



Contents lists available at ScienceDirect

Studies in History and Philosophy of Biological and Biomedical Sciences

journal homepage: www.elsevier.com/locate/shpsc

Imagining 'reactivity': allergy within the history of immunology

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ARTICLE INFO

Article history:
Available online xxxx

Keywords:
Allergy
Pirquet
Pasteur
History of immunology
Response
Reaction

ABSTRACT

An allergy is commonly understood to be an overreaction of the immune system to harmless substances that are misrecognised as foreign. This concept of allergy as an abnormal, misdirected immune response—a biological fault—stems from the idea that the immune system is an inherently defensive operation designed to protect the individual through an innate capacity to discriminate between the benign and toxic, or self and nonself. However, this definition of allergy represents a radical departure from its original formulation. Literally meaning 'altered reactivity', the term was coined in 1906 by Austrian paediatrician Clemens von Pirquet, to describe the fundamentally mutable nature of the immune response.

This paper argues that the conventional interpretation of allergy-as-pathology derives from specific concepts of 'organism', 'response', and 'normal' immune function that have—for over a century—governed the perception and study of immune phenomena within immunology. Through an examination of Louis Pasteur's conceptualisation of the host body/microorganism relationship, I argue that immunology is founded on a view of the organism as a discrete, autonomous entity, and on a concomitant notion of the immune response as essentially *reactive*. Revisiting the concept of 'altered reactivity', this paper points to the fact that allergy was initially posited as a general theory of immune responsiveness and, importantly, one that poses a significant challenge to orthodox notions of immunopathology. It suggests that Pirquet's unique view of immune responsiveness presents an account of organismic or biological identity that encapsulates, rather than reduces, its ecological complexity.

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When citing this paper, please use the full journal title *Studies in History and Philosophy of Biological and Biomedical Sciences*

1. Introduction

Most people understand allergies to be an overreaction or abnormal response of the immune system to innocuous substances that are, for reasons unknown, misrecognised as foreign or harmful. This account of allergy—which is widely embraced as *the* authoritative scientific definition—is one derived from contempo-

rary Western medicine and, specifically, the science and clinical practice of immunology. Within immunology, the branch of science and knowledge concerned with immunity,¹ allergy is figured as a pathological or misdirected immune response, a deviation or aberration of proper immune function. This notion of allergy as pathology is the direct product of a very specific conceptualisation of immune function; namely, one that views the immune system as

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¹ Interestingly, the etymology of the term 'immunity'—which derives from the Latin term, *immunitas*, meaning exemption from public service or charge—reveals the conceptual foundation of dominant immunological perspectives. In *A body worth defending: 'immunity', biopolitics, and the apotheosis of the modern body* (2009), Ed Cohen argues that immunity was originally a juridico-political term belonging to ancient Roman law. He explains that only in the late nineteenth century is the term adopted by Western biomedicine as a trope for the elaboration of organism–environment relations:

... as we go for vaccinations, take antibiotics, or avoid the things we are allergic to ... most of us remain ignorant of a basic historical fact: biological immunity as we know it does not exist until the late nineteenth century. Nor, for that matter, does the idea that organisms defend themselves at cellular and molecular levels. For nearly two thousand years, immunity, a legal concept first conjured in ancient Rome, has functioned almost exclusively as a political and juridical term. (Cohen, 2009, p. 3)

The linguistic origin of immunity, with its emphasis on 'exemption' and 'distinction' (ibid., pp. 38–45) brings to the fore a concept of the subject that is crucial to immunology: a body or citizen who exists within, but separately from, a larger governing system or ecology. This notion of an autonomous self—existent primarily *in*, rather than *of*, the world—is an enduring theme throughout the history of immunology, as will be discussed later in the article. For a critical examination of immunity's etymology and its history as a juridico-political concept, see Cohen (2009).

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doi:10.1016/j.shpsc.2010.10.016

Please cite this article in press as: Jamieson, M. Imagining 'reactivity': allergy within the history of immunology. *Studies in History and Philosophy of Biological and Biomedical Sciences* (2010), doi:10.1016/j.shpsc.2010.10.016

an inherently defensive operation designed to protect the individual through an innate capacity to discriminate between the benign and toxic, or self and nonself.² Central to this formulation is an acknowledgement that immunological activity, by its very nature, implies the presence of a coherent biological entity or self; that is, a fixed locus around which this activity is organised. As such, the interpretive frame of an immunological self has come to dominate the ways in which immune phenomena, such as allergies, have been and continue to be investigated, understood and imagined.³

Yet, this idea of allergy, which is premised on a seemingly self-evident understanding of what constitutes healthy or normal immune function, represents a serious departure from its original formulation over a century ago. The term ‘allergy’ was coined by Austrian paediatrician, Clemens von Pirquet, to mean ‘altered energy’ or ‘altered biological reactivity’ (Jackson, 2006, p. 10), and used specifically to describe the immunological phenomenon whereby an individual—upon exposure to *any* substance—experiences a change in his or her capacity to react. The original meaning of allergy was not limited to defining the spectrum of conditions that are today grouped under the rubric of immunopathology (for example, asthma, hay fever, eczema, and urticaria). In fact, the identification of these conditions or symptoms as pathological phenomena obscures the specific insight demonstrated by Pirquet’s work and the unique view of immune responsiveness it championed. From Pirquet’s perspective, allergy offered a conceptualisation of immune function and the immune response that troubled the conventional model of (and thus distinction between) healthy and pathological responses. As A. Barry Kay points out, Pirquet conceived of allergy more broadly as a general theory of immune responsiveness, and thus its introduction into the medical vocabulary signalled not a nosological contribution (the creation of another classificatory term), but rather the discovery of ‘a fundamental biological rule’ (Kay, 2006, p. 557).⁴ In short, Pirquet viewed allergy as a phenomenon that exemplified the nature of all immune responsiveness.

This unique account of the immune response challenged immunological orthodoxy. Pirquet’s emphasis on the capacity of the organism to *change* in its responses contradicted the widely held view of the immune response as the logical expression of a static, self-determining, biological organism or system (Tauber, 1994). Importantly, it implied a very different framework for conceptualising the identity of the immunological body: one based on the mutability, rather than stability and consistency, of immune responses.

The conceptual discrepancy between historical and contemporary definitions of allergy is a point of great interest for critical theorists, philosophers of immunology, historians of medicine, and the medical community alike. It forms the departure point of this analysis, which interrogates the notion of allergy-as-pathology by revisiting and critically examining the historical narrative that underwrites this definition. In particular, it draws attention to the epistemological conditions and philosophical assumptions that support this concept. Implicit in these divergent notions of allergy (‘altered reactivity’ and immunopathology) are two quite different interpretations of the immune response that correspond with different understandings of, or positions on, the immunological body. With respect to the underlying rationale of both perspectives, this article investigates why medical-scientific interpretations of

allergy have differed so dramatically, and considers the implications of this disparity.

In an effort to understand why Pirquet’s notion of ‘altered biological reactivity’ was not taken up within mainstream immunology, this paper examines the intellectual environment in which his work emerged and the way his ideas were received. Contextualising the reception of the allergy hypothesis in immunology’s history and intellectual heritage, it identifies the key ideas relating to organism, body, and physiological function that were characteristic of immunology at the beginning of the twentieth century. In doing so, it attempts to demonstrate why Pirquet’s theory was perceived as conceptually affronting and scientifically unconvincing, and consequently why it occupies a relatively minor position within histories of allergy and immunology.

Pirquet’s hypothesis was situated in an historical period during which immunology was establishing its identity as a discipline: a point at which the acceptance and rejection of certain ideas was instrumental to securing an object (the immunological self) and area of inquiry (epistemic community). At this time, the dominance of certain ideas that can now be considered intrinsic to the discipline—namely, a belief in the existence of a stable, immunological self, and a view of immune responsiveness as essentially or naturally protective—prevented a more detailed engagement with the provocative aspects of Pirquet’s work. That is, immunology’s conceptual development, discursive establishment, and legitimisation as an emerging scientific and clinical field revolved heavily around the concept of immunity. The centrality of this discourse meant that ideas which contradicted or challenged this basic principle inevitably did not receive the same recognition. As such, an historical analysis of Pirquet’s work demonstrates the extent to which the interpretive frame of an immunological self—along with its basis in a protective, benevolent immunity—has governed the direction of immunological thought and research, and thus also its historicisation.

This paper argues centrally for a reading of Pirquet’s allergy hypothesis that has figured less prominently in its historical renditions. Although there have been some recent and quite generous engagements with Pirquet’s work—most notably, Mark Jackson’s *Allergy: the history of a modern malady* (2006); Benedikt Huber’s *100 Jahre Allergie: Clemens von Pirquet—sein Allergiebegriff und das ihm zugrunde liegende Krankheitsverständnis, Teil 1: Leben und Werk* (2006a) and *Teil 2: Der Pirquet’sche Allergiebegriff* (2006b); and, to some extent, Gregg Mitman’s *Breathing space: how allergies shape our lives and landscapes* (2007)—I suggest that his hypothesis can be read as offering concepts of organismic identity and immune responsiveness that are distinct from those found in modern immunology. Specifically, Pirquet’s work proposes a schema for interpreting immune responsiveness that problematises an orthodox understanding of what constitutes normal and pathological immune phenomena. In challenging immunity’s status as the departure point for interpreting immune responsiveness, his model calls into question the very concept that anchors our ability to discriminate between normal and pathological. Importantly, the ecological view of the immune response that the allergy hypothesis proposes implies a notion of the organism as open, unbounded, and defined by the *alterability* of its responses to its environment, and, as such, contests the notion of a discrete, bounded, atomic entity whose responses are predictable. In this way, Pirquet’s work

² See Klein (1982) for a discussion of immunology as the science of self-nonself discrimination.

³ A large body of literature exists within historical and philosophical studies of immunology dealing with debates concerning the existence and nature of ‘the immunological self’. These accounts include discussions of whether this metaphor of immune function translates into an empirical, biological reality, and the role it plays in informing and/or inhibiting immunological research. See Tauber (1994) for an in-depth discussion of the concept of ‘the immune self’. See Löwy (1991, 1992) for discussions of how the concept of ‘self’ has been variously used to enable and direct investigations of immune phenomena. See Anderson and colleagues (1994) for a critical account of how the concept of ‘self’ has shaped the construction of the discipline’s history.

⁴ In *100 years of ‘Allergy’: can von Pirquet’s word be rescued?*, A. Barry Kay states that strict usage of Pirquet’s concept of allergy would have meant replacing the term ‘immune response’ for ‘allergic response’ (Kay, 2006, p. 557). Kay suggests that Pirquet understood allergy as a generalisable concept of immune responsiveness.

destabilises a conventional understanding of healthy or normal immune function, as it redefines this normativity in immune responsiveness as a capacity to fluctuate. Thus, it simultaneously disrupts a correlative notion of immunopathology: if normal immune function is inherently changeable or aberrant, then there is no immutable state (immunity) that acts as the physiological referent from which deviation (pathology) can be gauged. In other words, if the only constant is change, then the identities of the categories ‘normal’ and ‘pathological’ need to be rethought.⁵

2. Pirquet’s concept of ‘altered reactivity’

It is telling that ‘the study of allergy sprang from studies of the unpredictable effects of immunization’ (Moulin, 2000, p. 393). Throughout the late nineteenth and early twentieth centuries, investigations of immune phenomena had been primarily focused on elaborating the physiological mechanisms associated with immunity (Silverstein, 1989). Following the success of Louis Pasteur’s work with vaccination and Elie Metchnikoff’s discovery of phagocytosis (which completed Pasteur’s findings by identifying the biological mechanism in the host that accounted for the efficacy of vaccines), it was generally accepted that the role of the immune response was to affect immunity in the individual. At the time, scientists in this field had been conducting experiments into the effects of vaccination (both positive and negative) in the hope of discovering how immunity operated with respect to different infectious diseases, and thus how the body’s innate protective capacities could be mastered. For instance, Charles Richet and Paul Portier’s discovery of anaphylaxis in 1902 occurred accidentally while ‘attempting to immunize dogs against marine toxins’ (Kroker, 1999, p. 273). Kenton Kroker notes the significance of the concept of immunity in the identification of all immune phenomena; he explains that Richet, when confronted with a reaction that was incompatible with the logic of immunity, named it “anaphylaxis”, meaning “against protection” (ibid.).

This early emphasis on the body’s capacity for self-protection had an enormous impact on the way immune phenomena that appeared to disrupt the principle of immunity were perceived. As illustrated in the earlier example, the pervasiveness of this discourse made it impossible to conceptualise these phenomena in any other terms, as it was assumed that all immune phenomena could be understood with reference to immunity or some intending, biological ‘self’. Reactions viewed as contradictory to the notion of a defended, immunological self were frequently described in precisely these terms—as paradoxical reactions. Arthur Silverstein explains:

In the dawning years of the twentieth century, those investigators active in the young field of immunology had been brought up, with Metchnikoff and Ehrlich, to view the immune response as a superb Darwinian adaptation. It had evolved, presumably, to defend the organism against an outside world heavily populated by highly pathogenic organisms and virulent toxins. So deeply ingrained was this view of a benevolent immunity that the earliest observations that might have contradicted it were quickly attributed to other causes and mechanisms. (Silverstein, 1989, p. 214)

However, simultaneously, the obvious problems presented by pathological and altered reactions forced some investigators to question immunity’s status as the conceptual and physiological basis of all immune responsiveness. Silverstein points out that some of the earliest discoveries related to allergy and immunopathology were made by physiologists Charles Richet and Paul Portier (anaphylaxis), Maurice Arthus (local anaphylaxis), as well as paediatricians Clemens von Pirquet and Bela Schick (serum sickness)—in other words, practitioners who ‘were not part of the classical tradition of bacteriological immunology’ (Silverstein, 1989, p. 215). He argues that their training in different disciplines provided some freedom from an intellectual commitment to immunity, and thus allowed them ‘to speculate that these reactions might be an integral part of the “immune” response’ (ibid.). Among these latter investigators was the discoverer of allergy.

The word ‘allergy’ first appeared in 1906 as the title of a short article published in the journal *Munchener Medizinische Wochenschrift*.⁶ Written by the highly acclaimed Austrian paediatrician and immunologist Clemens von Pirquet, this piece presented a series of reflections on what were regarded as anomalous and contradictory manifestations of the immune response. Pirquet’s interest lay specifically in a number of reactions that were described by the scientific community of the time as ‘paradoxical’ (Pirquet, 1906, p. 1457). Evoking the entrenched immunity-centric perspective that governed work in this field, this characterisation foregrounds the extent to which investigations and interpretations of the immune response were mediated by an implicit understanding of the immunological self as a self-identical being. It was precisely this paradox—that is, the self-contradictory nature of the ‘immune’ response—that Pirquet sought to investigate. In his pithy meditation, Pirquet puzzled over the very existence of these reactions, given that their effects could not be easily or rationally reconciled with the general operation of immunity and the body exemplified by this model of immune function. Pirquet was perplexed as to how and, more importantly, in the service of what biological purpose inoculation could induce immunity and protection in some, and potentially dangerous, life-threatening responses in others. What logical processes would direct the body’s own armamentarium to generate harm (supersensitivity)⁷ in place of protection, and why? How could an inherently protective mechanism, in the service of the self, be responsible for self-harm?

As a way of addressing these questions, Pirquet reviewed his own clinical data alongside the findings of immunologists who had recorded similar reactions when conducting inoculation experiments with animals, and via this comparison he observed the existence of a definite pattern/rule. Pirquet noticed something both unusual and specific: in certain cases, in which an individual or animal had been previously inoculated against a particular disease/toxin, they would—upon reinfection (*second* exposure to the toxin)—exhibit an exaggerated and uncharacteristically different response to the one predicted. In other words, humans and animals that had been vaccinated against a disease and thus should have been protected from it, manifested unpredictable and often harmful reactions in place of the tolerant, non-pathological reactions typically associated with immunity. Furthermore, these deviant or altered responses seemed to represent a spectrum of changed immunological states, ranging from hypersensitivity (abnormally high and dangerous sensitivity to certain stimuli) to hypsensitivity

⁵ It is important to acknowledge that the philosophical and conceptual underpinnings of allergy have been productively explored by Parnes (2003), who examines allergy’s characterisation as ‘trouble from within’, and Löwy (2003), who gives an account of early understandings of allergy and anaphylaxis, and their relationship to studies of biological individuality. Additionally, there are a number of works that elucidate the evolutionary significance of allergy, for instance, Matzinger’s (2002) discussion of the danger model and Profet’s (1991) toxin hypothesis. Each of these critical commentaries makes a significant contribution to conceptual and philosophical engagements with allergy. However, these pieces (their specific concerns) are not within the scope of this article, as they adhere to a definition of allergy as a pathological immune response. In reviving Pirquet’s original allergy concept, this article explicitly interrogates the notion of allergy as pathology.

⁶ *Vienna Clinical Weekly Journal*.

⁷ In his article, *Allergie* (1906), Pirquet uses *supersensitivity* as an umbrella term to include a range of altered responses, from hypersensitivity to hypsensitivity.

(abnormally low sensitivity to stimuli), which varied in degrees of severity.

In an attempt to make sense of these anomalies, Pirquet advanced his own theory of immune responsiveness: he hypothesised that immunity and hypersensitivity were in fact closely interrelated phenomena that could be interpreted as different outcomes of a common biological mechanism (Pirquet, 1906). Pirquet proposed the need for “a new generalised term” which expressed the altered reactivity that followed contact with an antigen’ (Jackson, 2003, p. 386), and suggested the word *allergy*; a combination of the Greek words *allos*, meaning ‘other, different or strange’, and *ergon*, meaning ‘energy, activity or work’. Though it has been variously interpreted as changed reactivity, ‘altered biological reactivity’ (Jackson, 2006, p. 27), and an ‘altered capacity to react’ (Pulay, 1945, p. 13), Pirquet used the term to capture the organism’s fundamental ability to *change in its responses*.

By introducing ‘allergy’, Pirquet hoped to overcome the inadequacy of a pre-existing conceptual schema (immunity) for the purposes of studying the immune response in a way that would allow for the logical inclusion of anomalous reactions. Benedikt Huber writes:

All previous terminology seemed to [Pirquet] to have only a one-sided meaning, and he believed in the importance of studying the clinical reaction-ability of the organism without preconceptions. The term allergy was therefore, at first, a purely clinical expression “without any bacteriological, pathological or biological bias”. (Pirquet, 1908, cited in Huber, 2006b, p. 719)

‘Allergy’ enabled Pirquet to suspend his assumptions about the nature of immune responsiveness and observe these reactions with a naivety that he regarded as necessary and illuminating. He explains:

(...) the viewpoint of allergy [as a concept] had the effect that we would mainly look at the clinical alterations of the reaction without considering whether these were [evidence of] protective mechanisms of the organism or phenomena of other conditions. (Pirquet, 1910, cited in Huber, 2006b, p. 721)

In this sense, the concept of allergy allowed him to examine ‘altered reactivity’ as a general phenomenon, outside its specific physiological outcomes (their classification as normal or pathological states).

In 1910, Pirquet published a monograph (*Allergy*) devoted to elaborating allergy, which collated an extensive amount of experimental data and clinical findings relating to changes in reactivity. In this text, Pirquet attempts to map ‘reactivity’ as an object through a systematic, empirical study of the many forms that ‘changed reactivity’ takes in cases of certain infectious diseases. He writes ‘my plan is to take all the morbid entities in which symptoms of allergy are to be found one after the other, and then to collect those facts which all of them have in common’ (Pirquet, 1911, p. 263). As a project, the monograph attempts to produce an accurate picture of the scope of organismic reactivity by classifying and categorising different responses according to ‘the theoretical subdivision of [allergy], the altered reactivity relating to time, quality and quantity’ (Pirquet, 1910, cited in Huber, 2006b, 721). In other words, through an impressive array of examples, he shows that the immune response is capable of change and that the parameters of this change can be mapped. As such, Pirquet proposes a taxonomy of possible reaction outcomes, encompassing everything from anaphylaxis to immunity. This can be seen in the monograph’s conclusion, in which Pirquet’s studies are summed up in a table (titled ‘Divisions of allergy’) that organises all forms of ‘changed reactivity’ according to differences in time, quantity and quality. Crucially,

this diagram, which characterises all responses as particular instances or expressions of ‘reactivity’, illustrates that Pirquet regarded ‘reactivity’ (an undefined responsive capacity) as the common denominator of the immune response.⁸

This reinterpretation of the immune response was far removed from conventional ways of thinking about immune function and physiology generally, and, as such, experienced a brief and unsuccessful reception. As Jackson explains:

... von Pirquet’s ... approach to immunity and hypersensitivity was not well received by many of his contemporaries, who tended to regard the meticulous laboratory experiments more highly than the insights to be gained from clinical observation at the bedside. In the first instance, critics scathingly dismissed von Pirquet’s terminology. In promoting his own understanding of the precise mechanisms operating in anaphylaxis, for example, Charles Richet condemned the introduction of what he regarded as an unnecessary new term. Richet’s rejection of the term allergy was echoed elsewhere. When von Pirquet’s book was reviewed in the *Lancet* in 1911, the reviewer referred to the term as ‘not a happy combination’, and pointed out that Richet had already coined the word anaphylaxis to describe increased sensitivity to foreign substances. (Jackson, 2006, p. 40)

Here, Jackson highlights the fact that ‘allergy’ was interpreted by the immunological community as merely a re-description of immunopathology, already sufficiently encapsulated in the concept of anaphylaxis. Importantly, Pirquet’s notion of an open and uncommitted responsiveness (a schema for organising all immune responses) was overshadowed by an interpretation of allergy as pathology. His critics tended to focus on only one subset of reactions covered by the allergy hypothesis (namely, hypersensitivity) and thus neglected the broader scope of his findings and their implications. One could argue that Pirquet’s hypothesis was conceptually and philosophically unavailable to other immunologists of the time. This point is echoed in the dissatisfaction with the term expressed by American immunologists Robert A. Cooke and Arthur F. Coca. As Jackson states, from Cooke and Coca’s perspective, ‘von Pirquet’s original definition resulted in the inclusion of “phenomena of such different nature as to make their association valueless if not positively confusing”’ (Cooke & Coca, cited in Jackson, 2006, p. 40). Here, the terms ‘valueless’ and ‘confusing’ indicate just how obscure Pirquet’s ideas must have seemed.

In the context of an intellectual community that had worked hard to maintain a clear separation between immunity and disease, protection and pathology, the work of the ‘self’ and the work of an-other (a disease agent), the deliberate collapse of this distinction at a physiological level was perceived as a major transgression. Silverstein argues:

Just as Ehrlich’s maxim of horror autotoxicus inhibited free speculation and progress toward the understanding of autoimmune diseases, so did the general Darwinian teleological view of a benign immune apparatus inhibit acceptance of allergic disease as another facet of the same response. The continuing desire to keep allergy separate from immunity fostered early suggestions that substances other than antibodies ... were the immediate causes of these reactions. (Silverstein, 1989, p. 215)

By incorporating immunity into the repertoire of changed immunological states identified as instances or *types* of allergy, Pirquet subordinated immunity to allergy, and instated the latter as the governing principle of immune responsiveness. The suggestion that there existed a more fundamental concept than immunity—or a

⁸ For a detailed analysis of the concept of ‘altered reactivity’ and Pirquet’s monograph, see Jamieson (2008).

more logical interpretation of this innate physiological response—was fundamentally incongruous with the view of the organism, body, and/or self that is central to this discipline.

The reception of Pirquet's work illustrates that, in the early twentieth century, the field of immunology was itself allergic to the implications of his findings, in the conventional immunological sense. Within a discipline committed to the protective powers of immunity, the idea that the self could act against its own interests (its health) or that it demonstrated the potential to turn away from the task of self-protection, was literally perceived as pathological. If an allergy is an inability to tolerate some-thing or substance as self, or misrecognition of a benign entity as foreign and thus toxic to the self, it follows that immunology—as a field of study with a distinct disciplinary identity—would be unable to accommodate (to accept as self) the wider philosophical and conceptual implications of 'altered reactivity'. Immunology's early investment in an idea of the immune response as a unidirectional, purpose-driven reaction meant that Pirquet's notion of an 'uncommitted biological response' (Kay, 2006, p. 556) fell outside its discursive parameters (it was literally foreign to immunology, in the etymological sense of being 'on the outside, exterior'; *foranus*).

In drawing a primary connection between protective and pathological immune responses, Pirquet's studies implicitly raised questions about the *purpose* of immune responsiveness.⁹ If its purpose wasn't strictly protective, if it didn't serve an end that could be identified directly (maintenance of the self), then how could it be explained? Although informed by these notions of 'purpose' and 'self', it is arguable that Pirquet's investigations were oriented more towards discerning the *nature* or *character* of immune responsiveness. Rather than adopting immunity as an empirical and conceptual point of departure for interpreting anomalous reactions, Pirquet developed his own, broader schema for understanding immune phenomena that didn't rely upon this logic. At issue in his study was not how the body protects itself but, instead, how an organism or body formulates and manifests particular responses to specific substances at different points in time, and, crucially, patterns of change in this responsivity. Pirquet's studies, especially those documented in his monograph, foregrounded the complex biological interrelationship of organism and environment, as well as organism and antigen, as a vital factor in understanding immune responsiveness. More philosophically, these extended investigations pointed to the larger question of how organisms and antigens come to be materially (that is, responsively) inter-implicated, and yet constituted as separate, discrete entities.

Pirquet's insistence on the alterability of reactivity suggests a view of the biological body and its relationship to its environment that is at odds with the dominant notion of a defended, immunological self, entrenched in a context of otherness. His observation of the fundamental mutability of immune responsiveness challenges the idea of a fixed, stable immunological being that governs its responses to others, such that it remains consistent with (or identical to) itself. The discursive authority of immunity and its presumption of a discrete, autonomous organism have long precluded the question of how the body/self comes to exist as a clearly bounded entity—that is, how it acquires or establishes its borders (its biological identity) in a world where these physiological parameters are *negotiated rather than given*. The existence of an immune organism that responds instinctively to the intrusion of for-

eign elements is an axiom of modern immunology; importantly, it is not a question or puzzle in itself. However, I argue that it is precisely this question that Pirquet's work addresses. In examining and mapping the conditions of reactivity and, moreover, the conditions that give rise to its fluctuation, his studies rethink the nature of immunological identity.

3. Histories of allergy and immunology

The general response that Pirquet's hypothesis received at the beginning of the twentieth century (outlined earlier) is a position that has been maintained in critical and historical accounts of his work.¹⁰ The ways in and extent to which his findings were recognised by his contemporaries tends to be mirrored in the historicisation of his work: how it has been recorded, taken up, and critically elaborated with respect to immunology. Within histories of allergy and immunology, Pirquet's allergy hypothesis itself has not been extensively engaged. More apparently, the philosophical and theoretical implications of 'altered reactivity' for immunological interpretations of organismic identity have remained largely unexplored. Although Pirquet's work with Bela Schick on serum sickness is cited routinely as one of the key early twentieth-century discoveries of pathological immune responses (alongside anaphylaxis, local anaphylaxis, and the Arthus reaction), Pirquet's particular theory of allergy occupies a more ambiguous space in the narration of the field's history.

The literature in which Pirquet's work appears most frequently can be divided into a number of genres or types. First, Pirquet is cited in official histories of allergy and immunology that chronicle the key figures and discoveries in this discipline. This category includes accounts found in immunological textbooks and manuals (for example, Klein, 1982; Golub, 1991), articles devoted to figures and milestones in medicine (for example, Bendiner, 1981; Dworetzky and Cohen, 2002; Rapaport, 1974; Wagner, 1963), as well as more extended accounts within the history and philosophy of science and medicine that deal with the trajectory of the discipline and its concepts (for example, Moulin, 1991; Silverstein, 1989; Tauber, 1994). Second, Pirquet can be found in more recent histories and studies of allergy that contextualise the phenomenon socially, culturally and politically, as well as scientifically (for example, Jackson, 2006; Mitman, 2007; Keirns, 2008). These historiographical contributions typically pay more attention to the negotiation of ideas and scientific controversies that define the emergence of allergy as a proper immunological concept. Third, Pirquet is celebrated in articles devoted to anniversaries of the term allergy (for example, Kay, 2006; Huber, 2006a, 2006b; Ring, 2006).¹¹

While there are a few exceptions to these categories, they are nevertheless indicative of the ways and contexts in which Pirquet's work has been engaged, critically and historically. Within the above-mentioned literature, Pirquet is conventionally cited as the father of the term 'allergy', or as establishing the foundations for the development of a more specific conceptualisation of this type of immunopathology. However, the particular implications of 'altered reactivity' tend to be passed over, or else the term 'allergy' is re-interpreted in light of contemporary definitions of immunopathology (for example, Ring, 2006, p. 138; Porter, 1997, p. 447). Pirquet is often listed as a more minor figure among a host of relevant names that have come to exemplify scientific progress in this field (for example, Simons, 1994; Unger, 1960; Unger and

⁹ Many of the earliest investigations in immunology that document more confounding and seemingly illogical (paradoxical) responses raised questions about the purpose of these responses in relation to a biological self. A key example of this is the discovery of anaphylaxis (1902). As Kenton Kroger explains, Charles Richet spent years, following this discovery, trying to understand the biological and evolutionary necessity of anaphylaxis, and hypothesised that it served the wider purpose of maintaining the integrity and purity of species (Kroger, 1999, p. 274). For a detailed discussion of Richet's theories on this point, see Kroger (1999).

¹⁰ The primary exceptions to this rule are Jackson (2006) and Huber (2006a, 2006b).

¹¹ Many accounts of this style are published in German, Polish and other European languages. However, very few are available in English. This article deals only with texts published in (or translated into) English.

Harris, 1975).¹² Thus, despite widespread acknowledgement of Pirquet's work in historical texts, the insight that the allergy hypothesis provides into the problematic of immunological or biological identity has not been closely examined.

This lack of intimate engagement with the philosophical implications of Pirquet's concept within critical historical reflections on immunology has arguably reinforced the perception of 'altered reactivity' as an 'early' scientific concept. Its contextualisation within conventional immunological histories has secured its identity as a novel concept that aided the eventual discovery of allergy's correct (that is, current) meaning. In *Genesis and development of a scientific fact*, Ludwick Fleck describes this kind of early concept as a 'proto-' or 'pre-idea' (1979 [1935], p. 22). For him, proto-ideas are concepts that may or may not have an empirical foundation, but which contribute to the realisation of facts later regarded as proper to the history of science. He explains: 'Many very solidly established scientific facts are undeniably linked, in their development, to prescientific, somewhat hazy, related proto-ideas or pre-ideas, even though such links cannot be substantiated' (ibid., p. 23). Pirquet's hypothesis, as it figures in histories of allergy and immunology, takes the form of a proto-idea. In these narratives, 'altered reactivity' is situated in a developmental stage of the discipline's history and, as such, identified with an epistemological context in which the facts of allergy had yet to be deduced. Thus, as a proto-idea, 'altered reactivity' functions as a precursor to the contemporary, factual definition of allergy.

The contextualisation of Pirquet's work in these tomes raises the issue of the relationship between the work of history (the construction of historical accounts) and that of science (the discovery/construction of scientific facts). There is an intimate and complex connection between historical writing and the establishment and affirmation of scientific discourses and truths. As Jackson notes, official histories of allergy generally take the form of linear, progress narratives that frame the past as a series of basic but necessary insights that have enabled current scientists to access more correct scientific truths. In *Allergy and history*, he writes:

Most recent histories of allergy and allergic diseases have tended to adopt a positivist approach to the subject, regularly depicting allergy as a linear series of milestones or stepping stones of great discoveries, seminal publications and influential scientists that collectively freed the field of clinical immunology and allergy from a position of deep ignorance in the mid-nineteenth and early twentieth centuries to one of enlightened knowledge and therapeutic power in the modern world. (Jackson, 2003, p. 389)

Jackson emphasises that the histories we have are those, the narratives of which confirm the evolved and more advanced position of contemporary immunological research. Here, historical work and the production of scientific knowledge can be seen as different facets of the same project.

In *Toward an unnatural history of immunology*, Warwick Anderson and colleagues discuss the 'genealogies of "immunology"' (Anderson et al., 1994, p. 579) referred to by Jackson, and argue that these histories are predominantly written with an eye to the key immunological theories of the mid twentieth century. Emphasising the non-neutrality of this model for presenting past events, they insist that in the context of science, linear history is a form of representation that embodies its own politics of truth. Anderson

and colleagues are critical of widespread adherence to this model, and argue that this style of historical work presumes a position of enlightened knowledge from which the truth of things is naturally revealed through an objectivity provided by hindsight. They explain:

To position oneself at the end of history is no casual exercise. Rather, it is a powerful (if unwitting) means of defining the boundaries of one's discipline, and of securing the legitimacy of one's knowledge. Since Hegel, the end of history has implied a transition from a perplexing dialectical change to the rational functioning of Spirit—of immunological truth, in this case. (Anderson et al., 1994, p.576)

Anderson and colleagues argue that intrinsic to a teleological picture of history is a connection between past and present work that grounds and further entrenches contemporary scientific achievements in a clearly identifiable, locatable ancestry. They explain that immunology's history is often told using "a series of biographies linked by the principle of hereditary succession", which act to "validat[e] the family's legitimacy" (Spiegel, 1990, cited in Anderson et al., 1994, p. 582). These "filiative model[s]" of historical change' (ibid.) create the fiction of a pure and uninterrupted lineage that can be called upon to ground new findings and ideas, while actively prohibiting the intrusion of elements (concepts or events) that threaten its coherence. Hence:

A functional history will (for scientists) generally be one where the ancestors they read about can rewardingly be adopted as *their* ancestors, the ideas readily affiliated with *their* ideas; it will not be one that reveals the unnatural (or socially contingent) character of the field's boundaries. (Anderson et al., 1994, p. 582 [original emphasis])

Consequently, the figuration of Pirquet's hypothesis in these histories foregrounds what is vitally at stake in the maintenance of such orthodox narratives: a conceptual and philosophical investment in immunity, a self-centric model of immune function, and its implications for an enclosed, defended organism. That is, its historicisation (as exemplary of the way alternative concepts are incorporated into these accounts) demonstrates that immunity constitutes immunology's master narrative. In order to understand how and why this concept achieves such prominence, it is worth revisiting the intellectual origins—the formative events and ideas—that are fundamental to the discipline. This analysis will help to identify the assumptions about physiological function, body and self (definitive of immunological thought) and thus illustrate the processes by which a particular incarnation of the immunological body/self has emerged as significant to the field.

4. The conceptual foundations of immunology

The definitive concepts of immunology's history are almost always traced to a common, familiar legacy: developments in late nineteenth-century bacteriology and, specifically, Louis Pasteur's discovery of vaccination (1879).¹³ In the official historical accounts mentioned earlier, Pasteur appears repeatedly as an eponymous figure whose insights and achievements are widely recognised as foundational to immunology. This emphasis on Pasteur as a founding father means that his work has become synonymous with the birth of this discipline and, consequently, it is not unusual for his legacy to

¹² This treatment of Pirquet's work is summed up in an editorial published in *Allergy and Clinical Immunology International—Journal of the World Allergy Organization*. Author Johannes Ring describes Pirquet's *Allergie* (1906) as 'a "citation classic" of modern medicine' (Ring, 2006, p. 138), meaning that it has become an essential reference within proper histories of the field. That is, Pirquet's theory of allergy is cited as though its meaning were self-evident. In this sense, Pirquet's work has been engaged as *an historical reference*, rather than a text and body of work that remains open to critical reading and interpretation.

¹³ For examples, see Golub (1991) and Silverstein (1989). There have been attempts to critically rethink and disrupt this narrative and complicate its conceptual heritage. See Mazumdar (1995), as well as Tauber & Chernyak (1991).

be evoked as a point of departure for reconstructing a proper account of its history (Cohen, 2001, p. 198).

The perceived significance of Pasteur's findings for the establishment of this new scientific field has undoubtedly been supported by the achievements of important forerunners (for example, Edward Jenner's early work with vaccination against small pox) and descendants (for example, Elie Metchnikoff's discovery of phagocytosis). That is, his status as an historical figure is a product of retrospection, along with the reconstruction of events and ideas surrounding Pasteur's work that such a position entails. Yet, despite this, Pasteur's contributions are frequently identified as an historical and epistemological turning point—the crucial moment of transition from bacteriology to immunology.¹⁴ Regardless of the fact that his vaccination experiments didn't in and of themselves establish the principle of immunity, his work speaks of a familial connection between these fields, a thread that is visible in the evolution of specific immunological concepts (for example, immune response and immunological body) and the discursive construction of immunology's achievements. As such, the institution of Pasteur as an originary figure that bridges these disciplines has arguably secured an account of immunology's history that locates its conceptual and intellectual debt in a stable, scientific origin; namely, the discovery of vaccination.

It follows, then, that immunology's development into a distinct discipline is tied to the inheritance of concepts that are typically traced to Pasteur's experiments and his background in bacteriology. One of the most important and basic insights to come from his work (or more accurately, from the historical moment in science and medicine of which his experiments and ideas are exemplary) was the infective relation between the microorganism and host body. Pasteur's studies of fermentation, anthrax and rabies demonstrated the existence of microorganisms and their role in infectious diseases. These different investigations, which focused on isolating microbes, established a conceptual and ontological distinction between the host body and microbe (the vessel of disease and the agent of disease). This distinction proved central to the development of germ theories of disease, and thus to concepts of pathology in general. As Kodell Carter explains in *The rise of causal concepts of disease* (2003), the emergence of experiments proving that specific pathologies resulted from the presence of microorganisms led to 'a fundamental reorientation in how physicians thought about disease' (Carter, 2003, p.127).

With respect to Pasteur's work, I am interested in the function of the host–microbe interaction as a perceptual/conceptual framework for interpreting physiological events. In particular, I am curious about the concept of organismic identity that this legacy establishes as the foundation for immunological research and thought. Broadly speaking, the model of ecological relations that underpins both bacteriology and immunology—namely, an antagonism between host body and microbe—is one based on a view of the world as a system of discrete, bounded organisms. Within this framework, the organism emerges as a monadic body that interacts with others that are similarly autonomous and physically circumscribed. Put simply, it implies a view of 'the self as a distinct, circumscribed entity... divorced from its environment' (Tauber, 2008, p. 225 [original emphasis]), the primary mode of existence of which is an inherent opposition or defensiveness toward others. Consequently, immunology is grounded in a concept of ecology based on a strict demarcation of organism from environment, self from nonself, inside from outside, native from foreign. Crucially, it is not committed to any sense of the inter-implication or mutual embeddedness of these terms—an embeddedness that *conditions* these divisions.

This basic understanding of organismic identity lies at the heart of some of immunology's most fundamental ideas; in particular, its conceptualisation of the organism as a 'defended body' (Moulin, 2000, p. 385) or immunological self. Alfred Tauber explains, '[s]ince immunology was born during the decipherment of infectious diseases at the end of the nineteenth century, immunologists have generally adopted an insular perspective, where an entity is *defended*' (Tauber, 2008, p. 225 [original emphasis]). The defended body is a body that defines itself through an antagonistic or hostile relation with otherness—a relation predicated on the basis of intrinsic knowledge of what belongs to the self and what does not. From this position, all physiological events are subordinated to 'a common purpose: the defense and representation of the self' (Moulin, 2000, p. 395). This interpretation of biological function—which relates directly to the study of microbes and their characterisation as foreign, external agents—forms the dominant discursive framework of modern immunology.

Certainly, Pasteur is by no means solely responsible for the prevailing notion of a defended immunological self, and its corresponding vision of ecological relations. A much wider landscape of scientific thought and practice has contributed to the persuasiveness and self-evidence of this concept. Nor is he the only figure that historians have nominated as a founding father of the discipline. As with any other field, the precise origins of immunology form a subject of ongoing debate and contestation. Nevertheless, in this analysis the nomination of Pasteur as the father of a uniquely immunological perspective serves an important heuristic function: it allows for an examination more focused on the philosophical and conceptual investments that a conventional immunological model of life secures. Interpreting Pasteur's work as a provisional origin of these ideas is useful in anchoring a discussion of how a specific conceptualisation of immunological identity emerges. In particular, his vaccination experiments are valuable in illustrating how the logic of infection (one discrete entity penetrating and contaminating another discrete entity) arises as a principle for interpreting immune phenomena; they demonstrate the logic that underpins a conventional distinction between pathogen and host. In this way, Pasteur's work acts as a point from which to interrogate the conceptual bases of the defended immunological self.

5. Pasteur and the host body/microorganism relationship

From the beginning of his scientific career, Pasteur was fascinated with the lives of microorganisms. As a chemist turned microbiologist, he devoted an enormous amount of energy to studying the characteristics of these smaller life forms. Throughout his lifetime Pasteur argued that the study of microbes was central to understanding physiological and chemical phenomena that continued to puzzle scientists of the time; for example, the changed states of substances, such as fermentation and putrefaction. Importantly, Pasteur's major successes occurred at points when he was able to isolate the microbe and its effects to greater degrees. For instance, in the 1850s and 1860s he disproved the theory that fermentation was a chemical process and that ferments were inherently 'unstable chemical products', showing instead that fermentation was 'the result of the action of particular living micro-organisms' (Porter, 1997, p. 431). As Carter explains, '[b]y 1861 Pasteur was convinced that different forms of fermentation were associated with the life processes of distinct organized ferments' (Carter, 2003, p. 64). These experiments—which identified the microbe as an entity existent within, but distinct from, its environment—were the first step

¹⁴ Tauber & Chernyak (1991) argue that Elie Metchnikoff was the first to establish scientifically a theory of immunity, and as such, his work should be regarded as the origin of the discipline. For a detailed discussion of this contested origin, see Tauber & Chernyak (1991).

towards proving Pasteur's belief 'that different organic processes ... [were] caused by distinct organisms' (ibid., p. 65).¹⁵

In the years following these pioneering insights, Pasteur turned his attention to the relationship between microorganisms and disease, and in the late 1870s confidently hypothesised that 'microorganisms were responsible for disease, putrefaction and fermentation; that only particular organisms could produce specific conditions; and that once those organisms were known, prevention would be possible by developing vaccines' (Porter, 1997, p. 433). By 1879 this theory had been confirmed by a number of experiments that are now synonymous with the discovery of vaccination. Whilst conducting experiments with chicken cholera, Pasteur infected healthy chickens with "stale" cholera-causing microbes, two or more weeks old, which produced 'no serious disease' (ibid., p. 43). After failing to reinfect these same birds with a new virulent culture, he discovered they were protected from the disease. Confirmation of these results was achieved in a follow-up experiment that applied the same principle to anthrax in livestock. With these findings, Pasteur 'established the general principle that an organism [microorganism] can be altered (ATTENUATED) so that it does not cause disease but still retains the property of inducing immunity' (Golub, 1991, p. 5 [original emphasis]). In other words, he had discovered that by lowering the pathogenicity of infective organisms and injecting these into animals one could induce lessened disease effects in the host; that is, eliminate a pathological response to the same bacteria.¹⁶

The force with which the legacy of Pasteur is asserted in medical histories can be attributed to the enormous successes in bacteriology that accompanied these experiments. Pasteur's demonstration of the role of microorganisms in pathogenesis, paired with German physician Robert Koch's research into the identification of bacteria associated with specific diseases (the creation of his famous postulates), contributed to the eventual establishment and acceptance of germ theories of disease. Germ theory—which is typically (though erroneously) evoked in the singular—emerged in the late nineteenth century and is regarded as bacteriology's defining contribution to medical science and practice. In *Spreading germs: disease theories and medical practice in Britain, 1865–1900* (2000), Micheal Worboys notes that its significance is reflected in the fact that 'there are perhaps more celebratory histories of "the microbe revolution" than any other episode in medical history' (Worboys, 2000, p. 1). Importantly, he emphasises that there was never one definitive germ theory, only multiple conflicting theories (ibid.); indeed, 'the differences between germ-theorists were often as great as those between them and their opponents' (ibid., p. 4).¹⁷

While Worboys reminds us that there were marked differences between specific germ theories (or accounts of disease causation), Carter argues that these diverse perspectives were nevertheless

united by a common conceptual framework. According to Carter, all germ theories adhered to 'the etiological standpoint' (Carter, 2003, p. 1). Cited from the work of Koch, 'the etiological standpoint' refers to 'the belief that diseases are best controlled and understood by means of causes and, in particular, by causes that are *natural ... universal ... and necessary*' (ibid. [original emphasis]). Put simply, it refers to a concept of disease that is intimately tied to the investigation of causes. For Carter, the legacy of germ theories for modern concepts of disease can be seen in the endurance and entrenchment of an aetiological perspective, now evident in the intuitive or automatic connection made between the notions of 'pathology' and 'cause'. He explains that since the late nineteenth century, an 'interest in universal necessary causes' has been 'a defining characteristic of modern western thinking about disease' (ibid.).¹⁸

Widespread adoption of an aetiological standpoint radically altered understandings of pathogenesis in the scientific, medical and public imaginations. What emerged most explicitly from these conceptual developments was the establishment of a direct connection between the concepts of infection, causality and disease. From an aetiological position, disease is envisioned as the product of an infection, whereby one body (a microorganism or disease agent) infects another separate body (a host organism). That is, aetiology reconceptualises disease and its operation in/on the body by drawing a causal relationship between the presence of microorganisms and damage or harm experienced by the host body. Thus, this model of disease is one that presumes the prior existence of two independent bodies or entities that enter into relation with one another: here, disease is something generated by the interaction of these entities.

6. Anticipating immunity: the legacy of causal theories of disease

Pasteur's contributions to the development of an aetiological framework for interpreting disease (his experimental proofs of disease causation and work with vaccination) have had direct implications for the way pathology is construed in an immunological context. In making a correlation between the presence of microorganisms and changed pathological states, Pasteur's work established 'infection', and its assumption of a foreign disease agent and a stable immunological body, as a basic model of disease. Consequently, implicit in immunology's understanding of the body and bodily pathology is a material and ontological distinction between host and microbe, self and nonself, native and foreign.

A number of commentators have stressed that Pasteur's experiments with vaccination were driven *solely* by his interest in microorganisms (Cohen, 2001, p. 193; Moulin, 1991, p. 47). Cohen writes

¹⁵ Pasteur's demonstration of the existence of microorganisms famously disproved the theory of spontaneous generation—the idea that life can arise from nonlife. Spontaneous generation was a doctrine that emerged within natural philosophy, particularly in Germany, and rose to prominence in the early nineteenth century (Farley & Geison, 1974, p. 163). According to Farley and Geison, this theory was based on 'the notion that living organisms can arise independently of any parent, whether from inorganic matter (abiogenesis) or organic debris (heterogenesis)' (ibid.). In scientific histories, spontaneous generation is often recounted in terms of the famous debate between Felix Pouchet, a French naturalist who put forward a version of this theory in *Hétérogénéité* (1854), and Louis Pasteur, whose fermentation experiments were designed to directly disprove Pouchet's hypothesis. As a result of its contextualisation within narratives that treat Pasteur's work as the triumph of scientific method, spontaneous generation assumes the status of a myth that has been debunked. See Farley & Geison (1974) for a detailed examination of the Pasteur–Pouchet debate, and an analysis of how Pasteur's legacy has effected the perception of spontaneous generation as a scientific theory. Also see Pouchet (1859).

¹⁶ This brief sketch of Pasteur's famous experiments with vaccination focuses on the broad conceptual and scientific claims they produced. For a detailed discussion and contextualisation of these experiments, see Carter (2003).

¹⁷ Worboys argues that monolithic interpretations of germ theory are an artefact of the way the overall achievements of this period are remembered. His text, which recognises the plurality of germ theories, complicates an overly simplified or generalised view of the development of these concepts. For a detailed discussion of germ theories, see Worboys (2000).

¹⁸ The self-evidence of causality as a model for interpreting pathology is a phenomenon Carter problematises in his historical account of the emergence of concepts of disease causation (Carter, 2003). He stresses the historical specificity of causality as an intellectual apparatus for interpreting physiological events. Carter states that at the time at which Pasteur and Koch were competing to be the first to demonstrate causality experimentally, the concept was still in its infancy. Around the 1870s, 'there was a growing awareness of, and interest in, the concept of disease causation' (ibid., p. 73 [original emphasis]); however, ongoing disputes regarding the adequacy of experiments in proving causality (prior to the establishment of universal criteria) indicated that the precise meaning of the concept was still under debate.

that Pasteur's work 'focused almost exclusively on manipulating strains of bacteria that had been correlated with recognizable patterns of symptoms (a.k.a. "diseases") in the hope of mitigating the pathogenic effects produced and reproduced by their movements in the "external" world' (Cohen, 2001, pp. 193–194). Pasteur viewed the microbe as the centre or locus of biochemical activity—a natural, given point of reference for the investigation and explanation of phenomena related to physiological disturbance (or changed physiological states). In taking this position, he imagined all biochemical change to be in some way mediated by the activities of microbes. That is, Pasteur understood microbes as the primary site of agency and responsibility in relations among organisms and microorganisms. As such, he viewed them as the motor of change, or the source of the agency that instigates and produces change, within systems of organisms. For Pasteur, the microbe emerges as a key determinant of the ecological relations elaborated in his research.

However, in recognising the microbe as the principle source of agency in these events, Pasteur discounted the active role the host organism might play in disease processes. As Cohen explains, Pasteur imagined the body in stark opposition to the microbe, as a passive, internal space. Drawing an analogy between the body and the laboratory, he interpreted the host body as a similarly neutral and uncontaminated space through which the lives of microbes could be studied. This abstract view of the body as a 'medium of bacterial growth' (Cohen, 2001, p. 194) rendered the living processes of the host insignificant: it authorised a perception of the host body as a mere vessel for organismic activity, rather than a *participant* in these dynamic relations.¹⁹

In viewing the host organism purely as the microbe's other—or the context of its actions—Pasteur's interpretation of these physiological events was dramatically removed from any conceptualisation of the immune response, in the sense of an active responding on the part of the immunological body. 'Pasteurian medicine', writes Moulin, 'doesn't rely upon theoretical hypotheses concerning immunity, but on an empirical program of immunization which appeals to the attenuation of micro-organisms' (Moulin, 1991, cited in Cohen, 2001, p. 196). Thus, Pasteur's account of the conditions and processes that enabled vaccination did not factor in any theory of immunity or immune response. Indeed, he did not conceive of host–microbe relations within his own experimental systems in terms of a *response* at all. In his understanding, the actions of the host always appeared as the *effect* of an external provocation, as purely 'reactive' (rather than 'responsive'), mechanically determined, or lacking in the agency that presumably comes with intention, intellection and cognition.

Pasteur's emphasis on the microbe's role in determining pathological events firmly established a context—a concept of the environment or others—that the immunological body has arguably come to inhabit. In defining disease as a process catalysed by the intrusion of a foreign agent, he cemented a notion of pathology as something that does not properly or normally belong to the body, but which comes from 'outside' (consider contemporary definitions of allergy and infectious disease). Pasteur understood disease as 'the ecological disturbances effected by a pathogenic agent within an organic "culture"' (Cohen, 2001, p. 193); in other words, an event of penetration and contamination that disrupts or changes a given, normative state. As such, he created a framework for discriminating between normal and pathological states, which relied on a view of the microbe and host organism as biological entities fixed in an adversarial relation. According to the logic of this distinction, the body that exists separately from the microbe is one naturally free from infection (or prior to contagion), in the

sense of having had no previous encounter with, or knowledge of, its ecological other. In its state of inert passivity, it is an entity constantly acted upon, vulnerable to invasion, and thus physiologically naive. Consequently, the immunological body Pasteur conjures in his picture of disease is a body *in need of protection*.

In setting up this conceptual schema for thinking about the host body, Pasteur's work can be viewed as foundational to immunology's interpretation of immune responsiveness and its basic conceptualisation of *response*. From his view of organism relations—or what might be broadly described as ecological relations—response is figured as a predetermined interaction between stable, identifiable entities. It is imagined as the *outcome* of an encounter between discrete organisms, or a *consequence* that is already determined by the identities of the organisms involved. Here, response is reduced to fixed 'responsible parties' (either a disease agent or a malfunctioning immune system) and the disease-producing relationship of pathogen and host—the conditions that make contagion or infection possible—is neatly resolved or, more accurately, deferred, as in Pasteur's account of the microbe as the author of pathogenic events.

Pasteur's emphasis on the microbe (as opposed to the host) raises questions about the structure of relations that establish the microbe as the central player. Questions regarding the ecological complementarity of microbe and host—the very capacity of the former to be physiologically provocative for the latter—are inevitably buried under more pressing concerns to discover and eliminate the causes of disease. Pasteur's commitment to a series of distinctions implicit in his understanding of pathology (for instance, organism/antigen, self/other, inside/outside, agency/passivity, and cause/effect) means that he does not make sense of physiological disturbance or organismic identity in terms of the entangled ecological conditions that give rise to these phenomena. In beginning with the assumption of given organisms/entities, this interpretive framework obscures the inter-implication of organisms, which constitute the necessary conditions of infection. For this reason, his work passes over the philosophical issue of the ontological entanglement of stimulus (foreign, external agent) and response (defended, immunological body) and, consequently, relies on a concept of response as essentially *reactive*.

7. Refiguring the immunological body

This paper has argued that Pirquet's concept of allergy has historically been interpreted according to a conventional model of immunopathology. This reading of allergy-as-pathology is a product of the narration of immunology's history, and the tendency of these narratives to focus on this discipline as being one concerned centrally with immunity. As such, the notion of 'altered reactivity' as a general theory of immune responsiveness—and thus a concept that might replace immunity as the governing principle of immune function—has not figured prominently in the history. 'Altered reactivity' challenges the conceptual basis of immunity and, in doing so, proposes a very different understanding of organismic identity.

As shown, immunology's emphasis on immunity and its conceptualisation of the organism as a defended isolate can be traced to its reputed origins: Pasteur's discovery of vaccination and his work developing and proving a causal account of disease. Pasteur's investigations of microorganisms and their role in disease processes presumes a model of organism relations grounded in the prior separation of organisms from one another and their environment. Specifically, his understanding of pathology as the product of an infection—a causal interaction between different types of entities—confirms the view that the biological identity of organisms is given at the outset of life. The conceptual framework underpin-

¹⁹ For a detailed analysis of Pasteur's understanding of the host body/microorganism relationship, see Cohen (2009).

ning this reading of pathology is one that foreshadows the 'immune' organism. Pasteur's adoption of an aetiological perspective, coupled with his interest in discovering methods for ameliorating disease (vaccination), prefigured a notion of the organism as a given unit vulnerable to invasion by foreign, external elements.

More broadly, then, the idea of an immune organism (along with its implications of atomism, discretion, autonomy, and defendedness) stems from the aetiological approach to pathology that surfaced in the late nineteenth century. The notion of an immunological body first emerged in the context of debates about the relationship between disease and causality (or universal necessary causes). Specifically, it arose from studies of organismic interactions that clearly identified the microbe as a pathogenic stimulus responsible for causing or eliciting a reaction from a host body. Importantly, this emphasis on disease causation compartmentalises microbe from host, and stimulus from response, both conceptually and materially. In doing so, it obscures the ecological entanglement of these terms: in beginning with a fixed opposition between distinct entities, it negates the larger spatio-temporal conditions that constitute this relation.

In sum, the model of immunological identity that forms the starting point of immunological work is a discrete entity, whose material, responsive entanglement with the world is reduced to a series of predictable 'reactions' that correspond to contact with specific stimuli. In other words, it is an organism, the identity of which is defined negatively with respect to a pathogenic, microbial agent; or, rather, the nature of which is determined by the position it occupies within an aetiological schema.

I would like to suggest that, in contrast to immunity, 'altered reactivity' captures (rather than reduces) the ecological complexity of immune responsiveness and immunological identity. Rather than presuming a discrete monadic organism, Pirquet's concept of allergy begins with an open and uncircumscribed 'reactivity'. By insisting on the essentially mutable nature of reactivity, his work significantly complicates the possibility of a pure identity or fixed origin (an immunological self) that anchors immune responsiveness. Indeed, Pirquet's emphasis on the contextually embedded nature of all immune phenomena calls into question the existence of a coherent, contained, self-identical body that forms the departure point for interpreting immune events.

Pirquet's reading of the immune response as an open, mutable and ceaseless responsiveness or response-ability presents an account of organismic identity that resists any simple aggregation of ecological complexity into a series of brute reactions between isolated, pre-existent entities. In fact, it proposes a radical refiguration of the immunological body that has become basic to common-sense understandings of health (a protected, impermeable self) and disease (an attack by something essentially foreign). Pirquet's suggestion that the stability of immunological identity lies only in the perpetual fluctuation of reactivity requires us to rethink the terms and categories through which we have come to understand immunological being (normal/pathological, self/nonself, action/reaction). More precisely, his view of the organism as constantly mutating threatens the integrity of these bifurcations: if the organism's responsiveness cannot be explained in terms of the stability of a governing 'self', then it no longer makes sense to differentiate between normal and pathological responses, because what constitutes the self is always only provisional.

Pirquet's theory of immune responsiveness acknowledges that the self or organism is not separate from the world around it. For him, the 'self' cannot be completely 'other' to the bacteria that cause it to respond in predictable and patterned ways. 'Altered reactivity' is founded on a more ecological view of how the self—expressed in the specificity of its immune responses—is an existent of the world, not just in the world. Thus, it no longer makes sense to

start with the immunological self as a given entity; rather, it becomes necessary to ask the question of how a self emerges as itself. Pirquet imagined a 'response' as something open and uncommitted—an inherently unstable or changeable relation of the body with its environment—indeed, of the body with itself. In his work, immune responsiveness (and thus also immune function) begins with the volatility, dynamism and mutability of identity. It doesn't presume it.

Acknowledgements

I am very grateful to Vicki Kirby and Elizabeth Wilson for their feedback on early and later versions of this article, as well as the anonymous reviewers whose advice has helped me to improve and clarify it. Many thanks to Antje Kuenhast for generously translating Benedikt Huber's articles on Pirquet from German to English.

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