MEDICINA NEI SECOLI ARTE E SCIENZA, 20/1 (2008) 115-139
Journal of History of Medicine

Articoli/*Articles*

EVOLUTION BASED MEDICINE (EBM) AN EPISTEMOLOGICAL FRAMEWORK FOR THINKING OF, AND DEALING WITH THE SO CALLED "CRISIS OF MEDICINE"

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SUMMARY

A growing interest toward the evolutionary or Darwinian approaches in medicine stimulates today's debates about the future of medical knowledge and practice. A rising number of symposia, essays, and books are questioning if medicine still makes sense without evolution, arguing that an understanding of how natural selection shaped human vulnerability to disease could provide new insights into medical research and practice, and contribute to a more pertinent idea of health and disease than the ones emerging from the understanding of physiology and biochemistry. The aim of this paper is to provide an historical and epistemological perspective for an evolution based medicine (ebm). Starting from a schematic analysis of the most controversial issues debated within the literature dealing with the so called "crisis of medicine", I will guess that medical theory and philosophy of medicine find it difficult to manage the crisis because they are suffering from ahistorical fallacy. A schematic reconstruction of the historical advancements of medical epistemology, both at the level of theoretical thinking and of methodological strategies will then be put forward, to demonstrate the epistemological pluralism of medicine. Instead of considering medical pluralism as a demonstration that medical knowledge is socially constructed, the essay argues that it is a consequence of the fact that the living beings who become sick and those that try to

Key words : Evolutionary medicine - Darwinian thinking - Philosophy of medicine - Ahistorical fallacy - Principle of selection

understand how and why it happens are temporary endpoints of the ongoing process of biological evolution by natural selection. The main assumptions and theories which inspire "evolution based medicine" will finally be listed and analyzed in terms of their the epistemological implications, showing why and how an evolutionary and Darwinian perspective about medical knowledge and practice can improve and complete the epistemological understanding and foundation of medicine.

Introduction

After several years of teaching history of medicine in a medical faculty, and of trying to understand whether and how a historical perspective about medical thinking and practice could help medical students in their learning paths, I realized that most students attending the medical school didn't grasp the epistemological pluralism of medicine. In fact, they don't see that their teachers of epidemiology, immunology, pediatrics, etc. introduce them to quite different perspectives of medical research and practice. According to my experience, medical students acquire a schizophrenic and uncritical attitude towards the main theoretical and methodological components of basic and clinical knowledge. Even tough it seems that they survive well without knowing of their dissonant learning, I became interested in the investigation of such phenomenon. I advanced the hypothesis that student's epistemological schizophrenia was indeed due to a lack of historical perspective, at the level of the philosophical assumptions which informed the theoretical and technical transitions in medicine. So, I decided to teach a historical framework focused on the epistemological evolution of medical thinking and practice. As I turned to philosophy of medicine to find out the theoretical tools that could help me to understand why and how medical epistemology has evolved towards the present status, I could not find in the past and ongoing philosophical investigations any helpful suggestion to customize a historically coherent, pertinent and useful

(for my needs) epistemological framework of medicine. Moreover, I realized that medical philosophers, sociologists or commentators theorize the existence of something called a "crisis of medicine", and normally they suggest a supplementary teaching of medical humanities to deal with such crisis.
Philosophers of medicine seems more interested to explain how epistemological controversies work in medicine and defend some philosophical view, than to understand why those specific controversies exist, take the present form and could be solved not only philosophically, but also al the level of medical theory. As it is well known the main controversial issues, debated by medical philosopher are[1]:

- *whether health and disease are naturalistic (functional/nominalistic or ontological/essentialistic) or normative (cultural, holistic, etc.) concepts (e.g. Boorse vs. alia);*
- *whether clinical reasoning is deductive (how can it be formalize?) or inductive (but in term of frequentistic or bayesian probabilistic reasoning?) or abductive or intuitive;*
- *which kind of relationships lies between the scientific and practical dimensions of medical knowledge (which is the epistemological status of medicine?);*
- *whether a philosophy of medicine with its disciplinary peculiarities exists or not (e.g. Caplan vs. Pellegrino), and if it makes sense or not to separate philosophy of medicine from bioethics.*

These are certainly important philosophical issues, but quite rarely philosophers of medicine test their views about such topics with empirical studies (biological, historical, epidemiological, psychological, sociological, etc), or advance their ideas to offer scientists useful tools to improve the understanding of medical problems. Although some medical philosopher theorizes a cooperation between philosophy and medicine, most approaches don't really look for a perspective that provides a critical contribution to the theoretical and empirical dynamics that sustain changes in medical knowledge and practice.

According to William E. Stempsey philosophy of medicine can help "a society articulate a view about the purposes and ends of medicine" if it is "conceived of as a "social" philosophy" or as "medicine studies" consisting of a wedding of historical, philosophical and social studies of medicine[2].

In this paper I will first summarize the most controversial issues debated within the literature on the so called "crisis of medicine", and then I will show that physicians and philosophers of medicine find it difficult to manage the crisis because they are suffering from ahistorical fallacy. Therefore I will present a schematic reconstruction of the evolution of medical epistemology, both at the level of theoretical thinking and of methodological strategies, that will demonstrate the epistemological pluralism of medicine. Instead of considering the medical pluralism as a demonstration that medical knowledge is socially constructed, I will assume it as a consequence of the fact that the living beings who become sick and those that try to understand how and why it happens, are temporary endpoints of a process of biological evolution by natural selection. Therefore, I will drawn some consequences for the philosophical understanding of medicine from this fact.

Controversial issues concerning the status and perspectives of scientific medicine

According to several qualified analyses, medical systems are going through a critical phase, which is characterized by local crises at the multistratified and articulated levels of medical research and practice[3]. It is controversial whether the crisis is at the level of the medical way of thinking, or at the level of the physicians' ability to translate basic and technical knowledge into effective strategies to promote health and prevent or cure diseases, or whether the crisis concerns healthcare systems.

Maybe Kevin Wildes rises the right issue. "A crisis, – he writes - in its root meaning, is an inability to know which direction to take or which way one should turn. One can convincingly argue that there is a crisis in contemporary medicine in this most fundamental sense of the term. Traditional paradigms and self understandings of medicine are inadequate for contemporary medical practice. Although new paradigms and images have emerged, no one has become dominant for the field or the profession. Expectations about medicine are often influenced by idealistic, old-fashioned and sentimentalized images of the physician and patient together in the examination room. But these images do not represent the realities of contemporary health care and medical practice. The crisis of contemporary medicine has been brought about, to some extent, by the success of 'scientific "medicine'"[4].
In fact, there is no doubt that

- *people live longer and in better health than ever,*
- *scientific and technological progress continuously improves medical effectiveness,*
- *there is more respect for patients and more trust in doctors,*
- *expectations for further improvement in health conditions and health's demand are still very high.*

Moreover it is quiet evident that it is because of the success of scientific medicine that…

- *people who live in the most affluent and healthy countries, also are the most worried about their health;*
- *the request for complementary or alternative medicine in Western countries is increasing;*
- *patients and doctors are more unsatisfied than in the past with the contexts in which they interact;*
- *medical efficacy does not spontaneously become health efficiency;*
- *healthcare costs are out of control, and inequalities in health are increasing;*

- *private health marketing and promotion policies stimulate medicalisation and disease mongering.*

According to several medical educators and philosophers, to deal with such challenges tomorrow's doctors should be endowed more with moral and social qualities than with scientific and technical skills. A widespread view is that to stimulate the acquisition of more humane the most useful disciplines are humanities[5]. Is such a view supported by any evidence?

Empirical studies show that the teaching of medical humanities actually stimulates individual awareness toward social and psychological dimension of medical problems, and that problem based teaching, which concentrates on the practical on problem solving aspects of learning, improves clinical performances (clinical problem solving)[6]. Notwithstanding, other empirical studies show that today's medical education is not improving the acquisition of basic knowledge, the ability to generalize, and the consolidation of learning. Moreover, one can argue that some epistemological assumptions of problem based learning – like that adult learning is special and the superiority of constructivistic epistemology – cannot be maintained in the light of empirical and philosophical studies showing that adult learning doesn't exist and constructivist pedagogy is debatable[7]. The constructivist philosophy that inspires problem based teaching, together with the criticism against science and technology maintained by some humanistic discipline that are taught to medical students can promote epistemological relativism and opportunism among doctors[8].

Philosophers of medicine and medical educators tend to ignore that biomedicine is also dealing with several 'internal' challenges and problems, such as the emerging and re-emerging infectious diseases, the increasing morbidity (and mortality) due to allergic, chronic degenerative, neurologic and psychiatric disorders, the impact of genomic and post-genomic knowledge and techniques on medical thinking and

practice, the fragmentariness of medical teaching and learning and the epidemics of politics and bioethics within the biomedical discourses. Let me try to assume a different view. Perhaps medicine is also facing an epistemological crisis due to the present schizophrenic status of medical thinking. Medicine probably does not need more humanities in general – of course a humanistic education is good in general (not only for doctors) – and the usefulness of humanistic teaching depends on how it can functionally integrate and promote (not reduce) the scientific and practical skills needed by doctors. Medicine might need a new philosophical framework based on a scientific view of health and disease, and allowing the integration of empirical data categorized according to different objectives and strategies; an epistemological framework heuristically and explicatively more powerful than those presently defended and taught by the leading medical thinkers and teachers

Medicine is suffering of ahistorical fallacy, and the philosophy of medicine too

Why biomedical thinking is not evolving toward a more pertinent view of the limits of medical knowledge and practice? Why medical philosophers prefer to emphasize the contradictions instead of looking for theoretical links between different epistemological perspectives? Perhaps because both suffer from two different kinds ahistorical fallacies. The US neuroscientist and Editor for thirteen years (1993-1996) of the American Journal of Psychiatry, Nancy Andreasen, in 1994 suggested the 'diagnostic' category of "ahistorical fallacy" to explain the difficulties of psychiatrists and psychiatric institutions in US to improve the functioning of clinical definition of mental and neurological disease[9]. Andreasen claimed that the then ongoing discussion on psychiatric nosology could learn a lot from that historical investigation, but unfortunately individuals and institutions in the

United States were suffering from the peculiar failure to have a sense of the past. In Andreasen's words, to suffer from ahistorical fallacy means "to lack the capacity to see things within the context of the broad sweep of time, with all the ensuing richness of associations and sense of humility that result from perceiving things within a larger context"[10].

According to Andreasen the *ahistorical fallacy* rests on three faulty assumptions: a) that what the expert says must necessarily be true; b) that what has been said more recently must be truer than what was said previously; c) that "if information increases, knowledge increases as well". There is no doubt that these assumptions, to which may be added the misconception that knowledge grows linearly and progressively, are today widely spread among any field of biomedical research and practice, including most theoretical and philosophical investigations, and that they inform most attempts to reform medical curricula in Western medical schools.

A further kind of ahistorical fallacy works as an epistemological inclination of medical scientists and philosopher to assume functional explanations of disease as ahistorical. According to the pediatrician, geneticist and fine critics of medical theory, Barton Childs, the main epistemological limits of scientific biomedicine lays in its mechanistic and reductionistic view of the human body, metaphorically represented in pathology and physiology textbooks as a machine. "The machine model – says Childs – omits the arrow of time; it is essentially ahistorical"[11].

Such kind of ahistorical fallacy, that can be referred to the famous philosophical framework of biology worked out by Ernst Mayr[12] who formulated the distinction between proximate and ultimate causes, has recently been effectively reformulated by Alex Rosenberg in his last book. Rosenberg effectively argues that biological phenomena – and pathological process are biological – are histori-

cal by default as any explanation in biology needs to have sense in the light of evolution (by natural selection). "Biology is history, (…) for which the "iron laws" of historical change have been found, and codified in Darwin's theory of natural selection"[13].

The origins of the present status of medical epistemology: philosophical and methodological achievements and assumptions of the main traditions in medical thinking and practice

The evolution of medicine's theoretical foundations and methodologies can be represented as a long, entrenched and enduring cultural process during which medical concepts, theories and methods conceived by physicians in different historical phases has been undergo on the selective and changing pressures due to efforts aimed at validating or confuting them[14].

Today's medical thinking involves complex and dynamic interactions among different strategies and levels of categorization that try to make sense of non predefined events which can or cannot be medically relevant for the individual, the physician or the public health system, according to different criteria and contexts. In Figure 1, I attempt to simplistically illustrate that there are different pathways and level of analysis involved in the detection of medically relevant facts.

The complex status of today's medicine as well as of its internal tensions has come after a long theoretical and methodological history of medical thinking which is schematically resumed in Figure 2.

We can identify three main phases in the history of medical strategies aimed at explaining the nature and origins of disease and health[15]. At the beginning humans referred to preternatural ideas to explain their pains and sufferings. Such explanations came out from a specie-specific way of reasoning about hidden causes, selected for its higher inclusive fitness and hardwired into brain anatomy. Preternaturalistic ideas about disease and health, which are in fact more 'natural' than

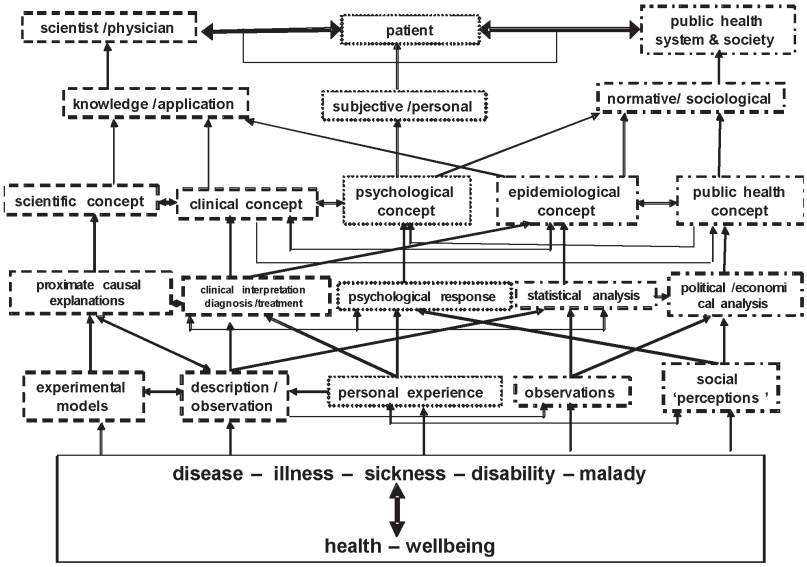

Fig. 1 - The strategies of categorization and conceptualization of medically or scientifically relevant phenomena concerning patient's disease are represented on the left of the scheme. The cognitive strategies which produce the social and political perceptions of the medical phenomena at the level of populations are sketched on the right. The patient's psychological perspective is shown in the middle of the diagram.

the 'naturalistic' ones still work even today among cultures and people far from any scientific literacy.

The Hippocratic revolution introduced and demonstrated the more practical instrumentality of an idea and of an explanation of health and diseases based on empirical facts and logical reasoning. The Hippocratic school suggested a functional concept of disease, based on a humoral theory, as alternative to the ontological one, preferred by priests and by those ancient medical schools that assumed a diagnostic stance. The history of scientific and technical improvements (as well as temporary worsening) of medicine can be represented as an almost dialectical process (in a Hegelian sense) characterized by the concurrent or parallel development of ontological and functional ideas of disease.

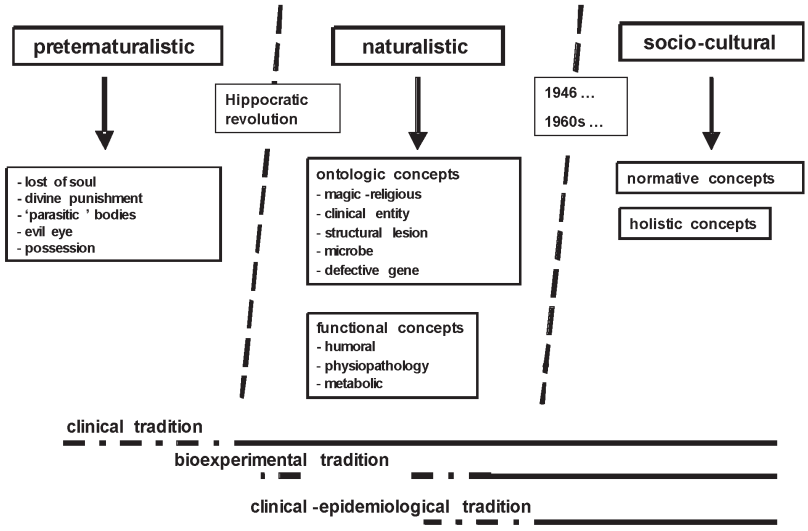

Fig. 2 - A schematic representation of the historical development of medical theories and methods. See text for explanatory comments.

After the Second World War, as the attention to the social and economic determinants of health and disease raised and spread rapidly and widely, the naturalistic or scientific approaches in medicine come under critics as unable to give and reach an objective definition or explanation of disease. New ideas, based on sociological, cultural, historical and philosophical analyses of medical knowledge and practice, which emphasized the normative dimensions of health and disease definitions, were put forwards. Of course the implicit assumption of normativists was and is that the origins of values and desires don't depend on or cannot be explained in term of a naturalistic or scientific characterization of the interactions between individual human physiology and the socio-cultural contexts in which such body used to live.

The conceptual and theoretical evolution of medical thinking was selectively directed toward the present state by three main method-

ological traditions based on different epistemological and practical assumptions[16]. These traditions are represented at the bottom of fig. 2.

Clinical tradition (Hippocrates → early 1900s)

- *based on observations and interpretations of symptoms and signs (naturally or artificially investigated/induced);*
- *starting from the late XVIIth century clinicians classifies symptoms and signs to create specific pattern useful to define clinical entities (ontological concepts) and make diagnoses*
- *emphasizes the singularity of clinical cases (individuality of patients)*

Physiopatological tradition (from 1855s → present)

- *develops explanatory theories and experimental models of diseases to identify the proximate causes that produce the functional alterations, and assume that clinical heterogeneity and individual variations depend on some intrinsic limitations of the experimental models on that are a sort of noise;*
- *disease are deviations from functional homeostasis (functional concepts), but can also be reified (ontologized) as germs, cancer cells, defective genes/protein;*
- *health means absence of disease: the goal of medicine is to treat or prevent diseases by rationally designing drugs and interventions on the basis of the understanding of the etiopathogenesis.*

Clinical-epidemiologic tradition (from 1950s → Evidence based medicine)

- *pays no attention to the functional mechanisms that cause the observed clinical phenomena;*
- *applies statistical methods to inductively establish causal correlations: clinical trials (based on frequentist statistics) has become the only reliable experimental design to test hypotheses and evaluate the effectiveness and efficiency of medical decisions;*
- *the major determinants of health and disease are environmental factors (prevalently social and economic), and the social function of medicine is to promote health.*

Given this broad picture, which shows the existence of an epistemological pluralism within medical thinking, we can ask how such a condition influences the understanding of medicine within and outside medical practice. In other words: is theoretical and methodological pluralism of today's medicine rightly interpreted, or is it a source of misunderstandings?
Methodological and theoretical pluralism of medicine is mainly a source of controversies that most times are addressed in term of typical philosophical issues, such as reductionism vs. antireductionism, rationalism vs. empiricism; etc., but that at a practical levels is represented by the theoretical and academic or political conflicts among clinicians, epidemiologists, pathologists and public health researchers. In the past decades a heated debate over the nature of evidences in medicine has been raised by the academic success of the evidence based medicine doctrine. However medical pluralism could be seen as a pragmatic necessity, due to the fact that human anatomy and physiology has emerged through biological evolution by natural selection. Let me try to control such an hypothesis and ask if the Darwinian view of biological dynamics could represent a useful heuristic stimulus for both medical theory and philosophy.

Which are the main ideas put forward by existing evolutionary or Darwinian approaches to medicine?

Everyone who is following today's theoretical debate in medicine should know that there is a growing interest toward the evolutionary of Darwinian approached to medical issues. "Does Medicine without Evolution Make Sense?", ask rhetorically an Editorial of PlosBiology that reports about the meeting on *Medicine and Evolution* organized in New York by the Society for the Study of Human Biology in late 2006[17]. According to the Senior Editor of PlosBiology, "and

understanding of how natural selection shapes vulnerability to disease can provide fundamental insights into medicine and health and is no less relevant than understanding of physiology and biochemistry" (p. 0697). If one queries through Pubmed using "Darwinian" or "evolutionary" and "health" or "medicine" can easily find about 100 reviews dealing with the Darwinian or evolutionary dimensions of medical and health care problems, more than two third published within the past five years.

There are several Darwinian or evolutionary medical traditions, which evolved along different theoretical and problematic paths, and that reached a few consistent understandings about the evolutionary dimensions of biomedical issues[18]. Here are the most philosophically relevant ideas which inspire the Darwinian or evolutionary approaches to medical problems.

1. Proximate causes cannot explain, by themselves, the origins and physiological or epidemiological dynamics of human diseases – remote or phylogenetic causes are also germane to the understanding of health and disease. Proximate causes are outcomes of remote causes.

Even though explanations in terms of proximate causes can detect how a physiological mechanism goes wrong and produce a malfunctioning or an harm, they cannot account for the origins any given cause-effect relationship empirically proved. While explanations of non living systems don't need to consider the genetic background of a cause-effect relationship, any biological system carries hereditary and somatic memories that predefine the specie-specific and the individual ways in which the system develops the malfunction or produce the harm as a consequence of environmental stimuli. So remote causes, phylogenetic and ontogenetic are relevant even though they often cannot be experimentally investigated or reproduced because of practical reasons[19]. The assumption of a spe-

cies-specific physiological design that should correspond to a statistically defined normalcy was and is indeed a useful instrumental simplification, but as any simplification doesn't correspond to any reality. Most important, it hides the historicity of the structural elements which produce the observed or detected morphological and physiological parameters.

There are several examples of risk factors that depend on our evolutionary and developmental histories, as for example from the fact that our body is not optimally designed because natural selection doesn't work as an engineer, or that our physiology was adapted to allow our ancestors to survive and reproduce in the Pleistocene savannas and as member of small tribes[20]. So changes in our nutritional, reproductive and affective lifestyles introduced since the agricultural revolution, creates health risks because they are at odds with our evolutionary predispositions[21].

Furthermore our interactions with infectious agents are ruled by evolutionary dynamics, as viral, microbial and macroparasitic populations undergo selective pressures, which include medical therapeutic and prophylactic measures that influence their transmission, pathogeneticity and virulence[22].

2. Health and disease are phenotypes.

From (1) it logically comes that phenotypic traits are not perfect, or that body is not a machine, nor the instantiation of a one-dimensional algorithm[23]. The best 'anthropomorphic' metaphor which describes natural selection is that of a *bricoleur*[24]. As living beings are not the result of an intelligent design, physiologically integrated and adaptive molecular interactions emerge as a result of selection processes or by the differential reproductive fitness that increases the frequencies of those genes that codify for the advantageous or not disadvantageous proteins that control cellular morphology and

physiology. As a consequence, phenotypic optimal functioning or individual wellbeing are not relevant from an evolutionary point of view, and several anatomical or physiological suboptimal traits, which can predispose human beings to sufferings and diseases could be, and were selected as advantageous at some lower level of selection (cells, proteins and nucleic acids)[25].

3. The level for a functional definition of health and disease are proteins that control the "unit steps of homeostasis"

Genes don't specify the phenotype, but "speak biochemistry"[26]. Therefore doesn't exist any gene "for" any given disease. Genes codify for peptides and proteins, which are the unitary and regulatory element of physiological homeostasis. The concept of "unit step of homeostasis", suggested by the paediatrician and geneticist Barton Childs, provides the best foundation for a functional and at the same time evolutionary definition of disease and for the explanation of the origins of malfunctioning and harm that are categorized as diseases[27]. Proteins that control physiological homeostasis passed the test of natural selection, and as natural selection promotes new adaptive or better integrated physiological processes in living systems using existing spontaneous variations among phenotypes, any protein necessarily exists in different structural forms and quantitative magnitudes within any individual. Qualitative and quantitative variations of proteins that control the unit steps of homeostasis explain biological individuality. The genetic recombination mechanisms and spontaneous mutations producing hereditary variability and the epigenetic mechanisms that amplify the protein repertoire by introducing further recombination and mutations during gene expression implement the phylogenetic and ontogenetic histories that set the internal physiological conditions, due to the singularity of homeostatic integrative dynamics ruled by proteins, of individual

vulnerability at a given time and in a given environment. Within such a perspective, a genetic defect is a special case of biochemical individuality. In fact, the effect of any genetic variation can only be appreciated through the impact of the modified protein on the integrated homeostasis.

The concept of unit step of homeostasis could be useful to suggest a more coherent and pertinent synthesis between medicine and biology, but also to immunize doctors against the deterministic view of the gene function, which is a misconception usually taught as a truth by most medical geneticists. Moreover, by focusing on the physiological function of proteins it would be possible to integrate the molecular and reductionistic approach, aimed at defining the proximate cause of the functional defect, with the biological approach, which regard malfunctions and harms as unavoidable consequences of the variability necessary for evolutionary changes, and with the clinical approach, which deals with the individual patient[28].

4. Each patient/person is a unique individual because of the singularity of his genome, of the epigenetic and physiologic interactions that happen during development at/between different levels of organization among several complex physiological systems.

It isn't necessary to appeal to a humanistic view as opposed to a biological one to understand that in their clinical practice doctors deal with singular cases, and that the right questions they should ask is "Why does this person suffer from such dysfunction now? In which way are his clinical conditions influenced by his genetic makeup and socio-cultural history? What can I do to restore this patient's unique attitude to the environment he lives in?" While a question such as "Which is the disease that affect this patient and how do I treat it?" can be misleading[29].

5. Diseases are not defects or alterations at the level of typical or species-specific functions: they reflect some individual physiological incongruence in relation to a given environment, due to complex interactions between a unique genetic constitution and environmental stimuli which are also unique.

From an evolutionary and biochemical point of view a disease represent then the outcome of some incongruence of variable homeostatic devices, which are the historical product of evolutionary and Darwinian dynamics, and of the environmental context[30]. In philosophical terms, an evolutionary concept of disease rests on a functional, nominalistic and historical definition[31]. From a biological point of view diseases are then deviations at the level of biochemical pathways caused by variants in protein structure and quantities which don't allow the pathway to maintain its functional integrity[32]. The remote causes, phylogenetic and ontogenetic set the individual predisposition to malfunction and to the consequent harm for the phenotype. As a consequence, no putative cause of disease is harmful by itself or independently from a historical and ecological contextualization, Moreover monocausal diseases don't exist, and the similarity between clinical cases depends on how much genetics and experiences they share[33].

6. As the concatenations of proximate causes are a consequence of both biological and social conditions, all diseases have a social component, and the evolutionary concept of disease takes into account the social, cultural and personal dimensions of patient's experience

Even though they give for granted the social, cultural and psychological dimensions disease categorizations, evolutionary or Darwinian approaches don't make any assumption about why and how individual experiences influence the personal categorization of disease.

In other words, that means that at the level of patient responses there are so much variability to the same malfunctioning or harm, and that given the same clinical case two doctors will follow different pathways to reach the final identical diagnosis.
Do we have some further biological insight to provide doctors with a more coherent theoretical perspective that explain them why individuals manage the same stimuli in different ways? Can we avoid any allusion to some immaterial essence of human cognition? Let me suggest that an epistemological framework for an evolution based medicine should include a further idea, which until know is not considered by most reviews concerning the theoretical and empirical foundation of Darwinian or evolutionary medicine.

7. The principle of selection also works during the somatic time to allow the acquisition of individual adaptive responses to unexpected stimuli, and such a biological fact explain the individual variability of patient and doctors strategies of dealing with medical problems

Except dualists or spiritualists, no one would context that both patient's and physician's categorizations of the different stimuli produced by physiological malfunctions related to illness and disease depend on or pass through individual brains. Human cognitive functions, in both their species-specific and individual expressions, are products of brain's physiological organizations. Therefore, to clarify the issues related to individual variability in responding to and reasoning about illness and disease we need to look at the functional logic of human brains, how it works and control behaviour on the bases of its evolutionary history and physiological dynamics. Neurobiological models based on an integrated understanding of brain anatomy and physiology show that human brain is a complex learning system, organized to collect and compare experiences,

which include emotional components that represent the physiological and basic levels of human normative dimensions[34]. The evolutionary history of human cognition was certainly at the origins of heuristics and biases that have been described by experimental psychologists, and that are heavily involved in several medical misconceptions[35]. But there is a further aspect of brain functioning to be considered.

Perhaps because of the specialization and ahistorical fallacies of medicine and medical philosophy, nobody has drawn the logical implications from the fact that during the second half of the past Century, biologists discovered that some physiological systems, immune and nervous system above all, actively manage internal and external stimuli by means of an articulated hierarchy of selective processes. From a philosophical perspective, as well as in term of medical theory it is quite relevant that a Darwinian heuristic was at the origins of the understanding of the physiological bases of brain plasticity. The discovery that some individual or somatic systems, like the nervous and the immune ones, can acquire new adaptive physiological responses or can learn from experience by working as selective or Darwinian systems, means that evolution by natural selection 'reinvented' or 'reutilize' Darwinian selection within complex somatic systems to provide them with a physiological plasticity or the ability to go far beyond the limits of the hereditary mechanisms to acquire new adaptations. It is also relevant that also some malfunctioning of our body, like, cancer, adopt an evolutionary or Darwinian dynamics to acquire new adaptive features and unfortunately progress toward more aggressive and deadly phenotypes[36].

We find evidences from neuroscience, cognitive and evolutionary psychology, and anthropology that the so called human values that modulate individual judgments and choices, as well as their communication, are processed by human brain according to both

species-specific preferences and predispositions hardwired within cerebral anatomical and physiological macro organization and individual preferences and predispositions resulting from the interaction between the individual biological endowments and the environmental context which modulate and/or modifies the predefined value setting[37]. Therefore it goes without saying that brain plasticity mechanisms are involved in the individualization of illnesses and diseases categorization as a consequence of the concatenations of all the remote and ultimate causes, including the social and cultural influences which raise so many problems to a value neutral definition of health and disease. Both the personal history of the patient and the learning and practical experiences of physician selectively set the individual brains status and thus personal attitudes and performances face a illness or disease phenomenology.

As a consequence of the properties of Darwinian or selective processes involved both in the evolutionary and somatic history of our brain, individual and sociocultural variability in dealing with illness and disease is unavoidable for natural, or scientifically understandable, reasons. A don't want to say that a scientific or biological analysis of medical issues will provide all the expected answers at the level of psychological and social understanding of medicine. We don't still and likely won't never have a complete or deterministic account of human behavior. So, as ways to actively process individual experiences or learn new adaptive behavioral strategies to deal with unpredictable problems, humanistic approaches can be and are indeed very useful. It is however epistemologically senseless, and to some extend misleading for doctors personal epistemology to teach them that there isn't a naturalistic explanation, at least in principle, of what they observe and feel. Fig. 3 represent the historical development of biomedical thinking with the integration of the evolutionary or Darwinian approach.

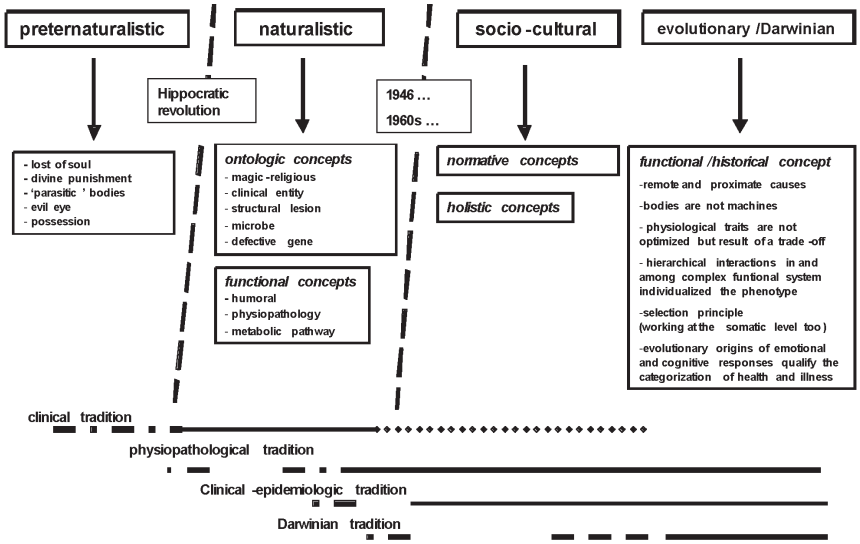

Fig. 3 - The theoretical and methodological approach which refers to evolutionary or Darwinian thinking has been integrated into the diagrammatic representation of the historical developments of medical theories and methods.

Conclusion

The so called Dobzhansky's dictum[38], with some minor modifications, can effectively synthesize the content of this article: nothing in biology [and medicine] makes sense except in the light of evolution (and Darwinian thinking).

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