Easy Medicine for Biologists

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This book first published 2020

Cambridge Scholars Publishing

Lady Stephenson Library, Newcastle upon Tyne, NE6 2PA, UK

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

ISBN (10): 1-5275-4342-0
ISBN (13): 978-1-5275-4342-3

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INTRODUCTION

People have mastered atomic energy, learned to fly, descended to the bottom of the oceans, and are able to study cosmic objects that are billions of lightyears from the Sun. However, we are subject to numerous diseases and the biological limit of a human's lifetime remains the same as in the Stone Age. Such a strange contradiction is not connected indifferently to our own existence. On the contrary, since ancient times people have been keenly interested in the causes of old age, diseases, and death. Interest in these issues is genetically programmed, since it is a meaningful manifestation of the self-preservation instinct; however, the answers require the accumulation of an extremely large amount of information about both man and wildlife. This accumulation of knowledge has been accomplished slowly, with stops and periods of degradation along the way. Therefore, it took almost five thousand years for medicine to approach its current state.

The centuries-long development of medical knowledge has evolved from the most common ideas about the nature of diseases to understanding their essence. Such a vector of development is absolutely natural, since only a detailed knowledge of a specific disease makes it possible to recognize and effectively treat it in a timely manner. The number of already known human diseases is extremely large, so while it is good to understand them all, this is an impossible task for any doctor. However, a doctor of any speciality should have a sufficient idea of what the disease is in general, its essence, the laws of its pathology development, and the principal differences in illness and health.

This knowledge is not only necessary for medical workers. Man emerged due to the evolution of organic matter over the course of billions of years. From his fossil ancestors, he inherited the principles of organizing the genome, an anatomical structure, a chain of metabolic processes, and a way to regulate physiological functions. Since these principles, chains, and methods are largely universal, one can learn a lot about the biology of other living beings that inhabit our planet when studying human medicine.

At the same time, people, as well as any living being, are born, live, and die in continuous interaction with a changing external environment. The unfavorable influence of the external environment can lead to the development of a variety of diseases. This occurs so often that disease must be considered as an optional, but practically unavoidable variant for not only human existence but also for all other species of animals, plants, fungi, myxomycetes, or microorganisms. It follows that a biologist needs a certain amount of medical knowledge. Meanwhile, under standard education programs, students of biological specialties are devoted to studying the laws of life processes in detail, mostly within the limits of the norm. For a biologist, everything that is outside the norm can seem to be a kind of chaos that goes beyond the laws of life and rational explanation; this is completely untrue. Yes, medicine is not an exact science, but it is surprisingly logical.

Where should we begin if we want to understand medicine?

It is best to start on the sea shore. The ocean has been filled with medicine throughout the history of mankind. In order to describe it, we have used a system of special terms and concepts. Without getting acquainted with the basics of this system, medicine cannot be understood. First of all, it is necessary to have an understanding of health and disease.

1

General Concepts

Health and Disease

Unfortunately, there are no precise criteria that make it possible to clearly separate the notions of "health" and "illness" and, for several thousand years, medicine has used approximate definitions. In particular, according to the definition by the World Health Organization (WHO), health should be understood as ***"a state of complete physical, spiritual and social well-being, and not only the absence of disease or physical defects"***.

The essence of such a definition is quite understandable, but reliable units to fully measure well-being have yet to be invented. Therefore, every time a person is recognized as either healthy or sick, it is not a question of the presence of one of these conditions but, instead, the degree of their probability. In order to assess the state of the body, a set of qualitative and quantitative data are compared with the standard values for body temperature, heart rate, cholesterol concentration in the blood, and many other indicators. This approach greatly simplifies the diagnosis of diseases; however, it does not eliminate all problems.

The first of such problems is the impossibility of establishing uniform norms for all people, due to the fact that they differ in terms of genotype, age, environmental conditions, way of life, and previous diseases. Ideally, we would be able to provide a definition of individual norms for each living human, for each period of their existence, and their response to every sharp change in environmental conditions. In practice, this cannot be done; therefore, averaged norms are used for separate, yet relatively homogeneous, populations: men, women, children, old people, inhabitants of different climatic zones, representatives of different professions, nationalities, followers of various diets, and so on.

Another age-old problem relates to determining the number of criteria needed to assess the likelihood of a disease or health issue in each particular case. The more such criteria are used, the more reliable the answer to the question will be; however, this will also increase the cost of determining the diagnosis. In practical medicine, when a disease is suspected it is necessary to establish a minimum acceptable list of indicators to be studied. It is clear that under such restrictions there can be no complete confidence in the results, although the additional factor of time helps: if the disease cannot be detected immediately, then after a certain period its signs may become more pronounced.

So, what is health? In addition to the World Health Organization's definition, health can be understood as *a* ***condition in which the body is able to maintain the optimal composition of its internal environment, to support the morphology given by the genome, and to have the sufficient reserve capacity of systems, organs, tissues, and cells.***

Therefore, disease[1] should be understood as the state of the organism in which at least one of these conditions is not fully met.

The quantitative characteristics of these conditions are variable, but the limits of the allowed values can be determined for them. Namely, these boundaries are used in practice to solve the "healthy/sick" dilemma. However, in addition to complying with classical anatomical features, we have to remember such boundaries are relatively arbitrary. For example, a person who has undergone a tooth extraction, or who has scars on their skin, should not be formally recognized as healthy, but also it would be wrong to treat them as sick. For this borderline category in medicine, the term "*practically healthy person*" has been adopted. This definition is used when a person has certain deviations from ideal health, but these deviations do not significantly affect his performance or his quality of life in general. In prosperous countries, the majority of the population conforms to the category of practically healthy people. However, this means that almost every person, excluding those defined as sick, has a health issue, even if it is small.

This situation is quite natural, if only because the number of already known human diseases is extremely high. The current International Classification of Diseases contains about 20,000 names and the number of options reaches 68,000, but these figures are not final because, according to some, estimates of the number of human diseases may stand at more than 100,000. Not surprisingly, with this number of diseases, the average probability of being sick is very high.

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[1] In medical literature, the term "*pathology*" is often used as a synonym for *"disease*".

There are so many diseases that it is impossible to compile a full list of them within the framework of a single classification. Relative clarity in this issue can only be achieved by using several basic criteria in parallel. Currently, the main classifications of human diseases are as follows:

Etiological classification: Depending on the etiology, all diseases are divided into infectious (bacterial, viral, fungal) and non-infectious (inflammatory, traumatic, toxic, allergic, professional, etc.).

Topographic-anatomical classification: Diseases are grouped according to the most affected organ: the heart, blood vessels, lungs, brain, liver, joints, teeth, and so on.

Classification by age and sex: Diseases of the prenatal period, newborns, children, adults, and seniors; diseases of men and women.

Classification by generality of pathogenesis: This is the main mechanism of the development of the disease and includes allergic diseases, oncological, inflammatory, hereditary, metabolic diseases, and adaptation.

Disease Periods

The disease is a complex biological phenomenon, which consists of numerous specific and relatively universal changes that occur in the affected organism. However, despite the huge variety of diseases, in most cases they develop according to the following pattern:

Fig. 1.1. General scheme of the disease.

Primary damage occurs due to the influence of an unfavorable factor from the external environment, the strength of which exceeds the resistance of tissues and which, at first, cannot be compensated for by the adaptive reactions of the organism.

The latent period begins from the moment of primary damage and continues until the appearance of the first external manifestations of the disease. The duration of this period is very variable. It can only be a fraction of a second for a mechanical trauma but, for some infectious diseases (e.g., leprosy, HIV infection, amebiasis) it can stretch for many years. The absence of external manifestations does not mean that the disease cannot be detected in the latent period, but this requires the use of instrumental or laboratory methods of patient examination. It should be noted that the term "latency period" is not synonymous for the term "incubation period", which refers to the time that passes between the moment of infection by a pathogenic microorganism and the moment at which the sick person becomes contagious.

Prodromal period (prodrome): This is the so-called "period of harbingers" (*Greek: προδρομος—harbinger*), albeit not entirely accurately, as the disease is already taking place. "Prodrome" means the interval of time between the appearance of the first manifestations of ill-health to their maximum extent. During this time, at first, nonspecific symptoms common to many diseases—such as fever, general weakness, sleep disorders, or loss of appetite—are found. However, at the end of the period, specific signs or specific combinations of symptoms are present: such as icteric sclera, skin and mucous membranes in acute hepatitis; a characteristic fruity odor in diabetes; tinnitus and so-called "flies before the eyes" in hypertensive disease.

The duration of the prodromal period is also variable, but not as much as the duration of the latent period. For infectious diseases, the time of the prodrome rarely exceeds three days, but it can last for several weeks at its worst. With severe radiation sickness, poisoning, and in especially dangerous infections, the prodromal period can be reduced to several hours; however, sometimes it is completely absent. Immediately after the latent phase, the height of the disease occurs, with the maximum severity of symptoms. This usually happens in the case of very serious diseases.

Period of pronounced manifestations, or height of illness: In the usual course of the disease, at this stage, the clinical picture becomes complete, and there are all, or most of, the inherent pathology signs. That said, in this period, the protective-adaptive capabilities of the body are also used to the fullest degree. In the acute course of the disease, the stress depletes the resources of cells, tissues, and organs. This means that the duration of the period of pronounced manifestations cannot be large, and it rarely exceeds two to three days, after which the outcome occurs.

However, in chronic diseases, the intensity of the process is significantly lower, and the duration of the period of pronounced manifestations can be stretched for weeks, or even months.

Outcome of disease: Recovering is the most favorable outcome of any disease and the most unfavorable outcome is death. Between these extremes, there are transitional options: incomplete recovery, chronic flow, recurrence, and the terminal states.

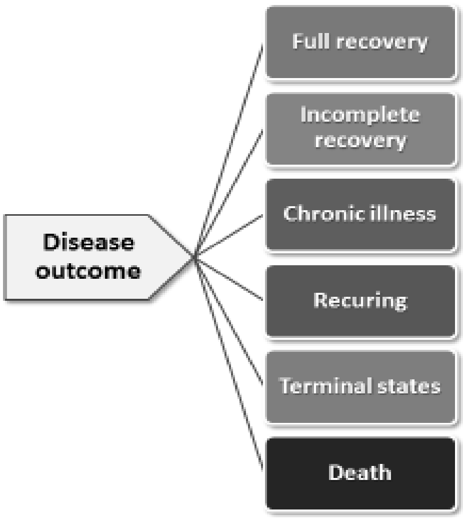

Fig. 1.2. Disease outcome

Recovering is the process of restoring damaged structures and disturbed functions. With complete recovery all the manifestations of the disease disappear and, although a return to the initial healthy state is observed, the formerly ill organism is never the same as it was before the disease. An incomplete recovery that is non-critical for the body can lead to violations of organ functions, anatomical defects in the form of scars, changes in the mass and shape of the organs, narrowing or widening of the blood vessels, and various physiological holes. Sometimes, as a result of additional treatment, an incomplete recovery can be turned into a complete one but, more often, recovery is still incomplete, and a person is recognized as "practically healthy".

The process of recovery is provided by urgent and long-term mechanisms:

The urgent (emergency) recovery mechanism includes protective unconditioned and conditioned reflexes: withdrawal of limbs from hot or too cold objects, sneezing, lacrimation, coughing, vomiting, sweating, and the narrowing of the pupils in bright light. These urgent mechanisms also belong to the defensive reactions of the regulatory systems that aim to preserve the body's homeostasis: internal temperature, optimal hemodynamics, osmotic pressure and pH of biological fluids, blood glucose concentration, and so on.

The long-term mechanisms of recovery are provided by energy and plastic cell reserves, and the possibility of activating the functions of tissues and organs. They are also due to the mutual assistance of adjacent systems of organs (for example, the respiratory and cardiovascular system). A very important part of long-term recovery is based on the ability of most human cells to divide. Cellular proliferation allows the dead cells to be replaced and the number of the immune system's protective cells to increase both in the right place and at the right time. The mechanisms of long-term recovery include the migration of phagocytic cells to the foci of pathology, phagocytosis and humoral immunity; increased blood supply to damaged tissues; poison detoxification processes; and connective tissue reactions (cicatricial wound healing, for example).

The coordination of various mechanisms of recovery is carried out by the nervous and endocrine systems, as well as by numerous protein factors of intercellular interaction.

Transition to chronic form, remission and recurring: There are situations when the amount of pathological change is counterbalanced by the protective and adaptive capabilities of the organism. In such cases, when the course of the disease continues for a long time, the disease becomes chronic.

Recurring is the term for the new manifestation of the disease (exacerbation) after remission (a period of relative well-being). A recurrent disease flow develops when the cause of the disease has not been completely eliminated. Under this condition, the accidental weakening of the body's defenses, by additional adverse environmental effects or premature cessation of treatment, causes the exacerbation of the dormant pathology. An important common feature of chronic and relapsing diseases is that both of these outcomes are not final. Sooner or later, they are replaced by either recovery or death.

Terminal states:

Pre-agony develops after a serious illness or massive trauma. At this stage, the central nervous system is upset due to the loss of consciousness. Violations in the regulation of the tone of the smooth muscles of the arteries lead to a sharp drop in blood pressure (systolic pressure can drop to 60mm Hg and below). The deterioration of the blood supply is manifested in cyanotic or pale skin; in addition, hypoxia causes a reflex increase in heart rate and dyspnea. Pre-agony can last from several hours to several days, after which it passes either into a state of terminal pause, or directly into agony.

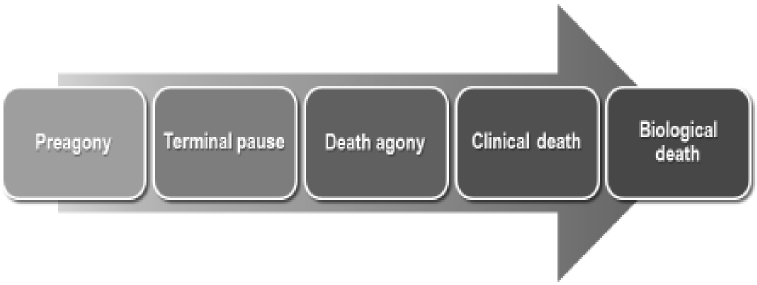

Fig. 1.3. Terminal states

Terminal pause has clear distinctive features. In this state, breathing stops for a few minutes. There are no diagnostically important corneal reflexes and a temporary cardiac arrest is possible. The duration of the terminal pause varies from a few seconds to several minutes, after which the agony begins.

Agony *(Greek: αγωνία—struggle)* can last up to several days. At the beginning of the period, in the absence of consciousness and when there is an inhibitory effect in the brain cortex, the activation of the brain's subcortical centers often occurs, which is manifested in uncoordinated motor excitement, resulting in convulsions. It might also involve the involuntary emptying of the bladder and intestines, as well as a short-term increase in blood pressure due to spasms in the blood vessels. Breathing will gradually become superficial and irregular. Arterial blood pressure will drop sharply and the pulse will only be detected on the carotid arteries. Pain sensitivity disappears. Skin covers are pale or cyanotic, as well as cold and wet. The agony ends with either another terminal pause, or clinical death.

Death (i.e., the final cessation of the life of the organism) happens for three reasons. Death can be considered to be natural when it happens as a result of aging but it can also occur as a result of an accident, murder, and suicide; in addition, when it is due to illness, it can be pathological. Except in cases of massive, life-incompatible injuries, death does not occur as a one-time phenomenon, but as a process of several successive phases called terminal states. Terminal states include pre-agony, terminal pause, agony, as well as clinical and biological death.

Clinical death is confirmed by the cessation of the activity of the main life-supporting systems (cardiovascular and respiratory), as well as the extinction of the most important diagnostic reflexes, such as the pupils' reaction to light. However, even with clinical death, there are still chances of reanimation. This is because at a cellular level, minimal metabolic processes remain for a while due to the accumulated stocks of proteins, carbohydrates, lipids, and the possibility of ATP synthesis in anaerobic glycolysis process. The lifetime of different cell types suffering from a deadly combination of anoxia, acidosis, and uncontrolled proteolysis is not the same. The most highly resistant cells are the least resistant. The viability of neurons in the cerebral cortex stops on average 5 to 7 minutes after the onset of clinical death. However, this interval can be increased to about two hours with significant cooling of the organism, which prevents the decay processes.

Biological death is an irreversible stage of dying, in which not only disorders and injuries occur, but also the death of critical cells in the cerebral cortex; this means the death of the human's personality. Subsequently, the disorganization and decay of other parts of the nervous system, internal secretion glands, internal organs, and integumentary tissues takes place. Biological death is distinguished by distinct external manifestations. In particular, the signs of biological death are rigor mortis, due to the accumulation of lactic acid in the muscles; the appearance of cadaveric spots, due to the accumulation of blood in the lower parts of the body; the opacity and drying of the eyes' corneas; and a decrease in body temperature to an ambient level.

The Disease's Atypical Flow

In conclusion, it should be noted that not every disease passes through all the stages listed above. Many things depend on the force of the harmful influence or the resistance of the effected organism, as well as whether the correct treatment has been received. Therefore, the combination of different factors determines the disease dynamics in each specific case. Due to the overall activity of the process, several variants of the flow (course) are possible for the same disease.

When the harmful influence is extremely dominant, an ***acute flow of pathology*** may develop, in which the outcome may occur immediately after a prodromal or even after a latent period and, here, the outcome can be unfavorable.

The ***chronic flow*** is characterized by a prolonged period of pronounced clinical manifestations, and this period repeatedly ends and resumes through the variant of the ***recurrent flow***.

When it is infected with viable, but not very active pathogens (tubercle bacillus, hepatitis viruses, some rickettsia), the ***latent flow*** of the disease is possible; although it is inhibited, in the same period, when there is a background of minimal symptomatology.

With proper treatment, or if there is a sharp activation of the body's protective-adaptive capabilities, any diseases can be stopped at an early stage and result in recovery. This is another version of the flow, which is called ***abortive*** (Latin: *abort* means "short"). Usually the abortive flow ends in a latent or in a prodromal period.

Etiology of Diseases

The study of the causes of diseases is devoted to a special section of medicine called **etiology** (*Greek: αἰτία—reason*). The cause is understood to be the primary impact that is the triggering event for the onset of the disease. For several centuries, the causes of diseases have traditionally been divided into external and internal ones. However, after clarifying the nature of hereditary diseases, it became clear that, in this case, the disease begins under the influence of mutagens and thus it is also the result of an external influence. Therefore, in order for the potential threat to have an effect, it must itself be strong enough, or the body has to be sufficiently weakened. If this happens, then the triggering effect that actually caused the disease is called the etiological factor.

The primary defect is the inevitable consequence—and thus indispensable evidence—of a realized ***etiological factor***. This is some kind of damage or violation, from which all other changes that are characteristic of a particular disease develop.

Environmental properties that are potentially dangerous to human health but have not yet caused the disease are considered to be ***pathogenic factors***.

Adverse effects that do not cause the disease itself but increase its possibility are ***risk factors***.

It should be borne in mind that the same adverse effects in different diseases may perform the role of any of these factors. For example, a low ambient temperature is considered to be a pathogenic factor, as it can cause harm to health; in addition, it can be a risk factor for pneumonia and, in the case of frostbite, a low temperature is already an etiological factor.

Historically, there were two opposing points of view on the causes of diseases. Proponents of the ***monocausal*** hypothesis believed that the reason is always singular; for example, infection by specific pathogenic microorganisms, or the impact of a solid thing. In contrast, the proponents of the ***conditionalism*** hypothesis adhered to the point of view that facilitating conditions are necessary—such as the action of risk factors, the weakening of the protective capabilities of the organism, or even both—in addition to the etiological factor.

The situation was clarified by Ivan Pavlov's (1849 – 1936) suggestion that unfavorable environmental factors were ranked according to the strength of their impact. It became clear that the impact of a very strong or especially harmful factor leads to violations or damages that are sufficient for disease to occur without any additional conditions. However, the influence of these extremely strong factors is rare. In reality, a person is much more likely to encounter either moderate or weak adverse effects, and the disease only occurs against a background of additional adverse effects.

It is also necessary to add that, at its onset, the duration, as well as the strength, of the etiological factor is important because with greater contact time, the likelihood of disease naturally increases. It is essential to take into account the peculiarities of the human genotype, since we all have sets of genes that differ in their degree of adaptation to the existing conditions of life. In a less adequate set, the higher the risk of disease, even with mild adverse effects on the body. Due to this, there are people with low resistance to infections and increased bone fragility, as well as a predisposition to obesity, allergies, malignant tumors, diabetes, atherosclerosis, and many other diseases.

Etiological factors

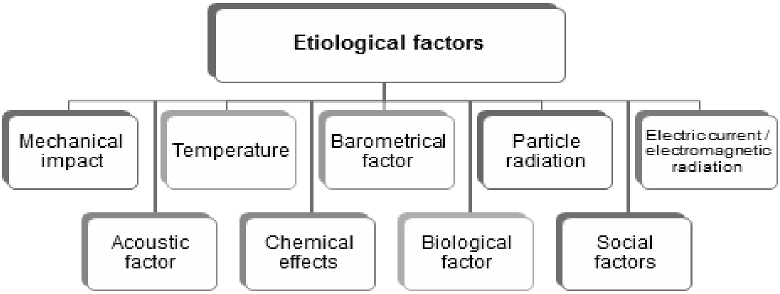

Fig. 1.4. Etiological factors

Mechanical effects: Falls from a height and impacts from solid or sharp bodies, as well as powerful jets of liquid or gas that exceed the limits of the elasticity and strength of human tissues, will cause various forms of injury, such as contusions, crush, bruises, wounds, sprains, or fractured bones. Pathological consequences can also be derived from prolonged contact with solid, vibrating surfaces. This can adversely affect the state of the sensory and motor nerve fiber tips and can lead to vibration disease.

Temperature: The human body is homoeothermic: i.e., able to maintain its internal temperature for a long time under adverse environmental conditions. However, this ability is not absolute and may not be sufficient. A relatively narrow range of ambient temperatures (approximately between +18°C and +26°C) is relatively comfortable for us. Prolonged exposure to low temperatures leads to the development of general overcooling or ***hypothermia***. Local exposure to low temperatures causes frostbite. At the other end of the spectrum, high environmental temperatures cause the body to overheat **(*hyperthermia*)**, which can develop into a state of thermal shock. This can lead to the brain overheating, thereby creating a substantial threat to life. Tissues that are severely overheated or that come into direct contact with fire will develop burns.

Barometric factor: Even minor changes in atmospheric pressure (within a few dozen mm of mercury) often exacerbate chronic diseases in the cardiovascular and respiratory systems of meteorically dependent people. Prolonged exposure to a reduced atmospheric pressure can trigger the onset of altitude sickness, which is also characterized by impaired activity in the circulatory and respiratory organs. This is associated with the impaired function of the nervous system. It is very dangerous to rapidly reduce external pressure when a diver rises from deep water (*decompression sickness*). This is because the nitrogen dissolved in the blood can form numerous bubbles that impede the movement of blood through the vessels, which can cause the blood circulation to stop completely. Finally, sharp and very significant fluctuations in atmospheric pressure arising from explosions cause contusions and barotrauma, such as a rupture in the eardrum or the lungs. Barotrauma may also be caused by depressurization in an aircraft at high altitude.

Radiation: When it has sufficient strength, any kind of radiation can cause disease. The degree of biological threat correlates with the penetrating ability of the radiation, which is determined by the energy and mass of the emitted particles. Radiation from the visible part of the spectrum, with a wavelength of 380–780nm, has a flux of low-energy quanta and does not have a significant penetrating power. Infrared rays with wavelengths from 740nm to 2000μm exert a predominantly surface thermal effect. However, ultraviolet radiation (λ = 10 – 400nm) penetrates inside the cover tissues and can damage nucleic acid molecules, and in particular can cause malignant tumors.

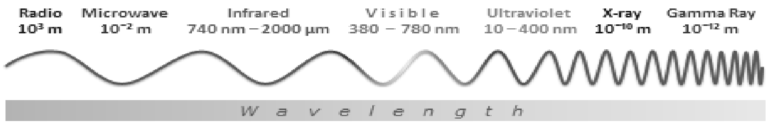

Fig. 1.5. The main types of the electromagnetic radiation

The danger of electromagnetic radiation is determined by its power, frequency, and the duration of exposure. Nervous, endocrine, and immune systems are the most sensitive to radiation and the disturbances in their functions form the basis of radio wave sickness. Strong radiation exacerbates chronic diseases in the nervous, cardiovascular, and endocrine systems, as well as oncological diseases. The same consequences can also occur with prolonged exposure to weak electromagnetic fields.

Sources of electromagnetic radiation are industrial power plants, electric motors, radars, high-voltage transmission lines, and some household electrical appliances. Solar flares also have a negative effect on the health of meteosensitive people. These result in showers of charged particles reaching the earth, causing sharp fluctuations in the intensity of the geomagnetic field.

The three classic types of ionizing radiation—α, β, and γ—have different degrees of penetrating power: the maximum is γ-quanta. High-velocity fluxes in heavy elementary particles, especially neutrons, also have a large penetrating power. Due to their substantial mass, they are more dangerous to health. Damage caused by various types of radiation breaks covalent bonds, which directly damages the biomolecules and also leads to the formation of a large number of free radicals causing damage to nucleic acids and proteins. As a result, ***radiation sickness*** can develop. When this occurs, the radiosensitive cells of the bone marrow and various kinds of epithelium are the most easily damaged but, when significant amounts of radiation are absorbed, even more resistant cells, including nervous ones, can be affected. Radiation sickness occurs in varying severity from mild to extreme, such as in the case of receiving radiation from lightning, in which a person dies in a few minutes, depending on the dose. In less dramatic cases and even when radiation sickness does not occur, the effect of ionizing radiation can have long-term consequences in the form of oncological or hereditary diseases.

Electric currents: The powerful flow of electrons disrupts the processes of depolarization and repolarization of cell membranes. It is able to disorganize the synapses and cause spasmodic contractions in the muscles and so it is especially dangerous for nerve cells and muscle tissues. The inhibition or cessation of the transmission of nerve impulses can lead to a loss of consciousness, cardiac arrest, or breathing difficulties.

When a current is struck by a living organism, there is always a place for the entrance and exit of the electron flow; these are the places where significant damage to tissues can occur and they can become charred. The path between these points is called a “loop current”. It will be deadly if it passes through the brain or heart. This threat is represented by a current of only 0.35A and a voltage of 36V.

Chemical exposure: Any substances entering the human body from the outside, or synthesized endogenously, even when useful and necessary, can pose a threat to health. Some of these substances are harmful due to the peculiarities of the structure of their molecules, while others are dangerous in excessive quantities. Complex biomolecules that perform informational, regulatory, and catalytic functions are most vulnerable to chemical damage. Poisons with a denaturing action—such as water-soluble salts of arsenic and other heavy metals—can damage protein molecules. Enzymatic proteins are sensitive to poisons and toxins that can cause irreversible inhibition of the catalytic center (e.g., hydrocyanic acid and its salts or neurotoxins synthesized by poisonous animals). Some end-products of normal metabolism, such as bilirubin or ammonia, have toxic properties; therefore, they are quickly eliminated from a healthy body. Many substances act as chemical mutagens, meaning that they damage nucleic acids. A number of substances possess ***teratogenic*** (*Greek: τέρας—monster*) properties—i.e., the ability to disrupt the interaction of cells in the fetal development of embryos—as a result of which various deformities develop. Finally, ***prions*** cause severe diseases in the nervous system.

Chemical factors are not always pathogenic because of their ability to damage other molecules or supramolecular structures. The excessive concentration of completely normal and necessary molecules can be harmful to the body. In particular, high blood glucose levels upset the osmotic balance between cells and the extracellular environment; extreme dietary lipid consumption increases the risk of disease in the blood vessels; and excessive synthesis of hormones underpins a number of endocrine diseases. In addition, many substances of industrial, plant, and animal origin can cause allergic reactions.

All medicinal substances, without exception, deserve special mention, and not only because they all have side effects. More importantly, the therapeutic effect itself can be toxic to the patient's body, in cases of an increased individual sensitivity to or an overdose of the drug; therefore, medications must be applied professionally and used for the minimum amount of time needed to heal.

Biological factors: The number of creatures that can harm a human is striking. The smallest of them are the viruses and pathogens of a number of diseases. A large number of diseases, including dangerous infections, are caused by bacteria. The simplest unicellular organisms (e.g., giardia and amoeba) and many fungi (ascomycetes, basidiomycetes, etc.) also have pathogenic importance. There is a group of infectious diseases caused by parasitism in the human body due to flatworms or roundworms. Different types of arthropods can be dangerous both in themselves (wasps, bees, scorpions) and due to their ability to carry the pathogens of serious infectious diseases (mosquitoes, cockroaches, fleas, lice, bugs). Small mammals, such as mice, rats, and ground squirrels, are also carriers of dangerous infections. Some infections can be easily transmitted from indoor pets—e.g., cats, dogs, birds, turtles, and even aquarium fishes. Poisons from snakes, as well as some amphibians and fishes, and mechanical injuries from large predatory animals pose an absolute threat to human health and life.

Generally, a significant number of the species that inhabit our planet are very unfriendly to humans; however, there are exceptions. Some bacteria that harmlessly live in the human intestine supply us with certain vitamins. Others can prevent the reproduction of dangerous microorganisms. Therefore, a balanced composition of intestinal microflora is one of the conditions for human health. The death of beneficial symbionts (e.g., as a result of oral antibiotics) is one of the causes of serious disorders in the digestive system.

Social factors: People live in constant communication with each other. A person's lifestyle, the nature of their professional and interpersonal relationships, and the accumulation of everyday problems all have a significant impact on the psyche. Since the nervous system regulates the activity of important organs, its state is naturally reflected in the organism as a whole. Additionally, the human nervous system is very sensitive to psychological overload. Strong emotions can cause real hormonal storms, leading to spasms in the blood vessels of smooth muscles and hollow organs. It can also have numerous effects at the molecular level, which interfere with the activity of regulated enzymes.

Imbalances in the metabolism contribute to the exacerbation of chronic diseases and the emergence of new ones. The endocrine, cardiovascular, digestive, reproductive, and nervous systems are very vulnerable to neurogenic factors. Therefore, social distress is a major risk factor for mental disorders, coronary heart disease, diseases of the stomach, intestines, biliary tract, pancreas, male and female infertility, and a number of hormonal pathologies. In addition, stress disrupts the work of the immune system, which leads to an increase in the likelihood of infectious and oncological diseases. Finally, strong negative feelings can provoke a state of passion in which individuals cannot control themselves, as they are in the grip of instincts, reflexes, and emotions. In extreme cases, this can lead them to commit murder or suicide.

2

LEVELS AND TYPES OF VIOLATIONS AND DAMAGE

Depending on the type, strength, and location of the etiological factor, the nature, size, and localization of pathological changes can be very different. ***Violations*** or ***disorders*** usually imply forced changes in functions, but distinct structural changes are called ***damages***. Depending on their severity and depth, pathological changes can be both reversible and irreversible. In addition, these changes are divided into local and general. Both of these involve the entire body; all local disorders and damages cause general body reactions. The difference lies in the intensity of the reactions.

The individual combination of disorders and injuries determines the nature and degree of activity in the developing disease. At the same time, pathological changes in ions, molecules, cells, tissues, organs, and organ systems have their own characteristics. The damage and disorders which dominate the organization of living matter depend largely on the specificity of the individual's medical history.

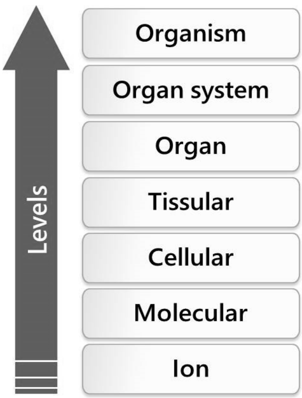

Fig. 2.1. Levels of disorders and damage

The Ions Level

The most important ions for humans are H^+, Na^+, K^+, Ca^{2+}, Cl^-, and HO^-; however, iron, magnesium, manganese, iodine, cobalt, zinc, selenium, and lithium also have biological significance. The number and ratio of different ions can have a great impact on the state of cellular structures and the whole human body. The most important indicators of the homeostasis of the human body, such as osmotic pressure and acid-base balance, depend on the content of various ions in biological fluids; without an optimal ratio of ions, bone mineralization is hampered, and the normal functioning of excitable tissues and implementation of the regulatory effects of some hormones are impossible. Finally, some ions act as coenzymes.

Ions can cause damage when there is a violation of their balance or their content in cells and biological fluids. These disorders are often secondary because they are generated by disorders in the endocrine, excretory, and digestive systems, or poor nutrition.

Ions not only enter the body but also leave it. The main organs performing the excretion of ions, in the absence of violations, are the kidneys, but most of the H^+, Na^+, Ca^{2+}, Cl^- and HO^- ions are reabsorbed and returned to the blood. However, when there is kidney disease, the efficiency of reabsorption may decrease, leading to a deficiency in different ions. Such deficiencies can also occur in cases of severe vomiting, excessive sweating, or prolonged diarrhea.

It is not only an abnormal number of ions but also their specific properties that can be harmful to health. Many metal ions are toxic, especially beryllium and arsenic, but almost all metals have toxic properties, including the ions in iodine, cobalt, selenium, zinc, and iron, despite the unconditional biological necessity of these elements.

Molecule Level

Due to the peculiarities of the chemical composition and structure of molecules, a huge number of substances represent a threat to human health and life. Strong inorganic acids and alkalis are capable of causing the denaturation of proteins, hydrolysis of peptide bonds, and extremely drastic changes in the pH of the medium with the subsequent development of either acidosis or alkalosis. The etiological factors of numerous allergic diseases are protein molecules, a variety of which can provoke abnormal reactions in the immune system. Substances that have a mutagenic, carcinogenic, or teratogenic effect constantly enter the human body via water, food, and air. Poisons of an organic nature, such as tubocurarine or tetrodotoxin, are very dangerous as they block the functions of the nerve synapses. Additionally, infectious prion proteins can transform normal human proteins into inoperable isomers.

Of course, molecular threats also include the nucleic acids of human-infectious viruses. In addition, some pathogenic microorganisms have a kind of “molecular weapon”. An example of this is the hyaluronidase enzyme used by microbes to destroy the non-cellular substance of the connective tissue in order to penetrate the human body. Neuraminidase is another substance that targets the cell membrane, breaking down its heteropolysaccharides, which facilitates its progress into the target cells. A number of pathogenic microorganisms—for example, penicillinase—are able to produce enzymes that destroy antibiotics. Many pathogenic microbes produce dangerous toxins (only one molecule of diphtheria toxin can kill a human cell).

Anti-enzymes are another molecular weapon produced by microbes, and it is because of these that intestinal parasites are not digested by human gastrointestinal tract enzymes. Anti-ferments of tissue and blood parasites block the actions of our phagocytic lytic enzymes. Leeches suck our blood with the help of anticoagulants such as hirudin and tabanin.

At the molecular level, there are disorders as well as damage. The reason for a number of diseases is the lack or violation of the composition and structure of the body’s own enzymes. Many diseases are caused by substances that are completely natural and necessary for normal life, when they accumulate in excessive amounts or appear in an inappropriate place. Violations of the content and/or ratios of organic molecules arise due to changes in their rate of synthesis and decomposition in the body, as well as the inadequate exchange between the body and the external environment. For each of these options, the discoordination of metabolic processes is inevitable. Under unfavorable conditions, it can develop into a disease.

Cell Level

Every second a huge number of chemical reactions take place in the cell, and many of these are in opposition to each other. They do not interfere with each other due to ***compartmentalization***: i.e., the spatial separation of incompatible reactions and their convergence.

The provision of the compartmentalization principle is a function of all intracellular structures, especially membranes, and a violation of this principle will occur in any injury. Since the initial cause of damage to both the organism as a whole and its individual cells is due to the action of external factors, the cell surface will be the first area to make contact with them. Disruption to the membrane transport functions causes further swelling in the cell. Numerous outgrowths appear and disappear on their surface and the cytoplasmic globules can separate from the cell membrane and remerge with it. Within the cell, pathological vacuoles are formed from swollen mitochondria and the cisterns of the endoplasmic reticulum; following this, a violation of compartmentalization and a decrease in the efficiency of metabolism occur. With an unfavorable outcome, edema leads to a special state of hydropic degeneration and then cell death.

Predominantly, damage to the plasma membrane is caused by the action of either physical or chemical pathogenic factors, while biological factors may act differently. In particular, viruses damage the membrane less, due to the fact that they cheat. Harmful particles and molecules get into the cell through the completely normal process of endocytosis; therefore, primary damage can occur in areas other than the plasma membrane. Often this happens when a cell suffers from a lack of oxygen, water, or nutrients, which immediately affects its energy metabolism. Lack of energy or amino acids inhibits the synthesis of critical proteins, including membrane proteins. Erosion of the membranes prevents the maintenance of a normal concentration gradient between the cell and the external environment, which creates a threat of secondary cell edema and the risk of releasing hydrolytic enzymes from lysosomes. These enzymes are able to digest their own cells from the inside. Additionally, lysosomes can be damaged by particles of coal, metals, asbestos, silica, quartz crystals, uric acid, and a number of other substances, which may be randomly absorbed by the cell.

Another sign of cellular distress is the excessive formation of various deposits. Although some cytoplasmic deposits of reserve lipids and carbohydrates are inherent in all healthy cells to a certain extent, disturbances in metabolic regulation can lead to the excessive accumulation of such inclusions, which leads to the degeneration of organelles and even cytolysis. Deposits can be of protein, lipid, carbohydrate, pigment, inorganic, or mixed.

A frequent variant of protein deposits is amyloid infiltration, or ***amyloidosis***. Amyloid is the three-dimensional fibrillar structure of glycoproteins that accumulates in both the extracellular space and the cytoplasm of cells after prolonged intoxication or depletion.

Hyaline has a similar structure but with a slightly different composition and the accumulation of this leads to the development of ***hyalinosis***, or the infiltration of hyaline into the cells and the extracellular medium.

Hyalinosis is not only a consequence of disease but it can also develop as a result of the natural aging of tissues.

Protein-carbohydrate deposits are accompanied by ***mucoid degeneration***, which is where mucus-like contents accumulate in the cells. Pure carbohydrate cytoplasmic deposits, such as glycogen deposits, are also possible.

Lipoproteins, phospholipids, triglycerides, and cholesterol and its esters can also accumulate in cells. Among pigment deposits, the excessive accumulation of melanin, hemosiderin, and colored products of fatty acid oxidation are frequent occurrences. The most common type of mineral deposit is calcification: i.e., the deposition of calcium salts in soft tissue cells. Deposits of iron salts and other metals are also possible.

A violation of metabolic processes that is of sufficient severity or duration can result in damage to intracellular structures. At first, vacuoles and various "garbage" inclusions appear in the nucleus, and, later, chromatin turns into a homogeneous mass (*karyopycnosis*). Then the volume of nucleoplasm is clearly reduced (*karyorrhexis*), after which the nucleus can decay (*karyolysis*). Similar processes (*plasmorexis* and *plasmolysis*) are possible in cytoplasm.

The destruction of the nucleus means the termination of the transcription process and the end of protein synthesis. In the course of progressive degradation, polysome complexes disintegrate; the number of ribosomes decrease; the Golgi apparatus disappears; and microtubule proteins and microfilaments are depolymerized. The number of mitochondria also decrease, while the surviving organoids swell and stretch. This leads to the disappearance of cristae, the spatial separation of the respiratory chain enzymes and the inhibition of the oxidative phosphorylation process. For some time, the cell can survive through the synthesis of ATP in anaerobic glycolysis, but damaged lysosomes quickly release proteases, which are able to catalyze the hydrolysis of peptide bonds in proteins, including glycolysis enzymes. As a result, cytolysis occurs: i.e., the final disintegration of the membranes and the dissolution of cell residues.

The Tissue Level

Biological tissue is a collection of cells of the same type that perform the same function. In humans and animals, there are four types of tissue: epithelial, connective, muscular, and nervous. With certain reservations, this list can also include a special liquid tissue: blood.

Biological tissue is more complex than single cells. This complication opens up both new functionality and new vulnerabilities to adverse factors. Additional opportunities are realized when combining the potential of related cells to meet the needs of the body. However, firstly, the provision of such needs can lead to the depletion of cellular resources and, secondly, synergism is provided by intercellular interactions where malfunctions are possible. For these reasons, integrated cell masses are subject to the additional risks of similar and simultaneous disorders. These disorders are manifested in changes in the state and/or number of cells.

The most frequent pathological change in the state of cells, tissues, and organs is an imbalance in the metabolic processes. Adverse factors rarely lead to increased anabolism, since any synthesis requires a source of energy and this is released during catabolism. Of course, this energy can be used to move cells around the body in order to perform phagocytosis, secretion, muscle contractions, and for the generation of nerve impulses. However, the long-term activation of catabolism means the expenditure of cellular resources, and it is difficult to complete this in a sick organism. As a result, cells, tissues, and organs are all threatened with exhaustion, involution, and the prospect of death.

Degradation may be a consequence of a prolonged decrease in the activity of healthy tissues or organs. This is because low functional activity involves a decrease in the blood supply, which inevitably impairs nutrition. In addition, each of the above reasons can lead to a state of dystrophy and atrophy.

Dystrophy (*Greek δισ—disorder, loss; τροφια—nutrition*): In a narrow sense, dystrophies are deposits of ballast or harmful substances in the cytoplasm of cells and in the extracellular space. In a broader sense, dystrophies imply metabolic disorders in tissues (e.g., muscle) and organs (e.g., kidney dystrophy) or they refer to the overall result of an imbalance in the metabolism between the human body and the environment.

Dystrophies result from:

- ***infiltration***: i.e., excessive income from the blood into the tissues of various substances (cholesterol, fatty acids, glucose)
- ***abnormal synthesis*** of substances that are unusual for healthy tissue (amyloid, hyaline)
- ***transformation*** of molecules of one type into metabolites of others (e.g., amino acids are converted into fatty acids or carbohydrates)