Singular Selves
Historical Issues and Contemporary Debates in Immunology
AM Moulin, A Cambrosio, Eds

Multiple splendor. The one and many versions of the immune system

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At first view, an interdisciplinary meeting on immunology would seem to be facilitated by the increasing circulation of immunological concepts in daily life, from the "Self" to "T4." The notions of immune system and immunity have spread far beyond the borders of the scientific community and generated a great wave of interest in a broad audience. This circulation reveals shared views between professionals and non-professionals of immunology on the meanings of defense and survival, identity and foreignness, recognition and rejection.

These popular views may be abhorrent to immunologists who prefer sophisticated[1] exchanges about refined theories of their own, when, for example, they strive to replace the antiquated Self/NonSelf framework with other theories such as the "danger" one, and rely on fastidious experimental procedures to test their hypotheses. These laboratory experiments are nevertheless human constructs. There is no doubt that the popularity of allegedly simplistic views on immunity bears witness to a profound resonance between specialised immunological topics and everyman's interest in self-defense and the curing powers of nature. This suggests the existence of an anthropological background[2] that articulates a network of meanings between scientists and their clients[3].

My chapter stands at the junction between the public and private (or scientific and cultural) uses of immunology. I suggest that common reveries underlie immunological concepts, and that the metaphysical character of the immune system turns it into an anthropological tool available for the interpretation of various cultural patterns. In other words, the immune system not only functions as a cultural frame inside the Western sphere, but may also be used as a transcultural key. The immune system behaves as a coded language[4] that can be reformatted, glossed, translated, distorted, but unquestionably is a tool for communication.

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1. "In the original sense of the word", as Rolk Zinkernagel remarks in his presentation of his model of the immune system. Localization, dose and time of antigens determine immune reactivity. Semin Immunol – Self-NonSelf revisited, 2000; 12: 169.
2. This chapter is a completely reformulated version of my earlier paper: Un objet scientifique à la charnière des sciences biologiques et sociales : le système immunitaire. Rio de Janeiro: Historia, Ciências, Saude, Manguinhos; 1996; 2. 300-18.
3. Kleinman A. Medicine's symbolic reality. On a central problem in the philosophy of medicine. Inquiry 1973; 16: 206-13.
4. Moulin AM. Text and context in biology. Poetics Today 1988, 9: 145-61.

Mythologies

Immunologists in their popular books often make reference to mythology:

> Myth is constituted by the loss of the historical quality of things, things lose the memory that they once were made. The world... comes out of myth as a harmonious display of essences[5].

The immune system is supposed to say something about the doings of Nature. In referring to myths, immunologists implicitly acknowledge the continuity between common sense and immunological concerns – what I call the anthropological background.

In his book "La sculpture du vivant,"[6] the immunologist Jean-Claude Ameisen refers to the myths of antique Greece on immortality. He recalls how mythology expressed dreams of immortalizing the human species and picks up Ariadne's thread that leads to contemporary attempts to postpone untimely death through manipulation of the immune system, defined as an ever-changing balance between destructive and constructive forces, embedded in its structure. He locates in mythology remote analogs of standardized immunological techniques. The magician Medea, for example, in order to rejuvenate his father-in-law Eson, opened up his veins and replaced his extenuated blood with plant juices and extracts from animals known for their longevity. In a similar way, the goddess Demeter anointed Eleusis king's son with ambrosia in order to turn him into an immortal. However, when she wanted to test his immunity by passing him through the flame, the glow of fire woke up the mother who wrought the child from his divine nurse[7]. It would be since this time that children cry when they are vaccinated...![8] In another tale, the story of Achillus's heel might also be quoted as a fair example of immunological defect.

But let us turn to harder texts.

Biology

Nowadays the immune system is currently conceived of as a network of cells and molecules endowed with a function in the body called immunity. Immunity, once pointing to a specific property, intervening only in very special cases for adaptive purposes to changes in the environment, has been turned into a general property incessantly involved in the survival of the organism. From an exceptional event linked to the onset of an epidemic or the meeting with a vaccinator's lancet, immunity has become a permanent function of the body, designed to sustain its ongoing combat against disease and death.

The immunological viewpoint is now accepted as one fundamental facet of bodily activities, of physiology and pathology, in the same way as evolution, development, or reproduction. Immunity has become a basic function, ranking beside the other great ones such as nutrition, circulation, respiration. The notion of immune system has led to convergence between scientists operating in distinct fields such as transplantation,

5 Barthes R. Mythologies. transl. by Lavers A. New York: Hill and Wang; 1972.
6. Paris: Seuil; 1999.
7. Chuvin P. La mythologie grecque. Paris: Fayard; 1992.
8. Moulin AM. Immunologie. In: Dictionnaire culturel des sciences. Paris: Editions du Regard; (in press).

zoology, genetics and favored the explosion of immunology[9] in the 1970s, which, in terms of grants and academic prestige, ranked high among the leading disciplines in biomedical sciences[10].

The definition of the immune system as an adaptive system evolving over time both raised and solved the issue of autoimmunity. Nineteenth century biologists had treated the possible existence of "autoimmunity" (immunity directed toward the components of the body) as a major taboo. Immunologists postulated the presence of ingenious mechanisms that would ensure the observation of the taboo by the cellular machinery[11]. Paul Ehrlich invented a regulatory mechanism consisting of antibodies able to knock out any emerging autoantibodies in the wake of immunization[12]. But the permanent destruction of elements belonging to the organism was contradictory per se[13]. This was a paradox: in order to maintain its integrity, the organism had to anticipate and destroy potentially obnoxious elements belonging to the fabric of the body.

This criticism led researchers to abandon Ehrlich's taboo of autotoxicity and to acknowledge a physiological level of silent autoimmunity. In the 1960s, it was hypothesized that this autoimmunity, once amplified, gave birth to autoimmune diseases, a framework which, firstly restricted to some rare anemias and experimental syndromes, soon included affections formerly recognized in other nosological frameworks and that were poorly understood, such as diabetes and multiple sclerosis. The idea that pathological autoimmunity was a mere amplification of a low-rate physiological reaction revived the so-called Broussais problem, i.e., the debate on the existence of a sharp divide between the normal and the pathological, subsequently discussed by Georges Canguilhem[14].

The theory of generalized autoimmunity acquired even more strength with the vogue of idiotypic regulatory networks[15]. Antonio Coutinho gave to this idiotypic regulation a literary formulation, when he tried to emphasize the conviviality of networks permanently regulating the mounting of an immune response. He was pictured in the French daily newspaper *Libération*, with two mice in his hand, one black and one white, and the following humorous caption: "Immunology, a school of tolerance!"[16] But Coutinho carefully refrained from saying what tolerance exactly was about: the enjoyment or the stoic acceptance of diversity, or the unawareness of differences, obviously corresponding to very different patterns of tolerance.

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9. Moulin AM. Le dernier langage de la médecine. De Pasteur au Sida. Paris: Presses universitaires de France; 1994.
10. Nossal GB. Trials and triumphs of immunology in the 1980s. Immunology Today 1988; 9: 286-91.
11. Silverstein AM. Cell Immunol 1986; 97: 173-88.
12. Ehrlich P. Zur Theorie der Lysinwirkung (Uber Haemolysine). Berl Klinische Wochenschr 1901, 38. 569.
13. See comments in Jacquemart F, Coutinho A. Observer, immune system and their respective objects. In: Sercarz EE, et al., eds. The semiotics of cellular communication in the immune system. NATO ASI Series H. Berlin: Springer Verlag; 1988; 23: 173.
14. Canguilhem G. Le normal et le pathologique. Paris: Presses universitaires de France; 1988. Moulin AM. La médecine moderne selon Georges Canguilhem. Concepts en attente. In: Georges Canguilhem, philosophe, historien des sciences. Paris: Albin Michel; 1993. p. 121-34.
15. Jerne NK. Towards a network theory of the immune system. Ann Immunol 1974; 125C. 373. Urbain J, et al. Idiotypic regulation of the immune system by the induction of antibodies against anti-idiotypic antibodies. Proc Natl Acad Sci USA 1977; 74: 5126. Jerne NK, Rolland J, Cazenave PA. Recurrent idiotypes and internal images. EMBO J 1982; 1: 243. Jerne NK. Idiotypic networks and other preconceived ideas. Immunol Rev 1984; 79: 5-24.
16. Liberation 22 May 1991, p. 20.

As autoimmunity no longer pointed to pathological reactions, it became available for more general functions hereafter: self-recognition and internal communication. Coutinho speculated about the existence of a distinction between a peripheral immune system and a central one featuring high "connectivity" and multireactivity[17]. He characterized the core system by a high level of regulation and oscillatory mode of work. In case of disease, the immune system tends to function according to an unusual clonal mode, including expansion and hyperproduction of deleterious molecules and antibodies. If one accepted Coutinho's suggestion, then one might consider as a form of therapeutics the introduction of autoantibodies, allowing the body to reconquer its usual balance and modify its microenvironment. The immune system would up- or downregulate the activity of antibodies directed against physiological targets belonging to other systems of the body such as the cardio-vascular, endocrine, or nervous systems.

The relationship between germs and their hosts covers a multiplicity of situations, from mutual assistance to irreconcilable fighting through oscillating phases. Parasites such as *Plasmodium*, the agent of malaria, offer fascinating models of this relationship. Adults, in endemic areas, survive with an enormous *Plasmodium* burden (multiple parasites in their blood cells) that would kill naive people (or young children) exposed for the first time to the infection.

Even if few therapeutics of this kind have passed into current use, some have suggested manipulating the immune system by introducing molecules directed against the self-components. Even if all diseases are not necessarily conceivable in immunological terms, they could be immunologically manipulated. Monoclonal antibodies offering the promise of "exquisite specificity," the Eldorado of immunologists, are candidate therapeutic agents to control hypertension. They might, in addition, neutralize the heat shock proteins released in acute infections in intensive care patients. Immunorestitution, a new password, points to the recovery of a putatively lost immune integrity. Here we may be forced to take into consideration Georges Canguilhem's caveat, "the cure never means the return to the cellular innocence."

Self/NonSelf in danger

A chapter of this book recalls in detail how Elie Metchnikoff elaborated his theory of immunity[18]. Metchnikoff's construct underwent sharp criticism by those who felt that it smelt of teleology and was heavily dependent on a philosophical agenda that included notions such as the pursuit of harmony and of a peaceful and timely mode of passing away, in short, natural death rather than immortality. Phagocytosis had for many years been relegated to a minor rank before being rehabilitated as innate immunity which is considered as a first line of defense against the hazards of life during evolution.

Following Burnet's work in the 1960s, the Self and NonSelf approach was adopted for several decades as a satisfactory background theory although from the very beginning, the

17. Coutinho A. Beyond clonal selection and network. Immunol Rev 1989; 110: 66-87.
18. Metchnikoff E. Leçons sur la pathologie comparée de l'inflammation. Paris: Masson; 1891. Tauber AI. Metchnikoff and the origins of immunology. From metaphor to theory. New York: Oxford University Press; 1991.

biological nature of the Self seemed elusive[19]. After some attempts at its characterization, its promoter Frank Macfarlane Burnet gave up trying to define it precisely. Yet many biologists resented the almost metaphysical assumptions underlying it and sought to drop it.

The so-called danger model was introduced by Polly Matzinger in the early 1990s[20] and reprised Melvin Cohn's proposal that whereas two cellular signals are required for the mounting of a specific immune response, one signal, if isolated, tolerizes the cell. Matzinger's idea is that one of these signals occurs when a cell is damaged (by a pathogen, for example) and when some inflammatory cytokines are released in the medium. A myriad of molecules, from NO oxides to heat-shock proteins act as chaperones and can thus trigger an immune response. The danger model, by interweaving non-specificity (damage) and specificity (recognition effected by antigen-presenting cells), follows the tradition of associating non specific and specific components, a "form" and a "matter," in the description of the immune response. The danger model epitomizes the famous statement that ontogeny reproduces phylogeny, the non-specific component being the more primitive.

But the phrasing of the "danger model" does no more to explain the explosion of an immune response than the Self-NonSelf model; it is not more natural for a cell to sense danger than to preserve its integrity. In other words, to feel danger is very analogous to looking after its own Self. As David Napier argues[21], sensing danger refers to the sense of the integrity and this integrity in turn refers to something or to a substance that might be a kind of Self.

Janeway, approved by Matzinger, has gone further by suggesting that all cells, when prompted to die before the due time for apoptosis, can deliver signals of the first kind[22]. For Janeway, this represents the most archaic line of defense. All cells, at the beginning of our era, were probably able to deliver such a pathetic cry for help. If we accept Janeway's proposal, the immune system would no longer stand apart in the body with its anatomical basis, its central and peripheral organs, reflex and regulatory pathways. Immunity would tend to become a general property of all cells and living tissues, as indeed was the case in organisms before the division of labor: this is the case of protozoa such as amoebas, a model favored by Cohn and Langman in their version of immunity[23]. In other words, the immune system would stand for the body.

Even if we question this way of animating the cellular dialogue and endowing the machinery of molecular biology with human affects and behavior, we must acknowledge the influence of this immune system talk on medical language.

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19. Moulin AM. La métaphore du soi et le tabou de l'autoimmunité In: Bessis M, Bernard J, Debru C, Eds Le soi et le non-soi. Paris: Seuil; 1990. p. 55-68 The so-called model of the peptidic self led to distinguish a somatic self and an immunological self: Kourilsky P, Claverie JM. Le modèle du soi peptidique Med/Sci 1988; 4: 177-83. Löwy I The immunological construction of the Self. In: Tauber AI, Ed. Organism and the origins of Self. Boston: Kluwer, 1991 p. 43-75.

20. Matzinger P. Tolerance, danger and the extended family. Ann Rev Immunol 1994; 12: 991-1045

21. Napier D. The age of immunology (forthcoming).

22. Janeway CA Jr Innate immunity: the virtues of a non clonal system of recognition. Cell 1997, 91: 295-98. Matzinger P. An innate sense of danger. Semin Immunol 1998; 10: 399-415.

23. Langman RE The immune system. San Diego: Academic Press; 1989.

Medical

Following the direction sketched above, the complexity of the immune system has considerably increased. If the definition of the immune system as a network of cells and molecules makes the link with the past, the identification of these cells and molecules has considerably progressed, and the tools of molecular biology have permitted the dissection of numerous receptors and cytokines[24] which foster great expectations from these new molecules. The popular metaphor of the immune system as an orchestra, once invented by the immunologist Fred Gershon, implies a variety of instruments and musicians, or possibly the replacement of the director by many secondary choir leaders. In keeping with the music metaphor, one might say that immunity is phrased as identification of signals and their integration into the cellular symphony. Genetic orientations are built into the fabric of the immune system and determine its power to mount a response against ordinary and extraordinary pathogens. Whether an imperfect response against an antigen is due to ineffective antibodies, and/or a genetic incapacity to mobilize appropriate categories of cells and/or the propensity to develop illness in a given organ, in any case, the global response for all these events has to be found in the immune system and its activity. The immune system has thus emerged as a cause, in the fullest, "Aristotelian" sense of the word: a formal, material, final cause of pathogenesis and recovery[25]. It has integrated the three time dimensions by including infections and traumas of the past, present encounters with environmental hazards, and prospective risks embodied in genes involved in susceptibility to disease. Among other issues, the immune system makes it possible to resume the traditional debate on "soil and germ".

But an epistemological difficulty is linked to the fluidity of the framework articulating medical discourse. So many reaction cascades are available for explaining a disorder that it is hard to choose between various explanatory pathways. Let us illustrate the case by telling a story about a patient who suffered from an intriguing infection. An intestinal worm, usually restricted to the guts, had honed in on the most bizarre locations; it had colonized the stomach in spite of the acidity of its content and passed the meningeal barrier, reputed to be impermeable to macroparasites. It was hard to decide whether some defect in immunity had caused this dissemination or whether this parasitic burden had induced an impairment of immunity. Furthermore, it was impossible, from a holistic point of view, to determine the sequence of the events (infections, misery, sexually-transmitted diseases...) that had led to the present condition. The discovery, years later, that the patient was infected by human T-cell leukemia virus (HTLV), introduced a further additional cause for immunosuppression, without solving the sequence of pathological phenomena.

The immune system conjures up a graph where it is possible to plot the onset, the development and the outcome of pathological processes. It provides a response to inquiries on pathogenesis for poorly understood disorders, somatic or even psychological. In Western countries, practitioners currently mention modified immunity to account for various

24. Moulin AM, Silverstein AM. History of immunophysiology. In: Oppenheim JJ, Schevach E, Eds. Immunophysiology. The role of cells and cytokines in immunity and inflammation. Oxford: Oxford University Press; 1990. p. 3-13.
25. Moulin AM. The dilemma of medical causality and the issue of biological individuality. In: Deleskamp-Hayes C, Gardell Cutter MA, Eds. Science, technology and the art of medicine: European-American dialogues. Dordrecht: Reidel; 1994. p. 153-64.

health problems: flu, common cold, chronic affections, or conversely incriminate pregnancy, sorrows, travelling, depression in a hypothetic immune dysfunction.

We have seen this before with the expansion of the notion of "stress" into a growing number of areas[26]. In the same way the immune system is now being presented as crucial for survival as well as quality of life, and immunomodulation is advertised as the most effective and softest management of disease, similarly, stress research in the past fostered the idea that the understanding of stress would yield clues for a healthier and happier life.

The concept of stress was invented by Hans Selye in the 1930s to account for the shock vascular syndrome in animal experimentation. It consisted of inflammatory reactions and corticoid secretion after aggression, and was soon extended to the response to various kinds of traumas. In the 1950s, in the context of cold war and messianic expectations of economic prosperity on the Western side, stress was endowed with new and extended meanings and became synonymous with mobilizing the energy of the organism and possibly responsible for deleterious side-effects. How Red Riding Hood meets the wolf and successfully overcomes her panic and runs away, has been told as a successful story of stress. According to Selye who greatly contributed to popularizing the notion[27], stress ultimately meant the hardship of life: unemployment, racial vexations, sorrow, mourning and suffering in general[28]. Stress was thereafter included in the factors influencing the level of immune defense and lately, stress has been incorporated into the domain of psycho-neuroimmunology[29].

Like stress, once primarily a scientific object modeled and studied in the laboratory, the immune system has become available as a framework for narratives of subjective experiences of illness and recovery. Solicited once by a journalist working for the tabloid press, I was surprised to be confronted with what I misunderstood as an appetite for the latest news about the immune system. I did my best to explain about apoptosis and lymphocyte stimulation, autoimmunity and the promise of new vaccines. The journalist listened to me earnestly without making notes and claimed that she understood everything. Imagine my surprise when upon reading the digest of my lectures in the next issue of the journal, I discovered how I had taught the reader and subsequently the readers how to manipulate his or her own immune system by feeding it with spinach and yolk egg and adopting the appropriate lifestyle. In short, a fashionable taste for immunology had crept into patients' complaints, taking its place beside the French *crise de foie* or the Japanese *katakori*[30], when immunity literally exploded onto the scene of popular culture with the AIDS epidemics[31].

A good example of the availability of the immune system as an explanatory framework in this period is the convergence of observations of an unknown syndrome that brought

26. Selye H. The development of the stress concept. In: Parvez H, et al , Eds. Advances in experimental medicine. A centenary tribute to C Bernard. North Holland Biomedical Press – Elsevier; 1980. p 43-69. See also Young A. The discourse on stress and the reproduction of conventional knowledge. Soc Sci Med 1980 ; 14B : 133-46. Moulin AM. Une devise pour l'organisme. In: Résister. Autrement, March 1994; 22-9.

27. Selye H. The stress of life. New York: McGraw Hill; 1956; Stress without distress. New York: Lippincott; 1974; The stress of my life. New York: Van Nostrand Reinhold; 1979.

28. Cooper EL, Ed. Stress, immunity and aging. New York: Marcel Dekker; 1984.

29. Locke A, Ader R, et al. Foundations of psychoneuroimmunology. New York: Aldine, 1985 Corson SA. Historical and philosophical background of immunoneuromodulation. Intern J Neurosci 1988; 39: 283-7.

30. Kuriyama S. The historical origins of katakori. Jpn Rev 1997; 9: 122-49.

31. Seytre B Sida, les secrets d'une polémique. Paris: Presses universitaires de France, 1993.

together infections by so-called opportunistic germs who displayed their pathogenicity in organisms of altered resistance (due sometimes to the iatrogenesis once vilified by Ivan Illich). The immune system suddenly appeared in everybody's intellectual armamentarium. The AIDS virus emerged as a virus specifically damaging for the immune system, adhering electively to receptors carried by those cells whose defensive action is crucial for survival.

The role played by T4 helpers in the development of the disease and the delayed failure of defense mechanisms has since become commonsense[32]. The meaning of the immune defeat went far beyond the tissular damage induced by retroviruses. Immune diseases strike not only those whose defenses are biologically compromised but those who have them socially altered (such as drug addicts, for example) and whom the collapse of social solidarity leaves helpless – groups most at risk in industrialized societies or poor populations of the developing world[33].

When in 2000, seizing the opportunity of the big AIDS meeting in Durban, President Mbeki of South Africa contested the current interpretation of AIDS as a contagious disease, he raised an uproar of protest. At first sight, it seemed that President Mbeki concurred with the American scholar Peter Duesberg who, at an early stage of AIDS research, had contested the scientific focus on HIV viruses[34] and had suggested scientists investigate other factors contributing to the emergence of the disease[35]. But was President Mbeki expressing a biological opinion when he said that political men would do better to address poverty than stick to the scientific issue of virus receptors? He pointed to factors important in contamination and the development of the disease such as the lack of education and the absence of decent means of living. He sent the political message that these factors and all factors alike might be actually more relevant than the virus itself and in short pleaded that the construction of immunity was as much culturally and socially as naturally grounded.

An object which so successfully links together disparate things and people is likely to involve a remarkable degree of semiotic flexibility or adaptability to successive contexts and variable purposes in users' circles. To the complexity of the construct corresponds a "fluid epistemology," a software with which are built up understandings and *faux sens*. But is it possible to develop a fruitful concept without a multiplicity of meanings which stimulate creative minds and potentially leads to falsification of the original contents?

Over centuries, doctors have elaborated a theoretical model of health and disease around a central tenet. The Hippocratic paradigm pivoted around ideas of depletion and plethora.

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32 Many novels have focused on the tribulations of the immune system in AIDS or cancer-stricken protagonists, such as Navarre Y. Ce sont amis que vent emporte; Camus R. Elégies pour quelques-uns; Barbedette G. Mémoires d'un jeune homme devenu vieux. Hervé Guibert described the clinical stages of the immune drama in: À l'ami qui ne m'a pas sauvé la vie; the opportunistic infections in: Cytomegalovirus: the clinical trials. in: Le protocole compassionnel (1991), before the ultimate Paradis of 1992. See also Lévy J, Nouss A. Sida-fiction. Essais d'anthropologie romanesque. Lyon: Presses universitaires de Lyon; 1994. Rémission is the title chosen by Alain Roger.

33. Brandt A. AIDS and metaphor. Toward the social meaning of social diseases. Soc Res 1988; 55: 413-32.

34. Duesberg P. HIV is not the cause of AIDS. Science 1988; 241: 514-6; Human immunodeficiency virus and acquired immunodeficiency syndrome. Correlation but not causation. Proc Natl Acad USA 1989 86: 755-64.

35. The Barbara McClintock Project (1993), supported by the association Act-Up, was named after the American biologist McClintock, whose non-conventional approach to genetics was crowned by the Nobel Prize. It aims at stimulating alternative hypotheses to the role of the virus.

Based obsessively on the paradigm of female physiology, the management of the disease consisted of dietetic guidance and regular bloodlettings aiming at maintaining or restoring humoral balance.

This paradigm has survived and has co-evolved from the end of the nineteenth century with a new vision centered around the fight between host and pathogen. At that point, doctors declared war on germs and aimed at the eradication of the enemy[36]. They speculated on the sterilization of the living medium, purified of all possible bacteria, not only the skin but the mazes of the intestines, the pulmonary passages... The idea of stamping out microbes and consequently disease in individuals by all possible means held sway on the physicians' minds and paved the way for the craze of eradication which seized international organizations in the second half of the twentieth century.

Today, a more sober discourse has prevailed, admitting the necessity of compromises. The awareness of resistances has led to strategies other than scorched earth, lest like in the Gospel, fiercer demons replace the former ones, previously chased from the home. From the idea of diseases emerging sporadically in an immunocompromised host, one can easily move to the idea of a compromise between every organism and the host of microorganisms besieging it both inside and outside. This idea that the immune system is constantly challenged and challenging is supported by the observations of the heretofore unnoticed immunological daily life. In Senegal, the village of Dielmo has been the seat of an epidemiological watch for the last 15 years. All inhabitants have been investigated around the clock for fevers or other symptoms. The unrelenting surveillance system has allowed researchers to detect transient drops in immunity, most notably in the post-partum period, leading to malaria development in mothers exposed to contamination, during the first term after delivery[37]. Casual encounters with pathogen agents incessantly shift the equilibrium in the body. Vaccination long viewed as unequivocally protective has been reconceptualized as the activation of multiple pathways in the body, with complex consequences difficult to assess which do not exclude a degree of rearrangement in immune receptivity.

Public/private images

We have surmised, from a rapid review of transitional forms of discourse between scientists and non-scientists, that immunological language can transmit general human concerns: this is probably what Melvin Cohn means when he mentions the "loaded"[38] character of the Self and NonSelf issue. It is not so much because scientists consciously attempt to popularize their esoteric knowledge than because scientists first address and convince themselves: they need, in the first place, to make nature intelligible to themselves. The danger theory illustrates how immunologists wrap (and need to wrap) in simple words complex biochemical reactions in a way that make sense for them and incidentally for their human fellows.

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36. Gradmann C. Invisible enemies: bacteriology and the language of politics in imperial Germany. Science in Context 2000; 13. 9-30.

37. Trape JF Criteria for diagnosing clinial malaria among a semi-immune population exposed to intense and perennial transmission. Trans R Soc Trop Med Hyg 1983. 435-42; Increased susceptibility to malaria during the early post-partum period. N Engl J Med 2000; 343: 598-603.

38. Langman RE, Cohn M. Editorial introduction. Semin Immunol 2000; 12: 159.

This transition between private and public science can be illustrated by a beautiful video-clip, produced in the 1990s by a senior immunologist[39]. He sketched the main lines of the immune system in terms of a fictive correspondence between a scientist and his mother. The choice of the protagonists is no mere chance. The mother, once an actor in the immunological drama of pregnancy, plays the *confident* in the tragedy. She allows the hero to express his beliefs and doubts. Mother and son were once fusional partners. Quite naturally, it is she who shelters and fosters the early version of a dialogue between Self and 'former' Self and mediates it between Self and the Other.

"How can I tell you how happy I am when you disclose to me your secret garden". The Garden of Eden once harbored universal knowledge. And it is again the metaphor of the garden that comes to the mother's pen during her initiation into the "field" of research: "I cannot help of thinking of the immune system as a big park with its trees, groves and alleys."

But a second metaphor competes with the former one: "I see the immune system as the big book where Grand Pa used to record the main family events: but it is difficult to single out changes in an ever-changing context." The difficulty of defining a changing bodily identity is echoed by the anthropologist Sarah Richardson in her article on the "End of the Self"[40]: "The Self is constantly being defined anew". But Richardson goes further by adding: "which is another way of saying that it doesn't really exist at all." The mother does not go to this extreme. She quietly addresses the Heraclitean dimension of life, the constant dissolution of elements that nevertheless maintain a form: "the system is our guardian, on a permanent watch and fulfills its duty by confronting continuously what exists today with what existed once."

The permeability of the border between the outside world and the interior of the organism[41] is also grasped as obvious: " We are open wide to the outside world: we are the milieu for a host of microbes: is it not to acknowledge that we are not alien to the milieu that surrounds us?" This is the intuition that beings originating from the outside (such as viruses, for instance) may have been part of our inner selves. The mother takes a similar intuitive approach to autoimmunity, which stands in symmetrical relation to the invasion from the outside.

Gaston Bachelard used to invite scientists and philosophers to explore and exploit jointly the resources of the unconscious, in the name of creative rationality. This poetical correspondence about the immune system, an official creation of contemporary biology, illustrates the kinship between biological and metaphysical thinking. The development of immunology as a broad biological science opened a new semantic field. It can be considered as a language into which it has become possible to express and potentially to solve general questions raised by the interaction between man and his environment, Self and the Other, seen as another kind of Self[42]. "*Aime ton prochain comme toi-même,*" says the

39. Daëron M. Cellular and clinical immunology. Paris: INSERM U 255, Institut Curie. The clip was produced by the INSERM for a broad audience and school students.
40. Richardson S. The end of the Self. Discover 1996; 17: 80. I thank David Napier for having attracted my attention to this quotation.
41. Moulin AM. Le dernier langage de la médecine. De Pasteur au Sida. Paris: Presses universitaires de France; 1991.
42. Daëron M. Le système immunitaire ou « Connais-toi toi même ». Colloque de Cérizy Praxis et Cognition, 1988.

Gospel, suggesting a strange and profound kinship between the various selves. Many cosmogonies commonly associate love and hatred as the principles of being.

Anthropology: the Self and the Other

The immune system is one of the rational constructs of our contemporary biomedicine: the identification of the body as a network of cells and molecules, strong and fragile like the web of life. This powerful representation challenges the imagination: any event registered in the Book of the system is determining for survival, until we reach, with our back turned to the future, the term fixed for the end. This system might contain part of the secret of biological individuality and the key to decay and destruction. Whoever detains the password of the Self and NonSelf and is able of manipulating the immune system becomes the master of life and survival.

While questioning the divide between the Self and the NonSelf, immunology first of all meets the philosophical queries such as in Plato's Meno: Is to know a form of remembrance, in which case NonSelf is identified with Self (see Descartes's innate ideas), or invention, and then how is recognition possible? Christ says to the mystic: "Thou would not look for Me if thou had not already found Me."

Anthropologists were eager to point to the convergence between biological systems and other semiotic products of our culture. Donna Haraway, in the wake of her work on cyborgs and post-modern beings, described the immune system as a typical post-modern icon: she views the body, either healthy or ailing, as a robot ready to be assessed and manipulated by the medical profession[43]. Following the adventure of smallpox inoculation[44] immunization campaigns against other pestilential diseases have tried to synchronize populations' immune reactions to pathogens. The state increasingly controls bodies, exploiting the "governmentality of life." The politics of public health have dramatically modified demographic trends. Donna Haraway conceives the manipulations of both individual and collective bodies as typical of modern science, obsessed with warfare and accounting, unable to turn away from dichotomic and mechanistic thinking stigmatised by Evelyn Fox-Keller[45]. Only in recent years have epidemiologists organized the careful registration of "vaccination-related adverse events," and discovered a long-neglected potential source for original clues to pending questions on individual pathways of immunity. Moreover, while acknowledging the output of public health measures on the modern rise of populations, historians point to the authoritarian character of such measures, the break in traditional lifestyle and social customs. They point to the risk of exclusion for some social groups targeted as "vectors" of diseases[46].

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43. Haraway D. The biopolitics of post-modern bodies: determination of Self in the immune system discourse. Journal of Feminist Cultural Studies 1989; 11: 3-43.

44. Moulin AM, Ed. L'aventure de la vaccination. Paris: Fayard; 1996.

45. Fox-Keller E. Refiguring life: metaphors of twentieth-century biology. New York: Columbia University Press; 1995 Napier D. Penser 'vaccinologiquement'. une sélection qui n'est pas vraiment naturelle, ou les modèles sociaux du monde microbien. In. Moulin AM, Ed. L'aventure humaine de la vaccination. Paris: Fayard; p. 409-22.

46 Rivet D. Hygiénisme colonial et médicalisation de la société marocaine au temps du protectorat français: 1912–1956. In: Longuenesse E, Ed. Santé, médecine et société dans le monde arabe. Paris: L'Harmattan; 1995. p. 105-28. Peter JP. Dimensions mythiques des épidémies et Sida. Action et recherches sociales 1989; 3: 15-29. Weindling P. Medicine and holocaust. The case of typhus In: Löwy I, Ed Medicine and change. historical and sociological studies of medical innovation. Montrouge: Editions INSERM/John Libbey; 1993. p. 447-64.

Another American anthropologist, Emily Martin, has analyzed the vision of the immune system, on the basis of research conducted, in a hospital, on the reception of immunological knowledge[47]. In the 1960s, the immune system was seen as composed of a central organ such as the thymus and peripheral effectors such as the lymphatic glands, and displayed centrifugal and centripetal pathways. The latest version of the system is different and exhibits the characteristics of economic life in advanced societies: mobility, polyvalence, and plasticity[48]. Hermann Wolf Fridman chose to call his popular essay on immunity "The mobile brain" (*Le cerveau mobile*)[49]. The immune system integrates the passwords of the globalized world, in the age of liberal economic thinking. Rolf Zinkernagel sees in the interplay of time, antigen dose and location in the body the secret of flexible autoimmunity regulation[1]. In some of the "danger models," we have seen that any damaged cells can deliver a signal and trigger an immune response.

The traits of contemporary American society are reflected as well in immunology as in the postulates of interactionist sociology of the Chicago School. In the market place, everything is negotiable, and standards are unstable. In the immune system, not only lymphocytes, but most tissues can be recruited for immunological tricks, in the "ball of cells," according to Lewis Thomas's title.

Ethnography

The immune system can be interpreted as a post-modern icon, influenced by the contemporary currents. However, although immunological language is a Western code rooted in twentieth century biomedical knowledge, its use is far from being restricted to industrialized societies[50]. It can function as a reference in comparative anthropological studies. From a cross-cultural perspective, the immune system can be used to explore various cultural views of illness, judged at first sight as incommensurable[51]. The immune system has created a semiotic field where one can project distinct cultural patterns of disease, belonging to remote pasts or exotic countries, and made it possible to detect hidden links between apparently distant narratives of illness.

The anthropologist Dominique Buchillet has detected a variant of king Mythridate's myth of immunization among the Desana of Amazonia[52]. The destitute Indians resent the apparent good health of their former invaders and their insolent immunity to epidemics

47. Martin E. Flexible bodies: tracking immunity in American culture from the days of polio to the age of AIDS. Boston: Beacon Press; 1994.

48. Martin E. The cultural construction of gendered bodies: biology and metaphors of production and destruction. Ethnos 1989; 54: 143-60. Toward an anthropology of immunology: the body as nation state. Med Anthrop Q 1990; 4: 410-26.

49. Fridman WH.Le cerveau mobile. Paris: Hermann; 1991.

50. For other examples, see Kleinman A. Concepts as a model for the comparison of medical systems and cultural systems. Soc Sci Med 1978; 12: 85-93.

51. It does not imply to create a continuity between various traditions or medical systems: see Zimmermann F. Généalogie des médecines douces. Paris: Presses universitaires de France; 1995. From classic texts to learned practice: methodological remarks on the study of Indian medicine. Soc Sci Med 1978; 12: 97-103. For translation matters related to the commensurability issue, see also Zimmermann F. Terminological problems in the process of editing and translating in Sanskrit medical texts. In: Unschuld PO, Ed. Approaches to traditional Chinese medical literature. Dordrecht: Kluwer; 1989. p. 141-50.

52. Buchillet D. Perles de verre, parures de blancs et « pots de paludisme ». Epidémiologie et représentations Desana de la maladie infectieuse (haut Rio Negro, Brésil). Journal de la Société des Américanistes 1995; 81: 181-206.

that are fatal to the tribes. They tell that the Whites did not flinch from drinking immortality with coca, while Indians were more squeamish. Since this time they pay the price for not having been brave.

Anthropologists have been attentive to the way populations adjust or distort in their myths and rituals scientific innovations from elsewhere. In the Meiji period, the Japanese reinvested the *Kamis*, geniuses that protected against smallpox (*Kami* is sometimes translated by guardian angel), with new meanings and linked their ancient rituals to the practice of Western vaccination[53]. Today, historians no longer consider popular resistance to scientific progress as a simple proof of backwardness but undertake a careful in-depth analysis of acceptance and rejection[54].

The American anthropologist David Napier has promoted a study of reactions to Western knowledge about AIDS in various cultures: how do Balinese, for example, integrate the western version of immunity into their religious beliefs and rituals?[55] He notes that they seem to understand and integrate current assumptions about the immune system and its role in HIV infection: the idea that a tiny invisible being has the power of investing and harming the body fits easily with their current demonology. Only those historians who think that bacteriology has been an absolute departure from the former beliefs into occult forces and invisible miasmas can deny the analogy between scientific beliefs in the multiple entities of the immune system[56] and such cultural demonology[57].

The immune system recapitulates the questions on the uncertain status of the body in Nature. It solicits queries on the boundaries between the body and other living beings, constantly renegotiated during the course of life[58]. On the one hand, ecologists complain that modern practices have inadvertently ignored the natural barriers between species (e.g., the bovine spongiform encephalopathy affair). However, 40 years ago grafting had already bypassed the dogma of the "uniqueness of the individual." The success of transplantation with living or deceased donors has pointed to the fluid relationship between the living and the dead or within the living community itself, again an open space for negotiation[59]. On the other hand, looking to the inside of the organism, no absolute guarantee against autoimmunity can be given, and the emergence of immunity may remain a matter of context, as Rolf Zinkernagel has indicated.

If the immune system is suggestive of the issue of limits between nature and culture, the Self and the Other, the living and the dead, it is possible to identify analogs in other cultures.

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53. Rotermund HO. Hôsôgami ou la petite vérole aisément. Paris. Maisonneuve et Larose: 1991.
54. Moulin AM. Premiers vaccins, premières réticences. Pour la science 1999; 264: 12-5.
55. Napier AD. Foreign bodies: performance, art and symbolic anthropology. Berkeley: California University Press; 1992 Also see Jacquemart F Préliminaires à une théorie générale anthropocentriste des objets mous [doctoral thesis in immunology]. Paris: University of Paris 6; 1990
56. Cambrosio A, Keating P. A matter of FACS: constituting novel entities in immunology. Med Anthrop Q 1992; 6: 362-84.
57. Napier D. The age of immunology (forthcoming).
58. Moulin AM. A science "dans le siècle": immunology or the science of boundaries. In: Krige J, Pestre D, Eds. Science in the twentieth century. Amsterdam: Harwood Academic Publishers; 1998. p. 475-95.
59. Moulin AM. Body parts: the modern dilemma Transplant Rev 1993; 95: 33-55. La crise éthique de la transplantation d'organes. À la recherche de la "compatibilité" culturelle. Diogène 1995; 172: 76-96; Postface. In. Carvais R, Sasportes M, Eds. La greffe humaine. Paris: Presses universitaires de France; 2000; p 749-64.

Among the Ngbaka villagers of Central Africa, along the Lobaye River, the genesis of disease works along two interpretive modes. Either disease is attributed to aggressive agents from the outside – flies, mosquitoes, melipones (wild honey flies which colonize the natural openings of the body in the rain forest) – or it is attributed to the doings of a wild beast crouched in the body, responsible for antagonistic effects. Alternatively, it stimulates and chastises, replenishes and starves the body, induces or restricts bleeding, stops or impedes the humoral flow[60]. This devouring beast, alternatively supportive or destructive, is a perfect illustration of the equivocacy of the Self to self-relationship, a strange relation associating fusion and autonomy, love and hatred.

Among the Avikam in Ivory Coast, a wound is perceived as a major hazard, putting the body at risk by disturbing the gentle flow in and out of the organism and canceling the concentration gradient, leading to homogenization and death[61]. The Avikam live on a lagoon, with log cabins built on woodpiles in a marine environment. Their daily life is an unrelenting battle against the invasion of salty water that destroys homes and drowns bodies, but that also provides the main resources for this population of fishermen. The story of the Avikam is similar to the epic story of Hans, the little Dutch hero, who kept his finger in a hole in the dike all night, waiting for help.

Surgery was, in the last century, celebrated as one of the greatest medical achievements and received almost unanimous applause. With the growing awareness of so-called nosocomial affections, a more sober view now prevails which considers surgical decisions as a potential harm whose consequences must be carefully weighted. As with the Avikam, any surgical intervention figures as a trauma with a risk of infection and pathological cascades. Practices such as the resuscitation of comatose patients, or the use of automated instruments to replace failing basic vital functions, need also to be reconsidered in this respect.

Any biological equilibrium is a negotiation with the fluctuating composition of the external and internal milieus, involving the up- and down-regulation of cells' capacity to proliferate, differentiate, secrete, adhere, or aggregate. Such was the message of the English immunologist Gell when he warned that the immune system is at risk of "bleeding to death"[62] when one of its branches is cut off or conversely is under the permanent threat of inflation by proliferation of cells or antibodies. Even immunization programs, unanimously praised for their major contribution to the decline of infant mortality, are not easily interpreted in a unilateral way. Vaccination activates multiple pathways in the body, varying with the type of antigen, leading to possibly contradictory effects. Some recent data suggest that some vaccines could, on the one hand, stimulate immunity and decrease infant mortality in an unspecific way, while other vaccines might increase atopy and raise

60. Amenorrhea or metrorrhagias are thus easy to explain. The amenorrhea corresponds to a period of nourishment for the parasite. This parasitic beast is necessary to the transmission of life;. Moulin AM, Lévi-Strauss à Kaka (République centrafricaine), CNRS typescript, Bangui 1983; Pagézy H, Couillot MF, Moulin AM. Enquête ethnographique sur la grossesse et l'allaitement, examens médicaux et considérations ethnomédicales. CNRS typescript, Paris, 1984.
61. Gely M. Le corps fragile: écologie du corps et syncrétisme médical chez les Avikam lagunaires de Côte d'Ivoire. Sci Soc Santé 1991; 9: 5.
62. Gell PG. Network concepts in science and the arts. In: Lefkovits I, Ed. The immune system; a Festschrift in honor of Niels Kaj Jerne. Basel: S Karger; 1980. p. 58.

mortality[63]. Moreover, the clarification of the immunological consequences of repeated inoculation of vaccine antigens remains to be worked out. The rise of lymphomas or autoimmune diseases, during the last two decades, has remained a controversial issue.

Metaphysical

Immunity emerges thus as a topic for reverie on the instability of biological borders and frontiers between beings. Literature elaborates in this mood the theme of a citadel where the enemy silently lurks inside or haunts, invisible, outside. The heroes of Dino Buzzati's "Desert of Tartars," wait on the battlements for a mysterious invader without precise indications of time and space. But who sets the limit between the Self and NonSelf, the citizen and the foreigner?

The time-space location suggested by Rolf Zinkernagel plays with thresholds and doses, light and darkness, hidden and exposed, latent and manifest antigens in the body. Ultimately, immunology illustrates a paradoxical element in recognition: the mixture of closeness and distance in the perception of the enemy, nonselves as other selves, the impossibility of identification in the absence of kinship, even inimical. Recognition is a gradual and complex phenomenon where the enemy is more easily recognized, different in that from the absolute foreigner whose name and essence are beyond all knowledge. This is the sense of the Greek distinction, the sociologist Georg Simmel used to recall, between the "meteque," alien in the city but belonging to it and depending on its laws, and the barbarian, who has no human language (the original meaning of barbarian) and no human bond.

A South African novel by Coetzee, "Waiting for Barbarians," depicts the odyssey of a judge settled on the frontier that protects the country from wild natives' invasion. A female prisoner is one day taken to him. The story of this judge who makes love with his prisoner and progressively identifies her as a human being, before being banned from his own society, is not only a political fable written in the apartheid country before the time came for political change, it is also a metaphysical and poetical tale about immunity with underpinnings on the arbitrary character of identities and the reversibility of categories.

But the making of identities is not necessarily the royal pathway to order and morals. Dealing with the case of the former Soviet Asian republics, the political scientist Olivier Roy breaks with the tradition that opposed "good" identities (cultural, linguistic, social) and "bad" identities (racial or pseudo-biological founded on skin, hair, blood...) and shows that the making of cultural identities can also be a source of violence and fantasy[64].

Conclusion

The concept of immune system has made its way both inside and outside the scientific community because it is the product of imagination focusing on the status of the body in the world and among the other bodies. The Western world distanced itself from cultures where disease is attributed to a divine or human maleficent volition. But with their helper, suppressor and dendritic cells, immunologists also have invented all kinds of entities

63. Aaby P, et al. Early BCG vaccination and reduction in atopy in Guinea-Bissau. Clin Exp Allergy 2000 ; 30 : 644-50. Non-specific beneficial effect of measles immunization: analysis of mortality studies from developing countries. Br Med J 1995; 311: 481-5.
64. Roy O. La fabrication des identités. Paris: Le Seuil: 1998.

endowed with intention. Dendritic cells may be reminiscent of some satanic monsters "quaerens quem devoret" (seeking to devour somebody).

The controversies where immunologists confront their views on the mechanisms of memory, recognition and defense, the connotations of the words they use or the affects to which they refer, manifest what I have called the anthropological background of a perhaps too human science. The awareness of this background might help – this is the gamble of interdisciplinary exchange – to discriminate more aptly between the contingent and the essential in the arguments and the underlying issues.

No immunologist would accept the reduction of his work to queries on the identification of the Self and boundaries between Self and the other selves, or to the medieval question of micro/macrocosm. But no philosopher would accept to deny that metaphysical queries underlie the experimental work of biology. The dialogue between both, at the extreme of their minds, harbors not only uncontested, at least I hope, pleasure, but a promise of mutual enrichment if not decisive progress toward a common truth.

In this chapter, I have not claimed that immunologists should refrain from using metaphors and attributing volitions and concerns to the immune system. I have not tried to stigmatize their transient use of non-scientific categories, but, instead, have tried to show that, while doing science, they interfere with categories profoundly relevant to human life and experience.

The Self and NonSelf debate, whether it is or not reformulated as the danger model, turns on an issue of the utmost importance: the overlapping and elusive character of identities. The immune system can be considered as an illustration of the ambivalent and reciprocal status of the Same and the Other[65]. If, in some versions of the immune system, the Other is viewed as the germ or the pathogen, the ideal target for eradication, other versions offer a more flexible, changing and adaptive picture. In this perspective, the immune system illustrates the cognitive and political problems of exploring the differences without abolishing or reifying identities. We suggested that the immune system may represent the central issue of anthropology or the encounter with the Other[66] how to structure this encounter and elude the danger of absorbing or being absorbed?

Definitions of Self and selves, crucial to guide one's way into chaos, are another possible source of closure and schizophrenia, hostility and fighting. Interdisciplinary exchange should serve the purpose of challenging the boundaries in which the scientists could be tempted to enclose themselves.

The immune system illustrates the importance of metaphor in science, one of the foundations that makes interdisciplinarity possible and fruitful, politically correct and epistemologically legitimate, a useful basis for a meeting and hopefully many others such as the one that took place in Saint-Julien, in Claude Bernard's home.

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65. Pouillon J. Malade et médecin: le même et/ou l'autre? (Remarques ethnologiques). Nouvelle Revue de Psychanalyse 1970; 1: 78-98. Segalen M, Ed. L'Autre et le Semblable. Regards sur l'ethnologie des sociétés contemporaines. Paris: Presses du CNRS; 1989.

66. Fabian J. Time and the Other. How anthropology makes its object. New York: Columbia University Press; 1983. Presence and representing the Other and anthropological inquiry. Crit Inquiry 1990; 16: 753-72.

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In Moulin Anne-Marie (ed.), Cambrosio A. (ed.). Singular selves : historical issues and contemporary debates in immunology.

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