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Scientific Method in Medicine: Bringing Unity to Research and Clinical Decision-Making.

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For many years, my family encouraged me to go to a medical school and become a physician. I considered pursuing medicine very seriously, until I realized during my senior year in high school that what fascinated me about the field was not the clinical work, but rather the scientific practice of medicine. I also quickly discovered that this interest is only a manifestation of my fascination with science; since then, I started to think about science as superior to all other academic disciplines, and I admired its commitment to explicate and take the universal laws apart, describe them down to the tiniest detail. In my mind, I pushed the clinical aspect of medicine into the margin of the scientific enterprise. Later however, I recognized that the medical and biomedical research that I so highly praised must have a purpose, and that great discoveries and technologies of medicine have direct application in clinical settings. The clinical practice is the scientific medicine's *raison d'être*. From this new approach, a unity between the two aspects emerges, and it is centered on the human body: the focus of both the innovative medical research, and its direct, clinical application. Many philosophical or ethical concepts can be credited with bringing about this unity between healthcare and medical research. The link between the two areas of medicine explored in this paper is the scientific method.

Arguably, medicine is different from all other sciences in its human aspect. Physicians may consider themselves scientists, especially if their main interest is performing research, but medicine cannot be divorced from healthcare, which includes caring for patients and improving the quality of their lives. This aspect, perhaps, makes medicine more pertinent to human life, but it also substantially complicates the scientific practice of medicine. A physician who diagnoses an individual case studies an individual, not a population; he does not repeat one trial to assess precision. Nor is he concerned about statistics the way biologists or chemists are. Yet at the same time, his diagnosis must be conclusive enough to allow correct treatment to be administered to a patient.

Medicine's human aspect clearly sets it apart from other natural sciences, and from this fundamental difference follow other characteristics unique to medicine. For example, the medical practice can be described on two different but complementary levels: diagnosis of individual patients, and medical research conducted on groups of patients. Both levels face ethical and practical difficulties from the scientific and humanist points of view. Clinical decision-making in individual cases must cope with generating correct diagnoses of symptoms unique to individuals, and it has no privilege of large sample size, multiple repetitions of trials, and statistical assessment. Medical research faces ethical problems, as the subject of its purely scientific analysis is human health. Scientific method, especially the close relationship between hypothesis and evidence, used on both levels of medical practice alleviates some of those dilemmas. In clinical decision-making, strict adherence to scientific method improves the quality of diagnoses; the more consciously a physician uses scientific method in his daily practice, the more correct his diagnoses are. In medical research, the principles of scientific method allow objectivity and progress, also reconciling ethical problems.

In his book Scientific Method in Practice, Hugh G. Gauch gives a definition of the scientific method as a set of principles that are common to every science, and include "such topics as hypothesis generation and testing, deductive and inductive logic, parsimony, and science's presuppositions, domain and limits"[6]. He also quotes the statement issued by American Association for the Advancement of Science: "the various scientific disciplines are alike in their reliance on evidence, the use of hypotheses and theories, the kinds of logic used and much more"[6]. In fact, hypotheses and evidence seem to be the key elements of the scientific method, present in all definitions of this difficult concept. Morris R. Cohen, in his Introduction to Logic and Scientific Method defines the scientific method as a method of reasoning in which "we test impressions, opinions, or surmises by examining the best available evidence for and against them"[2]. He argues that the scientific method is capable of producing more accurate results than logical methods based on habit, authority or intuition, simply because of its objectivity, and that it attains progress by encouraging possible doubt, which always promotes further verification and testing[2]. Scientific inquiry solves problems by forming possible explanations, or hypotheses, based on previous knowledge, which then guide the scientist's "search for order among facts" by directing his process of fact selection and interpretation of observations[2]. Hypotheses are always assessed according to evidence, and absolute certainty of one hypothesis attained by exclusion of all alternative hypotheses is possible only in theory. However, the more conclusive the evidence is, the more probable the most reasonable hypothesis is.

Arriving at a correct diagnosis, much like arriving at any other scientific conclusion, includes generating and testing of a hypothesis. To make a diagnosis, a physician must take advantage of his previous knowledge of medicine to identify likely ailments that cause the patient's symptoms. This task may be rather simple in some conditions, but it may also be difficult in others, where a variety of causes are likely to produce given symptoms. Narrowing down the possibilities corresponds to arriving at a hypothesis. Edward J. Noga, in his manual on diagnosing fish diseases, describes this process in a similar manner: first, he instructs veterinarians to perform water quality analysis, take the history from the fish owner, and to examine the fish for specific symptoms[8]. Those initial observations may lead to one or several hypotheses: for example, abnormal coloring in a fish may be an indicator of peripheral nerve damage as the nervous system transmits signals that control pigmentation[8]. It can also be an indicator of hemorrhage from an infection[8]. Abdominal swelling in a fish is a common indicator of an infectious peritonitis or a metabolic problem, such as renal failure[8]. Thus, the observation of the symptoms allows a veterinarian to perform a differential diagnosis of the most likely diseases that could cause the symptoms—this initial set of predictions is the hypothesis in the clinical decision making process.

Hypothesis has no bearing on the decision if it remains a hypothesis and is not evaluated. Only when one of the hypotheses is supported by available evidence better than others can it become a basis for a treatment. This is why in Edward J. Noga's manual the conclusive tests, such as skin and gill biopsies, blood tests, or post-mortem examination in extreme cases, follow the hypothesis generation[8]. When the evidence favors one of the hypothesized conditions more than others, the veterinarian usually accepts this condition and starts to treat it. It is worth noticing that the accepted hypothesis is, in the case of human medicine, a matter of treating a patient for a correct illness; improper treatment may result in complications and even death. This is where the use of scientific method in medicine becomes more difficult than its use in other scientific disciplines. A research scientist in biology, for example, may repeat his measurements multiple times; a physician usually does not have enough time or subjects. Medical personnel must be more certain of their conclusions; thus, they must have access to the best technology capable of generating the most conclusive evidence. The quality of available evidence influences the definiteness of the most reasonable hypothesis, which in medicine is the basis of the patient treatment.

Thus, medical technologies are designed to provide the best evidence for hypothesis evaluation. The variety of diagnostic tools available to physicians illustrates that modern medicine's success is a result of advancement in diagnostic tests. Medical imaging techniques are especially valuable, as they provide insight into the internal organs, otherwise accessible only by surgery. When a physician has a "window" into the patient's vital organs, he can make direct, empirical observations that still need skillful interpretation, but are less fallible than indirect results obtained from exterior physical examination.

Providing a means for a physician to look into the patient's body was the chief objective of medical technology research soon after the discovery of gamma radiation by Roentgen in 1895 and radioactivity by the Curies in 1898[11]. Current technologies may involve introducing a radiopharmaceutical into a patient's body where it is incorporated into metabolic processes emitting gamma radiation. The radiation is sensed and converted to a digital image giving rise to SPECT scan (Single Photon Emission Computed Tomography) or PET scan (Positron Emission Tomography), both of which project three-dimensional images of internal structures[11]. CT (Computed Tomography) achieves similar results using x-ray transmission, and MRI (Magnetic Resonance Imaging) projects images from measuring the response of atomic nuclei to electromagnetic pulses and an external magnetic field[11]. Thus, digital images from those instruments are non-invasive, but produce highly reliable digital images. Technology allows a physician to make empirical observations of the patient's vital structures and processes. Such direct, empirical evidence is among the most reliable when it comes to choosing the most reasonable hypothesis.

The process of diagnosing a condition, therefore, uses the scientific method in its generating of hypotheses and their assessment through facts and observations. The advancement in medical technologies illustrates that obtaining conclusive evidence is key to a correct diagnosis, which then becomes a purely scientific process of selection of the most reasonable hypothesis. However, it is also a very intuitive logical framework of solving problems. It has been argued that despite the presence of scientific method within the framework of clinical decision-making, many physicians diagnose unreflectively, following already-established, unquestioned expert guidelines. Those opinions, often voiced by advocates of evidence-based medicine, imply that when the scientific method is practiced consciously and explicitly, it is far more useful and productive in diagnosis.

The branch of medicine that formalizes the use of scientific method in clinical decision-making is the evidence-based medicine. The term evidence-based medicine was coined in early 1990's, and since then, it has described the use of the most current and best evidence from clinical trials to form diagnoses in individual patient cases[1, 4, 7, 9]. Many authors identify a set of rules for application of evidence-based medicine. A physician must first generate a set of questions that pertain to the individual patient, include a hypothetical treatment or test, and address an outcome[1, 9]. For example, according to Michael Bigby, a well-stated question in a case of a generally healthy, middle-aged man with dystrophic toenails could be, “In a patient with dystrophic toenails, should a potassium hydroxide (KOH) test or culture be done to establish a diagnosis of onychomycosis?”[1]. In this question, the hypothetical test is the KOH culture, and the likely outcome is identified as a diagnosis of onychomycosis. The questions are then answered by performing a literature search to locating reliable evidence, which is then assessed critically for quality and consistency[1, 9]. Once the best evidence has been identified, it can be applied to the case together with a physician’s clinical expertise and the patient’s personal preferences[1, 9]. This process is essentially one more variation of the hypothesis and evidence relationship in the scientific method; by asking a series of questions that can be answered with evidence, a physician generates hypotheses, then he searches for evidence not only by empirical observation in the form of diagnostic tests, but also by analysis of results of experiments performed by others. The data must be obtained instantaneously at the point of care, but it is not free of judgment. A physician must have some prior knowledge of what constitutes reliable evidence and how to use it. Thus, he performs a selection of facts in light of the initial hypothesis. The conclusion is, of course, appropriate treatment for a given case.

This approach to medicine is often contrasted with the traditional model of medicine that required physicians to strictly adhere to preexisting guidelines based on expert opinion[7]. Advocates of evidence-based medicine see the expert-approach as inferior. They argue that many ineffective treatments are practiced for too long before they are discredited, as the expert-approach rarely questions established treatments[5, 7]. Dan Meyer quotes such examples as treating pain with Vioxx, or using hormonereplacement therapy for menopause[7]. David M. Eddy also argues that before the evidence-based medicine became widely used by physicians, "medical decision-making" was not seen as a problem: it was expected that all physicians arrive at correct diagnoses using their education and clinical expertise alone[4]. However, studies performed by John Wennberg and colleagues in 1973, documented vast differences in recommendations made by different physicians in similar clinical cases. This was followed by another set of studies that documented a large proportion of physician recommendations being incorrect, when assessed by the experts[4]. Thus, evidence-based medicine is often seen as superior to the traditional, expert-based approach because it can prevent misdiagnoses that often arise from relying on a guideline or a framework. In addition, it provides a common criterion for medical decision-making that is far more objective than personal experience and personal knowledge of an individual physician. This common criterion is directly derived from the scientific method, which as a process, is also credited with objectivity that surpasses methods of reasoning based on intuition or habit.

The practice of evidence-based medicine also successfully bridges the gap between the two levels of medical practice: the clinical decision-making, and the scientific research. It requires the physician to have skills in critical reading and assessment of scientific papers, which often includes knowledge of scientific practices and statistical methods of data analysis[7, 9]. But it also requires availability of good and reliable evidence, which comes from the practice of medicine as a science, complete with scientific philosophy and scientific research.

Medicine traces its scientific beginnings to ancient Greek physician, Hippocrates, who is often called the Father of Modern Medicine: this of course implies that his practice constituted an early version of today's medical practice. What sets the Hippocratic approach apart from the earlier practices is that his diagnoses were based solely on reasoning and empirical knowledge. His works known as Hippocratic Corpus consisted of 72 books with 59 treatises on anatomy, physiology, treatment, surgery, and even mental illness[3]. Compared to his predecessors who saw justification of human health or disease only in religious beliefs, compiling a body of anatomical knowledge based on observations and then using it in the practice of healing made Hippocrates's medicine rational. Thus, the art of healing can be classified as medicine only when it uses logic and reason as the basis of its studies, or when it is scientific in approach.

Today's medicine comprises not only "applied" medical knowledge, or healthcare, but also the realm of medical research. Medical research is the second level of medical practice, which is different from clinical decision-making in many ways. The two, however, are closely entwined, as seen in the practice of evidence-based medicine that calls for evidence from clinical trials. In fact, randomized controlled trials (RCTs) are considered to be the best evidence available in medicine[10]. An RCT is an experiment that consists of two arms: a control arm, and an experimental arm, both of which include patients suffering from the same condition. The control arm is given an already accepted treatment, while the experimental arm is given a novel drug or treatment[10]. The selection of patients assigned to control, or experimental arm must be random to rule out any possibility of bias[10]. The adherence of the medical community to the RCT has raised ethical concerns in the past. John Worral presents a case study of the use of an innovative method to treat pulmonary hypertension in infants. In 1980, pulmonary hypertension had a mortality rate of 80% when treated conventionally; however, a group of scientists from the University of Michigan began to use a new treatment; ECMO, or Extracorporeal Membrane Oxygenation involved passing an infant's blood through a circuit where it was oxygenated, brought back to body temperature and transmitted back to the patient[10]. The ECMO treatment resulted in significantly higher survival rates for babies with pulmonary hypertension[10]. However, many experts in the medical community hesitated to accept the new treatment as no formal RCT was performed to assess its effectiveness[10]. The scientists who developed ECMO faced an ethical problem: babies from the control group treated with traditional methods had a substantially lesser chance of survival than those from the experimental branch[10]. They resorted to introducing modifications into the standard RCT format that were designed to minimize the possible damage done to the patients from the control branch, but there still was a significant body of opinion maintaining that only a properly conducted, traditional RCT could be a conclusive evidence of the ECMO's performance[10].

This case study may be the extreme, but the fact is that in order for evidence to be available, RCT with patient participation must be performed, and a physician who has to make a decision about his patient's participation in an RCT faces an ethical dilemma. This difficulty is resolved in the medical community by affirmation that an RCT is the only means of gaining conclusive evidence and introducing a concept of an "equipoise"—when a physician is in an "equipoise," he or she simply does not know which treatment is more effective, as personal impressions are not enough to support one method over another until conclusive evidence is obtained[10]. This concept illustrates two important aspects of the place of science in medicine. First, the subject of medical studies is the human body; therefore, what is considered neutral in other natural sciences, may raise ethical concerns in medicine. This means that medical research must compromise its human face with the scientific aspect. The goal of medicine is not purely the advancement of knowledge, it is also the improvement in the quality of the human life. Second, medicine is a science, accepting no hypothesis until its accuracy is proven with a rigorous experiment, in this case an RCT. Thus it makes profound use of scientific method, not only in the process of research itself, but also to reconcile some of its most difficult ethical dilemmas. The concept of equipoise derives from the assertion of scientific method, which maintains that no hypothesis can be rejected or accepted until an experiment is performed. Moreover, in cases like this one the scientific method calls physicians to have doubt, as doubt is a means of progress in science, even if entertaining doubt collides heavily with intuition.

The use of the scientific method, understood as the logical process that involves generating hypotheses and their assessment by examination of evidence, is present in healthcare. In diagnosis it is practiced either consciously or as a logical framework, but in both instances, it allows forming reliable diagnoses. When it is practiced consciously and explicitly, as in evidence-based medicine, it allows a physician to make judgments free of his personal habits and convictions, thus introducing scientific objectivity into clinical decision-making. This scientific objectivity and effectiveness of reasoning is especially important in diagnosis, where a physician must make a successful diagnosis in an individual, isolated case. Medical research faces a problem of different nature: it conducts research on representative groups of patients, thus potentially risking administering incorrect treatment to patients from one of the branches of the experiment. Scientific method is, of course, used in medical research in the same way as in other scientific fields, but it is also a powerful tool, which can reconcile some of the ethical dilemmas medical researchers face. It calls physicians whose patients participate in RCTs to entertain doubt, and not to accept any hypothesis without reliable evidence. Scientific method makes medicine a science, and when it is correctly applied unifies healthcare, clinical decision-making, and medical research, and thus, is a source of progress in the field.

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