FOUO

29 JANUARY 1979

JPRS L/8252

29 January 1979

[redacted]

USSR

[redacted]

[redacted]

THE CARDIOVASCULAR SYSTEM AND OCCUPATIONAL FACTORS

U. S. JOINT PUBLICATIONS RESEARCH SERVICE

[redacted]

NOTE

JPRS publications contain information primarily from foreign newspapers, periodicals and books, but also from news agency transmissions and broadcasts. Materials from foreign-language sources are translated; those from English-language sources are transcribed or reprinted, with the original phrasing and other characteristics retained.

Headlines, editorial reports, and material enclosed in brackets [] are supplied by JPRS. Processing indicators such as [Text] or [Excerpt] in the first line of each item, or following the last line of a brief, indicate how the original information was processed. Where no processing indicator is given, the information was summarized or extracted.

Unfamiliar names rendered phonetically or transliterated are enclosed in parentheses. Words or names preceded by a question mark and enclosed in parentheses were not clear in the original but have been supplied as appropriate in context. Other unattributed parenthetical notes within the body of an item originate with the source. Times within items are as given by source.

The contents of this publication in no way represent the policies, views or attitudes of the U.S. Government.

APPROVED FOR RELEASE: 2007/02/08: CIA-RDP82-00850R000100010059-5

50272-101

REPORT DOCUMENTATION PAGE	1. REPORT NO. JPRS L/8252	2.	3. Recipient's Accession No.
4. Title and Subtitle: THE CARDIOVASCULAR SYSTEM AND OCCUPATIONAL FACTORS			5. Report Date: 29 January 1979
			6.
7. Author(s): N. M. Konchalovskaya (editor)			8. Performing Organization Rept. No
9. Performing Organization Name and Address: Joint Publications Research Service, 1000 North Glebe Road, Arlington, Virginia 22201			10. Project/Task/Work Unit No.
			11. Contract(C) or Grant(G) No. (C) (G)
12. Sponsoring Organization Name and Address: As above			13. Type of Report & Period Covered
			14.

15. Supplementary Notes: SERDECHNO-SOSUDISTAYA SISTEMA PRI DEYSTVII PROFESSIONAL'NYKH FAKTOROV, Moscow, 1976

16. Abstract (Limit: 200 words)

This report contains clinical data pertaining to the state of the cardiovascular system of individuals whose work involves exposure to such occupational and industrial factors as noise, radio waves, ionizing radiation and chemicals. The book offers methodological approaches and defines the diagnostic possibilities with regard to evaluation of cardiovascular disturbances. Special attention is devoted to the mechanism of formation of cardiovascular reactions under the influence of various occupational factors. The authors singled out and described comprehensively the clinical cardiovascular disorders that are most frequently encountered among workers, as related to the nature and intensity of different occupational factors. Recommendations are offered for expert determination of disability, rational employment and rehabilitation therapy of states that develop.

17. Document Analysis a. Descriptors

USSR
Cardiovascular
Occupation
Noise
Radiation
Poisoning

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group: 6E, 6F, 6 J, 6S

18. Availability Statement	19. Security Class (This Report)	21. No. of Pages
For Official Use Only. Limited Number of Copies Available From JPRS.	UNCLASSIFIED	173
	20. Security Class (This Page) UNCLASSIFIED	22. Price

(See ANSI-Z39.18) See Instructions on Reverse OPTIONAL FORM 272 (4-77) (Formerly NTIS-35) Department of Commerce

JPRS L/8252

29 January 1979

THE CARDIOVASCULAR SYSTEM AND OCCUPATIONAL FACTORS

Moscow SERDECHNO-SOSUDISTAYA SISTEMA PRI DEYSTVII PROFESSIONAL'NYKH FAKTOROV in Russian 1976 signed to press 6 Aug 76 pp 2-26, 46-166, 200-255

[Annotation, table of contents, foreword, chapters 1, 3-6, 8, conclusions and bibliography for book edited by Professor N.M. Konchalovskaya, Izdatel'stvo Meditsina, 6,000 copies 256 pages]

CONTENTS PAGE

CONTENTS (Continued) Page

PUBLICATION DATA

English title	: THE CARDIOVASCULAR SYSTEM AND OCCUPATIONAL FACTORS
Russian title	: SERDECHNO-SOSUDISTAYA SISTEMA PRI DEYSTVII PROFESSIONAL'NYKH FAKTOROV, Moscow, 1976
Author (s)	:
Editor (s)	: N. M. Konchalovskaya
Publishing House	: Izdatel'stvo "Meditsina"
Place of Publication	: Moscow
Date of Publication	: 1976
Signed to press	: 6 Aug 76
Copies	: 6000
COPYRIGHT	: Izdatel'stvo "Meditsina" Moskva, 1976

ANNOTATION

[Text] This publication has been approved and recommended for publication by the Scientific Publication Council of the Presidium of the USSR Academy of Medical Sciences.

This monograph summarizes clinical data pertaining to the state of the cardiovascular system of individuals whose work involves exposure to such occupational and industrial factors as noise, radio waves, ionizing radiation and chemicals. The book offers methodological approaches and defines the diagnostic possibilities with regard to evaluation of cardiovascular disturbances. Special attention is devoted to the mechanism of formation of cardiovascular reactions under the influence of various occupational factors. The authors singled out and described comprehensively the clinical cardiovascular disorders that are most frequently encountered among workers, as related to the nature and intensity of different occupational factors. Recommendations are offered for expert determination of disability, rational employment and rehabilitation therapy of states that develop.

This book is intended for physicians specializing in occupational pathology.

The book includes 15 figures, 15 tables, and the bibliography lists 257 items.

FOREWORD

[Text] The planning and organizing of different public health services is based largely on information about the incidence of different diseases, their share of the morbidity and mortality structure, as well as the main, so-called clinical, patterns inherent in these forms. The increasing relative incidence of cardiovascular diseases and their role in changing general health of the public in the future are quite obvious to all highly developed countries. At the same time, the role of different occupational factors among causes that induce or alter the incidence and course of cardiovascular diseases is still far from clear.

An enormous amount of material has been accumulated, referable to the many years of observations of workers in different branches of industry, who were exposed to diverse toxic, allergenic, physical and dust factors varying in intensity. In these individuals, changes in cardiac and vascular function occupy a certain place, sometimes a significant one, in the clinical findings, and this requires definition of questions of syndrome diagnostics and expert evaluation of such states, as well as making substantiated decisions as to optimum job placement. At the same time, the special role of the circulatory system in the overall system of adaptation of the body to exogenous and endogenous factors, due to the constitutional distinctions and conditioning distinctions, the high incidence of influences known to be pathogenic for the cardiovascular system of a number of nonoccupational factors, as well as the nonspecific nature of changes, make it difficult both to differentiate between physiological and pathological deviations, and to establish the role of different factors in appearance thereof.

There have been substantial changes in the nature of work in the last few years. The comprehensive reduction of levels of occupational factors has extended the period of active work fitness and raised the mean age of workers with the corresponding change in general status, including that of the cardiovascular system as a premorbid background, against which changes of an occupational nature appear. The rare instances of possibly

severe effects on the circulatory system are presently set against the more common influence of factors with relatively low intensity, with a large contribution of intensive, complex mental labor, hypokinesia, processing of extensive information combined with the need to make responsible current decisions. Such is the work, for example, on control consoles, aircraft engine testing, adjustment of guidance [sighting] devices, etc. Unquestionably, overall reactivity of the body has also changed in view of the set of diverse toxic and allergenic influences.

In view of all of the foregoing, it was deemed expedient to shed light, in this monograph, on the basis of analysis of the literature and our own data, on the main pathogenetic mechanisms of action of the principal work-related factors on the condition of the heart and vessels, as well as methodology of studying the reactions thereof in different occupational groups; to systematize information about the condition of the heart and hemodynamics in individuals exposed to physical, toxic and dust factors; to determine the main variants of clinical syndromes, semeiotics, course and prognosis thereof; to define the possible place of different occupational factors in the overall structure of cardiovascular pathology and prediction of morbidity and mortality due to diseases in this group. As a result, it is planned to substantiate reasonable job placement, methods of treatment and prevention of long-term sequelae of the effects of working conditions on the cardiovascular system.

CHAPTER 1. PATHOGENESIS OF CARDIOVASCULAR REACTIONS TO VARIOUS OCCUPATIONAL FACTORS

[Text] Chief Mechanisms of Development of Cardiovascular Reactions

Many years of observations have shown that diverse changes in the cardiovascular system are observed in individuals engaged in the most varied occupations. Hypotheses have been expounded concerning a consistent link between the nature and incidence of some of them, on the one hand, and effects of working conditions, on the other. It is assumed that both the direct influence of some factors on the heart and vessels and an indirect influence, mediated by changes in neuroendocrine regulation of circulation, are involved. It is also unquestionable that, in the case of occupational poisoning (carbon monoxide, nitric oxide and others) and acute radiation sickness due to exposure to high doses of radiation, the cardiovascular changes occupy a prominent place in the symptomatology and largely determine the prognosis.

Let us consider successively the possible mechanisms of formation of reactions as a result of the direct effects of some occupational factors on the cardiovascular system. Thus, in the case of exposure to toxic agents with anoxemic action (carbon monoxide, cyanide compounds, amido and nitro derivatives of benzene, hydrogen arsenide, nitrogen oxides, phosgene), there is a reduction in blood oxygen capacity as a result of changes in structure, number and properties of erythrocytes and hemoglobin. In some cases, inadequate oxygenation of blood is related to involvement of the lungs (capillary-alveolar block of diverse genesis). There is also the possibility of direct injury to the neuromuscular system of the heart, vessels and their regulatory centers by high doses of radiation, intense heat, etc. In such cases, the symptoms of involvement of the cardiovascular system appear at an early stage and are prominent in the clinical manifestations of disease.

In the case of hypoxemic hypoxia, changes occur in cell metabolism of different body tissues and, first of all, in structures that are the most sensitive to hypoxia, which include the myocardium. G. F. Lang combined the disturbances referable to a complicated set of biochemical, physicochemical and bioenergetic processes in the myocardium in the concept of "myocardial dystrophy." There are grounds to assume that analogous pathogenetic mechanisms are involved in development of disturbances in carbohydrate-phosphorus, protein and mineral metabolism under the influence on the myocardium of a number of occupational factors, which were mentioned above. Some mechanisms have been discovered in special experimental studies of the effects of radiation on the heart (Ye. I. Vorob'yev et al., 1971, 1973), while others have yet to be submitted to clinical and experimental investigation.

Evidently, similar pathogenetic mechanisms are at the basis of changes in the cardiovascular system, in the presence of so-called foundry fever. However, here it is not so much the direct toxic effect on the myocardium as the unique sensitize effects of metal aerosols and compounds that play the leading role, and they lead to development of acute allergic myocarditis. The syndrome is polyetiological and occurs under the influence of certain infectious agents, toxic agents and drugs. The lesion is characterized by acutely developing morphological signs in one of three typical (according to Ya. L. Rapoport) variants: hypertrophy of muscle fibers alternating with fields of myolysis, perivascular lymphoid and plasma cell infiltration and plasmorrhagia. The main pathogenetic mechanisms are nonspecific, for which reason there are many features in common in the clinical signs of myocarditis, regardless of its etiology: acute onset, enlargement of the heart, dull sounds, persistent tachycardia, dysproteinemia with increase in share of coarsely dispersed proteins and α_2- and γ-globulin fractions, eosinophilia. The electrocardographic changes are not notable for stability. The previously held view of mandatory malignant course with mainly postmortem diagnostication has recently been shaken. Forms have been isolated that have a chronic, recurrent and occasionally more benign course (N. M. Konchalovskaya et al., 1965; M. I. Teodori, 1972; Gvozdijak, 1973).

A similar mechanisms is apparently involved with exposure to radiation in doses that elicit extensive destructive processes in tissues that are more radiosensitive than the myocardium. The toxemic form of radiation sickness has also been singled out (A. K. Gus'kova and G. D. Baysogolov, 1971). In this case, toxic and allergic influences are also expressed in the myocardium, and they can be the immediate cause of death, by analogy to the reaction of the heart at the toxic stage of burn injuries (N. S. Molchanov, 1973) or extensive traumatic crushing with the compression syndrome (Ye. V. Gembitskiy, 1973).

Another mechanism of direct effects on cardiovascular metabolism is expressed via neurohormones and the system of peripheral chemical mediation (epinephrine, norepinephrine, acetylcholine and others).

The effects of organophosphorus compounds and certain other toxic factors (lead and its ethylated derivatives) on the cardiovascular system are based

on structural and metabolic changes in the vascular wall and myocardium, synaptic activity of peripheral receptors of different classes, along with other symptoms of a myoneural block. Syndromes resembling acute angiitis with regional impairment of hemodynamics, crises with sudden circulatory insufficiency to the extent of coma, occupy a place in the symptomatology of poisoning by such substances. This is the topic covered by Ye. A. Lushnikov (1964) in his studies of patients with thiophos poisoning. Efforts at pathogenetic therapy of such states are related to such conceptions; they are directed toward reactivation of cholinesterases, normalization of catecholamine metabolism and adrenergic receptors (S. N. Golikov, 1971; A. L. Myasnikov, 1965, and others).

Not infrequently, in poisoning cases, there is development of atherosclerotic processes with the corresponding clinical manifestations as a result thereof. There is animated discussion in the literature (A. K. Gus'kova, V. P. Medvedev, 1973, and others) of the question of effects of some factors (radiation, lead, electromagnetic fields) on the higher incidence and earlier detection of atherosclerosis.

Vascular disturbances are based on local or general traumatization to vessels under the influence of vibration, overcooling and appearance of distinctive coagulopathy. The role of other mechanisms is also unquestionable; in particular, pathological afferentation from receptors (local irradiation, vibration, high-intensity radio waves).

Changes in the cardiovascular system occurring in connection with severe involvement of the lungs and associated with development of cor pulmonale occupy a special place in the symptomatology of occupational diseases. At first, there are compensatory changes in the cardiovascular system, directed toward elimination of hypoxia, then a set of successively and differently (depending on the nature of the main lesion) developing changes, which are indicative not only of involvement of various adaptive mechanisms, but signs of insufficiency of different elements of the circulatory system.

Under the influence of occupational toxic agents (carbon tetrachloride, polonium and others) with selective tropism for organs of the hepatolienal system and kidneys, signs of autotoxic myocardial lesions are added later on to the vascular component. However, the features of the primary effect of these toxic agents on the hepatic parenchyma persist and dominate in the clinical signs of the lesion. For this reason, it would be more correct to refer to secondary involvement of the cardiovascular system in the presence of the acute, toxic hepatorenal syndrome.

The period of active fitness for work and mean age of employed individuals increase in the case of a mild, but long-acting set of occupational factors.

In some occupations, there is increasingly distinct prevalence of mental and emotional tension over physical loads, and an increase in share of monotonous, stereotypic operations with minimal exercise. At the same time, the role of individual responsibility and need to process an enormous amount of

information are increasing, with reduction in active exercise (working on control consoles, production lines, etc.).

The possibility of intense and extreme factors will still be present in the immediate future for a small group of workers, with a significant contribution of mental and emotional stress (astronauts, individuals engaged in important overhaul work, seamen exposed to adverse climate, etc.).

Under such circumstances the role of other influences increases sharply: man's environment, working and living conditions, unreasonable nutrition, bad habits (smoking, alcohol abuse), hypokinesia, unwarranted extensive use of various drugs and use of chemistry in everyday life.

The cardiovascular system is highly reactive, it is functionally intimately related to the nervous and endocrine systems. For this reason, considerable difficulties arise in determining the etiological role of some occupational factor. In some cases, it is even impossible to single out the prime significance of a particular factor.

The main variants of neuroendocrine and nonspecific reactions consist, first of all, of diverse changes in the main indices of cardiac function and hemodynamics, that are within the ranges of rather broad physiological fluctuations. These reactions reflect, first of all, the congenital and hereditary constitutional distinctions of morphofunctional organization of regulation of circulation, which undergo specific changes in the course of ontogenesis and are substantially altered by conditioning, physical and psychological training, upbringing, living conditions, as well as, of course, prior diseases and consistency with the occupational work load. Congenital distinctions of the cardiovascular system undergo a certain evolution at different stages of life, and this does not occur smoothly; rather, they are intermittent, differing in males and females, with periodic changes inherent in different phases of sexual activity (menstrual cycle, pregnancy, involution of reproductive glands, etc.).

Of course, in view of the importance of the cardiovascular system to adaptation of the body to changing environmental conditions, including occupational factors, one should expect that, in the course of work, there would first be development of orienting reactions that are adaptive in direction.

Many of the functional changes in arterial pressure, pulse rate, tonus of the vascular wall, cardiac stroke volume and certain other parameters up to a certain limit should be interpreted as compensatory and adaptational, rather than pathological. Evidently, one could try to distinguish between some unique nonspecific reactions of the cardiovascular system inherent in the effects of specific occupational factors varying in mechanism of action on the basis of time of onset, appearance of certain associations of changes and fullness of effect reached with them.

First, let us touch upon some general nonspecific patterns of regulatory mechanisms that are significant to formation of reactions to any exogenous

factors. All researchers validly attribute a large role to the regulatory influence of the central nervous system, particularly some of its branches (hypothalamic and cortical regions of the vascular center); there condition is largely determined by the level of blood supply, while disturbances of these elements lead to functional changes in the cardiovascular system. Thus, changes in physiological activity and reactivity of median brain structures are recorded quite often with exposure to carbon disulfide, radio waves, ionizing radiation, etc. (D. A. Ginzburg et al.). Various changes are observed in bioelectric activity of the brain (periods and bursts of synchronized, high-amplitude oscillations of biopotentials at a frequency of 3-6/s). These changes are occasionally associated with clinical syndromes of diencephalic disorders and autonomic crises described by M. N. Ruzhkova, K. V. Glotova, A. M. Monayenkova and others. The incidence and severity of the vascular component are quite varied. The impression is gained that, under the influence of carbon disulfide and certain other toxic agents, vascular disorders are observed more often than manifestations of hypothalamic insufficiency, but the severity of both is similar. A. M. Monayenkova observed myocardial changes reliably more often in individuals with symptoms of impaired regulation of hypothalamic centers. The hyperdynamic type of vascular disorders demonstrated signs of neurogenic genesis thereof, as confirmed by the correlation between changes in indices of isometric contraction of the myocardium and signs of hyperactivity of the sympathoadrenal system (changes in catecholamine metabolism). Analogous correlations were observed by K. V. Glotova and G. G. Lysina (1972) under the influence of high-intensity, superhigh frequency electromagnetic fields.

Ye. A. Denisova et al. (1975), M. N. Sadchikova et al. (1972), Ye. V. Gembitskiy (1969) and others observed a different type of reaction, mainly in the vagotonic direction (bradycardia, arterial hypotension) under the influence of low doses of ionizing radiation and different intensities of radio waves. These hemodynamic changes were related to signs of altered peripheral afferentation and disturbances in the systems of such mediators as acetylcholine and cholinesterase. There was secondary appearance of changes in the catecholamine system and central regulation of hormone synthesis in the adrenal cortex (I. A. Kogan, N. I. Gorbarenko, 1971, and others).

There are data indicative of a considerable incidence of hypothalamic states among hot shop workers. Along with reflexly occurring changes in autonomic regulation of circulation, some place belongs to fluid-electrolyte balance disturbances in the pathogenesis of such states. The blood pH changes, and this affects the extracellular and intracellular concentrations of potassium and sodium ions and, consequently, the electrolyte gradient between the liquid phase and structural components of tissues. There may be changes in heart rate, frequency of cardiac contractions, widening of heart boundaries, dull sounds, arterial hypotension and electrocardiographic signs of weakened contractility of the myocardium, as well as symptoms of circulatory insufficiency of cardiac genesis.

Pathological afferentation from the periphery, primarily from vascular baroreceptors in the parts of the body subject to traumatization, plays a part in the pathogenesis of functional changes in the nervous system associated with local vibration. This is followed by development of vascular disorders due to impaired regulatory influence of the central nervous system on regional circulation. Such changes may also be observed under the effect of other factors (trauma, static pressure, cold, etc.) and, consequently, they cannot be viewed as the specific reaction only to the vibration factor. Changes can also occur under the influence of vibration on other innervation levels of vegetovascular regulation (spinal ganglia, autonomic centers located in the lateral cornua of the spinal cord). But disturbances in function of the reticular formation of the stem, in the region of the vestibular analyzer and diencephalic parts of the brain play a leading part.

The increased activity of thalamohypothalamic structures under the influence of general vibration is associated with attenuation of cortical activity. Synchronization of high-amplitude waves are recorded on the EEG, with appearance of slow waves and bursts, which characterize development of the diencephalohypothalamic syndrome. According to electromyographic findings, we can assume that there is a change in the usual correlations between excitability of segmental and suprasegmental parts of the spinal cord, excitation of the motor analyzer and increased exhaustion of motoneurons (L. G. Okhnyanskaya). Thus, in the case of both local and general vibration, complex interaction is demonstrable between different branches of the nervous system involved in hemodynamic regulation. Several concomitant influences are also of some significance: cold, trauma, static and muscular tension, noise and others, and this explains the uniqueness of the observed disturbances. Both compensatory reactions and disturbances related to the presence of static overstimulated foci, and changes in neurohumoral mediation are observed under the influence of vibration on extensive receptor fields of the central nervous system that regulate circulation. This leads to clinical symptoms of regional and systemic vascular circulatory disorders.

Predominantly cortical disturbances of hemodynamic regulation, prevalence of dysfunction and dystony of the hypertensive type are inherent in the pathogenesis of changes in cardiovascular organs under the influence of intermittent high-intensity noise in individuals whose work is not rhythmic, but very emotional and tense in nature (radio wave transmitter adjusters, individuals who assemble aircraft engines, administrative workers, etc.). Finally, there are in the symptomatology of occupational diseases extensive regional changes in circulation that are not associated with consistent changes in systemic hemodynamics and cardiac function. Regional syndromes occur under the influence of factors that are not uniform with regard to distribution of energy in different parts of the body (local irradiation, local vibration, tension of individual muscle groups, overcooling or overheating of specific parts of the body, static stress of the limbs, etc.). A pathogenetic link is observed here between the regional vascular disorders and changes in segmented innervation (vegetosensory mononeuritis and polyneuritis, ganglionitis and local circulatory disorders--acroangiospasm, trophic disorders occurring under the influence of carbon disulfide,

unsaturated hydrocarbons, with overcooling, electric trauma, local radiation lesion, local vibration). On the whole, it should also be stressed for this group that there is a pathogenetic link between regional and systemic hemodynamic disturbances, with predominant change in a given level of innervation and neurohumoral regulation, with a consistent sequence of changes, ranging from transient local to systemic hemodynamic ones. We can track the transition from predominantly adaptive vagal changes to sympathotonic ones, to the extent of development of circumscribed hypertensive crises, persistent arterial hypertension, i.e., more serious pathological circulatory conditions. At some stages, the brain and heart are affected secondarily, also via nonspecific mechanisms inherent in essential hypertension and ischemia, regardless of their etiology.

Aggravation has been observed in the course of existing cardiovascular diseases under the influence of occupational factors. However, we also know of serious diseases of the cardiovascular system that are unrelated to any particular occupation. At the same time, there is a consistent decline in number of diseases directly related to adverse working conditions, so that it is difficult to detect the link between some rather common, general diseases of the cardiovascular system and man's work. L. K. Khotsyanov (1960) and others indicate that there are substantial contradictions in the quantitative indices of cardiovascular morbidity among individuals in the same branches of industry and occupations, in different economic and geographic regions. This could be due both to the decisive influence of distinctions referable to local living conditions, diet, lifestyle and, unquestionably, to differences in diagnostic approaches to evaluation of the observed deviations. On the other hand, the significant change in work processes at the present time, increasing emotional and mental stress, and hypokinesia occupy a certain place in the genesis of cardiovascular pathology. They already demand the close scrutiny of general practitioners, occupational pathologists and industrial physiologists.

Development of the methodological bases for studying the effects of occupational factors on the cardiovascular system, strict unification of diagnostic and rating criteria, and choice of demonstrative groups, especially for detection of early stages of the above pathological states, are very important for obtaining reliable information on this score. Studies should be conducted in close contact with a number of specialists, both within one country and various international organizations that implement broad programs dealing with cardiovascular pathology in different countries of the world.

Several authors have indicated (and this has been confirmed by the data obtained from the dynamic observations of Ye. A. Denisova of individuals exposed to radiation) that some types of cardiovascular reactions are largely related to the initial type of regulation. Thus, arterial hypertension, pressory type vascular reactions and angina pectoris were inherent in only a limited group of people, and they were unrelated to the radiation dosage. At the same time, hypotensive reactions, particularly transient ones, were related to a greater extent to the effect of the occupational

factor at a specific intensity, and they are inherent in a considerable number of working people (to 2/3-4/5 of the individuals exposed to radiation in a dosage of 50-70 rem.

The significance of the background of neuroendocrine changes at particular stages of life should be assessed analogously with regard to development of hypertension, episodes of vascular disorders, especially in women, and ischemic patholgoy in men. These patterns are demonstrable at the late observation stages, including the period after contact with such factors as ionizing radiation, carbon disulfide, lead and others. Sex has some influence on the uniqueness of clinical variants of vascular pathology under the influence of other occupational factors as well. We were impressed by the high incidence of coronary and limb vascular lesions in men and signs of diencephalohypophyseal disorders and cerebrovascular disturbances in men (M. N. Ryzhkova, V. A. Soldatova and others).

Adaptation to pre-existing vascular disturbances among individuals in any professional group depends largely on the original background of regulation. Unquestionably, there is a number of adverse factors (overfatigue, intercurrent infection, pregnancy and lactation, menopause) involved in development of decompensation or appearance of new clinical symptoms in the presence of cardiovascular diseases in different occupational groups. In some cases, the demonstrated nonspecific symptoms are unjustifiably taken for the onset of an occupational disease.

At the late observation stages, different variants have been observed in involvement of the occupational factor in the genesis of the polyetiological cardiovascular syndrome: a) continued exposure to the occupational factor (deposition of long-lived radionuclides in the body, other toxic agents or metabolites thereof) or continuous progression of previously started pathological processes in the heart and vessels; b) the effect of the occupational factor is temporary; there is relatively complete repair of lesions with typical clinical signs of occupational disease in the past; other non-occupational influences continue to affect the body, inducing some pathological hemodynamic states or other (atherosclerosis, essential hypertension). The clinical syndrome may be similar under the effect of a number of factors (impaired cerebral circulation, ischemia); however, the role of the occupational factor should be then assessed as being quite negligible or insignificant in general.

Statistics should be taken into consideration to substantiate the role of an occupational factor in each specific case. It is expedient to use the following criteria as the basis for such evaluation: pathogenetic link between the effect of the occupational factor and clinical syndrome, and example of which is development of hypertensive reactions and essential hypertension among telephone operators working under great emotional and mental stress, under the influence of intensive noise; an increase in number of states suspected of being of occupational genesis in the group under study, as compared to a control group of individuals; uniqueness of the

polyetiological syndrome among individuals in the occupational group under study, with respect to time of onset, severity and predominant localization.

In the presence of the above conditions, it is logical to assume that an occupational factor plays some role in the origin of the clinical syndrome.

To return to the effort to single out, along with general features, some typical ones of the effects of a given factor on reactions of the cardiovascular system, one must take into consideration the distinctive features of the occupational factor. It has been noted that a direct deleterious effect on tissular structures of the cardiovascular system is inherent in only a very limited number of occupational agents (and they must be of a high intensity). This applies to the effects of massive doses (of the order of several kilorad) of ionizing radiation (A. K. Gus'kova, G. D. Baysogolov, 1971; Ye. I. Vorob'yev; Shippman, 1960, and others), extreme overheating and overcooling, electrotrauma. Even the classical "vascular toxic agents" (carbon disulfide, carbon monoxide, cyanide, phosgene and others) should be classified, according to mechanism of action, in the category of neurovascular or systemic toxic, anoxemia-inducing agents.

Thus, most occupational factors do not selectively affect the circulatory system and regulation thereof; rather, they have tropism for other organs and tissues, and there is secondary or concurrent involvement of the cardiovascular system in the process ("anemic heart" under the influence of benzene and ionizing radiation in acutely injuring doses, "cor pulmonale" in the case of dust-related pathology, radiation and toxic involvement of the bronchopulmonary system, central circulatory disorders under the influence of narcotics and neurotropic toxic agents). The changes in the cardiovascular system are a complex neurohumoral reflex of hemodynamics and cardiac function in response to stimulation from receptor fields, varying in size and localization, in which the primary interaction of the deleterious agent with the body occurs (superhigh frequency current, radiation, vibration, overheating, some toxic agents).

Depending on whether there is combined or isolated manifestation of the two chief mechanisms, there are some distinctions in the formation and subsequent course of cardiovascular disorders, as well as their outcome. In occupational situations, when nervous elements are stricken early (exposure to thiuram, narcotics and certain other toxic agents), the vascular disturbances are generalized; subsequently they are notable for considerable severity and stability, even if no changes develop in cardiac and vascular structure. Conversely, when the factor is localized on a narrow receptor field, on which the chief injury is expressed, apart from the most important reflexogenic regions (only the hand with local vibration or local radiation), for a long time there may be no systemic hemodynamic disorders.

A satisfactory condition of the heart, vessels and regulatory mechanisms of systemic hemodynamics is observed with exposure to a number of low-intensity factors, such as radiation, benzene, lead and many others.

Successive and prompt triggering of different compensatory mechanisms, and implementation of satisfactory resultant circulatory function also occur differently under the influence of different factors. This depends on the integrity of the different elements of neurohumoral regulation, systems of oxygen uptake and transport, nature of metabolic disturbances and integrity of the cardiovascular system itself under the influence of a specific agent. By comparing these mechanisms and relations between them at different stages of the pathological process, we can try to detect some specific features in the effects of different occupational factors on the circulatory system. Examples of such comparisons and definition of some pathogenetic distinctions will be supplied in the relevant sections of this monograph.

Classification and Brief Description of the Main Syndromes of Cardiovascular Disturbances Under the Influence of Various Occupational Factors

While we recognize that a number of pathogenetic mechanisms of development of cardiovascular reactions to diverse occupational factors are very complex and general, it is expedient to try to group them according to the prime features and to single out the most commonly encountered and circumscribed clinical syndromes (see Chart).

In view of the fact that a chart has some limitations, we should supply some explanations. First of all, a distinction is made between two main categories of factors that affect the cardiovascular system: a) primary or early selective; b) secondary. Physical factors (ionizing radiation, electromagnetic field radio waves, some toxic agents, as well as toxic and allergenic, emotiogenic influences) are typical in class "a." Their effects, in the case of low intensities or selective action, can be limited only to changes in regulation of the cardiovascular system or, in the case of massive or localized exposure (direct radiation, electric trauma, overheating and others), have a direct effect on the myocardium and vessels of different regions. The class "b" factors, which are not selectively tropic for the cardiovascular system, lead to secondary changes as a result of already existing pathology of organs and systems that are, consequently, more sensitive to occupational factors (lungs, bone marrow, liver and other systems and tissues that determine energy and metabolic processes in the body). This is how one should interpret the mechanism of development of changes in human cardiovascular function in the presence of occupational diseases of respiratory organs, toxic impairment of hemopoiesis, effects of systemic toxic agents that disrupt energy and metabolic processes.

While there is some phenomenological similarity of the main pathogenetic mechanisms of reactions, through which the cardiovascular system becomes involved in the pathological process in response to an occupational factor, there are substantial differences.

Primary neuroendocrine mechanisms of physiological regulation of cardiac function and circulation play a part in the genesis of early changes in the cardiovascular system. One may observe selective injury by toxic agents or physical factors to the myocardium and vessels, and impairment of physiological

functions. The latter is associated with development of dysmetabolic, dyshemic and neurodystrophic changes due to the direct effect of the deleterious factor.

The main routes of the other mechanism, secondary involvement of the cardiovascular system in the process, are compensatory and adaptive changes in its activity arising in response to respiratory insufficiency and hypoxia of diverse genesis. This is observed in the presence of diseases of respiratory organs, system of tissular transport and uptake of oxygen, acute circulatory insufficiency with impairment of systemic metabolism and energetic processes under the influence of extreme exogenous factors. It is logical that the adaptive and compensatory nature of the changes is lost at some stage, with regard to cardiovascular function. Clinical and physiological signs of insufficiency appear, and various syndromes of systemic and local circulatory insufficiency develop.

Concomitant or prior nonoccupational factors are very significant to both mechanisms of pathogenesis and variants of reactions. However, the nature and significance thereof vary. Thus, in the category of functional cardiovascular reactions that are primary with regard to mechanism, sex, age, endocrine and metabolic constitution play a large part. Prior and intercurrent diseases involving these organs, as well as the functional state of other organs that are the primary target of the pathological process (lungs, bone marrow and others), distinctions of biochemical and immunobiological changes, and level of general reactivity are instrumental in development of a primary occupational lesion to the heart and vessels.

It should be borne in mind that the reactions arising directly in the period of exposure to the most intensive occupational factor, usually in young people, cannot be confused with all the subsequent transformations that they undergo under the influence of diverse exogenous and physiological factors.

For this reason, we singled out on the Chart the reactions and syndromes inherent in the period of formation of disease, which are related to the occupational factors and are largely adaptive in nature. They change upon discontinuation or radical reduction in intensity of the occupational factor, when distinct compensatory and recovery processes develop. Thereafter, all changes should be qualified as polyetiological, with varying contribution of the occupational factor, which is appreciably complicated and neutralized by many other causes.

It is expedient to single out the following clinical syndromes during the period of formation of cardiovascular reactions to an occupational factor.

1. Neurocirculatory dystonia of the hypotensive and hypertensive types, and symptomatic hypotension and hypertension. In such cases, functional changes in cardiac function or only peripheral local circulation move to the fore in clinical semeiotics; a combination of symptoms of cardiac and vascular dysfunction.

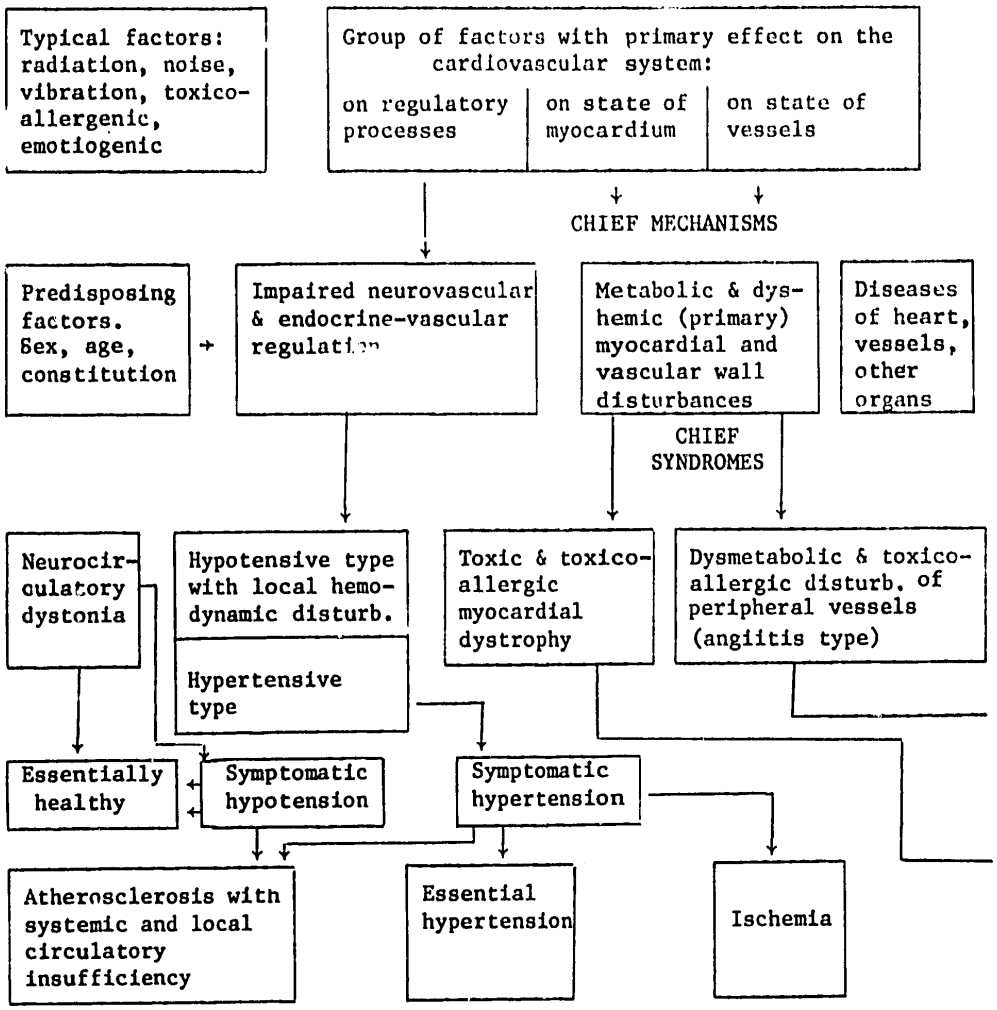


Chart. Grouping of reactions of the cardiovascular system to occupational factors (continued on the next page).

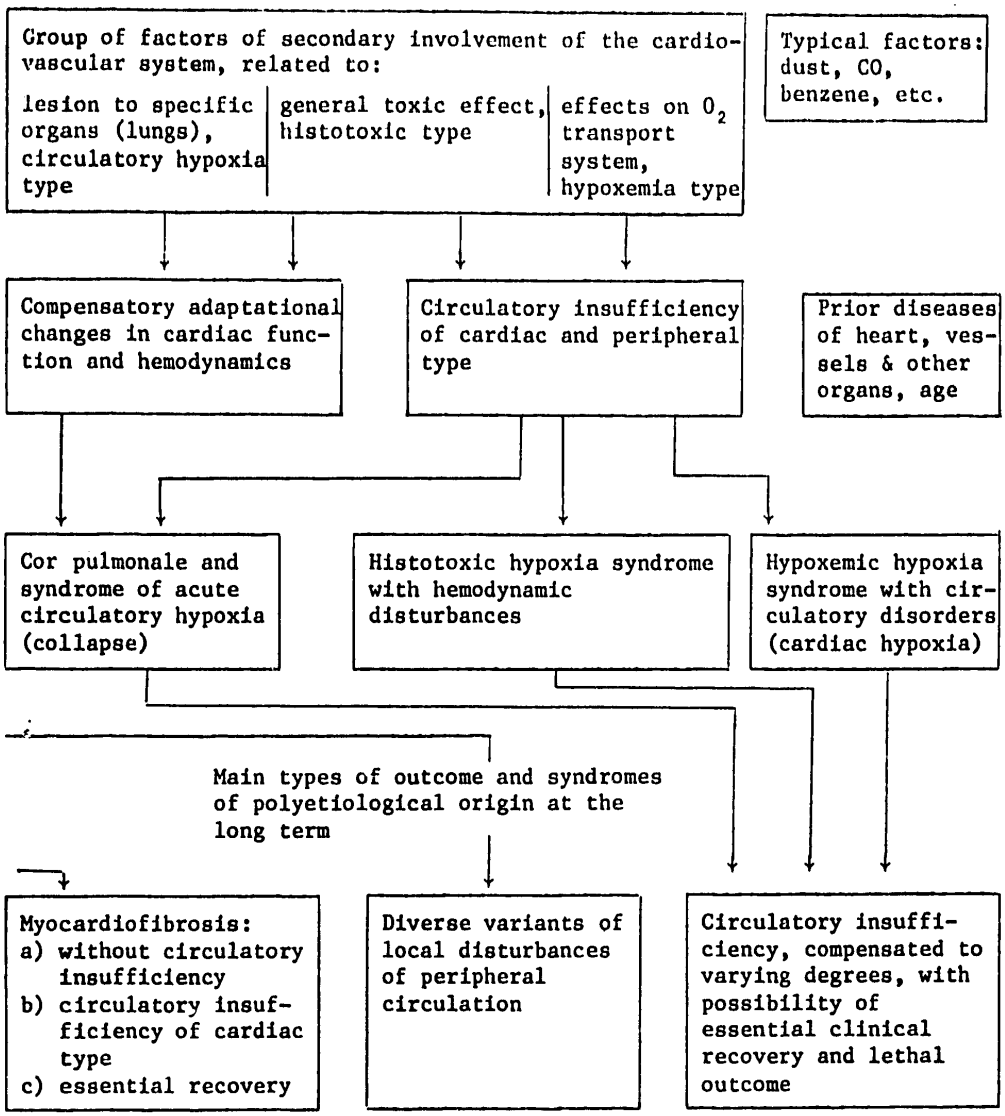


Chart (continued).

2. Toxicoallergic and metabolic-dyshemic (related to microcirculatory disorders) changes in the myocardium of the dystrophy type (G. F. Lang, 1958). The terms, "allergic myocarditis" (Fidler), "myocardosis" (V. Ionash, 1968), "myocarditis" (Ye. M. Tareyev, 1965) and many others for this group of syndromes are synonyms in our opinion. However, we prefer the term "myocardiodystrophy," as defined by G. F. Lang.

2. Dysmetabolic and toxicoallergic disturbances of peripheral vessels, of an exogenous nature, angiitis type, and regional dystony due to primary structural disturbances of the vascular wall, its microcirculation and local innervation system. There can be diverse variants of involvement of arteries of different caliber, veins and lymphatic vessels.

The following polyetiological syndromes may arise as the long-term sequelae of these states, with consideration of the concurrent and, occasionally, prime effects of other nonoccupational exogenous and endogenous factors: 1) hypotensive and hypertensive states that acquire features, at a certain stage, that bring them close to essential hypertension and ischemia; 2) myocardiofibrosis as the outcome of a toxicoallergic and dysmetabolic process in the myocardium, with varying degrees of circulatory insufficiency of the cardiac type; 3) atheromatous lesions to the heart, coronary, cerebral and great vessels of the limbs, with clinical signs of atherosclerotic cardiosclerosis and atherosclerosis of peripheral vessels, and local circulatory disturbances.

Among the reactions with secondary involvement of the cardiovascular system, we should make a distinction between the following syndromes during the period of formation of the process:

1. Cardiopulmonary syndrome developing as a result of diffuse pneumofibrosis, mainly of the restrictive type, and progressive chronic pulmonary insufficiency; bronchitis, bronchiolospasm and emphysema, with chronic respiratory insufficiency of the obstructive type and periodic acute respiratory disorders; toxic involvement of the alveolocapillary membrane with diffuse type of pulmonary insufficiency and acute, subacute or chronic course.

2. Acute circulatory disorders of the circulatory collapse type, related to poisoning by agents with systemic toxic action (carbon monoxide, cyanates, organophosphorus compounds and others) that the vital metabolic and energetic systems of the body. The main pathogenetic factor is histotoxic hypoxia.

3. "Anemic heart" (in the broad interpretation of the term): Development of this syndrome is attributable to toxic anemia, and it can also occur in cases of poisoning by agents that selectively strike the oxygen transport systems without involving erythropoiesis (carboxyhemoglobin and methemoglobin producers, and others); the pathogenesis is similar to that of hypoxemic and histotoxic circulatory disturbances.

The significance of the occupational factor to the outcome of the above syndromes is obvious; however, the initial status and intercurrent general somatic diseases also have a definite influence. This largely determines the course of an occupational disease, extent of involvement of the cardiovascular system and completeness of compensation at the long term.

In view of the fact that the authors of the next special chapters use the terminology we have cited, while the definitions are arbitrary to some extent, we consider it useful to briefly describe the chief elements of the syndromes that have been singled out.

1. Neurocirculatory dystonia occurs in one of two types:

a. Hypotensive type, with the following main etiological factors: radiation, radio wave emission, hypokinesia, emotional stress, toxic agents with neurotropic and mainly vascular action, overheating and others. The preclinical stage may last for a very long time. It is related to the prime pathogenetic mechanism, the change in regulation and reflex change mainly in local hemodynamics. Energy is adequately supplied to the body and the functions of vital organs and systems are also adequate for a long time. The main clinicophysiological manifestations required to make the syndromal diagnosis are: arterial hypotension, mainly vagoinsular type of regulation with corresponding signs of impairment (with loads) of segmental regional circulation, hypotension and dystonia of arteries and veins in different parts of the body. The changes constitute a set of adaptational and compensatory shifts of reflex origin, or they occur as a result of primary changes in central hemodynamic regulation. In most cases, the prognosis is good and there is no development of circulatory deficiency in vital organs. The main therapeutic and preventive measures amount to improvement of mechanisms of circulatory regulation and, when indicated, reduction of intensity of or discontinuation of exposure to the etiological factor.

b. Hypertensive type: The main etiological factors are emotionally intense work, exposure to noise, physical overloads, emissions from electromagnetic fields and radio waves, intensive heat. The following serve as substantiation of the clinical syndrome: hyperkinetic and spastic type of hemodynaic disorders with elevated or normal systemic arterial pressure. At a certain stage, this leads to appearance of signs of insufficiency of circulation, at first local and then system, combined with changes of a compensatory nature.

2. Myocardial dystrophy: The main etiological factors are: exposure of the cardiac region to massive doses of ionizing radiation, intake of organic metal compounds which are potential allergens in a specific state, extreme effects of excessively intense factors (overheating, electric trauma, barotrauma, toxic agents with sympathomimetic action). The clinical symptoms usually develop acutely, and they are characterized by signs of rapidly appearing circulatory insufficiency: tachycardia, drop of arterial pressure, change in electrocardiographic indices, indicative of diffuse involvement of the myocardium and cardiac innervation (blocked impulse conduction, arrhythmia, etc.).

3. Peripheral vascular syndromes (dysmetabolic and toxicoallergic local circulatory disturbances): The chief etiological factors are: some radioactive substances (polonium, plutonium), local vibration, overcooling and excessive strain of individual muscles, toxic agents with selective tropism for vessels (hydrogen sulfide, lead and others).

The preclinical stage may be protracted, and it is related primarily to innervation and dystonicdisturbances (in the presence of signs of compensated regional circulation). Subsequently, there is usually slow progression of anatomical structural and circulatory disorders in the arterial, venous and lymphatic systems.

The following serve as grounds for the clinical diagnosis of a full-fledged syndrome: clinical and physiological indices of altered tonus of peripheral vessels varying in nature, and insufficiency of regional and systemic circulation. The latter occur in the form of local and systemic crises, more often with hypertensive reactions. The clinical variants depend on the predominant localization of the process (veins, arteries, lymphatic vessels and capillaries in specific parts of the body).

The prognosis is determined, to a significant extent, by the localization and severity of morphological changes in the vascular wall, as well as lability of general regulatory systems of hemodynamics, hemocoagulation, metabolic constitution and age.

Ganglioblocking agents, products that improve trophics and microcirculation, regional hemodynamics, hypotensive and desensitizing agents, and anticoagulants are used for treatment.

4. Cor pulmonale: The following are causes of development of cor pulmonale:

a. Diffuse pneumofibrosis. Chief etiological factors are diverse types of dust, local irradiation of respiratory organs, intake via inhalation of some toxic agents. In typical cases, there is a lengthy preclinical stage of roentgenological and morphological changes. The prime clinical symptoms that substantiate the diagnosis are: roentgenological signs of diffuse fibrosis of lung tissue, moderate and slowly progressing respiratory insufficiency, mainly of the restrictive type, and regulatory disturbances of dynamics and structure of the respiratory act. In uncomplicated cases, the prognosis is relatively good. The main therapeutic and preventive measures should be directed toward arresting progression of fibrosis and collagen formation, with due consideration of all factors contributing to development of these mechanisms (polyvinylpyridine-N oxide, hormones, treatment of infections) and normalization of regulation of respiration.

b. Bronchitis, bronchiolospasm and emphysema. The main etiological factors are: irritant and allergenic substances, dust, some acutely toxic agents

in the heptyl and phenylhydrazine group. The infectious component plays a substantial role in the clinical course of the syndrome. The clinical diagnosis is backed up by typical symptoms of bronchitis, emphysema of the lungs and bronchiolospasm, early development of ventilation disorders, mainly of the obstructive type, signs of hypertension in the pulmonary circulation and, in acute cases, marked respiratory disturbances. The prognosis ranges from relative good, in the case of a chronic course, to extremely poor, with development of marked cardiopulmonary insufficiency and possibility of acute respiratory disturbances. The therapeutic measures should be directed, first of all, toward improving and normalizing bronchial patency and hemodynamics in the pulmonary circulation, as well as prevention and treatment of infectious complications.

c. Toxic or toxicoallergic involvement of the capillary-alveolar membrane. The chief etiological factors are: toxic agents with acute toxic effect on the bronchopulmonary system (phosgene, nitric oxide, chemical warfare agents, beryllium and some radioactive substances when the route of intake is by inhalation, which are very soluble and have a high specific activity--polonium and plutonium). In acute cases, the clinical course has distinctly circumscribed phases related to the main stages of pathogenesis: blocked transport of blood oxygen through the alveolar membrane, reflex change in hemodynamics, first in pulmonary and then systemic circulation, hypoxia and relatively rapidly developing circulatory insufficiency. The syndrome is established on the basis of conventional diagnostic criteria for pulmonary edema. This also governs the main directions of therapeutic measures, as well as prognosis.

In chronic cases (for example, berylliosis), the diagnosis is based on the presence of clinical signs of progressive respiratory deficiency, with distinct and early development of diffusion disturbances, against the background of clinical and roentgenological manifestations of diffuse granulomatosis or interstitial lesion to lung tissue. The prognosis depends on prompt discontinuation of contact with the toxic factor, early detection of the syndrome and its structure, with appropriate pathogenetic therapy directed toward normalizing the immunological status of the organism, eliminating or attenuating hypoxic disturbances and improving hemodynamics.

5. Acute circulatory disorders: Acute circulatory disorders develop under the influence of systemic toxic factors of an occupational nature (carbon monoxide, cyanates, etc.). These states do not require special identification; the chief clinical signs correspond to well-known syndromes of collapse, cardiogenic shock, vascular crisis, etc.

6. Hypoxic heart: The main etiological factors are: carboxyhemoglobin and methemoglobin producers, many nitro derivatives of benzene and other toxic agents with hemolytic and erythropoiesis-depressing action. Endogenous and exogenous factors of a nonoccupational nature play a large role. With respect to condition of the heart, the preclinical stage is related to the rate of development and severity of hypoxemia (anemia) and tissular

hypoxia. Clinical substantiation of the diagnosis and methods of treatment are the same as for well-known similar diseases of any other etiology ("anemic heart").

In this section, we have thus made an attempt to classify syndromes only of cardiovascular disorders as affected by various occupational factors. The implication is that they constitute a complicated clinical symptom complex of occupational disease of diverse etiology. In the diagnosis, formulation of the syndrome in accordance with its significance to the clinical course and prognosis are indicated, as well as link with a specific occupational situation.

The strict subdivision of syndromes is arbitrary; there may be transitional, combined variants of reactions, and this depends on the extent of involvement in the process of other organs and systems, as well as the general correlations established in the patient's organism. Depending on the concrete syndrome, its role at a given moment in the clinical findings and prognosis, as well as thanatogenesis, this part may vary as to the place it will hold in a comprehensive formulation of the diagnosis of an occupational disease.

CHAPTER 3. THE CARDIOVASCULAR SYSTEM AS RELATED TO INDUSTRIAL POISONING

[Text] One of the most important aspects of control of diseases of the heart and vessels is identification of the etiology and pathogenesis of such diseases. Industrial toxic agents are also of great interest in this regard. It is particularly important to study the condition of the cardiovascular system in the case of chronic exposure to such common industrial toxic agents as lead, carbon disulfide and benzene.

Soviet scientists have made a significant contribution to the study of the effects of carbon disulfide and benzene on the body (E. A. Dregichina, 1940, 1968; M. A. Kazakevich, 1954-1963; A. M. Rashevksaya, 1968; L. G. Okhnyanskaya, 1968; L. A. Zorina, 1965, 1971, and others). There is information in the literature about changes in the circulatory system in cases of lead poisoning (M. A. Kovnatskiy, 1961, 1964; V. A. Vasil'yeva, 1966, 1967; Toppich, 1963; Minden, 1963, and others), carbon disulfide poisoning (G. Ya. Bakeyeva, 1963, 1969; Vigliani, 1954, 1957, and others) and benzene poisoning (P. Mytnik, 1931; L. N. Khizhnyakova, 1964; Koelsch, 1935, and others). Most works dealing with the condition of the circulatory system are usually based on investigation of only some hemodynamic indices and on a small amount of material. For this reason, there is no agreement as to the nature of changes in the cardiovascular system under the influence of the above toxic agents. Nor are there data on the course and outcome of demonstrated circulatory disturbances. Yet, not only a correct conception of the essence of the pathological process of poisoning, but more effective treatment and proper answers to expert questions depend on solving these problems.

In addition to a comprehensive general clinical work-up on patients, a set of methods can be used (mechanocardiography, plethysmography, electrocardiography and polycardiography), which determine the main hemodynamic

parameters (all forms of arterial pressure, cardiac output, peripheral resistance, tonus of peripheral and cerebral vessels, bioelectric activity and contractile function of the myocardium), for in-depth studies of the functional state of the cardiovascular system.

The combined use of the above methods makes it possible to describe at one time the changes in various elements of hemodynamics and correlations between them, which permits detection of early disturbances in the circulatory system, more accurate description of clinical syndromes of cardiovascular disorders and mechanisms of their development.

Clinical Characteristics and State of Cardiovascular System in the Presence of Chronic Carbon Disulfide Poisoning

Carbon disulfide poisoning is known for over a century as an occupational disease. It is found primarily among workers in the viscose fiber industry. A radical change in the technological process in the viscose industry, which was made in the last few years, resulted in a significant decline in level of air pollution by carbon disulfide. Nevertheless, in virtually all countries of the world, carbon disulfide poisoning holds a prominent place among occupational diseases.

Carbon disulfide, which is a poison that strikes primarily the nervous system, causes acute, subacute and chronic poisoning. Numerous experimental and clinical studies dealing with its toxic effects are concerned mainly with changes in the nervous system (E. A. Drogichina, 1940; A. A. Model', 1957; Ye. Ts. Andreyeva-Galanina, 1958; M. A. Kazakevich, 1962; Zh. I. Abramova et al., 1967; N. B. Andreyeva, 1969; Pogorzelski, 1956; Straneo, 1961; Gobbato, 1964; Minden, 1967; Dorezak, 1968; Ferrero, 1969). In the case of acute poisoning, carbon disulfide has mainly a narcotic action. Acute and subacute poisoning can lead to persistent organic lesion to the central nervous system of the encephalomyelitis type, with loss of mental faculties (A. A. Kvvorkyan, 1955, and others). In the foreign literature (Attinger, 1948, 1952; Rechenberg, 1957; Weist, 1957; Vigliani, 1957, 1962; Navarro Martinez, Farina, 1969), there are descriptions mainly of severe chronic carbon disulfide poisoning associated with diverse forms of organic lesions to the central nervous system with development of signs of the extrapyramidal syndrome, pseudobulbar paralysis, hemiparesis, mental disorders with delirium or schizoid elements and, not infrequently, ending with feeble-mindedness. There are indications of severe lesions to the peripheral nervous system as well, in the form of polyneuritis with muscular atrophy.

In the Soviet Union, the broad implementation of sanitary and hygienic measures has aided in lowering significantly the concentration of carbon disulfide in air and virtually total disappearance of severe forms of poisoning. Clinical and physiological studies of individuals exposed to low concentrations of carbon disulfide (L. N. Gratsianskaya, G. Ye. Rozentsvit, 1950; M. A. Kazakevich, 1954, 1963; O. D. Chepik, 1957; L. M.

Kashin, 1966; E. A. Drogichina, 1968; L. Ye. Milkov, N. K. Byalko, 1969, and others) and experimental data (Ye. V. Lyadova, 1953; M. A. Kazakevich, M. S. Tolgskaya, 1960, and others) broadened the theoretical and clinical conception of the toxic process in chronic poisoning. It was noted that, under such conditions, the toxic process develops insidiously and may present few symptoms for a certain time (compensation).

It was established that, even at the earliest stages of exposure to carbon disulfide, there is development of disturbances of cortical processes, characterized by prevalence of inhibitory processes with concurrent increase in exhaustibility thereof. Clinically, the early stages of chronic poisoning are associated with functional disorders of the central and peripheral nervous system in the form of neurasthenia, autonomic and endocrine disturbances, signs of sensory polyneuritis. With continued contact with carbon disulfide, there may be progression of signs of poisoning, with a turn to the stage of organic changes, when diffuse involvement of the central nervous system occurs, on the order of encephalopolyneuritis or encephalomyelopolyneuritis.

In the last few years, clinicians have been concerned with the increasing number of patients suffering from diverse and, not infrequently, severe forms of diencephalitis ["diencephalosis"], with which no symptoms are demonstrable that are inherent in severe forms of chronic carbon disulfide poisoning (G. E. Rozentsvit, 1959; E. A. Drogichina, M. N. Ryzhkova, 1967; M. N. Ryzhkova, 1969; A. A. Model' et al., 1969, and others).

Little attention is given in the literature to the toxic effects of carbon disulfide on the circulatory system. Yet long-term observation of patients has shown that cardiovascular disturbances play a significant role in the symptomatology of chronic carbon disulfide poisoning.

In our experience (110 women and 41 men, mainly up to 40 years of age—81%, employed in spinning mills of a chemical fiber combine, who were exposed to relatively low concentrations of carbon disulfide for a long period of time), clinical signs of chronic poisoning usually appeared after 5-7 years of working in contact with carbon disulfide, and they were characterized by changes in the peripheral and central nervous system. In most cases (82%) they were functional in nature, in the form of vegetovascular dysfunction (32.5%) and asthenovegetative syndrome (44%), often combined with signs of vegetosensory polyneuritis and the polyneuritis syndrome (5.5%). Organic changes in the form of encephalopolyneuritis were seldom seen (18%). In addition, regardless of the functional or organic nature of nervous system disorder, 60% of the patients presented signs of involvement in the pathological process of the hypothalamodiencephalic region, and 34.4% of them periodically developed vegetovascular crises characterized by sudden worsening of wellbeing, appearance of severe headaches, chills, fever, numbness of the extremities, choking sensation, palpitations, cardiac pain and, not infrequently, elevation of arterial pressure. The symptomatology of the subjects, with regard to nature of complaints (headaches, vertigo,

increased irritability, sleep disorders, impaired memory, pain in the limbs and numbness) and changes in the nervous system (polymorphous symptoms inherent in a process localized in the mesencephalon, mild symptoms of reflex and sensory disorders, autonomic and emotional disturbances), was similar to that usually observed in poisoning cases (M. A. Kazakevich, 1962, 1963; M. N. Ryzhkova, 1971, and others). At the same time, in addition to neurological complaints, there were rather prominent complaints of cardiac pain varying in nature and intensity (86%), dyspnea (37%), palpitations and intermittent heart beats (34%). In patients with signs of hypothalamic involvement, cardiac pain was observed more often and it was more marked. In some cases, the cardiac symptoms were the chief ones in the clinical syndrome (angina pectoris, myocardial infarction). However, quite often complaints of heart pain were not associated with myocardial changes. Evidently, in some cases they are the result of marked neurasthenia, which is inherent in such patients.

Studies of the functional state of the cardiovascular system show that, along with changes in the nervous system, cardiovascular disorders are equally typical clinical signs of poisoning; they are characterized by changes in the main hemodynamic indices: arterial pressure, cardiac output, bioelectrical activity and contractility of the myocardium. Several authors (G. G. Lysina, 1958; G. Ye. Bakeyeva, 1969, and others) report a relatively high incidence of arterial pressure drop (23 to 59%). N. A. Vigdorchik (1938), Vigliani, Gobbato et al. (1957), Rechenberg (1957) and others classify carbon disulfide with toxic agents that elevate arterial pressure. Ye. N. Artem'yev and T. S. Konovalova, S. F. Shirokaya et al. (1963) indicate that unstable arterial pressure is observed with chronic exposure to carbon disulfide.

Studies involving tachyoscillographic recording from the right and left arm revealed a statistically reliable elevation of all forms of arterial pressure (as compared to a control group; $p<0.001$): end or maximum M_x (in 39% of the patients), lateral or true systolic N_w (48%), mean dynamic M_y (44%) and diastolic M_n in 40% of the patients. Table 1 lists data pertaining to the main hemodynamic indices of patients and individuals in the control group.

Concurrent elevation of all types of arterial pressure was observed in 38% of the patients, while 6%, with normal levels of M_x and M_n, presented elevation of M_y alone or combined with N_w.

Isolated elevation of mean or true pressure, as well as brief elevation and lability of pressure, are interpreted by many researchers as an early precursor of essential hypertension (Ye. M. Tareyev, 1948; V. G. Fleyshler, 1953; I. A. Ryvkin, 1971; Alam, Smirk, 1938, and others).

It is known that arterial pressure level depends on many circumstances, but it is determined chiefly by two factors: amount of blood pumped by the heart in the arterial system per unit time, i.e., minute blood volume (MV), and peripheral resistance (resistance blood encounters in vessels and especially in the precapillary region).

Table 1. Data referable to main hemodynamic indices of patients and control group of subjects

Hemodynamic indices	Carbon disulfide poisoning		Lead poisoning		Benzene poisoning		Control group		Adopted norms
	M±m	range	M±m	range	M±m	range	M±m	range	
Arterial pressure (mm Hg): minimum	82,9±0,9	56—116	80,5±0,9	58—108	68,5±0,81	50—90	72,0±0,69	60—86	60—85; over 40 yrs—90
mean	100,9±1,2	72—154	99,5±1,1	70—126	91,0±1,36	70—118	88,6±0,8	76—136	80—100
lateral	115,7±1,3	86—170	116,8±1,6	88—160	107,4±1,47	88—140	105±1,0	88—126	90—115
maximum	128,8±1,4	100—190	131,5±1,8	100—188	114,6±1,15	80—170	119,1±1,0	100—138	102—130; over 40 yrs-140
PWPV, cm/s: in elastic vessels (C_e)	730±9,5	520—1130	721±14,4	500—1220	673±20,48	500—960	612±12,3	420—850	300—750
in muscular vess. (C_m) brachial-radial arteries	1189±14,9	730—1680	1147±21,5	800—1880	878±30,7	600—1300	826±16,4	510—1120	600—1000
femoral-dorsal artery of foot segment	1087±15,4	600—1580	1050±18,1	650—1560	850±25,8	520—1170	817±12,5	560—1000	600—1000
Absolute modulus of elasticity of: elastic vessels (E_e)	7220±214,7	3650—17 200	7030±333,46	3370—20 110	6230±258,8	3330—12 450	5570±122,0	3770—8010	2100—7000
musc.vess. (E_m)	12430±270,4	4890—25 200	11440±514,73	5710—31 550	7010±238,9	4100—12 900	6480±103,8	4890—8750	3200—9000
C_m/C_e	1,60±0,02	1,0—2,63	1,54±0,01	1,08—2,03	1,31±0,02	0,86—1,76	1,30±0,01	1,10—1,50	1,0—1,40
E_m/E_e	1,76±0,04	0,70—3,65	1,65±0,07	0,76—4,57	1,16±0,04	0,50—1,93	1,16±0,02	0,71—1,70	1,0—1,40
Cardiac index(I)	2,23±0,03	1,40—3,73	2,18±0,04	1,42—3,70	2,58±0,06	1,63—3,75	—	—	2,0—2,45*
Peripheral resistance (w)	21,40±3,63	1600—3890	2140±77,6	1180—5080	1780±40,6	980—2410	—	—	1400—2500*
SPR	47,0±1,06	30,0—97,0	47,0±1,13	23,0—80,0	36,0±0,68	21,0—45,0	—	—	35,0—45,0*

Table 1. (continued)

Hemodynamic indices	Carbon disulfide poisoning		Lead poisoning		Benzene poisoning		Control group		Adopted norms
	M±m	range	M±m	range	M±m	range	M±m	range	
Ratio of total elastic resistance to peripheral (E_o/w)	0.52±0.01	0.26—0.95	0.53±0.01	0.30—0.82	0.59±0.02	0.32—1.17	—	—	0.37—0.56
Tonus (mm) of intra- & extracranial arteries & veins: a_{op}	11.89±1.43	1.43—21.0	16.31±1.2	6.3—35.76	14.24±1.6	1.21—34.96	10.01±0.4	5.17—17.0	8—13.0
h_{op}	81.06±8.3	12.65—300.0	106.0±10.0	20.0±260.0	100.4±13.1	5.5—280.0	56.43±3.03	19.8—95.0	40.0—73.5
a_{tp}	6.31±0.5	1.6—21.2	5.85±0.6	1.0—15.75	6.17±0.53	2.52—13.8	6.7±0.3	4.0—11.1	5.1—8.5
h_{tp}	39.77±4.8	4.4—172.0	47.0±5.8	13.2—153.0	44.74±9.6	5.4—207.0	30.71±2.6	10.0—61.05	16.1—16.0
Tonus (mm) of finger & toe arteries & veins a_{ppr}	6.96±0.44	1.76—17.10	10.33±1.05	0.48—26.25	9.23±0.85	2.2—21.85	12.19±0.79	6.17—19.6	7.1—17.55
h_{ppr}	41.19±2.45	8.0—92.3	46.18±3.37	11.6—104.0	41.42±3.46	17.6—90.0	33.26±3.55	12.0—72.0	21.0—55.0
a_{ppn}	3.43±0.63	0.81—22.0	3.63±0.33	1.07—9.09	4.08±0.57	0.96—13.0	3.54±0.23	2.0—8.9	2.4—5.0
h_{ppn}	15.12±1.52	2.5—34.45	23.04±2.59	4.0—66.0	17.94±2.18	4.4—50.0	17.30±1.08	6.0—32.0	10.1—25.0

*±10% of proper values.

Key:

a_{op}, h_{op}) tonus of intracranial arteries and veins (respectively), determined by orbital plethysmography

a_{tp}, h_{tp}) tonus of extracranial arteries and veins, determined by temporal plethysmography

a_{ppr}, a_{ppn}) tonus of peripheral digital arteries according to volumetric pulse on digital plethysmograms of hands and feet (respectively)

h_{ppr}, h_{ppn}) tonus of peripheral digital veins according to increment of obturation plateau on digital plesthysmograms of hands and feet (respectively)

PWPV) pulse wave propagation velocity

Studies have shown that the mechanism of elevation of arterial pressure in the presence of carbon disulfide poisoning, like that of essential hypertension, is based on disturbances of normal correlations between peripheral resistance and cardiac output. Increased peripheral resistance plays the leading role in elevation of arterial pressure. The findings of studies of the correlation between minute volume (MV) of blood and specific peripheral resistance (SPR) conducted on 146 patients are listed in Table 2.

Table 2. Correlation between MV and SPR in patients suffering from carbon disulfide poisoning (146 patients examined)

SPR \ MV	Below due level (by 15-30%)	At due level (±10%)	Above due levels (by 15-70%)
Below due levels (by 15-30%)	—	—	28
At due levels (±10%)	—	—	38
Above due levels (by 15-142%)	27	35	6

In 45 (31%) of 64 patients (44%) with elevated mean dynamic pressure, the rise was due to decreased patency of the precapillary system, i.e., spastic condition of precapillaries, and in only 19 cases (13%) was it due to an increase in MV.

Repeated readings of arterial pressure by the method of Korotokov revealed unstable indices M_x (ranging from 25 to 70 mm Hg) and M_n (fluctuations up to 40 mm Hg) in 66% of the patients, with a tendency toward hypotensive (22.5%) or hypertensive (43.7%) reactions.

The demonstrated instability of arterial pressure, combined with clinical data, is evaluated as neurocirculatory dystonia of the hypotensive and hypertensive types. And while the percentage of hypotensive reactions did not present any appreciable differences as related to different forms of poisoning and was unrelated to the condition of higher autonomic centers, the hypertensive reactions were observed more than twice as often (57%) in patients with signs of hypothalamic involvement than those without them (23%).

We failed to demonstrate a clearcut link between arterial pressure indices and ophthalmoscopic findings. However, changes in vessels of the fundus were the most marked (angiopathy) with elevation of arterial pressure.

We must concur with N. N. Savitskiy, that the term "neurocirculatory dystonia" characterizes not so much the tonus of vessels as it does impairment of tonus of the central system that regulates circulatory functions, a disturbance inherent in a normal level of vital function of higher branches of the central nervous system.

In view of the fact that the highest incidence of elevation of all forms of arterial pressure and hypertensive form of the neurocirculatory syndrome was observed in patients with signs of hypothalamic pathology, a link is suggested between these changes and disturbances of the hypothalamic region which, as we know, implements adaptational and regulatory functions in the body (N. I. Grashchenkov, 1963).

At the present time, one can consider it the most likely that the neurocirculatory syndrome is an expression of neurosis of higher autonomic centers in the hypothalamic region. With this syndrome, increased excitability and concurrent instability of higher vegetative centers are observed.

In view of the wide lability of arterial pressure, with a tendency toward hypertensive reactions and elevation of all types thereof in a considerable number of patients with chronic carbon disulfide poisoning, it can be concluded that the latter is associated with a tendency toward development of essential hypertension. This is also confirmed by the results of a dynamic study of patients with carbon disulfide poisoning over a period of several years, which indicated development of more persistent hypertension, with a turn to essential hypertension, in the case of stable and progressive course of intoxication.

On the basis of current data, which are indicative of impairment of cortical processes and injury to deep parts of the brain (hypothalamic region) under the influence of carbon disulfide (E. A. Drogichina, L. G. Okhnyanskaya et al., 1954; M. A. Kazakevich, 1963; A. A. Model' et al., 1969; M. N. Ryzhkova, 1971) and current conceptions of the pathogenesis of essential hypertension, it is justified to assume that development of the neurocirculatory syndrome and essential hypertension in cases of carbon disulfide poisoning depends on impairment of neuroreflex mechanisms of regulation of cardiovascular function as a result of exposure to carbon disulfide. One must also take into consideration the sequence of development of the clinical symptoms and prime role of the so-called specific symptom complex referable to the nervous system, which is inherent in poisoning.

The demonstrated incidence of increased tonus of the aorta and, particularly, of peripheral arteries of different caliber with asymmetry and different direction of changes in arterial tonus in different segments of the blood stream is also a result of impaired neurovascular regulation and one of the manifestations of the syndrome of neurocirculatory regulation, as well as one of the manifestations of the syndrome of neurocirculatory dystonia. Thus, the pulse wave propagation velocity (PWPV) in vessels of the elastic type (C_e) in the carotid-femoral artery (according to aorta) segment was above normal in one-third of the patients (37%).

An increase in PWPV in vessels of the muscular type (C_m) was observed much more often: in 79% of the patients in the brachial-radial artery segment (arm) and 68%, in the femoral artery-dorsal artery of the foot segment.

The elasticity modulus, expressed as the velocity of propagation of the pulse wave, which more accurately describes elasticity of the vascular wall, was elevated in vessels of the elastic type (E_e) in 48% and in vessels of the muscular type (E_m) in 75%.

The demonstrated elevation of ratio between velocities (C_m/C_e) and elasticity moduli (E_m/E_e) of vessels of the muscular and elastic type (over 1.4) found in 70% of the patients indicates that the elasticity properties of the walls of muscular arteries are greater in these patients than those of elastic arteries.

The incidence of elevated PWPV, high C_m/C_e and E_m/E_e was reliably higher among patients with signs of functional disturbances of the hypothalamic region than in patients without such signs.

According to volumetric pulse on digital plethysmograms, tonus of peripheral arteries with small caliber was accentuated in the fingers of most patients (60.7%) and toes of a considerable number of cases (43.6%).

A comparison of indices of pulse wave velocity and plethysmographic findings to such clinical signs as complaints of pain in the limbs, coldness and numbness thereof, revealed that pain of the extremities was associated with signs of vegetosensory polyneuritis, which are often seen in patients with normal and accentuated tonus of arteries of the limbs. Complaints of cold and numb limbs were clearly associated with elevated pulse wave indices. The higher incidence of increased tonus of peripheral arteries in patients with signs of hypothalamic involvement and increased sensations of cold and numbness in patients with signs of hypothalamic pathology at times of vegetative crises are indicate of a link between hypertonia of peripheral arteries and involvement of the hypothalamic region, which apparently includes structures that participated in regulation of vascular tonus.

In spite of the established opinion that tonus of cerebral arteries is increased in the presence of carbon disulfide poisoning, studies of cerebral circulation by the method of orbital and temporal plethysmography, using a cuff to occlude the cervical veins, indicate that a decrease in tonus of intracerebral arteries (42%) and veins (52%) is the most frequent cause of cerebral hemodynamic disorders, which are often dominant in the clinical syndrome of intoxication. V. P. Zhmurkin observed analogous changes in cerebral hemodynamics in the presence of essential hypertension.

Virtually all of the patients (95%) complained of headache. However, it was attributable to hypertension of cerebral arteries in only 16%, and a different mechanism of hypertension (neuralgia, migraine) was involved in 20%. In most cases (59%), headache was due to inadequate tonus of cerebral veins. Of the 59% cases with typical dull or excruciating headaches of occipital or frontal localization, which became worse when the body was inclined and often associated with vegetative disorders, 50% presented rather marked hypotonia of cerebral vessels (h_{op}>86 mm^3), and in 25% of the

cases it was associated with a decrease in tonus of cerebral arteries, causing difficult efflux of blood from the cranial cavity. In 9% of the patients, tonus of cerebral veins was normal, but a low arterial tonus (a_{op}>15 mm^3)* caused excessive influx (Table 1).

The role of hypotonia of cerebral veins in the genesis of headache was confirmed with particular distinction in pharmacological tests. Wellbeing of patients improved under the influence of a vasoactive agent (no-shpa [6, 7, 3',4'-tetraethoxy-1-benzal-1,2,3,4-tetrahydroisoquinolone hydrochloride]) along with increase in tonus of cerebral veins.

In the light of the foregoing, from the standpoint of therapy it is important to know which vascular disturbance (arterial or venous) is prominent in the clinical signs of poisoning.

The functional state of the myocardium is particularly significant in development of hemodynamic changes.

According to the data of most clinicians (G. G. Lysina, 1956; V. G. Belikov, G. G. Zakharov et al., 1965; G. Ya. Bakeyeva, 1969; Weist, 1957, and others), in the case of chronic exposure to carbon disulfide, contacts often present complaints and changes referable to the heart (unpleasant sensations, sharp or compressive pain, palpitations, dyspnea, dull sounds and systolic murmur over the heart). These symptoms and complaints progressed with increase in work tenure involving contact with carbon disulfide (Ye. N. Artem'yev, T. K. Konovalova, 1962, and others).

A. A. Model' and E. S. Navrotskaya (1958), who made an electrocardiographic study of 66 patients with early signs of chronic carbon disulfide poisoning, discovered changes in T wave, S-T interval and low voltage of the QRS complex, which they evaluated as a sign of functional weakness of the myocardium occurring as a result of impaired corticosubcortical regulation; these signs were present in addition to rhythm disturbances (bradycardia or, more often, tachycardia).

G. Ya. Bakeyeva (1963, 1969) found changes in the terinal part of the ventricular complex (shifting of S-T interval, decline or inversion of T wave) and signs of diminished myocardial contractility, indicative of hypodynamia of the mycoardium, along with functional disorders of the nervous system, in over one-third of the patients she examined. The physiological electrocardiographic, ballistocardiographic and polycardiographic changes she demonstrated, combined with the complaints and clinical manifestations of intoxication, were evaluated as myocardial dystrophy. V. A. Vasil'yeva et al. (1966) describe analogous changes and interpretation.

*H_{op} and a_{op}--tonus of cerebral veins and arteries, respectively, determined by orbital plethysmography.

Pathoanatomical and pathohistological data on animal organs in the presence of experimental chronic carbon disulfide poisoning (G. G. Lysina, 1956; M. A. Kazakevich and M. S. Tolgskaya, 1962) are also indicative of onset of dystrophic changes, not only in neurons of the central nervous system, but in other organs, including the myocardium.

Unlike the above-mentioned researchers, Gobbato et al. (1964), Lilis et al. (1965) and others attribute the decline of EKG waves with change in terminal part of the ventricular complex (in patients with chronic carbon disulfide poisoning) to atherosclerotic lesion to the heart and development of coronary insufficiency. Navarro Martinez and Farina (1969) observed signs of sclerosis of coronary vessels with development of of myocardial infarction (6.6%) in 15.6% of the patients with signs of severe, chronic carbon disulfide poisoning associated with atherosclerotic changes in cerebral and renal vessels. Ambrosio (1957) reported development of myocardial infarction in some patients with severe carbon disulfide poisoning, but he believes that coronary vessel involvement is rarely encountered under the influence of carbon disulfide.

Our electrocardiographic studies (Table 3) revealed disorders referable to cardiac rhythm (bradycardia in 14.7% of the patients and tachycardia in 20.8%) and changes in bioelectrical activity of the myocardium (decline, flattening or inversion of T wave), which were diffuse in most patients.

The signs of impairment of processes of myocardial repolarization in 36.2% of the patients, with due consideration of the entire symptomatology of the disease (cardiac pain, dull sounds, systolic murmur and others) can be evaluated as dystrophy of the myocardium.

The diffuse and dystrophic myocardia changes, as well as vascular dysfunction, are persistent and closely related to the severity of disturbances in the nervous system, and primarily in its superior vegetative centers.

Myocardial changes are observed more than twice as often (47%) among patients with signs of hypothalamic involvement as in patients without such signs (20%), and they are more marked.

Investigation of contractile function of the heart, which is the main resultant function of cardiac activity, made it possible to demonstrate the hyperdynamia and hypodynamia syndrome.

The phasic hyperdynamia syndrome, which was observed in 30% of the patients, was characterized by an increase in indices of efficiency of systole (intrasystolic index) to 91-97%, mainly as a result of shortening of the period of isometric contraction, i.e., the period of cardiac preparation for ejection of blood into the great vessels (0.01-0.02 s). These changes can be attributed to neurogenic intensification of cardiac function due to some tension of the sympathoadrenal system.

Table 3. Principal changes in electrocardiographic indices of patients with chronic carbon disulfide, lead and benzene poisoning

Factor involved and severity of poisoning	Number examined	Cardiac contractions		Conduction			Extra-systole	Decline, flattening or inversion of T			
		up to 60/min	81 or more	QRS = 0.09 s or more	QRS = 0.11 s or more	PQ = 0.17 s or more		$T_{I, II, III}$	$T_{V_{1-3}}$	$T_{V_{4-6}}$	moder-ate diffuse changes	marked diffuse changes
Carbon disulfide with signs of hypothalamic involvement	89	17	24	1	3	10	—	2	1	13	6	20
		(19.2%)	(27%)								47%	
without signs of hypotalnal.involvement	60	5	7	1	—	4	—	1	1	5	1	4
		(8.3%)	(11.7%)								20%	
total	149	22	31	2	3	14	—	3	2	18	7	24
		(14.7%)	(20.8%)			(9.4%)					36,2%	
Lead	102	42	6	2	2	5	4	4	1	11	10	1
											25%	
Benzene												
mild	87	21	7	1	1	10	2	—	2	4	18	5
		(24%)	(8%)			(11%)					33%	
moderate & severe	135	25	38	1	1	18	3	1	1	6	54	19
		(18%)	(28%)			13%					60%	
total	222	46	45	2	2	28	5	1	3	10	72	24
		(20,7%)	(20.2%)	0,9%	0,9%	13.5%	2%				49,5%	

The syndrome of cardiac hypodynamia, which was demonstrated in 36% of the patients, was characterized by a decline of indices of systolic efficiency (intrasystolic index constitutes 80-86%) and longer phase of pressure increment (0.04-0.06 s). It is attributable both to increase in peripheral resistance of the vascular system, which makes cardiac function difficult in the absence of myocardial pathology, and dystrophy of the myocardium, which induces very objective, though mild and compensated, decrease in contractile function of the heart.

The mechanism of development of the observed changes in the heart is quite complex in the presence of carbon disulfide poisoning. In view of the disorders of the nervous system and some parallel between them and the myocardial changes, it may be assumed that they are attributable to disturbances of metabolic trophic processes in the myocardium as a result of impaired central regulation. However, in view of the properties of carbon disulfide as a toxic agent for cells, we cannot rule out its immediate effect, as well as that of its metabolic products circulating in blood, on neural elements of the myocardium and muscle cells.

The results of studies of functional state of the cardiovascular system of patients with chronic carbon disulfide poisoning do not allow us to concur with the data of some foreign authors (Legge, Goodby, 1921; Richenberg, 1957; Vigliani, 1957, and others) who believe that carbon disulfide is not so much a toxic agent for nerves as it is for vessels, and they attribute the pathological changes that occur with intoxication, including encephalopathy, to sclerotic lesions to the arteries of the brain and other vascular regions.

The authors arrive at such conclusions solely on the basis of clinical examinations or studies of lipid metabolism.

Many authors have reported changes in lipid metabolism in the case of chronic exposure to carbon disulfide (M. A. Kazakevich, G. S. Konnikova, 1962; Nofer et al., 1964; Velvart, Ballog, 1961; Oleniczi, Plamioniak, 1963, and others). As a rule, these disturbances consist of increase in blood serum cholesterol, decreased bond between cholesterol and protein, reduced quantity of phospholipids and change in correlation between α- and β-lipoproteins, in the direction of an increase in the β-fraction.

In the opinion of most researchers, the changes in lipid metabolism with chronic exposure to carbon disulfide may be one of the factors involved in development of atherosclerosis.

At the same time, Prerovska et al. (1963, 1968) believe that one should proceed very cautiously in assessing the effect of carbon disulfide on development of atherosclerosis on the basis of the results of biochemical tests. In a group of young workers exposed for a long time to carbon disulfide, whom they had under dynamic observation, they found that, in spite of the higher levels of cholesterol and β-lipoproteins in the blood of these individuals (as compared to a control group), they did not present clinical

signs of vascular sclerosis, either at the first examination or later (after 6 years).

It is known that, although impairment of cholesterol and lipid metabolism in general plays a large part in the pathogenesis of atherosclerosis, this factor cannot be the primary cause. Enough facts have been accumulated to indicate that atherosclerosis cannot be viewed solely as the direct result of impaired lipid metabolism or excessive intake of cholesterol. Clinical observations, epidemiological studies and experimental data have led to recognition of the prime role of the neurogenic factor in development of atherosclerosis (P. Ye. Lukomskiy, 1963; A. L. Myasnikov, 1965, and others).

The cholesterol elevation and impairment of other types of metabolism (protein, carbohydrate, mediator), as well as biogenous amines (epinephrine and norepinephrine), which we observed in half the patients we examined, are apparently related to the toxic lesion and disturbances of central regulatory mechanisms, in particular, changes in functional state of higher vegetative centers.

Many years of patient follow-up indicate that the course of chronic carbon disulfide poisoning is adverse, involving prolonged stable or progressive symptoms, not only referable to the nervous system, but cardiovascular system, and that there is a correlation between circulatory changes and nervous system disorders.

The data obtained from dynamic studies warrant the belief that the changes in the cardiovascular system are not the only pathogenetic factors determining the clinical symptom complex of intoxication; on the contrary, they develop as a result of changes in the central and peripheral nervous system occurring under the influence of carbon disulfide.

We deem it opportune to illustrate this thesis with some examples that characterize the clinical findings and condition of the cardiovascular system.

> Patient G., 28 years old, has been working since 1961 as a mechanic servicing equipment and spinning machines at a chemical fiber plant; he comes in contact with carbon disulfide in concentrations up to 8 times higher than the maximum permissible levels. He was at the institute clinic due to chronic carbon disulfide poisoning, with the diagnosis of marked vegetovascular dysfunction with vegetative crises, asthenic state. His health was good in the past. In 1965, he had a mildly acute case of carbon disulfide poisoning, after which he began to have periodic headaches, complained of fatigability, irritability and sleep disorders. He became a poor traveler. In 1968, his condition worsened: more intensive attacks of headache associated with general weakness, compressing pain in the heart with irradiation

to the neck and left arm, cold extremities, pulsation and tremor of the entire body. He was hospitalized twice with such attacks, with the diagnosis of angina pectoris and suspected myocardial infarction. Such attacks (with elevation of arterial pressure and tachycardia) were again observed while the patient was in the clinic.

Objective findings when examined at the clinic: temperature 36.0-37.2°C, somewhat undernourished, pale integument. Asthenia. Irritable and quick-tempered. Positive Horner's symptom on the left. Fine tremor of the extended fingers. Lively tendon reflexes. Hypesthesia on the left of the segmented type. Tenderness of vegetative cervical elements. Pale pink dermographism. The hands and feet are cold and cyanotic. Poor pulsation on dorsal arteries of the feet. Arterial pressure in the range of 100/70 to 140/100 mm Hg. Pulse 75-100 per min. Heart boundaries are in the normal range. Sounds are loud and clear. No pathology of respiratory and digestive organs. Examination of fundus of the eye showed no change in retinal vessels. Blood test: hemoglobin 142 g/ℓ (1.42 g%); erythrocytes $3.8 \cdot 10^6$/μℓ (4,800,000); color index 0.89; leukocytes $8.7 \cdot 10^3$/μℓ (8700); lymphocytes 20%; monocytes 5%; eosinophils 4%; basophils 1%; stab 2%; segmented 67%; plasma cells 1%; erythrocyte sedimentation rate 7 mm/h. In blood serum: free carbon disulfide 0.00016 g/ℓ (0.016 mg%), bound 0.0002 g/ℓ (0.02 mg%); cholesterol 1.9 g/ℓ (190 mg%); sugar 0.85 g/ℓ (85 mg%), acetylcholine and acetylcholine-like substances 127 μg/mℓ, cholinesterase activity 0.4 false and 1.26 true. Sublimate test 2.1, formol test negative.

Epinephrine excretion in urine 16.4 μg/s and norepinephrine, 39.7 μg/s.

Tachyoscillographic examination of arterial pressure (mm Hg): $M_П$--86, $M_У$--106, N_W--118, $M_Х$--132, Δp--32, hemodynamic beat (HB)--14. PWPV in aorta 680 cm/s, in segment of brachial-radial artery 1220 (on the right) and 1200 cm/s (on the left), segment of femoral-dorsal artery of foot 1150 (right) and 1140 cm/s (left). SBV [systolic blood volume] 77.2 m ℓ actual MV is 54% greater than the proper level. The actual SPR is 14% less than due and 30% greater than the working level. E_o/E_w 0.66. No pathological changes on the EKG. Sinus rhythm, 75 beats/min. The electric axis of the heart is in normal location. Cardiac contractility is characterized by longer duration of pressure build-up (ic--0.05 s). Tension phase 0.09 and ejection phase 0.25 s (96% of proper level). KB [expansion unknown] 3.2, intra-systolic index (ISI) 83. After treatment with tranquilizers,

sedatives and vitamins (seduxen, Leonorus, devinkan, corvalol, vitamins C, B_1 and B_6), the patient was discharged in improved condition and transferred to work not involving contact with carbon disulfide and other toxic agents. The above treatment was continued under polyclinic [outpatient] conditions.

When readmitted to the clinic 1 year later, there was significant improvement of both subjective and objective signs. The patient was stronger and calmer. Temperature was normalized. There was reduction of vegetovascular dysfunction and virtual disappearance of vegetative crises. He is rarely troubled by pain in the heart and headache, and they occur mainly when he is overtired. Only some general weakness, pain in the arms and paresthesia of the limbs are reported.

Objective examination shows tenderness of muscles of the shoulder girdle. The hands and feet are warm. Heart sounds are clear. Arterial pressure 110/70-120/80 mm Hg. Examination of the cardiovascular system revealed normalization of its parameters.

Tachyoscillography revealed the following arterial pressure levels (mm Hg): M_n--74, M_y--98, N_w--108, M_x--120. PWPV in aorta 630 cm/s, in brachial-radial artery 850 (on the right) and 900 cm/s (on the left), femoral-dorsal artery of foot 870 (right) and 1000 cm/s (left). SBV 71.0 m , MV is 61% above proper level. Actual SPR is 18% less than proper and 25% more than working. The EKG is normal. Phase structure of systole is normalized (ic 0.02 s, ISI 93).

In this case, a young man who had worked for a long time in contact with carbon disulfide, after actue poisoning, gradually developed symptoms of chronic carbon disulfide poisoning associated with marked vegetovascular disturbances and vegetative crises. The cardiovascular disorders were manifested by changes in arterial pressure with a tendency toward hypertensive reactions, increased tonus of peripheral arteries, impairment of normal correlations between peripheral resistance and cardiac output, decreased efficiency of systole.

After treatment and discontinuation of contact with carbon disulfide, along with considerable improvement of his condition and attenuation of changes referable to the nervous system, there was also normalization of parameters characterizing the state of the circulatory system. This case is interesting in that the patient presented a combination of involvement of central and peripheral vegetative elements. Marked irritation of the inferior cervical sympathetic ganglion simulated attacks of angina.

Patient Zh., 35 years old, has worked for 9 years in contact with carbon disulfide in concentrations that were 3-5 times above the maximum permissible levels. In 1964, she was at the institute clinic due to chronic carbon disulfide poisoning, with the diagnosis of vegetovascular dysfunction with signs of hypothalamic insufficiency, hypertensive reactions and myocardial dystrophy. No burdens in history. For the last 2 years she has had headaches, pain in the hands and feed, coldness and numbness of the latter, sharp pain in the cardiac region and intermittent heart beat. She developed fatigability, irritability and sleep disorders. This was followed by attacks of headache associated with the feeling of "shortage" of air, rush of heat to the face, pressure pain in the heart, chills and tremor of the entire body, polyuria at the end of the attacks.

Objective examination revealed: normal body temperature, somewhat overnourished, pale integument. Emotionally excitable. Pupils are regular in shape, good reaction to light and convergence. Tendon reflexes uniformly active. Mile hypesthesia on the left, of the hemitype. Accentuated dermographism, persistent, red. Hands and feet are cold, cyanotic. Arterial pressure is unstable, with periodic elevations, 120/80-150/100 mm Hg. Pulse rate 70-80/min. Heart sounds are dull, systolic apical murmur. Roentgenoscopy of the heart revealed some enlargement of the left ventricle, no change in the aorta. No pathology of the lungs, digestive and reproductive organs.

Examination of the eye grounds revealed severe constriction of retinal arteries.

Blood test: hemoglobin 130 g/ℓ (13 g%), erythrocytes $4.55 \cdot 10^6$/μℓ (4,550,000), color index 0.85, leukocytes $4.8 \cdot 10^3$/μℓ (4800), lymphocytes 43%, monocytes 6%, eosinophils 3%, stab 5%, segmented 42%; erythrocyte sedimentation rate 15 mm/h. Blood serum: cholesterol 1.9 g/ℓ (190 mg%), sugar 0.91 g/ℓ (91 mg%), lipoid phosphorus 0.06 g/ℓ (6 mg%). Epinephrine excretion 10.5 μg/s, norepinephrine 12 μg/s. Wasserman negative.

Arterial pressure recorded by tachyoscillography (mm Hg): M_n--98, M_y--112, N_w--142, M_x--160, Δp--44, HB 18. PWPV in aorta 940 cm/s, brachial-radial artery 1250 cm/s, femoral-dorsal artery of foot 1090 cm/s.

SBV 50 m . Actual MV is 11% lower than proper level. SPR 58% above proper level and 40% above working level. E_o/w 0.54. On the EKG, sinus rhythm, 73/min, P-Q = 0.14 s,

QRS = 0.07 s, QRST = 0.35 (normal 0.36 s). $R_I = R_{II} > R_{III}$. R_{V_3} slightly notched Sv_3. ST_{II}, avf, V_{5-6} slightly low, T_{III} mildly negative, T_{avL}, avf low, T_{V_3} flattened, $T_{V_{4-6}}$ low. Normal position of electric axis of the heart. Moderate myocardial changes, mainly in left ventricle. Phase structure of systole: Q--first sound--0.04 s, sphygmic period 0.26 s (104% of due level), phase of pressure build-up 0.04 s, tension phase 0.08 s; KB 3.6, ISI 87.

After treatment (belloid, Leonorus, vitamins B_1 and B_6, dimedrol, calcium chloride), the patient's condition improved appreciably; she became calmer, sleep was normalized, there were fewer headaches and cardiac pain. She returned to her former job (contact with carbon disulfide), but soon headaches and irritability recurred. There was a significant deterioration in 1968. Upon readmission to the clinic 5 years later she reports worsening of her condition: the headaches became persistent, dull or intensive, mainly in the frontal and occipital regions, often accompanied by nausea. There was intensification of cardiac pain with irradiation to the left hand, and the above-described attacks occurred more often. Arterial pressure also rose more often. Memory was impaired. She developed fear of darkness.

Objective findings: she has gained weight, subfebrile temperature. The tongue is slightly deviated to the right. Mild flattening of the right nasolabial fold. Tender supraorbital, occipital and temporal points on the left. Mild hypesthesia of the left half of the head and face. Abdominal reflexes are diminished, and plantar ones absent. Arterial pressure is in the range of 145/85-150/100 to 170/105 mm Hg. There is intensification of the second sound over the aorta. Roentgenoscopy: unfolded type aorta. Examination of eye grounds: moderate constriction of retinal arteries and dilation of veins (angiopathy).

Tachyoscillographic recording of arterial pressure (mm Hg): M_n--104, M_y--124, N_w--142, M_x--160, p--38. HB 18, PWPV 1090 cm/s in aorta, 1280 cm/s in brachial-radial artery segment, 1160 cm/s in femoral artery-dorsal artery of foot, SBV 48.8 ml, actual MV is 5% above proper level. Actual SPR is 37% above due level and 44% above working level. E_o/w 0.57. No significant dynamics on EKG.

The changes in phase structure of systole were also persistent: Q--first sound 0.06 s, sphygmic phase 0.27 s (108% of due level), pressure phase 0.04 s, tension phase 0.10 s, KB 3.0, ISI 87.

In this case, a young women who had worked for a long time in contact with carbon disulfide and had never been sick in the past developed signs of chronic intoxication in the last 2 years, characterized by vegetovascular dysfunction with signs of hypothalamic involvement and cardiovascular disturbances (hypertensive reactions, increased arterial tonus and peripheral resistance, altered bioelectrical and contractile functions of the myocardium). In spite of significant improvement after treatment, when she continued to work in contact with carbon disulfide her condition worsened and there was progression of poisoning symptoms (increased signs of vegetative dysfunction, metabolic disorders, psychosensory phenomena). Along with progression of changes in the nervous system, there were also disturbances of the cardiovascular system. The periodic elevation of arterial pressure, in the form of hypertensive reactions, became more marked and persistent in the nature of grade IIB essential hypertension, which undoubtedly aggravates the course of intoxication.

> Patient U., 40 years old, worked for 12 years as an instrument control man at a chemical fiber plant, which involved contact with carbon disulfide in concentrations 3 or more times higher than permissible levels. He was at the institute clinic from 26 October to 6 December 1967 due to chronic carbon disulfide poisoning (marked asthenovegetative syndrome with signs of hypothalamic insufficiency, polyneuritis and sympathetic inflammation of the truncus [truncitis]).
>
> He considers himself to have been sick for about 3 years. No prior illnesses. He complains of persistent headache, pain in the arms and legs, coldness and numbness thereof, sharp or pressure pain in the cardiac region, sleep disorders, loss of memory. In the last year, he developed attacks of pressure pain in the region of the heart, associated with weakness and tremor of the body. He could no longer tolerate wine, heat or traveling. Vertigo and cloudiness of the eyes appear when he changes the position of his body.
>
> Objective examination: temperature 36-37.2°C, subcutaneous fatty layer is satisfactorily developed, integument is somewhat pale. Emotional instability (he cries). Asthenic. Corneal and conjunctival reflexes absent. Pupils dilated, d>s. Tender supraorbital and occipital points, Erb's point, neurovascular bundles on the forearms, legs, paravertebral points of the cervical and thoracic spine (D_1-D_7). Lively tendon and periostal reflexes, d = S; plantar: diminished on the left, absent on the right. Rocking in Romberg's position. Mild tremor of extended fingers. Hypersthesia of distal parts of the arms (C_6-D_1) and lower third of the thighs. Hands and feet are cold, with marbly skin. Pink dermographism appearing within 7-8 s and lasting over 6 min. Pulse 74/min.

Arterial pressure is in the range of 110/70 to 140/90 mm Hg. Heart boundaries are within normal range. Sounds are significantly dulled. No pathology of lungs and digestive organs. Examination of eye grounds revealed moderate dilatation of retinal veins.

Blood test: hemoglobin 144 g/ℓ (14.4 g%), erythrocytes $4.8 \cdot 10^6$/μℓ (4,800,000), color index 0.9, leukocytes $7.5 \cdot 10^3$/μℓ (7500), lymphocytes 31%, monocytes 6%, eosinophils 2%, basophils 2%, stab 5%, segmented 54%; erythrocyte sedimentation rate 2 mm/h. Blood serum: free carbon disulfide 0.03 mg%, bound 0.026 mg%, cholesterol 2.45 g/ℓ (245 mg%), sugar 0.94 g/ℓ (94 mg%), acetylcholine and acetylcholine-like substances 12 μg/mℓ, pseudocholinesterase activity 0.4, cholinesterase 0.96. Sublimate test 1.91, formol negative. Wassermann negative. Epinephrine excretion in urine 1.44 μg/s, norepinephrine 6.7 μm/s.

Tachyoscillographic recording of arterial pressure: M --90, M --112, N --124, M --160, Δp--34, HB 36. PWPV 770 cm/s in aorta, 1280 cm/s in brachial-radial artery, 1200 cm/s femoral artery-dorsal artery of food. SBV 60 mℓ, actual MV 6% above due level; actual SPR 25% above due level and 26% above working level; EKG: sinus rhythm, 76/min, $R_I = R_{II} > R_{III}$, $R_{V_4} > S_{V_4}$, QRS_{III} small, T_{III} low, T_{avL} flattened. Horizontal electric axis of the heart. Systolic phase structure: Q--first sound 0.06 s, sphygmic phase ξ 0.23 s (92% of due level), isometric contraction 0.05 s, tension phase 0.11 s; KB 2.4, ISI 82.

After treatment (glutamic acid, belloid, ATP, glucose with vitamins C and B_1, papaverine, adonisid, galvanic baths with naphthalane emulsion), the patient reported improvement. But very soon, in spite of discontinuing contact with carbon disulfide, his condition worsened. When admitted to the institute clinic 1 year later, there was no improvement of wellbeing and objective condition. Hemodynamic parameters presented no significant dynamics. Tachyoscillographic recording of arterial pressure (mm Hg): M_n--94, M_y--110, N_w--122, M_x-132, Δp--28, HB 10.

Pulse wave propagation in aorta 770 cm/s, in brachial-radial artery 1280 cm/s, femoral artery-dorsal artery of food 1060; SBV 45 m ; actual MV equals proper level; actual SPR is 30% above due level and 30% above working level. No dynamics demonstrable on EKG (with the exception of isolated supraventricular extrasystoles); the phase structure of the systole also remained stably altered: Q--first sound 0.04, sphygmic phase 0.25 s (95% of proper level), isometric contraction 0.05 s, tension phase 0.09 s; KB 2.8; ISI 82.

In this case, a patient whose work for 12 years involved contact with carbon disulfide, there was gradual development of symptoms of chronic poisoning, indicative of involvement of the central and peripheral nervous system (marked asthenovegetative syndrome with signs of hypothalamic involvement, signs of polyneuritis and sympathetic truncitis). In spite of treatment and discontinued contact with carbon disulfide, the changes in the nervous system are stable. Cardiovascular disturbances (hypertension, increased tonus of vessels and peripheral resistance, decreased systolic efficiency) are also persistent, and they aggravate the course of poisoning.

Patient D., 37 years old, has worked for 17 years as a spinner at a chemical fiber plant, has been in contact for the last few years with carbon disulfide in concentrations 4 times higher than permissible levels.

She was admitted to the institute clinic with complaints of headache and vertigo, pain in the arms and legs, coldness and numbness thereof, cramps of the legs, sharp pain in the cardiac region and palpitations, dyspnea upon physical exercise, irritability, poor memory, poor sleep with frightening dreams, tremor of right extremities.

For the first 2 years on the job (period when the shop was started up), the patient had several mild bouts of acute carbon disulfide poisoning; after working for 5 years, she developed headaches associated with nausea, vomiting and weakness. In 1957, she developed pain in the arms and legs, then numbness and cramps of the legs. Her condition worsened significantly in the last 3 years, with more frequent attacks of headache, which began to be associated with vertigo; appearance of tremor of the limbs, deterioration of memory; she began to tolerate poorly heat, odors and traveling (associated with headache). She has a history of eczema of the hands and cholecystitis.

Objective examination: temperature 36-37.2°C, well-developed subcutaneous fatty layer. Tremor of right extremities, deterioration of memory. Emotional instability, tearfulness and she is shaking throughout the examination. Pupils s = d, with attenuated reaction to light and convergence. The right corner of the mouth is descended, the tongue deviates to the right. Palatine and pharyngeal reflexes absent. Total hypesthesia of superficial sensibility, more marked on the limbs, better (but not normal) on the soles, around the oral and anal region. Mild retropulsation. Tonus of the legs increased, of the extrapyramidal type. Periosteal and tendon reflexes altered on the arms: d somewhat more than s. Knee reflexes (s = d) lively, abdominal (s = d) present but very transient, plantar diminished. There are elements of bradykinesia (slow performance

of tests). Rhythmic pulse 48-52/min. Arterial pressure in the range of 170/110 to 110/80 mm Hg, elevation first demonstrated and normalized 4 days after admission. Dull heart sounds over the apex; stronger second sound over aorta. Roentgenoscopy of the heart showed some enlargement of the left ventricle, no change in aorta. No change in vessels of the eye grounds.

Blood test: hemoglobin 128 g/ℓ (12.8 g%), erythrocytes $4.1 \cdot 10^6/\mu\ell$ (4,100,000), color index 0.94, leukocytes $4.1 \cdot 10^3/\mu\ell$ (4100), lymphocytes 32%, monocytes 6%, eosinophils 1%, basophils 1%, stab 4%, segmented 57%; erythrocyte sedimentation rate 11 mm/h. Blood serum: 0.020 mg% free carbon disulfide, no bound carbon disulfide, cholesterol 2.7 g/ℓ (w70 mg%), sugar 0.9 g/ℓ (90 mg%), lipoid phosphorus 0.073 g/ℓ (7.3 mg%), acetylcholine and acetylcholine-like substances 189 μg/mℓ. Pseudocholinesterase activity 0.320, cholinesterase 1.06. No epinephrine or norepinephrine in urine. Negative Wassermann. Analysis of duodenal contents negative.

Tachyoscillographic examination of arterial pressure (mm Hg): M_n--76, M_y--90, N_w--1-8, M_x--118, Δp--32, HB--10. PWPV 670 cm/s in aorta, 1220 cm/s (on the right) and 1150 cm/s (left) in brachial-radial artery, 700 cm/s (right) and 1300 cm/s (left) in femoral-dorsal artery of foot; SBV 68.2 mℓ. Actual MV 15% less than proper level, SPR 28% above proper level. EKG: sinus rhythm, 51-54/min PQ 0.16 s, QRS 0.08 s, QRST 0.40 s (normal 0.43 s). $R_I > R_{II} > R_{III}$, $R_{V_5} > S_{V_5}$, S II,III,avf accentuated, T_{II} mildly positive, $T_{III,avf,avl}$ flattened, T_{V_3} low, $T_{V_{4-5}}$ negative, T_{V_6} mildly negative. Sinus bradycardia. Electric axis of the heart deflected to the left. Marked myocardial changes. After therapy (tropacin, novocain, papaverine, dibazol) there was no appreciable change in the patient's condition (some decrease in headaches). Nor were there substantial changes in condition of the cardiovascular system. Auscultation shows that arterial pressure indices are in the range of normal fluctuations (110/80-130/90 mm Hg), but tachyoscillography revealed elevation of mean and lateral pressure.

Arterial pressure indices after 3 weeks (mm Hg): M_n--92, M_y--106, N_w--126, M_x--132, Δp--34, HB--6. PWPV 700 cm/s in aorta, 1630 cm/s (on the right) and 1530 cm/s (left) in brachial-radial artery, 1130 cm/s (right) and 1200 cm/s (left) in femoral artery-dorsal artery of foot. SBV 7.6 mℓ. Actual MV 5% below proper level. Actual SPR 28% higher than due and 24% higher than working level. EKG: mild positive dynamics. Sinus rhythm, 44-50/min, $T_{I,II,III}$ is no mildly positive, T_{V_6} mildly biphasic, $T_{V_{2,3}}$ positive, $T_{V_{4-5}}$ less negative.

In this case, a woman, with 17-year tenure on a job involving contact with carbon disulfide, who began to work when the mill was started, when there was significant gas level, and who suffered repeated bouts of mild acute carbon disulfide poisoning, developed signs of chronic poisoning within 5 years. Thereafter, with continued contact with carbon disulfide, her illness gradually progressed and, at the time of our examination, was consistent with the symptom complex of toxic encephalopolyneuritis with signs of extrapyramidal and hypothalamic involvement. Marked changes in the nervous system were combined with cardiovascular disorders (hypertensive reactions, increased tonus of peripheral arteries, impaired bioelectric and contractile functions of the myocardium), which persisted even after treatment.

Even of the changes in the cardiovascular system, as well as nervous system, do not lead to cardiac or coronary insufficiency, they still play a significant part in some cases in the symptomatology of intoxication. For this reason, the set of therapeutic measures should include, along with therapy directed toward restoration of nervous system function, agents that are directed toward elimination or attenuation of cardiovascular disorders.

Of course, when making expert determination of patient fitness for work, one must take into consideration, in each specific case, the nature and severity of functional disturbances of the cardiovascular system.

Individuals, in whom poisoning is associated with neurocirculatory disorders (with great lability of arterial pressure, persistent hypotension or hypertension) and diffuse dystrophic changes in the myocardium, should be transferred to jobs involving no contact with carbon disulfide or other toxic agents. Individuals presenting cardiovascular disorders that are not occupational in nature, in whom carbon disulfide could aggravate the course of these disorders, should also be transferred to work unrelated to exposure to carbon disulfide.

In the light of the above material, and in view of the influence of carbon disulfide on the circulatory system with possibility of development of the neurocirculatory syndrome, essential hypertension and syndrome of myocardial dystrophy in the case of chronic exposure, it should be noted that, in identifying chronic carbon disulfide poisoning, the demonstrated changes in the cardiovascular system (neurocirculatory dystonia with hypotensive or hypertensive reactions, essential hypertension, myocardial dystrophy) should be included in interpretation of the diagnosis.

Clinical Characteristics and Condition of Cardiovascular System in the Presence of Lead Poisoning

Lead poisoning, which is the most common occupational disease, has been the subject of numerous clinical and experimental studies since ancient times. Most researchers and clinicians (I. G. Gel'man, 1928; L. A. Zorina, 1965; A. T. Aldanazarov, 1968; A. M. Rashevskaya, L. A. Zorina, 1968; N. S. Sorkina,

1971; Schmidt, 1929; Koelsch, 1935; Lawer, 1955; Ambrosio, Secchi, 1968, and others) believe that lead is a polytropic poison with, however, predominant effect on the blood, nervous system, digestive organs and porphyrin metabolism.

In the opinion of many researchers, typical blood changes are among the early manifestations of lead poisoning: decreased hemoglobin and erythrocytes, increased reticulocytes and erythrocytes with basophil granulation.

According to the clinicophysiological studies of E. A. Drogichina, L. A. Okhnyanskaya et al. (1952), functional changes in higher branches of the central nervous system are early symptoms of lead poisoning, clinically manifested by attenuation of cortical activity with development of the asthenic syndrome and disturbances of the autonomic nervous system. In the Soviet Union, because of improvement of working conditions, serious organic disorders of the nervous system (lead paralysis, encephalopathy) are no longer observed in the presence of such poisoning. Severe lead colic has also become a very rare form of intoxication.

Clinical and laboratory studies of recent years have shown that impairment of porphyrin metabolism is the earliest sign of the effects of lead on the body (Yu. P. Yevlashko, 1965; N. S. Sorkina, 1971).

In the patients we examined (10 women and 92 men mainly up to 40 years of age, working in the most hazardous occupations--furnace operators, stokers, battery chargers and lead sheet coaters, who are exposed to lead fumes and dust for long periods of time), the clinical findings referable to the chief complaints (painful extremities, general weakness and fatigability, headache, more or less intense abdominal pain, etc.), changes in the blood, porphyrin metabolism, nervous system, gastrointestinal tract and other organs are consistent with the typical, commonly described clinical symptoms of lead poisoning. Out of 102 patients, 63 were mild poisoning cases, 32 were moderate and 7 were severe.

Unlike the patients with carbon disulfide poisoning, the patients with lead poisoning presented considerably fewer complaints referable to the nervous system, in the presence of inhibition and low lability of autonomic reactions. The changes in the nervous system were characterized by mild signs of the asthenovegetative syndrome (21%), asthenia (12%), vegetovascular dysfunction (12%) and some mild symptoms of vegetosensory polyneuritis (31%). Although many patients (55%) complained of pain in the cardiac region, this was not the prime element of symptomatology, and in most cases (51%) was manifested in the form of periodically occurring unpleasant sensations, sharp or boring pain.

On the whole, lead poisoning differs from chronic carbon disulfide poisoning in that the course is more favorable, with a tendency toward significant reduction and disappearance of signs of intoxication after treatment and discontinuing contact with lead.

It has been long known, on the basis of experimental and clinical studies, that lead has a spastic action. K. Kharchenko (1929), B. A. Atchabarov (1960), Minden (1963), Holstein (1964) and others interpret spasm of the cutaneous vessels as one of the cardinal symptoms of poisoning, "lead coloring" (distinctive pale earth color of the integument). Such a marked syndrome of intoxication as lead colic is a crisis with abrupt onset associated with excitation of the autonomic nervous system and spastic-atonic state of the intestine (E. A. Drogichina, 1952, and others). The persistent headaches, transient amblyopia and convulsive seizures, which are observed at the height of a lead colic attack, are related by researchers to cerebrovascular spasm. Diminished diuresis in the presence of lead colic is also attributed to spasm of renal vessels (Minden, 1963, and others).

The spastic effect of lead can extend to the coronary vessels as well. Thus, A. M. Breytburg observed severe spasm of coronary vessels under the influence of lead in experiments on animals. Spuhler (1940) demonstrated distinct coronary changes on the EKG of a 44-year-old patient with lead colic, whose earlier EKG presented no pathological changes or rapid normalization after disappearance of signs of acute poisoning.

A. I. Knopov (1958), N. M. Konchalovskaya et al. (1965), M. M. Abayeva (1967), Salvini (1953) and others have observed marked cardiovascular crises associated with EKG changes (appearance of coronary T waves) in the presence of severe lead colic. With disappearance of signs of lead colic, these changes regressed and even reverted back to normal.

In one case, a patient 26 years of age, we observed considerable diffuse lowering of T wave during a marked attack of lead colic associated with elevation of arterial pressure, increased peripheral resistance and tonus of arteries of the extremities, and the former disappeared 2 days after the attack. These very transient changes, along with complaints of pressure pain in the heart, can apparently b e related to impaired coronary circulation due to cardiovascular spasm.

Observation of patients suffering from lead poisoning revealed that the main cardiovascular changes (Table 1) are quite similar to those associated with carbon disulfide poisoning. In a considerable number of cases, there was a statistically reliable ($p<0.001$) elevation of all forms of arterial pressure: M_x in 38%, N_w in 54%, M_y in 45% and M_x in 29% of the patients. Concurrent elevation of all parameters of arterial pressure was noted in 29%, whereas isolated (3%) elevation of mean pressure, or in combination with elevation of N_w, was demonstrated in 16% of the patients with normal M_x and M_n indices.

In the patients examined, no clearcut correlation was demonstrated between arterial pressure indices and age, or severity of poisoning, with the exception of the patients with lead colic, in the presence of which elevation of all parameters of arterial pressure was observed.

Although elevation of arterial pressure is observed quite often in the presence of lead poisoning, unlike the cases of carbon disulfide poisoning, this elevation is characterized by a benign course in most cases: minor elevation of arterial pressure without a tendency toward progressing and worsening of general condition.

At the same time, in the course of prolonged dynamic observation, even in lead poisoning cases, we observed patients in whom previously demonstrated hypertension progressed and changed to essential hypertension against a background of persistent or residual signs of poisoning.

Observations revealed that the mechanism of elevation of arterial pressure in the presence of lead poisoning, as was the case in chronic carbon disulfide poisoning and essential hypertension, is based on impairment of normal correlations between peripheral resistance and cardiac output. As in the case of carbon disulfide poisoning, peripheral resistance plays the main role in elevation of arterial pressure.

Out of 45 patients, only 15 presented elevation of mean dynamic arterial pressure due to high MV and the other 30, due to increased patency of precapillaries.

Table 4 lists data on studies of (100 subjects) and correlation between MV and SPR levels.

Table 4. Correlation between MV and SPR in patients with lead poisoning (100 patients examined)

SPR \ MV	Below due level (by 12-35%)	At due level (±10%)	Above due level (by 12-50%)
Below due levels (by 15-35%)	—	2	12
At due level (±10%)	2	10	24
Above due levels (by 15-116%)	19	30	1

While elevation of arterial pressure in the presence of lead colic is not questioned (A. I. Knopov, 1952; G. Z. Zakirov, 1961; G. I. Tarabayeva, 1961; G. R. Gemke, 1966; Teleky, 1937; Toppich, 1961; Gobbato, Chiesura, 1968, and others), there is substantial disagreement as to the state of arterial pressure in the presence of chronic lead poisoning. N. A. Vigdorchik (1934, 1938) demonstrated on extensive material that lengthy tenure on jobs involving contact with lead is instrumental in development of hypertension. Other researchers have also reported elevation of arterial pressure in

pat. .s suffering from lead poisoning in other than periods of colic (S. A. Kipiani, 1954; Barbaso, 1950; Crepet et al., 1956, and others).

G. F. Lang (1950), R. N. Vol'fovskaya et al. (1968, 1970) have also mentioned the role of lead poisoning in the etiology of essential hypertension. I. G. Gel'man (1925), V. A. Shtriter (1950), Ts. G. Masevich (1954) and others adhere to the opposite view; they demonstrated more a tendency toward lowering of arterial pressure with chronic exposure to lead.

In the presence of lead poisoning, as is the case with carbon disulfide poisoning, the effect of these agents on onset of the neurocirculatory syndrome and essential hypertension should be interpreted as a triggering mechanism, and the subsequent pathological process develops in the presence of some predisposing or secondary mechanisms.

In the opinion of some authors (Schmidt, 1929; Cumings, 1959; Morgan et al., 1966, and others), the primary targets of lead are vessels, mainly of small and medium caliber, as well as capillaries. After reaching the blood stream, lead has a direct effect on the tunica intima of vessels, inducing proliferative changes. In a number of cases, endothelial hyperplasia led to significant constriction of vascular lumen and impaired circulation in tissues and organs.

N. I. Grashchenkov (1933) in experiments on animals, Ye. Freyfel'd (1933), S. A. Peysakh and Kh. M. Kadyrbayeva (1960), who made pathomorphological studies of victims of lead encephalopathy and lead colic, observed in addition to proliferation of endothelium hypertrophy of the muscular tunic of vessels, spasm thereof and proliferation of connective tissue around the vessel with invasion of the media and calcification. Most researchers consider endarteritis and atherosclerosis of small and medium arteries to be typical signs of lead poisoning. These changes, in the presence of lead poisoning, are observed mainly in vessels of the central nervous system, heart and kidneys.

Determination of pulse wave propagation velocity and modulus of elasticity of elastic and muscular vessels is indicative of statistically reliable enhancement of elastoviscous state (tonus) of arterial vessels. PWPV in elastic vessels (C_e) in the segment of the carotid-femoral artery (aorta) was above normal in one-third of the patients (34%). No clearcut correlation was observed between the increase in PWPV in the aorta, severity of poisoning and age of patients. A comparison of the findings to roentgenological examination of the aorta and parameters of mean dynamic arterial pressure revealed that the increased tonus of the aorta was most often due to high arterial pressure, rather than atherosclerotic changes in the vascular wall.

PWPV in vessels of the musclar type, both in the segment of the brachial-radial artery and segment of femoral artery-dorsal artery of the food, was increased in most patients (70 and 62%, respectively).

A study of correlation between velocity and elasticity modulus of muscular and elastic vessels revealed elevation of C_m/C_e in 71% of the cases and of E_m/E_e in 69%. In some cases, the elasticity modulus of walls of elastic type arteries was higher than for muscular ones, which was the reason for a decline of E_m/E_e (under 1) in 10% of the patients.

The results of digital plethysmography are indicative of increased tonus of peripheral arteries of the fingers (in 33%) and toes (26.5%).

In half the cases, the indices of specific peripheral resistance (SPR) were 115% higher than proper levels, which is indicative of decreased patency of the precapillary system of these patients. A 74% higher actual SPR, as compared to the working level, is indicative of the fact that the decrease in precapillary patency is inconsistent with the minute volume.

The demonstrated increase in arterial tonus in the extremities, as in the case of carbon disulfide poisoning, was not of substantial significance to genesis of pain. The pain in the limbs of patients with lead poisoning was also closely related to signs of vegetative polyneuritis, which were observed just as often in patients with increased (33%) and normal (30%) tonus of extremital arteries.

As for endarteritis obliterans, development of which with lead poisoning was reported by a number of authors (I. G. Gel'man, S. B. Braun, O. N. Chel'tsova, N. I. Kukin, 1937; A. A. Khavtasi, 1961; Boron, 1956, and others), of all the individuals we examined, only one presented clinical signs of endarteritis obliterans or thrombangiitis of the lower limbs (pain in the legs with intermittent lameness, absence of pulse on dorsal arteries and weak pulse on the posterior tibial arteries).

Some investigators make a distinction, among obliterative (occlusive) diseases of peripheral arteries, between two independent diseases: 1) endarteritis obliterans (or thrombangiitis); 2) obliterative atherosclerosis; and they believe that these are different diseases in etiology and pathogenesis (R. F. Akulova, 1955; N. I. Krakovskiy, P. N. Mazayev, R. M. Akhrem-Akhremovich, 1970, and others). In the opinion of these authors, an allergic state is important in the pathogenesis of thrombangiitis obliterans, along with impairment of regulatory functions of the central nervous system and its autonomic branch. This refers to changes in reactivity of the vascular system in response to various nonspecific stimuli (frostbite, cooling, infection, etc.).

Other researchers (V. D. Tsinzerling, 1958, and others) reject the existence of endarteritis as an independent nosological form, and they believe that atherosclerosis, the development of which is preceded by anbioneurosis, is the basis of all obliterative arterial pathology. At any rate, these two diseases are clinically similar and it is difficult to make a differential diagnosis.

In the light of the submitted data and observed changes in patients with lead poisoning, associated with hyporeactivity of peripheral vessels (T. A. Masich, 1970) and increased tonus of arteries of the limbs, it can apparently be assumed that, in the presence of lead poisoning, there are factors for development of obliterative diseases of peripheral arteries.

The spastic effect of lead on vessels, under appropriate conditions, can apparently lead to organic changes also. It is known that vasospasms, which alter the physicochemical state of arterial walls, are instrumental in degeneration and sclerosis (A. L. Myasnikov, 1965; V. B. Il'inskiy, 1970, and others).

There were already indications of development of atherosclerosis with lead poisoning in the last century (Frank, 1875, and others). M. A. Kovnatskiy et al. (1964), Moeshlin (1953) and others have reported appearance of atherosclerotic changes in vessels of the brain, kidneys, heart, and peripheral vessels under the influence of lead.

Cumings (1959) attributes development of encephalopathy with lead poisoning to atherosclerotic involvement of cerebral arteries.

Studies have shown that, as in the case of carbon disulfide poisoning, the most frequent cause of cerebral hemodynamic disorders in patients with lead poisoning is hypotonia of cerebral arteries (60%) and especially veins (66%), which is more marked during the period of lead colic. Such a symptom of impaired cerebral circulation as headache is related to changes in tonus of cerebral vessels; however, unlike the cases of carbon disulfide poisoning, headaches are usually rare and mild, with no dominant role in the clinical symptoms of poisoning, with the exception of the patients with lead colic. In some cases, however, in the presence of plethysmographic indications of some decrease in tonus of cerebral arteries and veins, the clinical sign of inadequate tonus, i.e., headache, was absent in individuals with mild poisoning and some cases of moderate poisoning. Evidently, the changes in tonus of cerebral arteries and veins in these patients were compensated and were not clinically manifested in any way.

Histomorphological studies are also indicative of the effects of lead, not only on arterial but venous vessels. Ye. Freyfel'd (1933) observed venous stasis in a patient who had suffered from lead encephalopathy and colic. S. A. Peysakh and Kh. M. Kadyrbayeva (1960) reported on postmortem venous stasis in cerebral vessels in a patient who had expired during a bout of lead colic.

Complex clinicophysiological and biochemical studies of workers exposed to lead for a long period of time and patients with lead poisoning, which were pursued by M. A. Kovnatskiy et al. (1961, 1964) and V. A. Vasil'yeva et al. (1966, 1967) revealed changes in the terminal part of the ventricular complex (displacement of S-T interval, lowering or inversion of T wave) and impaired contractility of the myocardium, which were closely related to

severity of poisoning. The demonstrated EKG and BKG [ballistocardiographic] changes, along with clinical data, were evaluated by the authors in most cases as myocardial dystrophy. But in some cases, the nature of EKG changes and corresponding clinical manifestations were also indicative of impaired coronary circulation. The changes in the cardiovascular system were combined, in a considerable number of cases, with impaired cholesterol metabolism (elevated total cholesterol, unbound and loosely bound with proteins, and decline of phospholipid to cholesterol ratio). In view of the results of clinicophysiological and biochemical studies (G. S. Konikova, 1961), as well as data (L. K. Cherednichenko, 1962; G. N. Kuz'minskaya, 1964) indicative of the significant influence of lead on development of atherosclerotic processes in the aorta, vessels of the heart and kidneys in experimental cholesterol atherosclerosis, the authors believe that lead may be instrumental in development of atherosclerosis. In the patients with lead poisoning, like those with chronic carbon disulfide poisoning, we failed to demonstrate a clearcut link between blood cholesterol content, hemodynamic changes and state of the myocardium. Elevation of blood cholesterol level was observed equally often among patients with normal and high parameters of arterial pressure, peripheral resistance and PWPV. There is no agreement either as to the state of the myocardium when the body is exposed to lead. A. M. Rashevskaya and S. V. Levina (1952), who made an EKG study of a considerable group of workers exposed to lead for a long time, observed rather often sinus bradycardia (25%), changes in P wave, QRS complex, S-T interval and T wave. However, the observed changes (diffuse lowering of T waves) were evaluated as myocardial dystrophy in only 8% of the cases. The authors considered these EKG changes to be secondary, appearing as a result of the effect of lead on the autonomic nervous system. This is confirmed by data obtained in the oculocardiac test on patients with lead poisoning. In these cases, the authors observed a severe vagal effect, manifested by slowing of heart rate (by 12-52/min) to the extent of cardiac arrest (1 to 6 s) and first grade atrioventricular block.

Other researchers (A. A. Orlova, 1954; A. N. Akhmedshin, 1964; M. M. Abayeva et al., 1968; Kosmider, Petelenz, 1961; Myerson, Eisenhauer, 1964, and others) also obtained analogous EKG changes in individuals exposed to lead for a long time and patients with lead poisoning; they believe that the EKG changes under the influence of lead are mainly functional and attributable to changes in the autonomic nervous system.

Other authors (Read, Williams, 1952; Kline, 1960) interpret analogous changes (transient changes in rhythm, conduction and T wave), in patients with lead poisoning, as "lead myocarditis" and relate it to the direct effect of lead on the myocardium.

In an electrocardiographic examination (see Table 3) we observed a tendency toward sinus bradycardia in 42% of the patients, and its incidence was not distinctly related to severity of poisoning. Some patients presented periodic ventricular extrasystoly, slow atrioventricular conduction (0.21-0.23 s) and longer electric ventricular systole. There were mild changes in bioelectric activity of the myocardium. A decline or, much less

often, flattening of the T wave was observed in 25% of the patients, but only 15% presented disturbances which were evaluated, in conjunction with the clinical data, as myocardial dystrophy. Disturbances of rhythm and processes of myocardial repolarization were closely linked with such signs of poisoning as anemia and autonomic nervous system disturbances, and they did not aggravate appreciably the clinical course of intoxication. In most cases, these changes were transient and regressed or disappeared under the influence of treatment, with regression of signs of poisoning and improvement of general condition.

The above changes in the heart were never associated with signs of circulatory insufficiency. Decreased efficiency of systole, observed in 38% of the patients, was closely related to such hemodynamic disturbances as elevation of arterial pressure and increased peripheral resistance.

The findings of observations pursued over many years indicate that the changes in the circulatory system of patients with lead poisoning were usually transient and reversible, and they progressed less often to development of essential hypertension, unlike the patients with carbon disulfide poisoning. The most marked hemodynamic disorders associated with lead poisoning are observed during periods of lead colic which, as we know, is a sort of autonomic crisis.

The results of our studies warrant the belief that all of the observed cardiovascular changes in patients with lead poisoning are due to disturbances of neurovascular regulation as a result of involvement of the autonomic nervous system in the pathological process, and that they are related to development of anemia only in a few cases. Normalization of parameters of the functional state of the circulatory system after treatment serves as more evidence of the thesis that the changes in the cardiovascular system are among the symptoms of the chief complaint.

As an illustration of the foregoing, a discussion of the following case history is of considerable interest:

> Patient K., 26 years old, is employed at a battery plant. Since 1963, he worked as a mechanic-tinsmith for industrial ventilation and came in contact with lead periodically. For the last 3 months he worked as a lead sheet coater and was in constant contact with high concentrations of lead (up to 0.3-0.8 mg/m^3).
>
> He was brought to the clinic with an attack of lead colic. When admitted he complained of severe, paroxysmal pain in the abdomen associated with nausea, vomiting and constipation for 5 days, weakness, pain in the extremities and heart. He became sick 3 days ago, when boring pain, paroxysmal at times, appeared in the abdomen, with nausea and vomiting (he had had some vodka the previous day). Gradually the pain became worse, then continuous, and pain also appeared in the limbs

and pressure pain in the heart. He was referred to the surgical department because of severe abdominal pain, where lead colic was suspected. It was learned from his history that he had been troubled periodically with abdominal pain, general weakness heavy feeling in the chest and dyspnea upon walking for the last several months. In the past, he had had scarlet fever, dysentery and exudative pleurisy on the right. Objective examination: temperature 36.6-37.4°C, undernourished, pale, there is lead band on the gums. He is restless because of the severe abdominal pain. Asthenic. Pulse 86/min. Arterial pressure 150/90 mm Hg. Heart sounds are loud, systolic apical murmur. The tongue is coated (white). The abdomen is distended, tender in all regions, no symptoms of peritoneal irritation. Blood test: hemoglobin 82 g/ℓ (8.2 g%), erythrocytes $2.88 \cdot 10^6$/μℓ (2,880,000), color index 0.89, reticulocytes 86%, basophilic granular erythrocytes 350/10,000, leukocytes $11 \cdot 10^3$/μℓ (11,000), lymphocytes 9%, monocytes 7%, juvenile 1%, stab 41%, segmented 42%; erythrocyte sedimentation rate 11 mm/h. The urine is red, coproporphyrin content +++++ according to Reznik-Fedorov, lead in urine 18.0 mg/ℓ. Direct blood serum bilirubin 0.38 mg%. Protoporphyrin 440 mg%. Plasma iron 1.67 μg/ℓ, total iron 200 μg/ℓ. In urine δALK [expansion unknown] 63 μg/g creatinine, porphobilinogen 4.9 μg/g, coproporphyrin 1706 μg/ℓ. Tachyoscillographic study of arterial pressure (mm Hg): M_n--104, M_y--124, N_y--140, M_x--156, Δp--36, HB--16. PWPV 610 cm/s in aorta, 1800 sm/s in segment of brachial-radial artery, 1560 cm/s in femoral artery-dorsal artery of food. SBV 48.3 m^3, actual MV 6% higher than due level. Actual SPR 34% higher than due and 57% higher than working level. Plethysmography: a_{op} 29.4 mm^3, h_{op} 181.3 mm^3, a_{tp} 6.4 mm^3, h_{tp} 39.6 mm^3, a_{ppr} 3.20 mm^3, h_{ppr} 39.0 mm^3, a_{ppn} 1.21 mm^3, h_{ppn} 24.42 mm^3 [see Table 1 for key]. Venous pressure 150 mm water. Blood flow 14 s.

The EKG (Figure 1) shows sinus rhythm, 82-96/min, RQ = 0.12. QRS = 0.07 s, QRST 0.32 s (normal 0.30 s). $R_I > R_{III}$, $R_{V_3} > S_{V_3}$, $S\text{-}T_{II,avF}$ slightly dropped with concavity up, $S\text{-}T_{2-3}$ arched upward and changing to a sharp biphasic ±T. Normal location of electric axis of the heart. Diffuse myocardial changes. Systolic phase structure: Q = first sound 0.06 s, sphygmic phase 0.21 s (92% of proper level), pressure build-up phase 0.01 s, tension phase 0.07 s; KB 3.7; ISI 95.

Complexon therapy (intravenous infusion of 10% $CaNa_2$ EDTA solution, 20 mℓ , 1 course, and 5% pentacin solution, 20 mℓ 2 courses), administration of iron, vitamins (B_1, C, B_{12}) rapidly led to attenuation and, after 4 days, cessation of abdominal pain, and then to significant improvement of well-being. The patient regained strength, gained 5 kg, dyspnea disappeared, arterial pressure reverted to normal (120/70 mm Hg),

there was attenuation of changes in peripheral blood and porphyrin metabolism. Blood test after treatment: hemoglobin 118 g/ℓ (11.8 g%), erythrocytes $3.75 \cdot 10^6$/μℓ (3,750,000), color index 0.96. Reticulocytes 14%, basophil granular erythrocytes 23/10,000 erythrocytes. Coproporphyrin 551 μg/ℓ. Examination of the cardiovascular system showed normalization of its changes also: arterial pressure (mm Hg): M_n--70, M_y--96, N_w--110, M_x--124, Δp--40, HB--14. PWPV 520 cm/s in aorta, 1150 cm/s in brachial-radial artery, 980 cm/s in femoral-dorsal artery of food. SBV 64.6 mℓ, actual MV 18% above due level. Actual SPR is at due level. There was also normalization of the EKG (Figure 1).

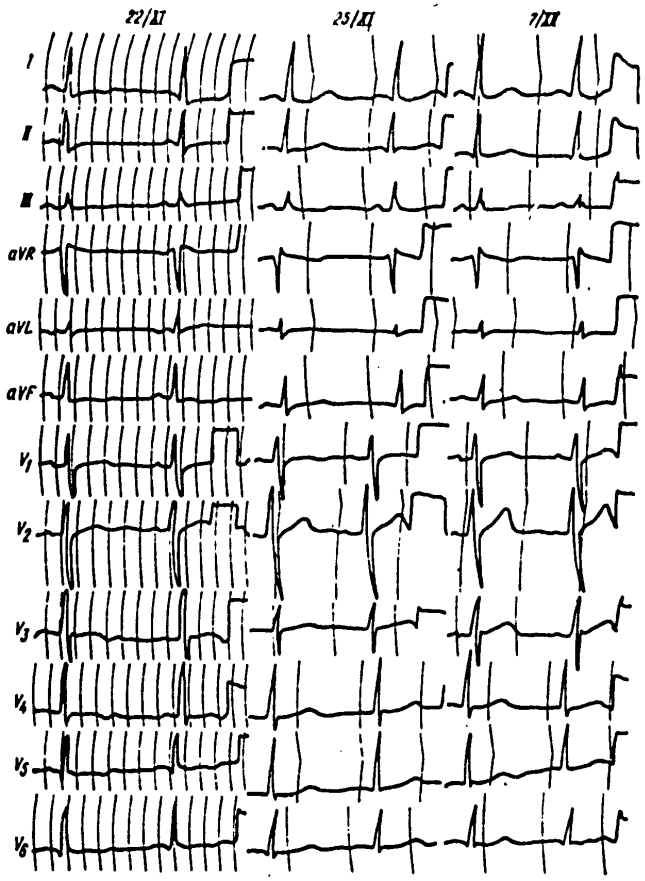


Figure 1. EKG of patient K. Explanation is given in text.

In this case, a young man who had relatively short tenure in work involving contact with lead developed severe lead poisoning with marked lead colic, anemic syndrome, impairment of porphyrin metabolism and changes in the cardiovascular system. The latter were characterized by arterial and venous hypertension, distinct increase in tonus of peripheral arteries with large and small caliber, arterioles and precapillaries (of the hands and feet), marked decrease in tonus of cerebral veins and arteries, diffuse changes in the myocardium. The rapid disappearance of the latter warrants relating them to disturbances of coronary circulation, apparently also due to spasm of cardiac vessels. With treatment, along with improvement in the patient's condition and regression of signs of intoxiation, there was also gradual normalization of changes in the circulatory system.

Patient B., 35 years old. Worked as furnace operator for 8 years at a nonferrous scrap metal plant; he came in contact with lead fumes and dust. When examined at the institute clinic, mild symptoms of lead poisoning were demonstrated (some elevation of reticulocytes to 27% and basophil granular erythrocytes to 62 per 10,000 erythrocytes), although the patient presented no complaints and did not consider himself sick. After 6 years, he began to notice fatigability, general weakness, pain in the hands and feet, unpleasant sensations in the epigastric region, tingling in the heart and palpitations.

When admitted to the clinic he was found to be undernourished, integument was pale. Heart souds were dull, mild systolic murmor over apex of the heart. Roentgenoscopy of the chest: some enlargement of the left ventricle and excited pulsation of the heart. Arterial pressure 130/80-120/70 mm Hg. No roentgenological signs of changes in respiratory organs and gastrointestinal tract. Eyegrounds: severe constriction of retinal arteries and veins. Blood test: hemoglobin 100 g/ℓ (10 g%), erythrocytes $3.73 \cdot 10^6$/μg (3,730,000), color index 0.81, reticulocytes 28%, basophilic granula erythrocytes 109/10,000 erythrocytes; leukocytes $4.3 \cdot 10^3$/μg (4300), lymphocytes 37%, monocytes 6%, eosinophils 1%, segmented 55%; erythrocyte sedimentation rate 5 mm/h. Blood serum direct bilirubin 0.4 mg%, total 0.75 mg%, cholesterol 225 mg%, lipoid phosphorus 6.5 mg%. Coproporphyrin in urine 50 μg/ℓ. Results of examination of cardiovascular system: arterial pressure (mm Hg): M_n--82, M_y--96, N_w--110, M_x--128, p--28, HB--18. PWPV 650 cm/s in aorta, 1150 cm/s on the right and 1040 cm/s on the left in brachial-radial artery, 1020 cm/s on the right and 1030 cm/s on the left in femoral-dorsal artery of foot. SBV 47.4 mℓ. Actual MV 30% less than due level; actual SPR 64% higher than proper level and 12% higher than working level. No EKG changes demonstrated. Sinus rhythm, 53-54/min. Normal position of electric axis.

Phase structure of systole: Q--first sound 0.06 s, sphygmic phase 0.25, pressure build-up phase 0.04 s, tension phase 0.10 s; KB 2.3; ISI 86%.

Rapid improvement of his condition and normalization of hematological indices after complexon therapy (3 courses of intravenous infusion of 10% $CaNa_2$ EDTA, 20 mℓ each) made it possible to diagnose mild lead poisoning, associated with changes in the blood and vascular disturbances (increased tonus of muscular type arteries and changes in retinal vessels).

The patient returned to his former job, but felt well only for a few months. He was soon troubled again by headaches, abdominal pain associated with constipation, intensification of pain in the hands and feet, general weakness and irritability.

When admitted to the clinic we observed pallor of the integument. Heart sounds were dull. Arterial pressure 105/60-135/80 mm Hg. Tenderness in the epigastric region and along the course of the intestine. Roentgenoscopy of the gastrointestinal tract revealed nonuniform haustration of the colon. Red, persistent dermographism. Hypesthesia of fingers and toes. Hands and feet are cold. Weak pulsation of dorsal arteries of the feet. Blood test: hemoglobin 94 g/ℓ (9.4 g%), erythrocytes $3.6 \cdot 10^6$/μℓ (3,600,000), color index 0.78, reticulocytes 46%, basophil granular erythrocytes 200/10,000 erythrocytes. Blood protoporphyrin 512.mg%, urine coproporphyrin 346 mg/day, lead content 0.4 mg/ℓ. Reexamination of the cardiovascular system showed progression of changes. Arterial pressure (mm Hg): M_n--80, M_y--106, N_w--114, M_x--130, Δp--34, HB--16, PWPV 710 cm/s in aorta, 1300 cm/s on the right and 1350 cm/s on the left in brachial-radial artery, 1100 cm/s in femoral-dorsal artery of food. SBV 53.1 mℓ; actual MV 19% less than proper level; SPR 52% above due level and 25% above working level.

This time, the demonstrated changes were evaluated as moderate lead poisoning associated with the anemic syndrome, impairment of prophyrin metabolism, mild signs of vegetative polyneuritis and vegetovascular (neurocirculatory) disorders. The latter were characterized by elevation of mean arterial pressure, increased tonus of muscular type arteries and impairment of normal correlations between peripheral resistance and cardiac output. Long-term treatment (3 courses of tetaksatsin and 2 courses of pentacin, iron products, vitamins B_6 and B_{12}) led to attenuation of symptoms of poisoning. The patient was transferred to a job not involving contact with lead, but his condition did not improve. He continued to complain of pain, coldness and numbness of the hands and feet, headache, sharp pain in the heart. When readmitted to the clinic,

disturbances of porphyrin metabolism (blood coproporphyrin 37.6 μg%, protoporphyrine 212.2 μg%, urine δALK 4.01 mg/g creatinine) and mild signs of vegetative polyneuritis were still present. Only a slight increase in basophil granular erythrocytes (72/10,000 erythrocytes) was found in the blood; there was progression of cardiovascular disorders. Arterial pressure in the range of 120/80 to 150/80 mm Hg. Results of tachyoscillography (mm Hg): M_n--94, M_y--112, N_w--136, M_x--144, Δp--42, HB--8, PWPV 920 cm/s in aorta, 1730 cm/s on the right and 1700 cm/s on the left in radial-brachial artery, 1180 cm/s on the right and 1120 cm/s on the left in femoral-dorsal artery of foot; SBV 56.0 mℓ; actual MV 26% below due level; actual SPR 77% above proper level and 31% above working level. Plethysmography: a_{op}--20.0 mm^3, h_{op}--260.0 mm^3, a_{tp}--7.20 mm^3, h_{tp}--72.0 mm^3, a_{ppr}--8.0 mm^3, h_{ppr}--80.0 mm^3, a_{ppn}--1.98 mm^3, h_{ppn}--9.9 mm^3. Venous pressure 110 mm water. Blood flow rate 16 s. EKG: sinus rhythm, 60-64/min. $R_I<R_{II}>R_{III}$, $R_{V_4}>S_{V_4}$, S-T_{III} interval slightly dropped; $T_{III,avF}$ low, T_{avl} mildly biphasic, $T_{V_{2-4}}$ high, with sharp apices. Systolic phase structure: Q--first sound 0.07 s, pressure build-up phase 0.05 s, tension phase 0.12 s, sphygmic phase 0.22 s; KB 2.4, ISI 81.

Work involving contact with lead was contraindicated due to progression of changes in the cardiovascular system (elevation of all parameters of arterial pressure, increased tonus of muscular and elastic types of arteries, decreased tonus of cerebral arteries and veins, significant decline of intra-systolic index--ISI). In spite of the lack of contact with lead, the patient's condition did not improve. On the contrary, there was intensification of headaches and sharp pain in the heart, appearance of dyspnea. When next admitted to the clinic after 3 years, no changes in the blood were demonstrated, and vegetovascular disorders were prominent. Arterial pressure was in the range of 125/80 to 160/105 mm Hg, and it was elevated more often. Examination of eyegrounds revealed constricted retinal arteries, nonuniform caliber, wide veins (retinal angiopathy). Tachyoscillography of arterial pressure: M_n--94, M_y--120, N_w--144, M_x--158, Δp--50, HB--14. PWPV 880 cm/s in aorta, 1320 and 1250 cm/s in brachial-radial artery, 1160 and 1120 cm/s in femoral-dorsal artery of food; SBV 93.0 mℓ; actual MV 27% above due level; SPR 12% above proper level and 42% above working level.

In this case, after 5 years of working in contact with lead and feeling well, the patient first presented mild signs of lead poisoning (changes in blood) that disappeared rapidly after treatment. Five to six years later, intoxication symptoms recurred, with changes in blood, porphyrin metabolism

and minor vegetovascular disturbances that reverted to normal after treatment; but after resuming contact with lead they rapidly reappeared, and after 1 year progressed with development of the anemic syndrome and progression of vegetovascular disturbances. In subsequent years, in spite of the lack of contact with lead and significant reduction of blood changes, prominent in the clinical signs of intoxication were vegetovascular disorders, the onset of which coincided with the period of the most marked hematological changes. Finally, as a result of prolonged vegetovascular disturbances, there was development of essential hypertension which determined the subsequent course of illness.

In view of the possibility of development of essential hypertension, questions of expert certification of fitness of patients with lead poisoning should be answered on an individual basis, with due consideration of the nature and severity of cardiovascular disturbances. Patients, in whom poisoning is associated with vegetovascular disturbances and persistent hypertension, regardless of severity of poisoning, should be transferred to work that does not involve contact with lead. In the case of lead poisoning, as is also the case in carbon disulfide poisoning, the demonstrated cardiovascular disorders must be included in interpretation of the diagnosis.

The differences in functional state of the cardiovascular system that one demonstrates in the presence of carbon disulfide and lead poisoning are apparently a manifestation of distinctions in the course of nervous processes in the presence of this pathology.

It should be noted that we failed to obtain data from comprehensive clinical and physiological examinations indicative of clinical signs of atherosclerosis of vessels of the brain, heart or other regions, either in the presence of lead poisoning or carbon disulfide poisoning. Nevertheless, the nature of the demonstrated changes is indicative of a very likely possibility of development of atherosclerosis in such poisoning cases. It is a known fact that such changes as hypertension, increased arterial tonus and impairment of lipid metabolism are "risk" factors instrumental in development of atherosclerosis (A. L. Myasnikov, 1965; B. V. Il'inskiy, 1970; I. A. Ryvkin, 1971, and others). While we admit there is a possibility of development of atherosclerotic vascular lesions in the presence of lead and carbon disulfide poisoning, we do not believe that any atherosclerotic process, or essential hypertension, in individuals working with lead or carbon disulfide should necessarily be tied in with the effects of these agents. One must take into consideration the clinical course, order of development of pathological processes and, of course, the leading role of the "specific" symptom complex inherent in a given type of poisoning.

Clinical Characteristics and State of the Cardiovascular System in the Presence of Chronic Benzene Poisoning

There are many works dealing with the effects of benzene on the body (P. Mytnik, 1934; S. M. Gusman, 1952; L. M. Omel'yanenko, 1953; L. A. Zorina,

1958, 1971; I. S. Gusev, 1966; Penatik Vigliani, 1938; Holstein, 1953; Merker, 1962; Richard, DeGowin, 1963, and others). Most researchers believe that benzene, which is an agent with systemic polytropic toxic action, strikes mainly the hemopoietic and nervous systems. Acute benzene poisoning is characterized by a narcotic effect with prevalence in the clinical signs of changes in the central nervous system. Changes related to involvement of hemopoietic function of bone marrow are the main and decisive clinical signs of chronic benzene poisoning. Benzene, which is toxic to hemopoietic tissue, can have a depressive and irritant effect on hemopoietic tissue, depending on dosage and individual distinctions of the organism as a whole and the hemopoietic system in particular. This could cause development of aplastic anemia or leukemia. In addition to changes in hemopoietic organs, in cases of chronic benzene poisoning one observes functional disturbances of the nervous system, in the nature of asthenic, asthenovegetative or asthenoneurotic reactions and vegetosensory polyneuritis.

There are very sparse data in the literature concerning the state of the cardiovascular system as related to chronic exposure to benzene. There are only a few experimental and clinical observations referable to changes in the heart and arterial pressure.

In the patients surveyed (258 women--86% and 42 men--14%, up to 40 years of age--55% and older--45%), the principal symptoms of chronic benzene poisoning were hematological changes (leukopenia, thrombocytopenia and anemia). Along with blood changes, there were rather frequent functional disorders of the nervous system in the form of the asthenovegetative syndrome and asthenia. The course was qualified as mild poisoning in 133 cases, moderate in 117 and severe in 50 (which included the 22 cases of leukemia). There was prevalence, in the clinical signs, of complaints of headache (not infrequently associated with vertigo), general weakness, bleeding (nosebleeds, bleeding gums, appearance of spontaneous bruises on the skin, longer menstrual cycle) which progressed with progression of intoxication. Although pain in the cardiac region was observed rather often (33%), it was not intense and usually in the nature of tingling or aching. Complaints of dyspnea (22%) and palpitations (18%) were closely related to severity of poisoning. Objectively, dull heart sounds and a systolic murmur were ausculted in a rather large number of cases (49%), and this was encountered equally often in different age groups, but most marked and most frequent in cases of severe poisoning. A venous hum was present in severe poisoning cases. The functional disturbances of the cardiovascular system of patients with benzene poisoning (Table 1) differed from the changes observed with lead and carbon disulfide poisoning. Opinions vary as to arterial pressure level in the presence of chronic benzene poisoning. Most researchers (P. Mytnik, 1934; M. E. Efendiyev, G. I. Amiroslanova, 1961; P. S. Kozlov, Yu. R. Tedder, 1965; Lande, and others) report a tendency toward decline thereof. V. A. Shtriter (1954), who analyzed arterial pressure indices in a large group of workers exposed to various occupational factors, reports that the incidence of hypotension is somewhat higher in individuals coming in contact with benzene than in a control group (10.8% and 9,9%,

respectively). However, in the group of individuals with signs of chronic benzene poisoning, the incidence of hypotension rises to 30.5%. According to another point of view, chronic exposure to benzene does not affect arterial pressure (E. M. Volovik, A. G. Ivanova and I. L. Miropol'skaya, 1957). The proponents of a third point of view believe that there is a tendency toward elevation of arterial pressure with chronic exposure to benzene (Z. E. Grigor'yev, 1956; Heim et al., 1924, and others).

Other investigations indicate that the parameters of all forms of arterial pressure fluctuate within the normal range in most patients. M_x was low in 20.4% of the patients and M_n, in 32.7%. The incidence of decline of arterial pressure indices is distinctly related, with statistical reliability ($p<0.001$) to severity of poisoning and hematological disturbances. Thus, such arterial pressure parameters are found in 7.5% for M_x and 21.8% for M_n in mild poisoning cases, 26.4 and 38.4%, respectively, in moderate cases, 40 and 48% of the patients in severe cases. There was reliably more frequent drop of arterial pressure in the presence of leukemia (M_x and M_n in 50%) and marked anemia (M_x--31%, M_n--41%), than in patients with moderate signs of anemia and without it (M --14.5%, M --29%). Some elevation of some forms of arterial pressure is observed in isolated cases, usually in patients over 45-50 years of age or those who had been given hormone therapy.

In view of the close link between arterial pressure parameters and blood changes, and first of all signs of anemia, as also confirmed by the results of dynamic observations indicative of normalization of arterial pressure with reduction and disappearance of signs of anemia, the hypotension associated with benzene poisoning should apparently be considered symptomatic.

Unlike the cases of lead and carbon disulfide poisoning, in the presence of benzene poisoning there is usually no change in tonus of elastic and muscular arterial vessels. Tonus of intracranial arteries was normal in only 25% of the subjects, in some cases it was increased, and in over half the patients (60%) it was decreased with statistical significance ($p<0.001$). While the incidence of arterial hypotonia in the brain does not present a clearcut relationship to severity of poisoning, in the group of patients with moderate and severe forms of poisoning it reaches higher levels and is closely linked to severity of anemia. Evidently, decreased tonus of cerebral arteries in the presence of anemia should not be considered solely a pathological phenomenon. In the presence of anemia, cerebral artery hypotonia may be also evaluated as a compensatory reaction, a "physiological defense measure," that prevents hypoxia of cerebral tissues. Increased tonus of external cranial arteries, observed in half the cases, can probably also be interpreted as an adaptive reaction to increase circulation in the system of the internal carotid.

A high level of influx of blood to the brain should also be associated with increased efflux, which could be provided by a higher tonus of cerebral veins. However, it was found to be low in most cases (67.8%). Hypotonia of cerebral veins is observed equally often with all grades of poisoning, but

it was the most marked (h_{op} 160 to 280 mm) with severe and moderate poisoning. Evidently, the decreased tonus of cerebral veins and arteries is the chief cause of heaches with elements of venous stasis, so often observed among the surveyed patients (75%).

The distinctive feature of the circulatory system in the presence of benzene poisoning is a tendency toward increased cardiac output (SBV and MV). SBV was high in 25% of the cases and MV was above proper levels (by 15-90%) in 74%. Maximum increase (over 30%) was observed in cases of severe and moderate poisoning. Cardiac output is determined by the body's oxygen requirement. For this reason, depending on conditions of vital functions, cardiac output changes over a wide range. The changes in cardiac output are adaptive and provide for the different requirements as to access of blood to all organs and tissues. This requirement is determined by many factors and, first of all, the condition of circulation. It is known that, in the presence of anemic states, the decreased transport function of blood is compensated by an increase in MV. According to the data of Stead et al. (1948), MV begins to increase when hemoglobin drops below 75 g/ℓ (7.5 g%); according to the data of V. I. Kuznetsov (1952), this happens when it drops below 122 g/ℓ (12.2 g%). However, there is no direct correlation between MV increment and degree of decrease in oxygenation of blood. Our data revealed that, in the vast majority of cases (55%), concurrently with increase of MV there was a decrease in peripheral resistance, i.e., increased patency of the precapillary system, which apparently is instrumental in increasing the percentage of oxygen uptake by tissues. The increase in MV in patients with benzene poisoning is a manifestation of intensified cardiac function in response to decreased oxygenation of blood, since it is believed that MV is the main regulated parameter in the body that characterizes the repose of the circulatory system to oxygen demand.

We believe that such changes in the circulatory system as increase in MV, increased patency of the precapillary system, faster blood flow, are compensatory in nature, since they are instrumental in supplying oxygen to tissues.

In the opinion of a number of researchers, the cardiac changes in the presence of chronic benzene poisoning are characterized by rather frequent complaints of diverse types of pain in the heart, palpitation and dyspnea, physical deviations in the form of widening of boundaries of the heart, dull sounds and presence of systolic murmur (P. Mytnik, 1934; N. S. Shubina, F. I. Midtsev, 1939; M. E. Efendiyev, G. I. Amiraslanova, 1961, and others). S. D. Reyzel'man (1935) found muffled and dull heart sounds in 45.2% of the cases in a routine examination of workers in the coal-tar chemical industry. These findings are evaluated as diseases of the myocardium (myocarditis, myocardiopathy, cardiosclerosis) and related to exposure to benzene. Electrocardiographic and roentgenokymographic studies of 57 patients with chronic benzene poisoning led L. N. Khizhnyakova (1962, 1964) to demonstrate slowing of atrioventricular and ventricular conduction shift of S-T interval, drop of T wave and changes in roentgenokymograms of the heart (pulsation and attenuation type changes) indicative of functional impairment of the

myocardium. These electrocardiographic and roentgenokymographic changes, with consideration of complaints and clinical manifestations, were evaluated as myocardial dystrophy in 39.4% of the cases. The author attributes the latter to the toxic effect of benzene on the myocardium. Cacurri (1948) relates the bradycardia, extrasystole and electrocardiographic changes in animal experiments to the direct effect of benzene on the myocardium and only partially to its effect on the autonomic nervous system. Other authors, however, believe that functional cardiac disturbances with marked EKG changes in the presence of chronic benzene poisoning are the secondary effects of development of anemia and panmyelophthisis (Buchner, 1939; Koelsch, 1936; H. Otto, 1953). In such cases, pathoanatomical examination revealed effusions of blood, fatty degeneration and embolisms in the myocardium.

In our EKG studies (see Table 3), most patients presented changes in T wave (drop, flattening, inversion). This myocardial changes, along with the clinical data, were consistent with the concept of myocardial dystrophy in 45.5% of the cases. The latter was unrelated to the patients' age (45% up to 40 years old and 50% over 40), but was reliable related to severity of intoxication and, primarily, of anemia. With moderate and severe poisoning, myocardial dystrophy was demonstrated in 60% of the patients and with mild poisoning, in 25.6%. While myocardial dystrophy associated with carbon disulfide and lead poisoning is related chiefly to disturbances of regulatory function of the autonomic nervous system, in the case of benzene poisoning its development is due to inadequate delivery of blood to the heart as a result of hypoxia. The observed decrease in efficiency of systole (33%) in most cases could be attributed to some impairment of myocardial contractility.

The results of many years of observations are indicative of the benign course of benzene poisoning. After treatment and discontinuation of contact with benzene, not only regression of signs of poisoning, but total recovery are possible.

The link between changes in bioelectric activity of the myocardium and anemia was also confirmed by the results of long-term observations. It was observed that, along with attenuation and disappearance of signs of intoxication (with high hemoglobin level), there was attenuation and disappearance of EKG signs of myocardial dystrophy. In cases of severe poisoning, progressive diffuse changes in the myocardium were noted with progression of anemia. The development of myocardial dystrophy in the presence of anemic states is related to metabolic disturbances in the myocardium resulting from hypoxia (G. F. Lang, 1954, and others).

There is information in the literature to the effect that attacks of angina pectoris and EKG signs of coronary insufficiency may be observed in the presence of severe anemia, as a result of severely marked myocardial hypoxia (G. S. Ayzen, 1942; Buchner, 1939, and others). Among the patients we examined, with chronic benzene poisoning, one patient with severe

poisoning presented anginal pain in the heart, along with decline of hemoglobin to 40-28 g/ℓ (4-2.8 g%) and worsening of EKG.

As an illustration of the foregoing thesis, we can submit the EKG of a patient who was under observation at the institute clinic due to chronic benzene poisoning.

Patient F., 48 years old, worked in contact with benzene and other solvents for 7 years. After 5 years she began to notice general weakness, rapid fatigability, headaches, dyspnea when walking, sharp pain in the heart. After 1 year, in a routine physical, blood changes were found for the first time (anemia, leukopenia and thrombocytopenia). Examination at the institute clinic revealed severe pallor of the integument and mucous membranes, and positive "pinch" symptom. Heart margins are in the normal range, sounds are clear, somewhat muffled, arterial pressure 120/60 mm Hg. Pancytopenia was found in peripheral blood: hemoglobin 101 g/ℓ (10.1 g%), erythrocytes $2.83 \cdot 10^6$/μℓ (2,830,000), reticulocytes 19%, leukocytes $3.4 \cdot 10^3$/μℓ (3400), lymphocytes 53%, monocytes 11%, eosinophils 0, stab 11%, segmented 25%; erythrocyte sedimentation rate 22 mm/h. Thrombocytes $8 \cdot 10^4$/μℓ (80,000), bleeding time 10 min. EKG (Figure 2) without particular changes. Sinus rhythm, 66/min. Horizontal electric axis.

Moderate grade of benzene poisoning was diagnosed. Therapy did not improve the hematological parameters and the patient's condition remained unchanged for the next 3-4 years. Three years later, when the patient was hospitalized, she reported more marked general weakness, dyspnea and cardiac pain. There was some widening of heart boundaries and a systolic murmur at all points. Arterial pressure 100/60 mm Hg. Blood test: hemoglobin 96 g/ℓ (9.6 g%), erythrocytes $2.6 \cdot 10^6$/μℓ (2,600,000), reticulocytes 13%, thrombocytes $7.6 \cdot 10^4$/μℓ (76,000), leukocytes $3 \cdot 10^3$/μℓ (3000), lymphocytes 58%, monocytes 11%, eosinophils 1%, stab 1%, segmented 26%. EKG (Figure 2) showed faster rhythm (85/min) and appearance of moderate myocardial changes with predominant localization in the left chest leads (lowering of $T_{I,II}$, $V_{3,4,5,6}$). The patient developed a hemolytic crisis soon after overcooling.

Thereafter, there were rather frequent hemolytic crises due to various factors (cooling, drugs) and they led to progressive hematological changes [periodic drop of hemoglobin to 28 g/ℓ (2.8 g%), erythrocytes to $1.05 \cdot 10^6$/μℓ (1,050,000), leukocytes to $1.15 \cdot 10^3$/μℓ (1150), with marked granulocytopenia (18%) and lymphocytosis (74%), thrombocytes to $4.4 \cdot 10^4$/μℓ (44,000)] and deterioration of the patient's wellbeing and condition (severe weakness, vertigo, dyspnea, pressure pain in the heart). There was worsening of EKG indices with progression of illness

and anemia. When the patient was readmitted to the clinic, the hemogram indices were low: hemoglobin 42 g/ℓ (4.2 g%), erythrocytes $1.98 \cdot 10^6/\mu\ell$ (1,980,000), thrombocytes $9.944 \cdot 10^4/\mu\ell$ (99,440), reticulocytes 45%, leukocytes $1.7 \cdot 10^3/\mu\ell$ (1700), lymphocytes 68%, monocytes 1%, basophils 3%, stab 4%, segmented 25%; erythrocyte sedimentation rate 55 mm/h.

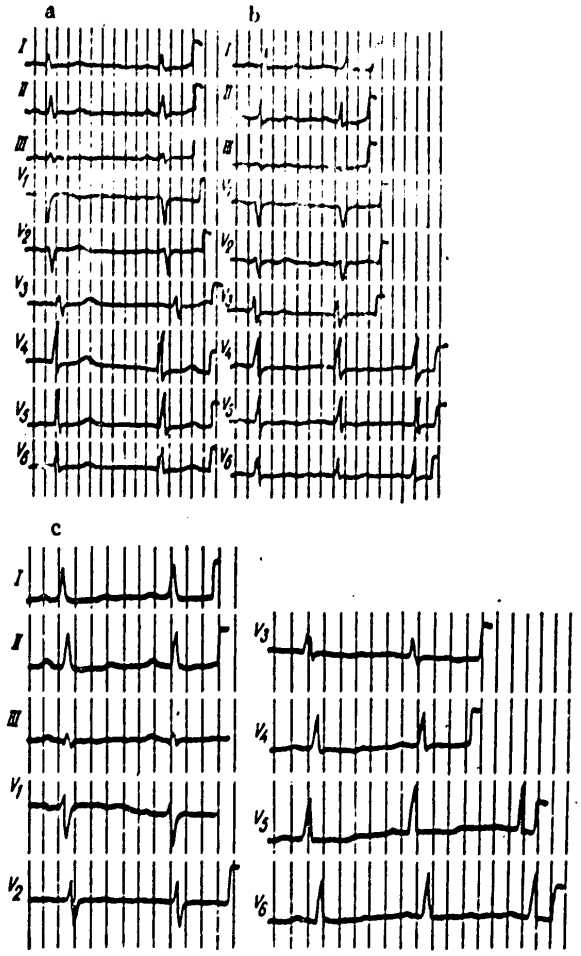


Figure 2. EKG of patient F.

a) at start of illness b) 2 years later c) 6 years later

On the EKG there was a sharp drop of T wave in standard and right chest leads, while V_{3-6} became negative in the left chest leads.

In view of the fact that the circulatory system is one of the chief mechanisms of compensation of hypoxia in the presence of anemic states, it must be conceded that diseases of the cardiovascular system are also a contraindication for work involving contact with benzene as well as a deterrent to continuing work with such contact.

Thus, the clinicophysiological studies of functional state of the cardiovascular system in the presence of three different occupational diseases are indicative of circulatory disturbances, which are, on the whole, in the nature of vegetovascular dysfunction (neurocirculatory syndrome) and myocardial dystrophy. They are not specific for any particular type of poisoning, since analogous cardiovascular changes are observed under the influence of other occupational factors, for example, with exposure to industrial noise and vibration, ionizing radiation, as well as other substances. At the same time, with each of the intoxications studied, we detect some distinctive features and uniqueness of changes in the circulatory system, the nature and severity of which are related to severity of the chief pathological process, determined by the predominant area of application of the deleterious factor and initial condition of the organism. Cardiovascular disturbances, which appear at the early stages of poisoning referable to some toxic agent or other, sometimes become the prime symptoms that determine the clinical course of intoxication.

CHAPTER 4. THE CARDIOVASCULAR SYSTEM AS RELATED TO EXPOSURE TO OCCUPATIONAL RADIATION

[Text] The reactions of the cardiovascular system are an inseperable part of the body's general response to radiation as one of many environmental stimuli, and they can also reflect the direct effects of injuries to structures that constitute the anatomical substrate of the cardiovascular system. There are a number of works dealing with investigation of the cardiovascular system with exposure to ionizing radiation; they summarize numerous investigations on animals in acute and chronic experiments, information about reactions of the cardiovascular system in the course of radiation therapy of various parts of the body, data on the state of cardiovascular function in individuals exposed to large doses of radiation and suffering from acute radiation sickness. There are relatively few works dealing with the cardiovascular system as related to long-term exposure to low doses of occupational radiation.

The biological effects of radiation on organs and tissues depend, first of all, on the magnitude of absorbed energy, its distribution in the body and time. A distinction is made of the more specific effect of radiation on the body, its direct deleterious effect on cell reproduction, associated with a change in the process of DNA synthesis. The nonspecific reaction to radiation is another biological mechanism, a response to an adequate stimulus of several systems with the property of excitability, reactivity. Interaction between these two classes of reactions is determined both by the characteristics of absorbed energy and distinctions referable to structure and radiosensitivity of tissues or organs.

The cardiovascular system is morphologically and functionally heterogeneous, and this also applies to the effects on it of ionizing radiation. As shown

In numerous studies, one should single out the reactions of the myocardium, great vessels, neuroregulatory mechanisms of cardiac function, capillaries, vascular endothelium and systemic hemodynamics. The myocardium is more radioresistant that capillaries or vascular endothelium which are highly sensitive to radiation. Myocardial changes also occur secondarily, as a result of disturbances in vessels that nourish the myocardium.

In addition to radiation dose (which could have a deleterious effect or elicit only functional stimulation with submicroscopic changes), the area exposed to radiation is important to reactions of the cardiovascular system to ionizing radiation. A distinction is made between total-body radiation and local exposure of a specific region: the immediate region of the heart, great vessels and reflexogenic vascular regions.

Numerous experimental studies have demonstrated the correlation between dosage and nature of radiation. Studies were made on different animal species of the condition of the heart, cardiac function systemic hemodynamics and local circulation, as well as reactivity of the cardiovascular system. Morphological changes in the heart were the most marked at the early stage following total-body and local exposure to radiation in doses exceeding 1000 rem. They consisted of appearance of stromal edema, perivascular infiltration, plethora, dystrophic and degenerative changes in the myocardium, as well as in nerve ganglia and fibers of the conduction system (N. A. Krayevskiy, 1954; O. V. Mikhaylova, 1964; B. M. Ariel', 1965; Ye. I. Vorob'yev, 1965-1973; Ye. F. Lushnikov et al., 1970, and others). At the late term, animals developed marked sclerotic changes in coronary vessels and the heart, leading to a reduction in weight of the heart. Somewhat less severe changes were present after exposure to doses of 500-600 rem, but their nature and outcome were the same. Along with vascular changes, dystrophy, fibrosis, hyalin and fatty degeneration of muscle fibers with necrosis thereof, signs of focal infarction, degeneration of nervous plexi and vascular receptors were observed (P. D. Gorizontov, 1960; O. V. Mikhaylova, 1964; L. L. Aver'yanova, 1967; I. A. Oyvin et al., 1971, 1972, and others). Most authors believe that lesions to blood vessels are the first to appear under the influence of radiation; they lead to dystrophic changes in muscle fibers, innervation system of the heart, autonomic neural pathways and conduction system of the heart. Myocardial circulatory disorders precede the changes in muscle fibers.

Along with structural changes in the heart, functional disturbances of the heart, systemic and local hemodynamics have been described with exposure both to total-body and local radiation of the cardiac region in high doses. It was demonstrated that there are phasic changes in arterial pressure and pulse rate corresponding to the phases of the acute radiation syndrome: tachycardia followed by bradycardia, transient hypertension followed by hypotension with drop of both diastolic and systolic pressure, decreased vascular tonus, slower blood flow and elevation of venous pressure (Ye. I. Vorob'yev, 1968; L. A. Yakovleva, 1972, and others).

The EKG changes are characterized by persistent decline of wave voltage, shifting of S-T interval and occasional appearance of atrioventricular block. The EKG changes are more marked with local irradiation of the cardiac region than with exposure of other parts of the body. Increased vascular permeability has also been noted. Changes in local circulation have been described at the early stages: significant dilatation of mesentery arteries, plethora of vessels in the pulmonary circulation or dystonia thereof, phasic changes in cerebral vessels, impairment of peripheral circulation in cutaneous vessels, dilatation, dystonia of vessels of the hands.

Investigation of sensitivity to various agents (chemical drugs, epinephrine, acetylcholine, low doses of radioactive substances and others) revealed that there were changes in cardiovascular reactions in some cases, and this was attributed to trophic changes in the myocardium and in the system of interoceptive analyzers (S. B. Daniyarov, 1953; N. A. Kurshakov, P. M. Kireyev, 1963, 1968; Sh. S. Melik-Israyelyan, 1969, and others). The experimental studies are corroborated by clinical findings.

The first information about acute radiation sickness in man appeared after 1945, when atomic bombs were dropped on the Japanese cities of Hiroshima and Nagasaki. With explosion of an atom bomb, there are other deleterious factors involved, in addition to radiation: shock wave which induces numerous traumatic lesions and luminous radiation that induces burns, i.e., there are combined lesions in a number of cases, and they have not been adequately followed up at that. More accurate ideas about changes in the cardiovascular system with exposure to acute radiation were obtained from studies of accidents. In the literature, there is a description of about 100 cases, including 26 in the USSR (N. A. Kurshakov et al., 1966; A. K. Gus'kova, G. D. Baysogolov, 1955-1971; A. I. Vorob'yev et al., 1973-1975; I. S. Glazunov et al., 1974; L. Gempel'man, G. Lisko, D. Gofman, 1954; Andrews, Balish, Edwards et al., 1969, and others). The dose levels ranged from a few dozen roentgens, which was not associated with formation of acute radiation sickness, to several hundred roentgens with severe lesions ending with death. Cardiovascular changes appeared early in the case of radiation doses of the order of 300-1000 rem. They consisted of tachycardia, drop of arterial pressure, appearance of apical systolic murmur, muffled heart sounds. As early as the 2d day of illness, the EKG presented signs of diffuse myocardial changes with slow intraventricular conduction, reduction of S-T interval, T wave and voltage in all leads. There were circulatory disturbances in the system of cerebral vessels, with appearance of transient focal neurological symptoms, decreased vascular tonus and oscillatory index. More marked cardiac changes were observed in the case of nonuniform radiation with a maximum dosage delivered to the region of the heart.

A. K. Guz'kova and G. D. Baysogolov (1971), in a summary of their clinical findings, described systemic hemodynamics in the presence of acute radiation sickness as follows: Already at the early stage of acute radiation sickness, there was appearance of changes in cardiovascular function related to impairment of neurovascular regulation. They are manifested by lability of

the pulse, especially when subject to loads, changes in arterial pressure with a tendency toward hypotension, lability of cutaneous vasomotors with excessive moistness of palms and feet, appearance of dyspnea, diminished vascular tonus and peripheral circulatory disorders.

With moderate and especially severe grade of sickness, hemorrhagic manifestations are observed, which reach a maximum in the 3d-4th week of illness. Changes appear on the EKG, which are first indicative of disorders referable to regulation of cardiac function and, later on, of signs of dystrophic myocardial changes with impaired conduction and contractility.

Early changes in cardiac function and vessels of a functional nature are due to impaired regulation, as proved by the reversibility of these changes, good restoration upon recovering from acute radiation sickness. A. V. Barabanova and A. K. Gus'kova (1964) describe one case, patient M., seen 10 years after he suffered acute radiation sickness as a result of an accident on the job. It was estimated that he was exposed to about 300 rem total-body gamma and neutron radiation. The clinical signs were typical for moderate grade of acute radiation sickness. The patient was essentially healthy and fit for work for all 10 subsequent years. A comprehensive clinical and physiological examination revealed only mild functional changes in the cardiovascular system in the form of asymmetric arterial pressure, lability and asymmetry of the oscillatory index, tendency toward tachycardia. No deviations from normal were demonstrable on the EKG, BKG [ballistocardiogram] and PKG [phonocardiogram]. In this case, the outcome of acute radiation sickness was a clinical recovery. Such a possibility is also confirmed by other authors (N. A. Kurshakov et al., 1966, and others). It is observed that the recovery period may end by the end of the first postradiation year, although some regulatory changes may persist for a longer time, depending on the radiation dose and severity of acute radiation sickness. In view of the direct deleterious effect of radiation, which induces changes in other organs and systems, basal metabolism and trophic disorders, clinical symptoms may also be present at a later time, and they are indicative of prior myocardial hypoxia with incomplete restoration. The initial state of organs and systems, including the heart and vessels, is significant to degree of recovery.

The numerous publications pertaining to the state of the cardiovascular system of patients exposed to radiation therapy for different diseases are quite contradictory. Aside from differences in dosage, this is also due to the area exposed to radiation, general condition and age of patients, nature of chief complain and initial state of the cardiovascular system. Changes in the cardiovascular system were observed in most cases, and they consisted of appearance of functional or morphological changes. In most cases, drop of arterial pressure, unstable pulse, appearance of changes on the EKG (rhythm disturbances, reduced voltage, changes in T wave and S-T interval, elevation of systolic index and others) were observed at the early postradiation stages. Impaired vascular permeability and capillary resistance were observed less often (A. V. Kozlova et al., 1968; Takaoka,

1968, and others). The changes occurred sooner with exposure of the head to smaller doses and they were more marked than with irradiation of other parts of the body. With exposure of the chest and immediate region of the heart, changes were demonstrated in arterial pressure in the direction of a drop, and with exposure of the abdominal cavity, in the direction of elevation. In some cases, changes were detected at the later stage (5-10 or more years after exposure) in the nature of sclerotic changes (myocardiosclerosis) and their link to irradiation was questionable (S. Kh. Sidorovich, 1969; A. V. Kozlova, 1969; Bompiani, Falcetti, 1967; Takaoka, Kaneda et al., 1968; Biran, 1969; Palmer, 1970; Giard, 1970; Huff, 1972, and others).

On the basis of the aggregate of data in the literature, one can conclude that there is early appearance of cardiovascular changes following both total-body and local exposure to high doses of radiation. They consist of appearance of compensated functional and morphological changes in the myocardium, vessels, capillaries, vascular nervous systems and receptors at first, then functional disturbances of the heart, systemic and local hemodynamics, and reactivity.

The mechanism of onset of the observed changes is complex. In the opinion of most authors, the functional disturbances of the cardiovascular system under the influence of total-body and local radiation to the heart in high doses are determined by a disorder of regulatory mechanisms leading to changes in neurovisceral regulation of the cardiovascular system and impairment of main functions of the heart, systemic and local hemodynamics, as well as changes in the structure proper of the heart. There are more marked changes in cardiac vessels when the region of the heart is exposed to local radiation. The direct deleterious effect of radiation is referable, first of all, to vessels, then the myocardium.

There are considerably fewer works dealing with investigation of the circulatory system as related to chronic exposure of animals to low doses of radiation.

The conditions of chronic experiments varied with regard to nature of exposure (external irradiation or intake of radioactive isotopes), radiation dosage and follow-up time, as well as methods of evaluating reactions (studying arterial pressure, pulse EKG, pulse wave propagation velocity, vascular permeability, blood flow, roentgenokymograms, metabolites, reactivity and morphological changes).

However, in spite of the existing differences, the same direction of changes in cardiovascular function was demonstrated in most cases. With exposure to 15-20 rem radiation, changes were demonstrated in arterial pressure, as well as lability thereof, unstable pulse, change in pulse wave propagation velocity [PWPV] and on the EKG, impaired rhythm, excitability, appearance of bradycardia, change in intraatrial and intraventrical conduction, drop of T wave, flattening or two phases thereof, change in reaction of arterial pressure and pulse to functional loads. The changes were more marked with

high doses of radiation (A. S. Amosov, 1966; V. G. Simavonyan, 1968, and others).

V. K. Sel'tser et al. (1970) report that no changes were demonstrated in EKG and PKG findings after exposing the rat heart to cumulative doses of up to 100 rem over a long period of time, and the main group of animals did not differ from the control. N. A. Zapol'skaya et al. (1968) found an increase in levels of biologically active metabolites--histamine, acetylcholine and others--in blood of rats exposed to ^{90}Sr for 2 years in doses of $4 \cdot 10^{-2}$ μCi/kg. There were no pathological deviations in rats given strontium in doses of $1 \cdot 10^{-3}$ μ i/kg. Ye. I. Vorob'yev (1967, 1973) examined the heart of rabbits exposed daily to gamma radiation in doses of 10 rem to a cumulative dosage of 400, 1500 and 2400 rem. Changes in muscle fibers of the heart, plethora of capillaries and veins, hemorrhages, edema of interstitial and perivascular connective tissue and dystrophy of muscle fibers were noted after 30 days, with focal or diffuse myofibrosis and sclerosis of the vascular wall after 3-6 months. G. A. Poddubskiy (1966), L. N. Burykina (1974), V. K. Sel'tser and N. V. Loseva (1971) and others report changes in the cardiovascular system at the long term following chronic exposure to radiation. The authors observe functional disturbances of the heart, most often demonstrable after functional tests, and they stress the greater significance of functional changes in the adrenals at the late postradiation term. In an interesting work conducted under the supervision of Yu. G. Grigor'yev (1972), a study was made of the chronic effects of external gamma radiation on the cardiovascular system, higher nervous activity, hemopoiesis, endocrine system and metabolic processes in dogs, with consideration of the animals' general condition. Several series of experiments were performed involving chronic irradiation of dogs at different dose levels (0.06-0.17-0.34 rem/day) as well as a combination of chronic and periodic single irradiation doses (18-42 rem); the cumulative dose over a 5-year period constituted 205, 315, 625 rem in the chronic experiments and 600, 940 rem in the combination of exposure. As shown by their studies, chronic irradiation did not elicit substantial disturbances of vital functions of dogs, although compensatory and adaptive capabilities were diminished. There was stabilization on a new functional level; however, there was inadequate adaptation of animals exposed to the highest dosage, as demonstrated by the functional tests. Histological studies of the heart and vessels were indicative of gradual development of signs similar to early age-related changes. These effects were related to dose rate and duration of exposure. Several parameters were restored after radiation was discontinued, but this occurred slower than after acute radiation.

In the case of chronic exposure to radiation, marked changes were noted in the cardiovascular system at the late stages, with poorer restoration of function and slower regeneration than after acute exposure (Ye. I. Vorob'yev, A. I. Stepanov, 1968; B. A. Markelov, 1972, and others).

Some interesting data were obtained by G. I. Lisenkova (1973). She demonstrated a stronger relation between the effect and radiation dose rate

than cumulative dosage, and this should also be taken into consideration when analyzing clinical findings. Thus, authors demonstrated changes in cardiovascular activity (morphological and functional) under the effect of chronic exposure to relatively low doses of ionizing radiation; the severity and duration of these changes were related to dose rate and cumulative dosage. The early reactions to chronic radiation were essentially due to neuroreflex regulatory changes in the cardiovascular system leading to changes in systemic and local hemodynamics (A. O. Saytanov, 1965; S. A. Keyzer, 1964; Yu. G. Grigor'yev et al., 1972, and others). Subsequently, as chronic radiation sickness develops, the functional disturbances of other organs and systems, as well as basal metabolism, changes in the circulatory system, are maintained by neuroreflex influences along with endocrine-hormonal and humoral changes.

Some authors consider it possible for cardiovascular changes to also occur as a result of the immediate effect of radiation on myoneural elements of the heart and vessels. At the long term, along with changes in reactivity, morphological changes are also observed in the cardiovascular system (G. I. Lisenkova, 1973; Ye. I. Vorob'yev et al., 1973, and others). As a rule, the cardiovascular changes are adequately compensated, and they are demonstrable only with loads (A. G. Izergina, 1972; V. I. Korchemkin, 1973, and others).

The results obtained on animals cannot be entirely extrapolated to man, although they can offer a general idea about the nature and direction of reactions to chronic radiation. When making extrapolations, one must take into consideration the species-specific distinctions of reactions. Thus, different reactions have been found in animals, depending on species and age. Rats were found to be more resistant than rabbits. Young animals are more sensitive and present stronger reactions.

Many difficulties are involved in identifying and properly evaluating changes in health status and, in particular, in the cardiovascular system of individuals whose work involves exposure to ionizing radiation. Numerous experimental and clinical studies show that the changes developing in individuals who have been exposed to low doses of radiation for long periods of time do not present strictly specific features. Several factors must be taken into consideration to demonstrate their link to radiation. In addition to comprehensive sanitary and hygienic characteristics with evaluation of all factors of working conditions, one needs to have information about the nature, incidence and severity of analogous deviations among properly selected control groups and be guided by the general theses on epidemiology of diseases of this class at a given time.

In view of improved working conditions, marked forms of chronic radiation sickness are virtually unseen in clinical practice of recent years. Investigation of the health status of individuals whose work involves exposure to low doses of ionizing radiation, doses close to the maximum permissible levels, as well as long-term sequelae of prior chronic radiation sickness

is acquiring much importance. Because of inadequate informedness of clinicians with regard to the main theses of clinical radiobiology, complexity of the phenomena that occurred and occasional lack of clearcut quantitative characteristics of the relationship between dosage and immediate somatic manifestations, at the early stages all changes demonstrated in health status of individuals, who had minimal contact with sources of ionizing radiation in some cases, regardless of dose levels, were attributed to signs of chronic radiation sickness. This also applies fully to evaluation of reactions of the cardiovascular system.

The first works were mainly descriptive, supplying the findings of single outpatient screening of some occupational groups, often very small ones, or else inpatient studies of deliberately selected individuals with some deviations or other in health status. There were usually no descriptions of sanitary and hygienic aspects of working conditions or information about individual radiation doses; nor were there data about the incidence and nature of dynamic changes, as compared to the initial results of screening essentially healthy people in a so-called control group. All this made it difficult to correctly evaluate the observed deviations as related to the effects of ionizing radiation.

Information about people working with sources of ionizing radiation is given in several works by M. N. Fateyeva et al. (1955, 1960), N. I. Shcherbakov (1966), G. G. Lysina (1962, 1968), Ye. I. Vorob'yev et al. (1965-1973) and others. Most authors observe changes in the cardiovascular system, manifested by muffled heart sounds, appearance of apical systolic murmur, enlargement of the left ventricle and changes in arterial pressure, mainly in the direction of decline. Thus, according to the data of V. I. Kuznetsov and G. A. Luk'yanov (1957) a decline of arterial pressure was observed in 61% of those examined and elevation, in 6.7%. There were also unstable pulse (tachycardia or bradycardia), changes in EKG indices (decreased wave voltage, changes in intraatrial and intraventricular conduction, decline of T wave, S-T interval and extension of Q-T). There was appearance of labile pulse with functional tests, changes in capillary circulation, attenuation of vascular reflexes in plethysmographic studies, inadequate and static reactions to cold and heat. The clinical changes were most often defined in terms of "asthenovegetative syndrome" or "vascular dystrophy." Along with signs of the asthenovegetative syndrome, some changes were noted in oxygenation, with development of hypoxia, occasionally demonstrable after functional tests (N. A. Kurshakov, P. M. Kireyev, 1963; G. G. Lysina, 1968, 1972), which authors related to impaired coordination between delivery of blood and aeration in the lungs.

According to Ye. I. Vorob'yev (1971), oxyhemometric and spirometric studies revealed the same incidence of deviations from normal in oxygenation of blood and external respiration function in individuals of the main (gamma flaw detectors) and control group. Blood flow in the pulmonary circulation, determined by the oxyhemometric method, was increased in 5.2% of the main group and 6.3% of the control, and decreased in 11.2 and 9%, respectively.

Decreased vascular tonus was often demonstrated on the basis of the results of measuring PWPV in vessels of the elastic and muscular types.

There have also been reports of changes in permeability of tissular membranes (hyaluronidase-hyaluronic acid system) and vessels (M. I. Smirnova, Ye. A. Denisova, 1969). The changes in histamine content were transient, and cholinesterase activity was not infrequently low.

In the early years of using sources of ionizing radiation in industry, changes in the cardiovascular system were also found more often because they were based on findings referable mainly to sick individuals who often sought medical aid. According to works of recent years, a comparison of findings on the main and control groups often fails to demonstrate appreciable changes in health status and condition of the cardiovascular system (A. K. Arnautov et al., 1966-1968; V. K. Sel'tser et al., 1966-1973, and others).

Some authors stress the exceptional sensitivity of the cardiovascular system to even low levels of radiation, without evaluating the effects of other factors. Thus, V. V. Volkovitskaya et al. (1966) found some physiological changes in individuals exposed to ionizing radiation in the form of brief episodes of doses in excess of the permissible level (during repair work on different elements of charged particle accelerators, when the radiation doses could reach 3 rem in 3-7 days). These changes were transient and did not exceed the range of the physiological norm, but they differed from base findings. In our opinion, it would be more correct to evaluate them as variants of normal physiological reactions to a set of occupational factors (excessive fatigue while doing repair and inspection work).

The most comprehensive data referable to dynamic observation of individuals working in contact with sources of ionizing radiation in the main branches of industry are contained in works of the last decade (A. K. Gus'kova, Ye. A. Denisova, V. A. Soldatova, N. I. Gorbarenko, R. A. Solodova, G. I. Kirsanova, E. N. L'vovskaya, A. V. Barabanova et al., 1963-1975, and others). A complete, rather than sampling, dynamic screening was made of individuals coming in contact with radiation while working with charged particle accelerators and atomic reactors used in scientific research, as well as medical roentgenologists and radiologists, industrial roentgenologists and flaw detectors, mine workers, individuals employed in scientific research institutions and those using radioactive isotopes in producing fluorescent substances of continuous action based on radium and mesothorium, and others. In all, there were 6000 people examined in the main group and about 500 in the control; they were under observation dynamically for 10-15 years, at 1-2-year intervals.

In view of the mildness, transience and reversibility of the observed changes in the cardiovascular and nervous systems, special investigative methods were used for early detection of deviations. The following techniques justified themselves the most: electrocardiography, rheography, sphygmography, determination of systolic and minute blood volumes, general peripheral

resistance, autonomic reflexes (Aschner-Dagnini oculocardiac reflex, oculostatic, postural reflexes, orthostatic and clinostatic), determination of skin temperature and perspiration, threshold levels of different forms of sensibility. All studies were conducted at rest and after functional loads, and this made it possible to demonstrate the reserve capabilities of the tested systems, as well as possible range of fluctuations in each individual case and the group as a whole.

The studies showed the chosen methods to be adequate for detection of early functional changes under the influence of radiation, and they made it possible to assess the health status of examined individuals as a whole. The medical findings were compared at different times, with consideration of cumulative radiation dose and its distribution in time. The results of clinical tests were processed in the direction of evaluating health status, and clinicophysiological characteristics of the cardiovascular system at different observation times, as related to radiation dose level; thus, a study was made of the stages of formation of reactions to chronic radiation in low doses, in the course of accretion of the dose load and as compared to findings for control groups examined at the same times. Concurrent examination of a control group yielded information about the incidence and direction, nature of changes in the cardiovascular system of essentially healthy individuals, made it possible to investigate the dynamics of their development at different ages, to assess their stability, direction, severity and to obtain information about the incidence of disease among essentially healthy people. The obtained facts were submitted to statistical processing. On the basis of the comprehensive work-up, a conclusion was made for each individual, with distinction of the following main categories: in good health (lack of complaints or objective deviations, even after special clinicophysiological tests); essentially healthy (history of compensated disease in the past or deviations in parameters of physiological functions that do not affect wellbeing and fitness of the subject and do not form a circumscribed syndrome of functional deficiency of any system); circumscribed syndromes of cardiovascular reaction: syndrome of vegetovascular dysfunction, vascular dystonia of the hypotensive or hypertensive type, occasionally combined with general asthenia (asthenovegetative syndrome); they are described in Chapter 1. In some cases, a general (nonoccupational) or occupational disease (chronic radiation sickness) was diagnosed at the time of the examination.

There was prevalence of men among those working with accelerators, atomic reactors and industrial roentgenologists, and more women among medical roentgenologists and radiologists. The mean age of those screened in the former group was under 40 years and in the latter, slightly over 40 years. Control groups were formed to correspond with the main groups, with regard to differences in sex, age and nature of work, as well as similarity of residences in specific economic and geographic regions.

The results of this study revealed that the first reactions to the entire set of occupational factors appeared in 80% of the subjects upon reaching

a cumulative radiation dose of 25-50 rem in 5-8 years. The incidence of deviations of some autonomic and hemodynamic indices rose appreciably, as compared to base data and results obtained in control groups. There were more individuals with complaints of an asthenoneurotic nature (increased fatigability, headaches, heaviness of the head, sleep disorders, irritability, quick temper, excessive perspiration). At the same time, no changes were demonstrated in viscera, the nervous system, eyes or blood of most subjects. Objective examination revealed muffled heart sounds (20% of the cases, versus 14% at the first examination), systolic apical murmur (17%, versus 6%) and rhythm disorders (31 and 16%, respectively). Onset of these deviations was apparently due to changes in regulatory influences of the autonomic nervous system on the myocardium. All of the deviations were moderate, and their incidence was lower than usually cited in the literature for individuals exposed to radiation under occupational conditions. Thus, V. I. Kuznetsov and G. A. Luk'yanov (1957) found dull heart sounds and appearance of systolic murmur in 58% of the cases and L. M. Omel'yanenko (1957), in 57%, and she considers these symptoms to be signs of dystrophic myocardial changes.

EKG examinations revealed a higher incidence of rhythm and excitability disorders of the myocardium (56 and 29%, respectively), and a more frequent tendency toward elevation of systolic index (26 and 11%, respectively). There was more marked tachycardia after a measured physical load. These deviations are also typical of disturbances of autonomic innervation, with changes in bioelectrical processes in the myocardium.

Many authors have reported changes in cardiac function, according to EKG findings, among individuals working with ionizing radiation, and most of them demonstrated changes in rhythm of heart function, negligible decline of wave voltage, flattening of P and T waves, extension of Q-T, evaluating them as manifestations of disturbances in tonus of the sympathetic and parasympathetic nervous system, with trophic changes in the myocardium, hypoxic and regulatory disturbances of biochemical processes in the myocardium (P. D. Gorizontov, B. B. Moroz, 1962; N. A. Kurshakov, 1963; Ye. I. Vorob'yev, 1973, and others). Upon reaching the above mentioned doses, increase in systolic and minute blood volumes, instability of total peripheral resistance with moderate decrease or, less often, increase thereof were observed more often in the main group. There were also more marked fluctuations of these parameters with the use of standard physiological loads. Although arterial pressure was consistent with the age norm in most subjects, more distinct fluctuations were observed in the course of the dynamic study, as compared to control groups: at the early stages, with radiation doses of 25-30 rem, arterial hypertension was found almost 3 times more often and hypotension less often; thereafter, with increase in radiation dosage there was an appreciable increase in incidence of hypotension, whereas in the control group the fluctuations of arterial pressure were insignificant throughout the observation period. The differences were statistically reliable, with regard to mean maximum arterial pressure in the main group at different times (118-106 mm Hg, $t = 3.0$). In the control group, there were negligible fluctuations of mean systolic arterial

pressure (116.6 117.4 mm Hg). A comparison of age-related indices of arterial pressure in the main and control groups revealed a more consistent elevation in the control group and, as we have already noted, it increased with increase in age. These findings are consistent with data in the literature (Z. M. Volynskiy et al., 1964; A. I. Syasnikov, 1964; I. A. Ryzkin, 1967, and others). In the main group, systolic pressure remained at lower levels. Perhaps this applies only to a specific range of doses. At the same times, we also observed changes in pulse rate. At the early stage, there was a tendency toward tachycardia and later on, bradycardia. The data in the literature on this score are contradictory. V. I. Kuznetsov and G. A. Luk'yanov (1957), N. S. Molchanov (1962) and others reported bradycardia; L. N. Omel'yanenko et al. (1957), on the contrary, observed tachycardia more often. Most authors report a tendency toward decline of arterial pressure (M. N. Fateyeva et al., 1960; A. A. Danilin et al., 1961; Ye. I. Vorob'yev et al., 1968, and others). Evidently, this contradiction is attributable to differences in examination time and dose levels.

Measurement of pressure in the central retinal artery (E. N. L'vovskaya, 1965, 1972) revealed a decline more often in the main group than the control (in all age groups), especially after 8-12 years of observation (32% versus 21% in the control). The drop of pressure in the central retinal artery coincided, in most cases, with systemic hemodynamic changes, and it was observed more often in individuals with arterial hypotension.

Studies of arterial pressure in symmetrical vascular regions of the upper and lower extremities by means of oscillography revealed a high incidence of asymmetrical arterial pressure in the main group, particularly in vessels of the arms (up to 25% of the cases). There was also frequent asymmetry of the oscillatory index in the main group (17-22% of the cases, versus 11% in the control).

Increased lability of arterial pressure and pulse was also noted in the functional tests, lability of arterial pressure being more marked in orthostatic position and lability of pulse, in clinostatic. After the physical load, there were more significant fluctuations of both arterial pressure and pulse than at the initial examination, which could be indicative of increased excitability of the autonomic nervous system.

Ye. I. Vorob'yev et al. (1965) demonstrated a distorted reaction and inertia of arterial pressure and pulse with functional tests, evaluating this as prevalence of parasympathetic reactions and more marked inhibitory processes in the cerebral cortex.

Sphygmographic studies of the vascular wall (determination of pulse wave propagation velocity--PWPV--in muscular and elastic vessels in segments of the femoral, radial arteries and aorta) revealed that changes in PWPV, mainly in muscular type vessels, were observed considerably more often in the main group of individuals than in the control. These changes were particularly noticeable at the early stages in subjects with unstable arterial pressure and a tendency toward elevation or decline. There were

less frequent changes in PWPV in vessels of the elastic type. A normal correlation between PWPV in muscular and elastic types of vessels was observed in 50% of the subjects. In all cases, the change was due to a change in PWPV in vessels of the muscular type. In the control group, the correlation between PWPV in vessels of the muscular and elastic types (C_m, C_e) was normal in most cases, and there was no appreciable change in the coefficient upon re-examination. A marked correlation was demonstrated between C_m and mean dynamic arterial pressure. C_m was accelerated in 68-87% of the individuals with high mean arterial pressure and slowing of the former was observed in 48-68% of the individuals with low arterial pressure.

The data we obtained may be indicative of some instability of indices of vascular tonus, mainly in arteries of the muscular type, and phasic nature of changes in tonus of large arteries. At the early stages, there was more often a tendency toward increased muscular tonus of the vascular wall and at the later stages, with higher doses of radiation, there was more often slower propagation of the pulse wave, indicative of decreased vascular tonus of arteries of the muscular type. The changes in tonus were also referable to smaller vessels (arteries, arterioles, veins), as indicated by rheographic studies that made it possible to evaluate both vascular tonus (overall) and blood supply to different vascular regions. The studies revealed that there were no gross disturbances, but decreased tonus of cerebral vessels with signs of venous stasis in some vascular regions were observed at the late stages. N. I. Shcherbakov (1960, 1966), Ye. I. Vorob'yev et al. (1968) and others reported on decreased vascular tonus on the basis of oscillographic studies (drop of mean arterial pressure, flattening of oscillographic curve, asymmetry of parameters of oscillogram curve, some elevation of oscillatory index); N. A. Kurshakov, O. M. Kireyev (1963) and others reported the same on the basis of data indicating slower PWPV in vessels of the muscular type.

Determination of systolic and minute blood volumes, as well as total peripheral resistance, made it possible to evaluate more fully the state of hemodynamics. The changes were related to observation period. At the early stages, with radiation doses of about 25-50 rem, one-third of the subjects in the main group presented above normal (62 ml) systolic volume. This could be indicative both of increased diastole and increased contractility of the myocardium as a result of the positive inotropic vagal effect (N. N. Savitskiy, 1970).

In the control group, the systolic volume was about the same at all examination times and there was a low incidence of deviations from normal. The difference between the main and control groups, with respect to incidence of deviations from normal systolic volume, was statistically significant at the early stages ($t = 2.75$). Minute volume was somewhat higher in the main group, as compared to the first examination, whereas there were virtually no differences in the control group. This was also reported by Ye. V. Gembitskiy (1967), N. S. Molchanov (1962) and others.

The correlation between actual and proper minute volume in the screened individuals revealed that the actual level was more often above the due level in the main group, especially at the early stages, and the differences from the control group were reliable ($t = 3.3$).

Total peripheral resistance was normal in most individuals of the main group and the control. A comparison of actual and proper total peripheral resistance revealed that deviations in the direction of lower and higher actual resistance were encountered equally often in the groups examined, but at the last examination there were more frequent deviations in the direction of higher actual peripheral resistance in the control group.

Along with changes in cardiac function and hemodynamics, there were also vegetosomatic nervous disorders, as indicated by skin temperature changes and disturbances on cutaneous thermotopography, perspiration, changes in reflex background of tendon reflexes with inconsistent asymmetry thereof, appearance of negative and distorted reactions to the Aschner-Dagnini test and demonstration of orthostatic and clinostatic reflexes, coordination disorders, changes in discrimination and vibration sensibility, lowered threshold of sensibility to pain and faster adaptation to pain. The incidence of these deviations constituted 20-30%. More often, changes in the cardiovascular and autonomic nervous system were found in the same subjects; they warranted the diagnosis of the syndrome of functional instability of regulation of the cardiovascular system, vegetovascular dystonia, apparently related to increased excitability of the autonomic branches of the nervous system. According to the data of A. B. Markizova and E. N. Mukhina (1968), V. K. Kamenetskiy (1968) and others, changes in autonomic reactions and reactivity were observed in about 30% of the cases, i.e., the incidence and time of appearance of these deviations were close to the figures we obtained.

It should be noted that the subjects often felt well and presented no complaints about their health status in the presence of objective changes in the autonomic nervous system or hemodynamics. Occasionally, changes were demonstrable only after a load, indicating increased reactivity of the autonomic nervous system.

All reactions to exposure in this range of radiation doses were moderate, they presented no strict specificity and it would have been difficult to detect and consider these deviations if we did not have the base data and results of dynamic observation, as well as data on the control group. It is only by means of dynamic comparison that we could relate them, not only to the effects of ionizing radiation, but the set of other industrial factors. According to our data, functions of vital organs are not affected, and they present variants of normal with some expansion of the range of vascular reactions, as also reported by other authors (N. S. Molchanov, 1962; Ye. V. Gembitskiy, 1969; A. K. Gus'kova et al., 1970, 1973; V. K. Sel'tser et al., 1973, and others). According to the data of A. K. Gus'kova, Ye. A. Denisova, V. K. Sel'tser and others, the above-described initial reaction lasted an average of 1-2 years; thereafter, in spite of continuing on the

same job, the deviations leveled off. The reversibility of changes in most subjects, their good general condition and negligible levels of deviations confirm the formed impression of neuroreflex mechanism of their appearance. We are justified in interpreting the observed changes as an adaptational reaction to altered environmental conditions, including exposure to ionizing radiation. Occasionally (17-20% of the cases) the changes did not disappear or even progressed somewhat, and with further increase in dosage there was development of the clinical syndrome of neurocirculatory dystonia of the hypotensive type, indicative of some deficiency mainly in regional circulation. The syndrome of neurocirculatory dystonia observed in this group of subjects was characterized by several clinical distinctions. The patients complained of headache (mainly long-lasting, almost constant, localized in the region of the forehead, temples and occiput), insomnia, increased fatigability, general weakness, vertigo, especially in the mornings. Their integument was pale. Dull heart sounds and an apical systolic murmur were found in half the subjects. There was arterial hypotension (90%) and bradycardia (31%). Vascular tonus was decreased (slow PWPV in vessels of the muscular type, slower propagation of the rheographic wave, change in type and quantitative parameters of rheograms) in peripheral and cerebral vessels, particularly veins, with signs of stasis. An increase or tendency toward increase was demonstrated in systolic and minute blood volumes, as well as decrease in total peripheral resistance. Analogous changes were also observed by Ye. V. Gembitskiy (1968) and many other authors.

Instability of vascular tonus and changes in reactivity were also demonstrated with the oscillographic, rheographic and plethysmographic methods, and capillaroscopy. More often there was diminished tonus of both large and small vessels, with spastic and atonic capillaries. Vascular tonus was not the same in different regions, and there was more frequent decrease in tonus of vessels of the head. Decreased tonus of cerebral veins was often demonstrated by means of rheography, orbital plethysmography, occlusion plethysmography and examination of vessels of the eyegrounds (V. P. Zhmurkin et al., 1965; G. I. Kirsanova, 1968, and others). Slower resorption of radioactive iodine from the intracutaneous reservoir was also indicative of changes in peripheral circulation (M. I. Smirnova, Ye. A. Denisova, 1969).

The fluctuations of arterial pressure and pulse rate with functional tests (orthostatic, clinostatic, physical load) were more marked than in essentially healthy individuals, and this is consistent with the data of Ye. V. Gembitskiy (1968) and others. Changes of a regular nature were demonstrated on the EKG of almost half the subjects (43.5%) and changes in bioelectrical processes in one-quarter (28.5%), indicative of diffuse changes in the myocardium of a dystrophic nature. They consisted of lowering of wave voltage, flattening, crenation of P wave, WRS complex and T wave, which could be indicative of slower conduction of excitatory impulses and slower contractions of specific muscles of the ventricles. Slowing of atrioventrical conduction and increase of the systolic index were observed less often. These changes could be indicative of the prevalent influence of the parasympathetic nervous system.

Evidently, along with regulatory changes in autonomic innervation, more profound changes are also observed, which lead to a change in myocardial metabolism. It is difficult to rule out the pathological influence of the vagus on onset thereof. They could be interpreted as dysmetabolic, dystrophic. This concept is consistent with the change in levels of metabolism in the myocardium (A. V. Ivanov, N. N. Kurshakova, 1962; Ye. F. Lushnikov, 1969, and others). At this stage of observation, these deviations do not weaken myocardial contractility, as indicated by hemodynamics and results of measurement of systolic and minute volumes.

Autonomic disturbances and a tendency toward lowering of skin temperature in distal parts of the limbs, asymmetry of skin temperature and perspiration, changes in sensitivity to pain in the distal parts (hypesthesia) were demonstrated in patients with neurocirculatory dystonia, which is indicative of disorders of receptor systems of a primary nature, as well as those related to circulatory disturbances. Postural reflexes (orthostatic, clinostatic), Aschner-Dagnini oculocardiac reflex, physical load tests were indicative of increased reactivity of the nervous system with considerable involvement of its parasympathetic branch.

Examination of biochemical indices failed to demonstrate appreciable disturbances, but there were changes inherent usually in older age groups (moderate increase in alpha-2 and gamma globulins, increase in beta lipoproteins, etc.), as also indicated by Ye. V. Gembitskiy (1969), V. N. Kozlovskiy (1972) and others. According to the data of G. G. Lysina (1975), maximum oxygen tension was also higher in the same individuals than in the control, while the index of tissular oxygen uptake was higher than the index of oxygen transport. After an oxygen load, there was less increment of oxygen than in the control, and this is probably attributable to the higher "initial level" of oxygen tension before the load. The overall indices of redox processes (oxygen disapperance rate in blood and urine) did not differ from data for the control group and corresponded to the lower range of normal. There was an increase in external respiration (increased minute volume of respiration and oxygen absorbed per minute), indicative of an increased oxygen requirement. The authors related the observed disturbances to disturbances of gas exchange regulation, and they considered them to be adaptational.

Not all subjects developed the syndrome of neurocirculatory dystonia. In most cases, there was only an initial reaction to radiation, apparently of an adaptive nature to adjust the body to new conditions.

In addition to ionizing radiation, individual discinctions of the body (extent of adaptability to environmental changes, level of development of functional systems, regulatory system), as well as the effects of other factors (psychoemotional loads, mental tension, trauma, prior diseases, bad habits, etc.), are probably of some significance, and they could create a certain background of increased sensitivity to exogenous factors.

With increase in cumulative radiation doses to 200-400 rem, changes may appear in other organs and systems, including the blood, gastrointestinal tract, respiratory organs, and some individuals develop chronic radiation sickness. In such cases, there is also secondary involvement in the process of the cardiovascular system due to injury to more radiosensitive organs and systems. This was observed in patients with chronic radiation sickness, for example, medical roentgenologists with long work tenure exposed to cumulative radiation of the order of 150-400 rem (V. A. Soldatova, 1967-1973), as well as individuals working with radium (R. A. Solodova, 1967).

Thus, with exposure to up to 100 rem there are no overt signs of radiation sickness, but there is impairment of neurovascular regulation and appearance of moderate changes in systemic and local (mainly) circulation. The initial reaction is adaptive in nature, and there is no substantial involvement of circulation in vital regions (brain, heart). This is associated with a good general condition and fitness of subjects. As a rule, the hemodynamic changes are compensatory in nature (drop of arterial pressure is associated with increase in systolic and minute volume; slowing of pulse and blood flow is combined with increased tissular oxygen uptake), i.e., the changes in some functions are compensated by others to provide the integral parameters inherent in normal circulation.

The transient nature of the reaction to continued exposure to radiation is indicative of its adaptive and physiological nature. The neurocirculatory dystonia syndrome, which develops in some people under the effect of the same radiation doses, may be indicative of aggravation of neuroregulatory disorders and changes in central and peripheral circulation inherent, to some extent, in these individuals previously. In such cases, the changes are functional and no profound disturbances of cardiac activity develop.

Progression of cardiovascular pathology may be observed with development of chronic radiation sickness.

In addition to changes in general hemodynamics and cardiac function, local disturbances of peripheral circulation (in the skin, limbs, brain) combined with drop of arterial pressure, venous stasis and venous hypotonia are inherent in chronic radiation sickness. The local circulatory disorders are aggravated under the influence of some provoking factors, they induce subjective disorders (headache, pain in the extremities, increased sensation of cold, general weakness and others) that may be the prime elements of the clinical syndrome. Transient focal neurological symptoms may appear, which are attributable to regional insufficiency of cerebral circulation and transient hypoxia of some parts of the brain. Objective examination reveals mild involvement of nerve trunks in the reaction. Some tenderness of the periosteum, vessels and, less often, muscles is demonstrable. Muscle tone is somewhat decreased in the limbs. Distal reduction of pain and vibration sensibility is often demonstrated. In-depth studies reveal the nature of asthenic disorders. The sensation of pain may be very long-lasting, and it is confirmed by means of adaptometry and other

electrophysiological tests (A. K. Gus'kova, I. K. Larionova, 1963). Signs of impaired peripheral circulation are also found: cyanosis, cold extremities, changes in oscillation curves, rheovasograms and capillary blood flow.

Inadequacy of cerebral circulation under the influence of radiation may be manifested in the form of predominant decrease or increase in tonus of cerebral arteries and veins (G. I. Kirsanova, 1968, 1971). Dull headache, occurring in the morning and becoming more intense at the end of the day, after spending time in a stuffy room, when overtired or after physical stress, is more typical of individuals with predominant decrease in arterial and venous tonus. Vertigo is rare, clinical signs of vestibular disorders are limited to vegetative manifestations and mild nystagmus, mild shakiness when walking and in Romberg's position; there is diffuse and mild decrease of muscle tone; tendon and periosteal reflexes are inconsistently asymmetrical. At the time of a headache, the severity of symptoms increases. Arterial pressure is low, including that of the central retinal artery; the veins of the eyegrounds are dilated and arteries are occasionally moderately constricted. The rheoencephalogram shows rapid ascent to the peak of the curve, marked additional waves on the descending leg, slower propagation of the rheographic wave, which is typical of decreased tonus of arteries and veins.

Constant and especially sporadic headaches related to diverse physical and emotional stress, changes in temperature, barometric pressure and other meteorological factors are more often present in individuals with increased tonus of cerebral arteries.

Arterial pressure is normal or moderately elevated. There is mild constriction of arteries of the optical fundus. Neurologically, there is prevalence of transient focal symptoms of the order of mild pyramidal insufficiency. The headaches are more often localized in the occipital region. During an access of headache, there is appearance of nystagmus and tenderness with extreme diversion of the eyeballs, with attenuation of the general background of reflexes and muscle tone, and reflex asymmetry. Rheoencephalograms show signs of increased arterial tonus and vascular asymmetry. These symptoms are more often observed in individuals over 40 years of age. There is prevalence of women among individuals with decreased vascular tonus.

The data in the literature (A. F. Bibikova, 1960; R. M. Lyubimova, 1962) are indicative of involvement of spinal fluid synthesizing structures and fluid-containing pathways in the reaction to radiation. Our observations reveal that, in the case of chronic exposure to radiation in the dose range of 150-400 rem, marked disturbances referable to spinal fluid dynamics are observed only when exposure to radiation is associated with a history of infection or trauma of the nervous system. They are more consistent in the case of local irradiation of the brain in doses reaching several thousand roentgens, and the direct effects of injury to the glial stroma are involved in onset thereof.

The changes in cardiac activity in the presence of chronic radiation sickness are characterized as changes that are mainly regulatory in nature, as well as disturbances of a metabolic nature in the myocardium proper, of the myocardiodystrophy type. Complaints appear of pain in the region of the heart, palpitations and dyspnea. Widening of boundaries of the heart, dull heart sounds and apical systolic murmur are demonstrable. On the EKG there is a decrease in voltage, flattening of T wave and decrease of S-T interval, widening of QRS complex, elevation of systolic index and moderate increase in ventricular electrical systole. The tendency toward intensified, inadequate and longer reactions to physical loads persists. It should be noted that all of the changes are more marked in the older individuals.

There may be structural changes in the heart and vessels with exposure to large cumulative doses of radiation, and they subsequently become quite persistent. Appearance of corresponding physical symptoms (dull sounds, wider boundaries, change in vascular tonus) is indicative of these changes.

Other variants of the syndrome of neurocirculatory dystonia (normotonic type with cardiac signs and hypertonic type) are not inherent in chronic exposure to radiation. Their incidence in the main groups does not differ from the control, and they are identical to analogous syndromes of nonradiation genesis with respect to clinical and physiological characteristics.

Investigation of morbidity among individuals in the main group revealed that the incidence of such diseases as vascular atherosclerosis and cardiac ischemia became somewhat higher at the end of the observation period than at the first examination. However, one must also take into consideration the corresponding advance by 12-15 years in mean age of the subjects and an analogous increase in incidence of these diseases in the control groups.

Analysis of diseases of the cardiovascular system as a function of working conditions and occupation (Table 5) indicates that there is a higher incidence of functional disorders among workers dealing with accelerators, medical radiologists and industrial radiographers, as well as those who work with radioactive isotopes at scientific research institutions. We were impressed by the somewhat higher incidence of essential hypertension and vascular atherosclerosis among medical roentgenologists and radiologists. The observed differences in morbidity structure of the main group are attributable to differences in age and sex composition of these groups. Moreover, the distinctive elements of their work, poor scheduling of work and rest, somatic burden and, in a number of cases, bad habits are apparently also significant. A comparison to a adequate control data may confirm this impression.

Analysis of observations, with consideration of the age of the subjects, enabled us to determine that hypotonic reactions are encountered more often in the main group and older subjects, whereas hypertonic reactions correspond to the control. In view of the fact that, at the present time, the age of most workers dealing with reactors, accelerators and industrial radiographers under 40 years, we deemed it necessary to continue the study.

Table 5. Incidence of cardiovascular syndromes among individuals in different occupational groups

Clinical syndromes	Incidence of cardiovasc. syndromes, %						
	workers		medical				
	with reactors	with accelerat.	roentgenologists	radiologists	industrial radiolog.	work with isotopes at SRI*	control group
Vegetative dysfunction	6,0	16,0	9,3	8,2	19,7	16,0	9,0--8,7
Neurocirculatory dystonia:							
hypotonic type	6,3	25,0	6,9	15,0	7,3	17,0	5,6--8,2
hypertonic type	2,8	4,7	13,0	4,0	15,0	7,2	6,7--5,0
Essential hypertension	0,7	2,1	10,0	6,9	4,7	5,2	6,0--8,2
Vascular atherosclerosis	0,2	6,7	11,4	17,3	1,8	6,0	8,5--13,8

*SRI--scientific research institutions.

The studies thus revealed that there are reliable differences from the control only in incidence of the syndrome of functional instability of cardiovascular regulation. Clinically, these reactions are not specific; they are analogous to those observed under the influence of other industrial factors, as well as in control groups, and they may be attributable to various causes (I. K. Shkhvatsabaya et al., 1974).

A study of some concomitant factors in some individuals, for example, bad habits (excessive smoking and drinking), revealed that their incidence is the same in both the main and control groups. In both groups, diseases were more often encountered among individuals who smoked or drank excessively. The differences between the main and control groups were significant only with regard to the syndrome of vegetovascular dystonia, which is encountered reliably more often in the main group.

However, bad habits may play an appreciable adverse role in the body's reactions to working conditions.

The earliest reactions to low doses of ionizing radiation are changes of a neuroreflex nature leading to functional changes in cardiovascular activity. Ionizing radiation acts like a nonspecific stimulus of the nervous system. At first, the reactions do not present a strict direction, and they are characterized by greater than normal lability, instability of the main hemodynamic parameters, as well as wider range of responses to functional tests. It has been demonstrated that some endocrine glands and related humoral mediatory systems (thyroid, adrenal cortex, hypophyseodiencephalic region, reproductive glands, catecholamines) are involved in formation of the changes. These changes can be evaluated as the syndrome of

vegetovascular dysfunction, which is adaptive at the early stages to the effects of ionizing radiation. Thereafter the functional deviations acquire more direction, the changes become more marked and stable, some signs appear of local circulatory disorders, changes in cardiac function, autonomic nervous system and endocrine glands, with impaired equilibrium of mediator systems and lability thereof. The changes in one phase are consistent with the syndrome of neurocirculatory dystonia of the hypotonic type (mainly), and it is also part of the clinical signs of chronic radiation sickness.

The question of significance of occupational radiation in doses close to the adopted maximum permissible levels with respect to onset or complication of circumscribed cardiovascular syndromes is debatable, and it should be further investigated. At this point in our observation period, it is valid to state that there is no reliable information indicative of a higher incidence or aggravation of essential hypertension. On the contrary, there is some delay in age-related transformation of arterial pressure in the direction of elevation and a tendency toward moderate arterial hypotension among individuals exposed to the maximum cumulative dose of radiation. This variant of vascular disorders does not consistently present visible disturbances of vascularization of the vital organs (brain, heart). We also failed to demonstrate conclusive changes from neurocirculatory dystonia of the hypotonic type to atherosclerosis, with signs of systemic and local circulatory insufficiency. However, the somewhat higher incidence and earlier demonstration of some signs of age-related involution with the highest radiation doses, according to the results of laboratory and instrument tests on individuals in the main groups (biochemical changes, changes in the lens), make it imperative to conduct a close epidemiological study of these groups.

CHAPTER 5. THE CARDIOVASCULAR SYSTEM AS AFFECTED BY EXPOSURE TO MICROWAVE RADIATION

[Text] Natural electromagnetic fields are a constant component of the environment of man. Changes in their intensity and frequency are related to fluctuations in solar activity. The fluctuations in intensity of natural electromagnetic fields also depend on electric conductivity of earth's atmosphere which, in turn, is related to humidity, temperature, rate of movement of air layers and other meteorological factors. Thus, in the course of evolution, animals and man had to adapt to natural electromagnetic fields and the significant fluctuations of their parameters.

At the present time, in view of development of electronics and use, in different branches of the national economy, of equipment that emits electromagnetic fields in the radiowave range, there are local changes in the natural electromagnetic background affecting limited groups of people.

In view of the urgency of the problem, many studies have been pursued in the last decades of the biological effects of electromagnetic fields (EMF). More comprehensive investigation has been made of the thermal effects of microwaves at a flux density (incident energy) of the order of 10 mW/cm^2 or more. On this energy level, the biophysical mechanism is related to transformation of electromagnetic energy into thermal energy when absorbed by tissues. Depending on the wavelength and properties of tissues, primary heating may occur at different depths from the surface of the body; deeper tissues are heated with exposure to decimeter waves, while exposure to centimeter and millimeter waves induces heating of superficial tissues, just like infrared and direct solar radiation. Poorly vascularized tissues are subject to more intensive heating. The change in tissue temperature leads to intensification of metabolic processes, irritation of excitable cells and injury to

tissular structures. The biophysical mechanisms have not been studied at a lower intensity of radiation, which is the case in modern industry (the energy levels are lower than those that cause a temperature change). It is believed that they are due to development of reactions on the molecular and cellular levels. This includes the effect of dielectric saturation (Schwan, 1958), the phenomenon of molecular resonance (Vogelman, 1968), the phenomenon of nonthermal denaturation of protein and change in membrane potential related to the change in permeability of the cell membrane (V. I. Shtemler, 1973; Portela, Vaccari, 1973, and others). There may also be impairment of electromagnetic regulation of functions in the integral organism (A. S. Presman, 1968).

The main mechanisms of these phenomena may be relaxation oscillations of ions and dipole molecules in the aqueous phase, rotation thereof and reorientation in space under the influence of the energy of electromagnetic radiation (Yu. A. Sebrant, 1969; Illinger, 1969). With specific parameters of radiation, not only redirection of side chains of large molecules, but separation thereof are possible. This effect becomes possible in the case of resonance absorption of electromagnetic energy by naturally oscillating molecules on the interface of media (Vogelman, 1968). The difficulty in studying the early physiological changes are attributable to the complexity of conducting an experiment, which includes electrophysiological studies, the difficulty in determining absorbed energy and its distribution in organs, tissues, physiological and submicroscopic structures. Research on the effects of electromagnetic waves on the integral organism is represented the most extensively in the literature, this applies to a lesser extent to different organs and cells, and very seldom to relatively simple subcellular models.

The hemodynamics related to microwave irradiation were investigated in experiments on the basis of pulse and arterial pressure of different animal species.

A comparison of studies conducted on large and small laboratory animals shows that microwaves lead to a significant change in pulse and arterial pressure of rats, rabbits, mice and pigeons (Z. V. Gordon, 1964; I. M. Yakovleva, 1973, and others), with negligible fluctuations of these parameters in dogs (Ye. V. Gembitskiy, D. Ye. Gavrilova, 1968; N. V. Tyagin, 1971; V. P. Svetlova, N. I. Chubarova, 1973). Brief exposure to a thermal mode leads to acceleration of heart rate, while exposure in the nonthermal mode induces persistent drop of arterial pressure and slowing of heart rate after a brief rise of arterial pressure or short latent phase. This led Z. V. Gordon to the conclusion that the hypotensive effect is a typical reaction to this factor. A. S. Presman (1964) believes that the effect depends largely on the localization and mode of exposure. N. A. Levitina (1964) and V. V. Markov (1973) established that intermittent irradiation elicits a more marked effect than continuous exposure.

The experiments of McAfee (1969) and others, involving anesthetization of the skin, warrant the belief that the changes in the cardiovascular system with exposure to microwaves depend largely on the direct effect of radiation on

on superficial reflexogenic zones and reflex change in hemodynamics, which is consistent with the usual conceptions of physiology of nervous regulation of the cardiovascular system.

Studies of ecological and species specificity of regulation of cardiac activity under the influence of superhigh-frequency (SHF) magnetic fields revealed that, in the course of ontogenesis, there is a decrease in extent of acceleration of cardiac contractions in response to microwaves, i.e., ecological and species specificity of function of the cardiovascular system has a substantial influence on the nature of animal reactivity. The change in cardiac function with exposure to microwaves reflects the general patterns of regulation of this system, formed in the course of evolutionary development of the animal kingdom (M. I. Yakovleva, 1973).

Hemodynamic reactions are an integral response of the cardiovascular system to a given factor, and they may be identical in the presence of different routes of expression and primary mechanisms of effects on the organism. For this reason, it is important to investigate primary and intermediate mechanisms to assess reactions to microwaves: to study structure and function of tissues that are the first to perceive radiation, their enzymatic activity, exchange of gases, electrolyte balance, microcirculation, etc., investigation of balance of humoral regulatory systems, in particular, the sympathoadrenal system, investigation of distinctions of reflex regulation of the circulatory system during exposure to microwaves and clinical manifestations of adaptation to this factor.

Many researchers have studied the morphological changes occurring under the influence of microwaves. Histochemical studies (G. K. Gerasmiya, 1963) of the heart of rats exposed to SHF electromagnetic waves of thermal intensity (density flux of 150-250 mW/cm^2) showed that there were marked vascular disorders and dystrophic changes in muscle fibers, to the extent of formation of areas of granular and clumped breakdown. A sharp decrease in glycogen content of the myocardium was observed in animals exposed to SHF radiation, as compared to control animals. The author interprets this as the result of stimulation of anaerobic glycolysis, which emerges as a process of functional compensation in this instance.

M. S. Tolgskaya and Z. V. Gordon (1971), who exposed animals to electromagnetic waves in the millimeter, centimeter and decimeter ranges at thermal intensity (140-100 mW/cm^2), found significant vascular disorders in the form of severe plethora, perivascular and percellular edema and multiple small hemorrhages in the myocardium. Exposure to all ranges of waves resulted in irregular staining and fragmentation of myocardial muscle fibers.

Morphological examination of animals exposed to low intensities (1-10 mW/cm^2 for 5-9 months) failed to demonstrate vascular disorders and dystrophic changes. M. S. Tolgskaya, Z. V. Gordon et al. (1973), who made a morphological study of the hypothalamic region, hypophysis, adrenals and thyroid during intermittent and continuous exposure to microwaves approximating

industrial conditions, demonstrated phasic changes in functional activity, which were reversible.

In a study of regulation of autonomic functions, M. I. Yakovleva (1973) demonstrated that changes may develop in the autonomic system under the influence of microwave energy as a result of impairment of function of higher autonomic centers, as well as changes in afferent and efferent elements of the autonomic nervous system.

Authors who investigated the effects of SHF on the central nervous system by means of electrograms observed that the hypothalamus and cortex (Yu. A. Kholodov, 1966, and others), stem regions and reticular formation (Mickey, 1963; M. S. Bychkov, 1973) and limbic structures of the brain (K. V. Sudakov, G. D. Antimoniy, 1973) are the most sensitive to this factor.

Experiments involving parallel recording of biopotentials of the cortex, mesencephalic reticular formation and posterior hypothalamus (exposure to a flux density of 100 $\mu W/cm^2$ for 30 min) revealed that changes occur in the cortex in the 5th-10th min after exposure. Changes were demonstrable, virtually simultaneously, in the hypothalamus and mesencephalic reticular formation 10 or more minutes after exposure to SHF fields (I. S. Dronov et al., 1973).

Analysis of electrographic data after exposing rabbits to a flux density of 50 $\mu W/cm^2$ revealed that the posterior hypothalamic region was more sensitive. The changes in background activity in the hypothalamic region either diminishes or remained at the former level 1-2 weeks after exposure. With this level of radiation, the authors failed to detect a cumulative effect; however, in their opinion, such a prolonged altered functional state of the diencephalic systems is a tension reaction close to stress. The observed electrographic changes in function of diencephalic systems are considered by the authors as direct proof of the hypothesis of diencephalic genesis of the main clinical syndromes in individuals exposed to low-intensity microwaves.

It was experimentally established that EMF have a selective effect on limbic structures of the brain (K. V. Sudakov, G. D. Antimoniy, 1973). These authors attribute to this the change in behavioral reactions, conditioned reflex activity in animals and mental disorders in man under the influence of EMF, since we know from numerous investigations that limbic structures have a direct bearing on formation of emotions, motivations and memory.

In assessing the findings of studies dealing with the effects of microwaves on the central nervous system and changes associated with this in the cardiovascular system, we must mention the significance of ecological factors, which influence experimental animals.

Another series of studies dealt with humoral regulation, electrolyte balance, exchange of gases and activity of other systems of the organism under the

influence of microwaves. Evidently, the demonstrated changes should be interpreted, on the one hand, as the consequence of the above-described changes in the central nervous system and its [illegible] branches and, on the other hand, as the possible result of local processes occurring in the regions of maximum absorption of energy.

S. N. Nikogosyan (1964) and V. A. Syngayevskaya (1968) demonstrated that a drop of blood and organ cholinesterase is observed in animals with exposure to microwaves. This warrants the assumption that there is an increase in acetylcholine content, to which the hypotensive and negative chronotropic effect observed by other authors may be related, to some extent.

It is known that the condition of the heart and vessels is closely related to oxygenation of tissues and level of redox processes. Studies of exchange of gases after exposure of animals to microwaves revealed that, at intensities under the level of the thermal effect, there is an increase in tissular oxygen requirement, in arteriovenous difference for oxygen, due to more intensive utilization of oxygen by tissues (L. A. Khasbazarova, 1968, and others), whereas at thermal intensities there is a decrease in tissular oxygen uptake, apparently due to chemical thermoregulation (V. I. Mirutenko, Ya. I. Serkiz, 1968).

Research on activity of oxidative and reduction enzymes supplements, to some extent, the studies of gas exchange; these investigations established that exposure to nonthermogenic intensities increases activity of succinate dehydrase and cytochromoxidase, while thermal radiation depresses their activity. In the opinion of V. A. Syngayevskaya, these processes depend on the intensity and duration of exposure, wavelength and initial state of the animal.

When studying the cardiovascular system, it is important to know the state of electrolyte balance. With exposure of rabbits to microwaves for 10 and 20 min at a flux density of 100 mW/cm^2, the potassium ion content of blood serum dropped from 23±0.92 to 20±0.92, that of sodium ions rose from 252±8.0 to 274±4.8 and that of calcium ions dropped from 13±0.40 to 8.2±0.5 (V. A. Syngayevskaya, 1970).

A chronic experiment, involving exposure of rats to decimeter waves at 40 mW/cm^2 (V. V. Kulakova, 1964), failed to demonstrate changes in sodium and potassium ions either in blood plasma or urine, while the calcium level rose substantially, first in plasma, then in urine.

In the experiments of N. R. Chepikova (1963) on rabbits and dogs, with contact exposure of the region of the heart and remote exposure of the ventral aspect of the body (λ = 12.6 cm, flux density 0.1-0.5 W/cm^2), the changes in blood and myocardial potassium ion content were phasic and in opposite directions.

We can comprehend the causes of impaired electrolyte balance by studying the works dealing with the state of cell membranes under the influence of

of microwave energy. V.I. Shtemler (1973) and E. Sh. Ismailov (1971), who investigated the effects of decimeter waves on permeability of human erythrocytes (flux density of 45 mW/cm^2) in vitro detected a significant increase in overall flow of potassium ions through the cell membrane out and that of sodium ions, within. The authors believe that this effect is due to a change in membrane permeability as a result of changes in properties of hydrated fluid in the cell membrane under the influence of decimeter waves. Obviously, changes in ion content on either side of the cell membrane must change its electrical potential. The results of these studies are quite comparable to the experiments of N. R. Chepikova. The decrease in potassium ion content of the myocardium, which she demonstrated, is apparently related to a change in membrane potential, which is related to the change in membrane permeability and impairment of depolarization processes.

At the present time, some significance is attributed to autoimmune reactions in pathology of the cardiovascular system (P. N. Yurenev, 1970; I. S. Golod et al., 1973, and others).

Experimental investigation of the effect of microwaves on immunological activity of the organism revealed that microwave energy of thermal intensity, in the case of total body exposure, depresses production of antibodies to foreign allergen and, at the same time, has a sensitizing effect, inducing production of autoantibodies in the irradiated organism (G. I. Vinogradov, I. M. Karandakova, Ye. M. Makarenko, 1972). Thus, we cannot rule out the possibility that autoimmune reactions, with fixation under specific conditions of "antigen--antibody" complexes on the vascular walls, which could probably lead to a change in vascular tonus and other undesirable reactions, also play some role in the complex mechanism of changes in cardiovascular system function under the influence of microwaves.

As we conclude this survey of the experimental data, we should dwell specially on the experiments of A. G. Subbota (1972), who established the deadaptational and decompensating effects of microwaves on the nervous and cardiovascular systems, with respect to developing resistance to diverse environmental factors (noise, high ambient temperature, physical load). In addition, this author demonstrated that one can develop adaptation in animals of their cardiovascular system to microwave energy of thermal and nonthermal intensities. It is manifested by hemodynamic stability, and it is related to involvement of the nervous system. The author evaluates progression of changes in these functions under the influence of microwave energy and appearance of symptoms of functional impairment of an organ or system as a manifestation of the cumulative effect of microwaves. A. G. Subbota interprets the signs of adaptation and accumulation, as well as reliability of adaptational mechanisms referable to microwaves as the main criteria for determination of radiosensitivty and radiovulnerability referable to microwaves.

To sum up the results of experimental studies, it can be assumed that the effect of microwaves on the cardiovascular system reflects several pathogenetic mechanisms:

1) direct effect of microwave energy on the central nervous system;
2) changes in the system of peripheral reception with absorption of energy;
3) reflex reactions of the heart and vessels in response to stimulation of exteroceptors and interoceptors that absorb radiation energy;
4) direct effect of radiation on the myocardium, vessels and nerve centers of cardiovascular regulation (at the appropriate wave lengths).

All these mechanisms undergo substantial modification, depending on the ecological and species specificity, and the original functional state of the nervous and cardiovascular systems.

In view of the similarity of action of primary biophysical mechanisms of microwave radiation on animals and man, let us discuss some of the clinical facts. First of all, it must be noted that, in the opinion of some authors, "cardiac" symptoms only appear when the changes in the nervous system reach a sufficient degree (V. M. Malyshev, F. A. Kolesnik, 1968). The nature and extent of functional changes in the nervous system depend on the intensity and duration of exposure, individual sensitivity of the organism and premorbid state.

Our studies and the data in the literature (N. V. Tyagin, 1962-1968; I. G. Ramzen-Yevdokimov, V. A. Sorokin, 1970; Klimkova-Deutschova, 1963, and others) enable us to single out three typical syndromes due to radiowaves: acthenic, which is observed at the early stages of illness; asthenovegetative, with vascular dysfunction, and hypothalamic. Efforts have been made to single out an independent nosological form of occupational disease, radiowave sickness, on the basis of investigation of the distinctions of development and order of formation of these clinical syndromes.

Studies of the cardiovascular system of individuals exposed to SHF radiation demonstrated objectively lability of the pulse and changes in arterial pressure (hypotension and hypertension). Tables 6 and 7 list data on the incidence of hypotension and hypertension, and they show that the highest percentage of cases of arterial hypotension was observed by authors who pursued their studies in 1948-1961, and the highest percentage of cases of hypertension, by those who worked in 1966-1973. We cannot rule out the possibility that this could be related to the general increase in incidence of arterial hypertension in the last few years, as well as the fact that the average age of workers is older.

The results of studies of peripheral circulation, according to findings from capillaroscopy and plethysmography, are quite contradictory and indicate both the presence of spams and atonia of capillaries and arterioles (M. T. Sverdlina, 1968, and others).

We failed to demonstrate pathology of the circulatory system in a rheographic study of the hands and feet of 59 patients with radiowave sickness.

Table 6. Incidence of arterial hypotension among individuals exposed for long periods of time to SHF fields (according to the data of different authors)

Author and year	Subjects' occupation	Number of subjects	Incidence of hypotension, %
A. A. Kevork'yan, 1948	Blue-collar worker	87	38
Yu. A. Osipov, 1952	" " "	108	22.2
V. A. Shipkova, 1959	Radar specialist	110	About 20
A. A. Orlova, 1960	Blue-collar worker	525	26-33
N. V. Uspenskaya, 1961	" " "	100	30
R. N. Vol'fovskaya et al., 1961	" " "	101	27-45
Ye. I. Smurova et al., 1962	" " "	54	53.7
L. T. Frolova, 1963	" " "	172	25.6
F. I. Komarov, L. V. Zakharov, F. A. Kolesnik, 1963	" " "	53	22.6
Ye. V. Gembitskiy, 1966	Radar specialist	210	14
M. N. Sadchikova, K. V. Nikonova, 1971	Blue- and white-collar workers	100	7-3

Table 7. Incidence of arterial hypertension under the chronic effect of SHF fields

Author and year	Subjects' occupation	Number of subjects	Incidence of hypotension, %
L. G. Frolova, 1963	Blue-collar worker	172	5.8
A. M. Kapitanenko, 1964	Operator	66	7.6
E. A. Drogichina et al., 1966	Blue-collar worker	100	17
G. G. Lysina, M. B. Rappoport, 1969	" " "	85	15
N. Ya. D'yachenko, 1970	Operator	62	29
M. N. Sadchikova, K. V. Nikonova, 1971	Blue-collar worker	215	14-23
V. I. Muratov, A. P. Turayeva, 1972	Operator	25	28
V. P. Medvedev, 1973	Mental labor	222	12.6

A study of central hemodynamics of healthy young people with short work tenure, as well as individuals with neurocirculatory dystonia of the hypotensive type, conducted by many authors, revealed increased blood minute volume and decreased peripheral resistance. In individuals with lengthy tenure, which of course means that they are older, as well as in those with neurocirculatory dystonia of the hypertensive type, the opposite findings were made for these parameters. Many have reported increased tonus of arteries of the muscular type.

Authors who studied circulation believe that changes in parameters thereof develop primarily as a result of impairment of structure and function of systems involved in maintaining homeostasis, namely the central nervous system, endocrine and neurohumoral systems.

Various authors studied exchange of gases in tissues and blood, as well as electrolyte balance of individuals subject to exposure to microwaves in order to investigate the pathogenetic mechanisms of hemodynamic disorders (I. V. Pavlova, E. A. Drogichina, M. N. Sadchikova, I. A. Gel'fon, 1968; G. G. Lysina, 1972). According to their findings, there is some decrease in oxygenation of blood and greater tissular capacity to absorb oxygen in individuals exposed to microwave radiation. The change in electrolyte balance consists of a drop in blood serum potassium and chlorides and elevation of sodium and chlorides in erythrocytes.

According to our data, hypercholesterolemia was demonstrated in over 50% of the cases of radiowave sickness. V. P. Medvedev (1973) observed hypercholesterolemia and alteration of blood lipid content, the mean indices of which differed appreciably from the corresponding age-related control, in essentially healthy individuals engaged in mental work related to sources of SHF radiation. This fact, along with the increased number of cases of essential hypertension and cardiac ischemia in the group engaged in mental labor, which currently or previously had contact with microwaves, led to the conclusion that contact with microwave radiation may be considered a substantial risk factor in development of essential hypertension and cardiac ischemia.

The results of observations of over 1500 individuals whose work involved exposure to EMF of high (HF) ultrahigh (UHF) and superhigh (SHF) frequencies enabled us to determine that deviations in function of the nervous and cardiovascular systems are observed primarily among workers involved with regulating, adjusting and testing the equipment of radar stations in the final completion shop of radio industry enterprises. The main clinical syndromes of cardiovascular disorders with exposure to SHF fields developed against the background of progressive asthenia (neurasthenia), more often after working for 5-10 years on jobs involving exposure to SHF EMF (flux density of up to several mW/cm^2). The clinical distinctions of the observed syndromes consisted of the following:

1. Asthenic (neurasthenic) syndrome, with vegetovascular dysfunction of the hypotensive type. Typically, there are complaints of headaches (heaviness of the head), increased fatigability, irritability, sleep disorders and periodic pain in the region of the heart. No organic pathology of the cardiovascular system was observed. Half the subjects presented periodic, moderate hypotension (systolic arterial pressure 90-95 mm Hg). Diastolic and pulse pressure were in the normal range. In some cases, arterial hypotension was associated with sinus bradycardia (pulse rate up to 59/min). The latter was observed less often in seated position (142 patients) and more often in supine position (222 people), which was indicative of lability of the

pulse when counted in orthostatic position. There was no substantial change in general condition on the days that low arterial pressure was recorded, and only a few people presented more complaints of an asthenic nature. Electrocardiography failed to demonstrate pathology. We should only mention that, in the presence of bradycardia, there was appearance of a high, sharp-peaked T wave, mainly in the chest leads and this, in view of the clinical data, is interpreted as a manifestation of vegetative dysfunction. As a rule, stroke and minute volumes, all forms of arterial pressure and peripheral resistance remained normal. Only a few individuals presented a minor drop of mean dynamic arterial pressure and increase in minute blood volume. Peripheral resistance was lower than it should be, but corresponded to the working, i.e., actual minute blood volume.

Thus, the increased minute volume in such patients could be considered an adequate reaction to decreased peirpheral resistance. Studies of cerebral circulation by the method of rheoencephalography failed to reveal disturbances with regard to pulse filling and tonus of intracranial and extracranial vessels. Consequently, the hypotensive reactions observed were mild, and they had no adverse effect on the condition of the heart and indices of systemic and local hemodynamics.

2. Asthenic (neurasthenic) syndrome with vegetovascular dysfunction of the hypertensive type proceeded, in some cases, with attacks of a sympathoadrenal nature and marked neurasthenic symptoms. The patients were excitable, emotionally labile, suffered from sleep disorders, diminished memory, sporadic headaches associated with nausea. Over one-third of the patients compalined of vertigo, brief fainting spells, noise in the head and obscured vision. Hyperhidrosis, bright red, diffuse and persistent dermographism, cooling and marbling of the integument of the limbs, palpebral and digital tremor, with the hands extended, were observed. In several cases, several years later, against such a background there was development of marked vegetovascular dysfunction of the hypertensive type, with periodic cerebral crises of the sympathoadrenal type. During an attack of severe headache, there was trembling, pallor or reddening of the face, generalized hyperhidrosis, marked emotional disorders and fainting spells. The patients reported compression pain in the region of the heart, the sensation of difficult breathing, "shortage of air"; as a rule, there was moderate elevation of arterial pressure, particularly diastolic (110 to 110 mm Hg) followed by severe weakness and normalization of arterial pressure. A typical finding was a change in sugar curves (diabetic and double), impairment of correlation between excretion of epinephrine and norepinephrine, especially during an attack. Between the paroxysmal attacks, administration of epinephrine (0.3 ml 0.1% solution) elicited marked vegetovascular reactions and a marked change in physiological dynamics of catecholamine excretion. Subfebrile temperature was not uncommon in patients with vegetovascular dysfunction. The chief complain was pain in the region of the heart, which was encountered in almost 70% of the cases. In 23%, the pains were of a compressing nature, with irradiation into the left hand and scapula. As a rule, the cardiac pain appeared against a marked neurasthenic background, with vivid emotional coloration; it was persistent and responded

poorly to treatment with vasodilating agents. Some patients reported periodic palpitations and arrhythmia in the region of the heart and dyspnea upon exercising. There was marked lability of the pulse when moving from horizontal to vertical position (tendency toward bradycardia in horizontal position in 22% of the cases and in seated position, in 7%; tachycardia in supine position in 20% and in seated position, in 36%). Arterial pressure was unstable, and it was elevated in almost 50% of the patients. Individuals with normal arterial pressure not infrequently presented a pathological reaction to a physical load, with elevation of systolic and, particularly, diastolic pressure. Constriction of retinal arteries was observed. Tachyoscillography revealed a tendency toward elevation of all forms of arterial pressure and an increase in peripheral resistance. If we consider that the rate of propagation of the pulse wave in musclar vessels was higher, which was also associated with an increase in correlations between modulus of elasticity of vessels of the musclar and elastic type, it may be assumed that the increase in resilient properties of vessels of the muscular type was due to angiospastic reactions.

More often, with elevation of arterial pressure blood minute volume decreased, and this was evaluated as an adequate reaction to increased peripheral resistance, which was above the proper level (by 20-30%), and in some cases working level, i.e., corresponding to a given minute volume. Thus, in this group of subjects, hypertension was spastic in nature.

In some patients with marked vegetovascular disturbances, we observed an increase in minute blood volume combined with elevation of all forms of arterial pressure and high indices of peripheral resistance. This was indicative of marked impairment of mechanisms that regulate the correlation between peripheral and central hemodynamics, and this was also consistent with the clinical findings. According to rheoencephalography, there was a decrease in intensity of pulsed filling, with predominant increase in tonus of intracranial and extracranial vessels (70%). The changes were functional in nature, as confirmed by the reaction to nitroglycerin. Some patients presented some extension of the margin of the heart to the left, due to hypertrophy of the left ventricle; heart tones were dull in almost half the cases, and in some of them there was a systolic murmur. Electrocardiography revealed a decline, smoothing or inversion of T wave, most often in the two standard or left chest leads, combined with a shift of the S-T segment in 32% of the patients with predominantly hypertensive reactions and especially vegetovascular attacks. These changes usually occurred during an attack; not infrequently, they were associated with persistent pain in the region of the heart. Vasodilating agents often failed to give relief (including nitroglycerin). In some cases, during the period of an attack, ventricular extrasystole was recorded, and one patient had attacks of paroxismal fibrillation. In most cases, the EKG changes were transient and rapidly regressed after an attack. Not infrequently, it was difficult to differentiate between the diagnosis of coronary insufficiency and metabolic disturbances, occurring as a result of vegetative dysfunction with output of catecholamines, in the presence of a persistent pain syndrome and lack of response to vasodilating agents. Dynamic observation of the patients acquired special importance to settle this question.

Let us submit two typical cases:

1. Patient R., began to work at the age of 27 years as a controller involving contact with microwave sources. There is no hereditary or prior history burden. After 5 years he developed increased fatigability, irritability, poor sleep, persistent headaches and pain in the region of the heart, which did not respond to vasodilating agents. No pathological changes were found in the cardiovascular system; arterial pressure 110/39 mm Hg. After 7 years he began to have attacks of severe general weakness with vertigo, sensation of "shortage of air," perspiration and brief elevation of arterial pressure (140-150/100 mm Hg). The EKG, taken during an attack, periodically showed ventricular extrasystole and decline of the T wave in the left chest leads ($T_{V_{4-6}}$). After the attack, the EKG reverted to normal relatively rapidly. Examination of the eye grounds revealed constriction of retinal arteries.

According to the results of mechanocardiography, recorded in a period free from attacks, when the patient had normal arterial pressure (120/70 mm Hg), there was a significant increase in peripheral resistance, 68% higher than it should be, there was a corresponding 30% decrease in minute blood volume. There was an increase in rate of propagation of the pulse wave, mainly in vessels of the muscular type, with increase in relationship between elasticity moduli (E_M/E_E 1.76). Thus, a patient, who had worked for a long time with radiowave sources in the SHF range, subsequently developed asthenoneurotic reactions, then attacks of the diencephalic type with elevation of arterial pressure and extrasystole. The clinical findings and results of instrument tests were indicative of the spastic nature of the hypertensive reactions.

2. Patient K., began to work as a controller at the age of 25 years and came in contact with microwave sources. There is no hereditary or prior history burden. After 5 years there was development of neurasthenic manifestations in the form of headache, increased fatigability, irritability and poor sleep. Arterial pressure was in the range of 120/70-130/80 mm Hg. Eight years after he started on that job, when he was 33 years old, he began to have frequent cerebral attacks: severe headache, trembling, reddening of the face, generalized hyperhidrosis, occasional, brief fainting spells; arterial pressure remained normal. After one of the attacks, marked changes were found on the EKG: S-$T_{V_{1-4}}$ interval is elevated in an arch and changes into a negative $T_{V_{1-4}}$ wave with biphasic $\pm T_{V_3}$. After 1.5 h, the EKG indices improved ($T_{V_{1-4}}$ wave became less negative) and reverted to normal after 1 month. The patient did not work with microwave sources for 1 year. The attacks stopped and arterial pressure was normal. The patient became calmer, but pain in the region of the heart persisted and was curbed only after intake of nitroglycerin.

Thus, a patient with no burden in his history (no history of head trauma, infections processes, hereditary predisposition for essential hypertension and cardiac ischemia, as well as no bad habits) developed marked vegetovascular dysfunction with signs of hypothalamic insufficiency, hypertensive reactions and angina pectoris after working for 13 years on a job involving exposure to EMF in the SHF range.

Observations revealed that the hypertensive reactions are gradually added to vegetative attacks. Such changes, with subsequent development of chronic coronary insufficiency, were diagnosed in 7% of the cases. In 4 of the individuals who had worked under adverse conditions for over 10 years, there was development of myocardial infarction, which was preceded by a long period of asthenoneurotic reactions and marked vegetovascular dysfunction. In isolated cases, there was dynamic impairment of cerebral circulation. At the long term, we observed development of essential hypertension (cerebral or cerebrocardiac form). Investigation of the order in which different symptoms develop, with due consideration of the nature of work, intensity of exposure and occupational tenure, is of special importance to determination of the etiological link between the above-mentioned nonspecific cardiovascular syndromes and effects of microwaves.

In order to define the distinctions of development of cardiovascular disorders, a dynamic study was made of a group of workers in the final shops for a period of 3-6 years, and in some cases 9-12 years.

Analysis of the data revealed that there were 3 groups, depending on the arterial pressure at the first examination: the first group of workers (17 people), with periodically recorded arterial hypotension (systolic pressure 90-100 mm Hg); second group (17) with normal arterial pressure; third group (9) with hypertensive reactions (arterial pressure of 145/90 mm Hg or higher). The mean age and work tenure of individuals in these groups were about the same (31 to 32 years of age; tenure of 7, 6 and 8 years, respectively).

Most of the 17 workers with a tendency toward arterial hypotension were in good health when first examined (asthenic syndrome in 9 cases and mild vegetovascular dysfunction in 3). Only 4 workers presented mild hypertensive reactions 3-6 and 9-12 years later. No pathology referable to the heart and vessels was found in any of the first group of patients. The first examination of the second and third groups of workers, with normal or high arterial pressure, revealed that only 5 out of 26 were in good health, asthenia with vegetovascular dysfunction was diagnosed in 11. After 3-5 years, 16 of the 26 workers in the second and third groups presented marked vegetovascular dysfunction with attacks of the diencephalic type, associated with elevation of systolic and, particularly, diastolic pressure to 105-110 mm Hg. Chronic coronary insufficiency developed in 7 workers and essential hypertension, in 3.

Thus, several years of observations revealed that, in controllers, reactions referable to the cardiovascular system follow changes in the nervous system, particularly its higher autonomic branches, while the nature and severity thereof depend on individual distinctions of the organism: in some cases, only mild asthenic reactions, with sinus bradycardia and arterial hypotension, without signs of systemic and local hemodynamic disorders, may be observed for a long time; in others (in whom hypotensive reactions were never observed), there is development of vegetovascular dysfunction of the hypertensive type, with signs of hypothalamic insufficiency and angiospastic reactions, which lead to impairment of cerebral and coronary circulation in a number of cases. P. M. Medvedev (1968), G. G. Lysina, M. B. Rappoport (1968) and others have also observed analogous changes in individuals working with SHF field sources.

The presence of hypotensive reactions with relatively benign course and hypertensive reactions with unfavorable course raises a number of questions, with respect to the role of the original state of pressor and depressor mechanisms in formation of adaptational and pathological reactions of the cardiovascular ysstem to SHF fields. Vegetovascular dysfunction with hypertensive reactions is of greatest clinical significance.

In order to form a prognosis, treat and make an expert determination of disability of such patients, it is quite important to evaluate the pathogenesis of the hypertensive syndrome, to pinpoint the role of disturbances in central and peripheral hemodynamics in development thereof. Depending on the distinctions of hemodynamic disturbances, two main forms of hypertension are identified; spastic, due to peripheral angiospasm, and hyperkinetic, which is due essentially to an increase in minute blood volume. The two forms are interrelated; the hyperkinetic one not uncommonly precedes the spastic (I. K. Shkhvatsabaya, 1972; Ye. M. Tareyev, A. V. Sumarokov, 1972; Richard, 1969, and others). Differential diagnostics of these forms of hypertension is of much practical significance, main for the choice of rational therapy. The angiospastic form of hypertension, with considerable increase in peripheral resistance, was present in virtually all of the patients under our observation.

The measured exercise test is of some value in detecting early vascular reactions. In a mass screening of essentially health individuals with long work tenure presenting normal arterial pressure at rest, not infrequently we observed elevation not only of systolic, but diastolic pressure after the physical load (60 hops in 30 s), which is indicative of impaired regulation of vascular tonus with a tendency toward angiospastic reactions. This conclusion is confirmed in the latest works of T. A. Sorokina (1972) and R. P. Kalyuzhnaya (1972), who demonstrated that significant activation of the sympathoadrenal system is observed in individuals with hypertension of any etiology, when submitted to the exercise test. In the patients we screened, a high output of catecholamines was observed during the attack periods. The submitted data confirm the nonspecificity of vegetovascular dysfunction in individuals whose work involves exposure to SHF EMF.

The changes referable to the heart are not specific either. Pain in the cardiac region, lability of pulse, extrasystole, not infrequent decline or rise of T wave on the resting EKG or after a load may be observed in the presence of vegetovascular dystonia of any etiology. Experimental and clinical observations warrant the assumption that the cardiac pain in most such cases is due primarily to lowering of the threshold of nociceptive sensitivty, impairment of central nervous regulation and, during sympathoadrenal attacks, to the effect of catecholamines. These factors may induce myocardial dystrophy, with impairment of its bioelectrical activity (I. B. Gordon, M. P. Stepanov, 1970; S. V. Rutsay, 1972; B. Yu. Dobrin, 1972, and others).

Coronary insufficiency, with the typical pain syndrome and EKG changes, may be related to exposure to SHF fields in some cases, with gradually developing and long-lasting vegetovascular dysfunction. These data are confirmed in experiments on animals and clinical observations (O. M. Gorbachev, 1965; Ye. F. Lobkova, M. Kh. Pluzhnikova, 1966, and others).

The lack of specificity of some symptoms and clinical syndromes of cardiovascular pathology, with reference to SHF fields, makes it necessary to take into consideration the set of all factors characterizing individual distinctions of the body (heredity, age, constitution, prior illnesses, bad habits) and working conditions (density flux, radiowave range, tenure of work under specific conditions, as well as other deleterious work-related factors, such as microclimate, intensity of physical and mental load, etc.) in order to determine the etiology of the disease.

Recognition of the leading role of SHF fields as a risk factor in development of illness, also makes it necessary for there to be a specific order of development of symptoms, with functional changes in the nervous system playing the leading role: long-term asthenic background with neurasthenic manifestations, marked emotional instability, then vegetovascular dysfunction, which often proceeds with periodic attacks and signs of hypothalamic insufficiency. The differential diagnosis must also be made, first of all, with reference to diencephalic syndromes of infectious and traumatic etiology, as well as essential hypertension. Essential hypertension, like cardiac ischemia, may be interpreted in some cases as the outcome of an occupational disease induced by microwaves. It is imperative to take into consideration other etiological causes (endocrine dysfunction due to thyrotoxicosis, menopause, etc.) in determining the role of SHF fields in development of vegetovascular dysfunction.

There is no specificity or independent diagnostic significance to cardiac changes demonstrable on the EKG, to which prime significance is sometimes attributed in determining the link between illness and SHF fields. Such symptoms as bradycardia, tachycardia, decline or elevation of T wave, are usually due to a change in autonomic regulation. The presence of persistent rhythm disturbances (blocking of the bundle of His limbs, fibrillation, persistent extrasystole) and considerable myocardial dystrophy with stasis rules out, rather than confirms a link between cardiac pathology and the

effects of SHF fields. Thus, comprehensive analysis of each specific case, with due consideration of the aggregate of industrial, domestic and clinical data, is required to determine the etiological role of electromagnetic waves at radio frequencies in development of vegetatovascular dysfunction, hypertension and cardiac ischemia.

Treatment of vegetovascular dysfunction in individuals whose work involves exposure to SHF fields should be administered with consideration of the etiology of the disease, individual distinctions of the organism and type of vegetative reactions with development of a given syndrome. It is imperative to remove patients from work involving contact with SHF fields for the duration of treatment (issuing a disability certificate for 1-2 months).

For patients with the asthenic syndrome, it is sufficient to prescribe general fortifying therapy and sedatives (bromides, Leonorus, valerian root, hawthorn, corvalol). Cholinolytics (atropine, amizil) and products with combined action (belloid, bellaspon) are recommended when there is prevalence of vegetovascular disorders. Occasionally, intravenous infusion of glucose preceded by administration of low doses of insulin elicits a good response. The therapy includes therapeutic exercise, hydrotherapy and psychotherapy.

In addition to general fortifying therapy, minor tranquiliziers, such as seduxen, elenium, trioxazine and antihistamines that potentiate their action (dimedrol, pipolphen, suprastin), as well as vasodilating agents are indicated for patients with vegetovascular dysfunction of the hypertensive type, especially if their are attacks of a sympathoadrenal nature. Of the wide assortment of modern hypotensive agents, it is preferable to prescribe magnesium sulfate, which has a sedative effect, combined with reserpine, which is a tranquilizer. If necessary, agents that have a direct effect on the vascular wall (papaverine, no-shpa [6, 7, 3',4'-tetraethoxy-1-benzal-1,2,3,4-tetrahydroisoquinolone hydrochloride] and others) are prescribed.

In the presence of ischemic heart disease, agents are required that improve coronary circulation (nitroglycerin, sustac) and metabolic processes in the myocardium (falicor, intensain and others). ATP and group B vitamins elicit a good therapeutic response. In view of the high sensitivity of patients, the choice of drugs requires a strict and individual approach. One should be particularly cautious in prescribing narcotics. In the presence of attacks (of the sympathoadrenal type), one can recommended low doses of aminazin, propazin, and occasionally pipolphen combined with injectable vasodilating agents is sufficient.

With proper organization of dispensary supervision and treatment of patients with the asthenic syndrome and negligible vegetovascular dysfunction, without hypertensive reactions, they can continue to work.

The results of many years of observations indicate that patients with marked vegetovascular dysfunction and hypertensive reactions, particularly with attacks, require rational counseling with regard to employment. One can

expect recovery or stabilization of a pathological process only with prompt transfer of such patients to another job, unrelated to SHF radiation.

The data in the literature and our own investigations enable us to summarize some of the pathogenetic mechanisms of biological effects of microwaves, to voice some general comments on clinical diagnostics of radiowave effects and outline the prospects of research on primary mechanisms, as well as detection of early preclinical signs of the effects of microwave energy on the cardiovascular system.

Experimental and clinical studies have shown that the cardiovascular system presents nonspecific reactions to microwaves; the changes in individuals whose work involves contact with such radiation are characterized by the syndrome of neurocirculatory dystonia. This syndrome probably develops as a result of the effects of microwave energy on peripheral reception and microcirculation, the myocardium, great vessels and interoceptors of internal organs (in the presence of the appropriate wavelengths), as well as various branches of the central nervous system related to regulation of cardiac function.

Expression of the reflex mechanism apparently begins with a change in properties of excitable cell membranes, which leads to an increased influx of afferent impulsation to specific branches of the central nervous system. Concurrently, there may also be a change in efferent impulsation, in view of the selective effect of radiation on radiosensitive structures: cortex, hypothalamus, reticular formation of the brain stem and limbic structures. Summation of these mechanisms evidently leads to impairment of normal neuroregulation in the organism, aggravating metabolic processes, already altered after the first contact with radiation, in tissues, thus closing a vicious circle.

The above-described pathogenetic mechanism is clinically manifested by lability of the pulse and arterial pressure, inadequate reactions of the cardiovascular system to physiological loads, as well as dosorders referable to correlations between central and peripheral hemodynamics.

The severity of cardiovascular disorders depends, as shown by several authors, on individual distinctions, ecological and species specificity of the nervous and cardiovascular systems.

Since the syndrome of neurocirculatory dystonia is not specific to the effects of microwaves and numerous other etiological factors play a significant role in its development, while the quantitative characteristics of radiation are unknown, it is difficult to determine the prime factor in the origin of illness and there are several important problems to solve for demonstration of reliable early signs of the reaction to microwaves in individuals engaged in different professions. It is interesting to investigate the role of pressor and depressor mechanisms in formation of adaptive and pathological reactions of the cardiovascular system to electromagnetic fields. The question of the role of microwave radiation

in development of essential hypertension and cardiac ischemia, which is presently debated in the literature, requires further investigation. Reliable results on this score can only be obtained by conducting epidemiological studies of large groups of people, using standard criteria for identifying these states.

10,657
CSO: 1870

CHAPTER 6. THE CARDIOVASCULAR SYSTEM AS AFFECTED BY INTENSIVE INDUSTRIAL NOISE

[Text] In the last few years there has been considerable interest in the matter of inadequate effects of noise on the human body and, first of all, its effect on the nervous and cardiovascular systems. It is known that noise elicits functional disturbances of the nervous system, which proceed in the nature of hypersthenic or hypasthenic neurosis combined with other neurosis-like manifestations, including local vascular disturbances. The nerve centers can influence the cardiovascular system directly through extracardiac nerves, which play a substantial role in regulation of circulation. For this reason, the changes that occur in the nervous system under the influence of a sonic (noise) stimulus can, of course, affect the functional state of the cardiovascular system.

According to data in the literature, noise can influence general and, in particular, cardiovascular morbidity. L. N. Vlasov, T. G. Isanina, R. G. Levina and V. A. Polyanskiy (1959) developed outpatient charts on individuals living in the vicinity of engine testing stations and residents of a "quiet" part of the city; essential hypertension and vascular hypotonia were observed 1.4 times more often among the former. I. S. Ivatsevich (1963) found essential hypertension and heart disease much more often among workers in the textile industry exposed to intense noise, than in workers in the radio engineering industry and instrument building, where there was virtually no noise. According to the observations of A. T. Rusinova (1973), essential hypertension, coronary cardiosclerosis, angina pectoris and myocardial infarction are encountered relatively often among individuals whose work involved exposure to intensive noise for a long period of time.

Graff, Bockmuhl and Tietze (1969) discovered that essential hypertension and other circulatory diseases are encountered considerably more often among boiler makers exposed to noise at a level of 95-110 dB, as compared

to individuals whose work did not involve exposure to noise. The highest incidence of hypertension was observed among individuals 25-35 years of age. In the authors' opinion, onset of essential hypertension with exposure to noise may be attributed to impairment of cerebrovisceral correlations.

Numerous observations of workers in "noisy" shops indicate that, in addition to specific complaints of impaired hearing, they often reported cardiac pain, palpitations and intermittent beats (M. Ye. Khaymovich, 1961; B. A. Krivoglaz, V. C. Boyko, L. A. Zaretskaya, D. P. Kachalay, 1966, and others). In these individuals, cardiac complaints do not occur with physical loads, but at rest and in the presence of nervous and emotional tension.

The data concerning the effects of intense noise on the cardiovascular system are quite contradictory. G. I. Vopilkina (1959), Grandjean (1959) observed a faster pulse, while T. A. Orlova (1965) and Lehmann (1956) discussed the reverse. L. Ye. Milkov (1963), who made a study of the pulse rate of individuals working with exposure to intense wide-band noise, found a tendency toward bradycardia before the start of the shift in almost one-third of the subjects. During the work day, however, their pulse changed both in the direction of becoming faster and slower.

In our observations of marked lability of the pulse under the influence of intense noise, we demonstrated temporary changes in rate thereof in the course of the work day and more constant changes with increase in work tenure with exposure to noise, and they were in the same direction, in the direction of slowing.

There are rather contradictory data concerning arterial pressure. There are indications of both the hypotensive and hypertensive effects of noise, which are usually related to its parameters--intensity and spectral composition.

A. I. Vozhzhova, I. A. Sapov (1960), A. A. Andryukin (1961), T. A. Orlova (1965), Holstein (1958), Steinmann, Taddi, Windmer (1955) and others, who examined essentially healthy individuals exposed to noise on their jobs, found their arterial pressure to be elevated. On the basis of a survey of a large group of workers in different shops at a ballbearing plant, A. A. Andryukin demonstrated a high incidence of essential hypertension among individuals exposed to noise. It was established that there was an increase in hyperreactive individuals with increase in work tenure under noisy conditions. Different results were obtained by G. I. Vopilkina (1959), A. A. Arkad'yevskiy (1963), Bugard (1958), Bode (1960) and others. According to their observations, arterial pressure drops under the influence of noise.

Of interest are data on arterial pressure in different occupational groups, with different characteristics of industrial noise, depending on work tenure under noisy conditions, as well as fluctuations of arterial pressure in the course of a work shift.

A. M. Volkov and T. L. Sosnova (1963) made a study, under laboratory conditions, of the effects of high-frequency noise on healthy individuals 20-25 years of age, the nature of whose usual work was unrelated to exposure to noise. After 5 minutes in noisy shops, the subjects presented a consistent elevation of arterial pressure corresponding to the increase in intensity of noise. But if the intensity of noise was not increased, individuals with signs of increased excitability of the cerebral cortex presented elevation of systolic pressure to 180 mm Hg after exposure for 5-10 min to 90 dB noise, whereas after repeated subsequent exposure the arterial pressure dropped critically (by 50-60 mm Hg) to the base level. The authors expound the hypothesis that intense noise is instrumental in the hypotensive state.

According to the data of I. A. Benyumov (1963), changes in arterial pressure depend on the functional state of the nervous system, work tenure, intensity and spectral composition of noise among individuals whose work involves exposure to noise. The author observes that hypotension is encountered with short work tenure and hypertension, among workers with long tenure.

G. I. Vopilkina (1959), who measured arterial pressure of women employed in the weaving and spinning industry every hour in the course of the work day, reported a consistent moderate decline for the first 4 h of work. After a 20-min rest, it rose, but was again low at the end of the shift.

N. N. Krylova (1958) screened women working in two shops at a knitwear factory, where the noise was of the order of 80 dB, of high frequency in one shop (3200-4800 Hz) and low frequency in the other (100-150 Hz). The author observed more marked changes in arterial pressure with exposure to high-frequency noise than low-frequency noise of the same volume; moreover, work tenure with exposure to noise was a factor. More often, changes appeared in individuals with less than 10 years of tenure. Dynamic measurement of arterial pressure during the shift revealed that a maximum elevation (by 20-30 mm Hg) is observed with high-frequency noise after working for 2 h. By the end of the shift, although pressure did drop it did not exceed the base level. With exposure to low-frequency noise, some elevation of arterial pressure was demonstrable by the end of the first hour of work; thereafter it slowly rose toward the end of the work day (by 10-15 mm Hg as compared to the base level). A study of the effects of high-frequency noise of the same volume on subjects revealed reactions in different directions: arterial pressure rose in some subjects and dropped somewhat in others (N. N. Krylova, 1958).

B. A. Krivoglaz, V. G. Boyko, L. A. Zaretskaya and D. P. Kachanay (1966) observed arterial hypotension combined with signs of myocardial dystrophy in workers of the doubler and weaving industry. I. I. Galakhov and A. I. Kachevskaya (1956), who studied the cardiovascular system of 400 workers in lathe, automatic and cigaret-making shops, where the volume of noise was in excessive of the permissible norms, demonstrated elevation of arterial pressure (by 10-20%) more often than among workers in other occupations. The arterial pressure rose in accordance with increase in work tenure.

G. T. Chukmasova (1957) studied changes in arterial pressure in workers of a nail-making shop (the noise level at the work places was in the range of 99-110 dB) and shoe factory (noise of 90-116 dB) in the course of the work day. She found that arterial pressure taken before the work shift, taken as the base level, was somewhat above normal values for the age of the subjects and directly related to work tenure. In the course of working, most subjects presented a 12-14% drop of arterial pressure by the end of the shift, as compared to the base level.

A study conducted by V. I. Skok (1963) revealed that arterial pressure may rise or drop in the course of the work day among workers in a nail-making shop, where the noise level was in the range of 95-105 dB. Elevation of arterial pressure was observed more often among older individuals than younger ones toward the end of the shift.

V. F. Rudenko (1963) screened two groups of diesel engine testers. The noise level at the work places of both groups was in the range of 110-120 dB and 110-115 dB; there was prevalence of moderate frequencies (320, 400, 500 Hz) in the noise spectrum of one group and high frequencies (maximum energy in the band of 2500 Hz or higher) of the other. The systolic arterial pressure was in the hypertensive range (140 mm Hg or higher) in the group exposed to moderate-frequency noise and 15.6% of those exposed to high-frequency noise. Dynamic studies of arterial pressure of engine testers in the course of the work shift (4-6 days) and after work were indicative of lability within the range of 35-40 mm Hg.

The above author singles out three types of reactions of systolic pressure by the end of the shift with exposure to noise: hyperdynamic (40 mm Hg elevation of systolic arterial pressure), hypodynamic (up to 40 mm Hg drop) and normodynamic (fluctuations in the range of ±10 mm Hg).

There are indications in several works of changes in different parameters of arterial pressure under the influence of noise. A. M. Volkov (1958), V. F. Rudenko (1959) and others believe that noise induces mainly elevation of systolic pressure.

Toddi and Windmer (1955) found elevation of diastolic pressure. According to the data of A. T. Rusinova (1963), L. Ya. Basamygina (1966) and others, unstable arterial pressure is observed with exposure to noise.

The studies we conducted revealed that lability of arterial pressure is demonstrable quite soon after regular exposure to intense noise. Along with hypertensive reactions, vascular hypotonia may also be observed in individuals with relatively short tenure of work involving exposure to noise. Tachy-oscillography made it possible to demonstrate that not only systolic and diastolic pressure, but mean dynamic pressure, which is the most constant parameter, changes under the influence of intense noise. Dynamic observations are also indicative of unstable arterial pressure on different days and in the course of a shift, in the same individuals. However, it can be

noted that systolic pressure more often rises while diastolic drops toward the end of the work shift. Evidently, the contradictory opinions concerning the hypotensive and hypertensive effects of noise can be attributed, to some extent, to instability of arterial pressure.

Since arterial pressure level depends largely on tonus of the vascular walls, peripheral circulation and function of the heart proper, it is of definite interest to study these hemodynamic parameters in individuals exposed to intense noise on their jobs. There is mention in the literature of changes in vascular tonus under the influence of noise; however, the authors did not pursue special studies to determine vascular tonus and included arterial pressure in this concept. By determining the pulse wave propagation velocity and modulus of elasticity of vascular walls, we established that there is increase in tonus of arterial vessels of the muscular type and, to a lesser extent, of the elastic type under the influence of intensive wide-band noise.

Some researchers measured arterial pressure, not only in brachial vessels but other regions: temporal artery and central retinal artery. L. Ye. Milkov (1963) failed to demonstrate substantial changes in pressure of the temporal artery or temporobrachial coefficient in individuals exposed to intensive noise (103 dB). At the same time, I. A. Benyumov (1963) found a change in temporobrachial coefficient in 33.4% of the workers in the doubler and weaving industry, exposed to high-frequency noise of 94-101 dB: it was low in 10.3% of the cases and high in 23.1%. There was prevalence of change in the temporobrachial coefficient among individuals with functional disturbances of the nervous system. According to the data of E. N. L'vovskaya (1964), elevation of diastolic pressure in the central retinal artery is often observed with noise of 85-122 dB. The results of capillaroscopy, tissular blood flow, plethysmography and peripheral resistance studies are indicative of changes in peripheral circulation under the influence of noise.

Data are submitted in the work of B. M. Shamardin (1974) that indicate impaired vascular tonus in the microcirculatory system. This author detected spastic and spastic-atonic states of fine vessels in different parts of the body (hands, legs, conjunctiva) among workers exposed to noise. L. Ye. Milkov often demonstrated capillary spasm of the nail bed and slow circulation in the hands of workers exposed to noise. N. N. Krylova (1958) found a direct correlation between the angiospastic reaction and noise volume under the influence of high-frequency noise at the level of 50-115 dB, on the basis of plethysmography, and this was confirmed in the studies of Oppliger and Grandjean (1959). According to the data of Rossi, Oppliger and Grandjean (1959), intermittent noise of the same level elicits even more marked vasoconstrictive effects.

Straneo and Seghizz (1962) investigated the reactions of workers whose occupation involved exposure to noise by the method of digital plethysmography in response to a pure tone of 3000 Hz and noise on the level of 87 dB.

According to their observations, a pure tone did not elicit changes in blood-filling volume, whereas it diminished with exposure to noise.

The works of Lehmann, Tamm (1956) and Lehmann (1962), who studied peripheral vascular resistance, merit attention. A change in vascular tonus, particularly in the capillary system, increased resistance of arterial flow and decreased systolic volume were noted in individuals exposed to high- and low-frequency noise. In another experiment, Lehmann (1962) observed constriction of precapillaries of the skin throughout the period of exposure to medium-frequency noise in 90-95% of the cases. With increase in peripheral resistance there was a corresponding decrease in volume of the heart beat. On the basis of these findings, the author believes that the demonstrated changes are not only a reaction of the precapillary region of the vascular system, but chiefly the result of increased resistance in most vessels of the entire circulatory system.

In order to determine the state of peripheral circulation in individuals regularly exposed to intense noise on their jobs, we measured specific peripheral resistance,* which gives an idea about the patency of the precapillary system and constitutes the overall resistance in the system of peripheral resistance as a function of body surface area. The obtained data indicate that the resistance in the system of peripheral vessels was more often increased, and in some individuals it was significantly higher than the proper level.

A comparison of actual specific peripheral resistance to working specific resistance, which is inherent in increased function of the circulatory system, revealed that in most subjects the actual specific peripheral resistance was also above the working resistance, i.e., the patency of their precapillaries is less than the corresponding level of minute volume of circulation.

There are works indicative of the possibility of development of coronary and cerebral circulatory disturbances under the influence of noise. In his studies, Koeppen (1955) attributed much importance to regular exposure to noise which, in his opinion, by inducing functional cardiovascular disturbances leads to development of coronary spasms. G. N. Aronova and T. A. Mayeva (1958), who studied coronary circulation in animals exposed to an intensive sonic (noise)stimulus, observed decreased circulation in vessels of the heart due to constriction of their lumen.

In the opinion of V. Ye. Lyubomudrova, B. N. Onopko and L. Ya. Basamygina (1968), in some cases noise can elicit coronary insufficiency with signs of anginal pectoris, as well as myocardial infarction.

*Actual, proper and working specific peripheral resistance was measured and calculated by a method proposed by N. N. Savitskiy (1963).

Vascular disturbances in the central nervous system in response to sonic stimuli are also reported by L. V. Krushinskiy, L. N. Molodkina, L. P. Pushkarskaya (1953) and G. L. Tokhadze (1956), who arrived at the conclusion, on the basis of experimental data on animals, that the immediate cause of their death following sonic trauma is impairment of cerebral circulation associated with effusion of blood in the brain and signs of neuronal hypoxia. This is usually preceded by a severe comatose state in the animals, with marked attenuation of reflexes, decreased muscle tone, impaired cardiac function and change in arterial pressure.

The studies of local circulation, conducted by I. B. Yevdokimova (1970) in individuals regularly exposed to varying intensities of noise on their jobs, are interesting. Using the rheographic method, she demonstrated changes in tonic tension and intensity of delivery of blood to vessels of the arm and brain. Changes in cerebral vessels were noted more often than in vessels of the extremities. At the same time, some distinctions were found in these changes as a function of intensity of noise. A noise of 85 dB induced mainly an increase in tonic pressure of vessels, with decline in blood supply to vessels of the limbs and increase to those of the brain. Tonic pressure and filling of extremital vessels increase, while the same parameters of cerebral vessels decrease under the influence of noise at 105-108 dB.

As for cardiac activity and condition of the myocardium with exposure to noise, the chief methods of studying them were determination of heart rate at rest, with a physical load, during orthostatic and clinostatic tests, oculocardiac reflex, determination of minute blood volume, electrocardiography, phonocardiography and ballistocardiography.

A. I. Vozhzhova and I. A. Sapov, who tested Aschner's oculocardiac reflex and the orthostatic reflex, demonstrated attenuation of parasympathetic influence on the heart and enhancement of the effects of sympathetic innervation. L. Ye. Milkov discovered a tendency toward attenuation of the oculocardiac reflex in different groups of workers exposed to noise at levels of 95, 103 and 120 dB; the decline of reactivity progressed with increase in intensity of noise. Testing of the ortho-clinostatic reflex failed to reveal substantial changes. There was some tendency toward a stronger vascular reaction in the course of the work day.

According to EKG data, changes indicative of functional impairment of the myocardium, mainly referable to rhythm and conduction, are sometimes observed under the influence of noise. Ye. Ts. Andreyeva-Galanina et al. (1968) demonstrated bradycardia, sinus arrhythmia, impaired electric conduction of the heart, reduced voltage, especially of the T wave, among those employed in the "noisy" professions.

The EKG studies conducted by A. A. Arkad'yevskiy (1961) and others on individuals exposed to noise on their jobs were indicative of changes in magnitude and shape of the T wave, longer diastole and decline of systolic index. According to the data of L. Ya. Basamygina (1966), slowing of

atrioventricular conduction and arrhythmia are observed more often with exposure to noise. M. L. Khaymovich and N. M. Esaiashvili (1968) reported rhythm and conduction disturbances.

The EKG changes under the influence of noise are corroborated by experimental data. A. V. Kadyskin (1966), who tested the effect of stable noise on experimental animals (rabbits), demonstrated an increase in P-Q interval, diminished electrical systole and reduction of systolic index. A. B. Strakhov (1963) observed impairment of heart rhythm and elevation of systolic index in experimental animals after prolonged exposure to high-frequency stable noise.

A survey of workers exposed to intensive wide-band noise often revealed changes on the EKG, in the form of sinus bradycardia and bradyarrhythmia, a tendency toward slower atrioventricular and intraventricular conduction. Since conduction is very rapidly restored after physical functional tests (running in one spot), it must be assumed that these disturbances are functional. Studies conducted in the course of a work day revealed a tendency toward slower rhythm toward the end of the shift and, in some cases, decline of T wave appearing concurrently with worsening of ballistocardiographic indices. According to the results of phase analysis of mechanical systole of ventricles, contractile function of the myocardium was not impaired in most subjects. The demonstrated changes are indicative of impairment of neuroreflex regulation. Their incidence increased with increase in work tenure involving exposure to noise and increase in its intensity.

On the basis of the submitted data, it can be concluded that the changes referable to the cardiovascular system due to exposure to intensive noise are indicative of development of the syndrome of neurocirculatory dysfunction, in the symptomatology of which there is prominence of generalized vascular disturbances with hypertensive reactions and a tendency toward turning to essential hypertension.

Questions pertaining to the distinctions of the effects of noise on the cardiovascular system, when combined with other factors of the industrial environment, merit attention. Ye. Ts. Andreyeva-Galanina, S. V. Alekseyev, G. A. Suvorov and A. V. Kadyskin (1972) indicate that the diversity of clinical manifestations with exposure to noise is attributable to the intensity of the noise, its spectral composition, concomitant deleterious environmental factors, as well as reactivity of the organism. According to the existing observations, intensive noise with prevalence of high frequency in its spectrum has the most deleterious effect on the body, in particular the cardiovascular system. We have indicated above some of the differences in effects of noise on the cardiovascular system as a function of its intensity. Tansen (1964) and others believe that the severity of functional changes in the cardiovascular system is directly related to the width of the noise spectrum. In the opinion of authors, a pure tone does not induce clearcut changes, while wide-band noise elicits statistically reliable ones. In recent times, much attention is being devoted to the study of pulsed noise. Our observations and the data of other authors

(Ye. Ts. Andreyeva-Galanina, 1968, and others) indicate that pulsed noise and noise associated with nervous and emotional tension have a more deleterious effect on the body than stable noise and noise that is not associated with nervous and emotional tension.

We still do not have clearcut data on the correlation between changes referable to the acoustic analyzer and the cardiovascular system. On the basis of a dynamic study of workers exposed to noise of 90-110 dB, Ye. Ts. Andreyeva-Galanina and V. G. Artamonova (1968) observe that appearance of vascular disturbances is not necessarily associated sith a change in functional state of the auditory analyzer. Observations show that hemodynamic changes, in particular, in arterial pressure, under the influence of noise may precede development of persistant disturbances of the auditory analyzer, i.e., they appear prior to demonstration of clinical signs of cochlear neuritis. All this indicates that the changes in the cardiovascular system may also be one of the early syndromes of exposure to noise. As already indicated at the beginning of this section, some researchers believe that noise affects the incidence of cardiovascular diseases, particularly essential hypertension and myocardial infarction. We cannot totally rule out the role of the noise factor in development of some cardiovascular diseases--essential hypertension, myocardial infarction and angina pectoris. However, continued observations and studies are required to answer this question definitively.

These data indicate that intensive noise is one of the deleterious industrial factors that induce a number of functional disorders referable to the cardiovascular system of the order of neurocirculatory dysfunction. There is reason to believe that, under specific conditions, neurocirculatory dysfunction may be considered one of the syndromes inherent in the effects of noise.

With exposure to noise, hemodynamic disturbances not infrequently precede development of persistant changes in the acoustic analyzer. Cardiovascular disorders under the influence of noise are based on disturbances of neuroreflex regulation of the circulatory system. Evidently, the functional disorders referable to hemodynamic regulation that arise initially under the influence of noise can, in time, lead to more persistent changes in vascular tonus. This is most likely the explanation for the high incidence of hypertensive states among individuals whose jobs involve exposure to intensive noise, especially when it is associated with nervous and emotional tension.

Differential diagnostics of neurocirculatory dysfunction due to noise often present great difficulties, especially in the absence of signs of occupational cochlear neuritis. For this reason, when establishing the diagnosis, one must rule out other etiological factors that are instrumental in onset of neurocirculatory dysfunction (psychological and emotional factors, organic disease of the nervous and cardiovascular systems, etc.). Moreover, in each individual case, one must take into consideration the entire diversity of factors involved in working conditions, work tenure with exposure to noise,

health status before starting to work, time of development of neurocirculatory dysfunction, presence and nature of changes referable to the nervous system and hearing.

Since neurocirculatory dysfunction associated with exposure to noise is due primarily to functional impairment of higher nervous activity and autonomic centers, the therapeutic measures in such cases should be directed toward regulating the nervous system and normalizing reflex reactions of the cardiovascular system. The following can be recommended in the set of therapeutic measures: general fortifying agents, sedatives and vitamins. Beneficial results are observed with the use of bromide and caffeine. Spasmolytic agents and ganglion-blocking agents are indicated for marked angiospasms. Gradual conditioning of the heart and vessels is very important, and this can be achieved by therapeutic exercise, which aids in regulating and coordinating all elements of the circulatory system, and also expands its reserve capabilities.

Fitness for work is usually unimpaired at the mild stages of neurocirculatory dysfunction. Proper adherence to a work shcedule and reasonable activity at leisure is the main recommendation in such cases for the restoration of impaired functions.

At the more marked stages, particularly when there are constant, disturbing subjective sensations, severe instability of pulse and arterial pressure, angiospastic signs, the question can be raised of transferring the subject to a job that does not involve exposure to intense noise. In finding jobs for such individuals, it must be borne in mind that, in addition to noise, tense work related to emotional factors is also contraindicated.

When settling expert questions of fitness and job placement, in addition to the condition of the cardiovascular system, one must definitely bear in mind the presence and severity of changes referable to other organs, in particular, the nervous system and ear.

CHAPTER 8. REACTIONS OF THE CARDIOVASCULAR SYSTEM TO ACUTE OCCUPATIONAL FACTORS

[Text] There are only a few reports in the literature concerning acute injury to the cardiovascular system by physical factors (ionizing radiation, electric trauma, superhigh-frequency waves) and chemicals (carbon monoxide, chlorine, cyanides and others).

The old opinion of Whit (1921), subsequently confirmed by Koelsch (1959), to the effect that there are no factors in industry that induce cardiovascular diseases is presently being questioned. If we agree that a cardiac poison refers to a substance, under the influence of which death occurs as a result of cardiac, rather than respiratory, arrest, several alkaloids can be classified as such substances: strophanthus, nicotine, colchicine, quinine, aconitine, fluorides, barium salts, snake venom, toad skin venom and others.

Regardless of whether the agent that induces poisoning is a selective poison for the nervous, hemopoietic system or parenchymatous organs, there are always disturbances in activity of the cardiovascular system. Moreover, changes referable to the cardiovascular system become the principal ones at a certain stage of many forms of occupational poisoning, and they determine the clinical course, outcome and prognosis.

As can be seen from the classification of factors and syndromes (Table 15), hypoxic states play a substantial role in cardiovascular disturbances. Thus, hypoxemic hypoxia, due to inadequate oxidation of blood in the lungs, is observed in cases of chlorine, phosgene and nitric oxide poisoning (acute pulmonary edema, acute cor pulmonale). Anemic hypoxia occupies an important place; it develops as a result of carbon monoxide poisoning (formation of carboxyhemoglobin), poisoning due to amidobenzene and nitrobenzene compounds,

phenylhydrazine (production of methemoglobin), hydrogen arsenide (hemolysis of erythrocytes), etc. Some agents (cyanides, hydrogen sulfide, insecticides and fungicides) induce tissular hypoxia (histotoxic hypoxia) as a result of primary impairment of cellular respiration (respiratory enzyme block). The cardiac changes are not inflammatory in nature, they are reversible in most cases and referred to in the Soviet literature by the term "myocardial dystrophy," which was proposed by G. F. Lang (1936). This term is specific, it has an etiological, pathogenetic and clinical basis, and in our observations it better defines the essence of processes occurring in the heart than the collective and vague term "myocardiopathy."

Industrial factors have both a direct and indirect effect on the cardiovascular system. Various industrial factors often induce the same deviations and, on the contrary, there may be different cardiovascular disturbances under the effect of the same factor. Systemic reactions of the allergic type, often in the nature of an autonomic "storm" (spelter's fever), often occur under the influence of some metals (copper, zinc, magnesium and others) in vapor (aerosol) form and certain other substances (tellurium, beryllium). Some substances (antibiotics, vitamins, ursol [p-phenylenediamine], methylchloride and others), which have allergenic action, occasionally induce marked reactions of the antigen-antibody type, and they often lead to involvement of the cardiovascular system. Agents with systemic toxic action affect the cardiovascular system in a more complex way: directly on tissue and organ cells, as well as via the central, autonomic nervous and endocrine systems. Local exposure to large doses of radiation induces local tissue lesions. High-tension electricity, SHF, UHF and electromagnetic fields of other ranges have mainly an indirect effect on the cardiovascular system. High ambient temperature, low and high atmospheric pressure have the same effect. A low oxygen content in inhaled air elicits cerebral hypoxia. Gas embolisms in vessels of various organs, which appear with a change from high to normal or low atmospheric pressure, may lead to serious complications.

With expsoure to various etiological factors, one must also bear in mind primary nonspecific neurohumoral effects (stress) and their important psychoemotional component, inducing early general reactions in the nervous system.

At the present time, the significance of hormonal changes to pathogenesis of cardiovascular disturbances has been proven. Considerable access of catecholamines in blood (epinephrine, norepinephrine) increases oxygen requirement of the myocardium and, when there are limited opportunities for delivery thereof (in the presence of lesion to cardiac vessels), this could lead to anoxia, myocardial dystrophy and necrobiosis. Impairment of electrolyte balance also plays a certain role (V. Raab, 1959; H. Sel'ye, 1960).

Changes in the Cardiovascular System Under the Effect of Some Metals and Aerosols Thereof

Copper, zinc, cobalt, magnesium oxide and tellurium are virtually nontoxic in solid or powder form. In melted and vapor state, they can

induce so-called spelter's fever (nonspecific allergic syndrome) associated with tachycardia, elevation of arterial pressure, chills (body temperature up to 38-39°), headache, aching of extremities and myocardial dystrophy (decline or inversion of T wave on the EKG).

The pathogenesis of this fever is attributable to destruction of cells of the alveolar endothelium and absorption of products of their decomposition, as a result of the active effects of metal aerosols.

As an example, let us describe the cardiovascular changes in the presence of "spelter's fever" induced by inhalation of tellurium fumes:

> Patient V., 21 years old, observed development of cough after working for a few minutes with melted tellurium,* which became worse toward the end of the work day; there were vertigo, general weakness and tremor of the extremities. When admitted to the clinic she complained of severe weakness, pressure under the sternum, cough and headache. Vertigo and repeated vomiting of food occurred when body position was changed. Objective findings: hyperemic face, cyanosis of lipids, nasopharyngeal mucosa and tongue are dark green. Strong putrid odor in the mouth. Respirations 32/min. Body temperature 38.2°C. Scattered dry rales ausculted over pulmonary fields. Pulse 120/min, rhythmic. Arterial pressure 130/90 mm Hg. No change in heart boundaries. Marked vegetovascular reaction: tachycardia, marked perspiration and diffuse dermographism. The following morning the patient felt considerably better. Pulse 74/min, rhythmic. Respiration 24/min. Arterial pressure 110/80. Heart sounds somewhat dull. No more rales in lungs. The EKG (Figure 6) shows sinus rhythm, 80/min. P-Q 0.17 s; QRS 0.08 s, Q-T 0.40 s (normal 0.37 s). Horizontal electric axis. $S\text{-}T_{1\text{-}2\text{-}3}$ slightly elevated, $T_{II\text{-}V_6}$ wave almost isoelectric, $TV_{1\text{-}2\text{-}3}$ negative, $T_{III}\text{-}V_4$ biphasic. EKG changes were indicative of significant diffuse changes in bioelectric activity of myocardium. Her condition imporved significantly in the next few days; no complaints. Isolated dry rales heard in lungs. Pulse 70-80/min, rhythmic; arterial pressure 110/60 mm Hg. Heart normal in size, but EKG remains changed. Complete normalization of EKG was observed only after 5 months.
>
> Thus, tellurium fume poisoning was acute in this patient, of the order of the nonspecific allergic syndrome associated with chills, fever, rales in lungs, headache, general severe weakness, marked vegetovascular reaction and changes in myocardial bioelectric processes. The clinical and EKG findings enable us to attribute myocardial dystrophy to metabolic disturbances in the body and myocardium.

*When tellurium compounds reach cells, they block several enzymatic systems: muscular oxidases, dehydrogenases and others (N. V. Lazarev, 1971).

Table 15. Classification of occupational factors that induce acutely developing changes in the cardiovascular system

Etiological factors	Pathophysiol. or funct. mechanisms	Pathoanatomical substrate	Frequent syndromes	Possible outcome
I. CHEMICAL				
1. Carbon monoxide, hydrogen arsenide, nitro and amido benzene compounds	Anemic hypoxia	Myocardial dystrophy; focal myocardial changes; vascular lesions	Cardiovasc. insuff. (I-II); collapse (not in all cases)	Angina pectors, myocardial infarction, coma, myocardial sclerosis
2. Chlorine, phosgene, nitric oxide, cadmium, etc.	Hypoxemic hypoxia	Pulmonary edema; acute cor pulmonale; myocardial dystrophy	Cardiopulmonary insuff. (I-II-III)	Cor pulmonale, coma
3. Cyanides, hydrogen sulfide, etc.	Tissular hypoxia	Myocardial dystrophy, necrobiosis	Vegetovasc. dysfunc., cardiovasc. insuff. (I-II), collapse (not in all cases)	Coma
4. Lead, copper, tellurium, zinc, magnesium, manganese, cobalt, etc. (vapor form)	Systemic reactions of allergic type	Lead colic, spelter's fever, myocard. dystrophy, allergic myocarditis	Vegetovasc. dysfunc., cardiovasc. insuff. (I-II) (not in all cases)	Collapse
5. Antibiotics, vitamins, etc.	Same	Myocard. dystrophy	Same	Same
6. Tetraethyl lead, mercury & compounds thereof, carbon tetrachloride, carbon disulfide, arsenic & comp. thereof, dichloroethane, gasoline [or benzine], methyl alcohol, insecticides, fungicides, ethylene chlorhydrin, nicotine, caffeine, etc.	Central & autonomic nervous system, parenchymatous organs, cellular enzymatic processes (respiratory enzyme block)	Encephalopathy, asthenovegetative syndrome, vegetovascular dysfunction, impaired metabolism & excretory function, hypoxia, myocard. dystrophy, fine necrotic foci in organs & tissues	Cardiovascular insufficiency (I-II) (not in all cases)	Collapse, coma

Table 15. (continued)

Etiological factors	Pathophysiol. or funct.mechanisms	Pathoanatomical substrate	Frequent syndromes	Possible outcome
II. PHYSICAL FACTORS				
1. Ionizing radiation	Radiation lesion to heart	Myocardial dystrophy, necrosis and necrobiosis of tissue	Vegetovasc. dysfunc., cardiovascular insufficiency (I-II) (not in all cases)	Collapse, coma
2. High-frequency current	Neuroendocrine and metabolic	Myocardial dystrophy, arrhythmia	Vegetovascular dysfunction	Collapse
3. Electric current	Myocardial dystrophy, focal necrosis & necrobiosis	Same	Vegetovascular dysfunct., cardiovasc. insuff. (I-II) (not in all cases)	Collapse, coma
4. Change in atmospheric pressure a) rise	Gas embolism	Myocardial dystrophy, focal myocardial changes	Cardiovasc. insuff. (I-II-III)(not in all cases)	Angina pectoris, myocard. infarction, myocardial sclerosis
b) drop	Hypoxic hypoxia	Myocardial dystrophy	Cardiovasc. insuff. (I-II) (not in all cases)	Collapse, coma
5. High ambient temperature and thermal radiation	Thermal overheating, heat stroke	Impairment of central nervous system (cerebral edema)	Same	Collapse, coma

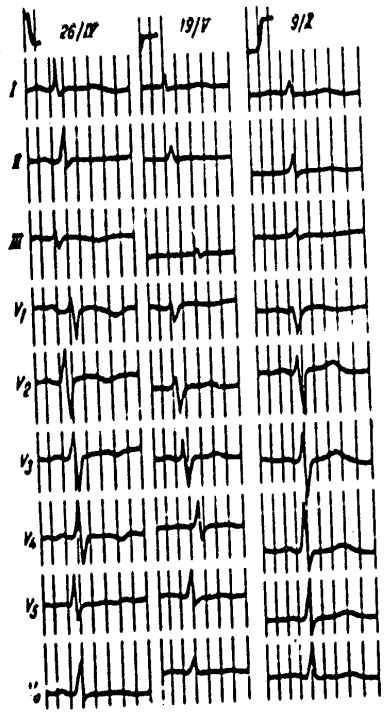


Figure 6.
EKG of patient V.; explained in text

Poisoning Due to Some Chemicals With General Toxic Action

Agents With Anoxemic Action

Hydrogen sulfide: In the case of acute poisoning, the nervous and cardiovascular systems are chiefly stricken. There is inhibition of intracellular tissular respiration (impairment of redox processes and their catalysts). For this reason the cell is incapable of utilizing blood oxygen. There is onset of hypoxia of tissues, organs and, what is particularly important, brain centers. Occasionally, death may occur immediately when there is a high concentration of hydrogen sulfide ("instantaneous form") as a result of cardiac paralysis; more often, death occurs due to development of asphyxia and comatose state. Patients complain of headache, pain in the region of the heart of a compressing type, sensation of intermitten pulse and general weakness. Clinically there are lability of pulse, tachycardia, mild elevation of arterial pressure followed by a decline, widening of heart borders and dull sounds. Not infrequently, there is development of toxic pulmonary edema associated with very marked dyspnea, cyanosis, moist rales in the lungs. On the EKG there is a decline of P and T waves, elongation of electrical systole of the ventricles, signs of myocardial hypoxia, "coronary" changes or focal lesions to the myocardium (Z. P. Kaluzhnikova, 1949; Schram, 1957, and others).

We submit a case history on a patient with acute hydrogen sulfide poisoning and "apoplectic" form of heart lesion:

> Patient O., 24 years old, a laboratory technician, was admitted to the rayon hospital on 21 December in serious condition due to acute hydrogen sulfide poisoning associated with comatose state and toxic edema of the lungs. She was unconscious for 10 h; there was cyanosis of the lips, pallor of the integument, gurgling respiration, tachycardia, dull heart sounds. Arterial pressure not demonstrable. Diffuse dry and moist rales in the lungs. Repeated vomiting of bile. After appropriate therapy the condition improved and arterial pressure

rose to 90/30 mm Hg. There was attenuation of tachycardia and signs of pulmonary edema.

From the very first days of hospitalization, the patient was troubled with squeezing pain in the heart. On the 40th day of illness (31 January) she was transferred to the institute clinic in satisfactory condition. She complained of dyspnea during physical exercise, periodic boring pain in the cardiac region (irradiating to the left scapula), moderate cough with production of sputum, headache, pain in the lumbar region, lower and upper extremities, marked weakness. The integument is pale pink, labial mucosa is slightly cyanotic and sclera are subicteric. Pulmonary sound in the lungs, vesicular, somewhat weak respiration. Pulse 70/min, rhythmic, good filling. Left margin of the heart shifted 1 cm laterally from the mediastinal-clavicular line. Heart sounds are somewhat dull. Systolic murmur at the apex and point V. Accented second tone in pulmonary artery. Arterial pressure 120/75 mm Hg. Venous pressure 40 mm water. Blood flow rate (lobeline test) 19 s. EKG (Figure 7) taken on 5th day of illness (a): correct sinus rhythm, 63/min; P-Q 0.15 s; QRS complex 0.08 s; Q-T 0.48 (normal 0.38 s). Electrical ventricular systole 0.1 s longer; $P_{V_{1-4-6}}$ accentuated; $R_I < R_{III}$; $R_{V_4} > S_{V_4}$; $S\text{-}T_{I-II,V_{4-4}}$ slightly elevated in the form of a convex arch and changes into negative, "coronary" type of T wave. Thus, the EKG was indicative of severe myocardial hypoxia and diffuse (dystrophic) changes mainly in the region of the apex and lateral part of the left ventricle. Phonocardiogram showed gross systolic murmur throughout the systole.

Unquestionably, the myocardial lesion was due to severe hypoxia, which apparently developed as a result of oxidative enzyme block (production of FeS complex). This cardiac lesion should be classified, according to G. F. Lang, in the category of toxic myocardial dystrophies.

Blood test (2 February): hemoglobin 126 g/ℓ (12.6 g%), erythrocytes $3.8 \cdot 10^6$/μℓ (3,800,000), leukocytes $5.3 \cdot 10^3$/μℓ (5300), lymphocytes 31%, monocytes 3%, eosinophils 5%, stab 6%, segmented 55%. Blood prothrombin 100%, total serum protein 77.8 g/ℓ, thrombocytes $24.7 \cdot 10^4$/μℓ (247,000), ESR [erythrocyte sedimentation rate] 3 mm/h (7.78 g%) (fractions unchanged). Urinalysis showed no deviations from normal. Thyroid function (^{131}I test) normal. Roentgenoscopy of the chest: heart in usual position, waistline flattened due to elongation of arch of pulmonary artery conus, left ventricle somewhat enlarged. Deep pulsation, rhythmic, adequate in force. Normal myocardial tonus. No change in aorta.

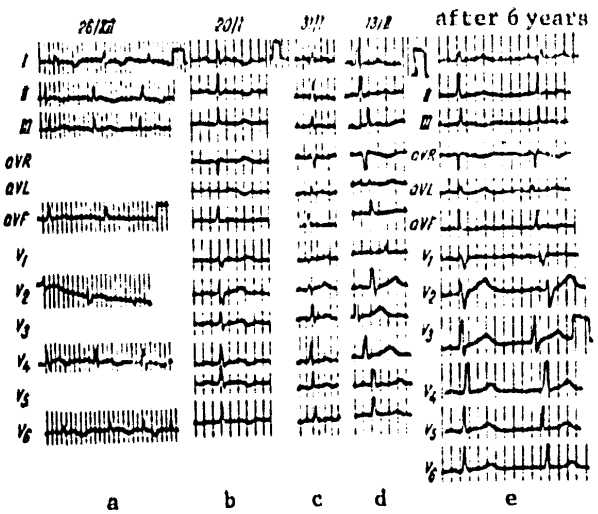


Figure 7. EKG of patient O. Explanation given in the text.

By the end of a month, there was some attenuation of general weakness and cardiac pain. Subfebrile temperature, dyspnea and tachycardia disappeared. The patient complained of general weakness, fatigability, headache, pain in the limbs and some cough. Dyspnea and palpitations appeared with mild physical exercise. Heart sounds became clear. EKG on 20 January (b) still showed signs of myocardial changes (negative $T_{I-II, V_{5-6}}$ wave). In the 2d month after poisoning, pain disappeared from the cardiac region, there was less dyspnea during exercise and fewer changes on the EKG. The EKG became normal after 2 months (c, d); the patient received general fortifying therapy, cardiovascular agents and sedatives; she was discharged from the clinic on 2 March (3.5 months after the poisoning) in satisfactory condition. There were no visible deviations in her health status. In the last examination on 11 February, EKG data (e) were normal.

Carbon monoxide: Clinical signs of such poisoning are characterized by impaired function of the cardiovascular and nervous systems due to hypoxemia, which resulted from production of carboxyhemoglobin. According to clinical and electrocardiographic dynamic observations, as well as data in the literature (I. Ya. Sosnovik, 1955; M. A. Kovnatskiy, 1961, and others), changes are often encountered in the cardiovascular system in the presence of acute carbon monoxide poisoning. At the early stage of acute and severe poisoning, the patients present general weakness, cardiac pain and tachycardia, widening of margins and dullness of heart sounds, occasionally rhythm disturbances and elevation of arterial pressure. When there is progression of functional

disorders of the heart and respiration, death may occur due to respiratory arrest. As shown by the EKG findings, there are often signs of diffuse, less often focal, myocardial lesion (S. Z. Kostyukova, 1941; S. I. Ashbel' et al., 1962, and others). In cases of mild and moderate poisoning, the EKG changes are transient and unstable in most cases; however, they may reappear during functional tests (physical load, orthostatic test, etc.). It should be stressed that there is no direct correlation between severity of poisoning and EKG changes. Heart lesions do not necessarily appear immediately, but within a few days and weeks (2-3 weeks), and they may vary in severity, ranging from mild diffuse changes to coronary-like and focal lesions.

> Patient M., 38 years old, a plumber, was delivered to the clinic in an unconscious state. He lost consciusness in a well while repairing water pipes. When admitted, there was severe rigidity of muscles of the upper and lower extremities, dilation of pupils, no reaction to light, bilateral Babinskiy symptom; visible mucosa and integument are pink, respiration rate 28/min; left margin of the heart is 1 cm lateral from the mediastinoclavicular line, heart sounds are sonorous. Pulse 100/min, arterial pressure 120/65 mm Hg. EKG (Figure 8): tachycardia (100 contractions/min); R-R 0.60 s, P-Q 0.16 s, QRS 0.10 s, Q-T 0.32 (normal 0.28). P_{II} moderately accentuated, $R_I > R_{III}$, $R_{V_3} > S_{V_3}$, $S\text{-}T_{I\text{-}II}$, v_{1-2} and especially $S\text{-}T_{V_{3,4,5,6}}$ are low. $T_{I\text{-}II}$ is low, $T_{V_{1,2,3,4,5,6}}$ is low and biphasic. The EKG data were indicative of myocardial infarction, mainly of the left ventricle. Blood test: hemoglobin 150 g/ℓ, leukocytes $4.6 \cdot 10^6$/μℓ, eosinophils 2%, basophils 0.5%, stab 1%, segmented 63%, lymphocytes 27%, monocytes 6.5%, ESR 18 mm/h. Oxygen in arterial blood 66%, coefficient of tissular oxygen uptake 0.16, CO_2 tension in arterial blood 34 mm Hg, lactic acid content 48.3 mg%. The patient regained consciousness after 14 h. His condition improved rapidly on the following days. He was discharged after 7 days in satisfactory condition. The EKG and blood findings were back to normal.

Thus, in a patient with acute and severe carbon monoxide poisoning, we observed involvement of the central nervous system and diffuse hypoxia (dystrophy) of the myocardium of a moderate grade, which were eliminated within a few days. Recovery may take several months and, in some cases, lead to chronic heart disease (myocardial sclerosis). A comparison of clinical and postmortem findings warrants the belief that in essence these changes consist of development of micronecrosis, often even without involvement of coronary vessels.

Roentgenological findings are also indicative of diffuse myocardial changes at the early stage of carbon monoxide poisoning; they show total widening of the heart and pulmonary artery within the first few days after poisoning, and in some victims (50% of the cases) dilatation of the superior vena cava.

These changes referable to the heart and vessels usually level off in a few days (3-7) and, according to EKG findings, are followed mainly by focal lesions. At the acute stage, when the changes are still mainly diffuse, there is a drop of arterial pressure (mainly mean and diastolic) and, in some cases, fine effusions of blood.

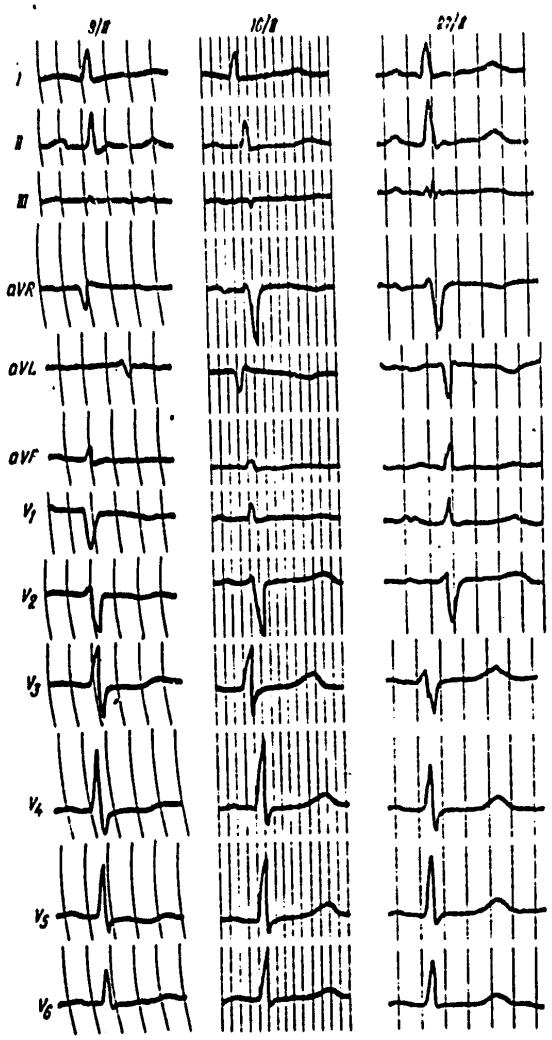


Figure 8. EKG of patient M. Explanation given in the text.

In serious cases there may be subarachnoidal effusion of blood, effusions along the optic nerve and in other important parts of the central nervous system; toxic pneumonia is observed (A. M. Rashevskaya, 1948). A few days after poisoning, there remain only mild dullness of sounds and hypotension, which persists for a long time. While the patient feels well and his temperature is normal, with no changes in blood, for a long time (3-5 weeks) the EKG shows marked focal changes, often resembling the changes observed in the presence of coronary insufficiency and pinpoint necrosis of the myocardium. These discrepancies between the minor clinical manifestations of poisoning and severity of EKG changes are very typical of heart disease following acute carbon monoxide poisoning. The genesis myocardial lesions is complex. It is based on dystrophic changes due to metabolic disturbances that are related to acute onset of myocardial hypoxia.

According to the EKG findings, diffuse myocardial changes persist in the vast majority of cases for a long time after disappearance of poisoning symptoms.

Thus, there are often marked changes in the myocardium and vascular system in the presence of acute carbon monoxide poisoning. It may be considered that the changes in the myocardium and hypotension are among the frequent long-term sequelae of acute (especially serious) carbon monoxide poisoning, and they are apparently attributable to a change in condition of autonomic centers.

Cyanides: Potassium, sodium, ammonia, hydrogen and other cyanides, even in small amounts, depress cellular respiration (they block oxidative enzymes) as a result of which there is development of organic and tissular hypoxia. The nerve centers are particularly sensitive to hypoxia and are the first to be involved. Death often occurs instantaneously due to paralysis of the respiratory center and reflex cardiac arrest. In the case of poisoning with small doses, there are complaints of weakness, headache, nausea, chest and heart pain, dyspnea and palpitations. With high concentrations, there are respiratory rhythm disturbances, severe dyspnea, fear, stunned state and then loss of consciousness. This may be followed by death. The EKG shows signs of hypoxic changes or "coronary-like" diffuse changes; occasionally there is extension of conduction (atrioventricular and ventricular). Koelsch (1959) reports lability of the pulse and arrhythmia at the long term after acute poisoning. Autopsies revealed light red, thin blood, fine effusions of blood in the lungs and pleura, pericardium, myocardium, as well as myocardial dystrophy and sites of softening of the brain.

We submit the following case history as an example of mild acute poisoning:

> Patient M., 31 years old, whose job involves manufacture of silver parts using silver cyanide and copper cyanide. While working she felt general weakness, vertigo, headache, sharp pain in the region of the heart. That day, the exhaust ventilation system had broken down. After working for 4-5 h she developed a feeling of pressure in the chest, shortage

of air, scratchy throat, intensification of pain in the region of the heart, with appearance of severe general weakness and dizziness. She was delivered to the clinic at 2100 hours. Examination revealed bright pink integument. Pulse 60/min, arterial pressure 130/80 mm Hg. Heart margins are in the normal range, sounds somewhat dull, systolic murmur over all points of the heart. EKG (Figure 9) shows marked diffuse (hypoxic) myocardial changes--myocardial dystrophy. Blood presented moderate neutrophil leukocytosis with left shift to 10% staff nuclears. General weakness, vertigo and stabbing pain in the region of the heart persisted for the next few days. Heart sounds gradually became clearer; leukocyte count reverted to normal and positive EKG dynamics were observed.

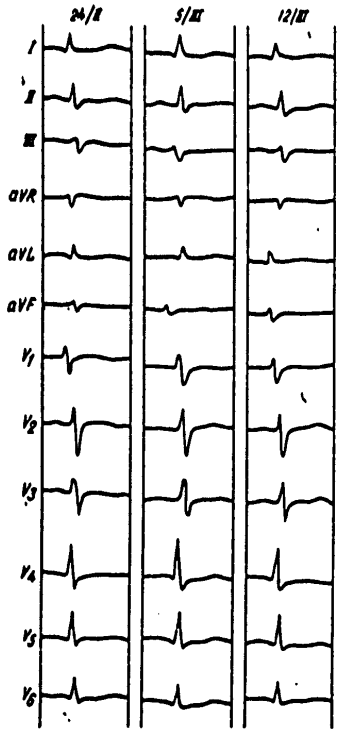


Figure 9.
EKG of patient M., explained in text.

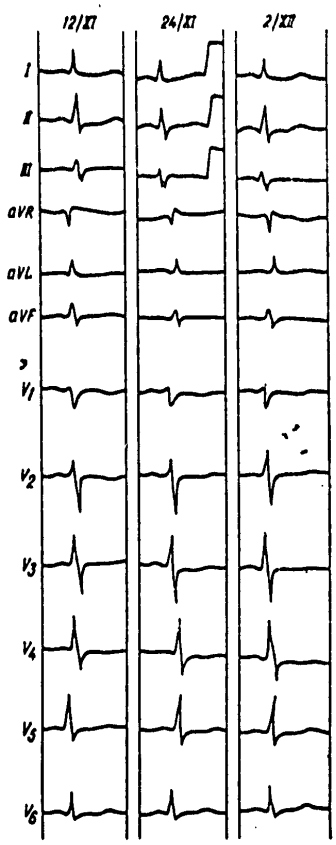


Figure 10.
EKG of patient Ye., explained in text.

Organochlorine compounds: Hexachlorane, dichlorodiphenyl trichloroethane, hexachlorocyclohexane, benzene hexachloride and others can induce systemic poisoning in acute cases: weakness, nausea, vomiting, gastric pain, headache, nose bleeds, as well as retrosternal pressure pain in the region of the heart, drop of arterial pressure, slowing of pulse and toxic lesion to the myocardium of the diffuse myocardial dystrophy type. In more serious cases one observes unconsciousness, cardiac weakness, occasionally pulmonary edema, collapse and encephalopathy syndrome (L. I. Medved', 1968).

We shall submit an example of acute poisoning by organochlorine compounds:

> Patient Ye., 32 years old, laboratory technician, worked for several hours with organochlorine compounds. Toward the end of the work day, she experienced severe headache, dizziness, general weakness, heaviness of the head, aching in the region of the heart, abdominal pain and nausea. There was repeated vomiting. When admitted to the clinic her condition was satisfactory: pulse 76/min, rhythmic, adequate filling. Arterial pressure 110/70 mm Hg. Heart boundaries in normal range; apical systolic murmur. Tongue is coated, abdomen soft, there is tenderness to palpation of the epigastric region and right subcostal space. The margin of the liver is palpable. Blood test is normal. The EKG (Figure 10) shows diffuse myocardial changes (flattened $T_{III,v_{3,4}}$ waves, biphasic $T_{v_{1,2}}$ and low $T_{v_{5,6}}$). Gradually her condition improved. EKG dynamics were positive (Figure 10): increase in $T_{I-IIv_{3-5-6}}$ and decreased biphasic nature of T wave in the V_2 lead.

The clinical and electrocardiographic findings made it possible to interpret these changes as myocardial dystrophy due to organochlorine poisoning. Perhaps the latter was due to increased sensitivity of the myocardium to epinephrine, elevation of which is observed in blood and tissues in the presence of such poisoning (N. V. Lazarev, 1971).

Changes in the Cardiovascular System Related to Poisoning by Agents Affecting Mainly the Central Nervous System

Acute poisoning may be observed under industrial conditions by agents with marked toxic properties (chlorohydrins, dichlorohydrins, ethylene chlorohydrins and others). Changes are observed in the nervous system and other organs (cardiovascular system, respiratory organs, kidneys, liver and others); there is development of severe collapse, coma, hemorrhagic syndrome; there may be edema of the lungs, lesion to the myocardium and parenchymatous organs. N. V. Lazarev (1971) describes a case of fatal ethylene chlorohydrin poisoning on the job. We submit our case:

> Patient Sh., 24 years old, was brought to the clinic at 2200 hours with suspected industrial poisoning. He worked in contact with ethylene chlorohydrin, a small amount of which (about 20 ml) was ingested by accident at 0600 hours. At

1900 hours he complained of nausea and vomiting. A gastric lavage was performed at the medical aid station and he was given "stomach" tablets. After this he returned to the shop. However, his condition worsened and he became weak; at 1940 hours he was sent home. On the way home he vomited many times and had frequent loose stool. The emergency center physician found the patient at home in a collaptoid state (arterial pressure 50/0 mm Hg). In spite of administration of tonics, his condition did not improve, and he was taken to the clinic. Upon admission: his condition is serious, clear consciousness, inhibited, responds to questions correctly and clearly. He reports general weakness, drowsiness and chills. Integument is pale with a grayish cast. The tip of the nose and ears are cyanotic. Respiration 26-30/min; vesicular respiration ausculted. Heart boundaries are normal, dull sounds, arterial pressure 80/60 mm Hg. Pulse 100/min, thready, rhythmic. Tongue is dryish with a whitish-yellow coat. The abdomen is soft, tender to palpation in the iliac region. Liver and spleen are not palpable. Pasternatskiy symptom mildly positive. Tonic and cardiac agents were given. At night, the patient was restless, thrashed about in bed, complained of pressure in the chest and had difficulty answering questions. On the 2d day, cyanosis of the lips, ear lobes and integument over the chest was more marked; shallow respiration, 42/min; weak pulse, 110/min, barely palpable; heart sounds are dull. Arterial pressure 60/40 mm Hg. Muscle tonus low. The patient does not have complete lateral movement of eyeballs, transient, nonrhythmic nystagmoid twitching of a horizontal nature appears when he fixes his glance. Periosteal and tendon reflexes of the hands very low; knee reflexes absent, Achilles reflexes low; no pathological reflexes. There was no spontaneous urination and no bowel movement. EKG (Figure 11)L sinus tachycardia, vertical position of electric axis of the heart. Minor changes in the myocardium, mainly the left ventricle (apices and lateral part of the heart). Chest x-ray showed no changes. Eyegrounds: hyperemic optic nerve disks, barely differing in color from the retinal background, boundaries vague, veins wide and somewhat tortuous. Blood test: leukocytosis--$23.75 \cdot 10^6$/μl (23,750) and stab nuclear shift (15%), marked elevation of transaminases (ATS 240 units, ALT 284 units), aldolase--34.2 units and residual nitrogen--300 mg%.

Urinalysis: albumin 6.6 g/l (0.66%), leukocytes 20/field, erythrocytes 203/field, altered renal epithelial cells in moderate amount. His condition was unchanged in the daytime. On the 3d day, his condition became extremely serious. The patient is stunned. Marked general cyanosis and acrocyanosis. Rapid respiration (40-48/min), shallow, intermittent. Vesicular

breathing. Pulse 100-108/min, deficient. Arterial pressure 100/80-120/90 mm Hg. Heart sounds dull, pericardial friction murmur in a circumscribed area (near the apex). Pupils constricted, no reaction to light. Tendon reflexes absent. No pathological reflexes. In this time (2 days) urine output only 200 mL. EKG taken on 3d day (Figure 11): "infarctoid" changes appeared, indicative of marked hypoxia and impairment of metabolic processes (electrolyte gradient) in the myocardium, dystrophy and, perhaps, noncoronarogenic myocardial lesion (mainly to the posterior wall of the left ventricle); considerable increase in electrical systole of the ventricles.

In view of worsening of his condition, the patient was transferred to the Institute imeni N. V. Sklifosovskiy where, in spite of intensive therapy and repeated peritoneal dialysis, he expired.

Anatomical findings: acute ethylene chlorohydrin poisoning (according to clinical data); numerous petechial and striate hemorrhages, nonuniform filling with blood of the myocardium, hemorrhages in the region of the anterior and posterolateral walls of the left ventricle (under the epicardium and near the superoposterior papillary muscle); isolated atheromatous plaques (which do not constrict lumen) in anterior and descending branches of the left coronary artery; dystrophy of the myocardium, kidneys (excretory nephrosis) and liver; severe edema of the brain and lungs; venous plethora of organs, thin blood.

Microscopy of myocardium: marked dystrophy and edema of the myocardium with areas of necrobiosis (Figure 11, c, d); fine droplet adiposity of hepatocytes of the liver; very severe dystrophy and autolysis of tubular epithelium of kidneys.

Thus, as a result of acute ethylene chlorohydrin poisoning, changes in the central nervous system caused impairment of respiration and organic hypoxia, appearance of severe collapse and impairment of renal excretory function (uremia). The occurring metabolic changes (protein, electrolyte, fluid-electrolyte, enzyme metabolism), as well as impairment of acid-base equilibrium, against the background of marked hypoxia, caused appearance of dystrophic and necrobiotic (noncoronarogenic) changes in the heart, involvement of the liver and kidneys.

Under industrial conditions, there are also cases of poisoning by substances with minimal toxic properties. In such cases, the acute states are apparently due to the large dosage of a substance or increased sensitivity of the body, or else both factors together. The reaction is associated with marked excitation of the sympathetic nervous system of the order of a stress reaction,

with increase in blood catecholamine content, which could cause injury to the myocardium and vessels.

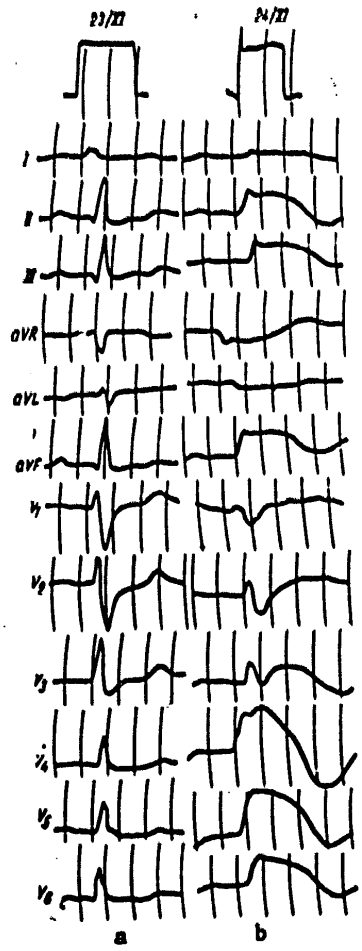


Figure 11.
Acute ethylene chlorohydrin poisoning
a) EKG taken on 2d day of illness
b) EKG taken on 3d day of illness

Patient T., 40 years old, instrument control man at a pharmaceutical plant (tenure of 8 years), was brought to the clinic at 1400 hours. He had worked for a long time on synthesis of sodium benzonate. In the past week he had to go down for 15-30 min, several times a day, to the desiccating department, where there was a large amount of caffeine powder. After this, he observed transient palpitations. During the night shift, he cleaned out the drying department, where there was about 500 kg of sodium benzonate of caffeine. He worked without a respirator. He developed a sensation of shortage of air, fever and general weakness after working for 1-1.5 h. General malaise, palpitations increased after 2-3 h, with appearance of mild vertigo, nausea and tremor of the body. At the end of his shift, on his way home, there was intensification of dyspnea and nausea. He vomited once. At home, there was appearance of sensation of pulsation in the temples, cramps in the legs and muscles of the upper abdomen, with intensification of palpitations and worsening of general condition. The emergency center physician rendered first aid and performed gastric lavage, after which the patient was taken to the clinic.

Upon admission: clear consciousness, hyperemic face and chest; rapid speech, somewhat slurred, body tremor, general excitation, motor restlessness, euphoria and dyspnea (26 respirations per minute); somewhat hard breathing; diffuse apical beat, accentuated sounds, heart boundaries in normal range; pulse 110/min, cordy, rhythmic; arterial pressure 160/80 mm Hg; abdomen soft, some tenderness upon palpation of muscles in the upper half; cranial nerves show no changes; testing of plantar reflexes showed tonic seizures of gastrocnemius; EKG taken on day of admission

(Figure 12a): diffuse myocardial changes; sinus tachycardia 110-105/min; normal position of electric axis; P-Q 0.13 s, QRS 0.10 s, Q-T 0.30 s (normal 0.27 s), $S-T_{II-III}$, $V_{3,4,5}$ slightly inclined, T_I flattened, $T_{II,III}$, $V_{5,6}$ low, biphasic.

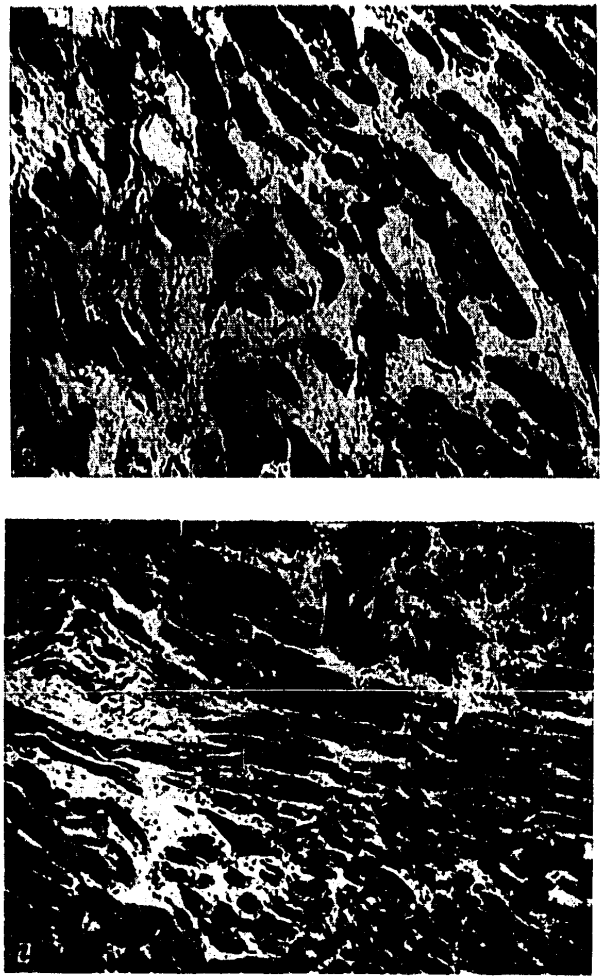


Figure 11. (continued) Acute ethylene chlorohydrin poisoning; histological preparation of myocardium: marked edema and dystrophy of myocardium (c[top]); necrobiotic regions (d[bottom])

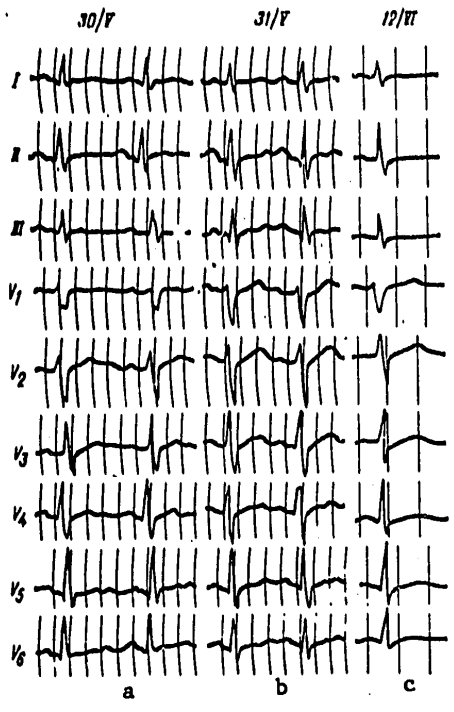


Figure 12.
EKG of patient T. Explained in text

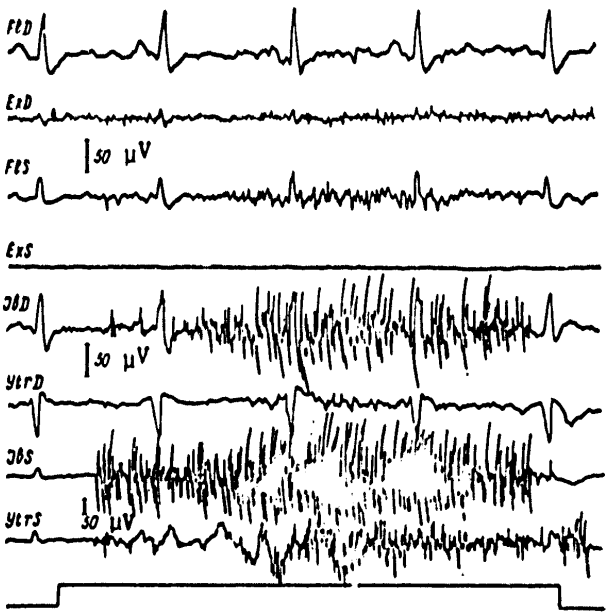
After intramusuclar injection of 10 mℓ 25% magnesium sulfate, 1 mℓ 2.5% aminazine with novocain, the patient slept for about 2 h. Upon awakening, he reported some improvement, but marked facial hyperemia, tremor of the entire body and hands persisted. Respiration rate 20/min, arterial pressure 140/80 mm Hg. There were brief and recurrent cramps in the gastrocnemius. After intake of 20 m 2% chloral hydrate he fell asleep. In the morning he was more mobile and euphoric. Marked hyperemia of all integument persisted, especially on the face, neck, back and chest. Respiration rate 20/min. Fine tremor of the body and hands, mild hyperesthesia of the feet. Tendon reflexes lively, abdominal s\d. Tenderness of gastrocnemius upon palpation.

EKG taken on 2d day (Figure 12b): more marked changes in the myocardium; tachycardia up to 150/min; electric ventricular systole up to 0.06 s. No changes demonstrable in blood and urine. On the next 2 days his condition improved appreciably. Pain in muscles of the legs and upper half of abdomen persisted. There was regression of cutaneous hyperemia; mild motor excitement, restlessness and elements of euphoria were observed. Roentgenoscopy of the chest failed to demonstrate deviations from the physiological norm. On the following days there was dyspnea upon exercise and rapid walking, increased perspiration and some tenderness in the right gastrocnemius. EKG on the 12th day of illness (Figure 12c) still showed changes in the myocardium (low T_I, II, $V_{4,6}$), against the background of generally positive dynamics.

Biochemical studies on the 7th-10th days of hospitalization showed elevation of aspartic transaminase to 82 units (normal 40 units). According to the results of electromyography (Figure 13) performed on the 5th day, there were deviations in bioelectrical activity of skeletal muscles. The changes in structure of the EMG were indicative of the stimulating effects of large doses of caffeine on the motor system.

He was discharged after 13 days in satisfactory condition, with the recommendation not to work in contact with chemicals for the next few months. When

examined 3 months later, no deviations referable to the internal organs were demonstrated.



Fiugre 13. Electromyogram of skeletal muscles of patient T. Explained in the text.

Thus, there were distinct clinical signs of excitation of the adrenergic system in the symptomatology of poisoning. This was apparently the chief cause of metabolic disturbances, deviations on the EKG and EMG indicative of dystrophic changes and fine necrotic foci in the myocardium. The EKG dynamics and elevation of aspartic (muscular) transaminase in blood serum could also be indicative of the latter.

In this case, the slow development of poisoning symptoms is apparently related to slower absorption of caffeine from the respiratory tract after inhalation, as compared to absorption from the gastrointestinal tract after intake by mouth.

Agents Inducing Acute Allergic States and Lesions in the Cardiovascular System

The data in the literature (Ye. M. Severova, 1962; Kh. I. Bronshteyn, L. Ye. Itkin, 1965; S. A. Ashbel', 1969) and our findings enable us to single out

allergic myocarditis and allergic myocardial dystrophy occurring under the influence of various industrial agents (antibiotics, vitamins, trace elements and others).

Myocarditis and myocardial dystrophy of allergic genesis were observed chiefly among young and middle-aged women working in the above industries. The disease was characterized by acute, recurrent or chronic course. In most patients, along with allergic manifestations (urticaria, Quincke type edema, etc.), there were varying degrees of pain in the cardiac region, as well as change in repolarization of the terminal part of the ventricular complex on the EKG, chiefly diffuse in nature.

We submit one of our case histories:

> Patient D., 48 years old, had worked for 22 years as a zootechnician and prepared feed for cattle (she was in constant contact with group B vitamins, choline chloride, trace elements and antibiotics). One month before she became sick, she began to observe edema on different parts of the body, mainly the left half of the face and neck, urticaria, first on the hands and legs, then all over the body. Eruptions and edema were associated with marked weakness, headache and mild pain in the region of the heart. At night, she developed excruciating pressure pain in the cardiac region irradiating to the left arm and left scapula, associated with a collaptoid state. Concurrently, there was development of extensive edema of the face and neck. She was hospitalized with the diagnosis of myocardial infarction. Peripheral blood revealed eosinophilia (10%) and leukopenia, $2 \cdot 10^6/\mu\ell$ (2000).
>
> Injections of vitamin B were prescribed. The first injection was associated with a severe allergic reaction and development of collaptoid state, with appearance of negative EKG dynamics. Hormone and desensitizing therapy improved her condition. In order to confirm the diagnosis and determine whether there was a link between her illness and occupation, she was transferred to the clinic. Upon admission she complained of weakness and periodic pain in the region of the heart, associated with edema of the face and neck. Objective examination revealed widening of the heart in both directions, dull heart sounds and tachycardia. Pulse 90-100/min, full. Arterial pressure 140/80 and 145/95 mm Hg. EKG (Figure 14) showed change in repolarization of ventricles (convex S-T segment and negative $T_{II,III,V_{1-4}}$ wave). Blood test: eosinophilia (10-12%), hypergammaglobulinemia (30%) sublimate test down to 1.49. On the basis of the clinical and EKG findings the diagnosis of toxic allergy was made (Quincke edema, urticaria), as well as acute allergic myocarditis. Her condition improved rapidly in response to hormone therapy, and there was normalization of EKG.

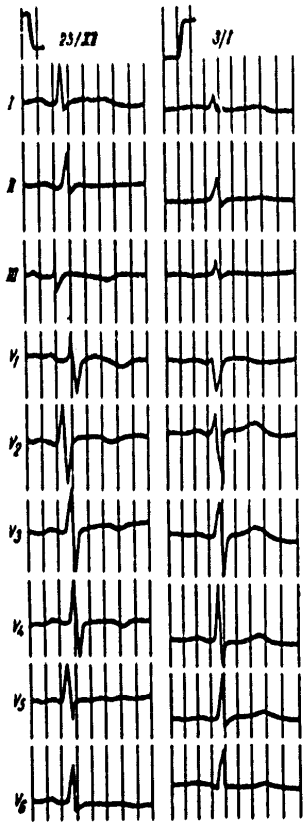


Figure 14.
EKG of patient D.
explained in text

In the described case, there was demonstration of similarity of nonspecific reactions to diverse industrial (occupational) and nonoccupational etiological factors in the presence of allergic heart disease.

Acute Effects of Physical Factors

Ionizing Radiation

The possibility of single exposure or delivery of large divided doses of radiation under occupational conditions exists only in exceptional (emergency) situations. There is even less possibility of selective exposure of the heart to a dose of radiation that would induce an acute lesion. Such lesions were observed in Los Alamos in connection with an accident (12,000 rad to the chest), the accident at Lokkart (1200-1500 rad to the head and neck, in one case 36,000 rad to the chest), and an accident described by N. A. Kurshakov et al. (800-1200 rad to the region of the heart). A. K. Gus'kova and G. D. Baysogolov, N. A. Kurshakov observed only transient changes in the EKG and some clinical paramaters with doses of several hundred rad. This clinical findings coincide with data in the literature concerning experimental studies, which were summarized by Ye. I. Vorob'yev (1971). In the last few years, some additional information was obtained about patients exposed to massive radiation to the chest for therapeutic purposes.

As an illustration, we submit the following example:

Patient S., 31 years of age, was brought to the clinic on 31 August 1972 due to acute local radiation lesion to the anterior chest wall and fingers of both hands. He worked as a flaw detector for 3 years. About 2 months ago, he had a vial of ^{137}Cs in his shirt pocket for about 2 h (^{137}Cs activity 2.5 to 5.3 g-equiv Ra). Tentative estimate of dosage: 30,000-38,000 R on the surface near the source, 16.5 to $22 \cdot 10^3$ rad at a depth of 1 cm, 1400-2000 rad at the level of the myocardium with maximum at the apex and 300-600 rad to other parts of the muscle. With contact radiation, the maximum dose was distributed in a narrow beam, with considerable decrease toward the periphery;

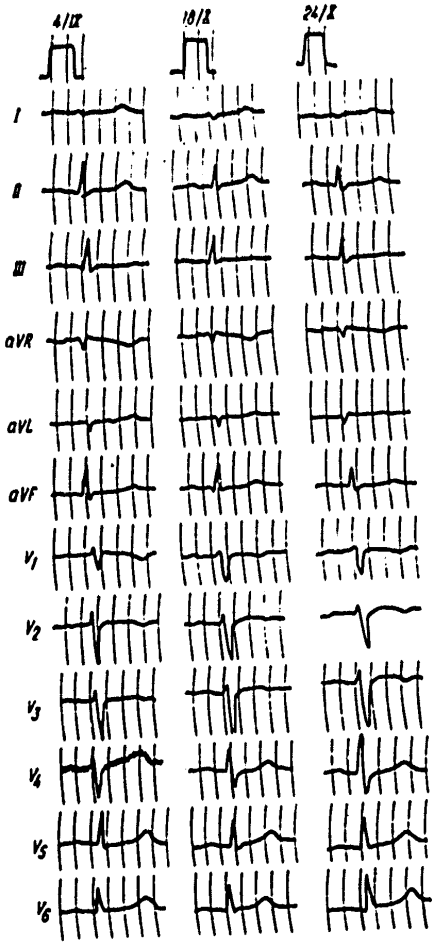


Figure 15.
EKG of patient S., explained in text

however, when the source is away from the skin, there could also be a different dose distribution with scatter from the beam along the surface.

The first signs of lesion appeared on the 3d day in the form of erythema under the left papilla, with subsequent formation of a necrotic site. Changes began to develop on the fingers of the right hand after 2 weeks, then on the left hand, with appearance of nausea and vomiting. The patient was hospitalized at the Institute of Hematology and Blood Transfusions, where a comprehensive examination (including trephine biopsy of both iliac bones) failed to demonstrate serious changes inherent in acute radiation sickness.

It was known from his history that the patient had had a brain concussion in 1964 (fell in a mine), he was treated by a neuropsychiatrist because of depression. When admitted his condition was satisfactory; consicousness clear. The integument over the anterior wall of the chest, from the level of the throat to the xiphoid process of the sternum and to the left up to the edge of the costal arch is hyperpigmented and scaly in many areas. The necrotic focus (2.5×3 cm) is surrounded by a zone of erosion with foci of epithelization totaling 6.5 cm in diameter in the region of the heart. Ulcerative necrotic changes in the fingers of the right hand (II-III) involve the terminal and middle phalanges and the main phalanx of the second finger. Percussion reveals a clear sound over the pulmonary fields and auscultation, vesicular respiration. The heart boundaries (percussed) could not be exactly defined due to a lesion in this region. Heart sounds are slightly dull. Arterial pressure 115/70 mm Hg. Pulse 80/min, rhythmic, full. Abdomen is soft, no tenderness, liver and spleen are not enlarged. Normal stool and urination. Neurologically: marked neurotic syndrome. Roentgenologically: no change in configuration and size of heart. EKG: (Figure 15) showed no changes.

Duirng the observation period there were positive dynamics with regard to state of involved areas. The ulcer on the chest diminished in size and there was epithelization of the eroded surface around it. Partial epithelization occurred in the sites of digital lesions on the right hand; only necrotic changes remained on the terminal phalanges of the second and third fingers of the right hand. Roentgenologically: osteoporosis of digital and metacarpal bones of the right hand.

The patient complained periodically of dull, sometimes stabbing pain of vague localization (sternum, costal border, epigastric region, less often in the region of the ulcer) lasting a few minutes to a few hours. He was active when he had such pain. Clinically, no deviations referable to the heart were demonstrable. His pulse was 60-80/min and arterial pressure 90/60-115/70 mm Hg. Dynamic comparisons failed to show pathological changes on the EKG. Clinical and roentgenological studies also failed to demonstrate changes in the lungs and pleura. Blood test, urinalysis and biochemical tests were normal. Total blood protein 74-81.9 g/l (7.4-8.19 g%). Normal proportion of protein fractions. Residual nitrogen 3.9 mg%, potassium 18 mg%, sodium 312.5 mg% in plasma, normal proportions. Sugar (85 mg%), cholesterol (200 mg%) and enzyme levels also failed to demonstrate deviations. Blood amylase 131 units, cholinesterase 45 units, creatine kinase 10.3 units, alkaline phosphatase 1.5 units; the following were slightly diminished: GASP [glutamic-aspartic transaminase?] 2.5 units, GALT [glutamic-alanine transaminase?].4.5 units, thymol test 2.5 units. Bone marrow taken from the sternum at the end of the 4th postradiation month was deficient in cells. The leuko-erythroblast ratio is altered due to reduction of erythroblasts.

The patient was treated with antibiotics, vitamins, antihistamines, mild tranquilizers, ganglion-blocking agents and physiotherapy; an intracutaneous and paravertebral T_1-T_4 novocain block was produced once.

The patient's condition was quite satisfactory. However, there was sudden occurrence of death. This outcome could be attributed to cardiac arrest, due to functional and organic changes in the heart, focal and diffusely dystrophic in nature, as a result of local exposure to radiation.

Pathoanatomical findings: acute, severe local radiation trauma to the left half of the chest with irradiation of the heart, left lung, sternum, and marked morphological changes in the skin, muscles, esophagus and serosa. Deep radiation ulcer at the stage of pyonecrotic changes in the skin, subcutaneous fatty tissue and muscles in the region of the sixth-seventh ribs along the left midclavicular line. Residual signs of radiation dermatitis on the left chest. Extensive, large-focus sclerosis on the anterioposterior wall of the pericardium and parietal pleura in the left pleural cavity, atrophy with cicatrized ulcers of the mucosa, sclerosis and thickening of the wall of the lower half of the esophagus. Radiation myocarditis with moderate cardiosclerosis. Venous plethora and edema of the lungs. Thrombosis of fine vessels of the lungs, mainly on the left. Small sites of pneumonia and infarction in the lower lobe of the left lung. Mild reticular

pneumosclerosis, mainly of the left lung. Radiation lesion to the second and third digits of the right hand, in the form of marked atrophy of the skin in the region of the middle and distal phalanges and dry necrosis of soft tissues of the distal phalanx corresponding to the level of the nail plate, phalangeal osteoporosis. Residual signs of lesion to the second finger of the left hand, in the form of partial atrophy of soft tissues of the distal phalanx.

Morphological signs are indicative of death of the asphyxia type: severe plethora of internal organs, subpleural ecchymosis, thin dark blood in heart cavities and vessels.

Death was due to cardiac arrest as a result of severe radiation trauma to the left half of the chest and cardiac lesion.

A comparison of this case to data referable to other patients exposed to predominant irradiation of the cardiac region (N. A. Kurshakov et al., 1965; A. K. Gus'kova, G. D. Gaysogolov, 1971, and others) indicates that it is unusual: relatively small dose of local radiation to part of the heart, rapid onset of death (within 4 months), suddenness of the latter, unique pathogenetic mechanisms that could not be totally explained on the basis of histological signs of cardiac lesion.

It may be assumed that there is a reflex mechanism involved in sudden functional disturbances of the heart as a result of pathological afferentation from periocardial involved regions of the heart and chest. This pathological reflex was expressed through activity of the heart, in circumscribed regions of which there were also postradiation and, perhaps, immunoallergic in genesis, moderate changes of the order of interstitial myocarditis and dystrophy of muscle fibers.

Effects of Atmospheric Pressure Changes

High pressure: The work of divers or caisson workers may be associated with functional disturbances of the cardiovascular system as a result of rapid transition from deep water to the surface. Decompression with excessively rapid lowering of atmospheric pressure could cause accumulation of gas (nitrogen) bubbles in blood, with the gas dissolved in body tissues. Not having had time to be eliminated through the lungs, they can induce emboli in the vessels of various organs and systems (lungs, brain, heart and others) and cause the corresponding clinical syndromes of caisson disease (A. P. Brestkin, 1952). Occlusion of branches of the pulmonary arteries could cause an acute strain of the right ventricle, with the corresponding EKG signs of cor pulmonale. Coronary vessel emboli induce transient attacks of angina pectoris or the syndrome of acute ventricular asystole, occasionally with edema of the lungs, focal lesions to the myocardium and ultimately death. Such patients complain of general weakness,

pain in the bones, joints and muscles. They present tachycardia and occasional elevation of arterial pressure. The EKG shows diffuse hypoxic changes, coronary changes or infarct-like deviations. This could lead to myocardial sclerosis.

Low pressure: When flying at high altitudes or working at a high altitude (in the mountains), lowering of atmospheric pressure and partial oxygen pressure could lead to decreased oxygenation of blood. There is an increase in dissociation of oxygen and hemoglobin in erythrocytes, followed by hypoxia and functional disorders of the cardiovascular and nervous systems. This may be particularly marked in individuals with vascular atherosclerosis (V. B. Malkin, V. I. Plakhatnyuk, 1974). The condition is associated with appearance of severe muscular weakness, drowsiness, impaired memory, slow responses to various stimuli, deeper and faster respiration, faster heart rate, drop of arterial pressure, with possible fainting or collapse, sinus tachycardia; there is appearance of signs of diffuse myocardial dystrophy on the KG; in the presence of atherosclerosis of coronary vessels there are focal changes in the myocardium.

Effects of High Temperature and Thermal Radiation

Overheating of the body and impaired heat regulation can be clinically manifested by symptoms varying in severity. In mild cases, faster pulse, dull heart sounds and hypertension are observed, against the background of general weakness, buzzing in the head and ears, thirst, occasionally nausea, vomiting and fast respiration (B. A. Krivoglaz, 1957; A. Yu. Tylis, P. Solomko, 1968).

In severe cases, the above syndrome may be the prodromal period, prior to development of heat (or sun) stroke. Then the respiration is fast, shallow, heart sounds become dull, pulse is fast (100-200/min), thready, and arterial pressure drops. The EKG shows extrasystole, transient block of the right branch of the atrioventricular bundle, increase of P_{II-III}, decline of S-T and T wave. Systolic and minute blood volumes diminish (A. N. Azhayev, N. A. Lapshina, 1971). Occasionally, there are epileptiform seizures, convulsions, mental disorders; later on there may be collapse and coma ending with death.

Effects of Electricity

When alternating current of 100 mA to 5A passes through the region of the heart, cardiac arrest may occur immediately (apparently as a result of ventricular fibrillation). In other cases, victims present autonomic disorders, pain in the cardiac region and transient rhythm disturbances. Occasionally, a few days after the accident there may be signs of diffuse or, less often, focal changes in the myocardium, as found on the EKG, which are indicative of injury to the myocardium.

Acute Effects of Radiofrequency (Short, Ultrashort, Superhigh) Electromagnetic Waves

The data in the literature (A. A. Orlova, 1960; E. A. Drogichina, M. A. Sadchikova, 1965; Z. V. Gordon, 1966; V. M. Malyshev, F. A. Kolesnik, 1968) indicate that electromagnetic fields in various frequency ranges influence the cardiovascular system.

In animal experiments, rhythm disturbances, vascular dilatation, longer phase of cardiac contraction, as well as acute onset of EKG and morphological changes of the myocardial dystrophy type were observed. Several authors (N. V. Uspenskaya, 1963; N. N. Molchanov, Ye. V. Gemibitskiy, 1973, and others) demonstrated changes in hemodynamic parameters and nonspecific changes on the EKG in chronic and acute experiments involving exposure to electromagnetic fields in different frequency ranges and of different intensity.

The mechanism of these changes has not yet been adequately investigated. F. A. Kolodub and G. Ye. Yevtushenko (1972) believe that they are based on changes in carbohydrate and nitrogen metabolism in myocardial cells.

Isolated cases of acute "wave sickness" have been described in man; it can occur under the influence of high-power generators, gross infraction of safety practices or an accident (V. M. Malyshev, F. A. Kolesnik, 1968, and others). The clinical signs and state of the cardiovascular system associated with this condition have not been sufficiently investigated. With exposure of the head, diencephalic symptoms are prominent in the clinical signs, with hypertensive reactions, tachycardia, attacks of paroxismal tachycardia, ataxia and autonomic syndromes (profuse perspiration and others). Death may occur due to collapse and acute overheating. McLaughlin (1957) and Grof (1958) described a case of fatal outcome after exposure of a 42-year man to SHF.

Some Questions of Etiology, Pathogenesis and Therapy of Acute Cardiovascular Syndromes of Occupational Etiology

There are several distinctions to the clinical syndromes referable to the cardiovascular system in the presence of acute states due to the effects of various occupational factors, although they retain the main patterns of nonspecific mechanisms, as well as clinical manifestations. One often observes signs of excitation of the central and autonomic nervous systems (vegetovascular dysfunction), adrenohypophyseal reactions (stress), redistributional leukocytosis, as well as changes in bioelectric processes (phases of repolarization of the myocardium) of the heart.

Some deviations or other are observed in the cardiovascular system, depending on the nature of the factor, its physicochemical properties, time and place of application, concentration of a toxic agent, type of energy and its distribution in tissues, condition of the nervous system, individual

reactivity of the body and severity of the overall pathological process. The severity of changes ranges from mild rhythm disturbances, fluctuations of arterial pressure and negligible dystrophic changes in the myocardium to development of hemorrhages, necrobiosis and necrosis of the myocardium, acute cardiovascular insufficiency, collapse and instantaneous death (in cases of poisoning by tetraethyl lead, ethylene chlorohydrin, methyl alcohol, gas embolism of coronary vessels and under the influence of certain other factors.

Sudden cardiac arrest may be the result of acute cyanide, hydrogen sulfide, barium salts, ethyl bromide, phenol, chlorinated hydrocarbon (methane) and other poisoning. In such cases, autopsies usually fail to demonstrate changes in the heart. If death did not occur immediately, post mortems often demonstrate fatty or protein dystrophy of the myocardium, necrobiosis and hemorrhages, edema of the tunics of the heart and parenchyma, change in vascular walls and other changes. The EKG shows significant changes in myocardial repolarization phase (lowering or inversion of T wave), mainly of an extensive nature, in both the left and right leads. The clinical and and EKG findings do not always permit attribution of these changes to vertical position of the heart, coronary insufficiency or acutely developed stress of the right ventricle. The demonstrated deviations are essentially consistent with the syndrome of diffuse myocardial dystrophy.

The pathogenesis of such functional disturbances of the heart is rather complex. In the first few minutes after exposure to occupational factors, it is due to specific and neuroemotional excitation, development of the hypothalamohypophyseoadrenal reaction that is common with any stress.

According to the data of H. Selye (1963) and Raab (1968), excessive accumulation of catecholamines in the heart is observed in the presence of stress states. This is associated with increase in heart function (contractions, stroke and minute volumes) and significant increase in myocardial oxygen uptake. The increased oxygen uptake is not always consistent with intake thereof, even in the presence of healthy coronary vessels, but especially with changes in the latter. As a result, there is onset of hypoxia, with impairment of metabolism (attenuation of processes of phosphorylation and glycolysis) and accumulation of incompletely oxidized products (lactic acid and others). Neuroendocrine and metabolic changes also occur as a result of the direct effect of the factor on the heart, and they induce disturbances in microstructures of myocardial cells. Evidently, the final and main result of such deviations is progressive hypoxia, which elicits changes in the heart in the nature of diffuse myocardial dystrophy, occasionally associated with necrobiosis or necrosis of the myocardium, involvement of the vascular wall and deviation of bioelectrical processes (Weiss, 1956).

G. F. Lang uses the term "myocardial dystrophy" to refer to functional changes, that are quite reversible at the early stages, related to some biochemical deviations or other (impairment of enzymatic systems, carbohydrate-phosphorus, protein, electrolyte or other forms of metabolism), as

well as impairment of redox processes in the myocardium. Thanks to the development of electron microscopy, the substrate of myocardial dystrophy is clearer. One observes enlargement of muscle cell nuclei, redistribution of nuclear substance, mitochondrial swelling, clearing of the matrix, destruction of septa and focal breakdown thereof. In the cell, there is a reduction in number of ribosomes; one observes dilatation of sarcoplasmic reticulum tubules, intracellular edema, disappearance of glycogen granules, appearance of fat droplets and other deviations. These changes are consistent with protein and fatty dystrophy observed under an ordinary microscope. The observed changes are not specific or stereotypic (D. S. Sarkisov, G. V. Vtyurin, 1971). The ultrastructural changes in myocardial cells are the same, regardless of their cause (toxic agents, hypoxia, increased load, circulatory disturbance, etc.). On the basis of clinical and experimental data, it was established that dystrophic myocardial changes are essentially reversible. After elimination of the pathogenic factor, the ultrastructures gradually revert to normal as a result of intracellular recovery processes (without increase in number of cellular elements). Destruction of muscle cells is compensated by hyperplastic processes (increased mass of specific ultrastructures) in remaining cells. This is associated with enlargement, hypertrophy, of cells. Thus, significant changes in myocardial function and dystrophy thereof are associated with structural changes on the subcellular level (D. S. Sarkisov, B. V. Vtyurin, 1971).

Myocardial dystrophy can be induced by various exogenous and endogenous factors.

Neurotrophic (dystrophic) changes in the ventricular myocardium were found by many researchers upon stimulation of peirpheral and central branches of the sympathetic and parasympathetic nervous system. Experimental stimulation of peripheral nerves produced so-called reflex myocardial dystrophy (A. Yu. Mal'kov, 1966; Z. I. Vedeneyeva, 1967; M. D. Vakar, 1969, and others). Some authors also observed flattening or inversion of the T wave on the EKG (S. M. Mints et al., 1970, and others).

Centrogenic myocardial dystrophy developed upon stimulation of hypothalamic nerve centers (I. K. Shkhvatsabaya, 1967; V. M. Tsinamzgvarshvili et al., 1971, and others). Changes were also demonstrated on the EKG, indicative of hypoxia, dystrophy and necrosis of the myocardium. There was also histological demonstration of necrosis and infarction-like changes in the cardiac muscle. These changes were largely due to intensification of the influence of the sympathoadrenal system on the order of Selye's stress reaction (M. G. Rayskina et al., 1966).

Experimental dystrophic changes were induced in the heart with injection of epinephrine (D. S. Sarkisov, B. V. Vtyurin and others). In such cases, the EKG showed some inversion of T wave and depression of S-T segment. Microscopic examination revealed fatty degeneration and areas of atrophy of muscle cells. After administration of epinephrine, lowering of T wave and enlargement of U wave are observed on the EKG. The experimental data

of A. V. Trubetskoy (1964), who detected myocardial dystrophy that developed as a result of brief cerebral ischemia. During surgery of the nervous system (Ye. Z. Ustinova, Ye. F. Drigo, 1963; S. P. Astrakhantseva, 1969; Burch, Gatath, 1954), patients presented high excretion of epinephrine in urine; on the EKG, the change in T wave; the change in St segment should be considered an indication of considerable metabolic disorders in the myocardium, which perhaps alter the function of the potassium-sodium "pump" (I. I. Isakov). The cardiac lesions induced by large doses of catecholamines (norepinephrine, epinephrine) may be prevented with adrenalytic agents. Alpha adrenalytic agents prevent injury induced by norepinephrine and beta adrenalytic agents, the deleterious effects of isoproterenol (Z. I. Vedeneyeva, 1967). The similarity of neurogenic dystrophy to lesions induced by large doses of catecholamines is also indicative of the possible pathogenetic action of the latter. The influence of the sympathetic nervous system on development of neurodystrophy is confirmed by depletion of the norepinephrine reserves of the myocardium following a strong stimulus. S. V. Anichkov (1971) believes that the decline of norepinephrine content in myocardial cells is one of the main mechanisms of neurogenic dystrophy that develops with strong and prolonged stimulation of the nervous system. Researchers have reported a decrease in blood epinephrine in the presence of cardiac insufficiency. In the light of the submitted data, we can understand appearance of signs of myocardial dystrophy in patients with neurocirculatory dystonia, hypothalamic disorders, various neuroses, autonomic dysfunction and manifestations of the diencephalocardiac syndrome. The presence of common collectors of autonomic and emotional afferentation in the hypothalamic region suggested the mechanism of appearance of dystrophic changes in the heart in the presence of some emotional states (P. V. Simonov, 1969). Dystrophic myocardial lesions can occur even with normal stimulation of the heart and, especially, in the presence of coronary sclerosis or other changes in the heart. Under such conditions, even an ordinary factor could cause heart disease. In the last decade, there has been considerable expansion of the teaching on myocardial dystrophies; however, not enough studies are being pursued of myocardial dystrophy as related to various occupational (especially acute) factors.

The clinical and EKG changes referable to the cardiovascular system with acute exposure to various factors, particularly occupational ones, are not specific.

Main Principles of Organization of Medical Care

The course and outcome of acute poisoning and lesions depend on the sophistication of organizing and proper use of a set medical and therapeutic measures administered at different stages of treating victims. It is imperative to make the utmost use of the advances in modern resuscitation practice, as well as of the most adequate ways and means of complex and intensive therapy.

Treatment is administered on a full scale and modern level; various pathogenetic agents are used: blood substitutes, extracorporeal hemodialysis,

prolonged oxygen therapy in a pressure chamber, cardiac defibrillation, administration of salt and protein mixtures, osmotic diuretics and specific antidotes. General practitioners, surgeons, resuscitation specialists, neuropathologists and other specialists participate in administering therapy.

Care of victims consists of rendering immediate medical aid at the site of the accident or in the nearest medical institution, with subsequent transfer to special (occupational, resuscitation, etc.) medical institutions.

In cases of serious injuries and poisoning, rapid delivery of the victim (by car or aircraft) to specialized institutions and early initiation of complex therapy increase significantly the incidence of favorable outcomes. The following therapeutic measures must be implemented: 1) rapid removal of toxic agent from the victim's body by means of well-known methods (inducing vomiting, gastric lavage, administration of appropriate antidotes), maintenance of cardiac and respiratory function; 2) systematic use of ways and means of resuscitation therapy directed toward restoring functions of vital organs (central nervous system, circulatory and respiratory organs); removal or neutralization of poison remaining in the organism (antidote therapy, lavage of gastrointestinal tract). Oxygen therapy, controlled respiration machine, artificial kidney, forced osmotic diuresis, infusion of blood and fluid are administered, with constant monitoring of fluid-electrolyte balance and metabolism.

Metabolic disturbances are corrected, and the possible secondary complications are averted in the light of the conceptions of mechanism of action of the deleterious factor at different stages of development of the process.

CONCLUSION

[Text] This monograph has submitted data describing the distinctive reactions of the human cardiovascular system to the most diverse occupational factors. The most common and, to some extent, circumscribed clinical syndromes, concomitant with different occupational diseases, have been described; their role is far from unequivocal. In some cases, they merely accompany the main clinical symptom complex that is directly related to the occupational factor (hemodynamic changes in the presence of radiation hypoplasia of hemopoiesis, cardiac symptom complex in the presence of anemia caused by benzene); in other cases, these syndromes are a typical element of the overall clinical manifestations of an occupational disease, although their appearance is secondary (cor pulmonale in the presence of silicosis, toxic pneumosclerosis, berylliosis). In some cases, the cardiovascular changes determine the symptomatology, course and outcome of disease, and they also affect the extent of disability (for example, with exposure to carbon disulfide, microwaves, etc.).

There are examples in the monograph of the direct deleterious effects of high-intensity occupational factors on the heart and vessels (overradiation, cooling, vibration and toxic effects).

All of the foregoing is indicative of the importance of the problem. Comprehensive details and identification of the cardiovascular component are needed to evaluate the health status of virtually all groups of workers and to make the diagnosis of an occupational disease. It is imperative to determine the extent of cardiovascular changes in the presence of certain other functional disturbances in the body that restrict occupational activity. The latter is closely linked with questions of expert certification of disability and medical rehabilitation.

In assessing the many years of experience in occupational medicine and data in the literature concerning cardiovascular pathology as a whole, it can be stated that we now have some rather comprehensive information that makes it possible not only to demonstrate a number of cardiovascular disturbances, but to classify them. Such systematization makes it possible to investigate the etiology and pathogenesis of occupational diseases, as well as clinical diversity of reactions that depend on the intensity and nature of factor involved and time of formation of pathological changes. It must be conceded that this work is far from completed, in view of the diversity of terms used by different authors, prevalence of special descriptions over general publications in which the different aspects of this complex problem would be analyzed. Distinctions are made of the more circumscribed forms and states: syndromes of neurocirculatory dystonia, myocardial dystrophy, involvement of peripheral vessels, systemic hemodynamic disturbances with circulatory insufficiency.

In view of the absence of results of properly organized epidemiological studies, the question remains debatable as to the role of some occupational factors in development of such forms of cardiovascular pathology as essential hypertension and cardiac ischemia.

Tests have not yet been fully refined for objective determination of the degree of limitation of fitness for general and specialized work in relation to changes in the cardiovascular system associated with various forms of occupational activity.

The expert decisions that presently being made, examples of which have been cited in this monograph, are indicative of the inadequacy of methodological capabilities and relative nature of decisions that are largely determined by a researcher's individual experience with a given factor.

In spite of the many reports on the fate of victims of occupational diseases, including patients with cardiovascular changes (workers in hot shops, individuals suffering from silicosis, those working with sources of radiowave radiation, carbon disulfide and others), we were unable to find in the available literature any specific studies dealing with analysis of the subsequent course of some cardiovascular syndromes as related to the decision made with regard to employment (with due consideration of age and other factors).

Diagnostics of cardiovascular pathology in the symptomatology of occupational diseases is based on the use of many modern and refined methods of examination. However, proper evaluation has not yet been made of the informativeness of different methods, and a set of procedures is only at the formative stage, with respect to adequate evaluation of the condition of the heart and vessels with exposure to a given occupational factor. In our opinion, some sort of general minimum level should be defined for exposure to all factors, which would make it possible to compare reactions to different factors according to severity and clinical importance.

Analysis of all the material submitted in this monograph shows a distinct prevalence of nonspecific reflex reactions of the heart and vessels to occupational factors. For this reason, identification, evaluation and interpretation thereof must be made by means of objective methods reflecting the extent of generalization and stability of reflex hemodynamic changes. The radioactive tracer method, with appropriate functional loads and electrocardiography are used for this purpose.

Microcirculation and oxygenation of different organs with exposure to occupational factors have been studied very little. Nor can we consider adequate the information at hand concerning pathological anatomy of the heart and vessels, especially in the case of chronic exposure to low-intensity occupational factors. Specialized experimental pathomorphological studies, as well as investigation of all available material about the condition of the heart and vessels in cases of incidental death of individuals who have worked for long periods of time with various occupational factors, are needed.

Of course, all these studies should be pursued in relation to the results of studies of control groups, that are adequate with respect to sex, age and living conditions, and they should be backed up by general knowhow in pathological anatomy of cardiovascular diseases.

It should be noted that, in view of the general physiological role of the cardiovascular system in the organism, the search for strict specificity of its reactions to different occupational factors is not considered too promising. There are more grounds to believe that these reactions may merely undergo some quantitative transformation and change in time of appearance and relation to other symptoms. And this leads to onset of other than strictly specific manifestations of cardiovascular disorders in response to exposure to an occupational factor. The possibility of development of ordinary and widespread cardiovascular diseases among individuals engaged in various occupations and having contact with the most diverse factors also plays a certain role. This gives even more importance to epidemiological investigation of the most common diseases of the heart and vessels, which is being done extensively at the present time.

A comparison of material referable to clinical observations related to different occupational factors shows that the most obvious changes in the cardiovascular system are those due to such occupational factors as massive radiation to the cardiac and vascular region, acute poisoning, toxic and allergenic agents, etc. The incidence of such cases is low; however, their occupational genesis is unquestionable. Equally unquestionable is the role of occupational factors in the origin of pulmonary and vascular pathology related to exposure to dust and toxic agents. However, in such cases, involvement of the heart in the process follows the laws of general pathology and does not present any strictly specific features.

The most common and, at the same time, difficult to interpret signs are neurocirculatory dystonia and mild dystrophic changes in the myocardium of individuals exposed to microwaves and ionizing radiation of low intensity, carbon disulfide, lead, unsaturated hydrocarbons and other toxic agents or mixed occupational factors (combination of noise and emotional stress, vibration and muscular tension). Success can be achieved in the study and evaluation of these diseases only after accumulation of extensive clinical statistical data that would indicate the possible link between clinical manifestations and dosage of occupational factor (with due consideration of known risk factors: hypokinesia, obesity, heredity and bad habits).

Future in-depth clinical studies could be pursued in the direction of establishing the correlations between different functional changes in the cardiovascular system and those present under physiological conditions. Mere accumulation of special characteristics on the basis of different manifestations and methodological approaches will not add clarity to this complex question. Attention should be concentrated on an overall evaluation of health status and generalized indices defining the adequacy of circulation. To define the effect of an occupational factor, the description of special but nonspecific cardiovascular reactions should be supplemented with a search of changes in systems and structures that are the most directly related to the mechanism of action of a given factor. It is only after detecting changes in these reflexogenic regions and determining the possible routes of involvement of hemodynamics in the reflex that one can suspect their causative link with an occupational factor. But even in such cases one must bear in mind the aggregate of all other influences on the heart and vessels, which is indicative of the multi-etiological nature of these syndromes.

Appearance of such disorders in various worker groups usually requires careful dispensary observation with administration of general fortifying and health-improving measures, after which an appreciable improvement is observed. At the same time, the syndromes that are related more to the effects of other factors, that are difficult to take into consideration (poorly organized lifestyle, bad habits, overeating, hypokinesia, conflict situations) do not present such beneficial dynamics and lead to development of various diseases (neurosis, cardiac ischemia, essential hypertension). The increase in mean age, occurring as the observation period is extended, affects the dynamics of symptoms in these individuals. It is very difficult, both clinically and etiologically, to evaluate full-fledged forms of cardiovascular pathology against a background of prior circulatory dysfunction, and this is well illustrated in the sections dealing with microwaves and toxic agents.

The accumulated experience enables us to offer some diagnostic criteria and terms defining the most common changes in cardiovascular function under the influence of occupational factors.

There are few cases of toxic and allergic myocarditis, marked hemodynamic disturbances related to acute poisoning and massive radiation that could be of independent significance in determining disability related to an occupational factor. In some cases, determination of the degree of disability is made only on the basis of the aggregate of data on other clinical manifestations of occupational and concomitant diseases. Examples of diagnostication in all these cases are given in the relevant chapters.

Therapeutic and preventive measures to prevent and attenuate cardiovascular disorders, in addition to improvement of special working conditions and use of the usual agents for symptomatic and pathogenetic therapy, should include as a very important element some general measures referable to organizing living conditions, the work process, physical and mental conditioning and reasonable diet. Implementation of such measures in various worker groups would improve the health status of society as a whole. This is attributable to the large number of groups screened and realistic organizational structure to implement the measures. For this reason, preliminary and regular physical examinations may become the first stage of complete dispensary care of the public with respect to cardiovascular aspects.

BIBLIOGRAPHY

1. Abayeva, M. M.; Adyrkhayev, A. G.; and Alferova, V. V. "Condition of the Heart of Individuals Whose Work Involves Contact With Lead," in "Tezisy dokl. 1-y Respublikansk. nauchn. konferentsii profpatologov Tadzhikistana" [Summaries of Papers Delivered at the First Tadzhik Republic Scientific Conference of Occupational Pathologists of Tadzhikistan], Dushanbe, 1968, pp 132-134.

2. Adler, A. M. "Oxyhemometry and Hemodynamic Indices of Patients With Acute Cor Pulmonale," candidatorial dissertation, Moscow, 1966.

3. Azhayev, A. N., and Lapshina, N. A. "Functional State of the Human Body When Overheated," GIG. TRUDA [Industrial Hygiene], No 6, 1971, pp 6-11.

4. Aldanazarov, A. T. "Changes in the Blood System in the Presence of Lead Poisoning," doctoral dissertation, Alma-Ata, 1970.

5. Alferova, V. V., and Kuznetsova, L. V. "Condition of Peripheral Vessels of Cyclotron Workers," MED. RAD. [Medical Radiology], No 12, 1962, pp 32-37.

6. Andreyeva, N. B. "Early Detection of Carbon Disulfide Poisoning," author abstract of candidatorial dissertstion, Leningrad, 1969.

7. Andryukin, A. A. "Arterial Pressure Level and Incidence of Essential Hypertension Among Individuals Working in Noisy Shops," GIG. TRUDA, No 12, 1961, pp 11-17.

8. Anichkov, S. V. "Pharmacological Analysis of Neurogenic Cardiac Dystrophies," in "Distrofiya miokarda" [Myocardial Dystrophy], Leningrad, 1971, pp 48-56.

9. Artem'yev, Ye. N., and Konovalova, T. K. "Symptomatology of Chronic Carbon Disulfide Poisoning," TER. ARKH. [Therapeutic Archives], No 11, 1962, pp 88-94.

10. Akhmedshin, A. N. "Condition of Cardiovascular System of Individuals in Contact With Lead," in "Materialy Otchetnoy nauchn. konferentsii Kazakh. nauchno-issled. in-ta krayevoy patologii" [Proceedings of Report-Back Scientific Conference of the Kazakh Scientific Research Institute of Regional Pathology], Alma-Ata, 1964, pp 95-96.

11. Akhrem-Akhremovich, R. M., and Lakshina, L. K. "Clinical Characteristics of Obliterative Diseases of Peripheral Arteries," KLIN. MED. [Clinical Medicine], No 11, 1970, pp 44-48.

12. Bakeyeva, G. Ya. "The Question of Cardiac Function With Long-Term Exposure to Low Concentrations of Carbon Disulfide," author abstract of candidatorial dissertation, Kalinin, 1969.

13. Basamygina, L. Ya. "The Cardiovascular Syndrome in the Presence of Vibration and Noise Sickness," in "Materialy 3-y Nauchno-praktich. konferentsii, posvyashch. vibratsionnoy, shumovoy boleznyam i ikh profilaktike" [Proceedings of 3d Scientific and Practical Conference on Vibration and Noise Sickness, and Prevention Thereof], Donetsk, 1966, pp 12-15.

14. Benyumov, I. A. "Arterial Pressure Changes in Workers Exposed to Noise in the Doubler and Weaving Industry," VRACH. DELO [Medical Record], No 4, 1963, pp 120-124.

15. Bespalova, L. A. "Morphological and Electron Microscopic Changes in the Myocardium of Dogs Exposed to Long-Term Chronic Gamma Radiation," KOSMICHESKAYA BIOL. [Space Biology], NO 3, 1973, pp 26-30.

16. Bongard, E. M.; Ostrovskaya, R. S.; and Podrez, Z. G. "Analysis of Acute Industrial Poisoning According to Data From the Clinic of Ufa Scientific Research Institute of Hygiene and Occupational Diseases Covering 1958-1960," in "Gigiyena truda i okhrana zdorov'ya rabochikh v neftyanoy i neftekhimicheskoy promyshlennosti" [Industrial Hygiene and Health Care of Workers in the Petroleum and Petrochemical Industry], Ufa, Vol 4, 1968, pp 140-143.

17. Brestkin, A. P. "Etiology of Caisson Disease," GIG. I SAN. [Hygiene and Sanitation], No 12, 1952, pp 26-36.

18. Bronshteyn, Kh. I., and Itkin, L. Ye. "Myocardial Lesion in Ursol Allergy (Allergic Ursol Myocarditis)," ZDRAVOOKHRANENIYE (Kishinev) [Public Health], No 1, 1965, pp 46-69.

19. Bystrova, Yu. A., and Kalashnikov, B. P. "Some Data on Retinal Vessels of Individuals Exposed to Occupational Radiation," in "Materialy Yubileynoy nauchn. sessii, posvyashch. 50-letiyu Tsentral'n. nauchno-issled. rentgeno-radiologicheskogo in-ta" [Proceedings of Jubilee Scientific Session Commemorating the 50th Anniversary of the Central Scientific Research Institute of Roentgenology and Radiology], Leningrad, 1968, pp 376-377.

20. Bychkov, M. S., and Dronov, I. S. "Electrocardiographic Data on the Effects of Very Low Doses of Microwaves on the Level of the Mesencephalic Reticular Formation--Hypothalamus--Cerebral Cortex System," in "O biologicheskom deystvii elektromagnitnykh poley radiochastot" [Biological Effects of Radiofrequency Electromagnetic Fields], Moscow, 1973, pp 58-65.

21. Vayl', S. S. "Functional Morphology of Functional Cardiac Disturbances," Leningrad, Medgiz, 1960.

22. Vasil'yeva, V. A.; Velikson, I. M.; and Konikova, G. S. "Comparative Data on the Effects of Some Chemicals (Lead, Carbon Disulfide, Benzene, Fluorides) on Development of Atherosclerosis," in "Professional'nyye intoksikatsiw" [Occupational Poisoning], Leningrad, 1966, pp 22-32.

23. Vigdorchik, N. A. "Blood Pressure Changes in the Presence of Some Chronic Industrial Poisoning," VRACH. DELO [Medical Record], No 11-12, 1938, pp 991-998.

24. Petrov, Prof I. R. (editor) "Effects of SHF Radiation on Man and Animals," Leningrad, Meditsina, 1970.

25. Volkov, T. M., and Sosnova, T. L. "Blood Pressure Changes in Individuals Exposed to Different Intensities of Noise Under Laboratory Conditions," in "Metodicheskiye voprosy izucheniya deystviya shuma na organizm" [Methodological Aspects of Studying the Effects of Noise on the Body], Moscow, 1963, pp 42-43.

26. Volovik, E. M.; Ivanova, A. G.; and Miropol'skaya, I. L. "Investigation of Morbidity Among Workers in the Chemical Industry," in "Materialy po voprosy gigiyeny truda i kliniki professional'nykh bolezney" [Data on Industrial Hygiene and Symptomatology of Occupational Diseases], Moscow, Vyp 7, 1957, pp 233-234.

27. Vol'fovskaya, R. N., and Makulova, I. D. "Analysis of Cases of Acute Industrial Poisoning in Leningrad Over a 10-Year Period (According to Institute Data)," in "Materialy Nauchn. sessi, posvyashch. 40-letiyu nauchno-issled. in-ta gigiyeny truda i professional'nykh zabolevaniy g. Leningrada" [Proceedings of Scientific Session Commemorating the 40th Anniversary of the Leningrad Scientific Research Institute of Industrial Hygiene and Occupational Diseases], Leningrad, 1964, pp 100-101.

28. Vol'fovskaya, R. N., and Makulova, I. D. "On the Effects of Lead on Development of Hypertensive States," GIG. TRUDA, No 9, 1968, pp 47-49.

29. Vorob'yev, Ye. I. "Radiation Cardiology," Moscow, Atomizdat, 1971.

30. Vorob'yev, Ye. I., and Stepanov, R. P. "Condition of Rabbit Myocardial Cells After Local Exposure of the Cardiac Region to Radiation," RADIOBIOLOGIYA [Radiobiology], No 6, 1973, pp 844-849.

31. Votchal, B. Ye. "Pathogenesis, Prevention and Treatment of Cor Pulmonale," in "Trudy 15-go Vsesoyuzn. s"yezda terapevtov" [Proceedings of 15th All-Union Congress of General Practitioners], Moscow, 1964, pp 189-191.

32. Gembitskiy, Ye. V. "Symptomatic (Secondary) Hypotension," TER. ARKH., No 1, 1969, pp 28-35.

33. Gemke, G. R. "Arterial Pressure of Individuals Working With Lead," Ibid, No 7, 1966, pp 26-32.

34. Gefter, A. I. "Pneumoconiosis and the 'Right Ventricular Angina' Syndrome," in "Trudy 15-go Vsesoyuzn. s"yezda terapevtov," Moscow, 1964, pp 466-468.

35. Gorbarenko, N. I. "Functional State of the Adrenals With Chronic Exposure to Radiation," in "Eksperimental'naya i klinicheskaya radiologiya" [Experimental and Clinical Radiology], Kiev, Vyp 7, 1971, pp 149-154.

36. Gorbachev, O. M. "Angina Pectors of Diencephalohypothalamic Origin," in "Fiziologiya i patologiya gipotalamusa" [Physiology and Pathology of Hypothalamus], Moscow, 1965, pp 74-76.

37. Gordon, Z. V. "Problems of Industrial Hygiene and Biological Effects of SHF Electromagnetic Fields," Leningrad, Meditsina, 1966.

38. Gordon, I. B., and Stepanova, M. P. "Pain in the Cardiac Region and EKG Changes With Physical Loads in Patients With Vegetovascular Form of the Hypotension Syndrome," TER. ARKH., No 8, 1970, pp 60-62.

39. Gorizontov, P. D. "Reactivity of Irradiated Organisms," in "Radiatsiya i organizm" [Radiation and the Organism], Obninsk, Pt 1, 1967, pp 5-9.

40. Grashchenkov, N. I. "Physiology and Pathology of the Diencephalic Region of the Brain," Moscow, Izd-vo AN [Academy of Sciences] SSSR, 1963.

41. Grigor'yev, Z. E. "Occupational Diseases of Painters Under the Combined Effect of Lead and Organic Solvents," in "Professional'nye intoksikatsii" [Occupational Poisoning], Leningrad, 1966, pp 65-73.

42. Grigor'yev, Yu. G. "Radiation Lesions and Compensation of Impaired Functions," Moscow, Atomizdat, 1963.

43. Gusev, I. S. "Comparative Toxicity and Hygienic Evaluation of Low Concentrations of Benzene, Toluene and Xylene," candidatorial dissertation, Leningrad, 1966.

44. Gusman, S. M. "Data on the Study of Chronic Benzene Poisoning," in "Sbornik trudov Azerbaydzhansk. in-ta usovershenstvovaniya vrachey" [Collected Works of the Azerbaydzhan Institute for Advanced Training of Physicians], Baku, Vyp 5, 1962, pp 115-121.

45. Gus'kova, A. K., and Baysogolov, G. D. "Evaluation of Health Status and Principles of Employment for Individuals Exposed to Ionizing Radiation," MED. RADIOL., No 5, 1968, pp 3-9.

46. Idem, "Radiation Sickness in Man," Moscow, Meditsina, 1971.

47. Daniyarov, S. B. "Adaptational Reactions of the Cardiovascular System to Exposure to Ionizing Radiation," in "Trudy Kirgizsk. med. in-ta" [Works of Kirgiz Medical Institute], Vyp 1, 1963, pp 121-129.

48. Dzhandzhagava, M. M. "Polycardiographic Studies of Rabbit Heart Function Under Normal Conditions and With Exposure to Ionizing Radiation," author abstract of candidatorial dissertation, Tbilisi, 1973.

49. Dobrin, B. Yu. "EKG Changes in Patients With Vegetative Paroxysms of Cerebral Genesis," TER. ARKH., No 9, 1972, pp 47-50.

50. Drogichina, E. A. "Occupational Diseases of the Nervous System," Moscow, Meditsina, 1968.

51. Drogichina, E. A., and Ryzhkova, M. N. "Symptomatology and Diagnostics of Diencephalic Pathology in the Presence of Occupational Poisoning," GIG. TRUDA, No 2, 1967, pp 20-24.

52. Drogichina, E. A., and Sadchikova, M. N. "Clinical Syndromes Associated With Exposure to Different Radiofrequency Ranges," Ibid, No 1, 1965, pp 17-21.

53. Yevdokimova, I. B. "Distinctions of Functional Changes in Local Circulation and Auditory Sensibility With Exposure to Intensive Industrial Noise," author abstract of candidatorial dissertation, Moscow, 1970.

54. Yevlashko, Yu. P. "Impairment of Porphyrin Metabolism and Its Significance to Pathogenesis of Lead Anemia," candidatorial dissertation, Moscow, 1965.

55. Zaytsev, G. P. "Endarteriosis (Endarteritis)," KLIN. MED., No 3, 1964, pp 145-149.

56. Zakirov, G. Z. "Arterial Vascular Crises in the Presence of Lead Colic," in "Trudy Orenburgsk. oblastn. otdeleniya Vserossiysk. nauchn. ob-va terapevtov" [Works of the Orenburgskaya Oblast Department of the All-Russian Scientific Society of General Practitioners], Orenburg, Vyp 2, 1961, pp 82-84.

57. Zaslavskaya, R. M. "Pharmacological Effects on Pulmonary Circulation," Moscow, Meditsina, 1974.

58. Zakharov, V. M. "Changes in Arterial Pressure Under the Influence of Low Doses of Internal Radiation From Radioactive Sodium," in "Reaktsiya organizma na deystviye malykh doz ioniziruyushchey radiatsii" [Reaction of the Body to the Effects of Low Doses of Ionizing Radiation], Moscow, 1962, pp 88-97.

59. Zorina, L. A. "Symptomatology, Diagnostics, Treatment and Prevention of Lead Poisoning," Moscow, Meditsina, 1965.

60. Idem, "Chronic Benzene Poisoning (Clinical and Experimental Study)," doctoral dissertation, Moscow, 1971.

61. Ivanov, A. Ye. "Pathoanatomical Diagnostics of Radiation Sickness," Moscow, Medgiz, 1960.

62. Ivanov, Yu. V. "Vascular Endothelium in the Presence of Acute Radiation Pathology (Mechanism of Development of the Hemorrhagic Syndrome)," author abstract of candidatorial dissertation, Moscow, 1970.

63. Tolgskaya, M. S.; Gordon, Z. V.; Markov, V. V.; and Vorontsov, R. S. "Changes in Secretory Activity of the Hypothalamus and Some of the Endocrine Glands With Exposure to Intermittent and Continuous Radiation," in "O biologicheskom deystvii elektromagnitnykh poley radiochastot" [Biological Effects of Radiofrequency Electromagnetic Fields], Moscow, 1973, pp 87-90.

64. Il'inskiy, B. V. "Problems of Vascular Pathology," Leningrad, 1970.

65. Il'inskiy, D. A.; Kuznetsov, V. I.; and Mozzhukhin, A. S. "Changes in Vascular Tonus in the Presence of Acute Radiation Sickness," in "Patogenez, eksperimental'naya profilaktika i terapiya luchevykh porazheniy" [Pathogenesis, Experimental Prevention and Therapy of Radiation Lesions], Moscow, 1964, pp 70-78.

66. Pavlova, I. V.; Drogichina, E. A.; Sadchikova, M. N.; and Gel'fon, I. A. "The Role of Some Biochemical Disturbances in the Pathogenesis of Radiowave Sickness," GIG. TRUDA, No 3, 1970, pp 20-23.

67. Kazakevich, M. A. "Some Results of Clinicophysiological Studies of Chronic Carbon Disulfide Poisoning," Ibid, No 7, 1963, pp 20-22.

68. Kazakevich, M. A., and Tolgskaya, M. S. "Experimental Study of Long-Term Sequelae of Chronic Carbon Disulfide Poisoning," in "Toksikologiya novykh promyshlennykh khimicheskikh veshchestv" [Toxicology of New Industrial Chemicals], Moscow, Vyp 4, 1962, pp 117-125.

69. Kashin, L. M. "Effects on the Body of Low Concentrations of Carbon Disulfide," author abstract of candidatorial dissertation, Kiev, 1966.

70. Kirsanova, G. I., and Sosnovskaya, F. M. "Clinicophysiological Characteristics of Venous Disturbances of Cerebral Circulation With Exposure to Radiation," MED. RADIOL., No 1, 1972, pp 16-22.

71. Kitsovskaya, I. A., and Polukhina, E. I. "Investigation of Functional State of the Hypothalamus--Hypophysis--Adrenal Cortex System Under the Influence of Intermittent and Continuous Radiation," in "O biologicheskom deystvii elektromagnitnykh poley radiochastot," Moscow, 1973, pp 76-79.

72. Knopov, A. I. "A Case of Lead Poisoning With Marked Cardiovascular Disturbances of Toxic Etiology," TER. ARKH., No 3, 1950, pp 55-58.

73. Kozlov, L. A.; Ivanov, I. G.; and L'vovskaya, E. N. "Pathogenesis of Occupational Deafness," GIG. TRUDA, No 3, 1964, pp 34-38.

74. Kozlov, P. S., and Tedder, Yu. R. "Complex Effects on the Body of Benzene and Unsaturated Hydrocarbons," in "Materialy 2-y Ob"yedinennoy nauchn. sessii, posvyashch. voprosam okhrany truda i professional'nykh bolezney i travmatizma" [Proceedings of 2d Joint Scientific Session Dealing With Labor Safety Practices, Occupational Diseases and Traumatism], Gor'kiy, 1965, pp 234-237.

75. Kozlova, A. V., and Lopatnikova, Z. F. "Radiation Therapy of Carcinoma of the Esophagus," MED. RADIOL., No 9, 1967, pp 17-23.

76. Kozlovskiy, V. N., and Denisova, Ye. A. "Lipoid and Protein Metabolism With Chronic Exposure to Radiation Under Occupational Conditions," Ibid, No 6, 1972, pp 63-67.

77. Kolodub, F. A., and Yevtushenko, G. I. "Metabolic Disturbances of the Heart With Exposure to Low Frequency Pulsed Electromagnetic Fields," KARDIOLOGIYA [Cardiology], No 7, 1972, pp 101-102.

78. Konikova, G. S. "Cholesterol Metabolism in Individuals Exposed to Lead for Long Periods of Time," TER. ARKH., No 7, 1961, pp 104-109.

79. Konchalovskaya, N. M.; Saytanov, A. O.; and Sorkina, N. S. "On the Question of Allergic Myocarditis," Ibid, No 9, 1965, pp 22-25.

80. Kostyukova, S. D. "Electrocardiographic Findings in Cases of Acute Carbon Monoxide Poisoning," KLIN. MED., No 2, 1951, pp 56-58.

81. Kruglikov, R. I. "Data on the Effects of SHF Electromagnetic Fields on Higher Branches of the Central Nervous System," author abstract of doctoral dissertation, Moscow, 1968.

82. Kuz'minskaya, G. N. "Experimental Atherosclerosis Against the Background of Lead Poisoning," ARKH. PAT. [Archives of Pathology], No 9, 1964, pp 21-24.

83. Kukin, N. N. "Effects of Lead on Development and Course of Endarteritis Obliterans," KHIRURGIYA [Surgery], No 2, 1937, pp 90-100.

84. Kurshakov, N. A., and Kireyev, P. M. "Myocardial Hypoxia With Acute and Chronic Exposure to Radiation," KARDIOLOGIYA, No 2, 1963, pp 3-9.

85. Kushelevskiy, B. P., and Zislin, D. M. "Syndromal Classification of Cardiopulmonary Insufficiency," in "Trudy 15-go Vsesoyuzn. s"yezda terapevtov," Moscow, 1964, pp 246-251.

86. Kushnev, A. I. "Visceral Pathology in the Presence of Chronic Carbon Disulfide Poisoning," in "Trudy Kalininsk. med. in-ta" [Works of Kalinin Medical Institute], Kalinin, Vol 11, 1965, pp 53-57.

87. Lang, G. F. "Pathology of the Circulatory System," Moscow, Medgiz, 2d edition, 1957.

88. Ledentsev, Yu. K. "Lipid Metabolism With Exposure to Low Temperature and Ionizing Radiation," in "Materialy 30-y Godichn. nauchn. sessii Sverdlovsk. med. in-ta" [Proceedings of 30th Annual Scientific Session of Sverdlovsk Medical Institute], Sverdlovsk, 1968, p 408.

89. Lobkova, Ye. F., and Pluzhnikova, M. Kh. "Some Distinctions of Circulatory Disorders in the Presence of Chronic Lesions to the Diencephalic Region," in "Zabolevaniya serdechno-sosudistoy, nervnoy sistemy i bolezni obmena veshchestv" [Pathology of the Cardiovascular and Nervous System, and Metabolic Diseases], Moscow, 1966, pp 179-184.

90. Lushnikov, Ye. F., and Lushnikov, G. A. "Role of Connective Tissue in Pathogenesis of Radiation Lesions to the Heart," in "Rol' soyedinitel'noy tkani i sistemy krovi pri luchevoy patologii" [Role of Connective Tissue and Blood in Radiation Pathology], Moscow, 1970, pp 132-135.

91. Lysina, G. G. "Condition of Internal Organs in the Presence of Chronic Carbon Disulfide Poisoning," GIG. TRUDA, No 6, 1958, pp 54-56.

92. Idem, "Oxygenation of the Body in Individuals Working With Sources of Ionizing Radiation for Long Periods of Time," VRACH. DELO, No 6, 1968, pp 100-103.

93. Idem, "Clinicophysiological Changes With Exposure to Occupational Radiation and Radiowaves," Ibid, No 11, 1975, pp 50-55.

94. Lyubomudrov, V. Ye.; Onopko, B. N.; and Basamygina, L. Ya. "Vibration and Noise Sickness," Kiev, Zdorov'ya, 1968.

95. Makel'skiy, V. V. "Hemodynamic Distinctions in Patients With Emphysema of the Lungs," KARDIOLOGIYA, No 7, 1967, pp 124-129.

96. Malkin, V. B., and Plakhatnyuk, V. I. "Electrocardiographic Changes in the Presence of Acute Hypoxia, and Their Significance," KOSMICHESKAYA BIOL., No 2, 1974, pp 54-61.

97. Malyshev, V. M., and Kolesnik, F. A. "Superhigh-Frequency Electromagnetic Waves and Their Effects on Man," Leningrad, Meditsina, 1968.

98. Markizova, A. B., and Mukhina, E. N. "State of Some Vegetative Vascular Reactions and Cutaneous Capillaries of Individuals Working With Sources of Ionizing Radiation," in "Materialy Yubileynoy nauchn. sessii, posvyashch. 50-letiyu Tsentral'n. nauchno-issled. rentgeno-radiologicheskogo in-ta," Leningrad, 1968, pp 375-376.

99. Masich, T. A. "Clinicophysiological Characteristics of the Vascular System of Patients With Chronic Lead and Carbon Disulfide Poisoning," author abstract of candidatorial dissertation, Moscow, 1970.

100. Kovnatskiy, V. A.; Vasil'yeva, V. A.; Kuz'minskaya, G. N.; and Cherednichenko, L. K. "Characteristics of States of the Cardiovascular System With Prolonged Exposure to Lead," in "Materialy Nauchn. sessii Nauchno-issled. in-ta gigiyeny truda i professional'nykh zabolevaniy Leningrada, posvyashch. itogam raboty in-ta za 1959-1960 gody" [Proceedings of Scientific Session of the Scientific Research Institute of Industrial Hygiene and Occupational Diseases of Leningrad, Dealing With Achievements of the Institute in 1959-1960], Leningrad, 1961, pp 31-32.

101. Vasil'yeva, V. A.; Velikson, I. M.; Kogan, A. G.; Konikova, G. S.; Kuz'minskaya, G. N.; and Cherednichenko, L. K. "Data on the Effects of Lead on Development of the Atherosclerotic Process," GIG. TRUDA, No 12, 1964, pp 6012.

102. Medvedev, V. P. "Cardiovascular Pathology in Individuals With Prior Exposure to SHF Electromagnetic Fields," Ibid, No 3, 1973, pp 6-8.

103. Milkov, L. Ye. "Effects of Intensive Industrial Noise on Nervous System Function," author abstract of candidatorial dissertation, Moscow, 1963.

104. Mikhnev, A. L., and Khomazyuk, A. I. "Pathogenesis of Hypertension in the Pulmonary Circulation in the Presence of Chronic Lung Disease," in "Trudy 15-go Vsesoyuzn. s"yeada terapevtov," Moscow, 1964, pp 239-240.

105. Model', A. A., and Navrotskaya, E. S. "Electrocardiographic Changes in the Presence of Chronic Carbon Disulfide Poisoning," VRACH. DELO, No 7, 1958, pp 755-756.

106. Molchanov, N. S., and Gembitskiy, Ye. V. "Problems of Names, Etiology and Pathogenesis of Hypotensive States," KLIN. MED., No 4, 1967, pp 6-13.

107. Mukharlyamov, N. M. "Cor Pulmonale," Moscow, Meditsina, 1973.

108. Mytnik, P. K. "Symptomatology, Early Detection, Therapy and Prevention of Chronic Benzene Poisoning," in "Promyshlennaya toksikologiya" [Industrial Toxicology], Moscow--Leningrad, 1934, pp 85-101.

109. Myasnikov, A. L. "Essential Hypertension and Atherosclerosis," Moscow, Meditsina, 1965.

110. Nadareyshvili, K. Sh. "Effects of Ionizing Radiation on the Cardiovascular System," Tbilisi, Metsniyereba, 1966.

111. Vol'fovskaya, R. N.; Asanova, T. P.; Zenkevich, Ye. S.; Makulova, I. D.; and Semenovskaya, N. A. "Neurocirculatory Disturbances in the Presence of Some Chronic Occupational Diseases," in "Tezisy dokladov Leningradsk. nauchno-issled. in-ta gigiyeny truda i profzabolevaniy" [Summaries of Papers Delivered at the Leningrad Scientific Research Institute of Industrial Hygiene and Occupational Diseases], Leningrad, 1970, pp 38-40.

112. Gus'kova, A. K.; Ponizovskaya, A. I.; Denisova, Ye. A.; L'vovskaya, E. N.; Kotova, E. S.; and Gribova, I. A. "Some Findings of Clinico-physiological Observations of Individuals Working on Accelerators," in "Biologicheskoye deystviye protonov vysokikh energiy" [Biological Effects of High-Energy Protons], Moscow, 1967, pp 67-84.

113. Drogichina, E. A.; Konchalovskaya, N. M.; Glotova, K. V.; Sadchikova, M. N.; and Snegova, G. V. "Vegetative and Cardiovascular Disturbances With Chronic Exposure to SHF Electromagnetic Fields," GIG. TRUDA, No 7, 1966, pp 13-17.

114. Il'inskiy, B. V.; Borisova, L. I.; Klbeva, S. K.; and Medvedev, V. P. "The Role of Hereditary and Some Industrial Factors in Development of Cardiac Ischemia," in "Tezisy dokl. 2-go Vsesoyuzn. s"yezda kardiologov" [Summaries of Papers Delivered at the 2d All-Union Congress of Cardiologists], Moscow, 1973, pp 34-36.

115. Dembo, G. A.; Dibner, R. D.; Teslenko, Zh. A.; and Proektor, M. L. "Left Ventricular Stress Syndrome in Healthy Individuals," KARDIOLOGIYA, No 3, 1962, pp 70-73.

116. Orlova, A. A. "Changes in Cardiac Function in Patients With Lead and Mercury Poisoning (According to EKG Findings)," candidatorial dissertation, Moscow, 1953.

117. Glazunov, I. S.; Blagoveshchenskaya, V. V.; Ivanov, V. V.; and Malakhova, T. "Acute Radiation Sickness Induced by Exposure to Gamma and Neutron Radiation," KLIN. MED., No 4, 1974, pp 55-61.

118. Peysakh, S. A., and Kadyrbayeva, Kh. M. "A Case of Death Due to Lead Poisoning," in "Trudy in-ta krayevoy patologii AN Kazakhsk. SSR" [Works of the Institute of Regional Pathology of the Kazakh Academy of Sciences], Alma-Ata, Vol 8, 1960, pp 227-234.

119. Poddubskiy, G. A. "Cardiac Function at the Long Postradiation Term," author abstract of candidatorial dissertation, Leningrad, 1966.

120. Pokrovskiy, N. N. "Effects of Industrial Noise on Blood Pressure of Workers in Machine-Building Plants," GIG. TRUDA, No 12, 1966, pp 44-46.

121. Rashevskaya, A. M., and Levina, S. V. "Symptomatology of Changes in Internal Organs in the Presence of Lead Poisoning," TRUDY AMN SSSR [Works of the USSR Academy of Medical Sciences], Moscow, Vol 16, 1952, pp 78-92.

122. Rashevskaya, A. M.; Molokanov, K. P.; and Orlova, A. A. "Berylliosis (Symptomatology, Diagnostics and Therapy). Expert Certification of Disability," Moscow, Meditsina, 1965.

123. Levin, Yu. M.; Nikitina, D. S.; Martsev, D. S.; and Kopnova, M. L. "Local Circulation and Microcirculation in the Systemic and Pulmonary Circulatory Systems in the Presence of Certain Radiation Lesions," in "Radiatsiya i organizm," Obninsk, Pt 1, 1967, pp 103-106.

124. Rozentsvit, G. E. "Occupational Paroxysmal Autonomic Syndromes and Treatment Thereof," in "Trudy Nauchn. sessii Leningradsk. nauchno-issled. in-ta gigiyeny truda i professional'nykh zabolevaniy za 1957 god" (Proceedings of Scientific Session of Leningrad Scientific Research Institute of Industrial Hygiene and Occupational Diseases in 1957], Leningrad, 1959, pp 121-126.

125. Rusinova, A. P. "Manifestations of Noise Sickness in Workers Engaged in Steel Cable Production," in "Kratkiye tezisy dokl. k Vserossiysk. konferentsii na temu 'Shum i shumovaya bolezn'. Voprosy profilaktiki'" [Brief Summaries of Papers Delivered at All-Russian Conference on "Noise and Noise Sickness. Problems of Prevention"], Leningrad, 1973, pp 134-136.

126. Rutsay, S. V. "Electrolyte Content of Rabbit Heart Tissues in the Presence of Hypothalamic Trauma," KARDIOLOGIYA, No 4, 1972, pp 124-125.

127. Savitskiy, N. N. "Biophysical Bases of Circulation and Clinical Methods of Studying Hemodynamics," Leningrad, Meditsina, 1974.

128. Sadchikova, M. N.; Osipova, V. F.; and Durneva, Z. N. "Some Data on Cerebral and Peripheral Circulation in the Presence of Radiowave Sickness, According to Rheographic Findings," GIG. TRUDA, No 9, 1972, pp 12-15.

129. Saytanov, A. O. "Functional State of the Heart With Chronic Exposure to Ionizing Radiation," KLIN. MED., No 6, 1969, pp 22-28.

130. Sarkisov, D. S., and Vtyurin, B. V. "Myocardial Dystrophy, Its Reversibility and Means of Prevention in Ultrastructural Aspect," in "Distrofiya miokarda" [Myocardial Dystrophy], Leningrad, 1971, pp 69-79.

131. Svistunov, N. T. "Effects of Electric Machine Noise on Functional State of Cardiovascular System of Testers," in "Materialy Nauchn. sessii po probleme 'Sovremennoye sostoyaniye ucheniya o proizvodstvennom shume i ul'trazvuke, ikh vliyanii na organism i profilaktike vrednogo deystviya'" [Proceedings of Scientific Session Dealing With the Problem "Present Status of Teaching on Industrial Noise and Ultrasound, Their Effects on the Body and Prevention of Deleterious Effects]"], Leningrad, 1968, pp 118-119.

132. Sel'tser, V. K. "Phase Structure of Cardiac Contraction in Irradiated Rabbits During Functional Tests," RADIOBIOLOGIYA, No 3, 1970, p 469.

133. Simavonyan, V. G. "Roentgenological Changes in Macaca Monkeys With Exposure to Radiation," in "Materialy Yubileynoy sessii, posvyashchennoy 50-letiyu Tsentral'n. nauchno-issled. rentgeno-radiologicheskogo in-ta," Leningrad, 1968, pp 49-50.

134. Simagina, V. A. "Condition of External Respiration and Circulation in Patients With Chronic Nonspecific Lung Disease at Different Stages of Illness," in "Trudy Orenburgsk. med. in-ta," Vyp 9, 1966, pp 169-177.

135. Slesarev, V. V. "Peripheral Circulation of Blood and Lymph With Exposure to Ionizing Radiation," MED. RADIOL., No 1, 1966, pp 59-66.

136. Smirnova, N. P. "Significance of Disturbances of Central Nervous Regulation to Involvement of Cardiovascular System With Exposure to Ionizing Radiation," RADIOBIOLOGIYA, No 1, 1962, p 228.

137. Soldatova, V. A. "Health Status and Clinical Distinctions of Reaction to Occupational Radiation in Medical Roentgenologists," author abstract of candidatorial dissertation, Moscow, 1968.

138. Sorkina, N. S. "Early Detection and Problems of Treatment of Chronic Lead Poisoning," candidatorial dissertation, Moscow, 1971.

139. Sosnovskaya, F. M. "Characteristics of Bioelectrical Activity of the Brain of Individuals Occupationally Exposed to Ionizing Radiation," author abstract of candidatorial dissertatin, Moscow, 1973.

140. Subbota, A. G. "Mechanism of Nonthermal Effects of Microwaves on Hemodynamics," in "Gigiyena truda i biologicheskoye deystviye elektromagnitnykh voln radiochastot," Moscow, 1968, pp 148-150.

141. Sudakov, K. V., and Amtimoniy, G. D. "Central Mechanism of Action of Electromagnetic Fields," USPEKHI FIZIOLOGICH. NAUK [Advances in Physiological Sciences], Vol 4, No 2, 1973, pp 101-135.

142. Teodori, M. I., and Mirochitskiy, S. M. "Key Issues in the Problem of Myocarditis," KLIN. MED., No 10, 1974, pp 6-14.

143. Teplov, S. I.; Sverdlov, V. S.; and Korovkin, B. F. "Myocardial Lesion in the Presence of Radiation Sickness and With Local Exposure of Cardiac Region to X-Rays," MED. RADIOL., No 3, 1959, pp 27-33.

144. Tikhonov, K. B. "Condition of Walls of Large Blood Vessels in the Presence of Acute Radiation Sickness," Ibid, No 4, 1965, pp 62-65.

145. Tolgskaya, M. S., and Gordon, Z. V. "Morphological Changes Under the Influence of Radio-Frequency Electromagnetic Waves," Leningrad, Meditsina, 1971.

146. Tyagin, N. V. "Clinical Aspects of SHF Radiation," Leningrad, Meditsina, 1971.

147. Fogel'son, L. I. "Correlation Between Diseases of the Cardiovascular System and Condition of Central Nervous System," KLIN. MED., No 7, 1964, pp 124-130.

148. Freyfel'd, Ye. K. "Pathological Anatomy of Lead Poisoning," in "Trudy 2-go Vsesoyuzn. s"yezda po professional'noy gigiyene i tekhnike bezopasnosti" [Proceedings of 2d All-Union Congress on Occupational Hygiene and Labor Safety Practices], Moscow, 1930, pp 202-204.

149. Khanina, S. B., and Shirinskaya, G. I. "Functional Cardiopathy," Moscow, Meditsina, 1971.

150. Khizhnyakova, L. N. "Effects of Benzene, Its Homologues and Their Nitroamido Derivatives on the Cardiovascular System," in "Gigiyena" [Hygiene], Kiev, 1964, pp 277-281.

151. Khovtasi, A. A. "Concerning Lead-Induced Endarteritis Obliterans," GIG. TRUDA, No 5, 1961, pp 57-58.

152. Tsigel'nik, A. Ya. "Problems of Modern Pneumology," KLIN. MED., No 4, 1962, pp 6-9.

153. Tsinzerling, V. D. "Morphological Changes in Lower Limb Arteries in the Presence of General Atherosclerosis, Essential Hypertension and Angioneurosis," in "Trudy 14-go Vsesoyuzn. s"yezda terapevtov," Moscow, 1958, pp 49-58.

154. Cherednichenko, L. K. "Effect of Lead Poisoning on Development of Experimental Atherosclerosis," GIG. I SAN. [Hygiene and Sanitation], No 3, 1962, pp 18-21.

155. Shamardin, B. M. "State of Microcirculation and Tonus of Peripheral Vessels in Workers in the Slate Industry as Related to Some Forms of Occupational Pathology," author abstract of doctoral dissertation, Tartu, 1974.

156. Shershevskiy, B. M. "Chronic Cor Pulmonale (Pathogenesis, Diagnostics and Therapy)," KLIN. MED., No 5, 1968, pp 17-25.

157. Shtriter, V. A. "Blood Pressure Levels in Different Occupational Groups," TER. ARKH., No 2, 1954, pp 50-55.

158. Andreyeva-Galanina, Ye. Ts. (editor) "Noise and Noise Sickness," Leningrad, Meditsina, 1972.

159. Shkhvatsabaya, I. K. "Some Problems of Pathogenesis of Essential Hypertension," KARDIOLOGIYA, No 8, 1972, pp 5-13.

160. Shcherbakov, N. I. "Some Hemodynamic Changes in Individuals Exposed for Long Periods of Time to Low Doses of Ionizing Radiation," author abstract of candidatorial dissertation, Leningrad, 1960.

161. Gromova, Ye. A.; Lebedeva, L. N.; Tkachenko, K. N.; and Fedotova, O. N. "Experimental Analysis of Functional and Metabolic Changes in the Heart in the Presence of Hypothalamic Lesions," KARDIOLOGIYA, No 4, 1972, pp 83-88.

162. Ryvkin, I. A. (editor) "Epidemiology of Arterial Hypertension and Coronary Atherosclerosis," Moscow, Meditsina, 1969.

163. Efendiyev, M. E., and Amiroslanova, G. I. "Chronic Effect of Benzene on the Human Body," in "Trudy Vyyezdnoy sessii AMN SSSR v Baku" [Proceedings of Visiting Session of the USSR Academy of Medical Sciences in Baku], Moscow, 1961, pp 28-36.

164. Yurenev, P. N., and Semenovich, N. I. "Symptomatology and Therapy of Allergic Pathology of the Heart and Vessels," Moscow, Meditsina, 1972.

165. Yakovlev, V. V. "Condition of Peripheral Vessels and Hemodynamics in the Presence of Acute Radiation Sickness," MED. RADIOL., No 4, 1966, pp 73-79.

166. Yakovleva, L. A. "Hemodynamics as Related to Experimental Local Irradiation of the Cardiac Region," KARDIOLOGIYA, No 6, 1972, pp 106-109.

167. Yakovleva, M. I. "Physiological Mechanisms of Action of Electromagnetic Fields," Leningrad, Meditsina, 1973.

168. Ambrosio, L., and Secchi, G. G. "The Central and Peripheral Nervous System as Related to Lead Poisoning," MED. D. LAVORO, Vol 59, 1968, pp 265-280.

169. Ambrosio, L.,; Marsico, F.; and Piccoli, P. "Occupational Carbon Disulfide Poisoning (Clinical Contribution to Information About Vascular Pathology Related to Carbon Disulfide)," FOLIA MED. (Naples), Vol 40, 1957, pp 544-569.

170. Andrews, G. A. "Radiation Accidents and Their Management," RADIAT. RES., Vol 7, 1967, pp 390-397.

171. Attinger, E. "Chronic Carbon Disulfide Poisoning, Pathogenesis, Early Detection and Prevention," SCHWEIZ. MED. WSCHR., Vol 31, 1954, pp 912-913.

172. Baldi, G., and Giubileo, M. "La Asotemia dei Saturnini e Degli Operal Esposti ad Assorbimeto di Piombo," MED. D. LAVORO, Vol 44, 1953, pp 42-428.

173. Battigelli, M. "L'Intossicazione Saturnina nei Demoliteri di Accumulatori," Ibid, Vol 46, 1955, pp 35-39.

174. Biran, S.; Hochmann, A.; and Stern, S. "Therapeutic Irradiation of the Chest and Electrocardiographic Changes," CLIN. RADIOL., Vol 20, 1969, pp 433-439.

175. Bolt, W., and Zorn, O. "Intracardiac Pressure in the Presence of Silicosis," BEITR. KLIN. TUBERK., Vol 105, 1951, pp 100-107.

176. Boron, P. "Zachowanie sie Cisnienia Tetniczego Krwi i Wskaznika Escylometrycznege u Robotnikow na Razonych na Dsvalanie Olowiu," MED. PRACY, 7, 1956, pp 47-50.

177. Cannan, R. K. "Atomic Bomb Casualty Commission: the First Fifteen Years," BULL. ATOMIC SCI., Vol 19, 1963, pp 45-50.

178. Harvey, R. M.; Enson, Y.; Cournand, A.; and Ferrer, M. I. "Cardiac Output in Cor Pulmonale," ARCH. KREISL.-G. FORSCH., Vol 46, 1965, pp 7-16.

179. Chapman, P. H., and Young, R. J. "Effect of Cobalt 60 Gamma Irradiation on Blood Pressure and Cerebral Blood Flow in the Macaca Mulatta," RADIAT. RES., Vol 35, 1968, pp 78-85.

180. Crepet, M.; Gobbato, F.; and Scansetti, G. "Cardiovascular Changes in Individuals Working With Lead," MINERVA MED., Vol 93, 1956, pp 1910-1918.

181. Cumings, J. "Heavy Metals and the Brain," Oxford, 1959.

182. Darmody, W. R.; Thomas, L. M.; and Gurdjama, E. S. "Postirradiation Vascular Insufficiency Syndrome (Case Report)," NEUROLOGY (Minneapolis), Vol 17, 1967, pp 1190-1192.

183. DeGowin, R. L. "Benzene Exposure and Aplastic Anemia Followed by Leukemia 15 Years Later," J.A.M.A., Vol 185, 1963, pp 748-751.

184. Dencker, H., and Holmdahl, K. H. "Mesenteric Angiography in Patients With Radiation Injury of the Bowel After Pelvic Irradiation," AM. J. ROENTGENOL., Vol 114, 1972, pp 476-481.

185. Dinischioty, G.; Radulescu, I.; and Muica, N. "Hemodynamic Studies of Industrial Lead Poisoning," ARCH. GEWERBEPATH. GEWERBEHYG., Vol 17, 1959, pp 148-167.

186. Dodge, C. H. "Clinical and Hygienic Aspects of Exposure to Electromagnetic Fields," in "Symposium on Biological Effects and Health Implications of Microwave Radiation," Richmond, 1969, pp 140-149.

187. Dorezak, W. "Ocena Czynnosei Watroby u Pracownikow Narazonych na Sawadowa Stycznose z Dwusiarczkeim Wegla Na Podstawie Niektorych Testow Enzymatycznych," MED. PRACY, Vol 19, 1968, pp 252-262.

188. Jerome, M.; Vaeth, M. D.; Lawrence, Z.; Feigenbaum, M. D.; Malcolm, D.; and Mertill, M. D. "Effect of Radiation on the Heart," RADIOLOGY, Vol 76, 1961, pp 80-86.

189. Takaoka, A.; Kandea, H.; Urano, M.; and Kikkawa, S. "Electrocardiographic Study of Cardiac Damage Secondary to Radiotherapy of Malignant Intrathoracic Tumors," RADIOL. CLIN. (Basel), Vol 37, 1968, pp 1-12.

190. Epstein, F. H., and Ostrander, L. D. "Detection of Individual Susceptibility Towards Coronary Disease," PROGR. CARDIOVASC. DIS., Vol 13, 1971, pp 324-342.

191. Fanger, H., and Lushbaugh, C. C. "Radiation Death From Cardiovascular Shock Following a Criticality Accident. Report of a Second Death From a Newly Defined Human Radiation Syndrome," ARCH. PATH., Vol 83, 1967, pp 446-460.

192. Ferrero, G. P. "Incidence of Diabetes Mellitus Among Workers Exposed to Carbon Disulfide," MED. D. LAVORO, Vol 60, 1969, pp 38-42.

193. Ferri, G.; Zacchi, C.; and Calzavara, R. "Histological and Histochemical Findings in the Heart Exposed to Ionizing Radiation," RADIOL. MED. (Torino), Vol 52, 1966, pp 728-729.

194. Flint, F. "Cor Pulmonale," LANCET, Vol 267, pp 51-58 [no date].

195. Frey, A. M. "Effects of Microwave and Radio Frequency Energy on the Central Nervous System," in "Symposium on Biological Effects and Health Implications of Microwave Radiation," Richmond, 1969, pp 134-139.

196. Fulton, R. "The Heart in Chronic Pulmonale Disease," QUART. J. MED., Vol 22, 1953, pp 43-47.

197. Giard, P. "Cardiopathy Related to Radiotherapy," J. SCI. MED. LILLE, Vol 88, 1970, pp 449-459.

198. Gobbato, F., and Chiesura, P. "Lead Nephropathy," MINERVA NEFROL., Vol 15, 1968, pp 12-24.

199. Gobbato, F.; Sequi, G.; and Turchetto, P. "Clinicostatistical Data on Vascular Changes in the Presence of Chronic Occupational Carbon Disulfide Poisoning," MINERVA MED., Vol 55, 1964, pp 4018-4021.

200. Greenfield, I., and Gray I. "Lead Poisoning. IX: The Failure of Lead Poisoning to Affect the Heart and Blood Vessels," AM. HEART H., Vol 39, 1950, pp 430435.

201. Gvozdjak, J. "Noncoronary Myocardiopathy," Bratislava, 1973.

202. Hassler, O. "Microangiographic Studies of Changes in the Cerebral Vessels After Irradiation. I: Proton Beam Lesions in the Rat," ACTA RADIOL. (Stockholm), Vol 4, 1966, pp 394-400.

203. Hempelmann, L.; Lisco, H.; and Hoffman, J. "Acute Radiation Syndrome," translated from English, Moscow, Izd-vo inostr. lit-ry [Foreign Literature Press], 1954.

204. Holstein, E. "Outline of Occupational Medicine," Leipzig, 1964.

205. Huff, H., and Sanders, E. M. "Coronary Artery Occlusion After Radiation," NEW ENGL. J. MED., Vol 286, 1972, p 780.

206. James, W. R., and Thomas, A. J. "Right Ventricular Hypertrophy and the Same in Small Pulmonary Arteries in Chronic Lung Disease," BRIT. HEART J., Vol 25, 1963, pp 583-588.

207. Jansen, G. "Effect of Noise on Physical Labor," INT. Z. ANGEW. PHYSIOL., Vol 20, 1964, pp 233-239.

208. Kannel, W. B.; Castelli, W. P.; and McNamara, P. M. "The Coronary Profile. Twelve-Year Following-Up in the Framingham Study," J. OCCUP. MED., Vol 9, 1967, pp 611-619.

209. Kleinert, H.; Kuttig, H.; and Wieland, C. "Electrocardiographic Studies During Cobalt 60 Teletherapy of the Cardiac Region," STRAHLENTHERAPIE, Vol 134, 1967, pp 339-349.

210. Kline, T. S. "Myocardial Changes in Lead Poisoning," AM. J. DIS. CHILD., Vol 99, 1960, pp 48-54.

211. Kosmider, S., and Petelenz, T. "Badania Elektrokardiografiezne w Przypadkach Przewlekeych Zstruc Zawodowych Olowiem," POL ARCH. MED. WEWNET, Vol 31, 1961, pp 1349-1357.

212. Bompiani, C.; Falcetti, E.; Matronola, V.; et al. "Systemic Arterial Pressure in Patients With Tumors At the Early Stages of Exposure to Ionizing Radiation," NUNT. RADIOL., Vol 32, 1967, pp 711-712.

213. Lauer, D. J. "Clinical Lead Intoxication From Brass Foundry Operations," ARCH. INDUSTR. HLTH., Vol II, No 2, 1955 pp 107-112.

214. Lee, G. "Physiology and Hemodynamics," in "Clinical Disorders of the Pulmonary Circulation," London, 1960, pp 7-33.

215. Legge, T., and Goadby, K. "Lead Poisoning and Lead Absorption," Berlin, 1921.

216. Lehmann, G. Effects of Noise," LANDARZT, Vol 38, 1962, pp 336-339.

217. Lushbaugh, C. C.; Comas, F.; and Hofstra, R. "Clinical Studies of Radiation Effects in Man," in "Space Radiation Biology," New York, 1967, pp 398-405.

218. McAfee, R. D. "The Neural and Hormonal Response to Microwave Stimulation of Peripheral Nerves," in "Symposium on Biological Effects and Health Implications of Microwave Radiation," Richmond, 1969, pp 150-153.

219. Merker, H. "Benzene and Early Detection of Its Effects on Blood," MED. KLIN., Vol 57, 1962, pp 1254-1262.

220. Michaelson, S. M. "Biological Effects of Microwave Exposure," in "Symposium on Biological Effects and Health Implications of Microwave Radiation," Richmond, 1969, pp 35-38.

221. Mickey, G. E. "Electromagnetism and Its Effects on Organisms," N.Y. ST. J. MED., Vol 63, 1963, pp 1935-1942.

222. Minden, H.; Gohlke, R.; and Rothe, R. "Report on Pathogenesis of Chronic Carbon Disulfide Poisoning," Z. GES. HYG., Vol 13, 1967, pp 815-822.

223. Morgan, J.; Hartley, M.; and Miller, R. "Nephropathy in Chronic Lead Poisoning," ARCH. INTERN. MED., Vol 118, 1966, pp 17-29.

224. Myerson, R. M., and Eisenhauer, J. H. "Atrioventricular Conduction Defects in Lead Poisoning," AM. J. CARDIOL., Vol II, 1963, pp 409-412.

225. Navarro Martinez, N., and Farina, G. "Clinicostatistical Contribution to the Study of Vascular Pathology Due to Carbon Disulfide: Analysis of 75 Cases," MED. D. LAVORO, Vol 60, 1969, pp 11-20.

226. Oleniacz, W., and Plamienisk, A. "Zaburzonia Gospedarki Tluszcowej w Przewleklym Ztruciu Dwuziarczkiem Wegla," POL. ARCH. MED. WEWNET., Vol 33, 1963, pp 1179-1182.

227. Oppliger, G., and Grandjean, E. "Vasomotor Skin Reaction to Noise," HELV. PHYSIOL. PHARMACOL. ACTA, Vol 17, 1959, pp 275-287.

228. Palmer, H. M.; Cocking, J. B.; and Emmanuel, J. G. "Irradiation Induced Constrictive Pericarditis in Intestinal Lymphangiectasis," BRIT. MED. J., Vol 4, 1970, pp 783-784.

229. Pierson, M. B., and Bachofer, C. S. "Alterations in Muscle Activity During Gamma Irradiation," RADIAT. RES., Vol 26, 1965, pp 403-412.

230. Prerovska, J., and Roth, Z. Z. "Sledovani Zamestancu z Rizika Sirouhliku Zamerennim na Rozvoj Arterioskelrozy," PRACOV. LEK., Vol 20, 1968, pp 6-10.

231. Raab, W. "Myocardial Metabolic Vulnerability--Key Problem in Pluricausal 'Coronary' Heart Diseases," CARDIOLOGIA (Basel), Vol 52, 1968, pp 305-317.

232. Read, J. L., and Williams, J. P. "Lead Myocarditis: Report of a Case," AM. HEART J., Vol 44, 1952, pp 797-802.

233. Rechenberg, J. K. "Carbon Disulfide Poisoning and Long-Term Carbon Disulfide Vascular Syndromes," ARCH. GEWERBEPATH. GEWERBEHYG., Vol 15, 1957, pp 483-530.

234. Rossi, L.; Oppliger, G.; and Grandjean, E. "Neurovegetative Effects on Man of Noises," MED. D. LAVORO, Vol 50, 1959, pp 332-337.

235. Salvini, M. "Lead Colic and Acute Coronary Insufficiency," FOLIA MED. (Naples), Vol 36, 1953, pp 423-439.

236. Idem, "Contribution to the Study of Cardiopathy Associated With Lead Poisoning," Ibid, pp 337-371.

237. Schwan, M. P. "Interaction of Microwave and Radio Frequency Radiation With Biological Systems," in "Symposium on Biological Effects and Health Implications of Microwave Radiation," Richmond, 1969, pp 13-33.

238. Simborg, D. W. "The Status of Risk Factors and Coronary Heart Disease," J. CHRON. DIS., Vol 22, 1970, pp 515-552.

239. Steimann, B.; Jaggi, M.; and Widmer, L. "Effects of Noise on Human Blood Pressure," CARDIOLOGIA (Basel), Vol 27, 1955, pp 223-229.

240. Sterner, G., and Eisenbud, M. "Epidemiology of Beryllium Intoxication," ARCH. INDUSTR. HYG., Vol 4, 1951, pp 123-151.

241. Stewart, J. R., and Fajardo, L. F. "Radiation Induced Heart Disease. Clinical and Experimental Aspects," RADIOL. CLIN. N. AMER., Vol 9, 1971, pp 511-531.

242. Straneo, G., and Caffi, M. "Contribution to Information about Carbon Disulfide Poisoning," FOLIA MED. (Naples), Vol 44, 1961, pp 917-940.

243. Straneo, G., and Seghizz, P. "Effects of Noise on the Peripheral Vascular System," Ibid, Vol 45, 1962, pp 6, 572-577.

244. Teleky, L. "Lead Poisoning," in "Handbuch der Sozialen Hygiene und Gesundheitsfursorge" [Handbook of Social Hygiene and Health Care], Berlin, 1926, pp 246-290.

245. Thomas, A. J. "Chronic Pulmonary Heart Disease," BRIT. HEART J., Vol 34, 1972, pp 653-657.

246. Toussaint, C.; Novac, J.; and Geiser-Toussaint, M. "Hemodynamic Changes As a Result of Pneumoconiosis of Coal Miners," REV. MED. LIEGE,

247. Toppich, E. "Demonstration of Coronary Lesion and Myocardial Pathology in Lead Poisoning," in "Aktuelle Themen auf den Gebiet der Berufsk Berufskrankheiten" [Current Problems in the Area of Occupational Diseases], Berlin, 1963, pp 43-49.

248. Uraki, Z. "Investigation of Long-Term Sequelae of Exposure to the Atom Bomb in Hiroshima," in "Investigation of Sequelae of Nuclear Explosions," Moscow, 1964, pp 74-75.

249. Velvart, J., and Ballog, O. "Vplyw Circuhlica na Rozvoj Aterosklerozy," PRACOV. LEK., Vol 13, 1961, pp 181-184.

250. Vidimski, G. "Chronic Cor Pulmonale," CARDIOLOGIYA, No 6, 1963, pp 31-36.

251. Vigliani, E. S. "Carbon Disulfide Poisoning in Viscose Rayon Factories," BRIT. J. INDUSTR. MED., Vol 11, 1954, pp 235-244.

252. Vigliani, E. C., and Pernis, B. "Atherosclerotic Encephalopathy Related to Chronic Carbon Disulfide Poisoning," in "Berufe Erkrank Durch Losemit," Leipzig, 1957, pp 57-58.

253. Vogelman, J. H. "Physical Characteristics of Microwave and Other Radio Frequency Radiation," in "Symposium on Biological Effects and Health Implications of Microwave Radiation," Richmond, 1969, pp 7-20.

254. Weist, H. J. "Toxic Parkinsonism With Quarelli Syndrome and Cardiovascular Damage Following Chronic Carbon Disulfide Poisoning," ARCH. GEWERBEPATH. GEWERBEHYG., Vol 15, 1957, pp 542-552.

255. Whitaker, W. "Pulmonary Hypertension in Congestive Heart Failure Complicating Chronic Lung Disease," QUART. J. MED., Vol 23, 1954, pp 57-73.

256. Wood, P. "Pulmonary Hypertension With Special Reference to the Vasoconstrictive Factor," BRIT. HEART J., Vol 20, 1958, pp 557-562.

257. Nofer, J.; Chojnowsski, J.; Kaweska, M.; et al. "Wplyw Zawedowego Norazenia na Dwusiarczek Wegla na Powstawanic Miazdzycy," MED. PRACY, Vol 12, 1961, pp 101-118.

10,657
CSO: 8144/0285

END