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HOW MEDICINE HAS BECOME A SCIENCE?

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ABSTRACT

The historical review of medical activities draws attention how late in its very long history therapies of proven effectiveness were introduced. Author attributes it to the late development of methods which would be capable to determine the causal relations which would scientifically justified identification the causes and risk factors of diseases as well as checking the effectiveness of preventive and therapeutic procedures. Among the fundamental tools for scientific knowledge of the causes and mechanisms of diseases, the author indicates: achievements of basic science and the development of epidemiological methods used to study causal relationships. In the author's opinion the results of basic research are an essential source of variables among which, with an increased likelihood could be found the causes and risk factors of studied conditions, including diseases. The author also stresses the role of medical technology, which is the primary source of potential medicines, other therapeutic procedures and diagnostic methods whose effectiveness is tested in experimental epidemiological studies. Medical technologies create also tools for the development of basic sciences.

Keywords: *scientificity, medicine, epidemiology, basic science*

INTRODUCTION

The need to find the causes of the phenomena is as old as civilization. Information about causal explanations can be found in the oldest written sources. Initially, in cases of unexplained phenomena reference was made to supernatural powers.

The departure, though not complete, from supernatural explanations of the causes of diseases medicine owes to Hippocrates. His work "Airs, waters and places" occurrence of diseases refers to the geographical and meteorological circumstances. Naturalistic approach of Hippocrates indicated the possibility of searching for the causes of diseases in the material world (1).

As it turned out, just move away from supernatural explanations, which is a necessary condition, for over two thousand years was not sufficient to know the causes of disease, or to achieve effective therapy. This problem was due to two main obstacles responsible why it took so long. The first was initial lack, and later poor development of basic sciences, which provide potential exposure variables, among which finding causes of diseases has increased initial probability, and thus increases the possibility to demonstrate causal relationships in a properly designed and conducted epidemiological studies. The second obstacle was the lack of a suitable methodology for epidemiological studies with particular emphasis on the representativeness of the samples and statistical tools which create the base for testing the hypotheses.

However, when it comes to assessment of the effectiveness of diagnostic and therapeutic procedures, even the most representative samples and most effective statistical tests couldn't contribute to improving the effectiveness of medical practice, without development of medical technology which provided therapeutic and diagnostic methods. This development occurred mostly in the twenties century.

CRITERION OF SCIENTIFICITY AND SEARCH FOR CAUSAL CONNECTIONS

It would seem that a natural starting point for considering the scientific nature of medicine should be a definition of science, and then determine how medicine fits this definition. However, this approach encounters major difficulties because the cultural variety of ways of understanding the word "science" makes obtaining universal agreement on the concept of science completely unrealistic. Science as a component of culture has such a wide range of meanings that cannot be denied that name to the educational activities of the medieval universities. The argument that from what then was taught in contemporary medicine remained almost nothing, cannot be a conclusive argument in the light of current pragmatics, since rejection and correction of previously recognized results is a constant component of the science. Therefore it is better to omit the cultural and institutional side of science and use scientific method as a criterion to adopt certain features of the activities that allow this activity to be considered scientific (2).

What are those features? First, the scientific activity in any field must concern the subject of this field. In the case of medicine, the subject is the human body and things, situations, characteristics and all other characteristics related to the construction and functioning of the human organism in the environment, both in health and in disease.

Furthermore, the knowledge belonging to the scientific discipline must be methodologically ordered. This means that within a given field cannot permanently persists statements contradicting each other, and each new observation that has been introduced to it, must be justified in a way of intersubjective communication and intersubjective verification both regarding the results obtained and the methods used to achieve them. While communication concerns clarity of language and the use of appropriate terminology, adapted to the field, the verification lies in the zone of observation or experimentation, which starting from the same premises enriched with new facts, should give an acceptable approximation of the same results. For the result to be possible to check there must be criteria which, if they meet, will lead to rejection of the hypothesis. For medicine, until the last century, the main problem was a serious deficiency of testing procedures, and inferences based on these tests. In this regard, a significant breakthrough did not occurred until the twentieth century.

It is obvious that in the empirical sciences, including medicine, claims of the absolute certainty is unattainable. Therefore, to a large extent checking the results and their broader generalizations involves falsification, i.e. rejection of the results such as causal interpretations which includes effectiveness of treatments and diagnostic procedures that cannot endure the testing procedures. The desired condition for testing hypotheses is the description of the conditions of accepting or rejecting hypothesis before checking it.

As long as studies are descriptive, without identifying the relationship between variables, issue of causality does not appear. Descriptive knowledge is mostly cumulative and rejection of its results is relatively rare. In contrast, where dependencies between variables are concerned, that is where we can put forward a hypothesis about causal relationships controversies may occur, and rejections of previously accepted results are more frequent. The causal interpretation takes place, for example, in the study of etiology, as the cause of the disease or other condition. The pathogenesis can be treated as a causal chain leading from the initial cause to the final effect in the form of the symptoms of the disease and its ways of outcome: recovery, a chronic condition, disability, or death. We have to deal with causal interpretation, when in intervention studies is tested the effectiveness of drugs or other therapeutic approaches and in the evaluation of diagnostic tests.

In some, usually singular, violent incidents causal connections are given directly to the observer. An example of it may be fracture of femur in the motorcycle accident. However, where we are looking for regular causal connections, simple observation does not provide information about these relationships in such an obvious way. Drawing conclusions based on our own observations and a few overheard events may easily lead to false conclusions.

Believe in a world structured in an uninterrupted causal chains converging to more and more general causes, and in extreme cases to a single Supreme Cause, dominated for centuries, and even today many people take it as the most convincing model. Even in modern times, some of the eminent epidemiologists required for accepting causation the specificity of the cause and effect.

Regardless of how intuitively convincing is strictly deterministic view of the world, it does not suit to the methodology of epidemiological studies. The results of statistical methods based on the conditional probability of an effect due to a given exposure first in the sample and then for the population. Complete assurance is never obtained. Therefore, the factors of exposure that alter the probability of the effect, we can call as protective or risk factors. If we give them a causal interpretation, it is important to realize that it almost always contains an element of subjective judgment.

Extremely deterministic model of causality goes beyond the empirical data, because it never be possible to consider all the circumstances of a particular phenomenon. Researcher choosing a research topic of phenomena preceding the effect, or accompanying it, refers to a limited number of variables which, in his opinion, have a higher prior probability of the relation to the effect (3.4).

Epidemiological tools by providing verifiability, the possibility of falsification and rejection of test results pave the way to ensure their scientific nature. Using in practice those verifiable and tested methods we assess the efficacy and safety of therapeutic and diagnostic procedures.

The purpose of this article is to show the role played by epidemiology in the transition from the practice of medicine based on intuition to activities based on the scientific foundation and the key role which was played in this process by basic sciences and medical technologies.

DIFFICULT ROAD OF MEDICINE TO BECOME A SCIENCE

Textbooks of history of medicine teach us to respect the intellectual power of ancient physicians, their ingenuity and courage, but rarely refer to the effectiveness of their actions. Meanwhile, until the twentieth century medicine was practiced intuitively and only a small oases of effectiveness appeared in the desert of helplessness and ineffective therapy. For centuries first the absence, and later the weakness of basic science made the causes of disease to be searched blindly and also blindly were pursued their remedies. Gaps of knowledge were filled with conjectures, that even if were formulated in natural terms, were not checked in the adequate studies. In the terms of rationality they frequently did not differ much, from supernatural explanations. The practical action based on those guesses, as opposed to the prayer, could be and were often harmful.

In such a situation, many important medical achievements relied on abandoning harmful practices previously implemented in the belief that they improved patient health. Example of such an important omission was the cessation of the pouring hot oil on wounds. *Ambroise Parre* when after the battle the hot oil stocks were exhausted noticed that wounded not treated with hot oil healed better than those that have been poured over with it.

Derived from the Hippocrates theory of "humors" idea, that diseases are caused by toxins contained in body fluids, in the nineteenth century found its expression in the "heroic medicine" which as the principle had the elimination of toxins with the body fluids through the bloodletting, laxatives, expectorants and emetics. The primary effect of these actions was induction of anemia, dehydration and imbalance of electrolytes, which often considerably worsen the patient's condition. This was accompanied by an impressive inventiveness of the methods of treatment. In the 1889 edition of the *Merck Manual of Medical Information* is mentioned about a hundred methods for the treatment of bronchitis, none of which, by today's standards, could be considered effective (5).

After centuries of use of bloodletting, which as we now know can be useful in a very limited number of diseases, in the nineteenth century *François Broussais* developed extensive theory which led to view that bloodletting is effective in the treatment of febrile diseases, including pneumonia.

This theory did not stay for a long time. Pierre Louis in 1835, has done pioneering methodological research which showed the ineffectiveness of the use of bloodletting in pneumonia (6). In his study he implemented the following principles:

- The introduction of a control group
- Selection of the compared groups with restrictions on age, diet, disease severity, and other procedures performed in patients. Today, this method still used in epidemiology as restrictive fit complementary to the much later introduced other methods, like matching or randomization.
- Addressing the differences to the population, not just to individual cases and for this purpose comparison of averages of the incidences.

Louis study is of particular importance because of methodological innovation and precision of calculations.

Disappointment at the lack of effectiveness of medicine based on observations of individual cases led in the mid-nineteenth century to the harsh criticism of the then state of medicine. In the U.S., a prominent skeptic about the effectiveness of contemporary medicine was *Jacob Bigelow*, who in 1836 wrote: *"The amount of death and disaster in the world would be less if all disease were left to itself"* (7). At the University of Vienna, *Karl Rokitansky*, who performed about 30,000 autopsies and had a special understanding of dubious efficacy of treatment methods, particularly surgical operations, together with his disciples and colleagues *Joseph Skoda* and *Jozef Dietl* expressed deep skepticism about the effectiveness of XIX century medicine.. Critics have called this attitude *"therapeutic nihilism"* but from the perspective of today's medical knowledge such an attitude had a large dose of rationality (8). Treatment methods contrived on the base of insufficient knowledge of basic science and not proven in epidemiological studies should be abandoned and leave free space for evidence-based medicine . But this process was not simple. It proceeded slowly and met with great resistance that we can observe even today.

But one cannot underestimate the achievements of the few scientists, who on the basis of the individual and not fully structured methodological observations were able to introduce effective measures to medicine. It should , however, be realized how fragile were their premises .

Author of the discovery that led to one of the greatest successes in the history of medicine, *Edward Jenner* (1749-1823) in 1796 vaccinate one boy with cowpox. He took flegm from blisters on udder of the cow suffering from cowpox, and rubbed it into the scratches made on the boy's shoulder . After a period of two weeks *Jenner* infected him with material taken from the pustules of a person with smallpox. The boy did not got sick. Jenner described his experiment in an article sent to the Royal Society in 1797 but the paper was rejected on the basis that the experiment performed on one subject is not sufficient. Undaunted, *Jenner* experimented on five other children, including his own 11 -month-old son. In 1798 , he published his results in as a self-released brochure: *"An Inquiry Into the Causes and Effects of the Variolæ Vaccinæ , or Cow- Pox"*.

Louis Pasteur, admittedly, did not perform experiments with the vaccine against rabies in humans and tested it on dogs, but after the first "effective" vaccination of 9-year-old Joseph Meister he began to use it as if tested completely.

With all due respect for the importance of *Jenner* and *Pasteur's* discoveries, it should be realized that the use of such methods for testing the effectiveness of medical procedures on a larger scale could lead to catastrophic consequences.

It was necessary to continue the path traced by *Louis* by introducing statistical methods to estimate the effectiveness of the proposed treatment and the health risks associated with their side effects. Wider awareness of this necessity could come only with the success of specific studies that were conducted by the researchers with methodological intuitions often much ahead of the era.

When the fleets of naval powers began to flow the oceans, scurvy became the most dangerous disease of seafarers. More sailors died from scurvy than from wounds inflicted in sea battles. *James Lindt* physician British fleet took up the challenge of finding an effective way to prevent scurvy and treatment of the disease (8). He chose 12 sailors suffering from scurvy and divided them into pairs. Everyone got standard diet of British seamen. Among them five pairs of patients received various remedies used to so far in the navy, and the two sailors got to eat two oranges and one lemon per day. *Lind* has observed a complete cure of the health of seafarers who were treated with citrus fruits and a small improvement in seafarers who drank cider. In the other there was no improvement. Despite the very small sample sizes, this study was a prototype intervention cohort study (8).

At the end of the nineteenth century, a different experiment conducted *Takaki* in the Japanese fleet. Japanese authorities gave him permission for a change of a standard diet based on husked rice to new one containing a whole grain barley. After this change, the beriberi disease no longer appeared in the Japanese fleet. Here was a population control group of seamen before changing the diet, and a group of sailors after its change as a test population. Thus, it was a form of *"crossover study"* although in this study the two populations were not completely overlapped.

In a further development of the methodology of epidemiological research a special role was played by *Golberger*, who used field cohort to study causes of pellagra in subjects on a diet consisting almost exclusively of maize (9).

Ignac Philip Semmelweis (1818-1865) was the first researcher who used the cohort study to trace the source of infection. He compared the incidence of puerperal fever in the maternity ward , where in births assisted midwives and the second ward where in births assisted students who come there immediately from the dissecting room. After finding that the majority of cases of puerperal fever occurs in women whose labors assisted the students, ordered them to wash their hands in a chloride disinfectant *"as long as the cadaverous smell disappears"* before entering the delivery room. The effect of this ordinance was to reduce the incidence of puerperal fever in the ward serviced by the students to the level of the branch supported by midwives . *Semmelweis* introduced to the epidemiology of infectious diseases observational cohort study, which he expanded to the intervention study. His intervention preceded the introduction of antiseptics by *Lister* for 29 years. (9).

As late as in the middle of the nineteenth century, during the cholera epidemic in London, a dispute was continued, whether cholera is caused by some infectious agent entering into the human body with food, or by *"miasma",* pestilence emanating from the *"bowels of the earth".* In the dispute participated two prominent British physicians: *John Snow* and *William Farr*. *Farr* in favor of the miasmatic theory expounded his observation that more cases of cholera occurred in the low-lying area in London's poor neighborhoods at the River Thames, which was closer to the *"bowels of the earth*", than in affluent suburban districts located above.

Snow reasoning started from the observation that cholera spreads along trade routes, which led him to the conclusion that the source of illness are sick people, but not the local air. The unsolved problem was the route of cholera transmission. To solve this problem he marked points on the map of London where occurred deaths from cholera. One large outbreak occurred in the Soho area at the vicinity of Broad st. *Snow* observed accumulation of deaths around the public well on the street and hypothesized that the cause of illness is the use of the water of this well . He ordered the removal of the pump handle and then the number of deaths in the region began to decline. Then performed a similar study in the districts supplied by different waterworks. In these studies showed that the use of waterworks, which fetch water from the Thames below sewage outlet *(Southwark Water Co.)*, led to greater incidence of cholera than the use of waterworks which fetch water above the sewage outlet. *(Lambeth Water Co.), (RR=8,5)*. His research has been particularly pioneering in that it applied the similar designs of the studies as are used today :

- Population studies
- Case-control studies
- Cohort studies

Snow showed convincingly relationship between occurrence of cholera and drinking water contaminated with feces. It was a big step on the road to detect the sources of infection by epidemiological studies, but to find an infectious agent of cholera one had to wait for the development of microbiology.

The next step in the direction of the recognizing of causes of infectious diseases was made in the second half of the nineteenth century by several eminent microbiologists, among whom special role played *Robert Koch*. Invention of solid media for bacterial cultures created the possibility to isolate bacterial strains and thus to identify the etiologic agents of infectious diseases. The crowning achievement of *Koch* research was formulation of the conditions to be met by an infectious agent to be identified it as the cause of the disease. Similar requirements formulated earlier *Jakob Henle*, and the *Friedrich Loeffler* worked with *Koch* on their final version known as Koch's postulates. On the Tenth International Congress of Medicine in Berlin in 1890, Koch announced his conditions in the following formulation (5, 10):

1. The parasite occurs in every case of the disease in question, and under circumstances which can account for the pathological changes and clinical course of the disease.
2. The parasite occurs in no other disease as a fortuitous and nonpathogenic parasite.
3. After being fully isolated from the body and repeatedly grown in pure culture, it can induce the disease anew.

This formulation was not sustained for a long time, since *Koch* himself observed asymptomatic carriers of *Vibrio cholerae*, which was contrary to the second postulate of which indicated the specificity of the effect. Currently, in most sources Koch postulates are formulated as follows:

1. The bacteria must be present in every case of the disease.
2. The bacteria must be isolated from the host with the disease and grown in pure culture.
3. The specific disease must be reproduced when a pure culture of the bacteria is inoculated into a healthy susceptible host.
4. The bacteria must be recoverable from the experimentally infected host

Koch constantly upheld the first postulate, which clearly underlines the specificity of the cause as the sole infectious agent able to cause the disease. For tuberculosis, the source disease in the formulation of *Koch's* postulates, it meant that it can be invoked only by *Mycobacterium tuberculosis*. *Koch* was present at the convened in 1908 in Washington, DC International Congress on Tuberculosis, where an American microbiologist *Post* presented a paper in which he linked the incidence of tuberculosis in children with drinking milk from cows infected with *Mycobacterium bovis*. *Koch* vigorously protested against this hypothesis, which hit the first of his postulates. Fortunately, American doctors, contrary to the Koch opinion, forced on sanitary authorities pasteurization of milk, and thus prevented the further spread of tuberculosis among children (5).

Koch's postulates are examples of strongly deterministic approach to causal explanations. They have played big role in determining the precise causes of some diseases of bacterial origin, but their application fails in the case of viral diseases, or of diseases caused by bacterial toxins.

The narrow understanding of disease causation by nineteenth-century illustrious medical scientists revealed itself in the dispute of *Koch* and *Virhoff* about the causes of tuberculosis. For *Koch* the one true cause of the illness was *Mycobacterium tuberculosis* infection. *Virhoff,* skeptical to the achievements of microbiology, claimed that the reason are harsh living conditions such as of coal miners in Silesia. Today we know that infection with *Mycobacterium tuberculosis* or *bovis* is a prerequisite for this disease, but among those who came into contact with the bacterium suffers only a certain percentage of infected and that is the greater the heavier are their living conditions. Thus, infection with Mycobacterium is the necessary cause of tuberculosis, but it is not sufficient since not all infected are ill and the living conditions are an important risk factor for the occurrence of this disease (11).

DEFINITIONS OF DISEASES ARE THE BASIS OF THEIR IDENTIFICATION IN CAUSAL RESEARCH

Koch's postulates are used almost exclusively as a tool for verifying the causes of infectious disease, but they also have a very important role in precise definitions. The definition of the disease in the case of infectious ones, in addition to clinical symptoms and pathological data, must refer to the etiological agent. And this reference gives the definition the highest accuracy - confirmed diagnosis.

In the case of non-communicable diseases almost always we have to deal with the entanglement of many factors and referring in the definitions to the etiology would be unreliable. For different disease groups diagnoses are based on different data sets from the history, physical examination and additional tests: biochemical, pathological, endoscopic, radiological, immunological and others depending on the type of disease. Without properly expanded list of definitions of diseases, emergence of epidemiology as a science would not be possible. To count the occurrence of diseases in the population, or assigning individuals to specified diseases, we must first define these diseases. Every epidemiological study begins with a description of the population or sample in terms of basic categories: who suffer from the disease, when and where.

The first records of deaths *(Bills of Mortality)* were introduced in England in 1532 and related primarily to distinction between deaths caused by epidemics and those which occur without any connection with them. Determining of the cause of death was initially not based on strict criteria and was dependent on the subjective judgment of the person authorized for that purpose. Defining disease entities appeared for the first time in the works of Thomas Sydenham (1624-1689), but Jacques Bertillon (1851-1922) is considered as the creator of the modern classification of diseases. In the years 1891-1893 he chaired the committee that introduced the classification of causes of death, later adopted as the basis of the International Classification of Diseases (ICD) (12). Precise definition of the disease was an important condition for scientific status of medicine. How discipline could have status of science if it subject would not be defined? How could be possible to investigate the causes of diseases if many of them would not be distinguishable?

In the 80's of twentieth century effective epidemiological methods were introduced to strictly define the cut-off points for diseases such as diabetes and hypertension, in which numerical values can be assigned to the severity of the disease. In diabetes, it was retrospective estimate of early increases in fasting plasma glucose levels in people who had indisputable diabetes qualities such as retinopathy or diabetic nephropathy.

CONTEMPORARY EPIDEMIOLOGY AS THE BASIS OF KNOWLEDGE AND MEDICAL PRACTICE

In Europe and in North America in the second half of the nineteenth century, and especially in the twentieth century, infectious diseases no longer were the most common causes of death. High and growing mortality was caused by cardiovascular diseases. Rising trend in cancer mortality was also observed. Sustained upward trend in the incidence and mortality of lung cancer, especially in men, emerged after World War II.

The development of microbiology gave a strong tools to determine the causes of infectious diseases. At the same time antisepsis, sterility and improved hygiene have created a reasonable ground to prevent these diseases. On the other hand the prevention of cardiovascular diseases and cancer, because insufficient knowledge about their causes had no scientific basis. Newly forming epidemiology of non-communicable diseases have to get the appropriate statistical tools and adapt them to the research focused on the search for the causes of the rising incidence of these diseases .

In relation to research on the causes of heart disease special role was played by field cohort which started in 1948 and is still operating in the town of Framingham in the Boston area. Among more than 2,000 publications based on the results of this cohort are numerous discoveries underpinning of modern knowledge about risk factors for heart disease. Even the term *"risk factor"* was introduced into epidemiology by researchers working in this cohort. Framingham study was initially focused on the plasma levels of selected substances and the results of physical examination. Gradually range of investigated problems widen to the life style, psycho-social and cultural factors such as mental stress or participating in social groups. In the last two decades, after forming additional cohorts of children and grandchildren of the participants in original cohort, research was dominated by the genetic determinants of cardiovascular disease (13).

The observed complexity of the causes of the diseases, dependence of their incidence on many factors evoked concerns of the separation of their individual roles. In this respect, the fundamental role played the Mantel - Henszel test and logistic regression.

For diseases with high mortality case fatality indicator was not sufficient as it provides a very superficial insight into the nature of the disease, as well as to the results of treatment. The methods of survival analysis and their further developments provided here the tools of higher precision.

Overview of the dates the availability of the tests fundamental to epidemiological analysis shows how recently basic tools of analytical epidemiology were provided for researchers:

- **Year 1900**. **Chi - square tes**t . Pearson , Karl (1900). "On the criterion That a given system of Deviations from the probable in the case of a correlated system of variables is such that it can be reasonably supposed to have arisen from random sampling" . Philosophical Magazine Series 5 50 (302): 157-175
- **Year 1908**. **"T -test"**, so called. Student's test, developed by William Sealy Gosset .
- **Year 1937**. **The confidence interval** for testing hypotheses, introduced by Jerzy Neyman .
- **Year 1923**. **Randomization** in sampling surveys has been used independently by J Neyman and RA Fisher.

Survival analysis:

- **Year 1958. Kaplan-Meier curves** (time to event) : Kaplan , EL , Meier, P. (1958). "Nonparametric estimation from incomplete Observations " . J. Amer. Statist . Assn. 53 (282) : 457-481
- **Year 1966 . Log- rank test** : Mantel N. "Evaluation of survival data and two new rank order statistics arising in its consideration". Cancer Chemother Rep . 1966 Mar 50 (3) :163 -70 .
- **Year 1972 . Cox proportional hazard model**, David R Cox (1972). "Regression Models and Life- Tables ." Journal of the Royal Statistical Society, Series B 34 (2): 187-220

Multivariate analysis:

- **Year 1959. Mantel- Henszel test :** Mantel Haenszel N & W. Statistical aspects of the analysis of data from retrospective studies of disease . J. Nat . Cancer Inst . 22:719-48, 1959.
- **Year 1961. Logistic regression:** Cornfield J , Gordon T, Smith HV. Quantal response curves for experimentally uncontrolled variables. Bull Int Stat Inst . 1961 ; 38:97-115 .

These tasts, an many other developed later, provide robust tools for the studies of the relationships between variables including those interpreted as causal ones in the observational studies. They also provide the basis for assessing the effectiveness of therapies in clinical interventions. The history of clinical trials is amazingly short. The first randomized clinical trials used to assess the efficacy of therapy were designed by Bradford Hill in 1946 , which concerned first the effectiveness of vaccines against pertussis, and the next one use of streptomycin in the treatment of tuberculosis. In this study, first time in history studied patients were assigned randomly to the control group and the intervention one. In addition, Hill based evaluation of lung X-ray examinations on opinion of radiologists not informed about the therapy of the patient (blinding). He also defined the fundamental ethical principles of experimental research on humans before the final formulation of the "Nuremberg Code ". He set the condition that the studies should be always focused on the welfare of the patient and introduced the requirement to obtain the consent of the candidate to study. (14).

In the thirties of the twentieth century was introduced an important new approach to statistical analysis. *A Wald*, based on previous studies of *Bayes*, pointed to the dependence of the power of test from the pre-test probability of the effect. *Wald* results were criticized by *RA Fisher*, who claimed that recourse to the uncertain initial assessments of the likelihood, decreases the precision of the study. *Fisher* authority only slowed, but not stopped Bayesian approach to epidemiological studies.

In applying the results of scientific research, in medical practice, very special role plays professional movement called *evidence-based medicine.* It sets principles which serve for adjustment of the results of epidemiological studies to particular groups of patients and to the individuals (15,16).

Traditional belief among scientists that practical conclusions could be inferred from the results of basic sciences, is not in accord with actual pragmatics of modern medicine. Basic science does not give today and can hardly be expected to have given in the foreseeable future so full and consistent picture of the human body and its environment in health and disease , that such a direct inference can be effective. In real practice, basic science and clinical experience is a principal source of variables to set hypotheses with the increased initial likelihood. The factual impact of these variables on the diseases progress or on the effectiveness of therapeutic and prophylactic methods require testing in suitably designed and properly executed epidemiological studies. On one hand epidemiology operating appropriate statistical methods is an essential tool for acquiring basic knowledge, but also is an important link between basic and clinical knowledge and the effective practical action.

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