

Darwinian aftershocks: repercussions in late twentieth century medicine

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Keywords: Darwin; Metchnikoff; health care; philosophy of medicine

As the USA is debating how medical insurance is to be revised and health care reformed, it might do well to consider the most difficult issue to address: expectations of health. There are obvious cultural determinants of the normal and the diseased. For instance: the French are prone to attribute all manner of dysfunction to a faulty liver; the Italians might seek out spas; Americans are more likely to take a laxative or an antacid for similar digestive complaints. Aside from such cross-cultural differences that illustrate the elusive manner in which we define and treat illness, there are some rather astounding historical statistics from my country to demonstrate the changing nature of our medical expectations. Sixty years ago, household interview surveys of a random sample of Americans reported 82 episodes of illness from all causes per 100 population over a period of several months. A similar poll in 1981 showed a 158% increase. This survey included all manner of 'illnesses', but if one limits the question to an illness requiring care, the average person today is 'sick' more than twice a year, as opposed to less than once a year on average in the 1920s¹ (p 296).

There are two components to an analysis of these morbidity rates. The first pertains to that most nebulous of issues, psychosomatic illness. In this regard, increasingly, Americans interpret internal sensations as illness today. We have altered the expression of many complaints into new, more socially acceptable diseases, a lesson well learned from anthropological studies: the normal is largely culturally defined. In a complex dialectic, the expression of illness has also changed as our medical models have evolved. In addition to the altered expression of illness (from muscle paralysis in the nineteenth century to pain or fatigue in our time) there is also an *increase* in complaints.

Only 5 to 14 percent of the general population do not experience symptoms in a given two-week period. The average adult has four symptoms of illness on one out of every four days¹ (p 296).

The second parameter pertains to the incidence of those more easily defined organic dysfunctions; eg anaemia (4-5% of the adult population), hyperuricaemia (3%), alcoholism (5%)² (p 19). Reasonable estimates of the prevalence of chronic disease (about 15%)² (p 20) and annual incidence rates of acute conditions alone (about 21%) (p 29) suggest at any one time, at least one third (and probably more) of a modern industrial society's population is characterized by some morbid condition. One must conclude that 'deviance, clinically or epidemiologically defined, is "normal"'² (p 15). By such standards, we are a sickly community.

The normal and the pathological

In fact, our language betrays confusion. Statistical normal is simply the most frequent³, whereas in common parlance, *normal* refers to the expected, the functional, and most widely understood, as encompassing health. The ascendant health-consciousness, or perhaps better, 'illness-consciousness' of Western society comprises a particular expectation of an ideal physical well-being. This elusive standard has seeped into our collective consciousness as 'the norm'. Beyond the biochemical assessment of bodily function, there is the patient's experience of discomfort or concern. This aspect of illness is highly subjective and translates into the patient's expectation of health care. The increased medicalization of daily life has brought unrealistic demands. Untreatable infirmities and unavoidable ailments are sources of growing concern to an apprehensive public. In a sense we are witnessing a 'paradox of health'⁴. As medical care becomes more available, the 'need' to see physicians rises. More medical attention is obviously a function of accessibility, but increasingly, Americans are willing to define themselves as patients and thus expect sophisticated clinical attention.

When one ponders the larger social issue of health care reform, we must recognize the expectations of what is normal, of which symptoms constitute significant illness, and how somatization provokes anxiety. Each are expressions of our collective experience. Health is a cultural construct that can hardly be defined solely by our armamentarium of diagnostic tests and images. There is a discretionary line drawn between the normal and the pathological, and implicit in health care reform is a revision of expectations. Beyond altering insurance coverage and enrollment is the far more revolutionary reorientation in the very boundary of what constitutes health and illness. That is a lesson Americans have hardly begun to address. The political debate is easily discernible, but I want to deal with some of the underlying theoretical concerns. I believe the overarching issue is that the normative in health is under scrutiny.

The normative is peculiar to each culture, and in its prescription, serves a regulative function. During the nineteenth century, the theoretical role of the physiological norm rode upon the broad shoulders of a newly defined normative based on positivist principles. This new standard may be simply stated as the application of an 'objective' natural science to physiology and health. The observer would distance himself as far as possible from the object of scrutiny. From the laws of physics

and chemistry, a new medicine would arise. And so it did, and we are its beneficiaries. This ethos has largely framed the agenda of medical science for the past 150 years, but the normative is a *cultural* construct, and the demands of late twentieth century patients are posed in quite different terms than those of their pre-Darwinian ancestors. What follows below is an attempt to chart the philosophical and historical basis of our public policy polemics. The debate over health care reform is actually a deep-seated restructuring of our cultural normative. Health care policy then should be viewed as one expression of changing expectation (from the norm to the ideal).

First, let me briefly trace the historical basis of this conclusion. Modern medicine emerged in the nineteenth century through two revolutionary changes in clinical orientation⁵. The first was the self-conscious endeavour to correlate anatomic pathology to clinical signs and symptoms. This clinico-anatomic approach was the clearest expression of a new scientific objectivism applied to medicine, and is largely credited to the Parisian School at the turn of the nineteenth century. The coupling of Pinel's *Nosologie Philosophique* (1798), an attempt to establish the typical picture of a disease and disregarding individual variations to Bichat's *Anatomie Generale* (1801), that related anatomic findings to pathology and clinical medicine, marks a radical departure from previous nosological endeavours. This clinical orientation led to the recognition of new disease entities, which seemed to favour an ontological concept of disease. This refers to the categorization of illness into a well-circumscribed species, arising from without and invading the body to become expressive of its own singular pathological character. This attitude toward disease as essentially autonomous was soon recognized as insufficient to explain or offer an understanding of cause. The response to this inadequacy was soon expounded by an alternate approach: physiology, an experimental science, was to distinguish an experimentally-based medicine. Broussais' early attempt at an alternate functional or physiological approach was crucial in establishing the basic principle that 'the phenomena of disease coincided essentially with those of health from which they differed only in terms of intensity'⁵ (p 49).

Although by the 1820s Broussais recognized that the normal and the pathological were to be viewed as varied values on a continuum of quantifiable function, this experimental ethos did not fully emerge until Bernard's classic studies of glucose metabolism in mid-century. The crucial step against an ontological organization of medical theory was taken in the recognition that a physiological conception of disease was not bound to a rigid, or self-contained definition of any particular malady. Since each individual differed from another, and since life was subjected to an infinite variety of changed conditions, every sick person really represented his own disease⁵. Bernard recognized this variation, and further appreciated that pathological predispositions were nothing but special physiological problems. Thus, nosology was no more than a practical makeshift to be disregarded by the medical scientist, and the line demarcating the normal from the abnormal, although drawn on a distribution curve of objectified criteria, truly took its meaning from the patient. The clinic no longer exclusively defined the disease but offered a context by which physiological function might be studied in its variation.

The competing theories of medicine

These competing approaches towards organizing a theory of medicine, the ontological versus the physiological, have persisted in a muted form today (muted because they have largely merged). The ontological approach remains as we seek single aetiological agents for disease, ie a bacterium or an altered gene. To bound disease by definite causes however is to forget Virchow's crucial cautionary note:

Not life under abnormal conditions, not the disturbances as such, engenders a disease, rather disease begins with insufficiency of the regulatory response⁶.

In other words, pathology may be initiated by a pathogen, but the disease is the response to the insult to organismal integrity. The struggle to maintain homeostasis is the disease proper, and this then revolves about the establishment of the normal physiology. Thus, the deviation, viz. pathology, is again construed in the context of the patient. It is this dialectic between an ontological self-sufficiency and an explanatory physiology that reflects a fundamental, and unanswered conflict in medical theory. The prevalent response of the physiologists was to search for ever-more fundamental units of function that might explain disease.

A profound irony emerged as medicine assumed its new legitimacy in laboratory-based sciences: medicine lost its own boundaries and focus. No longer possessing its own theory, medicine sought its explanatory roots in other scientific disciplines and accepted its nosological ontology as derivative *from* those endeavours. A medicine constructed on its own principles was subsumed to a medicine based on other sciences. These would define the basis of medical theory, offer it their criteria, and regulate disease as designations defined by sciences that had in fact no normative. Physics has no *value* in its descriptive practice, but physiology does in the context of suffering. The medical norm is derived from the patient in his cultural milieu, and the neutralist views physical states outside of such a relative construct. Disease is but an experiment of nature, a variation that confers the substrate for evolutionary dynamics. Illness is then the thwarting of goals normally open in that culture, pain or discomfort, or possibly dysaesthetic elements. In the neutralist view, disease becomes an explanation of illness states, and such designations are in some fundamental sense, arbitrary and require no special extra-physiological laws or concept for explanation. This was Broussais' view, and in the wake of his revolutionary thinking, he bestowed not only a new objectivity for medicine, but stole its own scientific ethos. We are left with that quandary.

Canguilhem traces how the mid-nineteenth century served as a crucible for sorting out our modern orientation towards disease, between these ontological and dynamic conceptions⁵. Pasteur's germ theory is an excellent representative of the former. However, the appreciation of the highly varied and complex state of an organism with regard to pathogenic agents or predisposition to disease has somewhat humbled even these erstwhile successful models. Numerous holistic schools of thought have developed from this position in the twentieth century, in the hope of logically extending nineteenth century homeostatic models of health. More dominant is the tradition of French and German reductionism, which was clearly expressed in the urgency to quantify physiological processes.

The prospect of quantitation has a dual nature - it offers the objectification that a chemo-mechanistic biology sought, and at the same time accurately reflects the instability and irregularity of biological processes. To what degree are arithmetic norms descriptive of individual behaviour, or more precisely, to what degree are organic phenomena reducible to chemo-mechanical laws? This question helps us to comprehend Bernard's notion of the pathological, and by historical extension, our own. He accepted the essential continuity of the normal-pathological axis, but at the same time that he regarded biochemistry and inorganic chemistry as following the same laws, he steadfastly held to the unique dynamics of biological systems. Canguilhem perceived the ambiguity in Bernard's scientific programme as a deceptive mingling of quantitative and qualitative concepts in describing the pathological, and the insecurity of defining disease as 'an objective reality accessible to quantitative scientific knowledge'⁵ (p 76). The story of nineteenth century physiology and medicine may largely be reduced to this problem. Does it remain as our own? We must return to this question.

The Darwinian watershed

It seems hardly reasonable to expect that a pre-Darwinian model of biological order and function suffices to construct a theoretical medicine. It is commonplace to note that with the publication of *Origin of Species*, a revolution in the manner in which we perceive the biological cosmos began. Only six generations later, we are still adjusting to a reorientation of Man in nature, jostled from his anthropocentric primacy, to a more circumspect view of himself. I need not argue whether *Origin of Species* was the beginning or the culmination of this evolutionary ethos, for in either case, it clearly was its watershed. Our anatomy, extending now to the gene, has been scrutinized and carefully examined from a new perspective. Slowly we continue to uncover ourselves in this light of Darwin's theory.

An important response to this challenge may be found in a science created in the wake of Darwinism's revolutionary challenge. Immunology is one of the unique products of the Darwinian age: born in the controversies of that fresh announcement that all species, including ourselves, were not static entities, but subject to change as a result of vicissitudes of time and happenstance. Each life form was thus challenged to respond in endless competition, and collectively adapt. Although not explicitly designated by Darwin, a crucial ingredient in this conception is a model of immunity that must be constructed in light of competitive dynamics. That Darwin's theory postulated an ever-changing species, defined by evolutionary necessity, immediately raises doubts as to what *is* the organism. In this schema, the organism is not *given*, but *evolves*. Always adapting, it is always changing. Thus the very core issue of identity is for the first time raised as a problem. The differentiation of self from non-self became a specific scientific problem. First, if the self is not given, it must be defined in process, which in turn requires a mechanism to identify, *self*, and second, in a dynamic interaction of self and other as an articulated problem, self-identifying processes must in turn recognize the other, the foreign. This latter concern confers the mechanism as fundamentally cognitive. The immune system assumes the role of identifying the foreign, a cognitive function, and

like the nervous system, it has the second function of response, ie effector mechanisms with which to defend. The first problem of self-identification is addressed by an immune system that defines the host. The linked destructive mechanisms protect that identity. Note, the first issue is *identity*, the secondary issue is host *integrity*. Together, establishment of identity and subsequent integrity-preservation functions, to a large extent determine the organism's capacity to compete with others. Darwinism then implicitly demanded an elaboration of an auxiliary science to deal with this aspect of such dynamic interaction.

Immunology is very much a post-Darwinian science. It began as the aetiological agents of infectious diseases were defined in the 1870s and 1880s, and the corresponding principle that these maladies were the expression of a conflict between species, man and pathogen. When Koch and Pasteur established the aetiological basis of infectious diseases as caused by bacteria, a powerful impetus was given to discern how the host reacted to such insult⁷. Infection is a complex equation of pathogen on one side and inflammatory responses on the other. This was a particular aspect of the problem of how species competed in the context of evolutionary concerns. For some, this was an explicit issue, but in most cases this broad view remained a hidden agenda. The common problem regarding the pathobiology of the host response, namely the inflammatory reaction, was soon discerned as a complex of both specific and non-specific reactions: those classically described symptoms and signs of inflammation (eg arising from wounds or aseptic fevers) were differentiated from the specific immune responses elicited by a particular infecting organism. Darwin did not deal with these issues, but they were articulated as an explicit problem ironically in the year of his death, 1882. The theoretical and experimental origins of immunology was first enunciated along those principles, by Elie Metchnikoff, a Russian zoologist who began his research career in the mid 1860s, shortly after the publication of *Origin of Species*. He was the first to recognize immunity as an active response of the host to infection. The immune reaction was comprised of specialized and directed inflammatory processes, which normally occurred upon any insult to the integrity of the organism. Thus immunity was a sub-set of inflammation that included common repair mechanisms stimulated by injury of any type, as well as surveillance and destruction of effete or malignant cells⁸⁻¹⁰.

In this scheme, the pathological was presented, not as a quantitative physiology or an anatomic structure-function correlation, but as a problem in the context of Darwinian dynamics. The theory of *orthobiosis* advocated by Elie Metchnikoff is not currently discussed as such, but its basic formulation, hidden under other guises, represents a very different orientation to health and disease^{11,12}. Metchnikoff postulated orthobiosis as a striving of the organism towards an ideal of harmonized growth, function and reproduction. 'Physiological inflammation' was the mechanism whereby the organism sought to mould disparate cellular lineages into common collective purpose¹³. This process, and it was very much construed as a dynamic biology, was understood to serve as the arbiter of organismal identity. Effete, senile, damaged, malignant or infected cells were eliminated by specialized cells of the immune apparatus. Metchnikoff revolutionized biology by

asserting that immunity was an active process; selfhood was under constant assault, and the phagocyte was the mediator of the process that defined host integrity. It was both teleological, and incipiently vitalistic, in the sense that for Metchnikoff, *what* determined selfless was simply the striving of the phagocytes for their aggrandizement. Their activity, competing with other cells lines, was Darwin's struggle of species turned inward into a struggle within the organism. (The argument has again been advocated by Buss¹⁴ and we have had occasion to critique this modern version elsewhere^{9,15}). Thus immunity, quickly subsumed beneath the banner of infectious diseases, was in fact originally proposed as the general purveyor of host identity. Only one of its functions was to preserve host integrity from invading pathogens; more fundamentally, immune processes were to *define* the organism by determining self from non-self and thereby confer *identity*^{9,10}.

One must not view Metchnikoff's formulation as totally unique, for the Darwinian paradigm was broadly applied. It was used to explain development¹⁶ and all kinds of adaptive behaviour and learning¹⁷. In the case of immunology, recall that Ehrlich first proposed a selectionist theory for antibody production. As he originally envisioned, antigen randomly selected 'receptors' by chemical affinity characteristics, which upon appropriate stimulation would secrete excess receptors [*sic*. antibodies] into the circulation¹⁸. Darwinian thinking was also widely applied to theories of the mind¹⁹, most notably by Sigmund Freud²⁰. Darwinian assumptions pervaded the discipline of child psychology from which Freud drew, but more generally the historical reductionism, the importance of sexuality and the archaic nature of the unconscious, as well as major psychical concepts like those of fixation and regression were directly derived from biological principles in vogue at the time. Freud himself was keenly aware of his indebtedness to Darwin and 'recommended that the study of evolution be included in every prospective psychoanalyst's program of training'²¹ (p 276). For our purposes, the common element to note is the essential characteristic of a disharmonious state. Freud, like Metchnikoff viewed the organism as composed of competing drives, striving for an unattainable ideal harmony. For Freud, the ego must contain and direct the *id*; the persona was a fractured entity actively seeking wholeness. With a model of appropriate psychosexual development providing the standard for the ideal state of mental health, Freudian psychoanalysis directs itself towards the same orthobiosis advocated by Metchnikoff, albeit in a different pathological context. In each case (Freud and Metchnikoff) health becomes the problematic ideal. As Freud stated, 'a normal ego . . . is, like normality in general, an ideal fiction'²² (p 79).

Darwinian medicine?

In response to Darwinism, a profoundly novel concept of health was proposed: no longer are the ancient humours in balance, but the organism's instinctual drives and cellular components are in conflict. Health is not given, it became an *ideal* to be actively sought. In this view, the potential disharmonious assembly of evolved constituents and drives must now strive for harmony. For Metchnikoff, this was an active process, one not given, but attained in conflict. He was severely monistic, not on an axis

of normal to pathological, but saw self-actualization as mediated by an essentially pathological process, the expression of a centre of activity, phagocytes, viz. immunity. It is at this interface of physiology (the present) and evolution (the historical) that a conceptual integration must be made. In large measure, Metchnikoff's end point is the same viz. pathology, in that his programme hoped to illustrate health, and more directly he endeavoured to harness his immune concepts to establish the ideal norm (harmony) and annul disease (through *orthobiosis*). But the derivative function of his thinking, like others profoundly influenced by Darwin, places him outside the thrust of pre-Darwinian conceptions concerning the nature of pathology and its dynamic role in defining health.

There has been little attention as to why the emergence of modern pathology was unable explicitly to incorporate the profound impact of the Darwinian hypothesis. The interface between evolutionary theory and the establishment of physiology as a biochemical discipline has rarely been explored. It is as if the two major themes of biology were enacted as a *pas de deux*, where each hardly acknowledged the other. Yet this is to deny a major conceptual revolution. The post-Darwinian orientation is completely reversed from Bernard's concepts. Bernard assumed a balanced physiology (quantitatively and qualitatively normalized). Metchnikoff allowed no such initial harmony, for as an evolutionist, he regarded the organism as forever striving towards perfection. Health was attained, actively, and never given: beginning with disharmony, harmonization became the ideal. Pathology then was potentially restorative; 'physiological inflammation' was his code for that curative process. Both agreed on the organism's striving for health, but Bernard assumed an organism defined by the ancient conception of humours in balance, what was only later called homeostasis. This view was based on the organism as a stable entity - as given. From evolutionary problematics, however, the organism is not regarded as 'given' at all, but is a complex product of its individual history in interaction with both its environment and its adapted selfhood.

The organism functions in a context of experience, ie complex interactive dynamics. Hierarchical, interactive networks defy a single molecular definition of selfhood. The adaptive organism resides squarely in our understanding of a *process* orientation. Such a view must then place cognitive processes at a key focus of any attempt to define the individual. Perceptual faculties are coordinated to effector responses and serve as a crucial dimension of registering adaptive criteria, to which we must relate not only traditional nervous system behaviour, but the entire cognitive axis that includes the immune system and the modulation of both by the psycho-endocrine systems²³. As these systems are in a sense open-ended to the world, they fail the negative feedback controls characteristic of simpler mechanical models of physiology, and rely instead on hierarchical systems that create emergent properties and exhibit self-organization. Only by appreciating the dialectical character of such an interactive individual can an organismal orientation account for the profound influence that experience confers on identity. In short, the given character of the organism, what we might now call its genetic signature, is an insufficient account of identity.

Conclusion

I have employed the conceptual origins of immunology as my case study of a post-Darwinian vision of the organism and the resultant thesis of the normative and health. There is little question that immunology, truly a science of the twentieth century, has exerted a profound influence on our conception of the organism. Here we have extended immunology well beyond the particular parameters of the discipline proper. I do so only to demarcate how a post-Darwinian view of the organism might be translated to our theoretic understanding of medicine. It is in this context of a theory of medicine that I believe our understanding of immunity, especially in the analysis of its generative theory, has broad-ranging implications for notions of health, disease, and the patient.

In summary, the pre-Darwinian notion of the *norm* has been challenged by another normative, the *ideal*. As the organism strives for its self-aggrandizement, adaptation and competition are the key features in an evolutionary world. To assume an organism is simply *maintaining* its own homeostatic balance is to ignore the dynamic requirements of an interactive entity defined in a context beyond self-regulation, to incorporate environmental adjustment as a crucial feature of its nature. The evolving organism is always striving for its ideal niche. The best adapted individuals survive, the species thus evolves. This was Darwin's crucial lesson, and beyond its implications for evolutionary biology *per se*, this revolutionary theory inexorably influenced our metaphysical understanding of life. I propose that this profound reorientation has also seeped into our medical consciousness as part of a new cultural normative. The 'normal' is being replaced with the 'ideal'. The general notion of progress, a distinctly Western concept²⁴, has become refined to a particular understanding not of a goal, but of an elusive perfection. To be normal is simply to quantitate the most frequent. To be ill, as the surveys show, is normal. To suffer ailments is expected. To become sick is likely. Health then is not *normal*, it has become an ideal. Like the biblical patriarchs, we now strive towards uninterrupted vigour for 120 years. That is the basis of health care reform: changing expectations derived from promises yet to be met and dreams yet to be dreamt.

Acknowledgments: Portions of this essay are excerpted from the forthcoming book, *The Immune Self: Theory or Metaphor?* Cambridge, UK: Cambridge University Press, 1994.

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(Accepted 21 July 1993)