The Factory Model of Disease

Neil Williams

from: *The Monist*, October 2007, Volume 90, Number 4, 555-584.

Introduction

The aim of the paper is to give an ontologically informed account of disease that can aid in the construction of disease ontologies. The paper begins by distinguishing cases of diseases from what are purely structural abnormalities, referred to as 'disorders'. The paper then presents a causal model apt for the understanding of disease that distinguishes diseases from both their causes and their potential effects. The analysis of disease defended treats disease in terms of distortions of standard cellular network processes, where those distortions are incapable of self remedy and produce biologically disadvantageous symptoms.

Part of the recent trend in systematizing the intractable masses of biomedical data has seen the construction of various *disease ontologies*.[1] If these disease ontologies are to succeed in making disease data computable, it is imperative that a coherent understanding should be developed of what should and should not be included within them. This means that in order to construct a satisfactory disease ontology a viable concept of disease is indispensable. My aim here will be to furnish such a concept.

What I offer is an analysis of 'disease' in terms of deviation from statistically determined norms. This is itself far from novel, statistical accounts of disease having long been present in the literature.[2] For this reason, I consider this account a *re*-defining, rather than just a defining of 'disease'. That said, my account presents a treatment of the concept of disease that departs from those that precede it with regards to both the causal model in which the account is articulated and the location of disease. Another important difference concerns the distinction between 'disease' and 'disorder', absent in most contemporary accounts.

The most basic version of the account is an analysis of disease in terms of statistical deviation understood in terms of cellular processes and analysed at the level of cellular networks. Cellular networks typically operate within a tightly constrained range; when those ranges far enough outside the norm that they are incapable of returning to the norm through standard processes of self-regulation, we have an instance of disease. The disease then is itself a *process*: a process of deviant cellular interaction outside of typical homeostasis.

Before turning to those matters, however, I want to offer a brief word of caution concerning the concept of disease. Much of the pertinent debate has concerned the extent to which 'disease' is a value-laden concept.[3] I will make no attempt to contribute to this issue here, except to say that I take it to be

largely off-target. Those interested in whether disease is a value-laden concept tend to be less interested in the definition of 'disease' per se, and more concerned with the *impact* various definitions might have for different communities of doctors or patients. Suppose, for instance, that a certain definition of disease happens to exclude a putative disease (a). Immediately questions are raised about the need for treatment for (a), the extent to which insurance companies should pay for the treatment of (a), whether folks with (a) should be freed from certain responsibilities, and so on. Though important, these worries are clearly *secondary* worries, and should be divorced from debates over the definition itself, which will be my exclusive concern here. Indeed when we turn below to the distinction between diseases and disorders, it will become clear that those conditions requiring treatment cannot be limited to diseases alone, as many disorders require (immediate) medical attention. In fact, I take it that being diseased is neither necessary nor sufficient for requiring (or having the right to receive) medical attention; the two are simply distinct issues.

It has been argued that we have no need for a disease concept, as the medical tradition does not require a concept of disease for discussions of ethical questions concerning treatment and punishment (Hesslow 1993). With regards to those issues in particular I am in complete agreement, but it would be a mistake to think that those are the only issues that might have need for a well-articulated concept of disease. Thus while we do not need a definition of disease in order to decide upon what conditions call for remedial attention in a given circumstance, if our aim is to construct a disease ontology, then such a definition is indispensable. What I offer is a value-free concept of disease, and while it is not my claim that a value-free ontological perspective is the only perspective from which to consider disease, it is the only one that can adequately serve the needs of bioinformatics who are developing disease ontologies, as well as promising to provide the most natural and straightforward response to the question of what a disease is.[4]

1. Disease versus Disorder

Part of establishing what it is to be a disease is figuring out what disease is not; this means distinguishing diseases from those things that have historically been counted as diseases but should not have been. The primary case I have in mind is a class of conditions I shall call 'disorders'. Distinguishing diseases from disorders will serve two purposes: first, of marking out an important family of non-disease conditions often requiring medical attention taken to fall within the confines of the disease concept belong outside it; and second, of giving us a distinct but in many ways parallel case against which better to understand the account of disease on offer.

I understand 'disorder' as a purely *structural* deviation from the norm, where 'structure' is an anatomical catch-all including: topography; shape; proportion; and number. Disorders are strictly anatomical abnormalities considered largely independently of the processes the body engages in. One might liken instances of disorder to a kind of abnormality of biological architecture. Functionality is not at issue, here the matter is one of form.[5] The class of disorders covers congenital deviations, as well as those brought on by environmental insult, disease, accident, genetics, or any other cause.

Disorders include such conditions as: broken legs, hernias, cataracts, reduced white blood cell counts, ingrown toenails, gall stones, tumours, lesions, and colour blindness. Regardless of how they might arise, disorders are states of the body that fall outside the standard range.[6] They are conditions that can be considered at a specific instant in time: given the snapshot of the body that captures a complete description of its state at a given time, the disorders are those conditions which differ sufficiently from the normal snapshot.[7]

The most basic case of disorder concerns a structural deviation with regard to the skeletal system. Let us consider a straightforward case of a skeletal disorder: that of a mid-thirties male with a broken arm. Though no two skeletons are exactly alike, when we restrict the comparison class to a relevantly similar group, we find a very high degree of similarity. This has led to well established skeletal norms. In this case the relevant class is that of males between the ages of 25 and 50. Within that group we find enough similarity to develop a *canonical skeleton*.[8] Like the 'average taxpayer', the canonical skeleton is no one person's skeleton—it is a statistical average that provides a great deal of information about what the skeletons of members of the comparison class tend to be like. This is the norm against which deviance is established. In the case of skeletons we literally have a snapshot through which the comparison can be made. With our well-established canonical skeleton at hand, we can produce x-rays of the broken arm of the mid-thirties male, and see that they deviate from the norm. This is the case of skeletal disorder.

Note that certain problems immediately arise for this model. What if everyone has broken arms? What if the male in question is exceedingly short, or exceedingly tall? The answer to both problems lies in how we interpret the canonical skeleton. Amongst the most important information we gain from the canonical skeleton concerns *topography*. Despite minor differences, we find that the way in which the skeleton is mapped out is uniform throughout a given comparison class. This makes disorders like breaks easy to see as deviations. With broken bones the topography is altered; broken and fractured bones admit of gaps not found in the canonical cases. This will hold irrespective of height. As well as information about topography, the canonical skeleton gives us information not just about the typical state of the skeleton (for that class), but about the *proto*typical or *arche*typical state (for that class). In this way, the canonical skeleton in fact differs importantly from the average tax-payer. Whereas the average tax-payer is nothing more than a statistical average and therefore varies according to contingent features of annual tax reporters, the canonical skeleton is borne our of averages but serves as an exemplar. This is not to suggest that the canonical skeleton represents the ideal skeleton (for whatever would count as ideal in this case?), but it is not a strict average either. Compare the case of the average tax-payer (based on actual annual reporting and incorporating undetected errors and fraud), with what would be the average had all taxes been accurately reported and filed. The latter is hardly the 'ideal tax-payer', but nor is the average either. In this way the canonical skeleton is impervious to minor contingent features that might arise, or regional peculiarities.[9]

Even with the canonical skeleton at our disposal, one might object that there remain structural deviations that are difficult to classify as disorders, because norms can differ and degree of deviation forms a continuum. The best line of response is to point to the successes of

treatment. Medical practitioners enjoy a high level of success in recognising, naming, and treating structural deviations concerning the human skeleton. And though at the margins we find the most difficult cases to classify, the success is to be judged according to the most prevalent cases—and there we find that the canonical skeletal is an excellent device for identification and treatment. Worries about perfect averages and radical deviations fall to the wayside—the model works in the majority of cases, and this is where it ought to be judged.

Such is the case for skeletons and bones. Other disorders are to be modelled on the skeletal case, as structural deviations from the norm. This will be the case for musculature, cells, organs, and organ systems. And though we are not quite as well off when it comes to these bodily features as we are for the skeletal system, we nevertheless have a very good account of what makes up the canonical body. Its architecture is well mapped out, providing prototypical structures for muscles, organs and so on. And as our knowledge of the body's structure grows, so does our understanding of the canonical. Against that canonical model we can then determine what count as deviations. And with that we get our complete concept of disorder.

With the concept of 'disorder' in place, why should we treat disorder as distinct from disease? The initial motivation comes from the way we use the corresponding terms. In standard parlance we rarely speak of the body's structural deviations from the norm as being diseases. This is true even when we take such deviations as requiring immediate medical attention, as with compound fractures. However life threatening the condition might be, our tendency is to differentiate structural maladies from diseases. Once we begin taking this differentiation seriously, and we look closely at how we might define the two terms, it becomes clear that the two deserve parallel but distinct definitions because they range over similar but yet clearly distinct types of condition. What gets slightly more confusing is when the two begin to intersect, and we find disorders contributing to the production of certain diseases, and diseases having amongst their symptoms various disorders. But as it turns out—and this is the primary motivation—the disease/disorder distinction helps make clearer the causal model for disease, and this helps us to understand what disease is. A complete statement of the contrast between disorder and disease will come later, once we have seen the account of disease, but it is important to see that we have removed from disease a wide range of cases that often get lumped together, and that this will help us develop a clearer picture of disease.

The final word on disorder concerns the model it provides for diseases. A disorder is a deviation from a structural norm. The treatment of disease will be similar, using the same idea of comparison to typical cases; in the case of disease, however, the comparison is to *standard processes of cellular interaction*. As cellular processes are much harder to map out, and case-by-case variation is of increased importance, the norms are much harder to establish. Nonetheless, disease will be understood in what follows according to this model, where hopefully the comparison with the disorder case will aid in understanding.

I turn now to the causal model. By rethinking the role of the cell within cellular networks, we get our first glimpse of the appropriate loci for disease, in addition to how disease is situated concerning cause and effect. This will

allow us to develop the right of picture of cellular processes needed for the total account.

2. Cellular Dispositionality and Cellular Networks

Part of what makes the present treatment of disease unique is the location it gives to disease within the hierarchy of the body's organisation. Disease exists primarily at the level of cellular interaction. This means that, in the most central cases, applications of the term 'disease' should be restricted to networks of interacting cells. Speaking less strictly of course, this supports a wider range of use. In other words we can perfectly well describe someone as 'being diseased', with the recognition that typically what we are claiming is that the individual in question has as a part a network of interacting cells whose processes deviate from the standard. Likewise for anything larger than groups of cells, such as organs or organ systems. It may not be the case—speaking more strictly—that someone has a diseased liver; but if a large enough subset of liver cells are engaged in sufficiently deviant processes then the predication fits well enough. In fact, should the number of cells involved be large enough, it could turn out that the liver as a whole (or even the entirety of the organ system to which it belongs) is diseased in a more strict sense, if the extent of deviant cellular action is appropriately widespread. In this way the cellular interaction case is the primary example of disease from which a more general use can be derived. Regardless, the primary application of 'disease' will be to cellular networks, and so we need a theoretical model for the site of cellular interaction.

Individual cells are what we might call biological 'power-centres'. Each cell is such that it has, as part of its programming, a wide range of capacities or abilities. The cell this is the seat of a wide range of potentiality. This potentiality prepares it for a wide range of types of causal interactions, the majority of which it will never exercise, regardless of its longevity. For instance, the cell is in a state of causal preparedness for what to do if its environment changes chemically, either through a change in the relative proportions of chemicals in its environment, or through the inclusion or exclusion of certain specific chemicals. Given a change in environment, the cell is prepared to act in some way or other. This reaction will typically involve something like a homeostatic response so as to enable to the cell to return to a typical state, but it night involve a reaction which enables the cell to exploit or avoid the chemical changes in its environment. But in any case, responding in one of these ways is something the cell is ready to do, as a result of its causal programming. Likewise where less positive results ensue—should a certain environmental change kill the cell, then this too is part of its causal programming. The death of the cell is just as much a programmed response as any other. That there is built in preparedness should not be thought of in terms of mere survival or adaptation. It is not the case that the cell is out for survival—this will often be the case, but it is better to think of the cell in terms of a much more fundamental and simple stimulus-response model. It simply *responds*; this response may favour its survival, it may even promote its longevity, but it may do nothing but maintain the status quo, or it have it might go into shock, or die, or what have you.[10] We should not think of the cell as an *agent*—it does choose

amongst options or act in order to obtain some goal, it simply responds. For whatever scenario that might arise (however fanciful), the cell has a built-in preparedness. It is in this sense that the cell is a 'power-centre'.

Under typical circumstances, the stability of its environment means the cell exercises just some small portion of its abilities. But the cell is also prepared for scenarios that might never occur. The range of scenarios includes fanciful encounters with as-of-yet-unknown bacterial agents, down to more pedestrian cases of change of location. That wider space of capacities provides one of the avenues from which disease can arise.

By way of analogy, we might think of the cell's existence as something like that of the traditional assembly-line factory worker. In the same way that factories can increase their output through specialisation, so our bodies are the result of a cellular division of labour. The complexity of our bodies owes a great amount to the ability of cells to organise themselves in such a way that tasks are divided amongst them. Without this division of labour, many of the high-level functions we enjoy would be impossible. Just as we increase factory output by restricting the number of tasks a given worker needs to perform, often by implementing mechanisms that bring the work to the worker (in the cell case that mechanism is often itself other specialised cells), the complexity the human body enjoys can be credited to cells engaged in specialised work. But just like the factory worker, no cell is limited to just that task it performs. In a certain well-defined environment, and in concert with other cells, it engages in specific well-defined activities; but these no more exhaust the capacities of the cell than do the menial tasks the factory worker is paid to do exhaust the range of the worker's capacities. This simplest case is that of re-assignment: the factory worker is relocated and now puts on bottle caps rather than boxing up packages. Similarly for the cell; a change in location can bring a change in task. In short, both the cell and the factory worker have a form of success brought about through specialisation; but those specialised tasks do nothing like exhaust the capacities of either.

As I have described it so far, the cell has a built in causal preparedness for various responses given environmental conditions. The tendency is to think of this environment chemically, as having specific concentrations of this or that molecule in the immediate vicinity of the cell. But the environment is of course not made up of molecules alone—a major portion of the environment with which the cell interacts is comprised of *other cells*. And just as each cell has prescribed responses to whatever chemical environment it may have, so each cell has a built in preparedness for interaction with other cells. Furthermore, the latter are likewise prepared for certain prescribed responses in the given cellular environments. The result is a mutual interaction between the cells: they jointly produce certain effects. What we have is a built in symmetry. Or better yet, as the contributions of each need not be the same or equal, we have an instance of causal *reciprocity*.[11] Each cell contributes to what is a mutual effect. The picture is one of cells responding to their environments, where those environments are composed of certain chemicals and other cells.[12]

In accordance with their built-in capacities, the standard processes a given cell contributes to are simply a matter of the cell responding to the specific arrangements of cells and chemicals in the cell's environment. With

changes in environment come changes in the specific responses; viewed over time these individual responses constitute cellular processes. When we begin to characterise these processes we begin to see the cells as forming *cellular networks*, which is to say groups of cells engaged in reciprocal production and response. This provides us with a second perspective from which to characterise cellular interaction: we can speak either in terms of the individual cells as power-centres and of the roles they contribute to the overall processes in virtue of their specific positions within the networks, or we can speak in terms of the larger groups of cells (cellular networks) and how their reciprocal engagements are the source of the processes that arise between them. This is the causal model on which our account of disease will be developed.

Returning to our factory analogy, and pushing it somewhat further, we can get a very rudimentary sense of the account of disease on offer when we imagine what might go wrong at the factory, and how production might be slowed, or even stopped altogether. The parallel here is with that of standard cellular processes: the breakdown or cessation of factory production is akin to distortions of typical cellular processes, and those distorted processes are diseases. In the factory, disruptions to the regular pattern of production might come from one or all of any number of places: (1) problems internal to the worker, (2) problems within co-workers, (3) lack of resources, (4) lack of power, and (5) physical occlusions. Difficulties of the first and second sort could be anything that stops the worker or her co-workers doing their jobs, but which are restricted to their physical or mental states. If the worker becomes weak, or hungry, or confused, she will not longer be able to perform her task as required. Similarly if she forgets what it is she is supposed to do, or how she is supposed to contribute, the factory line is slowed or stopped. As I have said, the factory worker has capacities well beyond those required by her task, and certain conditions internal to her may find her acting in ways other than that of her job description. The result is a slowing of production. The problems raised by the final three cases require no explanation: if we remove the required materials (or throw in additional ones) the worker cannot perform her task, similarly if power is lost or the line becomes blocked. This is all to be expected. Though perhaps undesirable and atypical, the slowing or cessation of production is an overall characterisation of a series of problems faced at the individual level.

How does this square with the cell? Like the worker, the cell has readied responses to all potential occurrences, but only some of those give rise to normal operating processes. When certain changes take place, either internal or external to the cell (or both), the processes that result fall outside the norm.[13] Each cell continues to respond in some way or other—there are still processes that result—but the productivity of the cellular network ceases to be typical. Depending on the process, it might even result in fatality. And with networks no longer operating within the range of standard processes, we may find that other networks begin to experience the same problems. Like the factory worker, the deviation from standard processes can arise from problems within the specific cells, or from without. On the internal side there are cases of cellular misinformation, generally connected with DNA problems, that lead to non-standard behaviour. Externally we have a host of problems concerning chemical changes in the environment, increases or reductions of energy, invasion of foreign agents (bacteria, viruses), and

absences (of chemicals or required compounds).[14] In each case these changes can cause the network of cells to operate in those non-standard ways which are at the core of the present account of disease.

Before turning to the specifics of the account, I want to complete the causal picture by contrasting the place of disorder with that of disease. We have just seen how a variety of factors internal and external to the individual cell can affect the overall process produced by the network. Disorders can be found at either end of this process. For instance, a lesion might be the site at which bacteria enter the body, and thereby disrupt certain processes. A disorder is then a contributing factor in the cause of some disease. Any structural deviation—especially brought on by traumatic environmental insult—could stand as partial cause of a disease process if it results on one of the factors listed above. It does this either by triggering the atypical responses of the cell directly (either alone or as a necessary part of a cause) or by contributing to a change in conditions that indirectly brings about the atypical responses. At the other end of things, disorders themselves can result from non-standard cellular processes, where they are often taken to be *symptoms* of the disease. There is a little more to being a symptom of a disease than just being an effect of it, but this is one way in which diseases and disorders can be connected.

3. Re-Defining 'Disease'

The core understanding of disease at work here is that of deviation from standard processes. But that alone is far too simplistic—many other details need to be included in order to get the appropriate refinement. After all, we should hardly take the most minor deviation to count as a disease, or we would find that everybody was diseased all of the time. Here we include the definition of a disease instance which results when we include the necessary extra factors:

x is a disease $=_{df}$ *x* is a prolonged distortion of standard cellular network processes, wherein the

activities of the network:

(i) fall outside an acceptable normal range for the organism's comparison class,

(ii) are not capable of remedy by the network itself without thereby distorting the processes of some other network (where that second network is likewise incapable of self-remedy without distorting the processes of yet another network, and so on), and

(iii) tend to reduce the organism's ability to cope with environmental pressures

As I have said, the core idea is that of a disease instance as a deviation from standard processes; the rest of the definition is there to restrict that class, as not all deviations are themselves diseases. This core idea is itself the portion most in need of defence, which will be provided in the next section, along with a discussion of the notion of 'standard' as it applies to standard cellular network processes, of what exactly a 'distortion' boils down to, and of what constitutes an 'acceptable normal range'. Throughout this section I will continue to unpack the remainder of the definition with the assumption that however controversial the notions of standard process and deviation might be, we nevertheless have a reasonable pre-theoretical understanding of what they are. Let us start with the first restriction, that the distortion of the standard cellular process be *prolonged*.

The need to insist that the distortion or deviation be prolonged is a reflection of the homeostatic features of cellular processes. What we might call the status quo of cellular processing is not something we would represent graphically as a straight line. What is normal for cellular processing is a regular ebb and flow as molecules and compounds are used and refilled and energy is stored and expended. The process is what we would expect of a homeostatic system: a constant back and forth between excess and shortage as various cells within the network consume, use, produce, and expel. From the perspective of the individual cell this is a largely repetitive series of responses to its environment, and minor blips of distortion are by no means unexpected or abnormal at all. But the distortions can get much bigger, even to the extent that the distorted processes barely resemble the standard processes, and yet still fail to be diseases. The reason, once again, has to do with homeostasis. Though perhaps not an ideal way of operating, distortions are common, and the cellular networks (either collectively or severally) are prepared for dealing with them. Most distortions are dealt with within a reasonable time period and at only a minor expense to the individual, where expense is understood in terms of energy and the redirection of resources. Using the factory analogy, the factory's output at this time may be limited, but the solution is kept in-house and all is up and running smoothly before too long. That is why the distortion must be prolonged. Most every network will go though periods when its processes are distorted, but only if these are prolonged do we have a disease.

Closely tied to the matter of the distortion's being prolonged is the second criterion, that of self-remedy. Here again we have a refinement that gives due recognition to the homeostasis the human organism enjoys. It is often overlooked just how resilient the human organism is; just how much it can persist through repeated internal and environmental challenges to survival. The condition of self-remedy is intended to work hand in hand with that of prolongedness: it is precisely because the body has such a great capacity to heal itself that a distortion needs to be prolonged to count as a disease. Over a short time frame many distortions will be remedied internally. However, even a distorted process that is (or could be) self-remedied might nevertheless count as a disease if the remedy itself causes the distortion of processes of *some other network*. For instance, we can imagine a distortion within a particular network that arises due to a lack of energy or resources. It may be the case that this network is able to remedy itself and return to standard processes, but does so at the expense of some other network, thereby distorting the processes of that second network. Assuming

the second network is unable to remedy itself, we have an instance of disease. Likewise if the second network is able to remedy itself only at the expense of a third network, and so on. What matters with regard to the presence of a disease is whether or not, somewhere down the line, there is a distorted process that is incapable of self-remedy. If there is, we have a disease.

When the cause of the distortion is some sort of pathogen, the immune system is the likely source of remedy. This means that the distortion in the original network has led to changes in another network, the immune system, and the immune system steps in to deal with the pathogen. However, this will not make for a disease instance unless the immune system is either unsuccessful in dealing with the pathogen within a reasonable time frame or compromises yet another network in the process. Dealing with pathogens is a typical process for the immune system, but when the process takes too long (or is indefinite) we have a disease; likewise if the processes of the immune system result in distortions of a third network.

Here we have an important feature of the account. If we have a case like that just described, where the first network is able to resume its standard processes only at the expense of a second, and the second becomes distorted and is unable to self-remedy (either entirely alone or at the expense of a third network), we have a disease. However, whereas most accounts would see the disease as arising with the second network (as more than likely the symptoms that the disease gives rise to will be as a result of the distorted process in the second network), the disease is clearly a product of problems with the first. However, because they are no longer distorted, we should not say that the now-remedied processes of the first network count as a disease. But it would likewise be mistaken to overlook the effects the first network has on the second when we describe the latter as diseased. Hence we have a clear location of the disease within the second network, but the cause of the disease is whatever is producing the problem with the first network. In instances of what we might call 'parasitical self-remedy', the disease moves to the last network that is distorted, but the cause remains with the first in the series. This feature of the account, owing largely to its causal model, allows medical practitioners to approach the diseased individual with an eye to identifying the genuine source of the disease, not just the most proximate diseased network.[15]

The third criterion introduces a restriction that Scadding (1967) calls a 'biological disadvantage.' Recognising that not all statistical deviations are diseases, Scadding introduces the restriction to ensure that diseases are *negative*—claiming that deviations that help are not to be thought of as diseases. Though I largely agree with Scadding, three points of clarification are required. The first concerns what exactly a 'biological disadvantage' comes to. The second is a lessening of the restriction to the *tendency* to result in biological disadvantage, and the third casts a small amount of doubt on the negativity dimension.

What then is a 'biological disadvantage'? Scadding unfortunately fails to elaborate. Kendell (1975) has suggested that it must include both increased mortality and reduced fertility. These should certainly form part of the notion. But common sense dictates that our definition of disease should be far more inclusive than this. Surely instances of disease are not just those that follow from the broadest of biological brushstrokes—it would seem that

many people live with diseases and have many children. Lennox disagrees, claiming that we should restrict accounts of disease to just survival and reproduction, because these are the two primary aims of life (Lennox 1995). But this is clearly too simplistic and does not gel with how we normally use the term 'disease'. A wider understanding is required, and my preference is for thinking of biological disadvantage in terms of a reduction in the organism's ability to cope with environmental pressures. This includes the severe cases of death and infertility, but many cases in between as well. A distorted process that has as a symptom tremors of the hand and arm (such as Parkinson disease) is as much a disease as one whose symptoms include fatalities (such as meningitis). Ideally, it would be nice to be to able specify exactly which cases count as reductions in the organism's ability to cope with environmental pressures, but beyond a widening from the most severe cases, it is difficult to be explicit about what those cases should be. I suggest we be quite inclusive—if the distorted process results in a condition that hampers one's ability to deal with the everyday tasks of life, then we ought to consider the distorted process a disease, even if the resultant reduction is quite trivial. The key here is to recall that having a disease does not necessitate being a candidate for medical attention, and the most trivial cases would surely not be something we spend much, if any, energy on. It turns out, unsurprisingly, that instances of disease form a continuum according to how much their potential symptoms tend to reduce the organism's ability to cope with environmental pressures. The worse cases involve fatality, but many will cause only minor disadvantages.

However, to insist that for a distorted cellular process to count as a disease it *must* result in a biological disadvantage is far too strong a criterion. This is where the second point of clarification regarding criterion (iii) comes in, as all we ought to require is the *capacity* to result in some biological disadvantage. Most of us find it unintuitive that any condition considered a biological disadvantage will be identical with the disease itself. What we consider when we look at potential disadvantages are *symptoms* of diseases: manifested observable effects of the disease, but not the disease itself (Reznek 1987). For instance, diabetes frequently results in blindness: it is the blindness that we recognise as a clear disadvantage, but the blindness is not the diabetes, it is a product thereof. It is a symptom of the disease. But the having of the disease is no guarantee that the symptom will ever arise. Symptoms are often good indicators of disease, but the absence of the indicator in no way indicates that the disease in question is absent. Consider an obvious case: a patient is given symptom-suppressing drugs for a disease we are unable to cure. The disease is present, the symptoms are not.[16] We can continue to associate specific symptoms with specific diseases, but that association must be understood as the *potential* to produce such symptoms, not the insistence that they arise.[17] Hence I have loosened the third criterion such that it need only have the *tendency* to reduce the organism's ability to cope with environmental pressures.

The third point of clarification also leans on the use of 'tends' in the definition, only this time the indication concerns the negativity of the biological disadvantage. This is by far the most suspect element of the definition, and the most radical departure from typical thinking about disease. The thought is this: disease need not be a negative. Or, more correctly, the symptoms a disease may give rise to need not be biological disadvantages—

rather, they may be *advantages*. It might be the case that the symptoms of a disease include increases of some sort, such as increased intelligence, or motor control, or speed. Let me be clear, I am not claiming that most diseases are good things. The great majority of diseases have bad, if not terrible effects, and are in no way positive. But nothing about the idea of the processes of a cellular network being distorted rules out its having positive effects (or at least the capacity to produce positive effects). The fact that the negativity must be stipulated is evidence enough for this. But all other accounts stipulate that the effects must be negative, so why not this one as well?

A first reason has to do with the potential dangers connected with positive symptoms. Recalling the factory worker case; an increase in output would surely be welcomed, but what is the cost of the increase? Perhaps by working harder the workers will become more tired, or perhaps the resources will be used up too quickly or the activities of different workers will no longer be synchronised. Returning to cellular networks, we should not overlook the fact that the distortion producing the positive effects remains a distortion. If the network is operating in non-standard ways, there is no telling what other networks might be experiencing distortions (or will do so in time), and these could have negative symptoms connected with them. The first worry then is more of a precautionary measure than anything else. Distortions are distortions, and we should be wary of them even if their effects are positive. Take the case of Olympic-quality long distance runners; these athletes are capable of covering much more ground on foot than most of us could ever run (in the same amount of time), but in order to get that way they reduce their percentage body fat to such low levels that other systems are effected adversely. The massive increased running abilities come at a cost. Moreover, should it turn out that the positive symptoms are in no way connected with potential problems elsewhere, it is still of medical interest to treat the relevant individuals as diseased. Such individuals are abnormal—and by recognising this we gain greater insight into normality, and better yet, potential insight into how negative abnormal cases might be remedied.

The second reason concerns the possible masking of negative symptoms. Symptoms that diseases are capable of producing need not arise. Should some positive symptoms arise from a distortion of network processes, it is no guarantee that negatives will not arise later. Additionally, it might be the case that the positive symptoms make it more difficult to notice negative symptoms that have arisen, but which happen to go unnoticed due to the positive ones. The worry here, much as it is above, is that the presence of the positive symptom clouds our judgement, causing us to ignore the fact that the symptom, albeit positive, nevertheless arises from a distorted process. And a distorted process is a deviation from the standard, whatever symptoms may arise.

4. Norms and Functions

The account of disease on offer is optimistic in one major respect: it anticipates our eventual ability to discern standards for cellular network activities. To some minor extent we are capable of that now, but the major advances are yet to come. Does this bring problems for the above account?

The answer is no—the *epistemic* difficultly of establishing exactly what those standards are does not stand in the way of our having an *ontological* treatment of what a disease is. That standard is independent of our awareness of it; our lack of knowledge provides a reasonable barrier to identifying which processes are the diseases, but not to what a disease is. Similarly the fact that we cannot yet use (much of) the cellular network analysis as an aid to diagnosis is an epistemological problem, that is being overcome, step by step, with our increasing knowledge.

The opposition here comes from what we might call the 'creationist' camp: those who deny that diseases are mind-independent features of our world, claiming that we have some role to play in their creation. Worries of this sort parallel (and sometimes incorporate) problems posed by those theorists who insist disease is a value-laden concept; both seek to undermine the *objectivity* of disease (DeVito 2000). For the present account, the question of objectivity does not concern the existence of some entity (as it might for a pathogen account of disease), but the status and determination of *standards* for cellular network processes against which distortions can be measured. But these worries about objectivity are entirely unwarranted. Distortions of cellular processes are no more reliant for their existence on our ability to identify them than the standards are. The distortions are just those processes that deviate from the standards—these are present whether we are aware of them or not. When we determine standards, it is a matter of *discovery*, not *creation*. The standards are present prior to our knowledge of them. As a simple demonstration, imagine testing for the average height amongst a group of one hundred people: whatever we find to be the average height was the average before our knowledge of it. What changes is our *awareness* of the average, we do not create the average.[18] We run into the same epistemic problems concerning a complete knowledge of diseases, but this in no way takes away from the account of what a disease is. For that reason I suggest we put the epistemic worries to one side. We do not now have a complete picture of what all the diseases are, but that is not a product of the account on offer, it is merely a statement about the present status of our medical knowledge. With an appropriate account of disease the hope is that various disease ontologies might help us approach more closely having that knowledge, but that will take time to develop. What we should concern ourselves with for now are problems that may arise the account of disease on offer, rather than epistemological concerns connected with its application.

Recall that the model here is intended to parallel the case of the standard skeleton for structural disorders. Part of what makes the skeletal case interesting is that it is derived from genuine cases, but is not itself any one skeleton in particular. It is an abstraction from the pure statistical average, devised so as to take into account fluctuations that we might find in the statistical data, but it is not an *ideal* or perfect case. Nor is it at all clear what it would mean to speak of an ideal or perfect skeleton. Perfect for whom? Ideal for what? What the standard gives us is an *exemplar* or a *prototype* against which deviation can be established, it is not a superlative or perfect case at all. The same fluctuations arise for cellular processing. Statistical averages for cellular network provide us with a central bandwidth, and working away from that bandwidth (accounting for fluctuations arising from regional contingencies and the like) we establish our exemplar. Again, the exemplar might in no way be ideal, but that is not what we are after in a statistical

model. The account of disease is that of deviation from the norm, not from an artificial ideal.

But problems do arise when determining standards for cellular processes, and so we need to be careful. For instance, what if everybody was stricken with a certain disease? In that case the 'disease' would be standard, so the disease itself should not count as a disease. How can such problems be avoided? It is no part of our concept of disease that everyone is *presently* diseased, so we can have a standard we can establish using present cases. We can then use that standard as the basis against which to judge the unfortunate future case where everyone is diseased as in fact being diseased. In this way we can use our standard to insulate the account against remote possibilities such the one mentioned. We still have a standard, we simply extend the time frame of that standard over some period greater than the present. As a consequence, we might similarly discover—using a lengthy enough time frame—that processes we presently do not take to be diseases are in fact diseases. This would occur just in case a vast history of cellular processing finds the present cases to be distorted. In this scenario we have applied our understanding to disease to a greater body of data, giving us a somewhat surprising, but entirely possible result. This is what we might think of as a problem for standardization that concerns contingent factors relative to a specific time-frame. We avoid those contingencies by extending the time frame as widely as possible.

Similar problems arise from contingent features associated with the environment. The people of a region that is always hot, humid, and teeming with nutrient rich fruits will run into different problems than those who live in cold, isolated regions that have limited resources. Does that mean that the processes of one count as diseases but not the other? In order to deal with regional differences the notion of standard requires a division between *universal* standards, and *local* or *regional* standards. All this requires is a restriction of the data set to similarly regionally located individuals in the *local* case, and no such restriction in the *universal* case. With these two standards, we can now judge an individual from a specific region according to both standards. The local standard will tell us if the cellular processes of the individual are relevantly similar to others in the region, and likewise if they differ from those universally. Assuming the other criteria are satisfied, if the processes are distorted in either case, we have an instance of disease. What is at issue is just a matter of using the relevant comparison class for the individual case.[19] If we are talking about a male in his twenties native to Aruba, the most relevant comparisons are with other males, of a similar age, and from a similar region. Or, in case we are worried that perhaps there is I disease that is distributed throughout an entire region, we utilise a less restricted (or unrestricted) comparison class to avoid the regional contingency.

The same applies to the individual case. For instance, though most people tend to maintain average temperatures between 98 and 99 degrees, some people have an average as high as 102 to 105 degrees (King 1954). Given adequate medical records, we can construct *personal* norms, and use these in addition to the local and universal ones (Fabrega 1979). This allows us to navigate the pitfalls that certain individual cases might produce.

The key here is that deviation from a standard is a relative notion, and that the relativity is not something that can be avoided. But its relativity does not undermine its objectivity or its value-free nature. It is not the case that there is a single objectively correct comparison class—nor need there be in order to maintain objectivity. These are facts about cellular processing that are compared to other facts about cellular processing, hence all comparisons remain objective. If certain difficulties arise that make us think we might want to adjust the comparison class, this is still no threat to objectivity. Even with placing restrictions on the comparison class (or removing restrictions altogether) determining what is a deviation from the standard remains problematic. But for the purpose of constructing disease ontologies, some sort of concept of disease is needed, and the aim—as with any definition—is to do right by the majority of cases. In that regard the present statistical deviation model fares very well.

Given some of the problems faced by statistical deviation models of disease, it might be asked why I have not opted for something less vulnerable to contingent features of populations. In particular, my account has a lot in common with Boorse's Functional account, so why not follow him in his functionalism? After all, if we can establish the *function* that a cellular network performs, we can treat disease as cessation of function, as Boorse does: "diseases are conditions foreign to the nature of the species," where "the nature of the species will be a functional design empirically shown typical of it," and "the basic notion of a function is of a contribution to a goal" (Boorse 1977: 554-555). There are a number of reasons I avoid a functional account, as well as similar accounts that propose an ideal for processes. The primary reason concerns the tendency of functional views to gloss over much of what goes on at the cellular level. Functional accounts treat bodies as machines: if the clock runs, all must be okay. But there are many ways of not being okay that do not threaten functionality. Some networks might shut down forcing others to take over, causing strain—function is not lost, but disease might still be present. Functionalism also promotes a kind of tunnel vision with regards to cells. If we think of a cell, or cellular network, or even an organ, is present just to perform some function, then we stop looking for diseases in the many ways the cells or networks might operate. Functional thinking is one dimensional, but the cells we are dealing with are not. Functionalism can also lead to misplacement of given diseases. If we have a case where one cellular network remedies its distortion at the expense of another, the functionalist will locate the problem with the second network, but the locus of the disease is clearly includes the first. Functionalism then leads to a potential masking of disease, a problem I would rather avoid.

Consider the comparison with any purely mechanical system, such as a car engine. Fixing a car engine is a matter of function—get the right parts working so that each function is performed, and all is well. In terms of a quick fix, and a starting place for diagnosis, this can be quite successful. Treat the body as a machine and get all the functions up and running and the job is done. But where is disease in this picture? There is no place for disease in a purely functional model. We do not consider broken engines to be diseased, even when function breaks down. The same should apply to the body as machine: treat the body in purely functional terms and there is no room for disease. Parts simply function or they fail to function; disease never enters the picture.

This is not to mention all the other problems that come with functional accounts. There are the difficulties (if not impossibilities) of assigning function. We can tell all the 'just so' stories we want, but pinning down functions is a devilishly hard task. Is this just an epistemic worry (which, *tu quoque*, the present treatment is also subject to)? That has yet to be seen. It is hard enough to determine function, but the thought that we can in principle discover the functions of bodily parts assumes that there are functions to be found. And despite the many positive defences of functions, this is an additional theoretical assumption that afflicts the functionalist account.[20] The present account has no such worries: the existence of standards are not in dispute. I am not endorsing scepticism about functions, but such scepticism is at least reasonable; whereas a similar scepticism about standards is not. Furthermore, many disorders result in dysfunction (broken arms do not work so well), but these do not look like diseases. And what should we say of body parts that have no function—can the appendix not be diseased? In the end, despite the problems associated with a statistical view, nothing is gained by appealing to deviations from nature's plan for an account of disease.

5. Problem Cases Considered

Part of considering an account of disease involves putting it to the test, that is, considering how it deals with problem cases. If an account fails to classify putative cases of diseases in what we intuitively think is the right way, we understandably become suspicious of the account. The problem cases I consider are classic cases that arise in the disease literature. That said, I have avoided discussion of a wide number of oft considered problem cases that clearly fall within the class of disorders, and not diseases. Hence by cleaving conditions correctly understood as disorders from those of disease I have already been able to remove a wide range of problem cases including blindness, fractures, bowleggedness, bullet wounds, and so on.

Mental Illness – Mental illness has proven difficult to capture within accounts of disease. The biggest concerns with cases of mental illness tend to be connected with ethical issues, relating to rights to treatment and freedom from responsibility. Naturally the present account is not intended as a basis for such judgements—as I argue in the introduction, an account of disease and the ethics of disease need to be kept separate. I still however need to address the definitional question: does this account of disease treat mental illness as a disease?

The response here largely echoes the response given by Szasz to the same question: unless there are physiological features wherein we find distorted cellular network processes (probably of brain cells, but not necessarily), then strictly speaking mental illnesses are not diseases (Szasz 1960, 1978). In as much as mental illnesses are *similar* to diseases in that case, the use of 'disease' to describe them is metaphorical. Of course, if distorted cellular processes are detected, then we learn that mental illnesses are diseases. In effect, the jury is still out: we are presently short of the kind of data we need to make a full determination. Nevertheless, we are increasingly

gathering this data and it seems more and more likely that most (if not all) mental illnesses are associated with non-standard (neurological) cellular network processes (Andreasen 2004, Pliszka 2004).

Some people are bound to find this response unsatisfactory. I suggest that in many of those cases—particularly those worried that mental illnesses might turn out not to be diseases—there is a failure to follow my advice of separating the ethical questions from the factive. To decide that mental illnesses are not diseases (assuming that the evidence points us that way), is merely to say that whatever goes on in the case of mental illness does not fall within our definition of disease. That is all. It does not rule out our having a definition of illness that is distinct from that of disease (a mental analogue, perhaps), nor does it rule out the need for care, the possible right to treatment, or the potential avoidance of responsibility in certain cases. These are distinct issues. Treating mental illnesses as a class of diseases no more decides these issues than ruling that mental illnesses are not diseases: the two are separate issues. In fact, if mental illnesses do not connect with distorted cellular processes (and so are not diseases), I suggest we take seriously the suggestion that illnesses and diseases be treated as distinct notions, and that 'illness' be so defined as to capture the mental case.[21]

Homosexuality – Homosexuality was once, and for quite some time, considered a disease (and might still be in some cultures). But that was according to very different accounts of disease than the one offered here, and was generally decided on the basis of poor evidence. So what does the present account have to say? As with mental illnesses, there is a great deal we do not know about homosexuality. But we can consider a few scenarios, and see what the definition tells us.

Here is a first scenario: homosexuality is strongly correlated with distorted cellular network processes. Does this make homosexuality a disease? Not on its own. In order to be a disease, it needs to satisfy the complete definition—and it is far from clear that it does. Case in point, I cannot see this causing any reduction in one's ability to cope with environmental pressures. Take the obvious candidate, reduced fertility. On the surface of it, homosexual preference seems to interfere with fertility as it tends to lead to homosexual partnerships, and homosexual partnerships cannot—in isolation—produce offspring. But this is only the surface. Homosexual preference does not always (and certainly need not) end in the formation of homosexual partnerships. And there is clearly no connection between physiological fertility and homosexuality, so homosexuality forms no real barrier to fertility. One might argue that strong preference would turn one away from partnerships that have offspring producing capabilities, but with a strong enough desire for children this can be avoided. Not to mention that *production* is far from the only means of having children. Homosexuality is consistent with both physiological fertility and the want for children (by conventional means or otherwise), so cannot meet the criteria for being a disease.

What of less drastic abilities to cope with environmental pressures? Homosexuality would still constitute a disease if we found the appropriate distorted cellular network processes made apparent some other kind of reduction in the ability to cope with environmental pressures. For instance,

one might claim that homosexual preference makes it harder to fit in, especially in communities where homosexuality is forbidden or shunned. This does not, however, count as a reduction of the relevant sort. For while there is no denying that in such cases we could trace a causal path from the distorted process to what we might call social discomfort. But the path is not an immediate one, and the social discomfort is not a *direct* result of the distorted process, so we should not count it as a symptom. In fact, it no more counts as a symptom than it would for any other genuine disease. Numerous diseases have symptoms that would make for social discomfort; most obvious are those that result in physical deformities or quite apparent disorders. In all cases this is too far removed from the disease itself to count as a symptom of the disease, and so cannot be a criterion by which we judge something to be a disease—symptoms must be more proximate effects. This becomes all to clear if we extend the case to the ridiculous extreme of increased mortality. Assume that instead of social discomfort we have a society rife with hate crimes, would we then want to claim that homosexuality is a disease because it results in increased mortality? Surely not—the problem here is severe criminality, not one that pertains to disease.

As many of us suspect, we are unlikely to find any sort of distorted cellular network processes that would count as the basis of homosexuality. If that is the case, then homosexuality is not a disease. Furthermore, even if we did find some distorted process, it does not seem that it would count as a disease, as it fails to reduce the organism's ability to cope with environmental pressures. Hence the account of disease on offer does not make homosexuality out to be a disease.

Syndromes – A syndrome is a cluster of symptoms that reliably arise together. The potential problem syndromes pose comes from the apparent lack of common cause. They are—for the most part—merely collections of symptoms. They are not, in any way we are as yet aware, connected to some underlying disease process. The problem then is what we ought to say about syndromes.

Without an underlying disease process, syndromes do not count as diseases. Hence, if syndromes are as they appear, then they are not, strictly speaking, instances of disease, and the best we can do is think of them as forming a class of disease-like maladies. Here the advice parallels that given for mental illnesses, should mental illnesses likewise fail to be cases of disease. Again, the same advice regarding the separation of ethical and remedial conclusions is offer.

But I suspect that syndromes are not as they appear. Rather I think that what we are dealing with in the case of syndromes is not an ontological classification, but an *epistemic* state regarding our knowledge of diseases. That is, a syndrome is just a set of symptoms whose underlying disease (or diseases) *has yet to be discovered*. Medical science has come a long way, but has really only begun to scratch the surface when it comes to a complete knowledge of disease. I suggest that we maintain a healthy optimism with regard to syndromes, and keep looking for the underlying disease that is the cause of the symptoms. In the meantime, of course, syndromes allow us to carry out the primary function of medical science: to diagnose and treat maladies. In as much as we can recognise and remedy syndromes, we are

part of the way there. But we are bound to get better at it when we can identify what is beneath it.

Pathogens – Pathogens are a class of microscopic entities that have historically been classified as diseases (Thagard 1996). As the present account of disease centres on the notion of distorted processes, it has no room for thinking of microscopic entities as diseases. Moreover, common phrases like 'communicable disease' tend to make sense when speaking of the microbes, but not processes.

The 'germ theory' of disease is typified by the claim that diseases should be identified with the microbes that cause them. It was thinking of disease in terms of the germ theory that led to rapid advances in our medical knowledge and our ability to treat, and most importantly prevent, a good many diseases at the end of the nineteenth century (Thagard 1996). But thinking of microbes as diseases is a conceptual error. Historically it proved to be a useful conceptual error; but it is an error nonetheless. The mistake is one of conflating a *source* or a *cause* of a certain disease with the disease itself. Just think about what is being claimed when one says that the microbe that causes syphilis (treponema pallidum) is itself a disease. One is not saying that persons have diseases, or that diseases afflict persons, but that the microbe itself is a disease. This is clearly an error. The source of the error is natural enough: microbes trigger the cellular responses in human organisms that give rise to distorted network processes (which may, in turn, produce various symptoms). If you can avoid the microbe, you can avoid the disease. Sound advice to be sure, but no reason to treat the microbe as a disease itself. Additionally, our present knowledge of diseases tells us that pathogen-caused diseases are merely a class of diseases. Many diseases have other causes (genetic factors for instance), so the thought that diseases might be identified with pathogens is clearly mistaken.

As for phrases like 'communicable disease', it is a mistake to interpret this as meaning that the disease itself—strictly speaking—can migrate from one person to the next. Rather what we have is a disease type whose cause is some type of microbe (often an airborne microbe), where either token instances of the disease process (directly or indirectly) produces more of the same type of microbe and redistributes them, or the token microbe independently reproduces itself and is then redistributed, such that other people can similarly come to have that same disease type. This is what communicability boils down to, and it does not require treating microbes as diseases.

Aging – We would all love to avoid the effects of aging, and would welcome a means by which to reverse the process. We are all, so to speak, afflicted—does this make aging a disease? After all, it is a process whose terminus is the always greatest of biological disadvantages. Aging is a natural process, and it is perfectly standard. For any age group, in any region, and for any gender, we find aging—and this is captured in the standards for cellular network processing for the group. The standards for eighty-year-old females differ from that of females in their twenties. Aging is captured within the standards for network processes, it therefore cannot be a disease. The only time we might become concerned is if the cellular processes for an individual are

incommensurate with the norms for their own age bracket, as found in cases of progeria: a process of rapid aging in children, resulting in conditions typical of much older age brackets, such as hair loss, arthritis and osteoporosis. The processes of the afflicted children are clearly non-standard, and the effects obviously disadvantageous, so we have a disease. But in the typical case, aging does not constitute a disease.

There are bound to be further problem cases not considered, and which might (if only *prima facie*) conflict with the account of disease on offer. Any account of disease is likely to have some putative counterexamples, if not genuine ones. Should this be cause for worry? An account with no counterexamples is better than one with them, but this perfect case might be impossible to achieve. Disease is a difficult concept to tame, but in an effort to produce disease ontologies some attempt must be made. As with any philosophical analysis, the most desirable result is one impervious to objection, but more often than not one has to make do with something less. If it can capture the best cases for which we have the strongest intuitions, and do well by many others, then it is an analysis we need to take seriously. I hazard that the present offering is such an analysis.

The next step in developing disease ontologies is to provide an account of the identity of diseases. When are two instances of disease tokens of the same type? When does one disease within a diseased person end, and the next begin? This must go hand in hand with further investigation into disease processes, and the causes and effects of disease processes. As our knowledge builds it becomes clearer what knowledge we are still missing, and where it is most likely to be found.

Conclusion

In my discussion of disease I have avoided saying anything about health. This has been no accident. Though it is commonplace in the literature to build a definition of disease out of that of health, or vice versa, I do not take this to be a sound practice. 'Health' and 'disease' are bound to be interdefined to some extent, but it is not going to be as simple as some theorists have suggested: there is more to health than the absence of disease. The WHO constitution opens with the following claim: "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."[22] Though I think the WHO overstates what is needed for health, the denial that health is merely the absence of disease is surely correct, but it seems to have been underappreciated in the theoretical discussions of health and disease.

In fact, what makes for health strikes me as far more complex than what makes for disease. Consequently, more study on what it is to be healthy is needed. Not just cases of failure, but of success. We need more information of what is going on in (putatively) healthy people; specifically we need a greater understanding of what is going on in their bodies at the cellular level. As we come closer to this knowledge, we not only learn more about health, we learn more about disease, and most importantly, we learn more about how to prevent and cure diseases.[23]

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ENDNOTES

[1] See for instance the OBO Disease Ontology at http://diseaseontology.sourceforge.net/.

[2] Most contemporary statistical treatments of the disease concept—now associated most closely with the work of Boorse (1975, 1977)—can be traced back to Cohen (1943).

[3] Reznek (1987) does an excellent job of presenting that debate, along with the presentation of his own value-laden account of disease.

[4] If one takes this as support for our having many concepts of disease, so be it, as long as those concepts are distinguished by purpose and the resulting definitions are not then incorrectly applied to other purposes.

[5] Disorders will be connected to function just as they will be tied up with (and result from) bodily processes; however, the existence and

assessment of disorders is irrespective of these connected functions and processes.

[6] I use 'state' and 'condition' interchangeably to mean the body's (or parts thereof) constitution at some given instance, as given by a physiological description including whatever attributes it exemplifies.

[7] The normal snapshot is sensitive to transient structural changes, as experienced when sitting or bending over as opposed to standing straight or lying flat.

[8] My understanding of the canonical skeleton is based—in part—on the Foundational Model of Anatomy as discussed in (Rosse and Mejino 2003).

[9] Section 4 continues the discussion of these kinds of problems.

[10] For more on the causal maintenance of the status quo, see Williams (2005).

[11] The notion of causal reciprocity—particularly as it applies to causal capacities—is adapted from the usage found in Martin (1993) and Heil (2003).

[12] This is a somewhat simplified picture of the cell's environment. There will be more the cell responds to than just chemicals and other cells (electromagnetic forces, for example), but excluding the increase in complexity the story here is just more of the same.

[13] This is certainly not the case for *all* changes. What is normal for cells and cellular processes is not entirely monotonous. Changes can be typical or atypical; it is the latter that matter for disease.

[14] Just like most factories, most cellular networks exhibit a degree of turnover; this is perfectly standard.

[15] For our purposes we can ignore the epistemic issues such a diagnosis would face. My claim is that armed with the appropriate metaphysical model, the medical practitioner is better prepared for dealing with the disease and identifying its cause.

[16] Thanks to Barry Smith for the example.

[17] Though we tend to describe a disease as having the potential to produce symptoms, the potentialities actually lie with the cells and networks themselves. As they operate in non-standard ways, they can give rise to symptoms (of effect other cells such that they might give rise to symptoms, and so on).

[18] Nor is the average affected by our interests. Our desire to know more about disease spurs our investigation of it, but here our values only direct what knowledge we seek to attain, they do not thereby taint that knowledge. Not, at least, any more than any other science is so tainted. With regards to the general question of values in science, in as much as it pertains to disease, we should only care if the situation for disease is worse than that for the rest of science.

[19] Compare Boorse (1977), pp. 556-8.

[20] Boorse's account of function can be found at (Boorse 1976).

[21] Here I follow the suggestion of Fabrega (1979) of keeping illness and disease distinct.

[22] Constitution of the World Health Organization, adopted and signed July 1946.

[23] Special thanks are due to Louis Goldberg for helping keep my biology in line, and for our many discussions on disease—many of the ideas in this paper had their beginnings in those discussions.