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IATROGENESIS HAS EXISTED AND CONTINUES TO THIS DAY

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Abstract: For the article "Iatrogenesis Has Existed and Continues to This Day": Ministry of Health of the Republic of Uzbekistan; Institute, Tashkent Medical Academya Department of Family Medicine–2 and Clinical Pharmacology; Khurramova Zahro, Khurshidbekova Dilsabo, Sotvoldiyeva Feruza, Tashkent Medical Academy, Department of Pathological Anatomy, Kholiyeva Nigora, Senior Lecturer

Worldwide, the problem of iatrogenesis continues to emerge repeatedly at new stages of development. Medicine and the medical industry have advanced to the forefront, and adverse effects have kept pace with this progress. Alongside advances in medical science, the risks associated with medical care have also increased, as have the number of iatrogenic diseases and deaths caused by them. Physicians should remember the words of E. C. Lambert: "There are patients who cannot be helped, but there are no patients who cannot be harmed."

Keywords: iatrogenesis, medicine, interventions, preventive and therapeutic measures, information, adverse effects.

At the present stage, the aggressiveness of treatment often exceeds the severity of the disease itself, and the problem of iatrogenesis continues to enter a new phase. The history of medicine tells us that Hippocrates also expressed the principle: "First, do no harm." Medicine and the medical industry have made tremendous advances; at the same time, however, adverse effects can be observed following all types of medical interventions. According to the International Classification of Diseases, any pathological process arising as a result of a medical intervention is considered iatrogenesis [8, 13, 20]. Statistical analyses have led to a proposal to classify "iatrogenic conditions" according to all causal factors, ranging from instrumental and diagnostic procedures to informational and preventive and therapeutic interventions. One of the major problems in modern medical practice is the change in the course of many diseases during pharmacotherapy. Iatrogenic diseases are generally considered to be illnesses of medical origin. However, leading clinicians E. M. Tareev and I. A. Kassirsky clarified and expanded this concept: it includes not only the adverse consequences of therapeutic procedures, but also any diagnostic interventions that cause a pathological condition (manipulative, diagnostic, surgical, resuscitative, etc.) [6, 7, 19, 22].

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A landmark that stimulated modern thinking about iatrogenesis was the publication in 1925 of O. Bumke's work "The Physician as a Cause of Mental Disorders" (quoted in [12]). In the subsequent period, the term "iatrogenesis" was used to describe diseases caused by the psychogenic influence of medical professionals.

According to S. Ya. Doletsky, "iatrogenesis" is an unintended and often unavoidable complication arising from communication with a patient, actions affecting the patient, or inaction by medical personnel during preventive, diagnostic, and therapeutic interventions [3, 4, 7].

Progress in medical science and the introduction of new, highly active medicines and vaccines into medical practice have shortened recovery times, improved the completeness of recovery, and reduced disability and mortality. On the other hand, however, the risks of medical care have increased in parallel, along with the number of iatrogenic diseases and deaths caused by them. In the words of H. B. Vuori, "medicine has reached a point at which any visit to a physician brings not only benefit but also the risk of losing one's health and even one's life" [2].

In 1969, R. H. Moser described the adverse effects of more than 5,000 medicinal products, including medical procedures and other commonly used methods of treatment (chemotherapy) [22].

A physician's professional activity is impossible to imagine without medicines, which number in the tens of thousands (Mashkovsky, Vidal). Every attending physician writes prescriptions for medicines daily to treat specific diseases. Prescribing decisions are based on advances in modern medical diagnosis and treatment, as well as on knowledge of widely advertised medicines. When prescribing drug therapy, the physician expects a positive response. It has long been known that modern, highly effective medicines can cause hidden or obvious damage to various organs and tissues because every medicine has adverse and toxic effects. According to the World Health Organization, an adverse drug reaction is "any harmful and unintended response to a medicine that occurs when it is used for the treatment, diagnosis, or prevention of a disease" [14, 17, 19, 20].

The widespread use of thalidomide as a sedative in pregnant women led to the birth of children with various congenital deformities. This tragic episode in the history of medicine became known as the "thalidomide disaster." The adverse effect occurred because the medicine had not been adequately studied for use during pregnancy. When prescribing a medicine, physicians must always remember that, in addition to known adverse effects, a drug may also have effects that have not yet been identified. Therefore, prescribing a large number of medicines can lead to unexpected and unfamiliar effects, sometimes severe enough to present as a "secondary disease" or as complications arising after the use of a medicine—iatrogenesis. The Great Encyclopedic Dictionary defines iatrogenesis as "a term denoting the negative influence of a physician on a patient, when, instead of a therapeutic effect, the patient develops beliefs that aggravate the illness or a psychological complex of a new disease." Today the term is used more broadly. Under ICD-10, iatrogenesis refers to any undesirable or adverse consequences of preventive, diagnostic, or therapeutic interventions or procedures that result in impaired bodily function, limitations in usual activities, disability, or death; it includes complications of medical interventions arising from both erroneous and correct actions by a physician [9, 10, 18, 21]. In other words, iatrogenesis is understood as "defective medical practice" [10, 15]. The principal of medicine expressed in the Hippocratic Oath is "Primum non nocere"—"first, do no harm"—and

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"Nihil nocere" ("do no harm under any circumstances"). This has been accepted as the physician's foremost commandment.

Many articles address various aspects of "iatrogenesis," but clinicians pay particular attention to complications arising during pharmacotherapy [3, 4, 7, 11, 14]. Such complications may occur when physicians have insufficient knowledge not only of age-related characteristics and psycho-emotional factors, but also of the pharmacological actions of highly active medicines. The widespread use by physicians of medicines whose efficacy has not been proven often leads to complications of pharmacotherapy.

According to the literature, most iatrogenic disorders take the form of adverse drug reactions. One of the most common manifestations is an allergic reaction, which may present as urticaria, angioedema (Quincke's edema), anaphylactic shock, or Lyell's and Stevens–Johnson syndromes. E. A. Arkin proposed the term "drug diseases" for drug-induced skin eruptions [1, 4]. Since the main manifestation of an adverse drug effect is a disease, and the cause of that disease is a medicine prescribed by a physician, the term "drug disease" may be extended to all clinical forms of illness associated with the direct or indirect damaging effects of specific components of medicinal products and their impurities. Objections to this term are based on understandable but subjective and, moreover, professional or corporate considerations. Most drug diseases are iatrogenic in nature [4, 7, 10]. There is no mandatory system for recording drug diseases. According to G. Mazhdrakov and I. Popkhristov, adverse reactions occur in 7% of patients; according to A. S. Lopatin and I. M. Stankovskaya, in 10–12%; and according to B. M. Pukhlik, in 15–40% of people taking medicines [10, p. 60; 16, p. 96]. In the United States, 1–2 million cases of adverse drug effects are recorded annually, and this condition accounts for 2–5% of all hospital admissions [12]. Approximately 30% of hospitalized patients develop a drug-induced disease during treatment. The frequency of adverse reactions to antimicrobial therapy ranges from 1% to 50%. Allergic reactions after taking medicines occur in 0.5–60% of individuals. P. F. Kalitievsky and A. V. Smolyannikov believe that any medicinal product, regardless of its structure or molecular weight, can act as an antigen and trigger an immune response. Complex high-molecular-weight compounds do not always possess antigenic properties; after entering a patient's body, they may become complete antigens by forming complexes with proteins. In other cases, medicines or their metabolites act as haptens, conjugating with proteins, polynucleotides, and polysaccharides to form antigenic complexes, which leads to increased tissue sensitivity [5, 18].

In recent years, the osteotoxic and myelotoxic effects of certain antibiotics and psychotropic medicines have been established; their use may be accompanied by the development of agranulocytosis and aplastic anemia [16]. Medicines can cause toxic effects when their doses increase as a result of accumulation in the body or when irrational combinations are used. Drug accumulation in the body is promoted by disturbances in metabolic processes, the condition of the patient's elimination organs, and concomitant diseases. For example, adverse effects of aminoglycosides such as nephrotoxicity, ototoxicity, and neurotoxicity may occur when renal excretory function is impaired [8, 9, 10]. High doses of medicines can also have toxic effects on the body's organs and tissues. Therefore, it is necessary to strictly observe dosage and administration schedules and monitor the function of elimination organs and interactions between medicines used simultaneously. Some medicines, when combined, impair elimination processes and increase toxic effects on specific organs.

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One example is the simultaneous use of second-generation cephalosporin antibiotics and furosemide, or their use together with aminoglycosides, which can lead to nephrotoxicity [8, 12, 14, 15, 17].

Iatrogenic conditions in patients may be caused by careless history-taking or review of the medical record by the physician, insufficient attention to laboratory and instrumental test results, unjustified ordering or performance of such tests, and inaccurate entries in the medical record. Professor B. E. Votchal once said: “We live in an age when surgery is becoming less and less dangerous, while medical treatment is becoming increasingly dangerous.”

In recent years, articles on drug-induced diseases have increasingly appeared. These are diseases associated with the use of medicines that have hepatotoxic, nephrotoxic, hematotoxic, and other effects. Among them, reports relating to liver pathology predominate. Drug-induced hepatitis (DIH) is one of the common iatrogenic forms of liver injury and is associated with the adverse toxic effects of various medicines—something physicians should always bear in mind. This is apparently related to the fact that the liver is the principal organ involved in detoxifying medicines and toxic substances. Acute drug-induced hepatitis may occur following the prescription of valproates, amiodarone, statins, erythromycin, methotrexate, and other medicines, even after a single dose or a short course of treatment. Chronic drug-induced hepatitis is less common than the acute form. It may be associated with the use of paracetamol, nimesulide, clarithromycin, and other medicines [7, 11, 18, 20].

Another cause of drug-induced iatrogenesis today is unjustified polypharmacy. When a large number of medicines are prescribed, it is difficult to predict and prevent adverse effects. Therefore, when treating various pathological conditions, attending physicians should follow applicable standards and avoid polypharmacy in order to prevent iatrogenesis. They should ensure timely monitoring of the pharmacotherapy being administered, taking into account pharmacodynamics, pharmacokinetics, drug interactions, and adverse effects, and comparing these with laboratory and instrumental test results.

One of the main tasks of clinical pharmacology is to monitor the effectiveness of pharmacotherapy and ensure its safety for each patient. This can be achieved only through knowledge of the adverse effects, contraindications, and interactions of the medicines being prescribed.

To monitor adverse reactions to medicinal products authorized for medical use, Order No. 36 of the Ministry of Health of the Republic of Uzbekistan dated 30 January 2008 was issued. This order is important for ensuring safe pharmacotherapy for patients. On the basis of this order, no more than six medicines are currently prescribed during pharmacotherapy for each patient.

Thus, preventing drug-induced iatrogenesis requires a trusting relationship between physician and patient, a thorough examination, careful history-taking, and the ordering of necessary laboratory and functional tests to confirm the diagnosis and assess the condition of the body’s elimination organs. The medical record should preferably contain a detailed description of the medicines the patient received during the illness, and the entries should reflect the effectiveness of the treatment provided.

Many physicians are familiar with E. C. Lambert’s statement: “There are patients who cannot be helped, but there are no patients who cannot be harmed.” Physicians should always remember this when prescribing medicines.

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