The application of philosophy and history of medicine in current medical practice. The Nephrotic Syndrome Example

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ABSTRACT
Current medicine has banished all philosophical theories and systems and preserves only the facts, the data and the results of experience. However, according the belief of authors medical history and philosophy still continue producing apparent results upon the treatment of dilemmas in current medical practice. As an evidence of this belief a peculiar approach of nephrotic syndrome (one of the most debated issues in nephrology) in parallel with the aspects of medical history and philosophy was attempted.
The first empirical references from the earliest times of medical art, follow more defined rational and methodic classifications such as the clinical-etiological of Bright, the current histological and probably the forthcoming omics classification, of medical science.
The mystic period and the sacred numbers of Egyptians and Babylonians, the mathematical theories of Pythagoras have now been replaced by the sacred number of p<0,001 and the mystic of statistic values of random controlled clinical trials (RCT). According to the mentioned above current doctors could be
considered as "eclectic" ones: they adopt the reports of beneficial experience (clinical guidelines), carefully and methodically controlled by RCT and follow the modern dogmas such as the individualization of therapy and cost/effectiveness relation combined with the diachronic one "the beneficence of the patient". The remains of medical antiquity may now have little interest, especially in a didactic point of
view; but they will always interest the "erudite" doctor, indicating the route followed by the science where the past is "dogmatic" in present and the present will be "empirical" in the future.

KEYWORDS: History, medicine, philosophy, nephrotic syndrome

Introduction

The nephrotic syndrome (NS), the glomerular disease (GD) in generally, is one of the most debated and challenging issue for the clinical nephrology. The uncertainty concerning the GD is reflected by the low grade of the existed clinical guidelines, (only 2% of clinical guidelines are grade as A (1) and the unwilling of nephrologists, (15-46%) to adopted them as it was recorded from a Canadian study (2) two years after the KDIGO guidelines.

The clinical nephrologist stands uncertain in front of the GD, where the cause is unknown, the treatment unsafe and the future uncertain. This uncertainty was expressed in ancient Greek philosophy (the aphorism quotes the first two lines of the Aphorismi) (3) by the ancient Greek physician Hippocrates:

"Life is short, and art long, opportunity fleeting, experimentations perilous, and judgment difficult."

The above mentioned observations were the trigger of wondering about the utility of medical history and philosophy in facing current dilemmas in daily medical practice. The belief that philosophy is a matter of great value when it can be redeemed in daily life and practice and additionally that philosophical theories still produce apparent results upon the current practice of medicine overarches the text below. In order to support this, a peculiar approach was attempted. The retrospection of history of medical science and philosophy in parallel with the history of NS and GD. This was an interesting challenge to consider: both continuity and change in the practices of medicine (what traditions did medical practitioners draw upon – even as they made radical innovations) and the relationship of medicine to its wider culture.

HISTORY OF SCIENCE, PHILOSOPHY SCIENCE AND HISTORY OF MEDICAL SCIENCE (4, 5)

Science represents the only robust and trustworthy way of knowing both the world and the Mankind and could be a part of "… a new humanism a project that could bridge social, national and intellectual divisions just as the humanist movement had done a millennium earlier…" (6). Anciently philosophy embraced the whole human knowledge (physics, natural history, medicine, morals, metaphysics, theology, mathematics etc). Gradually many of these branches have been detached from the main trunk and constituted separate sciences. Historians take also seriously the point that before the early 19thcentury there was no such a thing as science but instead there was something called, natural philosophy, with much broader ultimately religious aims.

The discipline of the **history of science concerns** the history of the way nature has been manipulated, modeled and understood by different societies. History of science constantly reattaches itself to other disciplines in the humanities and social sciences and embraces a wide range of approaches. These link history of science to history of philosophy, medical history, social history, history of

technology and many other historical disciplines.

In Europe a number of scientists turned to history to support their theories of scientific method what called **philosophy of science**. The assumption that the method and object of scientific practice demarcates it from all other human activities drew history of science and philosophy of science closely together. One could best discover a particular world view at any period or culture by looking at the sorts of problems addressed by its philosophers. In addition the central concepts of philosophy at any given time may be determining element of the nature of the scientific thought of that age. In the history of medicine, most of the medical theories derived more or less directly from some system of philosophy; consequently in estimating the merits of any theory or method of practice it becomes prominent to know from which of these emanated.

History of science has also allied itself move closely with developments in **sociology of science** and other historical disciplines (imperial history, economic and global history). This approach has to balance the intellectual history of science first to its social context (social history of science) and secondly to the technical accomplishments by adopting a more materialist view, with the integration of scientific instruments and their use (**science of technology**).

It is obvious that science has never flourished and been cultivated in the highest degree in any place where it has had no legal recognition. Science was usually conditioned by its social and historical contexts. In Ancient world the condition of organized theoretical knowledge or "episteme" had been that members of "leisured" classes devoted themselves to theory. Science had developed in the West from this disengaged basis and not elsewhere where there were great "bureaucracies" that were always hostile to independent scientific thought. The signal contribution of history of science has been to show the significance of relations between philosophical, historical, religious, social values in the development of science.

History of philosophy and medical science (7, 8) versus history of NS and GD

Science has been held to have a unique capacity to progress by providing us with true statements about nature. Scientific progress began when knowledge became more abstract and freed itself from its craft origins and then from unnecessary remaining metaphysical elements. Gradually became distinctive from other forms of human activity and progressed through operations that elevated it above and extricated itself from the plethora of superstitious metaphysical occultist and religious opinions that always held back its advance. The tenacious obedience to authority was disputed and there was a shift of human mind from the domain of purely speculative vague conjectures and dogmas to the actual study and collation of facts. New doctrines and scientific discoveries disputed the "authority" of the former time and surpassed dogmas which were not eliminated but attempts were made to reconstruct medicine upon "scientific" basis. **Dogmatics** who devoted themselves to philosophical speculations and the formation of theories gave their place to **Empirics** who gave their attention to the observation; their reasoning did not go beyond the observation and experience and placed nothing in the rank of positive and certain knowledge but the sensations.

The "scientists" started to observe the "unknown" and report the experience. Observation and memory which constitute experience were the principal faculties put in exercise: reason entered very little into their considerations.

Reports about NS dating back to Hippocrates. Generalized edema, referred to as dropsy in the earlier literature, and its correlation with renal disease has been documented by his observation: "when bubbles settle on the surface of the urine, it indicates a disease of the kidney and that the disease will be protracted (9). A rich history of observations and interpretations followed over the course of centuries until finally in 1827, an English clinician, Richard Bright, published his first book "Diseased Kidney in Dropsy" where a causal relationship between dropsy and anatomic changes in the kidney was established and the triad of generalized edema, proteinuria and kidney disease were the dominant features that defined the disease which from that time was called "Bright's disease" (10). In 1833 Bright gave the Goulstonian lectures and he first described the rising of blood urea with advancing renal impairment (11). The full description of the clinical and gross morbid anatomical features of all stages of glomerular disease in Bright's paper of 1836 is regarded as one of the classics of medical literature (12). The impact of his work was remarkable. His observations were quickly repeated in several centers and widely extended over the next decade. This was the empirical era of NS constituted only by observations concerning macroscopic symptoms where suggestions about reason were very cautious.

As the observations multiplied it became necessary to arrange them after a method which would impress them upon the previous acquired memory and experience. This was the origin of the first pathological classification. Mere experience report by occasional instinctive observations taken at hazard and gathered generally without taste or method; without the luxury of harmonious thought and premeditated design **is an Art**. It's the combination of intelligence that investigates beyond the phenomena, the reason and the systematically arrangement of observations that transforms Art into **Science**. The Empirics were succeeded by the **Methodists** and observations that tend towards a common end were arranged systematically; both signaled the passage from Art to the Science of Medicine. In accordance with the above mentioned, as the experience concerning GD increases and the information multiplies, it becomes more obvious the need of classify them under some system and method. The method used to classify GD was based on three axes: clinical observation, etio/pathogenesis and histological findings. The initial "rough" **clinical classification** based on Bright's Reports described cases of chronic NS. Acute nephritic related cases were also reported later. Another **classification based on etio/pathogenesis** arises as our knowledge and information about the causes of GD accumulated. Other immunological, genetic, metabolic causes are also involved in the pathogenesis of GD. However the "unknown" pathogenesis still has a dominant place and gives trigger for development of new theories and raising of new dilemmas and controversies.

The entrance of renal biopsy in 1950 was a revolution in the area of kidney disease and led to the emergence of a new specialty of nephropathology. There was a shift from the clinical/etiopathogenetic approach to the analysis of histological patterns. A grade range of morphological features appeared from "gross" findings on light microscopy (minimal change lesions, focal or diffused hypercellularity) to more complex and enriched descriptions with the support of immunofluorescence techniques and high revolution electron microscopy. Consequently the field of glomerular diseases dramatically augmented. New data are added in old clinical-histological entities and new diseases emerge such as immunotactoid GD, hereditary forms of GD, C3 glomerular disease. One the other hand the histological classification has

its limitations; the most prominent one is that we don't classify diseases but histological patterns and indeed patterns of limited "repertoire" since kidneys respond in a limited way to kidney damage. Therefore, certain histological patterns may be the end result of many different renal diseases and molecular pathways of progress of kidney injury. In other words different clinical manifestations may have similar histological findings while different histopathologies may be present to the same clinical entity. Consequently it became obvious in Renal Consensuses (13) that although the histological patterns are the only "scientific, objective observation" criteria we need to go beyond that to a more comprehensive classification where new data will be incorporated on the etiology/pathogenesis basis. **Observation and classification** are not enough in treating the GD. They may not be related to either clinical severity or prognosis and they do not always guarantee a clinical utility by determining the course of treatment.

Going back to the past. The Empirics assumed that in any given case only such remedies as had appeared to be valuable in similar cases, should be employed without any regard to the proximate cause of which they nothing reveals to us the mode of action. It was sufficient enough to show that they were able to cure in order to feel authorized to apply the same treatment to analogous cases. It was naturally supposed that the same remedy would relieve of a similar trouble and all similar cases should be treated in a like manner. No inquiry was made as to the mode of cure by the remedy. This attitude «treating without knowing" does not sound unfamiliar in medical practice even in recent days, representative examples the "early" use of aspirin and corticosteroids. The initial treatment of NS included resting and lowering the protein uptake in order to reduce the renal load, a therapeutic strategy that is followed even in now days. In 1950 the Nobel Prize in Physiology or Medicine was awarded jointly to Edward Calvin Kendall, Tadeus Reichstein and Philip Showalter Hench "for their discoveries relating to the hormones of the adrenal cortex, their structure and biological effects". The whole story began by **an observation**. Kendal in the course of his work he observed the favorable effects of jaundice on arthritic patients, causing remission of pain. Other bodily changes, for example pregnancy produced the same effect. These and other observations led him gradually to the conclusion that the pain-alleviating substance was steroid. In the period 1930-1938 Kendal and his collaborators had isolated several steroids from the adrenal gland cortex one of which was initially called Compound E. Working with physician Philip Showalter Hench, Compound E was used to treat rheumatoid arthritis. The compound was eventually named cortisone (14). The excellent response to new treatment mainly in cases of minimal change GD in pediatric patients and other types of GD had established corticosteroids as a corner stone not only for the treatment but also as a prognostic marker of the outcome of GD.

However, it was proved, once again that observation and empirical treatment is not enough. It has been several decades since then but there are still dilemmas that oscillate the clinicians. There is a need once again to go beyond the experience, behind the phenomena discovering new pathogenetic pathways. New players of humoral and cellular immunity are introduced in the field of renal injury. The recognition and understanding of their role has led to the introduction of new more specific, effective and targeted therapies (15). But the response to therapy is not always the desirable one. Except the cortico-resistant forms of GD, new forms of resistant nephrotic syndrome appear like cyclosporine, mycophenolate resistant forms. We could say that treatment strategies offer a picture of a republic delivered up to many rival factions which dominate but turns without ever obtaining lasting power. What exactly is going on? Maybe the past will help us to find the answer. A basic doctrine of the philosophy of causes says that the same factors placed under identical conditions will always produce the same result. But in medicine this is different: here nature and accidents ie. diseases, furnish us the opportunities of experimenting: but in the first place the elements (patients) of these experiments and the diseases (glomerulopathies with great heterogeneity) are never identical; and secondly it is impossible to isolate the patients from a multitude of influences that alter the therapeutical results. Another fundamental principal is expressed by the aphorism: contraria contrariis curantur. It was held that always exists a species of antagonism between the cause of the morbid phenomena and the active properties of the remedies that cured them; or rather between the pathological modification of the organism and the curative impulse given to the economy by the treatment.

Freedom of thought and expression are necessary prerequisites for any science to flourish. The right of free choice is the most dominant one. The history of medicine teach us that in the face of dilemmas about theories and treatments there was a cast of physicians the **Eclectics** who professed to select such principles and modes of practice as appeared to them the most valuable and beneficial for the patient. Their object seemed to be a reconciliation of the tenets of Methodists (classification of knowledge) with those of the Dogmatics (dogmas, principles and theories) and Empirics (observation and experience). Current doctors could be considered as "eclectic" ones: they adopt the reports of beneficial experience (clinical guidelines), carefully and methodically controlled by random controlled trials (RCT) and follow the modern dogmas such as the individualization of therapy and cost/effectiveness relation combined with the diachronic one "the beneficence of the patient".

As medical science gradually detached from philosophy and humanities was influenced and supported by other "applied" sciences such as physics, chemistry, mathematics. The first link was made at the time of Pythagoras, but the few fragments of this mathematical system that are left serve more as proof of its existence than for its understanding,. Those who wrote them use a "jargon" that is supposed to be known in the same way that modern scientists use algebraic, statistical characters etc. The language of the numbers used by the Pythagoreans is lost. Now days the sacred numbers 1, 2, 3 7 have been replaced by the sacred number of $p<0.001$ and the mystery of statistic values of randomized double blind studies. But in the case of GD they are "weak" due to: a) the few number of patients b)the slow progression of the disease c) the differences in data classification as well as in types of histological patterns. All these impede the reliable comparison of the data and the creation of a basic reliable multicenter study. Consequently the mathematically "evidence –based" well doing of treating GD has been limited by poor availability of large comprehensive registries.

The basic sciences, systems biology, molecular biology and omics are the rapidly advancing, innovating and promising fields in molecular mechanisms underlying the diverse etiologies of GD. It is the answer of now days offering a "storm" of new information and entirely new fields in its investigation. Large-scale gene, protein and metabolite measurements ('omics') have driven the resolution of biology to an unprecedented high definition. Passing from reductionism to a system- oriented perspective, medical

research will take advantage of these high-throughput technologies unveiling their full potential. The omic cascade, from the potentiality of 'what can happen'(genome) through 'what appears to happen' (transcriptome) and 'what makes it happen' (proteome) to 'what has happened' (metabolome), embodies the paradigm of what needs to be modelled. Integration will unveil the full potential of these high-throughput technologies leading to a comprehensive decoding of the upper emergent level, the phenotype and the key to decoding the underlying principles that govern the complex functions of living systems. Systems biology is a novel field pitched at decoding -omic dynamic interactions and adding an additional dimension to that of a classical homeostatic model of physiology (16, 17). In the near future omics will improve the **classification** of GD (in addition to clinical, etio/pathogenesis, histological the omics one) to a more sophisticated model. Finally there will be a radical moving from **empirical** to stratified and **individualized medicine** which will depend on refined molecular fingerprints.

These modern sciences will modify the traditional deductive model of scientific knowledge (scientific knowledge is hypothesis established on valid rationally and after research proven true statements) or even the more radical one related to Popper's philosophy of empirical falsification (A theory in the empirical sciences can never be proven, but it can be falsified) to an unbiased model without prior hypothesis but first gathering data and then generating hypothesis after analysis and modeling.

Churchill once said as he was "bombarding" by the claims of the Balkan nations that "…they produce more history than they can consume…" In analogy we now produce more information and data than we can incorporate into the daily clinical practice. This creating a demand for effective storage (data bases), management and exchange of rapidly generated data and research discoveries. Databases are divided into two categories: general databases with a broad information scope and kidney specific databases distinctively concentrated on kidney pathologies. In research, databases can be used as a rich source of information about pathophysiological mechanisms and molecular targets. In the future, databases will support clinicians with their decisions, providing better and faster diagnoses and setting the direction towards more preventive, personalized medicine.

It is a fact that modern medicine rejects from medical practice any kind of system and philosophical theories and insists on the value of pure scientific evidence based data alone. However this may sound utopian when the "philosophy of physician's attitude" about the welfare, disease and health determines his attitude towards healing. A science that deals with the mystery of life cannot be complete if it deals only with its empirical/scientific part. A major part of individualization of treatment in medicine relies on the "holistic" view of life and disease.

The clinical nephrologist still wanders around in the labyrinth of NS resulting usually in "minotauric dead ends" searching for the ball of yam (mitos) in order to find his way out.

Epilogue

This retrospection does not allude that that the progress of the science and the acquisition of knowledge is a circular game incessantly repeating. From Aristotle and Kant to Popper and model of systems biology, each era has its own "cognitive" model of approaching knowledge. Nevertheless knowing the history and philosophy of the science that we practice, it is not only a privilege of an erudite man but also make us more broad minded in, understanding, individualizing and treating current unknown under research issues indicating the route followed by the science where the past is dogmatic in the present and the present will be empirical in the future so that every current generation will be the empirical candidate of the future.

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