

Vaccine strategy when the smallpox model fails: 1. immune cognition, Malaria and the Fulani

Rodrick Wallace, PhD

The New York State Psychiatric Institute

Robert G Wallace

CUNY Graduate Center

and

Dept. of Biology

City College of New York*

July 2, 2001

We begin to examine the implications of IR Cohen's work on immune cognition [1-3] for vaccine strategies when simple elicitation of sterilizing immunity fails, as is the case for HIV, tuberculosis and malaria. Cohen's approach takes on a special importance in the context of recent work by Nisbett et al. [4] showing clearly that central nervous system (CNS) cognition is not universal, but rather differs fundamentally for populations having different cultural systems. A growing body of evolutionary anthropology indeed suggests that such effects are inevitable, since culture is as much a part of human biology 'as the enamel on our teeth'. Thus a successful vaccine strategy for use when the smallpox model fails must address a condensation of sociocultural and immune cognition, in the same sense that neuroimmunology and immunogenetics

*Address correspondence to Rodrick Wallace, PISCS Inc., 549 W 123 St., Suite 16F, New York, NY, 10027. Telephone (212) 865-4766, email rdwall@ix.netcom.com.

describe the condensation of CNS and genetic ‘languages’ with immune function. We reinterpret recent studies of African cultural variation in immune response to malaria from this perspective.

Introduction

HIV, malaria, and tuberculosis are major causes of morbidity and mortality for which no simple vaccine strategy has produced sterilizing immunity. HIV is an evolution machine, malaria has a complicated parasite life cycle with multiple and often changing, antigens, and tuberculosis, like other mycobacteria, has a thick waxy coat which hinders both immunization and antibiotic treatment. Analogously, many, if not most, infectious diseases have basic biological or ecological and life-cycle factors that obviate simple effective vaccination on the smallpox model, which indeed seems much the exception.

Recently, interactions between the central nervous system (CNS) and the immune system, and between the genetic heritage and the immune system have become officially recognized and indeed academically codified through journals with titles such as *Neuroimmunology* and *Immunogenetics*. Here we will argue that a cognitive socioculture – a social network embodying culture – in which individuals are embedded, and through which they are both acculturated and function to meet collective challenges of threat and opportunity, may interact strongly with individual immune function to produce a composite entity which might well be labeled an *Immunocultural Condensation* (ICC).

We first examine current visions of the interaction between genes and culture, and between the CNS and culture, and follow with a summary of Cohen’s view of immune cognition. Next we argue that immune cognition and cognitive socioculture can become fused into a composite entity, and make an application to recent observations of culturally-specific immune response to malaria in Africa. We conclude with some discussion of larger implications.

Genes, cognition, and culture

Increasingly, biologists are roundly excoriating simple genetic reductionism which neglects the role of environment. Lewontin [5], for example, explains that genomes are not ‘blueprints,’ a favorite public relations metaphor, as genes do not ‘encode’ for phenotypes. Organisms are instead outgrowths

of fluid, conditional interactions between genes and their environments, as well as developmental ‘noise.’ Organisms, in turn, shape their environments, generating what Lewontin terms a triple helix of cause and effect. Such interpenetration of causal factors may be embodied by an array of organismal phenomena, including, as we shall discuss, culture’s relationships with the brain and the immune system. We propose reinterpreting immune function in this light, with profound implications for medical and public health interventions for infectious diseases where the smallpox model fails.

The current vision of human biology among evolutionary anthropologists is consistent with Lewontin’s analysis and is summarized by Durham [6] as follows:

“...[G]enes and culture constitute two distinct but interacting systems of inheritance within human populations... [and] information of both kinds has influence, actual or potential, over ... behaviors [which] creates a real and unambiguous symmetry between genes and phenotypes on the one hand, and culture and phenotypes on the other...

[G]enes and culture are best represented as two parallel lines or ‘tracks’ of hereditary influence on phenotypes...”

With regard to such melding, over hominid evolution genes came to encode for increasing hypersociality, learning, and language skills, so the complex cultural structures which better aid in buffering the local environment became widespread in successful populations [7].

Every successful human population seems to have a core of tool usage, sophisticated language, oral tradition, mythology and music, focused on relatively small family/extended family groupings of various forms. More complex social structures are build on the periphery of this basic genetic/cultural object [8].

At the level of the individual human, the genetic-cultural object appears to be mediated by what evolutionary psychologists postulate are cognitive modules within the human mind [9]. Each module was shaped by natural selection in response to specific environmental and social conundrums Pleistocene hunter-gatherers faced. One set of such domain-specific cognitive adaptations addresses problems of social interchange [10]. The human species’ very identity may rest, in part, on its unique evolved capacities for social mediation and cultural transmission. Anthropologist Robert Boyd has

remarked that culture is as much a part of human biology as the enamel on our teeth.

Indeed, a brain-and-culture condensation has been adopted as a kind of new orthodoxy in recent studies of human cognition. For example Nisbett et al. [4] review an extensive literature on empirical studies of basic cognitive differences between individuals raised in what they call ‘East Asian’ and ‘Western’ cultural heritages. They view Western-based pattern cognition as ‘analytic’ and East-Asian as ‘holistic.’ Nisbett et al. [4] find that

1. Social organization directs attention to some aspects of the perceptual field at the expense of others.

2. What is attended to influences metaphysics.

3. Metaphysics guides tacit epistemology, that is, beliefs about the nature of the world and causality.

4. Epistemology dictates the development and application of some cognitive processes at the expense of others.

5. Social organization can directly affect the plausibility of metaphysical assumptions, such as whether causality should be regarded as residing in the field vs. in the object.

6. Social organization and social practices can directly influence the development and use of cognitive processes such as dialectical vs. logical ones.

Nisbett et al. [4] conclude that tools of thought embody a culture’s intellectual history, that tools have theories build into them, and that users accept these theories, albeit unknowingly, when they use these tools.

We may assume, then, the existence of gene-culture and brain-culture condensations.

Immune cognition

Recently Atlan and IR Cohen [3] have proposed an information-theoretic adaptation of IR Cohen’s [1, 2] ‘cognitive principle’ model of immune function and process, a paradigm incorporating pattern recognition behaviors analogous to those of the central nervous system.

We paraphrase Atlan and Cohen’s [3] description of immune system cognitive pattern recognition-and-response behavior as follows:

The meaning of an antigen can be reduced to the type of response the antigen generates. That is, the meaning of an antigen is functionally defined by the response of the immune system. The meaning of an antigen to the system is discernible in the type of immune response produced, not merely

whether or not the antigen is perceived by the receptor repertoire. Because the meaning is defined by the type of response there is indeed a response repertoire and not only a receptor repertoire.

To account for immune interpretation IR Cohen [1] has proposed a cognitive paradigm for the immune system. The immune system can respond to a given antigen in various ways, it has ‘options.’ Thus the particular response we observe is the outcome of internal processes of weighing and integrating information about the antigen.

In contrast to Burnet’s view of the immune response as a simple reflex, it is seen to exercise cognition by the interpolation of a level of information processing between the antigen stimulus and the immune response. A cognitive immune system organizes the information borne by the antigen stimulus within a given context and creates a format suitable for internal processing; the antigen and its context are transcribed internally into the ‘chemical language’ of the immune system.

IR Cohen’s cognitive paradigm suggests a language metaphor to describe immune communication by a string of chemical signals. This metaphor is apt because the human and immune languages can be seen to manifest several similarities such as syntax and abstraction. Syntax, for example, enhances both linguistic and immune meaning.

Although individual words and even letters can have their own meanings, an unconnected subject or an unconnected predicate will tend to mean less than does the sentence generated by their connection.

The immune system, in Atlan and Cohen’s view, creates a ‘language’ by linking two ontogenetically different classes of molecules in a syntactical fashion. One class of molecules are the T and B cell receptors for antigens. These molecules are not inherited, but are somatically generated in each individual. The other class of molecules responsible for internal information processing is encoded in the individual’s germline.

Meaning, the chosen type of immune response, is the outcome of the concrete connection between the antigen subject and the germline predicate signals.

The transcription of the antigens into processed peptides embedded in a context of germline ancillary signals constitutes the functional ‘language’ of the immune system. Despite the logic of clonal selection, the immune system does not respond to antigens as they are, but to abstractions of antigens-in-context.

Immune cognition and culture

It is possible to give Atlan and Cohen's language metaphor of meaning-from-response a precise information-theoretic characterization, and to place that characterization within a context of recent developments which propose the 'coevolutionary' mutual entrainment – in a large sense – of different information sources to create larger metalanguages containing the original as subdialects [11-16]. This work also permits treating gene-culture and brain-culture condensations using a similar, unified, conceptual framework of information source 'coevolutionary condensation'. Cohen's immune cognition model suggests, then, the possibility that human culture and the human immune system may be jointly convoluted: That is, there would appear to be, in the sense of the gene-culture and brain-culture condensations of the previous section, an immune-culture condensation as well. To the terms neuroimmunology and immunogenetics we must add 'immunocultural condensation.'

Malaria, tuberculosis and HIV share the distinction of having no effective available vaccines or vaccine strategies, in considerable contrast to the 'smallpox model' in which a single, simple, vaccine dosage almost always gives lifelong, or at least very long-term, immunity from disease. The evolutionary anthropologists' vision of the world, as we have interpreted it, sees language, culture, gene pool, and individual CNS and immune cognition as intrinsically melded and synergistic. We propose, then, that where the smallpox vaccine model fails, culture and immune cognition may become a joint entity in determining the kind of vaccine strategy which may be effective, 'confounded' by the distinct population genetics associated with linguistic and cultural isolation.

Africa, as the human homeland, contains the greatest known linguistic, cultural, and indeed genetic, diversity. This suggests the probable need for severe local refining and monitoring of any vaccine strategy in Africa, and implies that traditional 'case-control' studies of vaccine strategies may be profoundly affected by linguistic and cultural differences, as convoluted with the associated genetic divergence.

In sum, population differences of immune function heretofore attributed to genetic factors alone may, rather, represent differences in immune cognition driven by profound cultural differences. This would, in our view, particularly affect development of vaccine strategies for culturally diverse populations where the smallpox model fails.

We reinterpret recent observations of malaria in Burkina Faso from this

perspective.

Malaria and the Fulani

Modiano et al. [17, 18, 19], whom we paraphrase at some length, have conducted comparative surveys on three roughly co-resident West African ethnic groups – which they describe as ‘sympatric’ – exposed to the same strains of malaria. The Fulani, Mossi, and Rimaibe live in the same conditions of hyperendemic transmission in a Sudan savanna area northeast of Ouagadougou, Burkina Faso. The Mossi and Rimaibe are Sudanese Negroid populations with a long tradition of sedentary farming, while the Fulani are nomadic pastoralists, partly settled and characterized by non-Negroid features of possible Caucasoid origin.

Parasitological, clinical, and immunological investigations showed consistent interethnic differences in *P falciparum* infection rates, malaria morbidity, and prevalence and levels of antibodies to various *P falciparum* antigens. The data point to a remarkably similar response to malaria in the Mossi and Rimaibe, while the Fulani are clearly less parasitized, less affected by the disease, and more responsive to all antigens tested. No difference in the use of malaria protective measures was demonstrated that could account for these findings. Known genetic factors of resistance to malaria showed markedly *lower* frequencies in the Fulani [19]. The differences in the immune response were not explained by the entomological observations, which indicated substantially uniform exposure to infective bites.

Modiano et al. [17] conclude that

“...[S]ociocultural... factors do not seem to be involved... The available data support the existence of unknown genetic factors, possibly related to humoral immune responses, determining interethnic differences in the susceptibility to malaria.”

In spite of later finding the Fulani in their study region have significantly *reduced* frequencies of the classic malaria-resistance genes compared to the other ‘sympatric’ ethnic groups, Modiano et al. [19] again conclude that

“This evidence... supports the existence in [the Fulani] of unknown genetic factor(s) of resistance to malaria...”

Much in the spirit of Lewontin [5], we beg to differ, as ad hoc presumptions of genetic causality paper over alternatives consistent with the results.

Recently Andrew Gordon, a medical anthropologist, published an exhaustive study of Fulani cultural identity and illness, based on participant-observation in Guinea [20]. His findings are remarkable:

“Cultural identity – who the Fulani think they are – informs thinking on illnesses they suffer. Conversely, illness, so very prevalent in sub-Saharan Africa, provides Fulani with a consistent reminder of their distinctive condition... How they approach being ill also tells Fulani about themselves. The manner in which Fulani think they are sick expresses their sense of difference from other ethnic groups. Schemas of [individual] illness and of collective identity draw deeply from the same well and web of thoughts... As individuals disclose or conceal illness, as they discuss illness and the problem of others, they reflect standards of Fulani life – being strong of character not necessarily of body, being disciplined, rigorously Moslem, and leaders among lessors... to be in step with others and with cultural norms is to have pride in the self and the foundations of Fulani life.”

The Fulani carried the Islamic invasion of Africa into the sub-Sahara, enslaving and deculturating a number ethnic groups, and replacing the native languages with their own. This is much the way African Americans were enslaved, deculturated, and taught English.

As Gordon puts it.

“ ‘True Fulani’ see themselves as distinguished by their aristocratic descent, religious commitments, and personal qualities that clearly differ from lowland cultivators. Those in the lowland are, historically, Fulani subjects who came to act like and speak Fulani, but they are thought to be without the right genealogical descent. The separation between pastoralists and agriculturists repeats itself in settlements across Africa. The terms vary from place to place in Guinea, the terms are Fulbhe for the nobles and the agriculturalist Bhalebhe or Maatyubhee; in Burkina Faso, Fulbhe and the agricultural Rimaybhe; and in Nigeria, the Red Fulani and the agricultural Black Fulani... The schemas for the

Fulani body describe the differences between them and others. These are differences that justify pride in being Fulani and not Bhalebhe, Maatyubhe, Rimaybhe, or Black Fulani. In Guinea, the word ‘Bhalebhe’ means ‘the black one’. The term ‘Bhalebhe’ carries the same meaning as ‘Negro’ did for Africans brought to North America. It effaces any tribal identity...

The control a Fulani exercises over the body is an essential feature of ‘the Fulani way.’ Being out of control is shameful and not at all Fulani-like... To act without restraint is to be what is traditionally thought of as Bhalebhe...

Being afflicted with malaria – and handling it well – is a significant proof of ethnicity. How Fulani handle malaria may be telling. What they lack in physical resistance to disease they make up in persistence. Though sickly, Fulani men only reluctantly give into malaria and forgo work. To give into physical discomfort is not *dimò*. When malaria is severe for a man he is likely not to succumb to bed, but instead to sit outside of his home socializing.”

Parenthetically, many primate studies [e.g. 21] show that dominance rank, an important psychosocial factor, strongly and positively affects immune response in a stable social setting, while a vast body of parasitological observation and theory [e.g. 22] shows the ‘overdispersion’ of parasites within affected populations – i.e. relative concentration – is closely but inversely related to social dominance.

The Occam’s Razor hypothesis, then, is that the observed significant difference in malarial parasitization between the dominant Fulani and co-resident ethnic groups in the Ouagadougou region of Burkina Faso can be largely accounted for by factors of immunocultural condensation, particularly in view of the observed *lower* frequencies of classic malaria-resistance genes found in the Fulani.

Given their protective ICC, the Fulani simply may not need those classic genes.

Conclusions and speculations

We have characterized the interaction between immune and sociocultural cognition as an immunocultural condensation, and used the concept to propose an Occam’s Razor explanation of observed differences between rates

and intensity of malarial parasitization among co-resident ethnic groups in a section of Burkina Faso. We suspect that comparison of the ‘neuroimmunological spectra’ of biochemical mechanisms between these ethnic groups, in a large sense, would show differences consistent with the strictly immunological findings, and might illuminate mechanisms by which the proposed ICC operates.

The particular relation between the Fulani and, at least, the Rimaibe, somewhat mirrors the relation between ‘White’ and ‘Black’ residents of the US. Thus we suspect that differences of ICC may play a role in the ‘health disparities’ evident between those groups, an effect which persists even in the face of statistical procedures which supposedly adjust for differences of income between the groups. This suggests the continuing burdens of history, what organizational ecologists have come to call ‘path dependence.’

AIDS and tuberculosis are, it is widely understood, particular diseases of marginalization and poverty. They spread along the structural flaws of a society like water through cracks in ice. Our work here leads us to suppose that cross-sectional marginalization and deprivation are synergistic with longitudinal path dependent, i.e. historically driven, structures of ICC to define the ecology of these infections.

As we have described it, immunocultural condensation presents both a challenge and opportunity in the development of vaccine strategies where the smallpox model fails. To the degree that factors of ICC dominate a disease ecology, there is unlikely to be an effective, single, one-size-fits-all vaccine strategy. On the other hand, a more flexible vaccine strategy which makes appropriate use of ICC mechanisms may enjoy a considerable synergistic boost in effectiveness, at least among those who do not bear the burdens of history.

Nobody said it would be easy.

References

- [1] Cohen IR, 1992, The cognitive principle challenges clonal selection, *Immunology Today*, **13**, 441-444.
- [2] Cohen IR, 2000, *Tending Adam’s Garden: evolving the cognitive immune self*, Academic Press, New York.
- [3] Atlan H and IR Cohen, 1998, Immune information, self-organization and meaning, *International Immunology*, **10**, 711-717.

- [4] Nisbett R, K Peng, C Incheol and A Norenzayan, 2001, Culture and systems of thought: holistic vs. analytic cognition, *Psychological Review*, **108**, 291-310.
- [5] Lewontin R, 2000, *The Triple Helix: Gene, Organism and Environment*, Harvard University Press, Cambridge, MA.
- [6] Durham W, 1991, *Coevolution: Genes, Culture and Human Diversity*, Stanford University Press, Palo Alto, CA.
- [7] Bonner J, 1980, *The Evolution of Culture in Animals*, Princeton University Press, Princeton, NJ.
- [8] Richerson P and R Boyd, 1995, The evolution of human hypersociality. Paper for Ringberg Castle Symposium on Ideology, Warfare and Indoctrinability (January, 1995), and for HBES meeting, 1995.
- [9] Barkow J, L Cosmides and J Tooby (eds.), 1992, *The Adapted Mind: Biological approaches to mind and culture*, University of Toronto Press.
- [10] Cosmides L and J Tooby, 1992, Cognitive adaptations for social exchange, in *The Adapted Mind: Evolutionary Psychology and the Generation of Culture*, Oxford University Press, New York.
- [11] Wallace R and RG Wallace, 1998, Information theory, scaling laws and the thermodynamics of evolution, *Journal of Theoretical Biology*, **192**, 545-559.
- [12] Wallace R and RG Wallace, 1999, Organisms, organizations and interactions: an information theory approach to biocultural evolution, *BioSystems*, **51**, 101-119.
- [13] Wallace R, 2000, Language and coherent neural amplification in hierarchical systems: Renormalization and the dual information source of a generalized spatiotemporal stochastic resonance, *International Journal of Bifurcation and Chaos*, **10**, 493-502.
- [14] Wallace R, 2000, Information resonance and pattern recognition in classical and quantum systems: toward a 'language model' of hierarchical neural structure and process,
www.ma.utexas.edu/mp_arc-bin/mpa?yn=00-190.
- [15] Wallace R, 2001, Adaptation, punctuation and rate distortion: non-cognitive 'learning plateaus' in evolutionary process,
www.ma.utexas.edu/mp_arc-bin/mpa?yn=01-163
- [16] Wallace R, 2001, Selection pressure and organizational cognition: implications for the social determinants of health, cogprints.soton.ac.uk, Manuscript number cog00001526,

- [17] Modiano D, V Petrarca, B Sirma, I Nebie, D Diallo, F Esposito and M Coluzzi, 1996, "Different response to *Plasmodium falciparum* malaria in West African sympatric ethnic groups, *Proceedings of the National Academy of Sciences*, **93**, 13206-13211.
- [18] Modiano D, G Luoni, V Petrarca, B Sodiomon Sirima, M De Luca, J Simpure, M Coluzzi, J Bodmer and G Modiano, 2001, "HLA class I in three West African ethnic groups: genetic distances from sub-Saharan and Caucasoid populations", *Tissue Antigen*, **57**, 128-137.
- [19] Modiano D, G Luoni, B Sirima, A Lanfrancotti, V Petrarca, F Cruciani, J Simpure, B Ciminelli, E Foglietta, P Grisanti, I Bianco, G Modiano and M Coluzzi, 2001, "The lower susceptibility to Plasmodium falciparum malaria of Fulani of Burkina Faso (west Africa) is associated with low frequencies of classic malaria-resistance genes," *Transactions of the Royal Society of Tropical Hygiene and Medicine*, **95**, 149-152.
- [20] Gordon A, 2000, "Cultural identity and illness: Fulani views," *Culture, Medicine and Psychiatry*, **24**, 297-330.
- [21] Schapiro S, P Nehete, J Perlman, M Bloomsmith and K Sastry, 1998, "Effects of dominance status and environmental enrichment on cell-mediated immunity in rhesus macaques," *Applied Animal Behavioral Science*, **56**, 319-332.
- [22] Crofton H, 1971, "Model of host-parasite relationships," *Parasitology*, **63**, 343-390.