaust pipes of engines. A ring reaction takes place with the formation of ozone. In the presence of light and hydrocarbons, nitrogen dioxide is reconverted into nitric oxide, and the reaction proceeds as long as sunlight is present. Ozone in turn reacts with the olefins.

As a result of complex and diverse reactions resulting in the formation of free radicals, ozonides, and various peroxides, a variety of organic substances

are formed in the atmosphere which differ considerably in chemical activity. Irritation of the mucous membranes of the eye associated with lachrymation, damage to vegetation, corrosion of rubber products, and a decrease of visibility are observed. The main complaints of the population concern the lachrymating effect of the photochemical fog. Prolonged efforts to determine precisely what specific compound is responsible for the phenomenon of the photochemical fog have been unsuccessful thus far. It is possible that each of its effects is due to a different chemical agent. A new compound named peroxyacetyl nitrate has been successfully extracted from atmospheric air. It displays the same effects as the photochemical fog, but has not yet been proven to be the active agent of the Los Angeles smog. In any event, it has now been established that the photochemical fog is formed as a result of pollution of atmospheric air with exhaust gases in the presence of sufficient insolation and temperature inversion.

The appearance of the photochemical fog in Los Angeles for the first time was attributed to the presence of specific conditions: the lack of public urban transportation and the consequent excessive saturation of the city with private automobiles whose number is measured in the millions, the tendency of this entire region toward anticyclonic weather, and the abundance and constancy of solar radiation. Wherever such conditions exist, such adverse consequences are possible in various degrees. In the last few years, in addition to Los Angeles, the photochemical fog has begun to appear in many other cities of the U.S.A., including San Francisco, Washington, New York, etc. The areas covered by the photochemical fog expand each year, and the number of cities affected by it is growing. The photochemical fog is becoming the most "modern" disease of American cities.

It would be difficult to assume that the harmful influence of the photochemical fog is limited solely to the lachrymating effect, although the latter alone is enough to make life miserable for the entire population (in Los Angeles, a fog of this type is observed for up to 100 days per year). This is most probably associated with chronic illnesses that thus far have not been successfully identified.

The expanding use of automobiles throughout the world is causing the adverse effects of exhaust gases to increase steadily; phenomena analogous to the photochemical fog may also arise in other countries. In any case, the time has come to tackle this problem in the Soviet Union as well.

The A. N. Sysin Institute of General and Communal Hygiene of the USSR Academy of Medical Sciences has begun some exploratory studies along these lines. The chemist V. A. Popov has adopted the pheolphthalein method used in the United States for determining the so-called oxidants in atmospheric air. Tentative studies in Moscow, Baku and Batumi have shown that in the summertime, i.e., in the presence of sunlight, oxidants, which are products of photochemical conversions of exhaust gases, may be detected in the air of these cities.

Although their concentrations are very slight (approximately eight times lower than in American cities), they nevertheless approach the limit permissible by the California standard. As the number of automobiles grows, the concentrations of oxidants will rise, and if no decisive steps are taken to reduce the emission of exhaust gases, it will be impossible to avoid the appearance of the disease of American cities in the Soviet Union as well.

The universal presence of motor transport and its volume, the steady growth of the number of automobiles, emission of noxious substances in the zone where people breathe, ability of the components of these gases to undergo various photochemical conversions with the participation of highly reactive free radicals - all of these factors make the pollution of atmospheric air with automobile emissions the most threatening factor from the standpoint of modern sanitation. It is also necessary to consider that the exhaust gases contain many other ingredients such as aerosols of lead compounds, carbon monoxide, and carcinogens.

It may be stated therefore that at the present stage, the urgency of this problem has supplanted the importance earlier justifiably accorded by hygienists throughout the world to the combustion products of mineral fuel. This problem should become one of the first priorities in our scientific and environmental efforts.

However, the means of solving this problem do exist. Suffice it to mention the coordination of intracity transportation, checking of the operating condition of cars, the removal of transit transport beyond the city limits, conversion of automobile engines to liquefied gas operation, etc. The main objective is of course the conversion of automobile transportation to electric power. Scientific research efforts should be concentrated primarily in this direction. Our country, which is building interstellar spacecraft, is certainly capable of constructing electric cars, that meet all the requirements of economy, comfort, convenience of use, and hygienic safety.

We shall not stop to discuss the problem of radioactive contamination of atmospheric air, first because this is an entirely specialized problem, and secondly because the road to the solution of the problem of protection of atmospheric air from radioactive contaminants is a matter of international policy, not medicine.

However, it is indispensable to consider that aspect of the problem which is connected with the development of industrial chemistry, a most acute and topical problem of the modern era.

The role of chemistry in the acceleration of the building of Communist society is very prominent. The 23rd Congress of the Communist Party of the Soviet Union set forth high rates of development of the chemical and petrochemical industries. Chemistry and its products widely permeate all aspects

of production and living conditions of the population. The production of raw materials, semifinished products and finished articles from synthetic materials will become on of the most common, complex, and largest sources of pollution of the envirnoment and particularly atmospheric air, and will present the danger of a harmful effect on man if hygienists, chemists, and engineers do not study these compounds from the standpoint of their nature, biological characteristics, and danger for man, and do not learn to determine them (which will require specific and high sensitive methods of investigation) and to prevent their presence in atmospheric air in concentrations adverse to man.

Interest in the pollution of the environment with chemical substances has been increased throughout the world. In March 1963, the world Health Organization convened in Geneva a special international symposium on michrochemical pollutants of the envirnoment. According to the data of this symposium, hundreds of new organic compounds are being synthesized every year throughout the world. Many of them find practical applications and constitute a source of environmental pollution. The mere enumeration of the various areas of application of new chemical compounds would require considerable space. They include various fertilizers, pesticides, defoliants, plastic articles used in machine building, in housing, and in municipal services, new fabrics for clothing, shoes, objects for everyday use, packaging, effective washing agents, detergents, bonding materials, synthetic drugs, vitamins, antioxidants for fats, liquid fuel additives, etc.

The acuteness of the situation is made worse by the fact that the majority of these organic compounds have not been studied from the toxicological and physiological points of view, and no methods have been developed for their determination in complex mixtures and low concentrations.

The possibility of their combined action, transformation in the environment, and the lack of their study from the standpoint of hygienic, carcinogenic, and teratogenic effects compound the situation considerably. Moreover, the planners require data on the harmlessness of the new substances, which will come in contact with the workers and engineers in the course of production, with the population around the plants, and with millions of consumers utilizing the products of industrial chemistry in all parts of the country.

For this reason, chemistry should now be at the center of attention of public health science and in particular, atmospheric sanitation. The objectives are large and, therefore, sometimes appear unreachable. However, this spurious appearance should be resolutely rebuffed. It is necessary to mobilize all the available resources, plan the sequence of the work closely, and allocate the efforts appropriately.

It is perfectly obvious, for example, that additional resources should be directed primarily at reinforcing scientific groups that have already formed and proven themselves. Where qualified personnel, modern equipment and an experimental base already exist, it is easier to achieve a marked increase in the yield of practical research than in cases where all of this must be created from scratch. It is therefore necessary to give support as rapidly

as possible to scientific centers that are already doing work in the areas of toxicology and chemistry, and in the area of new synthetic compounds and pollutants of the environment, including atmospheric air, associated with their production.

Problems subject to investigation should be planned in a more serious and active manner. Accelerated research methods should be adopted, with priority given to those research areas that are absolutely indispensable for the formulation of practical conclusions; studies that are less urgent and merely confirm the conclusions reached should be postponed.

The work of graduate students should be switched broadly to problems of industrial chemistry, particularly synthetic chemistry. Priority and even express handling should be accorded to the publication of materials dealing with research in the area of industrial chemistry.

Atmospheric pollutants associated with the development of industrial chemistry have a number of characteristics which permit one to formulate the trend and prospects of measures aimed at preventing their harmful action and the ways of eliminating them.

For the most part, these are organic compounds characterized by a considerable volatility, a distinct odor, and an irritant action on the mucous membranes, particularly those of the upper respiratory tract. They can be neutralized in the following ways.

1. Method of combustion in special furnaces. Unfortuantely, their combustion sometimes requires the consumption of fuel because of the low concentration of pollutants and an insufficient heat of combustion. A drawback of this method is the destruction of valuable organic compounds instead of their recovery and utilization in the national economy. However, in cases where no other means of neutralization of these compounds exist, the combustion method remains available.
2. Compounds of this type usually condense readily, and hence, are capable of being separated by means of units producing low temperatures. Once the bulk of a compound has been separated by the condensation method, the remaining amounts, which are no longer of any value, can be subjected to combustion.
3. Compounds of this type undergo purification by means of sorption fairly readily, this being followed by desorption of the products obtained and regeneration of the filters. This is the chief method of recovery, and should be widely employed in practice as one of the most universal means of controlling the emissions of organic compounds.

The combination of these three methods makes it possible to find a satisfactory solution to the most diverse emissions of synthetic chemistry.

In the case of substances marked by a low threhold of action, it is necessary to find ways of eliminating them from the chemical process, with substitution of less toxic compounds or the introduction of a technology based on fundamentally different methods not requiring the use of toxic substances.

Thus, for example, the high-temperature heat carrier Dowtherm, widely employed in synthetic chemistry and creating large zones of atmospheric pollution around synthetic fiber plants, can be replaced by electric heating. The development of this progressive method should be given considerably more attention in the plans of the technological institutes concerned.

By comining the various enumerated trends in the prophylaxis of atmospheric pollutants consisting of emissions of synthetic chemistry (altering the chemical process, replacing noxious reactants by harmless ones, recovery, combustion of residual effluent, etc.), one can always find the necessary means of neutralizing industrial emissions. However, this requires two conditions:

1. Hygienists and toxicologists should become involved in the work of scientific technological institutes dealing with the development of technological schemes for new branches of industry.
2. Studies on the biological and toxicological effects of new chemical compounds being placed in production, with the establishment of their maximum permissible concentrations and with the development of specific and highly sensitive methods of their determination, should be intensified and accelerated as much as possible.

As is evident from the above, the problem of atmospheric pollution has become considerably more complex and difficult during its one-hundred-year history. New problems have arisen which have gradually superseded the routine considerations that used to prevail in this area during the first half of the 20th century.

Industrial chemistry and the struggle with automobile exhausts have become the primary concern. In order to supply answers to the vital practical questions, the priority of research in the area of industrial chemistry, must be ensured.

LITERATURE CITED

Note: References mentioned in this paper are to be found at the end of the volume in the 1967 bibliography.

COMBINED EFFECT OF HYDROGEN FLUORIDE AND SULFUR DIOXIDE ON THE BODY OF MAN AND ANIMALS

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From Akademiya Meditsinakikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 11, Izdatel'stvo "Meditsina" Moskva, p. 32-43, (1968).

For quite some time, we have studied the pollution of the environment by discharges of a large superphosphate plant producing superphosphate, sulfuric acid (by the Mills-Packard process), and as a by-product, ammonium fluoride.

The numerous studies have demonstrated that the superphosphate plant constitutes a major source of pollution of atmospheric air with sulfur dioxide, sulfuric acid aerosol, nitrogen oxides, and fluorine compounds whose concentrations at a distance of 2000 m from the plant exceed the maximum permissible levels. The main ingredients of the discharges of the superphosphate plant are hydrogen fluoride and sulfur dioxide.

Our purpose was to study the combined action of low concentrations of hydrogen fluoride and sulfur dioxide and to obtain data for substantiating the maximum permissible concentrations of these substances when they are jointly present in atmospheric air.

The isolated action of sulfur dioxide as well as hydrogen fluoride has been adequately studied thus far, and the maximum permissible concentrations of each of them in atmospheric air have been established and approved. In order to substantiate the highest permissible single concentration of a combination of these two substances, we determined the thresholds of olfactory perception and reflex effect of sulfur dioxide and hydrogen fluoride on the light sensitivity of the visual system.

F. I. Dubrovskaya established the olfactory threshold of sulfur dioxide for the most sensitive persons at the level of 1.6-2 mg/m^3. According to the data of M. S. Sadilova, this threshold for hydrogen fluoride is at a level of 0.11-0.03 mg/m^3. The determination of the threshold of smell of the gaseous mixture was preceded by a separate verification of the thresholds of olfactory perception of sulfur dioxide and hydrogen fluoride.

The observations were made on 17 persons. The threshold of smell of sulfur dioxide for the most sensitive persons (eight people) was established

at a level of 1.6 mg/m^3; the concentration of 1.3 mg/m^3 was imperceptible. The threshold of smell for hydrogen fluoride for the most sensitive persons (six people) was established at a level of 0.04 mg/m^3, the maximum imperceptible concentration being 0.02 mg/m^3. Thus, the results of our studies are close to the data of F. I. Dubrovskaya and M. S. Sadilova. Data on the determination of the odor threshold for mixtures of the concentrations of sulfur dioxide and hydrogen fluoride studied are listed in Table 1.

Table 1

Determination of the Odor Threshold of Hydrogen Fluoride-Sulfur Dioxide Mixtures

Concentration in mg/m^3		Fractions of Threshold During Isolated Action		Sum of Fractions of Threshold for Isolated Action	Number of Persons	
Hydrogen Fluoride	Sulfur Dioxide	Hydrogen Fluoride	Sulfur Dioxide		Perceiving the odor	Failing to perceive the odor
0,04	1,6	$\frac{0,04}{0,04}=1$	$\frac{1,6}{1,6}=1$	2	17	—
0,03	1,2	$\frac{0,03}{0,04}=0,75$	$\frac{0,2}{1,6}=0,70$	1,45	17	—
0,02	0,8	$\frac{0,02}{0,04}=0,5$	$\frac{0,8}{1,6}=0,5$	1	12	5
0,01	0,65	$\frac{0,01}{0,04}=0,25$	$\frac{0,65}{1,6}=0,4$	0,65	—	17

It is apparent from Table 1 that the minimum perceptible concentrations in the mixture are 0.02 mg/m^3 hydrogen fluoride and 0.8 mg/m^3 sulfur dioxide for a sum of relative concentrations equal to 1. The odor of the mixture is not perceived if the sum of the relative concentrations is less than 1.

The results obtained suggest that a complete summation of the action of hydrogen fluoride and sulfur dioxide is noted in this case.

We studied the reflex effect of small hydrogen fluoride and sulfur dioxide concentrations on the functional state of the central nervous system by determining the light sensitivity of the eye under dark adaptation conditions.

F. I. Dubrovskaya (1957) established that sulfur dioxide in a concentration of 0.6 mg/m^3 causes threshold changes (an increase) in the light sensitivity of the eye. For hydrogen fluoride (according to the data of M. S. Sadilova, 1965), the concentration having a threshold effect on the course of the dark adaptation curve is 0.03 mg/m^3, while 0.02 mg/m^3 is inactive.

Our observations were made on four persons 26-38 years old, most sensitive to the threshold of smell, with a normal visual acuity.

A procedure recommended by V. A. Ryazanov, K. A. Bushtuyeva and Yu. V. Novikov (1957) was employed.

To measure the light sensitivity of the eye, we used an "ADM" adaptometer. The hydrogen fluoride-sulfur dioxide mixture was supplied in the 15th minute of dark adaptation for 5 minutes. The light sensitivity of the eye was determined every 5 minutes up to the 30th minute and in the 40th minute. The tests were made three times with each concentration.

We carried out observations with the following concentrations: sulfur dioxide 0.3 mg/m^3, hydrogen fluoride 0.015 mg/m^3, sulfur dioxide + hydrogen fluoride in concentrations of 0.25 + 0.01 mg/m^3, and sulfur dioxide + hydrogen fluoride in concentrations of 0.3 + 0.015 mg/m^3.

In all four subjects, the concentrations of sulfur dioxide (0.3 mg/m^3) and hydrogen fluoride (0.015 mg/m^3) and also the sum of sulfur dioxide and hydrogen fluoride (0.25 + 0.01 mg/m^3) did not cause any changes in the light sensitivity of the eye.

During inhalation of sulfur dioxide with hydrogen fluoride in concentrations of 0.3 + 0.015 mg/m^3, the light sensitivity of the eye in the 20th and 25th minutes increased considerably when compared with the normal sensitivity in three subjects (Fig. 1) and in the 20th minute in one subject.

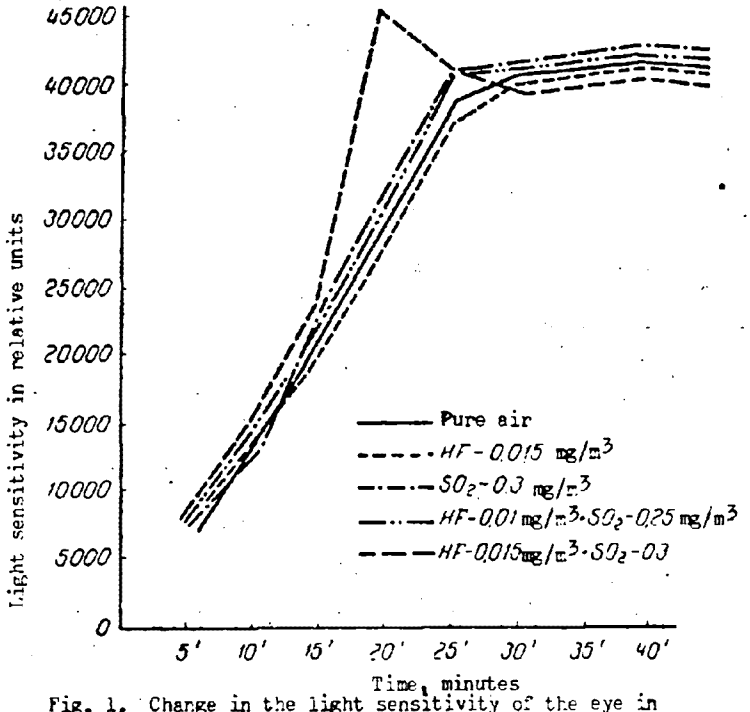

Fig. 1. Change in the light sensitivity of the eye in subject L.

Statistical treatment of the data obtained showed that the apparent changes of the light sensitivity of the eye were significant. Thus, the threshold of the reflex effect of the sulfur dioxide - hydrogen fluoride mixture on the light sensitivity of the eye was $0.3 + 0.015$ mg/m^3. The fractions obtained by dividing the concentrations studied into threshold concentrations during isolated action add up to 0.74 for the first mixture and to 1 for the second mixture. The only active mixture was the second one, whose inhalation caused first an increase and then a decrease in the light sensitivity of the eye. A mixture of sulfur dioxide and hydrogen fluoride of lower concentrations with a sum of the parts of threshold concentrations equal to 0.74 was found to be inactive for all the subjects. In this case, there is a total summation of the effects of each substance.

In order to detect the resorptive effect of low concentrations of hydrogen fluoride and sulfur dioxide in a mixture, we subjected 90 white male rats weighing from 80 to 95 g to chronic exposure for three months. The animals were divided into six groups.

The concentrations of the substances in the chambers during the period of exposure are shown in Table 2.

Table 2

Concentrations of Sulfur Dioxide and Hydrogen Fluoride in Experimental Chambers

Number of Chamber	Specified Concentrations in mg/m^3		Actual Concentrations in mg/m^3	
	Sulfur Dioxide	Hydrogen Fluoride	Sulfur Dioxide	Hydrogen Fluoride
I	5,0	—	5,01±0,063	—
II	—	0,3	—	0,297±0,0708
III	0,15	0,01	0,147±0,0004	0,0099±0,00039
IV	0,25	0,01	0,249±0,003	0,0099±0,00038
V	5,0	0,3	4,99±0,048	0,3±0,0048
VI	Control			

For one month prior to the exposure, the general state of health of the animals was observed, and the following indices were determined: their weight, the motor chronaxy of antagonist muscles, cholinesterase activity, amount of coproporphyrin in the urine, morphological composition of peripheral blood, and the amount of calcium, inorganic phosphorus, sugar, and catalase in the blood. These indices were also studied during the exposure of the animals. Rats of the third, fourth and control groups were healthy, active, and gained weight normally in the course of the experiment.

Rats of the first, second and particularly fifth group were less active. Beginning with the fourth week of exposure, the fur of the rats in the second

and fifth groups lost its natural luster and bristled up. Irritation of the mucosa of the eyes was observed in rats of the fifth group.

The motor chronaxy of the flexors and extensors of the shin was determined by means of an ISE-01 pulsed electronic stimulator. The tests were carried out on five rats of each group once every 10 days under the same conditions.

Fig. 2 shows the chronaxy of antagonist muscles of rats exposed to hydrogen fluoride, sulfur dioxide and their mixture (average data for the groups).

Reliable changes in the ratio of chronaxies of extensors and flexors were noted in rats of the second and fifth groups in the fourth week of exposure, and in rats of the first group, in the fifth week. In rats of the third and fourth groups, a change in the ratio of chronaxies of antagonist muscles was observed in the third month of exposure.

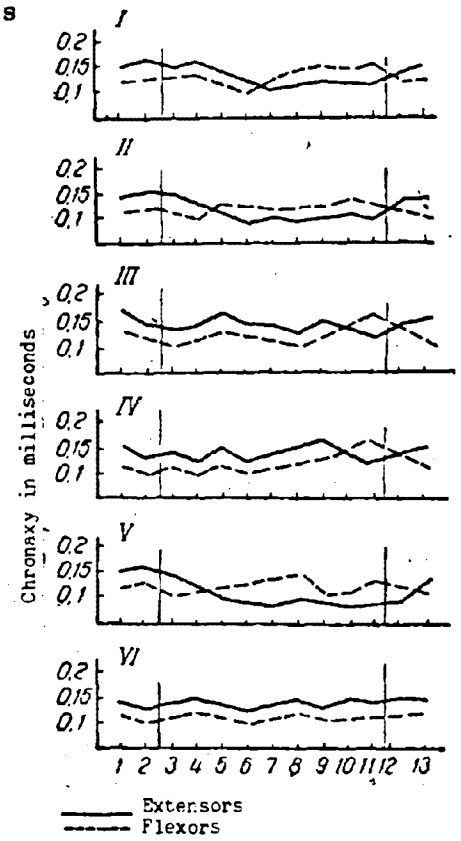

Fig. 2. Motor chronaxy of antagonist muscles in rats of different groups.

Cholinesterase plays an important part in the process of functional activity of the nervous system. The cholinesterase activity in the blood was studied on a photoelectrocolorimeter in five rats of each group once every ten days by using the Fleischer-Pope method as modified by N. N. Pushkina and N. V. Klimkina. The blood for the study was taken from the tail vein by incising the tail, asepsis rules being observed. The cholinesterase activity was expressed in micromoles of acetylcholine per 2 ml of blood.

The change of cholinesterase activity in rats of different groups is shown in Fig. 3.

In animals of the first, second and fifth groups, beginning with the third week from the start of exposure, a statistically reliable increase of cholinesterase activity was observed, and at the end of the experiment, there was a decrease of this activity.

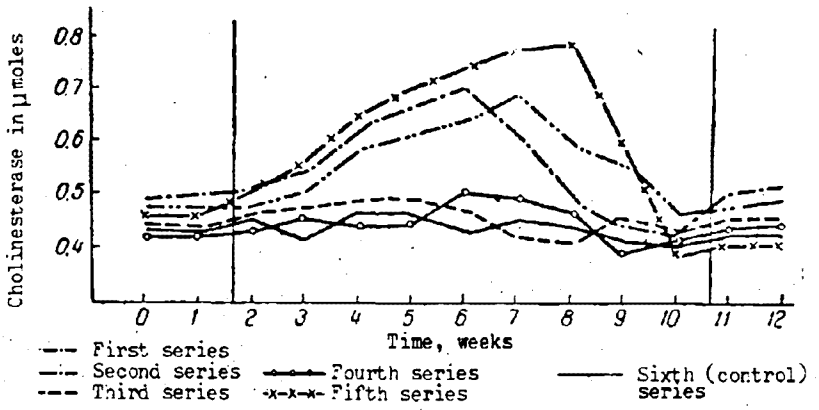

Fig. 3. Change of cholinesterase activity in rats of different groups.

We studied the chronic effect of hydrogen fluoride, sulfur dioxide and their mixture on metabolism on the basis of the change of the porphyrin metabolism in the body of the animals. A spectrophotometric method (M. I. Gusev and Yu. K. Smirnov, 1960) was used to determine porphyrin. A graphic representation of the results obtained is given in Fig. 4.

In rats of the first, second and particularly fifth groups, the amount of porphyrin excreted with the urine increased during the exposure.

A study of the morphological composition of peripheral blood showed an increase in the number of leucocytes in animals of the first, second and fifth groups. The number of erythrocytes and amount of hemoglobin in the blood of rats of the first, second and fifth groups decreased in the course of the experiment. A study of the blood of animals of the second and fifth groups showed a tendency toward hypocalcemia, hypoglycemia, and a decrease of blood catalase.

After the completion of chronic round-the-clock exposure, some of the rats of each group were killed. Autopsy of the animals subjected to the combined action of hydrogen fluoride in 0.3 mg/m^3 concentration and sulfur dioxide in 5 mg/m^3 concentration showed distinctly visible changes in the lungs. On their surface, areas of normal tissue alternated with areas of dark red color. No visible changes were observed in other organs.

Histological analysis of the organs revealed considerable changes in the lungs of rats of the fifth and also of the first and second groups. There was a marked thickening of alveolar septa in the lungs, an inflammatory infiltration in the stroma and around the bronchi (interstitial pneumonia, peribronchitis), and emphysema in some areas (Fig. 5).

The lungs of animals of the third and fourth groups had areas of emphysema, a thickening of the alveolar septa, and areas of interstitial

pneumonia (Fig. 6).

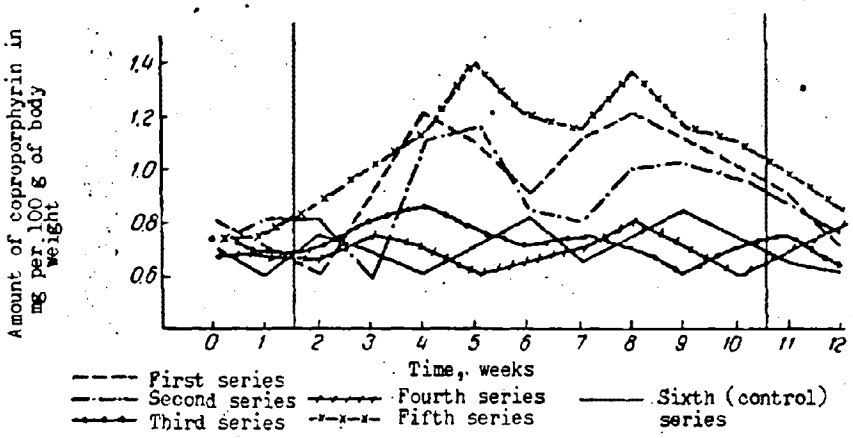

Fig. 4. Content of coproporphyrins in the urine of animals of all groups.

Rats of the fifth group had an inflammatory infiltration in the stroma of the kidneys, primarily around the glomeruli (Fig. 7). Histochemical analysis of the respiratory organs and kidneys in rats of the first, second, and, particularly, fifth groups showed the accumulation of neutral mucopolysaccharides in the walls of the bronchi and in the glomeruli of the kidneys.

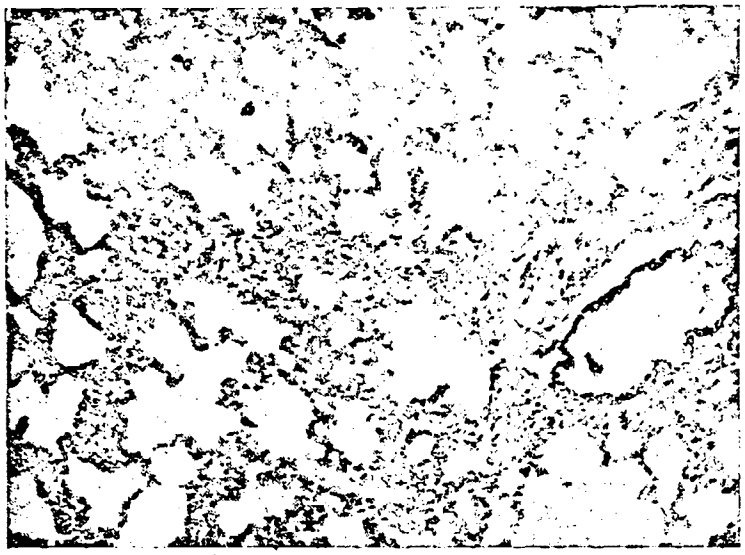

Fig. 5. Rats of fifth series. Changes in the lungs. Magnification 40 x 10. Inflammatory infiltration in the stroma, thickening of interalveolar septa (interstitial pneumonia), sometimes emphysema and edema. Peribronchitis.

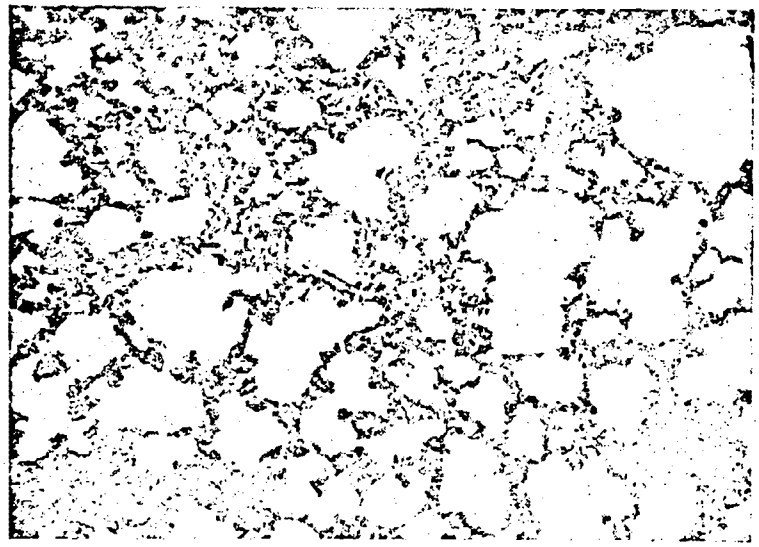

Fig. 6. Rats of fourth series. Changes in lungs. Occasional emphysema, thickening of interalveolar septa with cellular infiltration (as reaction to irritation).

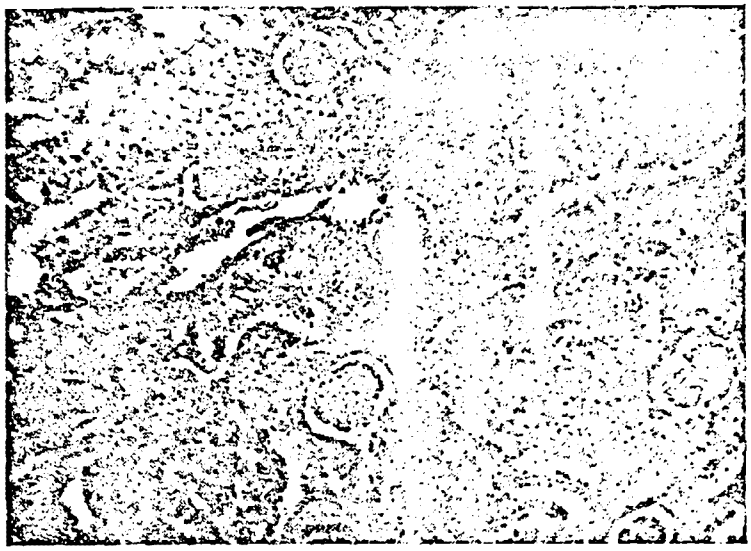

Fig. 7. Rats of fifth series. Changes in kidneys. Magnification 4C x 10. Photograph shows inflammatory infiltrate in stroma, chiefly around glomeruli.

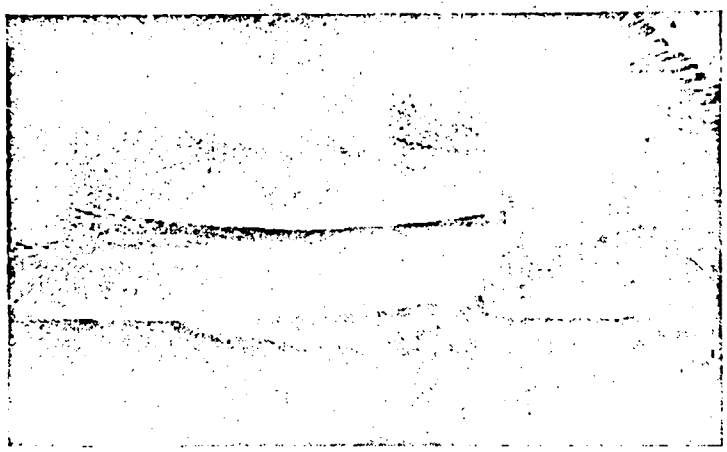

Fig. 8. Striation of enamel of lower incisors in experimental rats of fifth series.

An increase of fluorine was found in the bones of rats of the second and fifth groups. The amount of fluorine in the bones of rats of the second group was 6.6 mg, in rats of the fifth group 6.8 mg, and in the control, 4.8 mg per 100 g of dry substance. In rats of the second and fifth groups, early signs of fluorosis were detected in the form of striation of tooth enamel (Fig. 8).

Thus, a prolonged inhalation of a mixture of 0.3 mg/m^3 hydrogen fluoride and 5 mg/m^3 sulfur dioxide caused considerable changes in the rats: in the ratio of motor chronaxies of antagonist muscles; in cholinesterase activity; in the excretion of coproporphyrin with the urine; an increase in the number of leucocytes; a decrease in the number of erythrocytes and amount of blood hemoglobin; and also changes in the lung tissue and in the kidneys.

In rats that inhaled a mixture of 0.01 mg/m^3 hydrogen fluoride and 0.25 mg/m^3 sulfur dioxide (inactive concentration of the mixture for short-term inhalation) and also in rats exposed to a mixture of hydrogen fluoride and sulfur dioxide at the level of maximum permissible concentrations (0.01 mg/m^3 for hydrogen fluoride and 0.15 mg/m^3 for sulfur dioxide), the changes in cholinesterase activity, in the excretion of coproporphyrin with the urine and in the morphological composition of the blood were insignificant. Changes in the ratio of chronaxia of the antagonist muscles were reliable. A histological examination of the organs of the animals of these series showed significant changes in the lungs in the form of a thickening of the alveolar septa, areas of interstitial pneumonia, and emphysema.

Thus, the studies showed that the combined presence of sulfur dioxide and hydrogen fluoride in the atmospheric air of populated areas at the level of the existing mean daily maximum permissible concentrations for each substance is inadmissible.

The total mean daily concentration of sulfur dioxide and hydrogen fluoride present together, expressed in fractions of the maximum permissible values established for each of them, should not exceed unity.

Conclusions

1. The effect of complete summation was established in a study of the reflex and resorptive effect of a mixture of sulfur dioxide and hydrogen fluoride.

2. When sulfur dioxide and hydrogen fluoride are present together in atmospheric air, their highest single and mean daily maximum permissible concentrations, expressed in fractions of the individual maximum permissible concentrations, must not exceed unity.

LITERATURE CITED

Note: References mentioned in this paper are to be found at the end of the volume in the 1968 bibliography.

NEW DATA FOR THE VALIDATION OF THE MEAN DAILY MAXIMUM PERMISSIBLE CONCENTRATION OF HYDROGEN FLUORIDE IN ATMOSPHERIC AIR

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From Akademiya Meditsinakikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 11, Izdatel'stvo "Meditsina" Moskva, p. 5-15, (1968).

In the available literature on the toxicological characteristics of inorganic fluorine compounds, there are no convincing data on changes induced in the organism by the inhalation of comparatively low fluorine concentrations, and no data whatsoever on the threshold and inactive concentrations. The permissible fluorine concentrations of atmospheric air adopted earlier were not subjected to experimental verification and no account was taken of possible differences in the biological action of the various fluorides (S. V. Miller, 1955). And yet, the national economy plan specifies a further development of aluminum plants, the production of superphosphates, the expansion of the production of fluorine salts and of concerns for the enrichment of fluorspar and other branches of industry utilizing fluorine compounds. In view of these objectives, the problem of a scientific validation of the safe level of fluorine content in the air of populated areas assumes a major importance.

The present report and two other studies of the present collection present the results of several series of investigations which provide a toxicological assessment and make it possible to determine the parameters of the noxious effect on the organism of gaseous and pulverized fluorine compounds marked by different solubilities in biological media.

In 1965, on the basis of experimental studies, we proposed a permissible mean daily concentration of hydrogen fluoride (HF) in atmospheric air at a level of 0.01 mg/m^3, which was shown by tests to be the maximum inactive concentration.

In order to refine certain problems of the mechanism of action of fluoride ions and to study the phosphorus-potassium metabolism by using isotopic tracing, we continued the studies with HF at the level of the concentrations investigated earlier: 0.10-0.03 and 0.01 mg/m^3. In the course of exposure of the animals, the following quantities were also refined: 1) activity of alkaline phosphatase of the blood; 2) degree of excretion of fluorine from the body through the kidneys and the gastrointestinal tract; 3) accumulation of fluorine in the teeth and bone tissue.

All the conditions of the previous (first) experimental series were observed: 1) the HF concentrations in the chambers during the period of exposure were 0.10 ± 0.002, 0.03 ± 0.001 and 0.01 ± 0.0009 mg/m^3; 2) the experiment involved female rats two months old kept on the same food and water diet as the animals of the first series; 3) the animals were subjected to a five-month round-the-clock exposure followed by a one-month period of recovery.

In the first series of studies, inhibition phenomena in the central nervous system were observed in animals of the first and second groups. In order to determine better the mechanism of the inhibitory effect of fluorine ions on the central nervous system, we studied the activity of brain and blood cholinesterase, the content of pyruvic acid in the blood, the content of sulfhydryl groups in the brain, and the state of nerve cells and interneuronal connections.

It is well known that cholinesterase, which decomposes acetylcholine into choline and acetic acid, plays an important part in the synaptic transfer of nerve impulses. The activity of pure cholinesterase present in the gray matter of the brain was studied at the end of the exposure and at the end of the one-month recovery period (the activity of the enzyme was determined in 7-8 animals of each group after a Fleischer-Pope homogenization as modified by N. N. Pushkina and N. V. Klimkina). Our studies did not show any differences in the activity of the brain enzyme in the "fluorinated" and control animals. However, we did record a statistically reliable depression of the blood cholinesterase in animals of the first and second groups in the first two months of exposure, at its end, and after the recovery period.

In the normal process of synthesis of acetylcholinelike substances in cells, conjugated synthetic processes take place between choline, which is a product of phosphatide metabolism, and a product of carbohydrate metabolism capable of acetylating choline. The formation of acetylating agents in the conversion cycle of carbohydrates proceeds via the stage of pyruvic acid (Kh. S. Koshtoyants). Our determination of pyruvic acid by the Friedemann-Haugen method confirms the presence of a "fluoride block" in animals of the first and second groups. An increased content of pyruvic acid was also observed one month after the end of exposure (Table 1). These data attest to the depression of carboxylase, an enzyme decomposing pyruvic acid.

Many researchers have shown that an enormous number of enzymes participating in the conversion cycle of pyruvic acid and also cholinesterase require for their activity the presence of sulfhydryl groups in the protein component of their molecules. The binding or blockage of sulfhydryl groups depresses the activity of many enzymes of protein and carbohydrate metabolism. According to Koshtoyants, they are of major importance in normal

processes of stimulation and inhibition of the nervous system, since the activity of the receptor is determined by the presence of free sulfhydryl groups in the protein molecule. In the determination of the content of sulfhydryl groups by the Kolthoff and Harris method, we observed their decrease in the brain tissue at the end of exposure in animals that inhaled HF in a concentration of 0.10 mg/m^3. After the one-month recovery period, the content of sulfhydryl groups returned to normal.

After the completion of exposure of animals in the first group, a study of the histological specimens of the cerebral cortex showed a distortion of the nerve cells, disappearance of the Nissl substance, and pyknosis and lysis of the nuclei. Extended areas with damage to the apical dendrites were observed. The dendrites had beaded enlargements, and were broken down into fragments: the specimens showed black dots that were not connected to each other by strands of cytoplasm. Histopathologic changes of the nerve cells and dendrites in animals of the first group were also observed after the one-month recovery period.

There were also changes in the cerebral cortex in animals of the second group. However, these changes were less pronounced. Nerve cells with granular cytoplasm containing clear vacuoles were found only occasionally. Cells were observed whose dendrites had enlarged beads. Changes of neurons in the presence of 0.03 mg/m^3 HF were reversible in character.

In animals inhaling HF in a concentration of 0.01 mg/m^3, no pathologic changes were detected in the neurons.

Table 1

Concentration of Pyruvic Acid (in milligram-percent) in the Blood of the Animals

Group of Animals	At the End of Chronic Exposure				At End of One-Month Recovery Period			
	Statistical Criteria							
	n	$X \pm Sx$	t	P	n	$X \pm Sx$	t	P
First	6	4,8±0,05	8,74	<0,001	6	1,6±0,14	5,85	<0,001
Second	6	4,2±0,15	3,41	<0,01	6	4,2±0,16	3,65	<0,01
Third	6	3,6±0,28	0,32	>0,05	6	3,7±0,16	1,37	>0,05
Control	6	3,5±0,14	—	—	6	3,4±0,15	—	—

Thus, the shifts in the functional state of the central nervous system which we observed in the first series of experiments resulted from the inhibitory influence of fluoride ions on enzyme systems involved in the transfer of nerve stimulation and from the histopathologic damage to nerve cells and interneuronal connections.

Disturbances in the phosphorus-calcium metabolism and in the architectonics of bones are attributed by researchers to the inhibition of phosphatase activity. From esters of phosphoric acid phosphatase liberates inorganic phosphorus, which combines with calcium to form the phosphorus-calcium salts necessary for building bone tissue. Kutscher and Wust, Massart and Dufait, Smith, and others explain the mechanism of phosphatase depression by fluorine by the fact that magnesium, which enters into the enzyme complex and is the enzyme activator, forms a nondissociable form on combining with fluorine. The degree of phosphatase inhibition does not always correspond to the concentration of fluorine ions; high concentrations either do or do not cause a lesser inhibition effect than intermediate or relatively low concentrations. On the basis of their studies, Reiner, Tsuboi, and Hudson believe that fluorine, by undergoing polymerization in the organism, forms a dimer and a tetramer. The dimer is formed when low concentrations of fluorine enter the organism, and a tetramer is formed in the presence of high concentrations. The dimer combines with the active center of the enzyme. The tetramer also combines with the active center, but may be replaced by a substrate, and the enzyme inhibition effect decreases at high fluorine concentrations. We studied the activity of alkaline blood phosphatase under dynamic conditions according to G. K. Shlygin and S. Ya. Mikhlin in six animals of each group. In the presence of hydrogen fluoride in a concentration of 0.10 mg/m^3, the inhibition of alkaline phosphatase of the blood was observed only during the second month of exposure of the animals. A more pronounced effect was detected as a result of inhalation of HF in a concentration of 0.03 mg/m^3: inhibition of the enzyme was observed during the second, third, and fifth months of exposure. Even as low an HF concentration as 0.01 mg/m^3 can depress the enzyme activity: a statistically reliable shift was observed at the end of the fifth month of exposure.

We studied the rate of phosphorus and calcium metabolism in the body by means of isotopic tracers. The radioisotopes P^{32} and Ca^{45} in tracer doses were introduced into the animals intraperitoneally at the end of chronic exposure and at the end of the one-month recovery period. Twenty-four hours after the introduction of the isotopes, the animals were sacrificed by decapitation. The analysis was performed on the teeth, humerus, femur, blood, and liver. The teeth and tubular bones were thoroughly cleaned to remove the soft tissues. All the specimens were then weighed, brought to a constant weight at 105°C., and ground into a powder. From each specimen, portions weighing 30 mg were evenly spread over aluminum targets. The activity was measured with a type B counter. The total activity produced by the radiation of P^{32} and Ca^{45} was determined first, then the activity of Ca^{45} was completely cut off with an aluminum filter, and the activity due to P^{32} was calculated. In calculating the activity, necessary corrections were introduced for the natural decay of the isotopes, absorption in the specimens, etc. The isotopic tracer method revealed a statistically reliable retardation of the inclusion of phosphorus and calcium in the biological substrates studied. More pronounced changes were found in the phosphorus metabolism in animals of the first and second groups; phosphorus was included more slowly in all the specimens studied than in the control. Even when the lowest EF concentration

Table 2

Inclusion of Radioisotopes P^{32} and Ca^{45} in Tissues and Blood of Animals at End of Five-Month Exposure to HF (in 1 g of Moist Tissue in Percent of Activity Introduced into Body)

Biosubstrate	Isotope	Statistical Criteria	Group of Animals			
			First	Second	Third	Control
Teeth	P^{32}	n	7	6	8	8
		$X \pm Sx$	0,75±0,12	1,00±0,05	1,20±0,10	1,35±0,12
		t	4,24	2,56	1,00	—
		P	<0,001	<0,05	>0,05	—
	Ca^{45}	n	8	7	7	6
		$X \pm Sx$	3,00±0,36	3,34±0,25	3,88±0,26	3,82±0,25
		t	1,87	1,35	0,01	—
		p	>0,05	>0,05	>0,05	—
Femur	P^{32}	n	7	7	8	8
		$X \pm Sx$	0,43±0,05	0,52±0,11	0,72±0,02	0,93±0,06
		t	6,66	3,18	3,35	—
		p	<0,001	0,01	<0,01	—
	Ca^{45}	n	8	7	7	8
		$X \pm Sx$	1,66±0,11	1,88±0,22	2,54±0,11	2,68±0,16
		t	5,18	2,54	0,74	—
		p	<0,001	<0,05	>0,05	—
Humerus	P^{32}	n	7	7	8	8
		$X \pm Sx$	0,45±0,05	0,56±0,09	0,69±0,04	0,85±0,08
		t	4,08	2,36	1,83	—
		p	<0,002	<0,05	>0,05	—
	Ca^{45}	n	8	6	8	8
		$X \pm Sx$	1,96±0,14	2,17±0,28	2,59±0,13	2,91±0,24
		t	3,44	2,00	1,19	—
		p	<0,01	>0,05	>0,05	—
Blood	P^{32}	n	7	6	6	8
		$X \pm Sx$	0,060±0,006	0,060±0,010	0,090±0,005	0,110±0,005
		t	7,00	5,00	2,86	—
		p	<0,001	<0,001	<0,05	—
	Ca^{45}	n	8	6	6	8
		$X \pm Sx$	0,030±0,001	0,030±0,004	0,040±0,007	0,040±0,007
		t	1,40	1,20	0	—
		p	>0,05	>0,05	>0,05	—
Liver	P^{32}	n	7	6	8	8
		$X \pm Sx$	0,61±0,05	0,70±0,04	0,78±0,05	0,95±0,06
		t	4,07	3,54	2,30	—
		p	<0,002	<0,01	<0,05	—

(0.01 mg/m^3) was acting on the organism, a delayed inclusion of radioactive phosphorus was noted in the femur, liver and blood. Disturbances in the calcium metabolism were noted only in animals of the first and second groups (Table 2). Changes in the phosphorus-calcium metabolism continued to be observed in all three "fluorinated" groups of animals and after the one-month recovery period. It is necessary to postulate that the observed mottling of tooth enamel and the histologic changes in the bone tissue in animals of the first and second groups resulted from a disturbance of the phosphorus-calcium metabolism.

Repeat determinations of the fluorine content of the urine in the second series of experiments confirmed a high level of excretion of fluorine from the body. A higher fluorine concentration, which occurred during the second month of exposure in the urine of certain groups of animals, was retained until the end of the inhalation period. The fluorine content of the urine was almost directly proportional to the concentration of hydrogen fluoride in the air inhaled. A reliable increase of fluorine in the urine and in animals of the third group was observed.

We were interested in the problem of the level of fluorine excretion from the body through the kidneys and through the intestines. These studies were made at the end of the chronic exposure on animals of the first group and on the controls. It was found that in animals subjected to the inhalation of hydrogen fluoride, over 78% of the fluorine is excreted through the kidneys, and 15% through the intestines. In the control group, the reverse relationship was observed. These data lead to the conclusion that the gaseous fluorine that has entered the body is excreted through the kidneys as a result of a complete absorption in the respiratory organs (I. D. Gadaskina) and penetration of the general circulatory system. The fluorine retained in the body is deposited in the teeth and bone tissue. A higher degree of fluorine accumulation was observed after exposure to the higher hydrogen fluoride concentration (Table 3).

After the chronic exposure was completed, histological analyses were carried out which showed that HF in 0.10 mg/m^3 concentration causes changes in all the internal organs.

In the study of the upper respiratory tract, the main changes were observed in the mucous membrane and submucous layer. The mucous membrane is thinned out in some places and swollen in others. In some areas the epithelium is absent, cast off, or lies in the lumen of the air tube. Leucocytes, erythrocytes and lymphocytes are visible among cells of the cast-off epithelium. Large leucocytic clumps are present on the mucous membrane that remains. In the submucous layer, the capillaries and vessels are greatly enlarged. There are hemorrhages. The same type of changes were observed in the bronchial epithelium. In some areas, the cast-off epithelium fills the bronchial lumen, obstructing the bronchi completely. In the submucosa of the

Table 3

Fluorine Content of Teeth, Humerus and Femur (in Milligram-Percent of Moist Substance) after Exposure of the Animals to Hydrogen Fluoride.

Animal Group	Teeth				Humerus				Femur			
	Statistical Indices											
	n	$X \pm Sx$	*t*	*P*	*n*	$X \pm Sx$	*t*	*P*	*n*	$X \pm Sx$	*t*	*P*
First	8	75,5±2,19	23,66	<0,001	8	73,1±1,67	27,76	<0,001	8	80,3±2,76	25,5	<0,001
Second	7	33,0±1,47	8,96	<0,001	7	37,9±1,96	10,31	<0,001	7	23,9±3,49	3,33	<0,01
Third	8	17,3±1,38	0,91	>0,05	8	18,5±2,29	1,96	7>0,05	8	13,2±2,12	1	>0,05
Control	8	15,6±1,27	—	—	8	13,3±1,36	—	—	8	12,3±0,61	—	—

bronchioles, a polymorphous cellular infiltration is visible which sometimes destroys the epithelium and comes out into the bronchial lumen. An acute hyperplasia of the peribronchial lymphatic nodes resulting in the deformation of the bronchi was detected. The hyperplastic nodes extend under the mucous membrane, causing it to bulge out in the lumen and form outgrowths, thus destroying the muscle layer of the bronchi, causing its segmentation and atrophy. This in turn causes the formation of bronchiectases. The interalveolar septa are enlarged because of the dilatation of the capillaries and their congestion with erythrocytes, and also the appearance of lymphocytes and histiocytes in them. The space of many alveoli is filled with a transudate containing cast-off epithelial cells, leucocytes, and erythrocytes. In some areas, there are so many erythrocytes in the alveolar lumen that the contents assume a hemorrhagic character. A perivascular edema is observed. In isolated cases, bronchopneumonia is superimposed on the process described.

In the liver, kidneys, adrenal glands, and spleen, congestion phenomena are observed in the form of an expansion and overfilling of capillaries with erythrocytes and the formation of hemorrhages. Degeneratively dystrophic changes are represented by pyknosis of the nuclei of renal convoluted tubules and of liver and Kupffer cells. In addition, a development of infiltrative-proliferative processes around the liver vessels is noted. The formation of clear foci consisting of erythrocytes, cellular fragments with pyknotic nuclei, and reticuloendothelial cells was observed in the liver.

Congestion in the red pulp, a certain loss of follicles and an increase of the reticuloendothelial elements in them were observed in the spleen.

Changes were also noted in the cardiac muscle, i.e., the disappearance of transverse striation and disjunction of the myofibrils.

A hydrogen fluoride concentration of 0.03 mg/m^3 causes changes in the liver only. The nature of the injury is similar to the above. No histopathologic changes in the internal organs were detected following exposure to a hydrogen fluoride concentration of 0.01 mg/m^3.

Conclusions

1. Round-the-clock exposure to hydrogen fluoride concentrations of 0.10 and 0.03 mg/m^3 causes inhibition in the central nervous system, decreases the activity of a number of enzymes, impairs the phosphorus-calcium metabolism, and causes the accumulation of fluorine in the body and damage to the internal organs and bone tissue.

2. A hydrogen fluoride concentration of 0.01 mg/m^3 should be regarded as the threshold concentration. Its effects on the body of the animals showed changes in the phosphorus metabolism only (inhibition of alkaline blood

phosphatase and a delayed inclusion of radiophosphorus in bone tissue, liver, and blood at the end of a five-month exposure of the animals).

3. The mean daily maximum permissible concentration of hydrogen fluoride in the air of populated areas, adopted earlier as 0.01 mg/m^3, should be lowered to 0.005 mg/m^3.

LITERATURE CITED

Note: References mentioned in this paper are to be found at the end of the volume in the 1968 bibliography.

SANITARY EVALUATION OF FLUORIDES READILY SOLUBLE IN BIOLOGICAL MEDIA

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From Akademiya Meditsinakikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 11, Izdatel'stvo "Meditsina" Moskva, p. 16-26, (1968).

Having studied the nature of the action of hydrogen fluoride, we considered it necessary to investigate fluoride salts as well, since we suspected that gaseous and powdered fluorine compounds may differ in the degree of their toxic effect on the body. These differences may be due to different levels of retention of fluorides in the respiratory organs and their different solubilities in biological media.

It is known from studies made by I. D. Gadaskina and T. A. Shtessel' that HF is completely absorbed in the respiratory organs. The behavior of fluorine salts present in a finely dispersed state in air is partially indicated in Table 1, taken from a handbook on the toxicology of radioisotopes.

Table 1

Distribution of Fine Particles in the Respiratory Organs of a "Standard" Person.

Nature of Distribution \ Compounds	Readily Soluble Compounds, %	Other Compounds, %
Excreted with exhaled air	25	25
Deposits in upper respiratory tract, then ingested	50	50
Deposits in the lungs	25[1]	25[2]

[1] This part assimilated in the body

[2] Of this, one-half is excreted by the lungs and ingested in the first 24 hours, so that the fraction of swallowed particles increases to 62.5%. The remaining 12.5% reach the body fluids.

It is evident from Table 1 that for one and the same concentration of gaseous and powdered fluorine compounds in air, different amounts of F^- will enter the human body.

Table 2

Solubility of Fluorides in Different Media (Average Data for Three Observations)[1]

Time of Withdrawal of Samples for Analysis	Ringer-Tyrode solution (pH = 7.2)				Gastric Juice (pH = 2.5)			
	NaF	AlF_3	Na_3AlF_6	CaF_2	NaF	AlF_3	Na_3AlF_6	CaF_2
	Percent of Amount of Fluorine Introduced							
After 1 hour	94,9	3,9	0,0	0,0	48,4	0,0	0,0	0,0
» 2 hours	98,8	3,9	2,9	0,0	48,4	0,0	0,0	0,0
» 5 hours	98,8	3,9	2,9	0,0	48,4	0,0	0,0	0,0
» 24 hours	96,6	5,9	3,9	0,0	82,5	0,0	0,0	0,0
» 5 days	100,0	5,9	12,9	1,9	82,5	9,7	4,8	4,8
» 10 »	100,0	21,2	29,9	3,9	100,0	9,7	4,9	21,1
» 20 »	100,0	38,7	37,5	21,2	100,0	9,9	9,7	35,0

[1] The minimum amounts were taken for the study of solubility - 0.16 mg of F in 100 ml of solution.

The data we obtained on the degree of solubility of different fluorides in biological media are listed in Table 2.

The highest solubility in biological media was displayed by sodium fluoride. It is completely soluble in weakly alkaline media. In acid medium (gastric juice) during the first five hours, which are of practical importance, the solubility of NaF was also higher - 48.4% of the fluorine introduced. As the period of exposure increased, the solubility of NaF in the gastric juice increased to 82.5-100%.

Aluminum fluoride and cryolite are very similar in their degree of solubility in the Ringer-Tyrode solution. During the first 24 hours, the solubility of aluminum fluoride and cryolite is equal to 4-6% of the amount of fluorine introduced; calcium fluoride is insoluble. As the period of contact increases, the solubility of aluminum fluoride and cryolite increases, and on the 20th day reaches 38%; the solubility of calcium fluoride is slightly lower. Aluminum fluoride, cryolite and calcium fluoride are insoluble in gastric juice during the first 24 hours. These data permit the assumption that the NaF retained in the body dissolves completely in certain biological fluids. Aluminum fluoride, cryolite, and particularly calcium fluoride will not dissolve completely in biological fluids and hence may have a lesser toxic effect than HF or NaF.

To study the fluorine salts, we set up a special experimental apparatus which enabled us to obtain a condensation aerosol. The experimental influence of fluorine condensation aerosols on the body frequently corresponds to actual conditions (aluminum and other industries where high temperature processes

are employed). The experimental assembly was equipped with automatic blocking of the air supply instruments and with signaling that came on when the operating conditions of its main units were impaired.

Table 3

Light Sensitivity of the Eye During Inhalation of Sodium Fluoride by Subject L.

NaF Concentration, mg/m³	Statistical Criteria	Observation Time in Minutes[1]			
		20	25	30	40
Pure Air	$X \pm Sx$	126,3±7,6	183,0±21,3	223,5±17,9	281,9±31,5
0,07	$X \pm Sx$	198,1±8,3	195,4±11,1	324,4±48,0	399,4±18,8
	t	6,35	0,51	1,96	3,2
	p	0,01	>0,05	>0,05	<0,05
0,05	$X \pm Sx$	154,1±1,1	166,1±2,0	215,3±16,5	299,3±40,3
	t	3,61	0,78	0,34	0,34
	p	0,02	>0,05	>0,05	>0,05
0,03	$X \pm Sx$	134,0±3,9	216,1±9,2	259,7±10,9	304,5±17,3
	t	0,89	1,41	1,73	0,63
	p	>0,05	>0,05	>0,05	>0,05

[1] In percent of 15-minute dark adaptation, taken as 100.

In order to standardize the highest single maximum permissible concentration of NaF, the reflex effect of the latter on the light sensitivity of the eye was studied by using the common method of dark adaptation in three persons with normal vision. The study of the reflex effect of NaF showed that a concentration of 0.07 mg/m^3 causes an increase of the light sensitivity of the eye in all the subjects, and a concentration of 0.05 mg/m^3 does so in one person only. A concentration of 0.03 mg/m^3 of NaF did not cause any deviation of dark adaptation (Table 3).

To compare the results of the study with those obtained in the experiments with HF, a chronic exposure of the animals to sodium fluoride was also carried out round the clock over the course of five months. The NaF concentrations were checked four times a day. The withdrawl of air samples from the chambers for the purpose of analysis for the degree of absorption of F^- was carried out by using dinitrocellulose membrane filters No. 2 in combination with absorbers filled with double-distilled water. Fluorine was determined by the alizarin-thorium procedure (sensitivity of the method, 0.001 mg/m^3). Since in the chronic exposure of animals the HF concentration of 0.01 mg/m^3 was found to be the threshold value, only two concentrations, 0.10 and 0.03 mg/m^3, were studied in the experiment with NaF, which

is incompletely retained in the body and in our view should be less toxic. The actual NaF concentrations in the chambers during the period of exposure are indicated in Table 4.

Table 4

Mean Daily NaF Concentrations (in terms of F^-) During the Period of Exposure.

Chamber No. 1; Given Concentration 0.10 mg/m³		Chamber No. 2; Given Concentration 0.03 mg/m³	
Variation Limits	%	Variation Limits	%
0,07	0,8	0,028—0,033	56,0
0,09—0,11	86,9	0,034—0,040	25,4
0,12—0,15	12,3	0,041—0,050	13,8
		0,050	3,8
$X \pm Sx$	0,10±0,007	$X \pm Sx$	0,036±0,003

NaF dust, which entered the exposure chambers, must be classified as highly dispersed: particles of up to 1μ comprise 75.0-89.2%, and those of 1-2μ, 10.8-25%. The natural content of F^- in the food and water was the same as in the experiment with HF (the daily intake of F^- with the food was 0.045 mg, and with water, 0.007 mg).

During the first month of exposure, as in the case of HF, some of the animals of the second group were stimulated. The "fluorinated" and control animals did not differ in weight over the course of the experiment.

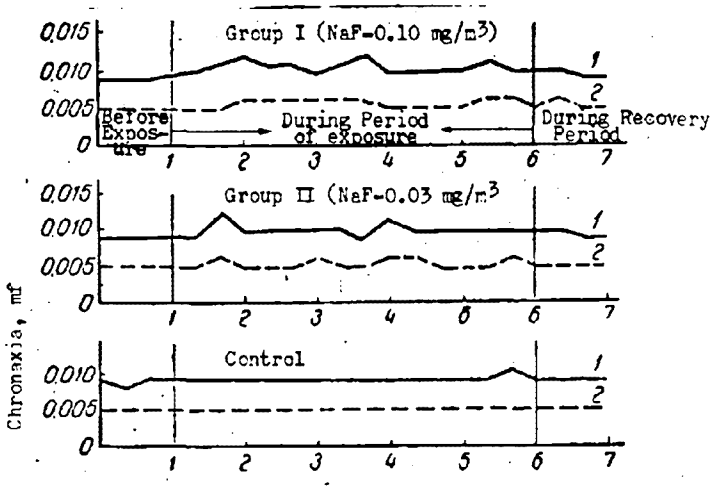

Fig. 1. Average data for the chronaxy of antagonist muscles in each group.
1 - extensors; 2 - flexors

The functional state of the nervous system was studied by the method of motor chronaximetry on ten animals of each group. In animals of the first and second groups, a slight but statistically significant prolongation of the chronaxy of the extensors and flexors was recorded. No disturbances of the ratio of chronaxies of antagonist muscles were noted (Fig. 1). Data from the measurement of motor chronaxy attest to a certain inhibition of the processes in the central nervous system, under the influence of NaF. Under the influence of similar HF concentrations, a prolongation, equalization and inverse ratio of the chronaxies of the antagonist muscles were observed in the animals.

At the end of exposure of animals of the first group, morphologic changes were observed in the cerebral cortex: deformation of dendrites, nerve cells of enlarged volume with clarified cytoplasm and vanished Nissl substance. In addition, there was a wrinkling of the nerve cells and pyknosis of the nuclei. The process was focal in character. After the one-month recovery period, altered neurons occurred much more seldom than immediately after the exposure. An HF concentration of 0.10 mg/m^3 caused more profound destructive changes in the cerebral cortex, up to and including the destruction of nerve cell nuclei and neuronophagia.

During exposure to NaF in a concentration of 0.03 mg/m^3, the animals of the second group showed slight changes of neurons which could be regarded as functional and reversible, i.e., they were not observed one month after the exposure.

The content of active sulfhydryl groups in the brain tissue, determined by the Kolthoff and Harris* method, was the same in the "fluorinated" as in the control animals.

A study of blood cholinesterase activity on eight animals of each group using the Fleischer-Pope** method showed that both NaF concentrations, like HF, had an inhibiting effect on this enzyme beginning with the first month of exposure (Fig. 2).

Sodium fluoride also has an inhibitory effect on the activity of blood alkaline phosphatase (the phosphatase activity was determined on six animals of each group according to G. K. Shlygin and S. Ya. Mikhlin). An NaF concentration of 0.10 mg/m^3 causes an inhibition of the activity of the enzyme in the animals over the entire period of exposure. During exposure to 0.03 mg/m^3 NaF, there was an obvious tendency toward a decrease in the activity of the enzyme, but statistically reliable differences from the control occurred only during the first two months of exposure (Fig. 3).

Having established the fact of the inhibitory effect of NaF on phosphatase, which is involved in the phosphorus and calcium metabolism and in the processes of bone formation, we thought it desirable to study the phosphorus-

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* [Translator's note: Kol'tgoff and Garis, Fleysher and Poup, according to the transliteration of
** Russian reference.]

calcium metabolism as well, by using the method of isotopic tracers. Upon intraperitoneal administration of the P^{32} and Ca^{45} radioisotopes, it was noted that the phosphorus metabolism tended to speed up in the bone tissue and humerus and that there was a retardation of the calcium metabolism in the femur. After the one-month recovery period, the phosphorus-calcium metabolism returned to normal. The content of stable P and Ca elements in the bones, determined by spectral analysis, did not change under the influence of the NaF concentrations studied.

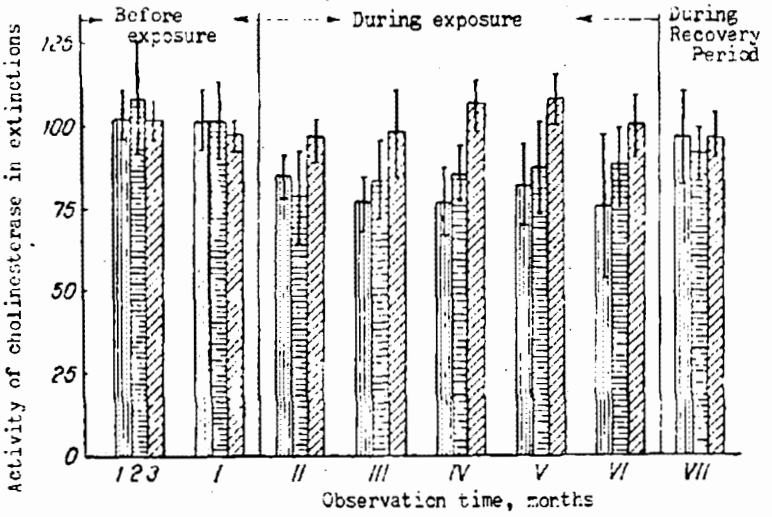

Fig. 2. Blood cholinesterase activity of experimental animals.
1 - NaF - 0.10 mg/m^3; 2 - NaF - 0.03 mg/m^3; 3 - control.

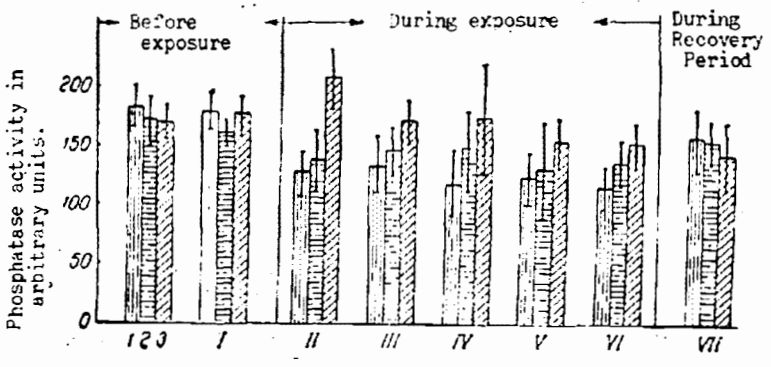

Fig. 3. Activity of blood alkaline phosphatase of experimental animals.
Notation same as in Fig. 2.

During the exposure, observations were made every month to determine the excretion of fluorine from the body through the kidneys, and at the end of the exposure, the deposition of fluorine in the bone tissue was determined (fluorine was determined by ion exchange chromatography). It was found that in the first and second groups of animals during the exposure, the fluorine content in the urine was respectively 4-5 and 2-3 times that of the control group (Fig. 4). However, the fluorine that had entered the body was not excreted, and it accumulated in the skeleton. After the exposure, the fluorine level in the bone tissue of animals of the first group surpassed the control level by a factor of 5-7, and that of the second group, by a factor of 1 1/2-3 times, but it was 2-3 times lower than during exposure to hydrogen fluoride (Table 5). There was no damage to the tooth enamel under the influence of the NaF concentrations studied. Histological analyses of the bone tissue established certain disturbances in animals of the first group only. Focal changes of osteocytes in the form of a faint color and lysis of the nuclei and also an irregular and frequently substantial deposition of lime were occasionally observed in the dense substance of the humerus, femur and pelvic bone. After the one-month recovery period, the altered nuclei of osteocytes had almost disappeared, but an irregular deposition of lime was observed as before.

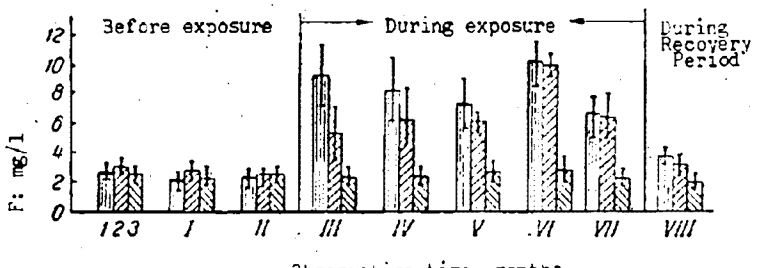

Fig. 4. Fluorine content in the urine of experimental animals, with confidence limits.
Notation same as in Fig. 2.

The state of the respiratory organs deserves some attention. In contrast to the experiment with HF (an irritant gas with a low pH), the upper respiratory tract remains unchanged during inhalation of a finely dispersed sodium fluoride dust. The latter penetrates into the deep reaches of the respiratory organs, causing injury to the lungs at the 0.10 mg/m^3 concentration. The interalveolar septa are enlarged as a result of being infiltrated by lymphocytes, histiocytes and epithelioid cells. The capillaries of interalveolar septa are expanded and overfilled with erythrocytes. Numerous fine-focus hemorrhages and areas of desquamative alveolitis are observed. Pulmonary emphysema is pronounced. Some changes in the lungs were also detected one month after the exposure was discontinued (enlargements of the interalveolar

Table 5

Fluorine Content (in Milligram-Percent of Moist Substance) in Teeth, Humerus and Femur.

Group of Animals	Teeth				Humerus				Femur			
	Statistical Criteria											
	n	$X \pm Sx$	t	P	n	$X \pm Sx$	t	P	n	$X \pm Sx$	t	P
First	6	52,4±5,4	8,06	<0,001	6	42,5±6,5	5,29	<0,001	8	35,5±4,6	5,97	<0,001
Second	6	17,5±2,4	3,64	<0,01	7	22,4±2,9	4,86	<0,001	7	11,7±0,9	2,58	<0,05
Control	5	7,2±1,5	—	—	7	7,9±0,7	—	—	6	6,8±1,4	—	—

septa and emphysema). The 0.03 mg/m^3 NaF concentration does not cause any serious changes in the lungs.

Histological analysis of the liver in animals of the first group showed a varied staining of the protoplasm of the liver cells. The tissue was mottled in appearance - clear foci with unstained cytoplasm alternated with normally stained areas. Clear nodules from fragments of hepatic cells and reticuloendothelial type cells were observed. There was a lymphohistiocytic infiltration around the vessels. No appreciable histomorphologic changes in the liver were found in animals of the second group.

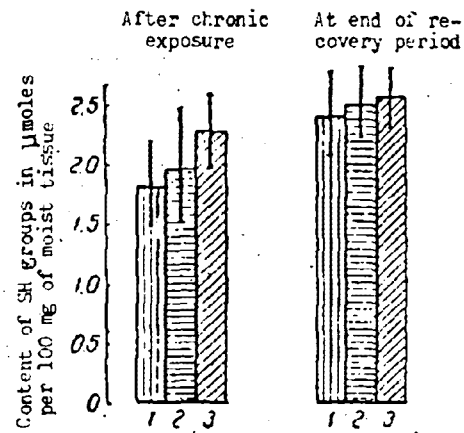

Fig. 5. Content of SH groups in the liver tissue of experimental animals. Notation same as in Fig. 2.

During both periods of observation, i.e., at the end of the exposure and at the end of the one-month recovery period, the content of active SH groups in the liver of "fluorinated" animals was lower than in the controls. However, statistically reliable differences were established only in the first group at the end of exposure (Fig. 5).

The heart, kidneys, adrenals, and spleen were not damaged by the action of the sodium fluoride concentrations studied.

Conclusions

1. The threshold of the reflex effect of NaF on the human body established by the method of dark adaptation is 0.05 mg/m^3.

2. NaF concentrations of 0.10 and 0.03 mg/m^3 during round-the-clock chronic exposure of the animals have a generally toxic effect and cause the accumulation of fluorine in the bone tissue. The extent of the changes observed in the body depends on the NaF concentration in air.

3. Because of the neutral properties of sodium fluoride dust and its incomplete absorption in the body after penetration through the respiratory organs, its toxic influence is less than that of similar hydrogen fluoride concentrations.

4. The highest single NaF concentration in the air of populated areas should not exceed 0.03 mg/m^3, and the mean daily concentration should not exceed 0.01 mg/m^3.

LITERATURE CITED

Note: References mentioned in this paper are to be found at the end of the volume in the 1968 bibliography.

BIOLOGICAL EFFECT OF POORLY SOLUBLE FLUORIDES

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From Akademiya Meditsinakikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 11, Izdatel'stvo "Meditsina" Moskva, p. 26-32, (1968)

Aluminum fluoride, a typical representative of poorly soluble fluorides, was selected for the study. The experiments were carried out with a condensation aerosol of AlF_3 (at a sublimation temperature of about 700°C).

To substantiate the highest single maximum permissible concentration of AlF_3, the light sensitivity of the eye was studied on three persons. An AlF_3 concentration of 0.3 mg/m^3 was found to cause a reliable increase of the light sensitivity of the eye in all the subjects; a 0.1 mg/m^3 concentration was found to be inactive. Data on the light sensitivity of the eye for one of the subjects are listed in Table 1.

As in the experiment with HF and NaF, a chronic exposure of the animals to AlF_3 was carried out around the clock over the course of five months. The concentrations of fluorine in the chambers were checked three times a day. The withdrawal of air samples from the chambers was performed in the same way as in the case of exposure of the animals to HF and NaF. Considering the fact that aluminum fluoride forms the hydrated complex ions AlF^{++} and AlF_2, which are insoluble in water and decrease the effective quantity of the fluoride ion in the sample by 30%, in determining the AlF_3 concentration we introduced a correction factor of 1.33. The correction factor was established on the basis of experiments on the determination of the fluoride ion content in AlF_3 by the method of volatilization and dissolution of AlF_3 collected on a filter in a 0.2 N solution of alkali.

The animals were exposed to highly dispersed AlF_3 powder: in the air of the exposure chambers, particles up to 1μ comprise 67.6%; 1-2μ, 29.9%; and 2-4μ, 2.5%.

The experimental animals (white female rats two months old) were divided into three groups, with 20-23 rats in each: the first group included animals exposed to aluminum fluoride in 0.10 mg/m^3 concentration, the second group to 0.03 mg/m^3, and the third group was the control. The aluminum fluoride concentrations in the experimental chambers during the period of exposure are listed in Table 2.

Table 1

Light Sensitivity of the Eye During Inhalation of Aluminum Fluoride in Subject L.

AlF_3 Concentration in mg/m^3	Statistical Criteria	Observation Time in Minutes[1]			
		20	25	30	40
Pure Air	$X \pm Sx$	126,3±7,6	183±21,5	223,5±17,9	281,9±31,5
0,3	$X \pm Sx$	163,6±7,2	169,2±12,7	206,2±8,9	258,4±20,8
	t	3,58	0,55	0,86	0,62
	p	<0,05	>0,05	>0,05	>0,05
0,1	$X \pm Sx$	123,0±1,7	149,1±4,2	190,9±17,4	237,9±26,1
	t	0,42	1,50	1,30	1,07
	p	>0,05	>0,05	<0,05	>0,05

[1]In percent of 15-minute dark adaptation taken as 100.

Table 2

Aluminum Fluoride Concentration (in Terms of F^-) During Exposure Period.

Chamber No. 1; Specified Concentration, 0.10 mg/m^3		Chamber No. 2; Specified Concentration 0.03 mg/m^3	
Variation Limits	%	Variation Limits	%
0,06—0,08	13,8	0,018—0,02	6,9
0,09—0,11	77,7	0,034—0,04	70,0
0,12—0,16	8,5	0,041—0,05	21,6
		<0,05	1,5
$X \pm Sx$ 0,010±0,0013		$X \pm Sx$ 0,036 ± 0,00056	

The fluorine content of the food was the same as in the experiments with HF and NaF. In the course of the experiment it was found that AlF_3 in the concentrations studied does not affect the weight of the animals.

In animals of both experimental groups, a slight but statistically reliable prolongation of the chronaxies of extensors was noted (by only 1 mF, compared with the control). The method of functional loading was used to enhance the toxic effect. At the end of the exposure, each animal was given 0.003 ml of a 40% alcohol solution per gram of body weight, but

no statistically reliable differences were observed in the neuromuscular excitability of the "fluorinated" and control animals. A very slight prolongation of the chronaxy of antagonist muscles, observed during the period of exposure, immediately disappeared when the action of AlF_3 was discontinued. Thus, whereas serious disturbances of the subordinational influences were found in the central nervous system, observable even during the recovery period, less significant changes of the motor chronaxy were found during exposure of the animals to NaF, and they were still less significant during the action of AlF_3, which also produces an inhibition effect on the blood enzymes later than NaF does.

AlF_3 has an inhibitory influence on the activity of the blood cholinesterase, studied on eight animals of each group by the Fleischer-Pope method, only with the 0.10 mg/m^3 concentration, beginning with the end of the third month of exposure (Fig. 1). An inhibition of the activity of alkaline phosphatase, determined according to G. K. Shlygin and S. Ya. Mikhlin in seven animals per group, was observed during the fourth and fifth months of exposure under the influence of AlF_3 in concentrations of 0.10 and 0.03 mg/m^3 (Fig. 2).

The mineral metabolism, studied at the end of the experiment by isotopic tracer and spectral analysis methods, is not disturbed during exposure of the animals to low concentrations of aluminum fluoride; tooth enamel is not damaged either.

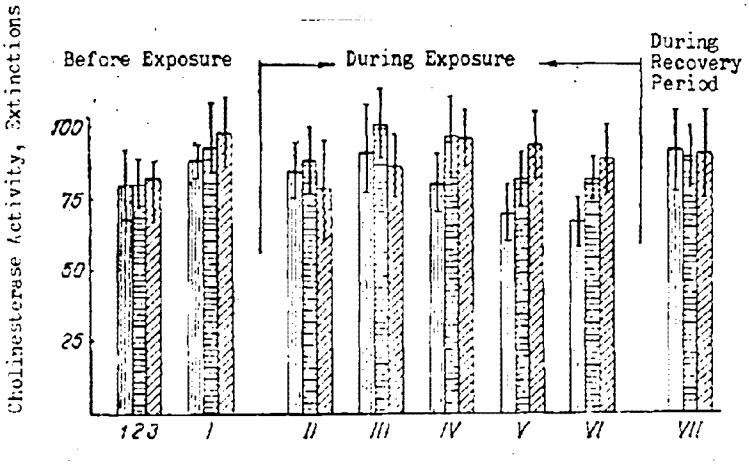

Fig. 1. Activity of blood cholinesterase of experimental animals.
1 - AlF_3 0.10 mg/m^3; 2 - 0.03 mg/m^3; 3 - control

The fluorine content in the urine of animals subjected to the inhalational action of aluminum fluoride during the period of exposure was higher than in the control by a factor of 1 1/2 (Fig. 3), but it was considerably lower than for animals in the experiment with HF and even NaF.

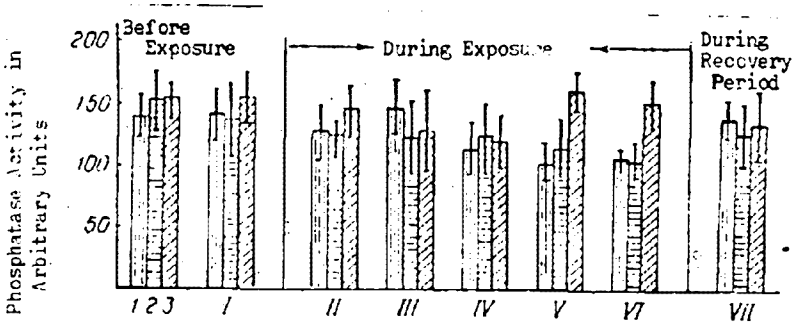

Fig. 2. Activity of blood alkaline phosphatase of experimental animals.

Notation same as in Fig. 1.

Our experiments have shown that during inhalation of HF, the excretion of fluorine by the body takes place mainly through the kidneys (about 90%); during inhalational exposure to AlF_3, the excretion of fluorine is greater through the intestines (about 62%) than through the kidneys (28%). These differences may be explained by the fact that HF is completely absorbed in the respiratory organs, enters the blood, exerts a generally toxic influence, accumulating partly in the bone tissue, and the remaining fluorine is excreted from the body through the kidneys. AlF_3 is swallowed in considerable amounts from the upper respiratory tract and enters the stomach. Insoluble in acid media, it passes into the intestines with the food, and thence, judging from the solubility of AlF_3 in the Ringer-Tyrode solution, may be absorbed in the blood in small amounts only; most of the unabsorbed AlF_3, however, is excreted from the body with the stool.

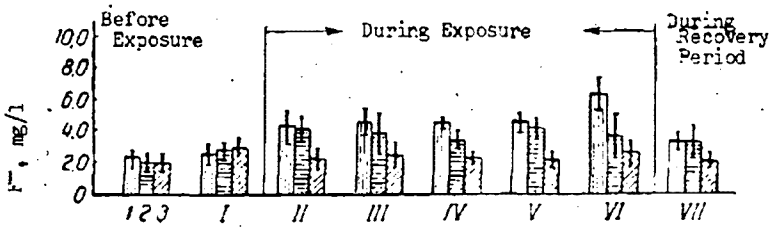

Fig. 3. Fluorine content in the urine of experimental animals.

Notation same as in Fig. 1.

Because of its poor solubility in biological media, AlF_3 has a slight cumulative capacity. The level in the bone tissue during exposure of the animals to AlF_3 is considerably lower than during exposure to HF and NaF. After the animals were exposed to AlF_3 in 0.03 mg/m^3 concentration, statistically reliable differences in the accumulation of fluorine (as compared with the control) were observed only in the teeth. In tubular bones (shoulder and hip) only a tendency toward an increase of the deposition of fluorine

was observed (Table 3).

Table 3

Fluorine Content (in Milligram Percent of Moist Substance) in Teeth, Humerus and Femur.

Group of Animals	Teeth				Humerus				Femur			
	Statistical Criteria											
	n	$X \pm Sx$	t	P	n	$X \pm Sx$	t	P	n	$X \pm Sx$	t	P
First	9	22,8±3,8	2,85	<0,02	9	24,9±1,7	2,50	<0,05	9	25,0±2,3	4,23	<0,001
Second	9	16,7±1,4	3,13	<0,01	9	22,1±2,3	2,21	>0,05	8	16,1±2,0	0,90	>0,05
Control	8	11,8±0,7	—	—	8	18,5±1,9	—	—	8	14,0±1,2	—	—

Analysis of the individual indices shows that the fluorine content of the bone tissue of the controls and "fluorinated" animals is frequently the same.

At the end of the exposure, we determined the content of SH groups in the liver tissue by the Kolthoff-Harris* method, but no reliable changes were found.

A histological analysis of the internal organs and bone tissue of the animals did not reveal any appreciable changes either. Slight changes in the lungs in the form of focal enlargements of interalveolar septa were observed in only a few animals of the first group (at the 0.10 mg/m^3 AlF_3 concentration).

Thus, during round-the-clock exposure of animals to concentrations of 0.10 and 0.03 mg/m^3, AlF_3 has only a slight generally toxic effect. The 0.03 mg/m^3 aluminum fluoride concentration may be regarded as a subthreshold value that causes no accumulation of fluorine in the body and produces no histopathologic changes in the organs and tissues.

During inhalational action on the body, gaseous compounds of fluorine (HF) are first in toxicity, next are fluorine salts, which are highly soluble in biological media (NaF), and last are poorly soluble fluorides (AlF_3, Na_3Alf_6, CaF_2).

Conclusions

1. The threshold of the reflex effect of fluorides poorly soluble in biological media, established by the adaptometric method, is 0.3 mg/m^3, and the concentration of 0.03 mg/m^3 during chronic exposure of the animals is the subthreshold value.

* [Translator's note: Kol'tgoff and Garis, according to the transliteration of Russian reference.]

2. In atmospheric air, the highest single maximum permissible concentration of fluorides (AlF_3, Na_3AlF_6, and CaF_2) sparingly soluble in biological media is recommended at the level of 0.2 mg/m^3, and the mean daily value, 0.03 mg/m^3.

LITERATURE CITED

Note: References mentioned in this paper are to be found at the end of the volume in the 1968 bibliography.

MATERIAL FOR STANDARDIZATION OF THE MAXIMUM PERMISSIBLE CONCENTRATION OF HYDROGEN FLUORIDE IN THE AIR OF POPULATED AREAS

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From Akademiya Meditsinskikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 10, Izdatel'stvo "Meditsina" Moskva, p. 186-201, (1967).

The literature in the Soviet Union and abroad contains extensive material on the toxicology of fluorine and the clinical course of industrial fluorosis (Ye. Ya. Girskaya, 1959, and others). The effect of fluorine in drinking water has also been adequately studied. However, the importance of the relatively low fluorine concentrations present in atmospheric air as a result of industrial discharges has been insufficiently studied thus far.

For a number of years, we conducted studies to determine the level of pollution of atmospheric air in the areas around the aluminum and cryolite industries of the Urals. The zonal distribution of fluorine in air was investigated in connection with the setting up of industrial discharges at various heights (M. S. Sadilova, 1958, 1959, 1964).

Simultaneously with the study of the air medium, an investigation was made into the health of children residing within the effective range of fluorine-containing industrial discharges. It was found that in children subjected to the influence of fluorine compounds, the level of general morbidity and diseases of respiratory organs is higher, and an affection specific for fluorine is observed - mottling of tooth enamel and a higher fluorine content in the urine. In children who live in regions where aluminum plants are located, an increased deposition of fluorine in the bone system was noted. These observations showed that fluorine in atmospheric air should be regarded as one of the major factors in the pathology of the juvenile population (M. S. Sadilova, 1957, 1962; A. F. Aksyuk and G. V. Bulychev, 1962).

Further growth of the aluminum, cryolite, superphosphate, and other industries requires the elucidation of questions concerning the safe concentration of fluorine in atmospheric air.

It should be noted that S. V. Miller (1955) has proposed maximum permissible concentrations of fluorine in the air of populated areas on the basis of calculations. In validating the standard, Miller used the maximum permissible concentration of fluorine in drinking water, 1.5mg/l, assuming that the fluorine compounds in water and air are equally toxic, that the amount

of drinking water consumed is 1.5-2 l per day, and that the amount of air passing through the lungs is 15-20 m^3 per day; the author thus calculated that the concentration of fluorine in inhaled air should not exceed 0.15 mg/m^3. In other words, Miller considers a fluorine concentration of 0.15 mg/m^3 (in terms of the ion) as the threshold value. Considering the fact that fluorine has a significantly unfavorable effect on domestic animals in areas around plants with fluorine-containing discharges into the atmosphere (because of the penetration of fluorine not only with inhaled air, but also in large quantities with grass and vegetation), Miller recommends a maximum permissible concentration with a 15-fold margin coefficient: a highest single concentration of 0.03 mg/m^3, and a mean daily concentration of 0.01 mg/m^3, both of which were adopted.

In our experiment, we studied the influence of several concentrations of hydrogen fluoride, which is the most toxic compound present in industrial discharges of plants. Further stages of the investigation will deal with the influence of hydrogen fluoride and fluorine-containing dust (present both separately and together). An experimental device was used to determine the threshold of olfactory perception of hydrogen fluoride in accordance with a procedure adopted in the Soviet Union. The constancy of the concentrations was checked by collecting samples of inhaled air before and after the study.

The threshold of olfactory perception was determined in 17 subjects with a normal sense of smell. A total of 672 determinations were made, and hydrogen fluoride concentrations from 0.22 to 0.02 mg/m^3 were studied. The minimum perceptible concentration ranged from 0.03 to 0.11 mg/m^3. For the majority of the subjects (10), it amounted to 0.03 mg/m^3.

The maximum imperceptible concentration was 0.02 mg/m^3 (Table 1).

Table 1

Concentrations of hydrogen fluoride studied in the determination of its odor threshold.

Number of Subjects	Number of Observations	Concentration, mg/m^3	
		Threshold	Subliminal
1	43	0,111	0,054
1	37	0,106	0,054
2	76	0,052	0,042
3	123	0,042	0,032
10	393	0,030	0,020

The next stage of our study consisted in the determination of the effect of hydrogen fluoride on the central nervous system via the receptors of the upper respiratory tract. We studied the change in the light sensitivity of the eye of three persons with normal vision, using a procedure commonly

employed in hygiene. Concentrations of 0.02, 0.03, and 0.06 mg/m^3 were studied. Data of the observations showed that the inhalation of hydrogen fluoride in a concentration of 0.03 mg/m^3 and especially 0.06 mg/m^3 causes a marked increase in the light sensitivity of the eye. A concentration of 0.02 mg/m^3 as well as inhalation of pure air did not cause any change in the light sensitivity of the eye (the results are statistically significant). Fig. 1 shows data on the light sensitivity of the eye for one of the subjects.

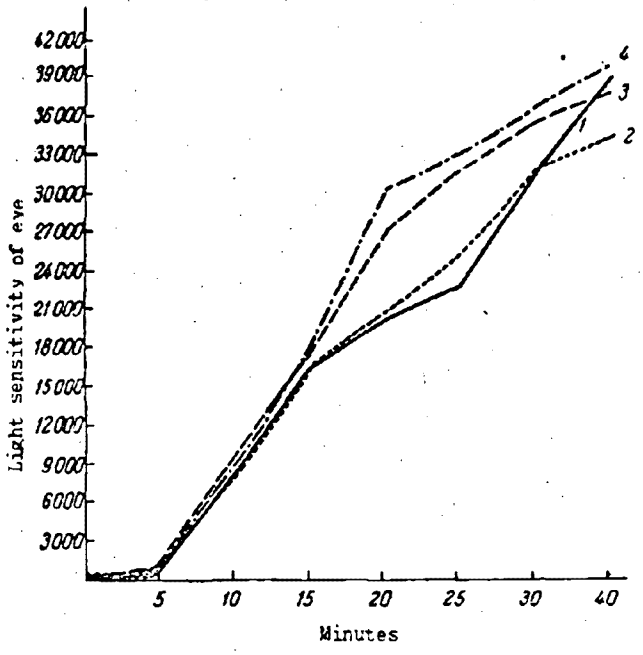


Fig. 1. Light sensitivity of the eye in one of the subjects during inhalation of pure air (1), and hydrogen fluoride in concentrations of 0.02 mg/m^3 (2), 0.03 mg/m^3 (3) and 0.06 mg/m^3 (4).

Thus, the odor threshold and threshold of the reflex effect of hydrogen fluoride on the functional state of the cerebral cortex, determined by the method of adaptometry, are at the same level, 0.03 mg/m^3. These data make it possible to classify hydrogen fluoride among substances with a trigeminal effect.

A chronic round-the-clock exposure of the experimental animals was carried out over the course of 5 months.

The animals were exposed in exposure chambers. The hydrogen fluoride was dispensed by a special device whose glass section was coated with paraffin (in order to prevent the glass from corroding). Distilling flasks were filled with hydrofluoric acid, whose vapors, appropriately diluted with pure air

(18 l/min), were supplied to the exposure chambers. The air leaving the chambers was purified by passing through glass vessels filled with water.

Before the start of the experiment, the concentrations studied - 0.10, 0.03, and 0.01 mg/m^3 - were adjusted so that they were constant in the exposure chambers. The work involved in producing different concentrations of hydrogen fluoride proved to be extremely time-consuming, since the degree of dilution of hydro-fluoric acid had to be determined empirically. The initial solution taken was 40% hydrofluoric acid. It was found that in order to produce a concentration of 0.10 mg/m^3 in the chamber, hydrofluoric acid must be diluted with water in the proportion of 1:27; for a concentration of 0.03 mg/m^3, 1:500; and for a concentration of 0.01 mg/m^3, 1:40,000. The samples of air from the chambers were collected in a filter holder on an ashless membrane filter No. 2, and then in two absorption units connected in sequence and containing doubly distilled water. Fluorine was determined by the alizarin-thorium procedure of S. K. Chirkov (1957). The sensitivity of the procedure was 0.001 mg/m^3. During the exposure, the concentrations of hydrogen fluoride in chambers 1 and 2 were checked five times a day, and in chamber 3 four times. The predetermined concentrations in the chambers showed only insignificant fluctuations.

The experiments were performed on four groups of white female rats with 19-22 rats in each group. Animals two months old were used.

Group I - concentration of hydrogen fluoride 0.10 $\pm$ 0.002 mg/m^3. Group II - 0.03 $\pm$ 0.0001 mg/m^3. Group III - 0.01 $\pm$ 0.00009 mg/m^3. Group IV - control.

The fluorine content in the food ration of the rats was normal: wheaten bread 0.13 mg %, black bread 0.36 mg %, cabbage 0.17 mg %, oat grains 0.17 mg %, dry matter, milk 0.14 mg/l. The animals drank boiled tap water with a fluorine content of 0.7 mg/l. Before and after the experiment, the general state of the animals, their weight, and the composition of peripheral blood were observed. It was noted that the majority of the animals of group II during the first month of exposure were excited (the animals bit each other and also showed aggressiveness toward the experimenter). Subsequently they became as quiet as the animals of the other groups. No weight changes were detected. The composition of peripheral blood (hemoglobin, erythrocytes, reticulocytes, leucocytes, differential leucocyte count) did not show any significant deviations from the norm.

In setting up the chronic experiment, particular attention was paid to the study of the functional state of the central nervous system of the experimental animals. We studied the state of the central nervous system by using the methods of conditioned reflexes and chronaximetry. The method of neurohistology was also employed. The tests were conducted on 8-11 animals of each group.

In the study of the conditioned reflex activity against a background of chronic exposure, use was made of an accelerated variant of the motor-food method for small animals. In animals in Kotlyarevskiy's chamber, two positive conditioned reflexes were developed - to a bell and to red light, and one negative reflex - to a buzzer. After reinforcing the positive reflexes, a stereotype was developed. The stereotype included seven signals that were alternated in a definite sequence: bell, light, light, bell, buzzer, bell, light.

The influence of fluorine on the conditioned reflex activity was estimated from the rate of formation and reinforcement of the reflexes, the number of correct responses, and the length of the latent period. In the development of the stereotype, account was also taken of the state of the differential inhibition, successive inhibition, and character of the intensity relationships of reflexes to stimuli of different intensities. The chronic action of hydrogen fluoride in concentrations of 0.03 and 0.01 mg/m^3 was also studied against a background of functional loads.

The studies showed that hydrogen fluoride in a concentration of 0.10 mg/m^3 causes serious disturbances in the conditioned reflex activity of experimental animals: a retardation of the reinforcement of positive reflexes, an insufficient stability of the latter, and a lengthening of the latent period (Table 2).

Table 2

Formation and Stability of Positive Conditioned Reflexes in Experimental Animals Under the Influence of Hydrogen Fluoride

Concentration, mg/m^3	Statistical Indices	Bell			Light		
		Reflex Appeared	Reflex was Reinforced	Percentage of Loss of Reflexes	Reflex Appeared	Reflex was Reinforced	Percentage of Loss of Reflexes
0,10	M±m t	4,2±0,5 1,6 (c)*	15,1±2,9 3,6 (b)	6,3±0,8 5,7 (c)	5,7±0,8 4,1 (c)	38,1±7,6 4,3 (c)	17,0±1,5 9,8 (c)
0,03	M±m t	4,3±0,3 3,0 (b)	9,5±2,3 2,1 (a)	5,5±1,7 2,3 (a)	3,9±0,4 2,3 (a)	11,3±4,5 1,5 (o)	6,3±1,0 4,0 (b)
0,01	M±m t	3,3±0,1 1,6 (o)	4,7±1,1 0,2 (o)	1,3±0,4 0,2 (o)	2,4±0,2 0 (o)	4,3±1,0 0,1 (o)	1,8±0,4 0,6 (o)
Control	M±m	3,4±0,1	4,5±0,6	1,4±0,3	2,4±0,2	4,5±0,9	2,1±0,3

* Degree of significance: a - 95%; b - 99%; c - 99.9%; o - not significant

In the development of the stereotype in these animals, there was recorded a large percentage of cases of successive inhibition and disinhibition of differentiations as compared with the groups of animals exposed to lower concentrations of hydrogen fluoride and with the control group. Also observed were disturbances of the intensity relationships of conditioned reflexes to the weak and strong stimuli (appearance of equalizing and paradoxical phases, Table 3).

Table 3

Effect of Hydrogen Fluoride on the Conditioned Reflex Activity of Experimental Animals in the Process of Formation and Reinforcement of the Organism.

Indices	Statistical Indices	Concentration, mg/m³			Control
		0.10	0.03	0.01	
Latent period: To bell	M ± m t	1,37 ± 0,03 16,7 (c)*	0,63 ± 0,04 2,0(o)	0,69 ± 0,02 1,1 (o)	0,65 ± 0,03
To light	M ± m t	2,09 ± 0,05 11,5 (c)	1,38 ± 0,03 0,7(o)	1,49 ± 0,03 1,8 (o)	1,41 ± 0,03
Disturbance of Intensity Relationships:					
Equalizing phase	M ± m t	3,3 ± 1,8 1,3 (o)	3,0 ± 0,9 1,0(o)	Her —	1,8 ± 0,7
Paradoxical phase	M ± m t	6,3 ± 1,40 4,5 (c)	2,7 ± 0,9 3,0 (b)	Her —	Her
Loss of reflex:					
To bell	M ± m t	3,0 ± 0,45 6,6 (c)	Her —	0,11 ± 0,1 1,1 (o)	Her
To light	M ± m t	13,0 ± 1,2 10,4 (c)	2,6 ± 2,6 3,6 (b)	0,33 ± 0,18 0,1 (o)	0,36 ± 0,12
Successive Inhibition: To bell	M ± m t	23,3 ± 4,02 5,7 (c)	13,3 ± 3,3 3,9 (c)	0,33 ± 0,18 0,6 (o)	0,1 ± 0,13
To light	M ± m t	31,0 ± 5,1 5,9 (c)	17,7 ± 4,7 3,3 (b)	0,77 ± 0,29 0,32 (o)	0,9 ± 0,3

* Degree of significance: a - 95%; b - 99%; c - 99.9%; o - not significant.

Changes in the conditioned reflex activity were also noted in animals subjected to the action of hydrogen fluoride in a concentration of 0.03 mg/m^3, but they were observed with particular clarity against the background of functional loads (24-hour starvation). After the 24-hour starvation, animals of this group showed an increase in the number of losses of conditioned reflexes to light and an increase in cases of successive inhibition.

A concentration of 0.01 mg/m^3 caused no changes in the conditioned reflex activity of the animals.

Toward the end of the one-month recovery period, the conditioned reflex activity of the animals subjected to the action of hydrogen fluoride in a concentration of 0.10 mg/m^3 improved somewhat, but remained altered relative to the control. The conditioned reflex activity of the animals which inhaled hydrogen fluoride in a concentration of 0.03 mg/m^3 was restored completely.

The motor chronaxy of antagonist muscles was measured on the shin of the right hind limb. The tests were performed with a GIF condenser chronaximeter an average of three times a month at a fixed time and under the same conditions. The nerve cords were stimulated by the unipolar method. Average data on the measurement of the chronaxy of antagonist muscles according to groups are shown in Fig. 2.

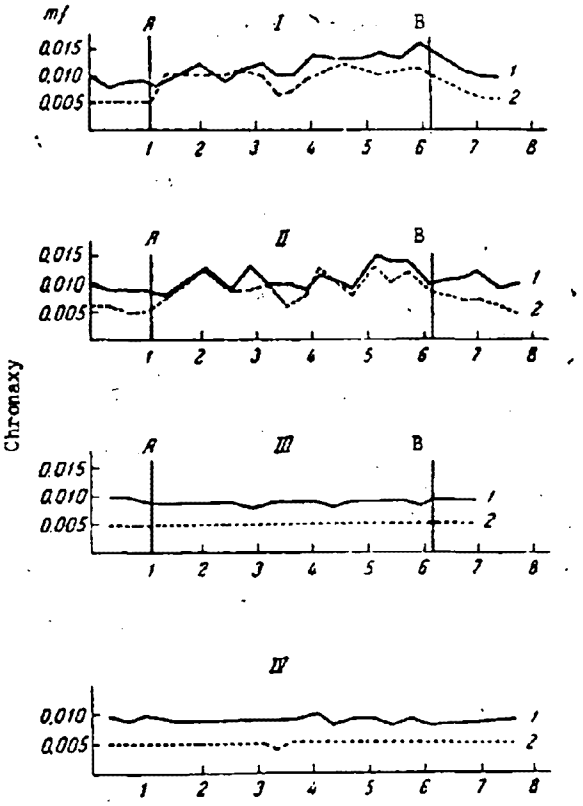
In rats of groups III and IV (control), the subordinational influences of the brain were within the normal range.

In the experimental animals of groups I and II, changes in chronaxy were observed immediately after the start of exposure and were manifested in a prolongation, equalization, and reversed ratio of the chronaxies of antagonist muscles. It should be noted in this connection that the prolongation of the chronaxies in animals of groups I and II was characteristic chiefly of flexors, whereas a prolongation of the chronaxies of extensors was observed in 38.4 and 30.8% of the cases respectively. The results of the tests are statistically significant.

The changes which we observed in the activity of the central nervous system may be regarded as a manifestation of a deep inhibition encompassing the complex system of cortical and subcortical subordination centers. In the experimental animals of groups I and II, there was established a statistically significant depression of the activity of cholinesterase, the enzyme involved in the transmission of nervous excitation.

Neurohistological studies* of the brain were conducted in the area of motor and sensory systems. Interneuronal connections and the state of the nerve cells were studied in this case.

* The histological examinations were performed by O. K. Shturkina (Sverdlovsk Medical Institute).



Fig, 2. Chronaxy of antagonist muscles in rats during their exposure to hydrogen fluoride in groups I, II, III, and IV.

1 - extensor muscles; 2 - flexor muxcles; AB - period of exposure.

The following symptoms were observed in animals of group I: hyperemia of vessels of the membranes and substance of the brain, perivascular edema, thickening of dendrites with the formation of beaded swellings on them and the disappearance of cytoplasmic outgrowths, the so-called spines. With regard to the nerve cells, a change of their structure consisting of an uneven staining of the Nissl substance, its partial lysis, thickening, swelling, and shriveling of the cytoplasm were established. In some nerve cells, death of the nuclei and neuronophagia were observed. At the end of the three-month recovery period, some shifts tending to offset the process were noted: the destructive changes in the nerve cells were less distinct, and the spines on the dendrites were seen more distinctly. The process was not completely compensated, since in some nerve cells profound destructive changes were observed, i. e., cells with lost nuclei. These data account for the fact that the conditioned reflex

activity of animals of group I during the recovery period continued to be altered. For this group of animals, disturbances of the nervous activity cannot be considered to be exclusively functional.

Some authors (De Eds, 1936; Roholm, 1937; Thomas, Wilson, and De Eds, 1935) attribute the changes in bone tissues characteristic of fluorosis to a disturbance of the phosphorus-calcium metabolism as a result of the inhibitory action of fluorine on the enzyme phosphatase. These authors postulate that phosphatase participates in processes of bone formation by liberating inorganic phosphorus from esters of phosphoric acid; this phosphorus combined with calcium ions forms phosphorus-calcium salts necessary for building bone tissues. Roholm (1937) ascribes in these processes a prime importance to alkaline phosphatase. However, literature data on the effect of fluorine on the activity of phosphatases are very contradictory.

Our observations on alkaline phosphatase were carried out on 6 animals of each group. The phosphatase activity was determined by using the procedure of G. K. Shlygin and S. Ya. Mikhlin. It was found that the initial period of increase in the activity of the enzyme in animals of groups I and II is followed by a decrease in this activity. The activity of alkaline phosphatase in animals of group III, exposed to hydrogen fluoride in a concentration of 0.01 mg/m^3, was at the level of the control.

Despite the fluctuations in the activity of alkaline phosphatase during certain periods of exposure, the inorganic phosphorus content of the blood was practically stable and did not exceed the limits of the physiological norm. This is apparently because the phosphorus level in the blood is not maintained by the activity of phosphatases alone. It is known that the activity of phosphatases even in a healthy organism is not a constant, while the content of inorganic phosphorus fluctuates within very narrow linits. Probably the mechanism by which inorganic phosphorus is maintained at a constant level in the blood is complex and varied. It has been established that phosphoric acid salts can immediately enter the blood from their reserve in the bones when the inorganic phosphorus content of the blood has dropped.

Since the literature contains indications of a decrease in the activity of bone phosphatase in rats acted upon by fluorine, we also checked its activity in our experimental animals after the end of exposure. Bone phosphatase was determined in the tibia of 6-11 animals of each group using A. Bogdanskiy's procedure with slight modifications by Ye. P. Yeremin and Z. A. Kasparskaya (1950). Our studies did not show any change in the activity of bone phosphatase under the influence of the hydrogen fluoride concentrations studied. As soon as clinical symptoms of fluorosis became known, it was commonly accepted that one of its early manifestations was the mottling of tooth enamel.

Before the start of the experiment, the condition of the teeth was checked in animals of all the groups, and was subsequently checked regularly in the course of exposure. The tooth damage was evaluated on a 4-point scale. Our observations (Table 4) confirmed that the mottling of tooth enamel is indeed an early specific manifestation of morphological changes under the influence of fluorine. In white rats, the color of healthy teeth is yellowish, and the teeth are shiny and resemble amber. In 5 animals of group I, as early as after the first month of exposure, the teeth became transparent, whitened, and lost their shine. As the period of exposure grew longer, the extent of damage increased, and toward the end of the 5th month, all the animals showed a moderate form of damage: the upper and lower incisors resembled marble, they were rough, streaked, and the ends of the incisors were worn down.

In animals of group II, the changes in the teeth were less marked and appeared later than in group I.

Table 4

Mottling of Tooth Enamel in Experimental Animals

Number of Animals Observed	Degree of Damage	Time of Observation During the Period of Exposure, Months				
		1	2	3	4	5
		Number of Animals with Damaged Teeth				
	Group I					
19	Very little	1	9	2		
	Little	4	4	2	2	
	Moderately		2	15	17	19
	Markedly					
	Group II					
20	Very little			2	2	4
	Little		1	2	6	7
	Moderately					
	Markedly					
	Group III					
22	Very little					2
	Little					
	Moderately					
	Markedly					

At the end of exposure, histological analyses of animals in groups I and II showed a thinning of the enamel and dislocation of the enamel prisms. In the animals of these groups, definite changes in the bone tissue were also noted. In animals of group I, a narrowing of the bone-marrow channel of tubular bones was observed, and the outlines of the periosteum were irregular. In the pelvic bones there was disturbance to the structure of the osteons*, lysis

* Editor's note: probably bone tissues.

of osteocytes, and in the region of the periosteum, a focal resorption of the osseous substance with growth of connective tissue. Calcium was deposited unevenly in the bones. In animals of group II, the changes were less pronounced and were localized primarily in the lumbar section of the spinal column and in the pelvic bones. An irregularity of the periosteum, focal disorganization of the structure of osteons, and an irregular deposition of calcium were noted.

The changes observed in the teeth and bone tissue constitute an irrefutable proof of a disturbance of the phosphorus-calcium metabolism under the influence of hydrogen fluoride.

H. Christiani attaches considerable importance to the level of deposition of fluorine in the bone skeleton, assuming that an increased fluorine content of bones constitutes a diagnostic means of detecting early symptoms of fluorine intoxication. He also holds that the severity of osseous changes is related to the extent of deposition of fluorine. After the completion of exposure, we determined the deposition of fluorine in the teeth and tibia of 6 animals of each group. The teeth and bones were carefully separated from the soft tissues, dried to a constant weight, ground up, then a sample of 0.03 g was taken, calcinated, and dissolved in 3 drops of 1:1 hydrochlpric acid, then passed through an ion exchange column with an AV-17 anion exchanger. The amount of fluorine evolved from the column was then determined by the alizerin thorium procedure. The analyses showed that hydrogen fluoride concentrations of 0.10 and 0.03 mg/m^3 cause the accumulation of fluorine in the organism.

We can draw a certain parallel between the osseous changes and the level of deposition of fluorine in the bones, and in this respect our data are in accord with H. Christiani's point of view.

Table 5

Fluorine Content in the Tooth and Bone Tissues of Experimental Animals (in milligram-percent of dry substance).

Group of Animals	Teeth		Tibia	
	M±m	t	M±m	t
I	110,5±5,60	17,27 (c)	121,3±8,70	9,57 (c)
II	18,2±1,20	3,87 (b)	51,4±3,20	5,12 (c)
III	15,2±2,14	1,27 (o)	28,9±2,85	1,11 (o)
Control	12,2±0,98		23,3±4,0	

* Degree of confidence: b - 99%; c - 99.9%; o - not significant

During the experiment, we followed the fluorine content in the urine. Fluorine in the urine is also determined by ion exhange chromatography, which was first used for this purpose in the U. S. A. (Harold, Nielsen, Logan, Utan, 1960; Talvitie, Brewer).

An increase of the fluorine concentration in the urine was noted starting with the 2nd month of exposure, and its highest level, which substantially exceeded the control in all the experimental groups, was established toward the end of exposure. Despite the high degree of excretion of fluorine, the latter, as indicated above, was deposited in the bone system.

Histological analysis of the viscera (after the completion of exposure) in animals of group I showed in the upper respiratory tract, desquamation of epithelial cells with the baring of the basal layer, hyperemia of the vessels, and focal inflammatory infiltration with lymphocytes, leucocytes, and histiocytes. Symptoms of acute focal inflammation of the nasal mucosa were pronounced in all the animals, but in different degrees. Symptoms of bronchitis and peribronchitis were observed in the bronchi. The vessels of the lungs were hyperemic, and symptoms of focal pneumonia were noted in two cases out of 5. In the liver there was protein and fatty degeneration, and in the kidneys, protein degeneration and an increased permeability of the arterioles. In the spleen, hyperemia of the vessels of the red pulp was noted, and in the white pulp there was a reduction of certain lymphoid follicles and hyperplasia of reticular cells. The walls of the central artery of the spleen were thickened as a result of plasma infiltration. Changes in the myocardium were characterized by the disappearance of cross striation and separation of myofibrils.

In animals of group II, the changes were less pronounced. In some areas, the nasal mucosa was thinned (the structure of the cells was not distinctly visible), and in some cases, on the contrary, proliferation of the epithelium was noted. Hypersecretion and desquamation of the epithelium was present in the bronchi. Hyperemia was noted in the lungs and in parenchymatous organs.

In animals of group III, the histological analysis did not uncover any changes.

Conclusions

1. The threshold of odor and the threshold of the reflex effect of hydrogen fluoride on the human organism, established by the method of dark adaptation, are both at the same level, 0.03 mg/m^3.

2. In a five-month exposure, hydrogen fluoride concentrations of 0.10 and 0.03 mg/m^3 cause a number of disturbances in the organism of warm-blooded animals:

a) Phenomena of inhibition in the central nervous system, with the 0.10 mg/m^3 concentration causing irreversible destructive changes in the nerve cells;

b) Change in the phosphorus-calcium metabolism;

c) Accumulation of fluorine in the bone system;
d) Histopathological changes in the teeth, bone system, and viscera.

3. The extent of the changes observed in the organism is related to the concentration of hydrogen fluoride in the inhaled air.

4. A hydrogen fluoride concentration of 0.01 mg/m^3 causes no changes in the organism of the experimental animals.

5. Our investigations showed that:
a) A hydrogen fluoride concentration of 0.15 mg/m^3 (in terms of the fluoride ion 0.147 mg/m^3) cannot be regarded as the threshold concentration;
b) A hydrogen fluoride concentration of 0.03 mg/m^3 cannot be the maximum permissible highest single concentration.

6. The highest single concentration of hydrogen fluoride must not exceed 0.02 mg/m^3, and the mean daily concentration, 0.01 mg/m^3.

LITERATURE CITED

Note: References mentioned in this paper are to be found at the end of the volume in the 1967 bibliography.

REFLEX EFFECT ON THE HUMAN ORGANISM OF LOW CONCENTRATIONS OF ACETIC ACID AND ACETIC ANHYDRIDE PRESENT SEPARATELY AND TOGETHER IN ATMOSPHERIC AIR

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From Akademiya Meditsinakikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 11, Izdatel'stvo "Meditsina" Moskva, p. 73-91, (1968).

Acetic acid, CH_3COOH (methanecarboxylic acid), is a monobasic organic acid of the fatty series. It has a pungent acid odor; it is miscible with water and organic solvents (alcohol, ether) in all proportions, solidifies at a low temperature, its melting point is +16.7°C., boiling point 118.1°C., and specific gravity at 20°C., 1.049. Acetic anhydride, $(CH_3CO)_2O$, is an organic compound, the simplest of the carboxylic acid anhydrides, a colorless liquid with a sharp stifling odor; its boiling point is 139.6°C, melting point 73°C., and specific gravity at 20°C., 1.082. It dissolves in cold water to the extent of 12% and dissolves well in alcohol and ether.

Acetic acid has been known in Europe since the ninth century, and is widely employed as a mordant or solvent in the textile industry, in dye works, in the production of linoleum, cellulose acetate, alkylacetates, and in many organic syntheses (production of esters, acetates, etc.).

Acetic anhydride is used in the chemical industry for the production of cellulose acetate and many drugs and in the manufacture of certain explosives.

Sources of atmospheric pollution with acetic acid and acetic anhydride may be plants that either produce or consume them in their technological processes. The literature contains no data on acetic acid or acetic anhydride as atmospheric pollutants, but data from sanitary studies of the air of industrial buildings confirm the possibility of such pollution.

According to the data of Ye. N. Kuprits and B. S. Shender, a study of an acetic acid plant revealed acetic acid vapors in concentrations from 62 to 120 mg/m^3 in the air of a plant section. S. L. Danishevskiy (1951), in a study of plants producing acetic acid and acetic anhydride by dehydration of ketene, found vapors of ketene, acetic acid and acetic anhydride in total concentrations ranging from 1 to 70 mg/m^3.

High concentrations of acetic acid vapors (125-440 mg/m^3) were found in 1957 by Ghiringhelli Di Fabio in the production of cellulose acetate. G. N. Nazyrov studied the air of sections in three hydrolysis plants where

acetic acid was formed as a by-product. According to his data, the highest concentrations of acetic acid vapors in the air of a plant section amount to 50 mg/m^3. Since acetic acid and acetic anhydride in the air of plant buildings and in atmospheric air are in the form of vapors, they enter the human body mainly via the respiratory tract. Acetic acid vapors cause considerable irritation of the mucous membrances of the respiratory tract and eyes, resulting in lacrimation, cough, and restriction of breathing. The problem of the toxic effect of acetic acid has been insufficiently treated in the literature.

The effect of high concentrations of acetic acid is discussed in the works of Flyuri and Tsernik, N. V. Lazarev, Ghiringhelli Di Fabio, B. V. Vladykin, A. I. Shibkov, G. G. Zakharov, Jamado, M. G. Ibragimov and Ye. Z. Lisnyanskiy, and others. The chronic action of acetic acid vapors causes affections of the nose, nasopharynx, mouth, larynx and also conjunctivitis and bronchitis among workers. The concentrations responsible range from 62 to 125 mg/m^3 (Shender, Ye. N. Kuprits, Ghiringhelli Di Fabio). The maximum permissible concentration of acetic acid for plant buildings adopted in the Soviet Union is 5 mg/m^3. In the USA, it is five times as high as the concentration adopted in the USSR for acetic acid and is equal to 10 parts per million (by volume), i.e., to 24.5 mg/m^3.

Literature data on the toxicity of acetic anhydride are very limited. The toxic effect of acetic anhydride vapors is qualitatively analogous to that of acetic acid, but is stronger and more dangerous because of the removal of water from the tissues (F. Flyuri, F. Tsernik, N. V. Lazarev). The maximum permissible concentration of acetic anhydride for plant shops has not been established.

Thus, neither in the Soviet nor in the foreign literature have we found any studies dealing with the influence of low concentrations of acetic acid and acetic anhydride vapors (of the order of the maximum permissible values for plant sections or lower) on the human and animal organism. Their odor threshold concentrations have also been unknown. In view of this fact, we decided to substantiate experimentally the highest single maximum permissible concentrations of acetic acid and acetic anhydride present separately and together in the air of populated areas.

To determine acetic acid under experimental conditions, we used a colorimetric method developed by Yu. V. Dyuzheva (1960). The method involves a preliminary transfer of acetic acid into ether and its determination with hydroxylamine and ferric chloride. The sensitivity of the method is 5 mg per 3 ml. The method is nonspecific: the total monobasic carboxylic acids are determined; esters interfere with the determination. However, these impurities were absent in our studies. The air was drawn at a rate of 0.5-0.6 l/min through two absorbers with porous plates No. 1 filled with 2 ml of alcohol.

The samples may be withdrawn by using ASM silica gel with a grain size of 1-2 mm (2 g of silica gel is placed in one modified Zaytsev absorber) at a rate of 5 ℓ/min (M. V. Alekseyeva).

The method of determination of acetic anhydride in air was developed by Ye. V. Deyanova (1964). The method is based on the preparation of hydroxamic acid by the reaction of acetic anhydride with hydroxylamine hydrochloride and involves the colorimetric determination of hydroxamic acid with ferric chloride. The sensitivity is 0.01 mg per 3 ml (according to the author). In accordance with the author's recommendation, we raised the sensitivity of the method to 0.005 mg in a volume of 3 ml. Specificity: acetic acid does not interfere with the determination. The air samples were drawn at a rate of 0.8-1 l/min into two absorbers connected in succession and containing porous plate No. 1, filled with 4 ml of a 1% alcohol solution of hydroxylamine. In the determination of the combined action of acetic acid and acetic anhydride, each substance was determined separately.

Table 1

Thresholds of Olfactory Perception of Acetic Acid and Acetic Anhydride.

Number of Subjects	Concentration, mg/m³		Total Number of Tests
	Minimum Perceptible	Imperceptible	
Acetic Acid			
1	1,57	1,22	24
3	1,22	0,92	69
5	0,92	0,81	119
10	0,81	0,60	253
5	0,70	0,60	102
6	0,60	0,51	162
Total 30			731
Acetic Anhydride			
1	1,20	1,03	24
2	1,03	0,80	49
7	0,80	0,60	195
6	0,60	0,51	137
5	0,49—0,51	0,41	122
Total 21			533

In order to determine the highest single maximum permissible concentration of acetic acid and acetic anhydride in atmospheric air, we used the methods recommended by the department of sanitary protection of atmospheric air. We studied the threshold of olfactory perception of acetic acid vapors in 30 persons. Ten acetic acid concentrations ranging from 5.51 to 0.51 mg/m^3 were investigated. In all, 731 observations were made. The threshold of olfactory perception was determined for acetic anhydride in 21 persons. Eleven acetic anhydride concentrations were studied, ranging from 4.50 to 0.41 mg/m^3, and 533 determinations were made. The results are given in Table 1.

As is evident from this table, the threshold of olfactory perception of acetic acid in the most sensitive persons is 0.60 mg/m^3, and that of acetic anhydride, 0.49 mg/m^3. Concentrations of 0.51 mg/m^3 acetic acid and 0.41 mg/m^3 acetic anhydride were found to be imperceptible.

The threshold of the reflex effect of low acetic acid and acetic anhydride concentrations on the light sensitivity of the eye was determined with an ADM adaptometer using a common procedure. Three persons 17, 18, and 30 years participated in the study. In all, 120 observations were carried out.

The data obtained show that the inhalation of acetic acid vapors in a concentration of 0.60 mg/m^3 causes a marked increase of the light sensitivity in the 20th minute in all the subjects. A concentration of 0.48 mg/m^3 caused a statistically reliable increase of the light sensitivity in two persons. A concentration of 0.37 mg/m^3 was found to be inactive in all three subjects.

Results of adaptometric studies with acetic anhydride showed that a concentration of 0.50 mg/m^3 causes a statistically reliable change in the course of the dark adaptation curve in all three subjects, a concentration of 0.36 mg/m^3 in only two subjects, and a concentration of 0.25 mg/m^3 did not produce any changes in the subjects.

Results of the effect of the substances studied on the light sensitivity of the eye are presented in Table 2.

Thus, the threshold of the reflex effect of acetic acid on the functional state of the cerebral cortex, determined by the adaptometric method, is equal in the most sensitive individuals to 0.48 mg/m^3, and the threshold of acetic anhydride, 0.36 mg/m^3. The inactive concentration for acetic acid is 0.37 mg/m^3, and for acetic anhydride, 0.25 mg/m^3.

The next stage of our study consisted in determining the threshold of the effect of acetic acid and acetic anhydride vapors on the electrical activity

Table 2

Light Sensitivity of Eyes in the 20th and 25th Minutes of Adaptation During Inhalation of Acetic Acid and Acetic Anhydride Vapors in Percent of 15th Minute.

Subject	Minute of Test	Pure Air	Acetic Acid Concentration mg/m³			Pure Air	Acetic Anhydride Concentration mg/m³		
			0,60	0,48	0,37		0,50	0,36	0,25
N.	20-	146,0	254,0 (c)	246,0 (c)	149,0 (o)	144,6	223,4 (c)	211,6 (c)	147,5 (o)
	25-	187,0	225,8 (c)	192,8 (o)	193,0 (o)	190,3	217,0 (c)	217,4 (c)	192,0 (o)
T.	20-	176,5	269,0 (c)	217,1 (c)	178,5 (o)	173,8	214,7 (c)	206,2 (c)	179,2 (o)
	25-	242,8	190,8 (c)	239,1 (o)	237,5 (o)	235,1	197,7 (c)	225,6 (b)	244,5 (o)
A.	20-	139,5	177,0 (c)	152,0 (o)	146,0 (o)	145,2	174,0 (c)	149,2 (o)	141,2 (o)
	25-	204,8	184,1 (b)	198,2 (o)	194,9 (o)	208,9	247,4 (b)	206,9 (o)	204,4 (o)

Note. Confidence factor: a - 95%, b - 99%, c - 99.9%, o - unreliable.

of the brain by means of the electrocortical conditioned reflex method described by K. A. Bushtuyeva, Ye. F. Polezhayev and A. D. Semenenko (1960).

Our observations were carried out on an eight-channel Hungarian electroencephalograph (Orion Budapest). The biocurrents were recorded from the temporal and occipital parts of both cerebral hemispheres of the subjects, using the bipolar method. The experiment involved five persons with a normal function of the olfactory system and a distinct alpha rhythm.

We studied the influence of inhalation of three acetic acid concentrations (0.36, 0.29, and 0.18 mg/m^3) as well as three acetic anhydride concentrations (0.25, 0.18, and 0.11 mg/m^3) on the change of the electrical activity of the brain. The tests were conducted four times for each concentration, with alternation of the test with pure air. In all, 140 observations were made.

The data obtained were treated and checked for statistical reliability.

The material of the electroencephalograms was treated in the following manner: in each pairing of light and gas in the first ten seconds (before the light was turned on), the duration of desynchronization was calculated in seconds (desynchronization smaller than 40% of the amplitude of the basic rhythm and lasting less than 0.5 second was not considered in the calculation), both during the action of pure air and in the presence of the specified concentration of acetic acid and acetic anhydride.

The statistical treatment was carried out in two variants:

In the first variant, the values of the duration of desynchronization were summed up for all 25 pairings during the action of both pure air and the substance studied;

In the second variant, the values of the duration of desynchronization of the alpha rhythm were also summed up, but only if they blended with desynchronization caused by the light, also over 25 pairings, in the presence of both pure air and the substance studied.

Statistical treatment according to the two variants gave almost the same results.

Data obtained by studying the influence of acetic acid vapors on the electrical activity of the brain showed that of the five subjects tested, the threshold of formation of the electrocortical conditioned reflex is an acetic acid concentration of 0.36 mg/m^3 for two subjects, and 0.29 mg/m^3 for the remaining three (Fig. 1). The 0.18 mg/m^3 concentration was found to be inactive for all the subjects.

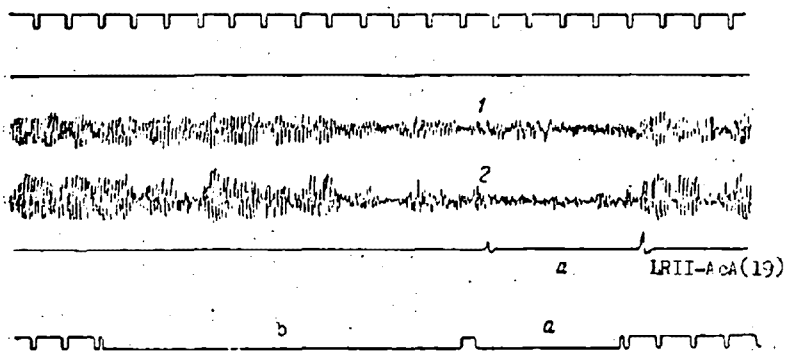

Fig. 1. Electroencephalogram of subject L. R. Conditioned reflex desynchronization occurred during inhalation of acetic acid in a concentration of 0.29 mg/m³ (at the 19th pairing).

1 - electroencephalogram from the left temporal-occipital area; 2 - electroencephalogram from the right temporal-occipital area; a - mark indicating light was turned on; b - mark indicating supply of gas.

Results of the study of the influence of acetic anhydride vapors showed that in three subjects, the conditioned electrocortical reflex was formed at acetic anhydride concentrations of 0.25 mg/m^3; the 0.18 mg/m^3 concentration produced a conditioned reflex desynchronization in two subjects (Fig. 2). The 0.11 mg/m^3 concentration was found to be inactive for all the subjects (Fig. 3).

The changes we obtained were statistically reliable. In attempting to give a general evaluation of the observations made in the study of the conditioned reflex effect of acetic acid and acetic anhydride on the electrical activity of the brain, we note that the conditioned reflex (or desynchronization of the alpha rhythm) was developed in the course of a single experimental day, usually at the 7th-9th pairing of light and gas (acetic acid and acetic anhydride) and was retained until the 22nd-23rd pairing, after which it became extinguished (Fig. 4 and 5). Desynchronization of the alpha rhythm appeared with a minimum latent period (2-5 seconds) and continued until the light was turned on.

Thus, we have established that in the most sensitive persons, the threshold of the conditioned-reflex change of the brain's electrical activity for acetic acid lies at a level of 0.29 mg/m^3 and for acetic anhydride, at 0.18 mg/m^3. The inactive concentration for acetic acid was found to be 0.18 mg/m^3 and for acetic anhydride, 0.11 mg/m^3.

Combined data on the odor thresholds and reflex effects of acetic acid and acetic anhydride are listed in Table 3.

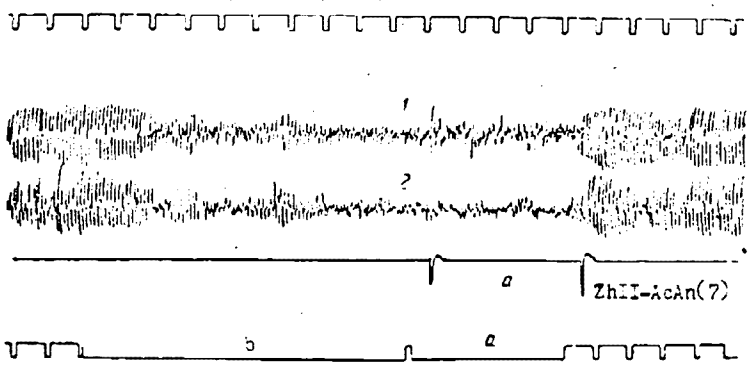

Fig. 2. Electroencephalogram of subject Zh. N. Conditioned-reflex desynchronization occurred during inhalation of acetic anhydride in a concentration of 0.18 mg/m³ (7th pairing). Notation same as in Fig. 1.

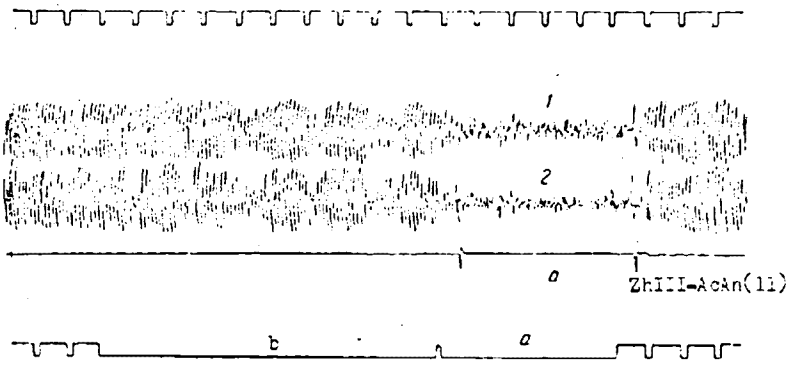

Fig. 3. Electroencephalogram of subject Zh. N. Conditioned-reflex desynchronization did not occur during inhalation of acetic anhydride in a concentration of 0.11 mg/m³ (11th pairing). Notation same as in Fig. 1.

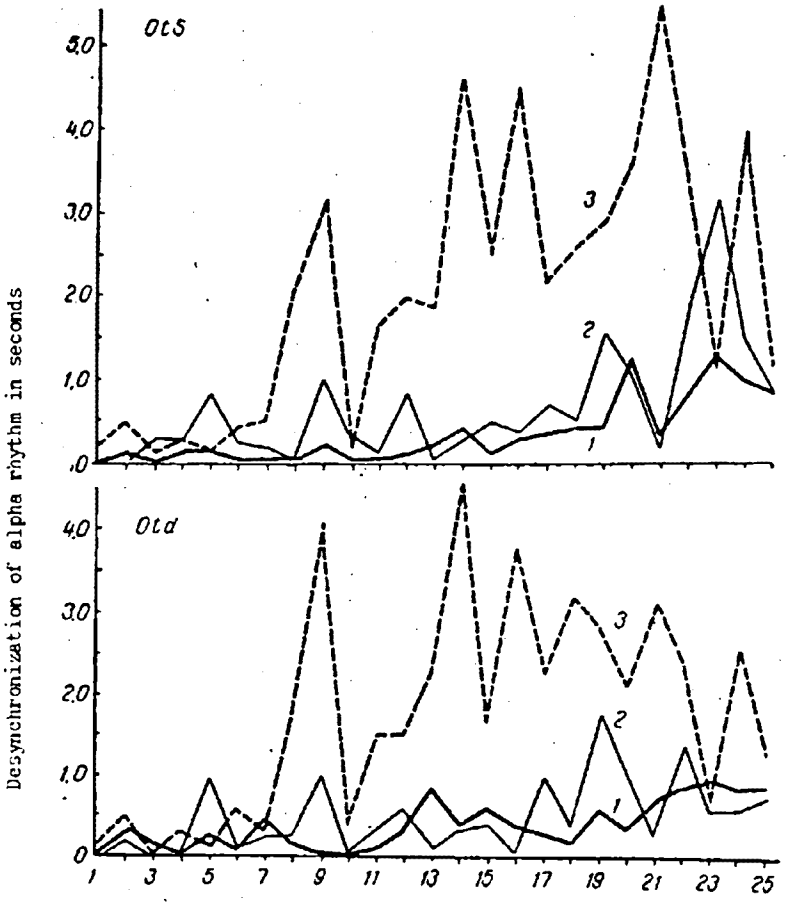

Fig. 4. Change in the electrical activity of the brain in subject L. R. during inhalation of different concentrations of acetic acid.

1 - pure air; 2 - 0.18 mg/m^3; 3 - 0.29 mg/m^3

Table 3

Thresholds of the Effect of Acetic Acid and Acetic Anhydride on Man

Substance	Olfactory Perception		Light Sensitivity of the Eye		Electrocortical conditioned reflex		Highest Single MPC
	Perceptible	Imperceptible	Active	Inactive	Active	Inactive	
	Concentrations, mg/m³						
Acetic Acid	0,60	0,51	0,48	0,37	0,29	0,18	0,2
Acetic Anhydride	0,49	0,41	0,36	0,25	0,18	0,11	0,1
Combinations: Acetic Acid	0,16	0,19	0,25	0,15	0,15	0,145	
Combinations: Acetic Anhydride	0,35	0,24	0,18	0,18	0,087	0,06	
Sum of Fractions of Effect Threshold	0,94	0,80	1,06	0,81	0,99	0,83	

Sum of fractions of maximum permissible concentration: active - 1.62; inactive - 1.32.

On the basis of all of the above data, we propose 0.2 mg/m^3 as the highest single maximum permissible concentration of acetic acid in atmospheric air, and 0.1 mg/m^3 for acetic anhydride.

In recent years, the combined action of low concentrations of atmospheric pollutants has been widely investigated. Studies have been made on the combined action of sulfur dioxide and sulfuric acid aerosol (K. A. Bushtuyeva, 1961), chlorine and hydrogen chloride (V. M. Styazhkin, 1962), carbon disulfide and hydrogen sulfide (B. K. Baykov, 1963), carbon disulfide, hydrogen sulfide and Dowtherm (Kh. Kh. Mannanova, 1964), acetone and acetophenone (N. Z. Tkach, 1965), phenol and acetophenone (Yu. Ye. Korneyev, 1965), etc. The authors showed that the character of the effect of a mixture of two and three atmospheric pollutants on the human and animal body is determined as a total or partial summation. In one case, during inhalation of a mixture of hydrogen sulfide, carbon disulfide and Dowtherm, a certain potentiation of their effect was noted. For this reason, the next objective of our study was to investigate the combined action of acetic acid and acetic anhydride on the human organism. The

study of this combination is of major sanitary importance: the source of

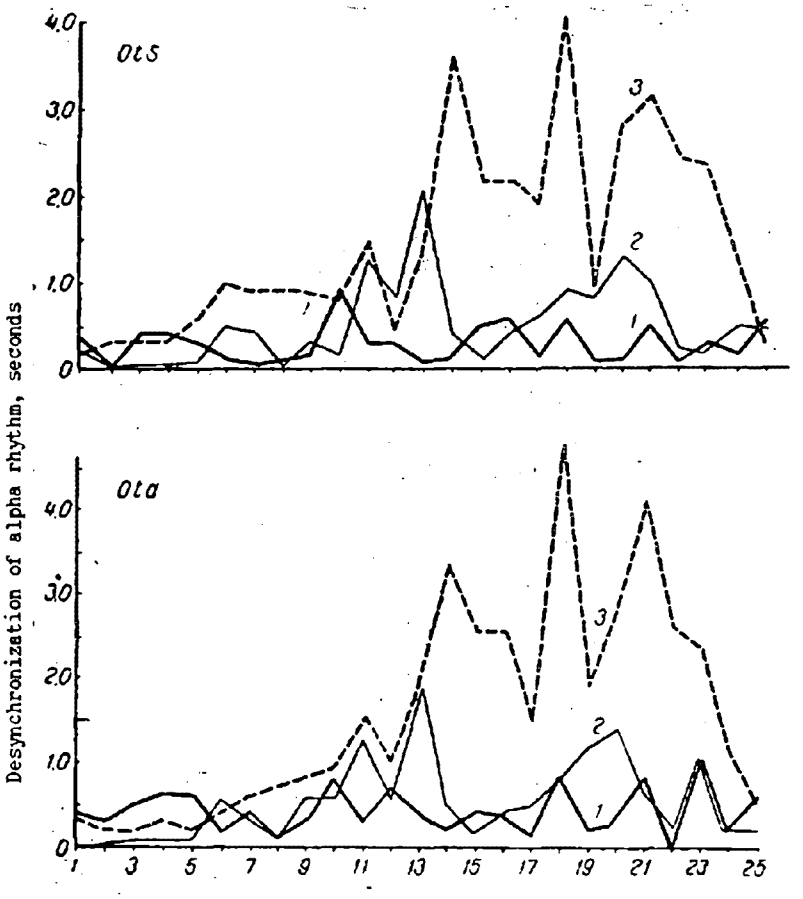

Fig. 5. Change in the electrical activity of the brain of subject Zh. N. during inhalation of different concentrations of acetic anhydride.
1 - pure air; 2 - 0.11 mg/m^3; 3 - 0.18 mg/m^3

study of this combination is of major sanitary importance: the source of their combined discharge into the atmosphere are plants producing acetic acid and acetic anhydride, and also cellulose acetate plants, whose number and output are increasing considerably, particularly because of a growing consumption of cellulose acetate in the production of rayon, plastics, synthetic lacquers and other products.

In order to determine the character of the combined action of acetic acid and acetic anhydride, after determining the threshold of smell of each ingredient separately, we began the determination of the odor thresholds of acetic acid and acetic anhydride in their mixture.

Seven mixtures of different concentrations of acetic acid and acetic anhydride were studied in 20 subjects. In all, 338 observations were made.

Results of the studies are listed in Table 4.

Table 4

Odor Thresholds of Acetic Acid and Acetic Anhydride for Their Combined Presence.

Number of Subjects	Threshold Concentrations in mg/m³	Sum of Fractions	Subthreshold Concentrations in mg/m³	Sum of Fractions
	$CH_3COOH + (CH_3CO)_2$		$CH_3COOH + (CH_3CO)_2$	
2	0,60+0,25	1,05	0,29+0,45	0,80
3	0,37+0,28	0,98	0,29+0,24	0,80
4	0,60+0,25	0,96	0,20+0,45	0,77
2	0,29+0,24	0,96	0,19+0,24	0,80
3	0,16+0,35	0,94	0,20+0,25	0,82
3	0,40+0,25	0,90	0,30+0,25	0,78
1	0,30+0,25	0,78	0,20+0,25	0,65
2	—	—	0,60+0,25	0,71

The studies performed showed that the odor thresholds for the most sensitive persons correspond to the following concentrations of the mixture of acetic acid and acetic anhydride: 0.16 + 0.35 mg/m³ and 0.29 + 0.24 mg/m³. The imperceptible concentration of acetic acid in the mixture was 0.19 mg/m³, and of acetic anhydride, 0.24 mg/m³.

The material obtained should be treated from the standpoint of determination of the nature of the combined effect of acetic acid and acetic anhydride, i.e., it should be determined whether we are dealing with synergism, potentiation, or antagonism. In order to obtain comparable data, the concentrations studied should be expressed in fractions of the threshold values for each of them. In other words, in order to determine the character of the combined action of these two substances, the acetic acid and acetic anhydride concentrations studied should be split into their threshold concentrations for each subject and summed up. Thus one can obtain the total concentrations of the mixture in fractions of the individual effect threshold. As is evident from Table 4, the odor was perceived in cases where the sum of the relative concentrations of acetic acid and acetic anhydride was close to unity (0.90-1.05). The odor of the mixture was imperceptible if the sum of the relative concentrations amounted to 0.82 and lower. For only one subject was the index of the total concentration of the active mixture equal to 0.78, and that of the inactive mixture, to 0.65. She was more sensitive to the mixture of these gases.

The next section of our study involved the determination of the effect of low acetic acid and acetic anhydride concentrations present together on

the reflex change of the light sensitivity of the eye. We studied the following mixtures of acetic acid and acetic anhydride: 0.31 + 0.25 mg/m^3; 0.25 + 0.18 mg/m^3; and 0.15 + 0.18 mg/m^3. Three persons participated in the experiment. In all, 60 determinations were carried out.

The effect was evaluated in the same manner as in the determination of the threshold of olfactory perception. The data obtained are listed in Table 5 and Fig. 6.

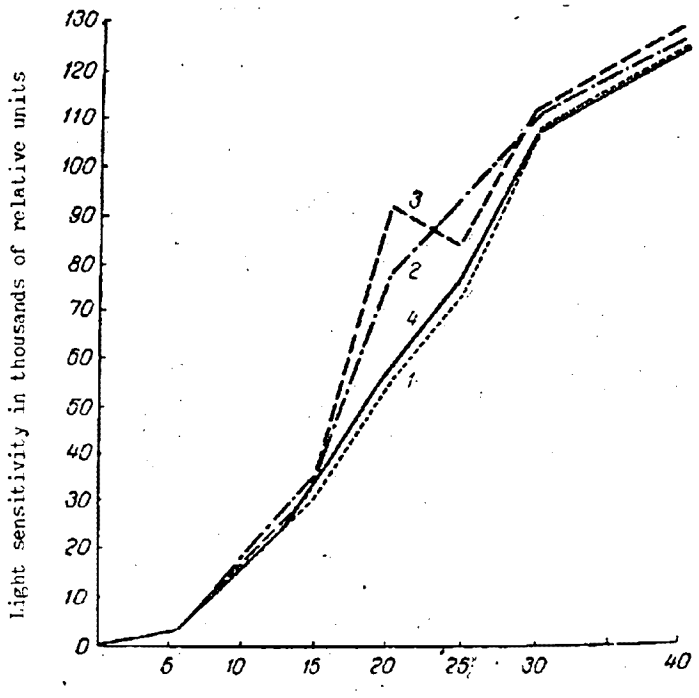

Fig. 6. Change of the light sensitivity of the eye in subject T. R. during inhalation of acetic acid and acetic anhydride.
1 - acetic acid 0.15 + acetic anhydride 0.18 mg/m^3;
2 - acetic acid 0.25 + acetic anhydride 0.18 mg/m^3;
3 - acetic acid 0.31 + acetic anhydride 0.25 mg/m^3; 4 - pure air

From Table 5 and Fig. 6 it is also evident that the reflex change of the light sensitivity takes place in the most sensitive persons at the concentration of a mixture of 0.25 mg/m^3 acetic acid and 0.18 mg/m^3 acetic anhydride. The concentration of a mixture of 0.15 mg/m^3 acetic acid and 0.18 mg/m^3 acetic anhydride was found to be inactive with respect to the course of the curve of dark adaptation of the eye.

The index of total concentration of the active mixture (with respect to the adaptometric thresholds) is 1.06, and that of the inactive mixture, 0.81. Thus, an effect of complete summation is observed during the combined effect of acetic acid and acetic anhydride on the light sensitivity of the eye.

Table 5

Threshold of Reflex Change of the Light Sensitivity of the Eye in the 20th Minute During Inhalation of a Mixture of Acetic Acid and Acetic Anhydride.

Subjects	Threshold Concentrations, mg/m³	Sum of Fractions of Adaptometric Threshold	Subthreshold Concentrations, mg/m³	Sum of Fractions of Adaptometric Threshold
	$CH_3COOH + (CH_3CO)_2O$		$CH_3COOH + (CH_3CO)_2O$	
N.	0,25+0,18 (c)	1,00	0,15+0,18 (o)	0,81
T.	0,25+0,18 (c)	1,01	0,15+0,18 (c)	0,81
A.	0,31+0,25 (b)	1,01	0,25+0,18 (o)	0,77

Note. Confidence factor: b - 99%, c - 99.9%, o - unreliable

The third stage of our study dealt with the effect of subthreshold concentrations of the acetic acid-acetic anhydride mixture on the electrical activity of the brain as determined by the method of the electrocortical conditioned reflex.

The following mixtures of vapors of acetic acid and acetic anhydride were investigated: 0.18 mg/m^3 + 0.13 mg/m^3; 0.15 mg/m^3 + 0.087 mg/m^3; and 0.145 mg/m^3 + 0.06 mg/m^3. In all, 75 observations were made. Five persons with a distinct alpha rhythm participated in the experiment. In all the subjects, the threshold of formation of the electrocortical conditioned reflex was determined for acetic acid and acetic anhydride taken separately.

According to the results of the determination of the threshold of the electrocortical conditioned reflex during inhalation of the mixture of acetic acid and acetic anhydride vapors and according to the statistical treatment of the data, in three out of the five subjects the threshold of formation of the electrocortical conditioned reflex corresponded to a mixture of 0.18 mg/m^3 acetic acid vapors and 0.13 mg/m^3 acetic anhydride vapors, with a total concentration index of 1.02 (relative to the individual threshold in the study of the isolated effect of these substances). For two subjects, the threshold mixture consisted of 0.15 mg/m^3 acetic acid vapors and 0.087 mg/m^3 acetic anhydride vapors (the sum of the relative concentrations of this mixture was 0.99 for them). The subthreshold (inactive) mixture in the electroencephalographic tests for three subjects consisted of 0.15 mg/m^3 acetic acid and 0.087 mg/m^3 acetic anhydride (the total concentration index of the inactive mixture was 0.75). For the remaining two subjects, the index of the total concentration of the inactive mixture was 0.83, for an inactive concentration of the mixture of acetic acid - 0.145 mg/m^3 and acetic anhydride - 0.06 mg/m^3.

Fig. 7 shows graphs of the change of the brain's electrical activity during inhalation of different concentrations of a mixture of acetic acid

and acetic anhydride.

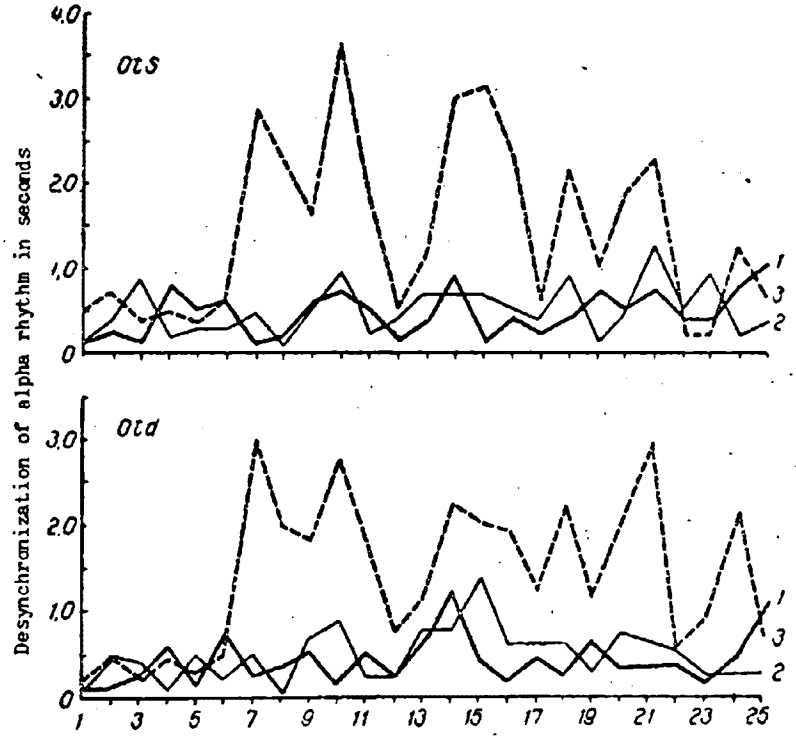

Fig. 7. Change in the electrical activity of the brain of subject Zh. N. during inhalation of different concentrations of a mixture of acetic acid and acetic anhydride.

1 - pure air; 2 - 0.145 + 0.06 mg/m^3; 3 - 0.15 + 0.087 mg/m^3

Thus, analysis of the results obtained from the determination of the threshold of the electrocortical conditioned reflex during the combined action of acetic acid and acetic anhydride vapors, both for the determination of the threshold of olfactory perception and of the threshold of reflex change of the light sensitivity of the eye, indicates a complete summation of the effect of these substances, i.e., the sum of the active concentrations expressed in fractions of the threshold values is close to unity, and the sum of the inactive concentration is less than unity (0.83).

In converting the threshold concentrations of the acetic acid-acetic anhydride mixture (based on the electroencephalographic test) to values relative to the maximum permissible concentrations of the ingredients for isolated action, the minimum total active concentration in fractions of the maximum permissible concentrations of the components was found to be

$$\frac{0.15 \text{ mg/m}^3}{0.2 \text{ mg/m}^3} + \frac{0.087 \text{ mg/m}^3}{0.1 \text{ mg/m}^3} = 0.75 + 0.87 = 1.62.$$

The maximum inactive concentration is the total concentration at a level of:

$$\frac{0.145 \text{ mg/m}^3}{0.2 \text{ mg/m}^3} + \frac{0.06 \text{ mg/m}^3}{0.1 \text{ mg/m}^3} = 0.72 + 0.60 = 1.32.$$

It follows that for the combined presence in atmospheric air of acetic acid and acetic anhydride vapors, their total concentration expressed in fractions of the recommended maximum permissible concentrations of each of the substances for isolated action should not exceed 1.3.

Conclusions

1. The threshold of olfactory perception of acetic acid in the most sensitive persons is 0.60 mg/m^3, and that of acetic anhydride, 0.49 mg/m^3.

2. The threshold of reflex change of the light sensitivity of the eye during inhalation of acetic acid is 0.48 mg/m^3, and that of acetic anhydride, 0.36 mg/m^3.

3. The threshold of formation of the electrocortical conditioned reflex for acetic acid is 0.29 mg/m^3, and that of acetic anhydride, 0.18 mg/m^3. Concentrations of 0.18 mg/m^3 acetic acid and 0.11 mg/m^3 acetic anhydride did not have a reflex effect on the electrical activity of the brain.

4. The proposed highest single maximum permissible concentration of acetic acid in atmospheric air is 0.2 mg/m^3, and that of acetic anhydride, 0.1 mg/m^3.

5. During the combined action of acetic acid and acetic anhydride vapors (according to data from the determination of the threshold of smell, adaptometry, and electroencephalography), an effect of complete summation takes place.

6. The threshold mixture in electroencephalographic tests consists of acetic acid (0.15 mg/m^3) and acetic anhydride (0.087 mg/m^3) with a total concentration index of 0.99. The total concentration index of the inactive mixture is 0.83 (acetic acid 0.145 mg/m^3 and acetic anhydride 0.06 mg/m^3).

7. When acetic acid and acetic anhydride vapors are jointly present in atmospheric air, their total concentration expressed in fractions of the adopted maximum permissible concentrations of each of the substances should not exceed 1.3.

LITERATURE CITED

Note: References mentioned in this paper are to be found at the end of the volume in the 1968 bibliography.

THRESHOLD CONCENTRATIONS OF PARAFFINS IN SHORT-TERM AND LONG-TERM INHALATION

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From Akademiya Meditsinakikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 11, Izdatel'stvo "Meditsina" Moskva, p. 43-50, (1968).

In connection with the rapid rate of development of petroleum refining and petrochemical branches of industry and an ever-increasing role of large-capacity refineries and petrochemical enterprises, a major importance is assumed by the study of the biological effect of hydrocarbons and their sanitary standardization in atmospheric air.

The chief atmospheric pollutants in the area of a refinery are aliphatic hydrocarbons (olefins and paraffins).

The present article is devoted to the study of paraffin hydrocarbons as atmospheric pollutants.

The data available in the literature (Kochmann, 1923; Eulenberg, 1925; Nelson et al. 1943; N. V. Lazarev, 1954; Z. Kh. Filipova, 1961) indicate a relatively slight toxicity of paraffin hydrocarbons. Nevertheless, their sanitary standardization is considered necessary for the following reasons.

1. In areas around petroleum refineries, paraffins are the chief hydrocarbon pollutants. A number of studies dealing with the content of hydrocarbons in atmospheric air around petroleum refineries have been published (B. P. Gurinov, 1958; R. S. Gil'denskiol'd, 1958, and others). However, a sanitary evaluation of the data obtained and further observations are complicated by the lack of sanitary standards.

2. In areas around petroleum refinery plants, paraffin hydrocarbons enter into the composition of organic pollutants of the atmosphere and make up a significant part of the "sum" of hydrocarbons widely employed in sanitary practice. Because of the great variety of hydrocarbons in atmospheric air, the inconstancy of their composition and varying toxicity, the concept of a "sum" has no sanitary meaning and requires an interpretation.

Paraffins (methane hydrocarbons) are open-chain saturated compounds. Paraffins with up to four carbon atoms are gaseous substances, those with 5 to 15 carbon atoms are liquids, and higher representatives of the series (with C_{16}) at room temperature are solids. Paraffin hydrocarbons are narcotics

whose narcotic effect increases with the number of carbon atoms in the chain. In the body, paraffins do not undergo chemical transformations and do not accumulate.

In dealing with the problems of atmospheric sanitation, the hydrocarbons of greatest interest are the gaseoux ones and the first liquid homologs, since they are the chief atmospheric pollutants and, because of their physical properties, spread over considerable distances.

We studied the reflex effect of butane and pentane, the most toxic lower hydrocarbons of the series found in atmospheric air.

The thresholds of olfactory perception and thresholds of the effect on the electrical activity of the brain were determined. The study of the threshold of olfactory perception was made on twelve practically healthy volunteers ranging in age from 18 to 48 years.

The experiment with every concentration was repeated three times. We studied the concentrations of 777, 498, 355, 242 and 305 mg/m^3 for butane and 328, 257, 217 and 155 mg/m^3 for pentane. In all, 327 determinations were made. The results are shown in Table 1.

Table 1

Thresholds of Olfactory Perception of Aliphatic Hydrocarbons (Butane, Pentane).

Number of Subjects	Concentration in mg/m^3	
	Maximum Inactive	Minimum Active
	Pentane	
4	155	217
6	217	257
2	257	328
	Butane	
9	242	305
3	305	355

Thus, it was found that the odor threshold concentration in the most sensitive persons was 217 mg/m^3 for pentane and 305 mg/m^3 for butane.

The threshold of the effect on the electrical activity of the brain was studied by the electrocortical reflex method on four subjects whose threshold of smell had first been determined. The results are given in Table 2.

Table 2

Threshold Concentrations Causing Formation of Electrocortical Conditioned Reflex During Inhalation.

Subject	Hydrocarbon Concentrations, mg/m³						
	Pentane			Butane			
	150	130	100	350	320	280	200
S. A.	+	+	—	+	+	—	—
I. R.	+	+	—	+	+	—	—
V. T.	+	—	—	+	+	—	—
Kh. E.	+	+	—				

Conventional symbols: + electrocortical reflex formed; - not formed.

The minimum concentrations causing the formation of the electrocortical reflex during short-term inhalation lie at the imperceptible level and are 130 mg/m^3 for pentane and 280 mg/m^3 for butane.

In view of the fact that hydrocarbons of the paraffin series are constantly present in atmospheric air, we studied the character of their combined action. The tests were conducted on three persons whose thresholds of olfactory perception and of the isolated effect of these substances on the electrical activity of the brain had first been determined. The effect of the hydrocarbons was determined in the following combinations:

Combination I: maximum inactive concentration of pentane + maximum inactive concentration of butane;

Combination II: 1/2 maximum inactive concentration of pentane + 1/2 maximum inactive concentration of butane;

Combination III: 1/2 maximum inactive concentration of pentane + 1/4 maximum inactive concentration of butane (Table 3).

Hence, all the combinations of paraffin hydrocarbons for which their sum is greater than or equal to 1 (in fractions of the maximum inactive concentration of each substance) cause a conditioned-reflex desynchronization of the α rhythm.

With a combination of pentane and butane whose concentrations (in fractions of the maximum inactive value) added up to less than 1, no electrocortical conditioned reflex could be formed.

Table 3

Results of Study of the Combined Effect of Pentane and Butane on the Formation of the Electrocortical Conditioned Reflex.

Pentane + Butane	Subjects		
	S.A.	F.R.	V.T.
1 + 1	+	+	+
1/2 + 1/2	+	+	+
1/2 + 1/4	—	—	—

Note. Concentrations of pentane and butane given in fractions of maximum inactive values.

In order to study the chronic effect of paraffin hydrocarbons, white male rats weighing 85-95 g were subjected to a chronic round-the-clock exposure. Exposure to the first liquid homolog, pentane, was tested.

The choice of concentrations was due to the following considerations: 30 mg/m^3 is one-third the highest single (proposed mean daily) concentration; 100 mg/m^3 is at the level of the highest single concentration; 300 mg/m^3 corresponds to the maximum permissible value for plant shops; 800 mg/m^3 was taken in order to obtain a pronounced effect.

The following tests were used in the study: weight and behavior of the animals, blood pressure, chronaxy of antagonist muscles, cholinesterase activity of the blood, and determination of the number of blood leucocytes. Before the end of the exposure, the adsorptive capacity of certain tissues and organs was studied by vital staining.

The exposure was carried out for 117 days with the exception of series IV of the experiments (exposure to pentane in a concentration of 800 mg/m^3). The exposure of animals of this group lasted 66 days until the appearance of distinct changes.

Table 4

Pentane Concentration During Chronic Exposure

Series of Experiments	Concentrations, mg/m^3	
	Specified	Actual
I	30,0	25,5
II	100,0	116±2,5
III	300	332±7
IV	800	800±20,7
V	Control	

At the end of the experiment, some of the animals were killed for the purpose of vital staining of the organs and histopathological analyses; the remaining animals were left alive for observation for 12 days during the recovery period. In the course of the entire exposure, the behavior of the experimental animals was no different from that of the intact animals. The initial weight of animals of all groups was practically the same (the differences were statistically unreliable). Observations of the weight dynamics did not show any changes at subsequent stages of the exposure either.

The initial blood pressure level in all the rats was in the range of the physiological norm for this species of animals and amounted to 113-110 mm Hg in the various groups. A statistically reliable drop of the blood pressure level was observed after a one-month exposure in animals exposed to pentane in

concentrations of 800 and 332 mg/m^3. The drop of the blood pressure level became more pronounced in subsequent stages of the exposure. Pentane in a concentration of 116 mg/m^3 also showed a hypotensive effect after a two-month exposure. The blood pressure level in animals exposed to the action of pentane in a concentration of 25 mg/m^3 remained unchanged.

A distinct distortion of the chronaxies of the flexors and extensors was established after two months of the experiment in animals exposed to pentane in concentrations of 800, 332 and 116 mg/m^3. Pentane in a concentration of 25 mg/m^3 did not cause any change of subordinative chronaxy (Table 5).

Table 5

Ratio of Chronaxies of Antagonist Muscles in Experimental and Control Animals Before and During the Experiment.

Date of Study	Series I 30 mg/m^3 $M \pm m$	Series II 116 mg/m^3 $M \pm m$	Series III 332 mg/m^3 $M \pm m$	Series IV 800 mg/m^3 $M \pm m$	Control
7/X 1965 r.	1,69±0,28	1,67±0,22	1,45±1,12	1,82±0,32	1,49±0,19
10/X	1,48±0,12	1,18±0,22	1,14±0,12	1,29±0,27	1,36±0,34
10/X	1,44±0,12	0,75±0,08	0,71±0,12	0,54±0,12	1,4 ±0,12
10/I 1966 r.	1,69±0,21	0,46±0,05	0,98±0,08		1,86±0,15
1/II	1,56±0,19	0,87±0,11	0,72±0,19		1,47±0,12

The cholinesterase activity was determined by using a modified Fleischer-Pope* method. During the entire exposure, the cholinesterase activity of the blood (in micromoles of decomposed acetylcholine) in all the experimental animals did not differ appreciably from the control. A statistically reliable difference as compared with the initial level was not found in any of the observed groups either.

The number of blood leucocytes in the experimental and control animals during the exposure did not exceed the limits of the physiological norm and amounted to 8825-15580.

The method of vital staining was determined by the degree of absorption of the dye by the various organs (method of D. N. Nasonov and V. Ya. Aleksandrov).

Combined data on the accumulation of the vital dye (neutral red) by the various organs are listed in Table 6.

As is evident from the above data, the degree of absorption of the vital dye by the brain tissue in animals of series II and III of the experiments is approximately twice (1.9-2.3) as high as in the intact animals. According to the remaining data, the differences are insignificant.

* [Translator's note: Fleysher and Poup, according to the transliteration of Russian reference.]

Table 6

Index of Accumulation of Vital Dye (in milligrams per gram of tissue weight) in Experimental and Control Animals.

Organ \ Series of Experiments	I (Concentration 25,5 mg/m³)	II (Concentration 11,6 mg/m³)	III (Concentration 332 mg/m³)	Control
Brain	24,7±3,3	67±9,0	53±8,5	29±8,6
Heart	106±6,4	108±7,3	103±4,7	9,6±7,3
Liver	260±50,5	247±48,3	170±16	155±16

All the tests were carried out two weeks after the end of exposure. Tests that revealed changes in the course of exposure established a return to the physiological norm at the end of the recovery period.

Studies of atmospheric air in areas around petroleum refineries established the content of the paraffin hydrocarbons (Table 7).

Table 7

Content of Aliphatic Hydrocarbons in the Atmospheric Air of a Residential Area.

Component	Single Concentrations in mg/m³			Mean Daily Concentrations in mg/m³		
	Maximum	Minimum	Average	Maximum	Minimum	Average
Sthane	2,56	0,58	1,4	2,15	0,85	1,41
Propane	12,9	0,46	3,05	21	0,305	3,59
Butane	4,05	0,32	1,88	2,76	0,74	1,09
Pentane	33,6	0,52	7,45	4,05	0,70	2,70

Conclusions

1. The lower paraffins (butane, pentane) have an olfactory effect whose threshold for the most sensitive persons is 305 and 217 mg/m³ respectively.

2. The minimum concentrations at which the formation of the electrocortical reflex is possible in the most sensitive persons are 130 mg/m³ for pentane and 280 mg/m³ for butane. The maximum inactive concentrations were 100 and 200 mg/m³ respectively.

3. The highest single maximum permissible concentrations of paraffins which are proposed are below the thresholds causing olfactory perception and reflex shifts in the most sensitive persons: 100 mg/m^3 for pentane and 200 mg/m^3 for butane.

4. In the combined action of butane and pentane, an additive effect takes place, established by the most sensitive test, the EEG reflex. Thus, when these substances are jointly present in atmospheric air, the permissible concentrations are such that when expressed in fractions of the maximum permissible concentration, they do not exceed a sum of 1.

5. After a prolonged exposure of the experimental animals to the action of paraffins (pentane), the blood pressure decreases, the subordinative chronaxy is distorted, and the adsorptive capacity of the nervous tissue (brain) changes. The changes already take place at pentane concentrations of 116 and 332 mg/m^3.

6. Pentane in a concentration of 25 mg/m^3 during chronic round-the-clock exposure does not cause any appreciable shifts in the body of the animals. This concentration is proposed as the mean daily maximum permissible concentration of pentane in atmospheric air.

7. Petroleum refineries pollute atmospheric air with paraffins having up to C_5 carbon atoms.

8. The results of the studies demonstrate the usefulness of the concept of the "sum" of hydrocarbons and the need for a differentiated definition of diverse classes of organic compounds in a sanitary evaluation of atmospheric pollutants.

LITERATURE CITED

Note: References mentioned in this paper are to be found at the end of the volume in the 1968 bibliography.

BIOLOGICAL EFFECT AND HYGIENIC EVALUATION OF POLLUTION OF ATMOSPHERIC AIR WITH PHTHALIC ANHYDRIDE

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From Akademiya Meditsinskikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 10, Izdatel'stvo "Meditsina" Moskva, p. 86-96, (1967)

Phthalic anhydride is the anhydride of ortho-benzenedicarboxylic acid. Its boiling point is 284.5°C, and its melting point, 128-131°C. It has the odor of bitter almonds.

Phthalic anhydride sublimes readily. Its solubility in water is 0.6 g in 100 ml of water at 25°C. When dissolved in hot water, it converts into phthalic acid. It is soluble in carbon disulfide, alcohol, ether, benzene. Phthalic anhydride is marketed in the form of flat, white, frequently rhombic crystals.

Phthalic anhydride is used in various branches of industry. It is widely employed in the production of dyes: phthaleins, rhodamines, indigo, anthranilic acid, derivatives of anthraquinone, phthalocyanines. Esters of ortho-phthalic acid are used as plasticizers in the production of glyptal, polyester, and epoxy resins. Phthalic anhydride is used in the pharmaceutical and leather industries.

Its ability to enter into a series of characteristic reactions makes it widely applicable in chemical laboratories.

There are several methods of preparing phthalic anhydride. The most popular method used in industry is based on the oxidation of naphthalene in the presence of a catalyst at 350-500°C. The preparation and use of phthalic anhydride are associated with its pollution of the atmosphere.

The waste gases of phthalic production after purification in scrubbers are discharged into the atmospheric air. Part of the phthalic anhydride is discharged with ventilation gases. In the literature accessible to us, we were unable to find any studies dealing with the presence of phthalic anhydride in the air around industrial enterprises.

The effect of phthalic anhydride on the human and animal organism has been studied by many investigators. Several authors (Friebel et al., 1956; L. A. Titunov and A. A. Denisenko, 1957; Yu. K. Korotkova, 1957, 1960; S. N. Kremneva and M. S. Tolgskaya, 1961) studied the toxicity of phthalic anhydride introduced into the gastrointestinal tract.

Kremneva and Tolgskaya (1961) administered intratracheally a 2% emulsion of phthalic anhydride to white rats under anesthesia. Doses above 30 mg/kg were found to be absolutely fatal. Death of the animals occurred within the next few hours or within a day.

An inhalational exposure to dust and vapors of phthalic anhydride was carried out by Friebal et al. (1956) on guinea pigs. The concentrations of vapors were maintained at the level of 644.5 mg/m^3, and those of dust, at 8.5 mg/m^3.

In such concentrations, the product irritates the conjunctiva and respiratory tract. An admixture of naphthoquinone and maleic acid increases the irritant effect.

An inhalational exposure of 10 guinea pigs to phthalic anhydride dust for 30 days, 15 minutes once a day, at a concentration of 600 mg/m^3, was carried out by Korotkova (1959). The concentrations were determined gravimetrically. During the exposure, coughing and sneezing were observed in the animals. In three guinea pigs after the first exposures, edema of the eyelids, hyperemia of the conjunctiva of the eyes and liquid discharges from the nose were observed. In some cases, a weight loss was noted. Autopsy revealed a hyperemia of the mucous membrane of the trachea and bronchi, adhesions in the pleural cavities, and a moderate hyperemia of the internal organs.

Kremneva and Tolgskaya (1961) carried out a static exposure for 6 months, 6 days a week and 3 hours a day, to phthalic anhydride concentrations of 5-12 mg/m^3. At the end of the 6th month, the level of arterial pressure was 70% of the normal. Eosinophilia was observed in the majority of cases over the entire course of exposure. Concentrations of 1-2 mg/m^3 were found to be inactive under the same conditions.

It is evident that only high concentrations of phthalic anhydride during periods of moderate duration were studied. The effect of low concentrations in a round-the-clock exposure was not studied on the experimental animals. The maximum permissible concentration of phthalic anhydride for industrial buildings was adopted at a level of 1 mg/m^3, and has not been established for atmospheric air.

The wide use of phthalic anhydride in industry, the inadequate study of its toxic properties, and the presence of sources of atmospheric pollution indicate that the sanitary evaluation of this compound is quite urgent. The purpose of the present study was to give an experimental validation of the maximum permissible concentration of phthalic anhydride in atmospheric air.

This was done by determining the odor threshold and studying the reflex effect of phthalic anhydride on the light sensitivity of the eyes.

Under the conditions of the experiment, the determination of phthalic anhydride in a current of air was carried out by using a spectrophotometric method proposed by M. D. Manita.

The threshold of olfactory perception of phthalic anhydride was determined on 27 practically healthy persons (374 observations). The results are given in Table 1.

Table 1

Threshold of Olfactory Perception of Phthalic Anhydride

Number of Subjects	Number of Observations	Minimum Perceptible Concentration, mg/m^3	Maximum Imperceptible Concentration, mg/m^3
6	100	0,32	0,22
4	66	0,53	0,32
17	208	0,72	0,53

It is evident from Table 1 that the minimum perceptible concentrations of phthalic anhydride in different persons ranged from 0.32 to 0.72 mg/m^3. The threshold of odor perception in the most sensitive persons was 0.32 mg/m^3. The maximum imperceptible concentration was found to be 0.22 mg/m^3. The concentrations studied had no irritant effect on the subjects.

In recent years, the study of the effect of vapors of various toxic compounds on the light sensitivity of the eyes has been widely used for validating the highest single maximum permissible concentrations.

The effect of phthalic anhydride on the light sensitivity of the eyes was studied on three persons by means of an ADM adaptometer, using a widely accepted procedure. The light sensitivity was measured up to the 40th minute every 5 minutes. The effect of each concentration on the light sensitivity of the eyes was studied no fewer than 3 times (Table 2).

Thus, a phthalic anhydride concentration of 0.96 mg/m^3 caused significant changes in the 20th minute of dark adaptation in all the subjects. A concentration of 0.55 mg/m^3 was found to be inactive.

In 2 out of 3 subjects under adaptometric observations, the threshold of odor perception was observed at a level of 0.72 mg/m^3, and in the third subject, the perception threshold was not determined.

Based on what appeared to be a primarily trigeminal action of phthalic anhydride, the data of our studies make it possible to recommend the highest single maximum permissible concentration of phthalic anhydride in atmospheric air at the level of 0.2 mg/m^3.

Table 2

Results of Adaptometric Studies

Subject	Concentrations of Phthalic Anhydride, mg/m³	Light Sensitivity in the 20th Minute of Dark Adaptation, 1/ε
E.	Pure Air	23 533.
	0,50—0,55	21 066 (o)
	0,96—1,09	30 700 (b)
	1,49—1,79	45 899 (c)
P.	Pure Air	41 330
	0,50—0,55	39 933 (o)
	0,96—1,09	59 433 (b)
	1,64—1,79	77 100 (c)
P.	Pure Air	21 067
	0,50—0,55	21 333 (o)
	0,96—1,09	35 367 (a)
	1,64—1,79	41 633 (b)

Note. Degree of significance: a - 95%; b - 99%; c - 99.9%; o - insignificant.

In order to validate the mean daily maximum permissible concentration of phthalic anhydride, we studied the influence of its low concentrations in a 70-day round-the-clock inhalational exposure. The experiments were conducted on 60 white male rats in 100 l chambers. Each chamber was supplied with 20-23 l/min of air to which was first passed through FPP-15 filters. Group I of the rats was exposed to phthalic anhydride in a concentration of 1.52 mg/m^3, group II, to 0.54 mg/m^3, group III, to 0.18 mg/m^3. The animals of group IV were the controls. The concentrations were chosen on the basis of the following considerations. The concentration of 1.32 mg/m^3 was taken as the value close to the maximum permissible concentration for the air of industrial buildings. The concentration of 0.18 mg/m^3 in the subliminal value from the standpoint of olfactory perception and is close to our recommended highest single maximum permissible concentration. The concentration of 0.54 mg/m^3 was chosen as one that is frequently encountered at a distance of 500 m from the phthalic anhydride plant in the atmospheric air of residential areas.

During the chronic experiment, observations were made on the general condition of the animals, their weight, motor chronaxy of antagonist muscles, cholinesterase activity, and morphological composition of the blood. The behavior and activity of the rats of all three groups did not differ from those of the controls. Rats of all the groups gained weight in uniform fashion.

Studies by numerous authors have shown the high sensitivity of the study of the ratio of motor chronaxy of antagonist muscles as a method for characterizing the functional state of the central nervous system (Yu. N. Uflyand, 1941; A. N. Magnitskiy, 1948; A. F. Makarchenko, 1956). In the establishment of the mean daily maximum permissible concentrations of noxious substances in atmospheric air, this index was first used and widely employed by the staff of the department of communal hygiene of the Central Institute for Advanced Training of Physicians. We used this test to study the effect of low concentrations of phthalic anhydride on the organism of the experimental animals. The studies were carried out on an ISE-01 electronic pulse stimulator. The chronaxy of the antagonist muscles was determined on the right hind leg in 5 rats of each group once every 10 days under the same conditions. A disturbance of the normal ratio of motor chronaxy of flexors and extensors in rats of group I occurred on the 31st day of exposure and returned to normal two weeks after the end of exposure. In rats of group II, the changes were less pronounced. In the animals of group III, no such changes were observed (Fig. 1).

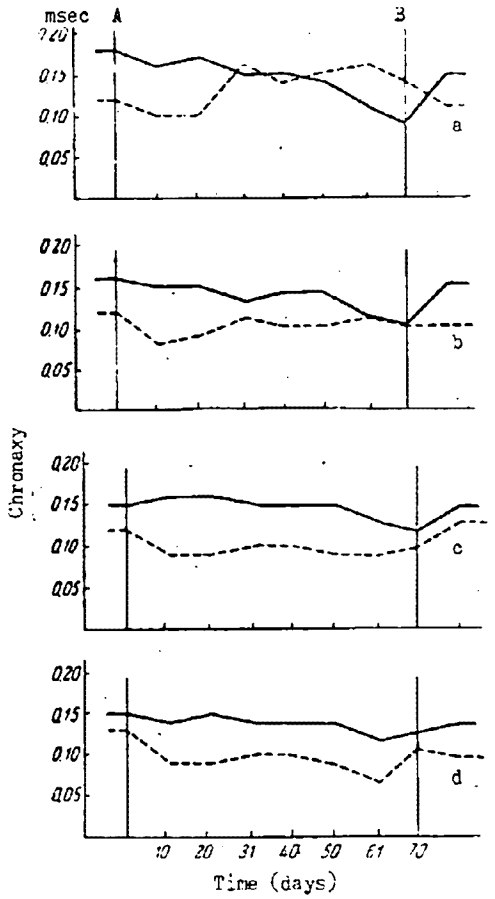

Fig. 1. Effect of phthalic anhydride on the motor chronaxy of antagonist muscles of rats in group I (a); group II (b); group III (c) and group IV (d). Solid line refers to extensors and dashed line to flexors; AB - period of exposure.

Numerous experiments established that the cholinesterase activity changes in many pathological conditions of the organism. This method found applications in sanitary standardization practice. G. I. Solomin (1961), V. I. Filatova (1962), D. G. Odoshashvili (1962), and V. A. Chizhikov (1963) confirm that the cholinesterase content changes under the influence of chemical substances.

The cholinesterase activity of whole blood was stuided by a chemical method of A. A. Pokrovskiy's (1953), modified by A. P. Martynova (1957). The cholinesterase activity during the experiment was evaluated from the change in the time of decomposition of acetylcholine. The determination was made on rats of each group once every two weeks. On the 42nd day of exposure, a depression of cholinesterase activity occurred in animals of group I. The time of acetylcholine hydrolysis increased to 49 minutes. In rats of group II, statistically significant but less pronounced changes were also observed. The time of acetylcholine hydrolysis for animals of group III did not differ from the control (Fig. 2).

According to the literature data, phthalic anhydride acts on the blood-forming system (k. Ye, Bakaleynik, 1960; S. N. Kremneva and M. S. Tolgskaya, 1961; V. S. Anatovskaya, 1961). This served as the basis for our study of the morphological composition of the blood. The blood analysis included determinations of the amount of hemoglobin, erythrocytes, thrombocytes, leucocytes, and a differential leucocyte count. On the 70th day of exposure, we obtained a change in the thrombocytes in animals of groups I and II. The leucocyte count did not change appreciably. The content of hemoglobin and erythrocytes fluctuated within normal limits.

Thus, in the course of chronic exposure it was possible to establish a change in the ratio of the motor chronaxy of antagonist muscles and in cholinesterase activity, and an increase in the thrombocyte count in rats of group I exposed to phthalic anhydride in a concentration of 1.32 mg/m^3. Less pronounced changes and later ones were observed in animals of group II. In the course of the two-week recovery period, the disturbances which occurred returned to normal. No deviations could be established in rats of group III. The data obtained from the chronic exposure were subjected to statistical treatment and confirmed our conclusions. On the basis of the chronic exposure, we propose a mean daily maximum permissible concentration at the level of the highest single concentration, 0.2 mg/m^3.

Studies of pollution of atmospheric air with emissions from the phthalic anhydride plant were conducted by using a polarographic method (I. G. Kogan, 1961).

The samples were collected on an FPP-15 filter mounted in a special holder and in two absorbers connected in series and containing porous plate No. 2. The absorbing liquid was 96° ethanol.

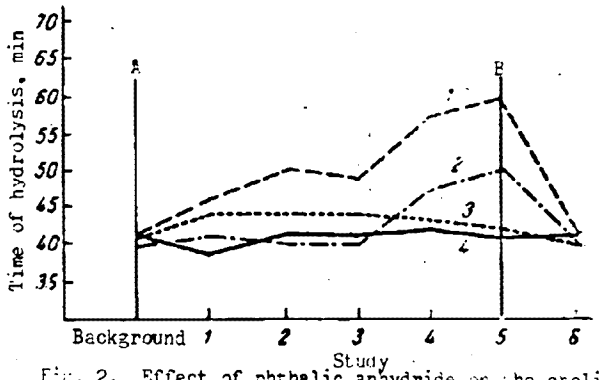

Fig. 2. Effect of phthalic anhydride on the cholinesterase activity of the blood.
1 - group I; 2 - group II; 3 - group III; 4 - group IV (control); AB - period of exposure

To determine the possibility of the spread of vapors and condensation aerosol of phthalic anhydride in the atmosphere, we conducted studies around plants producing phthalic anhydride. The output of the plants was over 10,000 tons of phthalic anhydride per year. Data on the degree of pollution with vapors and condensation aerosol of phthalic anhydride are present in Table 3. From the latter it is evident that only at a distance of 1000 m were the concentrations obtained lower than our proposed maximum permissible concentration (0.2 mg/m^3).

Table 3

Pollution of atmospheric air with phthalic anhydride in the area of the chemical plant complex on the leeward side.

Distance from Source of Discharge, m	Number of Collected Samples	Number of Samples Above the Sensitivity Limit of Method	Maximum Concentrations, mg/m^3	Average Concentrations, mg/m^3
250	17	9	0,134	0,031
500	37	22	0,652	0,064
1 000	32	17	0,1510	0,084
1 500	10	3	0,055	0,017

A sanitary protective zone of no less than 1000 m must be provided for this plant. The sanitary protective zone (500 m) adopted in accordance with the standards of the building code for enterprises with an output of over 10,000 t must be considered inadequate.

Conclusions

1. The threshold of olfactory perception of phthalic anhydride for the most sensitive persons is 0.32 mg/m^3, and the subliminal concentration is 0.22 mg/m^3.

2. A study of the curve of dark adaptation during short-term inhalation of phthalic anhydride indicates that the threshold at which it is affected is 0.92 mg/m^3, and the subthreshold concentration is 0.55 mg/m^3.

3. The highest single maximum permissible concentration which must be recommended is 0.2 mg/m^3.

4. Chronic round-the-clock exposure to vapors and condensation aerosol of phthalic anhydride in concentrations of 1.32 and 0.54 mg/m^3 for 70 days causes significant changes in the ratio of chronaxies of flexors and extensors, changes in the activity of whole blood cholinesterase, and an increase in the thrombocyte count. A concentration of 0.2 mg/m^3 was found to be inactive and may be recommended as the mean daily maximum permissible concentration.

5. The atmospheric air around phthalic anhydride plants with a capacity of 10,000 tons per year is polluted. In the presence of purification equipment, phthalic anhydride is observed in concentrations below our recommended maximum permissible value only at a distance of 1,000 m. For this reason, the sanitary protective zone for this plant should be no less than 1000 m.

LITERATURE CITED

Note: References mentioned in this paper are to be found at the end of the volume in the 1967 bibliography.

DATA FOR A SANITARY ASSESSMENT OF METHANOL IN ATMOSPHERIC AIR

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From Akademiya Meditsinakikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 10, Izdatel'stvo "Meditsina" Moskva, p. 65-74, (1967).

At the present time, methanol is obtained in huge amounts by synthesis, and also by hydrolysis of plant raw material. Methanol finds extensive applications in the manufacture of organic dyes, chemicopharmaceutical preparations, formaldehyde, and other chemical compounds.

The chief sources of pollution of atmospheric air with methanol are paint-and-varnish plants, wood-processing plants, metal-working shops, furniture factories, and many other enterprises.

In the nature of its action, methanol is a nerve and vascular poison with a marked cumulative property.

L. I. Kaza (1925) and V. M. Rozhkova (1948) held that an essential role in the mechanism of action of methanol is played by the primary product of its oxidation in the organism - formaldehyde, which paralyzes cellular respiration and inhibits the oxidation processes.

The action of low methanol concentrations on the human and animal organisms was first studied by Chao Cheng-ch'i (1959). The author experimentally determined the thresholds of the odor of methanol (4.1 mg/m^3) and of its reflex effect on the light sensitivity of the eye (3.3 mg/m^3), and also carried out a chronic exposure of white rats to methanol vapor in concentrations of 50 and 1.77 mg/m^3 in the course of three months for 12 hours a day.

On the basis of these studies, the highest single and mean daily maximum permissible concentrations of methanol in atmospheric air were established at 1.5 and 0.5 mg/m^3 respectively.

However, in his investigations, this author did not use the most sensitive method, which is the study of the electrical activity of the cerebral cortex for the purpose of validating the highest single maximum permissible concentration. Moreover, a continuous, round-the-clock exposure was not carried out in the chronic experiment. Therefore, we decided to refine these norms by using the most modern experimental methods.

To determine methanol in atmospheric air, we used the method of M. V. Alekseyeva (1963).

We began the study of the problem by determining the odor threshold of methanol in 25 persons aged 18 to 40 years. Nine concentrations from 12.2 to 3.9 mg/m^3 were tested (Table 1).

Table 1

Results of Determination of the Threshold of Olfactory Perception of Methanol Vapor

Number of Subjects	Minimum Perceptible Concentration, mg/m^3	Maximum Imperceptible Concentration, mg/m^3
3	10,3	9,7
5	8,4	7,5
4	7,5	6,5
2	6,5	5,6
5	5,6	4,5
6	4,5	3,9

As is evident from Table 1, the odor threshold in subjects with different sensitivities ranged from 10.3 to 4.5 mg/m^3. The threshold concentration in the most sensitive persons was found to be 4.5 mg/m^3, and the maximum imperceptible concentration, 3.9 mg/m^3. Thus, our data almost coincided with those of Chao Cheng-ch'i (4.1 mg/m^3). We then studied the effect of low concentrations of methanol on the light sensitivity of the eye by means of an ADM adaptometer on three subjects ranging in age from 18 to 25 years. The study was made daily at a strictly defined time once a day under identical conditions for each subject.

A physiological background was developed in each subject, i.e, a standard curve of dark adaptation, during inhalation of pure air between the 15th and 20th minute for 8 days. Concentrations of 4.11, 3.53, and 3.06 mg/m^3 were tested. The 4.11 mg/m^3 methanol concentration caused a marked change of the light sensitivity of the eye in all the subjects, and the 3.53 mg/m^3 concentration did so in only one subject. For the latter, the 3.06 mg/m^3 concentration proved to be inactive (Fig. 1).

The effect of low methanol concentrations on the electrical activity of the cerebral cortex was studied on the 6 persons with the lowest odor threshold (Table 2) by the method of A. D. Semenenko (1963) with the aid of an 8-channel electroencephalograph. The test was conducted no fewer than 4 times with each concentration and was regularly alternated with pure air.

The studies showed that methanol in a concentration of 1.46 mg/m^3 affected the magnitude of the amplitude of the alpha rhythm and caused statistically significant changes in all 6 subjects, whereas a concentration of 1.17 mg/m^3 did so in only two subjects.

The inactive concentration for all the subjects was 1.01 mg/m^3. The results of the studies are summarized in Table 3. They show that the highest single maximum permissible concentration of methanol established earlier at 1.5 mg/m^3 should be reduced to 1 mg/m^3.

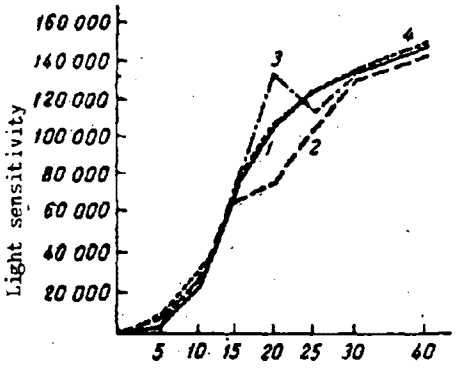

Fig. 1. Changes in the light sensitivity of the eyes during inhalation of methanol vapor. 1 - pure air; 2 - concentration 4.11 mg/m^3; 3 - 3.53 mg/m^3; 4 - 3.06 mg/m^3

Table 2

Results of Study of the Threshold of the Reflex Effect of Methanol Vapor on the Electrical Activity of the Cerebral Cortex.

Subject	Methanol Concentration, mg/m^3		
	1.46	1.17	1.01
G. K.	+	+	—
R. K.	+	—	—
T. A.	+	Not Studied	—
M. K.	+	—	—
L. T.	+	+	—
L. M.	+	Not Studied	—

Note. + statistically significant changes, - insignificant changes.

To check the mean daily maximum permissible concentration of methanol, a round-the-clock exposure of 45 white male rats weighing 100-120 g (three groups of 15 animals each) was carried out in the course of 90 days; group I was exposed to methanol vapors in a concentration of 5 mg/m^3, which slightly exceeded the odor threshold, group II to 0.5 mg/m^3, which was the existing mean daily maximum permissible concentration, and group III was the control.

During the entire period of exposure, the air temperature and methanol concentration in each chamber were measured daily. In group I, the average concentration was 5.31 $\pm$ 0.62 mg/m^3, and in group II, 0.57 mg/m^3 $\pm$ 0.59 mg/m^3.

In the course of chronic exposure, the animals of all the groups were healthy, active, and gained weight moderately. However, toward the end of the period of exposure, a slight lag was noted in the weight of animals of the control group.

Table 3

Results of Study of the Odor Threshold and Reflex Effect of Methanol on the Human Organism

Threshold	Data of Chao Cheng-ch'ü		Our Data	
	Concentrations, mg/m³			
	Minimum Active	Maximum Inactive	Minimum Active	Maximum Inactive
Olfactory Perception	4,1	3,7	4,5	3,9
Light Sensitivity of the Eye	3,3	2,4	3,53	3,06
Electrical Activity of Cerebral Cortex	Not studied		1,17	1,01

The study of the motor chronaxy of antagonist muscles was carried out on 5 rats in each group once every 10 days. The results show that a prolonged inhalation of the methanol vapors in a concentration of 5.3 mg/m³ in rats of group I starting with the 6th week of exposure causes statistically significant changes in the chronaxy of antagonist muscles with the appearance of a reversed ratio of their indices. Toward the end of the recovery period, the ratio of the chronaxy of flexors and extensors returned to normal.

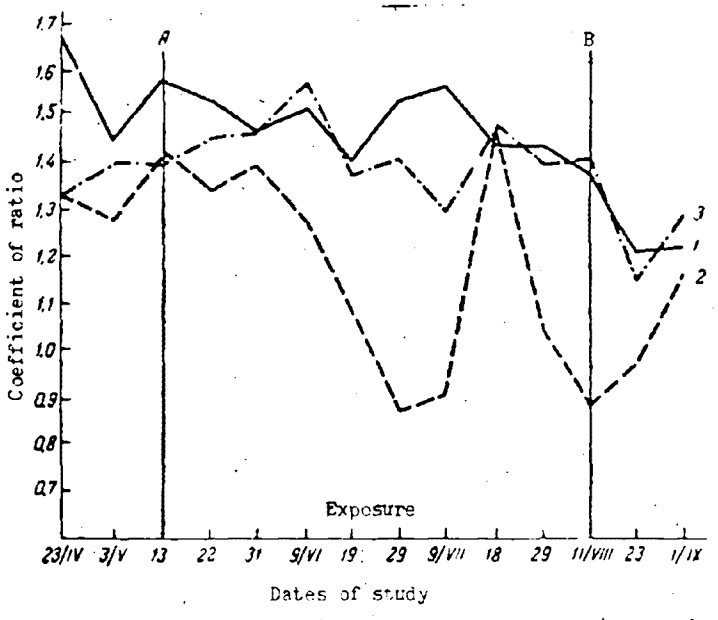

Fig. 2. Change in the ratio of chronaxy of antagonist muscles in rats during inhalation of methanol vapors.
A and B - period of exposure; 1 - pure air; 2 - concentration 5.31 mg/m³; 3 - concentration 0.57 mg/m³.

No changes in the chronaxy indices occured in rats of group II (Fig. 2).

Several authors (M. I. Gusev, 1960; K. A. Bushtuyeva, 1964; B. M. Mukhitov, 1961, and others) observed changes in the excretion of coproporphyrin with the urine in animals exposed to a prolonged action of certain noxious chemical compounds. We also used this method in our studies. The daily portion of urine from each group of animals (5 rats in each) was collected in special receiver chambers made of glass. The extraction of porphyrins from the urine was carried out by Fischer's method, and coproporphyrin was determined quantitatively on an SF-4 spectrophotometer in the wavelength range of 400-410 . The coproporphyrin was determined once every two weeks. In rats of group I (5.31 mg/m^3), the excretion of coproporphyrin with the urine per 100 g of weight starting with the 7th week of exposure decreased sharply and remained at this level until the end of exposure (Fig. 3). Normalization occurred after 20 days of the recovery period. In rats of group II (0.57 mg/m^3), no significant changes were observed.

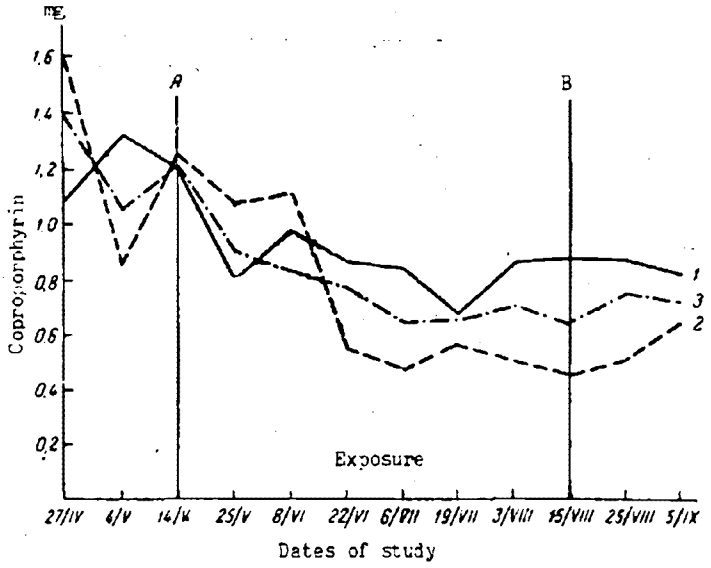

Fig. 3. Excretion of coproporphyrin with the urine in rats during inhalation of methanol vapors.
Notation same as in Fig. 2.

We studied the activity of whole blood cholinesterase by using A. A. Pokrovskiy's method (1953) modified by A. P. Martynova (1957).

The cholinesterase activity was determined in 5 rats of each group twice a month. Before the exposure, the original levels of acetylcholine hydrolysis amounted to an average of 38-39 minutes. In rats of group I, starting with the 6th week of exposure, the time of hydrolysis increased to 41 minutes, i.e., a decrease in cholinesterase activity was noted. At the end of exposure,

it amounted to 43 minutes (Fig. 4), and returned to normal at the end of the recovery period. In rats of group II, no significant changes were observed.

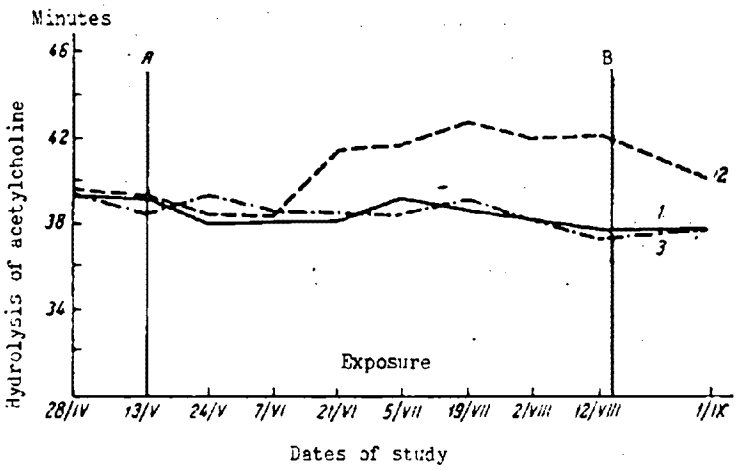

Fig. 4. Change in the activity of whole blood cholinesterase in rats during inhalation of methanol vapors.

Notation same as in Fig. 2.

The literature contains many papers indicating a change in the total amount of blood protein or in its individual fractions in various diseases and during the action of certain chemical compounds on the organism (R. Ubaydullayev, 1961; V. A. Chizhikov, 1964; P. G. Tkachev, 1964; Granati and Sekavo, 1956; Mario and Carlo, 1957).

In a chronic experiment, we studied the effect of low methanol concentrations on the protein fractions of the blood serum of rats by using paper electrophoresis. The protein fractions of 5 rats of each group were studied. The blooed was taken from the tail of an empy stomach every 15 days.

In group I, changes appeared 7 weeks after the start of exposure. This was associated with a decrease in the content of albumins and an increase in the amount of gamma globulins and beta globulins. There was no change in alpha globulins as compared with the control. In rats of group II, the fractional composition of the proteins remained unchanged (Table 4).

No changes were observed in the total proteins of the rats. Results of the study show that a continuous exposure of white rats to methanol vapors in the course of 90 days caused changes in animals of group I only (5.31 mg/m^3).

The 0.57 mg/m^3 concentration was found to be inactive, On this basis, we consider it possible to recommend 0.5 mg/m^3 as the mean daily maximum permissible concentration.

Table 4

Total proteins and protein fractions of the blood serum during chronic exposure of white rats to methanol vapors.

Period of Exposure	Group	Total Proteins	Albumins	Globulins			Albumin-Globulin Ratio
				Alpha	Beta	Gamma	
Before exposure	I	9,02	41,8	24,6	20,7	12,9	0,72
	II	9,31	44,8	23,2	19,4	12,6	0,81
	III (Control)	8,91	45,1	23,3	19,2	12,4	0,83
On 45th day of exposure	I	8,79	34,7	24,0	24,0	17,3	0,53
	II	9,01	44,1	21,5	20,2	14,2	0,79
	III (Control)	9,02	43,6	20,9	20,9	14,6	0,87
On 90th day of exposure	I	9,17	32,8	23,3	25,8	18,1	0,49
	II	9,16	42,0	21,8	21,9	14,3	0,72
	III (Control)	8,89	42,9	21,8	21,2	14,1	0,76
On 20th day of recovery period	I	9,27	39,4	25,3	21,2	14,1	0,65
	II	9,05	42,2	20,2	22,1	15,5	0,73
	III (Control)	8,79	44,2	20,2	22,9	12,7	0,80

Table 5

Pollution of atmospheric air with methanol vapors around the hydrolysis plants of Uzbekistan.

Distance From Source of Discharge	Number of Samples	Single Concentrations, mg/m³		Number of Samples with Concentration, mg/m³	
		Maximum	Minimum	1 and Above	Under 1
Andizhan Plant					
100	16	2,26	0,46	10	6
200	18	1,67	0,11	5	13
300	27	0,33	0,05	—	27
500	18	0,14	—	—	18
Fergana Plant					
100	17	4,49	0,89	16	1
200	15	2,2	0,1	9	6
300	25	0,83	0,11	—	25
500	19	0,3	—	—	19
Yangiyul' Plant					
100	14	1,15	0,1	3	11
200	24	0,55	1	—	24
300	14	0,05	—	—	14

In order to make a sanitary evaluation of the pollution of atmospheric air around the Andizhan, Fergana and Yangiyul' hydrolysis plants of Uzbekistan, we studied the range of pollution of atmospheric air with methanol vapors. The tests were taken in May and August 1962 at distances from 100 to 500 m on the leeward side of the source of the discharge (Table 5).

It is evident from Table 5 that at distances of 100 and 200 m from the andizhan and Fergana plants, the methanol concentrations exceeded the recommended maximum permissible concentration 1 mg/m^3). At the Yangiyul' plant, this excess was observed only at a distance of 100 m. At larger distances from the plants, all the concentrations were below 1 mg/m^3.

Conclusions

1. Atmospheric air around hydrolysis plants producing methanol is polluted by its vapors at a distance of up to 200 m.
2. A study of the effect of methanol on the human organism showed that in the most sensitive persons, the threshold of olfactory perception of methanol is 4.5 mg/m^3, the threshold of reflex change of the light sensitivity of the eye is 3.35 mg/m^3, and the threshold of action on the electrical activity of the brain is 1.17 mg/m^3.
3. The highest single maximum permissible concentration of methanol in atmospheric air should be no higher than 1 mg/m^3.
4. Chronic round-the-clock exposure to methanol in a concentration of 5.3 mg/m^3 over the course of 90 days caused changes in the normal ratio of chronaxy of antagonist muscles, activity of whole blood cholinesterase, excretion of coproporphyrin with the urine, and protein fractions of the blood serum in the experimental rats.

A concentration of 0.57 mg/m^3 had no effect on the rat organism.

5. The mean daily maximum permissible concentration of methanol which can be recommended is 0.5 mg/m^3.

LITERATURE CITED

Note: References mentioned in this paper are to be found at the end of the volume in the 1967 bibliography.

DATA FOR THE VALIDATION OF THE MAXIMUM PERMISSIBLE CONCENTRATION OF AMMONIA IN ATMOSPHERIC AIR

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From Akademiya Meditsinskikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 10, Izdatel'stvo "Meditsina" Moskva, p. 108-122; (1967).

Ammonia is the simplest compound of nitrogen and hydrogen, a colorless gas with a sharp suffocating odor and a pungent taste. Under pressure or on cooling, it passes to the liquid state. It is soluble in ether, alcohol, and fats. It dissolves readily and in large quantities in water, forming ammonium hydroxide. It reacts actively with acids and other compounds. Ammonia is obtained chiefly from nitrogen and hydrogen (I. D. Fotonich, 1965; S. A. Beskov, 1962).

Ammonia is a valuable nitrogen-containing liquid fertilizer and also the main raw material in the production of nitric acid and ammonium fertilizers. It is used in considerable amounts in the manufacture of ammonium hydroxide and ammonium chloride. Ammonia is widely used in refrigeration engineering, in the production of soda, and in nitriding steel products.

The chief sources of discharge of ammonia into atmospheric air are nitrogen fertilizer plants, enterprises producing nitric acid and ammonium salts, refrigeration units, coking and leather plants, and livestock breeding farms.

The largest of these sources are nitrogen fertilizer plants and coking sections of ferrous metallurgical enterprises. Small amounts of ammonia reach the air from the soil and from open water reservoirs.

However, the literature available to us gives scant data on the quantitative content of ammonia either in the air of industrial buildings or in the atmospheric air of populated areas.

According to the data of V. A. Ryazanov (1961), at the site of one of the largest chemical plants around the ammonia synthesis section, single concentrations from 20.1 to 57 mg/m^3 were observed at a distance of 10 m, and from 0.1 to 0.2 mg/m^3 at a distance of 1 km. The mean daily concentrations at different points of the plant site ranged from 0.216 to 3.309 mg/m^3. In the air of the town located at a distance of 2 km from this chemical plant, the ammonia concentrations did not exceed 0.004-0.005 mg/m^3.

To study the degree of pollution of atmospheric air with ammonia around metallurgical plants, the Novolipetsk Metallurgical Plant, the largest source of discharge of ammonia into atmospheric air, was investigated. The coking and nitrogen fertilizer sections are located on the territory of the plant. In the coking section, ammonia is present in the composition of the coke-oven gas and of the tar water. Ammonia reaches the atmospheric air as a result of the discharge of coke-oven gas at various points of the plant through leaks in gas lines and units (scrubbers, exhausters). The gases are also emitted from open reservoirs (storage tanks, measuring tanks) where ammonia water or tar water is stored.

The nitrogen fertilizer plant synthesizes ammonia from coke-oven gas supplied by the coking plant. The entire technological process of this plant takes place in a closed system; the discharge of the gas into atmospheric air takes place during repairs, during purging of the system and dispensing of the finished liquid ammonia into tanks, and also during distribution among the consumers.

We studied the atmospheric air around the Novolipetsk Metallurgical Plant in September-October 1963 and in May-June 1964 and 1965. The latter study was made in connection with the start-up of a new nitrogen fertilizer plant synthesizing liquid ammonia. The air samples were taken on the leeward side of the emission source at a level of 1.5 m above ground. A total of 400 air samples were taken.

Results of the studies are given in Table 1.

As is evident from Table 1, the highest concentrations of ammonia were found at distances of 500 and 1000 m. In 1965, as a result of the starting of a nitrogen fertilizer plant synthesizing ammonia, the concentration of the latter at close distances increased even more.

Table 1

Pollution of Atmospheric Air with Ammonia Around the Novolipetsk Metallurgical Plant.

Distance From Source, m	Ammonia, mg/m^3					
	1963 г.		1964 г.		1965 г.	
	Maximum	Average	Maximum	Average	Maximum	Average
500	1,40	0,31	3,60	0,62	4,68	2,19
1 000	3,5	0,5	0,39	0,18	1,73	0,91
3 000	2,25	0,45	1,30	0,26	0,39	0,24
5 000	1,0	0,16	1,30	0,18	0,28	0,22
7 000	0,20	0,09	1,20	0,19	0,17	0,16
10 000					0,13	0,12

A number of authors studied the pollution of atmospheric air around more minor sources of discharge of ammonia.

Z. D. Markova (1941) detected ammonia in concentrations of 0.02 to 0.05 mg/m^3 in the residential areas of Rostov-on-Don, whereas in the city parks, the concentration did not exceed 0.02 mg/m^3.

V. A. Kononova and V. B. Aksenova (1963) found ammonia in amounts from 0.015 to 0.057 mg/m^3 in the air around livestock farms in a zone of up to 150 m.

According to the data of American authors, in areas with pure air, the concentration of ammonia in Chicago ranged from 0.0058 to 0.0143 mg/m^3 (cited by V. A. Ryazanov, 1961). According to the data of Stoklaz, the concentration of ammonia in pure air varies from 0.02 to 0.04 mg/m^3, which according to Ryazanov (1961) is exaggerated. Thus, from the literature data cited it is evident that, depending on the source of pollution, the concentration of ammonia in atmospheric air ranges from 0.015 to 0.057 mg/m^3, and in air where special pollution sources are absent, the content of ammonia ranges from 0.003 to 0.005 mg/m^3.

Ammonia is an irritating gas which affects primarily the mucous membranes of the respiratory tract and the central nervous system. This effect of ammonia is due to its high solubility on the moist surfaces of mucous membranes and its ready absorption into the blood stream.

Cases have been described involving an acute poisoning with ammonia as a result of the rupture of cylinders during production or when pouring ammonium hydroxide in everyday use (R. N. Vol'fovskaya and G. N. Davydova, 1945; Ye. I. Lyublina, 1948; V. K. Trutnev and N. V. Velikorussova, 1955; K. V. Yegorov, 1959, and others).

Vol'fovskaya and Davydova (1945), Trutnev, Lehmann (1886-1889), Horvath (1926, 1929) and others classify ammonia among suffocating poisons with a marked inflammatory-necrotic effect. Vol'fovskaya and Davydova also admit the possibility of a resorptive effect.

Injury to the nervous system is manifested in the loss of consciousness and a strong excitation to the point of violent delirium.

According to the observations of I. P. Pavlov (1896), ammonia in a dose of 50 mg per kg of animal weight caused drosiness and ataxia, and when the dose was increased by a factor of 2½, convulsions followed by death of the experimental animals were observed. Studies made by V. V. Pravdich-Neminskiy (1958), Ye. A. Vladimirova (1938), E. E. Kosyakov (1962), N. B. Kozlov (1962), E. E. Martinson (1962) and others confirmed Pavlov's observations.

Studies made by Recine (1956) showed that in poisoning with ammonia, because of its action on prothrombin, the coagulability of the blood is impaired, and the content of residual nitrogen in the blood increases.

An increased content of ammonia in the blood and tissues is accompanied by changes in the physicochemical properties and structure of the tissue proteins, a disturbance of the ion exchange and acetylcholine exchange, and a depression of tissue respiration (N. B. Kozlov, 1962).

The chronic action of gaseous ammonia in low concentrations is manifested in the form of inflammation of the upper respiratory tract, conjunctivitis, and a lowering of the resistance of the organism to infectious diseases.

Workers of the municipal sewer network, who because of the requirements of their work are exposed for long periods of time to an atmosphere containing small amounts of ammonia and hydrogen sulfide, have displayed chronic hypertrophic catarrhs changing into atrophic ones (M. D. Ayzenberg, 1927; T. V. Ass, V. V. Vol et al., 1926).

Abadie, Trachta, and Trousseau (cited by R. M. Zhmudskaya, 1933) revealed conjunctivitis involving ulcerations of the cornea in workers exposed for a long time to the action of low concentrations of ammonia.

According to the data of Henderson and Haggard (1930), the threshold of perception of ammonia for man is 37 mg/m^3. According to I. M. Alpatov (1964), the threshold of the reflex effect of ammonia for man is 22 mg/m^3. According to Lehman (1886), Silverman, Whittenberger, and Muller (1949), the highest permissible concentration of ammonia for lengthy exposure is 69mg/m^3. The maximum permissible concentration of ammonia for the air of industrial buildings, adopted in 1930 in accordance with a proposal of the Moscow Institute of Labor Protection, is 20 mg/m^3.

Despite a considerable number of sources of discharge, ammonia as an atmospheric pollutant has been inadequately studied. The existing studies give contradictory data. The maximum permissible concentration of ammonia in atmospheric air has not been established thus far. The object of our study was to give an experimental validation of the highest single and mean daily maximum permissible concentrations of ammonia in atmospheric air.

The gas in the experiment was obtained by using a 25% solution of ammonia in a distilling flask.

The concentrations of ammonia in air were determined by a colorimetric method based on the yellowish-brown coloration of solutions formed when ammonia acts with Nessler's reagent. The sensitivity of the method is 0.3μg of ammonia in the volume analyzed.

To validate the highest single maximum permissible concentration of ammonia in atmospheric air, we determined the threshold of olfactory perception by using a method proposed by the Committee on Sanitary Protection of Atmospheric Air (1957). The tests were conducted on 22 practically healthy persons aged 17 to 48 years. A total of 432 tests with concentrations from 5 to 0.4 mg/m^3 were performed (Table 2).

Table 2

Threshold of Olfactory Perception of Ammonia.

Number of Subjects	Number of Observations	Concentration of NH_3, mg/m^3	
		Minimum Perceptible	Maximum Imperceptible
2	36	1,95	1,0
7	138	0,98	0,75
9	200	0,70	0,55
4	58	0,50	0,45

As can be seen from Table 2, the threshold of olfactory perception of ammonia in the most sensitive persons is 0.5 mg/m^3, and the subthreshold concentration is 0.45 mg/m^3.

Numerous studies established that fragrant substances in concentrations of undetectable odor can cause definite reflex responses in the human organism. Such reflex changes arise in the visual system and in the cerebral cortex, and we utilized them in the study of the subsensible effect of ammonia on the human organism.

Adaptometric studies were performed with the aid of an ADM adaptometer on 3 subjects whose threshold of olfactory perception of ammonia was first determined.

The tests were conducted with concentrations of 0.65 and 0.51 mg/m^3 for one subject and 0.51, 0.45, and 0.32 mg/m^3 for the other two. This distribution was due to the subjects' different thresholds of perception of ammonia odor. The effect of each concentration was studied no fewer than three times. The data obtained show that ammonia in a concentration of 0.45 mg/m^3 decreases the light sensitivity of the eyes in two subjects (D. N. and L. N.), whereas a concentration of 0.32 mg/m^3 was found to be inactive for them (Fig. 1). In the third subject (Sh. L.), the threshold concentration for the change of the light sensitivity of the eyes was found to be 0.65 mg/m^3, and the subthreshold concentration, 0.5 mg/m^3.

To determine the threshold of the electric activity of the brain, we used the method of recording the flare-up of the alpha rhythm during the action of intermittent light timed to the intrinsic potentials of the brain.

The work was performed in the department of communal hygiene of the Central Institute for Advanced Training of Physicians.

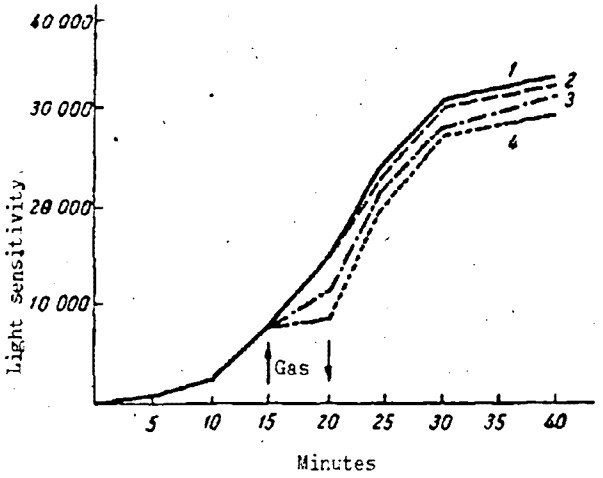

Fig. 1. Change in the light sensitivity of the eye in subject D. N. during inhalation of different concentrations of ammonia.

1 - pure air; 2 - concentration 0.32 mg/m^3; 3 - concentration 0.45 mg/m^3; 4 - concentration 0.5 mg/m^3.

The studies were conducted on 5 subjects aged 18 to 24 years, whose ammonia odor threshold was first determined. The changes in biopotentials were recorded on an 8-channel Kaiser electroencephalograph. The total activity of the human cerebral cortex was analyzed with the aid of a multichannel integrator of B. N. Balashev's system (1964). The biocurrents were taken off in the bipolar manner. Rhythmic photic stimulation was carried out by means of a photostimulator at a frequency of 8 flickers per second and an intensity of 0.1, 0.2, and 0.6 J. Three observations were carried out with each concentration, and 2-3 observations with pure air for the control. The total bioelectric activity for the entire period of action of the light was calculated by means of an integrator. The results obtained were expressed in percent. The average acticity calculated for the first three minutes was taken as 100%.

In 3 subjects with an odor threshold of 0.55 mg/m^3, a concentration of 0.35 mg/m^3 had a substantial effect on the electrical activity of the brain; in two subjects (Kh. V. and K. V.), an attenuation of the total bioelectric activity was observed during the first minute of supply of the gas, and a reinforcement was observed in subject D. M. In all three, an ammonia concentration of 0.22 mg/m^3 caused no changes (Fig. 2).

In two subjects (D. N. and I. N.) with an odor threshold of 0.76 mg/m^3, the active concentration was found to be 0.44 mg/m^3, and the inactive concentration, 0.32 mg/m^3. Ammonia had the most pronounced effect in the fourth

minute of the experiment with a gradual attenuation in the 5th-6th minute. A more pronounced effect on the organism when ammonia first begins to act is also observed when the threshold of olfactory perception is established and when the light sensitivity of the eyes is studied.

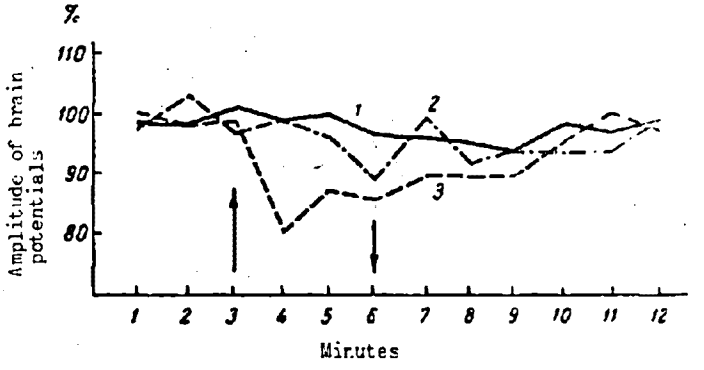

Fig. 2. Amplitude of brain potentials in subject K. V. during inhalation of different concentrations of ammonia. 1 - pure air; 2 - concentration 0.22 mg/m^3; 3 - concentration 0.35 mg/m^3. Arrows indicate the time of inhalation of the gas.

Table 3 shows the thresholds of the reflex effect of ammonia on man.

Thus, the concentration of 0.2 mg/m^3, which was found to be the subthreshold value according to the most sensitive method, may be recommended as the highest single maximum permissible concentration for atmospheric air.

Table 3

Thresholds of the Reflex Effect of Ammonia.

Effect Studied	Concentration, mg/m^3	
	Threshold	Subthreshold
Olfactory perception	0,50	0,45
Change of the light sensitivity of the eyes	0,45	0,32
Change of the electrical activity of the brain	0,35	0,22

In order to establish the mean daily maximum permissible concentration of ammonia in atmospheric air, we studied its chronic effect on the animal organism. A continuous round-the-clock exposure of white rats to gaseous ammonia was carried out for 84 days in the following concentrations: group I, 20 ± 0.1 mg/m^3 (level of the maximum permissible concentration for industrial buildings), group II, 2.0 ± 0.061 mg/m^3, and group III, 0.2 ± 0.0072 mg/m^3 (level which we propose for the highest single maximum permissible concentration for atmospheric air); group IV was the control.

Sixty white male rats weighing 105-150 g were selected for the chronic exposure. The latter was carried out in 100-l chambers. Purified air mixed with gaseous ammonia in definite concentrations was supplied to the chambers at a rate of 28-30 l/min. Samples of air for analysis were taken from the chambers every day.

In the course of the chronic experiment, the general condition of the animals, their weight, state of the latent reflex time, porphyrin metabolism and ammonia content in the urine were observed. In the blood of the animals, the cholinesterase activity, oxidation-reduction function, number of fluorescent* leucocytes, hemoglobin, erythrocytes, and nucleic acids were determined. At the end of the exposure and recovery period, part of the animals were killed and subjected to anatomico-pathologic analyses. The results of the experiment were evaluated by calculating the reliability between the indices of the control and experimental groups of animals, obtained by statistical treatment using the range method.

In the course of the experiment, the rats were healthy and active in all the groups, and no weight lag was observed in comparison with the controls.

Measurement of the latent time of the reflex response permits an evaluation of the functional state of the central nervous system for different actions of toxic substances on the organism (A. A. Minayev, 1965; A. P. Fomin, 1965). We used for this purpose a "chronoreflexogenometer" instrument proposed by S. I. Gorshkov (1964). The time (in sigmas) of the appearance of the motor response to the action of the pain stimulus (electric current) was determined.

Results of the studies are given in Table 4 and Fig. 3

In our studies, a significant shortening of the reflex time was observed during the first month of exposure only in group I during the action of ammonia in a concentration of 20 mg/m^3.

We determined the cholinesterase activity of the blood by the Fleischer-Pauns procedure modified by N. N. Pushkina and N. V. Klimkina (N. N. Pushkina, 1963). A depression of cholinesterase activity occurred in rats of group I. No changes were observed in the other groups (Fig. 4).

The oxidation-reduction function of the blood serum was determined by using a modified method of Tumberg (Yu. L. Anin, 1964). The method is based on the change in the color of methylene blue with blood serum during boiling on a water bath and the determination of the time of its total bleaching.

* Editor's note: For the Russian use of the terms "luminescent" and "luminescence" in this paper, we have substituted "fluorescent" and "fluorescence", on the basis of the definitions of these terms.

A lengthening of the time of total bleaching as compared with the control group occurred in rats of groups I and II (Table 5, Fig. 5). This phenomenon characterizes a depression of the oxidation-reduction processes in the animal organism.

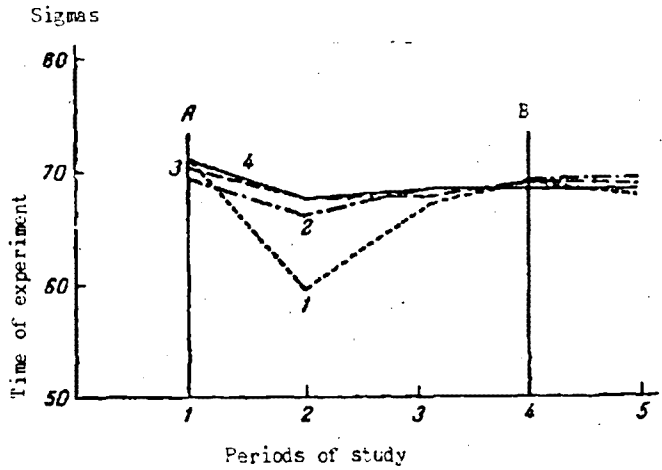

Fig. 3. Change in the latent reflex time in rats under the influence of different concentrations of ammonia.
1 - group I (20 mg/m^3); 2 - group II (2 mg/m^3);
3 - group III (0.2 mg/m^3); 4 - control group IV;
AB - period of exposure

Table 4

Change in the Latent Reflex Time in Rats

Periods	Group I (20 mg/m^3)	II (2 mg/m^3)	III (0.2 mg/m^3)	IV (control)
Before exposure	71,4(o)	69,2(o)	70,4(o)	71,3
1st month exposure	57,6(c)	66,4(o)	67,8(o)	67,0
2nd month exposure	66,3(o)	68,0(o)	67,6(o)	68,3
3rd month exposure	68,3(o)	68,4(o)	68,4(o)	68,1
Recovery period	68,0(o)	68,8(c)	68,0(o)	68,2

Note. Degree of significance: c - 99.9%; o - insignificant

One of the methods of determining the early qualitative changes in the formed elements of white blood cells is fluorescent microscopy. The method is based on the ability of nuclear nucleoproteins of degenerating cells to combine with acridine dyes in a different manner than the nucleoproteins of undamaged cells (M. N. Meysel' and V. A. Sondak, 1956). However, during the exposure we failed to observe any degenerative changes in the leucocytes in the blood of the experimental rats as compared with the control group.

Nor were we able to detect any changes by studying the blood for the content of erythrocytes, hemoglobin and total quantity of nucleic acids.

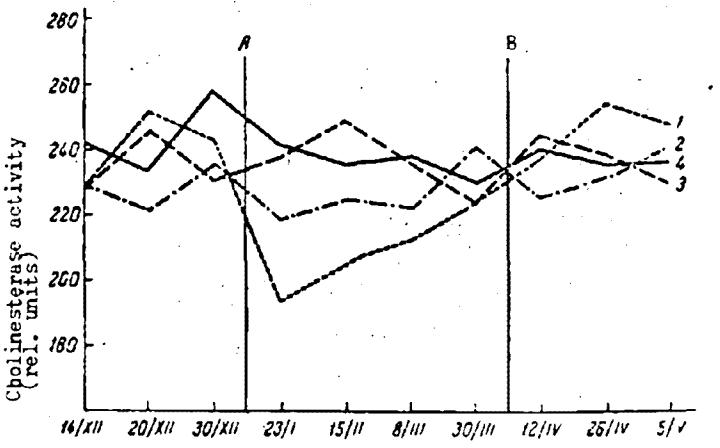

Fig. 4. Change of cholinesterase activity in the blood of rats under the influence of ammonia. Notation same as in Fig. 3.

Table 5

Change of the Oxidation-Reduction Function of the Blood Serum in Rats (Time in Minutes)

Periods	Group I (20 mg/m³)	II (2 mg/m³)	III (0.2 mg/m³)	IV (Control)
Before exposure	10,53(o)	10,93(o)	10,46(o)	10,66
Exposure	19,10(c)	15,0(c)	12,20(o)	12,05
Recovery period	12,66(o)	12,73(o)	12,63(o)	12,66

Note. Confidence factor: c - 99.9%; o - insignificant.

In order to characterize the chronic action of ammonia on the organism of the experimental animals, we also studied the porphyrin metabolism.

Yu. K. Smirnov (1953) showed that excitation of the nervous system causes an increase in the porphyrin metabolism, and inhibition causes a decrease. M. I. Gusev (1960) was the first to study the porphyrin metabolism in connection with a sanitary standardization of lead in atmospheric air. Subsequent studies by G. I. Solomin (1961), Li Sheng (1961), V. I. Filatova

(1961), B. M. Mukhitov (1963), and others confirmed the high sensitivity of this method. The content of coproporphyrins in the urine was determined spectrophotometrically. It was found that during the exposure, an increase in coproporphyrin occurred only in group I of the animals (Fig. 6).

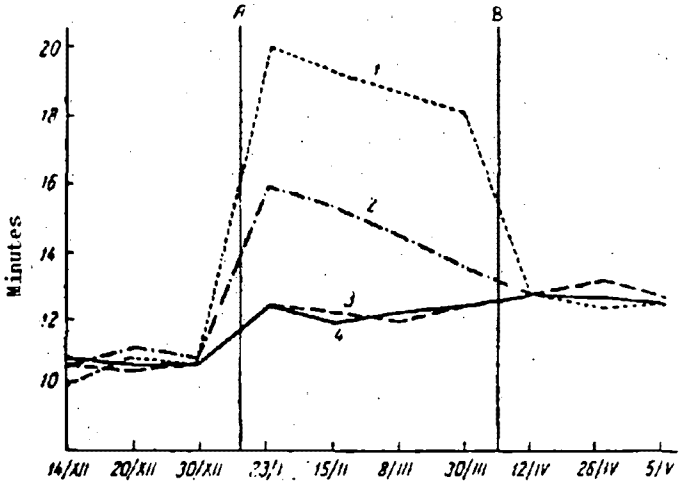

Fig. 5. Effect of ammonia on the oxidation-reduction function of the blood serum of rats.
Notation same as in Fig. 3.

Simultaneously, we determined the content of ammonia in the urine of the animals. An increase in the ammonia content was also noted only in group I.

From the round-the-clock chronic exposure of white rats which was performed, it was found that ammonia in a concentration of 20 mg/m^3 caused a shortening of the time of the reflex response, a depression of cholinesterase activity and oxidation-reduction function of the blood, and also an increase in the excretion of coproporphyrin and ammonia in the urine.

Ammonia in a concentration of 2 mg/m^3 caused only a depression of the oxidation-reduction function of the blood serum. A concentration of 0.2 mg/m^3 was found to be inactive.

Histopathological examinations did not show any changes in the internal organs and central nervous system in animals of the experimental groups as compared to the control group.

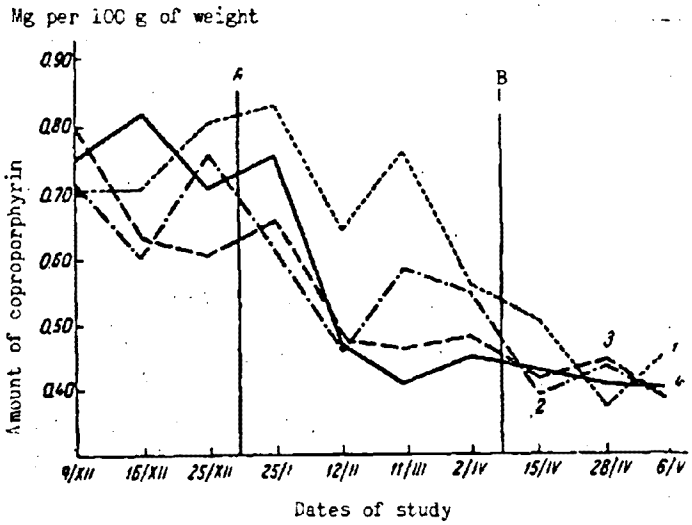

Fig. 6. Effect of ammonia on the coproporphyrin exchange of rats. Notation same as in Fig. 3.

Conclusions

1. A whole series of enterprises including metallurgical plants whose composition includes coking and nitrogen fertilizer sections constitute major sources of pollution of atmospheric air with ammonia.

2. The subliminal concentration of ammonia which did not cause a change in the biopotentials of the brain, equal to 0.2 mg/m^3, is proposed as the highest single maximum permissible concentration in atmospheric air.

3. A similar concentration of ammonia (0.2 mg/m^3) during around-the-clock chronic exposure was found to be inactive and can therefore also be recommended as the mean daily maximum permissible concentration in atmospheric air.

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Note: References mentioned in this paper are to be found at the end of the volume in the 1967 bibliography.

POLLUTION OF ATMOSPHERIC AIR WITH VAPORS OF HYDROLYTIC ETHYL ALCOHOL AND ITS EFFECT ON THE ORGANISM

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From Akademiya Meditsinskikh Nauk SSSR. "Biologicheskoe deystvie i gigienicheskoe znachenie atmosfernykh zagryazneniy". Red. V. A. Ryazanova. Vypusk 10, Izdatel'stvo "Meditsina" Moskva, p. 74-86. (1967)

Hydrolytic alcohol is ethyl alcohol (ethanol) containing different impurities of acids (in terms of acetic acid, 0.036-0.12 g/l), unsaturated compounds (in terms of allyl alcohol, 0.07-0.89 g/l), 3-6.2 g/l of methyl alcohol, carbonyl compounds (in terms of acetaldehyde 1.7-21.6 g/l), 0-0.24 g/l of furfural, and higher alcohols (in terms of isobutyl alcohol, 2.3 g/l).

Ethanol is a transparent, colorless, volatile liquid with a specific odor and a boiling point of 78.4°C. Ethanol is miscible in all proportions with water, ether, and chloroform; it dissolves inorganic salts, particularly chlorides, nitrates, and acetates, essential oils, and some fatty oils.

Ordinary ethanol is obtained by alcoholic fermentation of such starch-containing materials as potatoes, cereals, rice, and also molasses; synthetic ethanol is obtained from ethylene and acetylene.

In the ethanol-producing industry hydrolytic alcohol has become the most common product. Its production is based on the fermentation of hexose sugar, obtainable from hexose-containing plants. Ethanol finds applications as a solvent in the manufacture of lacquers and varnishes, and is used as the starting material in the synthesis of many organic compounds, in the preparation of synthetic rubber by Lebedev's method, as a fuel for internal combustion engines, in the food industry, in medicine, and in many other branches of the national economy.

In the nature of its action, ethanol is a narcotic and a nerve poison. In high concentrations, it first causes stimulation, and then paralysis of the central nervous system. Prolonged chronic exposure to large doses may cause serious organic diseases of the nervous system, digestive tract, cardiovascular system, liver, etc.

There are no literature data on the effect of low ethanol concentrations on man and animals during inhalation. Its maximum permissible concentration in atmospheric air has not been established. Nor are there any data on the pollution of atmospheric air with ethanol around the plants producing it. The object of the present study was to elucidate these questions.

The determination of ethyl alcohol in atmospheric air was made with the aid of I. A. Pinigina's method (1961), based on the reaction of alcohol with the vanadium-hydroxyquinoline complex with the formation of an orange color. The sensitivity of the method is 0.002 mg in a volume of 2.5 ml. To obtain the desired concentration in the experimental mixture of air and ethanol, we passed air through a distilling flask filled with hydrolytic alcohol. Before the start of the experiments, the constancy of the ethanol concentrations in the cylinder was studied for several days, and found to remain at the same level with only slight fluctuations. To determine the odor threshold, 25 persons aged from 18 to 40 years were chosen. A total of 385 determinations of the odor threshold were made with 7 concentrations (from 14.8 to 6.3 mg/m^3) (Table 1).

Table 1

Results of Determination of the Odor Threshold of Hydrolytic Ethyl Alcohol

Number of Subjects	Concentration, mg/m^3	
	Minimum Perceptible	Maximum Imperceptible
1	10,2	9,4
7	8,7	8,0
7	8,0	7,3
4	7,3	7,0
6	7,1	6,3

Thus, the threshold of olfactory perception of hydrolytic alcohol in the most sensitive persons of this group was found to be 7.1 mg/m^3, and the subthreshold concentration, 6.3 mg/m^3. We then determined the effect of low ethanol concentrations on the light sensitivity of the eye by the dark adaptation method. A total of 42 tests on persons aged 18 to 27 years were carried out. Concentrations of 8.29, 6.97, and 6.12 mg/m^3 were studied.

An ethanol concentration of 8.29 mg/m^3 caused a change in the course of the dark adaptation curve in all four subjects. For the most sensitive two person, the minimum active concentration of ethanol with respect to the light sensitivity of the eyes was found to be 6.97 mg/m^3. The inactive concentration for these persons was 6.12 mg/m^3 (Table 2).

In studying the effect of low ethanol concentrations on the electrical activity of the cerebral cortex, we used A. D. Semenenko's method (1963) of a reflex response involving a flare-up of the alpha rhythm in man during simultaneous stimulation of the subject with intermittent light whose frequency corresponds to his rhythm and with sound whose intensity was varied continually Superimposed on the background of the functional load was a reinforcement of the intrinsic alpha rhythm of the subject, and under the influence of the inhaled gas mixture with the active ethanol concentration, there was a change in the character of the recorded surves, indicating a change in the dynamics of the nervous processes occuring in the cortex of the cerebral hemispheres.

Table 2

Threshold of Reflex Variation of the Light Sensitivity of the Eyes During Inhalation of Vapors of Hydrolytic Ethyl Alcohol (in 20th minute in percent of 15th minute)

Subject	Pure Air	Concentration, mg/m³				
		8,29	6.97	6.12	Threshold	Subthreshold
I. L.	158,6 (o)	194,8 (b)	150,0 (o)	—	8,29	6,97
B. Ye.	156,0 (o)	226,7 (b)	155,6 (o)	—	8,29	6,97
Ch. A.	133,5 (o)	223,6 (c)	151,9 (b)	134,3 (o)	6,97	6,12
B. V.	148,0 (o)	214,4 (b)	130,7 (b)	147,8 (o)	6,97	6,12

Note. Degree of significance: a - 95%; b - 99%; c - 99.9%; o - insignificant.

The curves were recorded on an eight-channel Hungarian electroencephalograph of the Orion Budapest Co. The study was made on five persons with the lowest odor threshold under the same conditions and at the same time.

Ethanol concentrations of 6.14 and 4.9 mg/m^3 were studied. The experiment was conducted no fewer than 4-5 times with each concentration. Results of the study and analysis of the statistical treatment of the data show that a concentration of 6.1 mg/m^3 was active for all five subjects. The inactive concentration was 4.9 mg/m^3 (Table 3).

Results of all the studies of the reflex effect of ethanol are summarized in Table 4.

On the basis of the study of the reflex response of man, we propose 5 mg/m^3 as the highest single maximum permissible concentration of hydrolytic ethanol in atmospheric air.

To validate the mean daily maximum permissible concentration of ethanol in atmospheric air, we conducted a 90-day round-the-clock dynamic exposure of 45 white male rats weighing 100-120 g, which were divided into three groups.

In selecting the concentrations for the exposure, we used the results of the study of the reflex effect of ethanol on the human organism. Group II of rats was exposed to ethanol vapors in a concentration of 5 mg/m^3 at the level of our proposed highest single maximum permissible concentration, and in group I, the ethanol concentration was five times as high.

Group III of the rats was the control group. To evaluate the effect of ethanol vapors on the organism of the animals, we studied the behavior and weight dynamics of the animals, motor chronaxy of antagonist muscles, excretion of coproporphyrins with the urine, activity of blood cholinesterase, to-

tal proteins, and protein fractions of the blood serum. All the numerical data obtained were subjected to statistical treatment.

Table 3

Effect of Low Concentrations of Hydrolytic Ethanol on the Electrical Activity of the Cerebral Cortex

Subject	6,1 mg/m³		4.9 mg/m³	
	Hemisphere		Hemisphere	
	Left	Right	Left	Right
I. S.	+	±	—	—
L. M.	+	+	—	—
R. K.	+	—	—	—
L. B.	+	+	—	—
M. K.	+	+	—	—

Note: + statistically significant changes,
- insignificant changes.

Table 4

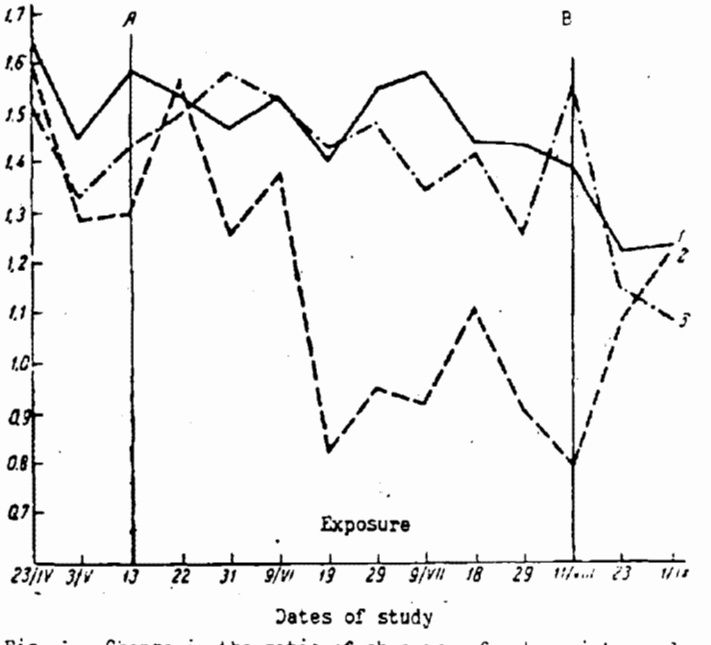
Effect of Low Concentrations of Hydrolytic Ethanol on Receptors of Respiratory Organs.

Function	Concentration, mg/m³	
	Threshold	Subthreshold
Odor perception	7,1	6,3
Light sensitivity of eye	6,9	6,1
Electrical activity of cerebral cortex	6,1	4,9

The experimental mixture of air with a given ethanol concentration was supplied to the chamber at the rate of 35 l/min. Such a rate of supply of air produces the most favorable conditions for the animals (V. A. Popov, 1964). The actual ethanol concentrations in the chambers were: in group I, 29.25 ± 2.1 mg/m³, and in group II, 5.59 ± 0.45 mg/m³. During the exposure, the animals of all the groups were healthy, active, and gained weight moderately. However, a slight weight lag was observed in rats of group I. We determined the chronaxy of antagonist muscles every 10 days in five rats of each group at the same time and under the same conditions, using an ISE-01 electronic pulse stimulator (Table 5 and Fig. 1).

The above data indicate that in rats of group I, a distrubance of the normal ratio of the chronaxy of extensors and flexors occurred on the 6th day of exposure. At the end of the recovery period, all the ratios returned to normal.

In rats of group II, there were no statistically significant changes as compared with the animals of the control group. The activity of whole blood cholinesterase was determined by the method of A. A. Pokrovskiy (1953) and A. P. Martynova (1957) in five rats of each group.



Dates of study

Fig. 1. Change in the ratio of chronaxy of antagonist muscles during inhalation of vapors of hydrolytic ethanol.
A-B - period of exposure; 1 - pure air; 2 - concentration 29.25 mg/m³; 3 - concentration 5.57 mg/m³.

Table 5

Ratio of Chronaxy of Antagonist Muscles in Rats During Inhalation of Vapors of Hydrolytic Ethanol

Periods	Date of Study	Group I	Group II	Control, III
		Ratio of Chronaxia of Extensors to Chronaxy of Flexors		
Before exposure	23/IV	1,62 (o)	1,53 (o)	1,65
	3/V	1,29 (o)	1,33 (o)	1,45
	13/V	1,30 (o)	1,43 (o)	1,58
Exposure	22/V	1,55 (o)	1,50 (o)	1,54
	31/V	1,26 (o)	1,58 (o)	1,48
	9/VI	1,37 (o)	1,53 (o)	1,53
	19/VI	0,82 (c)	1,42 (o)	1,41
	29/VI	0,93 (c)	1,49 (o)	1,54
	9/VII	0,91 (b)	1,35 (o)	1,57
	18/VII	1,1 (o)	1,42 (o)	1,14
	29/VII	0,91 (a)	1,26 (o)	1,14
	11/VIII	0,79 (o)	1,56 (o)	1,39
Recovery	23/VIII	1,08 (o)	1,15 (o)	1,22
	1/IX	1,23 (o)	1,09 (o)	1,23

Note. Degree of significance: a - 95%; b - 99.9%; c - 99.9%; o - insignificant.

Table 6

Change of Cholinesterase Activity in Rats During Inhalation of Vapors of Hydrolytic Ethanol (in minutes of hydrolysis of acetylcholine).

Period	Date	Groups I (29.2 mg/m³)	II (5.59 mg/m³)	Control III
Before exposure	28/IV	37,6 (o)	37,0 (o)	39,2
Exposure	13/V	37,8 (o)	38,8 (o)	39,2
	24/V	39,8 (o)	31,4 (o)	38,0
	7/VI	39,0 (o)	39,2 (o)	38,0
	21/VI	42,0 (c)	38,6 (o)	38,2
	5/VII	42,2 (b)	38,8 (o)	38,8
	19/VII	39,8 (o)	37,4 (o)	38,8
	2/VIII	41,8 (a)	37,8 (o)	38,0
	12/VIII	42,2 (a)	37,8 (o)	37,6
Recovery	1/IX	38,7 (o)	38,0 (o)	37,4

Note. Degree of significance: a - 95%; b - 99%; c - 99.9%; o - insignificant.

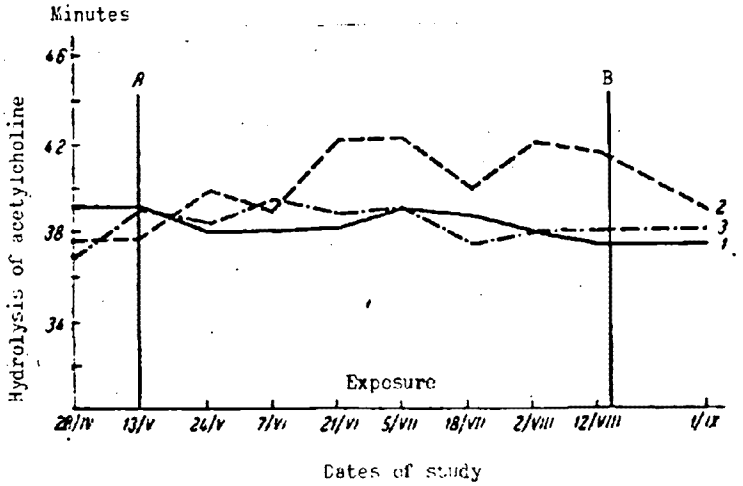


Fig. 2. Change in cholinesterase activity during inhalation of vapors of hydrolytic ethanol.
Notation same as in Fig. 1.

The blood was taken from a caudal vein under aseptic conditions once every 15 days. Normally, the time of acetylcholine hydrolysis was 37-39 minutes (Table 6, Fig. 2). At the end of the 6th week of exposure, a certain depression of cholinesterase activity occurred in animals of group I, and the time of acetylcholine hydrolysis increased to 42 minutes. However, at the end of the 9th week of exposure, it returned to normal, and in the 10th-11th week it increased again. This was obviously due to the defensive function of the

animal organism. After 20 days of the recovery period, the time of acetylcholine hydrolysis returned to normal. No changes were observed in rats of group II as compared to the control.

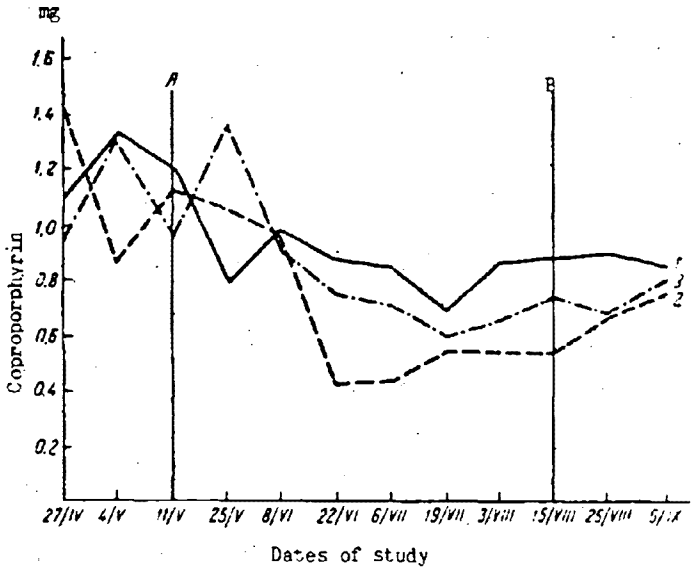


Fig. 3. Change in the excretion of coproporphyrin with the urine during inhalation of vapors of hydrolytic ethanol. Notation same as in Fig. 1.

We evaluated the effect of low concentrations of ethanol vapors on the metabolism from the change in the porphyrin metabolism in the animal organism. The coproporphyrin was determined by Fischer's method. The extraction of porphyrin from the urine was carried out with ether, and the quantitative determination, on an SF-4 spectrophotometer in the 400-410mμ region. The daily portion of urine from each group of animals (with 5 rats in each group) was collected in special glass containers.

Coproporphyrin was determined once every two weeks, and its amount was recalculated in terms of 100 g of the animals' weight. In rats of group I, the excretion of coproporphyrin with the urine starting with the 6th week of exposure decreased sharply, and remained at this level until the end of exposure (Fig. 3). Normalization occurred at the end of the recovery period. No statistically significant changes were found in rats of group II as compared with the control group. In the chronic experiment, the effect of low concentrations of ethanol vapors on the total proteins was also studied, and their fractional composition in the blood serum was determined with the aid of paper electrophoresis. The blood was taken on an empty stomach, from the tail every 15 days. In rats of group I, by the end of the 2nd month of exposure, the content of albumins decreased, and the gamma globulin fraction increased. This increase was statistically significant and lasted until the end of exposure. Even during the recovery period, the albumin-globulin ratio did not return to normal (Table 7 and Fig. 4).

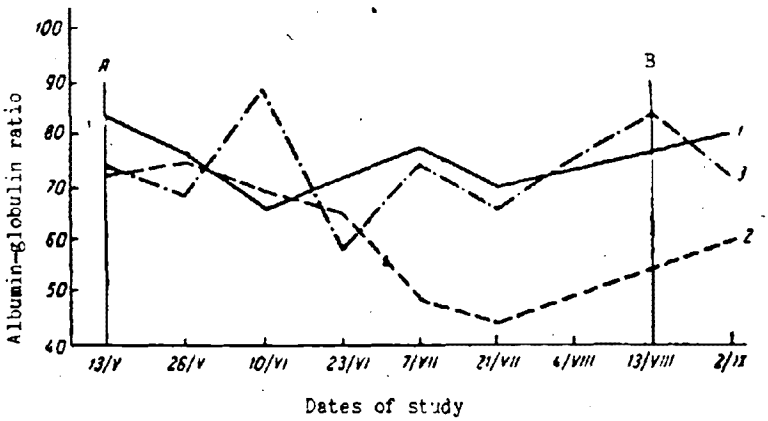


Fig. 4. Change in the protein fractions of the blood serum during inhalation of hydrolytic ethanol vapors.
Notation same as in Fig. 1.

No changes whatsoever were observed in rats of group II. No change was noted in the total proteins of the rats in any of the groups.

Thus, continuous exposure for 90 days had a marked effect on animals of group I (29.1 ± 2.1 mg/m^3), but had no effect on those of group II (5.59 ± 0.045 mg/m^3). On the basis of these data, we can recommend that the mean daily maximum permissible concentration of hydrolytic alcohol be taken at the level of the highest single concentration, 5 mg/m^3. In order to obtain a sanitary evaluation of atmospheric pollution with vapors of hydrolytic ethanol, we conducted a survey of three hydrolysis plants in Uzbekistan. A total of 186 air samples were collected at distances of 100, 200, and 300 meters on the leeward side of the source of discharge. The samples were collected by suction into two absorbers containing activated carbon. From 10 to 40 l of air was collected in each sample at a rate of 1 l/min. The air temperature during the sampling ranged from 20 to 35°C, and the relative humidity, from 25 to 70%; the barometric pressure was 730-750 mm Hg, and the wind velocity, from 1 to 5 m/sec. During the sampling, the weather was dry and clear (Table 8).

It is evident from Table 8 that at a distance of 100 m and farther from the source of discharge around the three Uzbekistan hydrolysis plants studied, the ethanol concentrations were below our proposed highest maximum permissible concentration of 5 mg/m^3.

Table 7

Change in the Total Proteins and Protein Fractions of the Blood Serum During Chronic Exposure of White Rats to Vapors of Hydrolytic Ethanol

Period	Group	Total Proteins	Albumins	Globulins			Albumin-Globulin Ratio
				Alpha	Betta	Gamma	
Before exposure	I	9,09	42,3	23,8	19,5	14,4	0,73
	II	9,05	42,6	22,9	20,4	14,1	0,74
	III (Control)	8,91	45,1	22,9	19,4	12,6	0,83
On 50th day of exposure	I	8,89	32,3	24,6	26,0	17,1	0,48
	II	9,04	42,6	21,6	21,4	14,1	0,74
	III (Control)	9,88	43,7	20,8	20,9	14,6	0,77
On 90th day of exposure	I	9,40	36,3	23,4	23,5	16,8	0,54
	II	8,63	45,4	21,1	21,1	12,4	0,84
	III (Control)	8,73	42,9	21,8	21,1	14,2	0,76
Recovery	I	9,38	37,9	24,0	22,6	15,5	0,60
	II	8,67	44,8	21,1	21,8	12,3	0,83
	III (Control)	8,79	44,2	19,8	23,4	12,6	0,80

Table 8

Results of Study of the Pollution of Atmospheric Air with Ethanol Vapors Around Hydrolysis Plants in Uzbekistan

Distance From Discharge m	Number of Samples	Single Concentrations, mg/m³		Number of Samples with Concentration of, mg/m³		
		Maximum	Minimum	2 and above	From 1 to 2	Below 1
Fergana Plant						
100	26	2,79	0,55	6	9	11
200	17	0,16	—	—	—	17
300	27	0,018	—	—	—	27
Andizhan Plant						
100	25	4,52	0,45	10	10	5
200	16	1,68	—	—	2	14
300	27	0,37	—	—	—	26
Yangiyul' Plant						
100	44	2,2	—	4	10	10
200	25	0,5	—	—	—	25

Conclusions

1. The atmospheric air around the surveyed Uzbekistan hydrolysis plants is slightly polluted with vapors of hydrolytic ethanol.

2. A study of the biological effect of hydrolytic ethanol vapors showed that the threshold of olfactory perception in the most sensitive persons is 7.1 mg/m^3. The threshold of change of the light sensitivity of the eyes is 6.97 mg/m^3, and the threshold of the reflex effect on the activity of the cerebral cortex is 6.1 mg/m^3. The maximum inactive concentration according to the most sensitive test is 4.9 mg/m^3.

3. The highest single maximum permissible concentration of hydrolytic ethanol may be established at a level of 5 mg/m^3.

4. Chronic round-the-clock exposure of the experimental rats to ethanol vapors in a concentration of 29.25 mg/m^3 for 90 days caused changes in the normal ratio of the chronaxy of flexors and extensors, cholinesterase activity, excretion of coproporphyrin with the urine, and in the relative amounts of the protein fractions of the blood serum. Ethanol in a concentration of 5.59 mg/m^3 had no effect on the rat organism.

5. The mean daily permissible concentration of hydrolytic ethanol in atmospheric air based on the data of the chronic experiment may be recommended at the level of the highest single concentration, 5 mg/m^3.

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