

## “Disease Entity” as the Key Theoretical Concept of Medicine

PETER HUCKLENBROICH\*

*University of Münster, Münster, Germany*

\*Address correspondence to: Peter Hucklenbroich, MD, PhD, University of Münster, Institute for Ethics, History, and Theory of Medicine, Von-Esmarch-Strasse 62, D-48149 Münster, Germany. E-mail: [hucklen@ukmuenster.de](mailto:hucklen@ukmuenster.de)

*Philosophical debates about the concept of disease, particularly of mental disease, might benefit from reconsideration and a closer look at the established terminology and conceptual structure of contemporary medical pathology and clinical nosology. The concepts and principles of medicine differ, to a considerable extent, from the ideas and notions of philosophical theories of disease. In medical theory, the concepts of disease entity and pathogenicity are, besides the concept of disease itself, of fundamental importance, and they are essentially connected to the concepts cause of disease or etiological factor, natural course or natural history of disease, and pathological disposition. It is the concept of disease entity that is of key importance for understanding medical pathology and theory of disease. Its central role is shown by a short reconstruction of its main features and its intrinsic connection to the concept of pathogenicity. The meaning of pathogenicity is elucidated by explicating the underlying criteria.*

**Keywords:** *Boorse, disease, disease entity, medical pathology, pathogenicity*

### I. INTRODUCTION: RECONSIDERING THE ESTABLISHED CONCEPTUAL FRAMEWORK OF MEDICAL PATHOLOGY IN PHILOSOPHICAL DEBATES ON THE CONCEPT OF DISEASE

The more recent discussion concerning the concept of disease<sup>1</sup> started in the late fifties of the 20th century. It was provoked, mainly, by criticism of the traditional conception of mental diseases as diseases of the brain that are explainable by etiological factors in the realm of neuropathology (Griesinger, 1845).<sup>2</sup>

Criticism of this concept started with publications that postulated a different etiology that referred to family dynamics and pathological patterns of communication—for example, the famous “double bind” interaction (Bateson et al., 1956). Criticism of this kind was escalated and exaggerated up to the thesis that there are no mental diseases at all but only problems of life; the concept of mental disease was declared a “myth” (Szasz, 1960, 1961). This thesis formed the hard core of “antipsychiatry” and stimulated many attempts to design a new definition of disease or develop a comprehensive philosophical theory of health and disease.<sup>3</sup> This highly controversial debate has lasted until now and seems still to be going strong, as can be observed in a striking number of collections of papers.<sup>4</sup> Among all other definitions of disease hitherto brought forward, the theory of Christopher Boorse is probably the most well known and most debated one. This attention might be due to two factors: first, this theory is well entrenched in philosophy of biology and refers to well-known biological and statistical notions; second, it advocates an unequivocally non-normative, naturalistic position. Because of the latter feature, it is frequently taken to be the definition that is used in medicine and medical science; and, apparently, there is no protest by Boorse himself against this attribution.

But this assumption is at least questionable. Indeed, the medical concept of disease does not presuppose or imply the acceptance of any norm or value in order to be correctly applicable; hence, it is a descriptive concept. But medical pathology (German “*Krankheitslehre*”) differs clearly and considerably regarding its terminology and conceptual structure from Boorse’s so-called “Bio-statistical theory” (BST). The fundamental concepts of BST are the concepts of physiological *function*, *functional ability*, *efficiency* of a function or functional ability, and *contribution* (causal contribution) of a function to individual *survival* and *reproduction*. Using these concepts as primitives, *disease* and *health* are defined.<sup>5</sup> Indeed, talk of functions, dysfunctions, and loss or disturbance of functions is widespread in medicine, too. But there are two important differences compared to BST: first, there is no terminological, systematic use of “function” or “dysfunction” in medicine, because there is no system of functions in medical (biological) theory or physiology that could yield a causal model of the human organism. The alleged hierarchical system of functions in BST, targeted at the ultimate goals of survival and reproduction, is nothing but the dream of a philosopher. The real organization of processes in biological organisms is a cyclical, feedback, self-referential, and self-processing network of structures and processes that cannot be flattened to form a plane, unidirectional hierarchy.<sup>6</sup> Further, there are no operational, quantitative definitions of the concepts “efficiency” and “causal contribution” of a function/functional ability in the sense of BST that could provide a method of determination and measurement concerning their magnitudes. Therefore, it is not possible to determine something like an unambiguous (even causal) contribution of “functions” to survival and reproduction; instead, the biological processes are polyvalent, changing,

and ambivalent concerning their causal and biological meaning. There is no hierarchical system of physiological functions, and Boorse has never tried to give but a sketch of it, or a hint where we could look it up. This nonexistence of a hierarchical system of functions is responsible for three consequences: first, it is not possible to construct a systematic *pathology* from the functional view, because meaning and causal consequences (for health and/or disease) of alleged functions and losses of functions are indeterminate and *equivocal*. Second, the diagnostic value and meaning of functional loss is equivocal, too. Dysfunctions and functional impairment may be symptoms of many different diseases that cause the same functional disability. Third, there are no general laws or rules that determine the respective thresholds of functional disability or impairment separating normal variation from pathological deviation. There is no theoretically justified criterion for establishing statistical thresholds of this kind. To sum up: the basic concepts of BST—function and functional ability, as well as their impairment and loss—are not suitable for constructing a systematic, unequivocal pathology, diagnostics, and therapy of disease.

Note that in medical terminology, the term “pathology” has two slightly different meanings: first, it is used as shorthand for the general and overall theory of diseases and pathological phenomena, including pathological anatomy, pathophysiology, pathobiochemistry, psychopathology, clinical nosology, and symptomatology. Second, in a biologically restricted sense, it designates the morphological discipline of pathological anatomy or pathoanatomy, including pathohistology and pathocytology. This ambiguity is carried over to the term “pathological,” particularly in the phrase “pathological condition.” In this paper, I use the terms “pathology,” “pathological,” and “pathological condition” *always* in the first, general sense. If I refer to special aspects, I will explicitly speak of, for example, pathoanatomical, pathophysiological, clinical, or subjectively experienced conditions or phenomena. The exact theoretical meaning of the term “pathological” is elaborated in Section IV, which is on the concept of pathologicity.

## II. THE CONCEPT OF DISEASE ENTITY: CORE IDEAS

The modern medical concept of disease entity was invented in the 17th century by Thomas Sydenham.<sup>7</sup> In the 18th century, Francois Boissier de Sauvages, stimulated by the paradigm of Linné’s taxonomical systems in biology, tried to establish for the first time in medical history a *system* of all disease entities—a *nosology*.

The fundamental idea lying behind the concept of disease entities is this: disease is a phenomenon neither totally uniform nor totally variable concerning its form of appearance; rather, it presents itself in the form of certain definite, natural *kinds* or *classes* of disease. This feature of disease is analogous to the conceptual structures of *plant* and *animal* in biology

and *substance* or *material* in chemistry. Just as there are *species* of animals and plants, and *classes* of chemical substances in nature, there are natural kinds of diseases, called *species morborum* or *disease entities*. Biological taxonomies and the periodic table of elements in chemistry arrange their objects in proper, systematic order by natural criteria; likewise, the diseases are arranged in proper order by *nosology*. Therefore, any disease entity—like *influenza*—is a theoretical entity of medicine, like any element—for example, *oxygen*—is a theoretical entity of chemistry. From that it follows that a main task of medical research consists in the discovery, definition, and characterization of all disease entities that occur in empirical reality, and to build a comprehensive system reflecting all their similarities and differences. This system, viz. medical nosology, will form the basis for diagnostics and differential diagnostics, and eventually for specific therapy.

The system of Boissier did not endure; neither did the systems of his successors in the 18th and 19th centuries. Prior to success and acceptance, some very important problems had to be solved: what are the fundamental processes in

- origin and causation of diseases (e.g., by Louis Pasteur and Robert Koch),
- pathological alterations of morphology (e.g., Giovanni Battista Morgagni),
- pathological alterations of physiology (e.g., Claude Bernard), and
- which processes on the level of cells are involved (e.g., Rudolf Virchow)?

The investigation and solution of these problems took about 100 years, until the beginning of the 20th century. Then, over the course of the 20th century, medical research succeeded in integrating the knowledge of all clinical specialties into one comprehensive, multibranching nosological system based on empirical evidence. However, this is not to say that we already have knowledge of all existing disease entities and their complete descriptions and explanations. Instead, the discovery and explanation of disease entities is a stepwise process, developing from clinical syndromes and pictures, through the stage when we can clinically describe a disease entity, to its definite explanation by etiology and pathogenesis. This development frequently includes, besides specifications and refinements, also conceptual revisions and reclassifications. But at the beginning of the 21st century, we can state that all medical specialties possess a mature, full-fledged nosology. Really, all? No. *Psychiatry* is the exception that proves the rule. Most clinical pictures, syndromes, and disorders of psychiatry lack a pathophysiological and pathoanatomical explanation. After all, this was the crucial reason for the “antipsychiatric” turn in the middle of the 20th century, mentioned above. Only now does biological psychiatry accept the challenge of bridging the gap between biology and psychology and establishing a proper psychiatric

nosology. Of course, much work still has to be done. But that may be a good reason to remember, and to clarify further, what the essential conceptual structure of disease entities is.

### III. DISEASE ENTITY: SOME MAIN CONCEPTUAL FEATURES

*Disease entity* is a theoretical concept of science (medical science). In this respect, it is similar to the concepts of, for example, *particle*, *elementary particle*, and *field* (in physics), or of *element* and *compound* (in chemistry), or of *species*, *genus*, and *clade* (in biology). It is *theoretical* insofar as it is not definable by purely empirical, observational terms. But it is an extremely fruitful concept for structuring and explaining empirical facts and clinical observations. Standard textbooks of clinical medicine, such as *Harrison's Principles of Internal Medicine*, present the medical knowledge according to its nosological structure, that is, as a system of disease entities (Longo et al., 2012). This is true for all clinical disciplines of medicine, at least in present-day theory and practice.<sup>8</sup> Particularly, disease entities subsume not only diseases of internal medicine such as infectious or metabolic disorders but also surgical diseases (injuries, wounds, and burns), intoxications (poisoning), inborn and acquired disfigurements and malformations, and some further kinds of pathological conditions that are distinguished and separated from diseases only by commonsense, *lay* understanding—not by medical terminology. But what is a disease entity *exactly*? In the following, I shall list some of the most important conceptual features in a very abridged, compressed manner.

#### Diseases and Disease Entities: Principles of Completeness and Unambiguousness of Nosology

“Disease entity” is a category used for theoretical interpretation and explanation of individual cases of being ill and for the practical purpose of diagnosis. The term “disease” designates the *whole* course of the *individual* case, from its very beginning or *first cause* to its *outcome*, in contrast to single manifestations, symptoms, or findings in this case. The term “disease entity” designates the *type* or *pattern* to which a disease belongs. That is to say, every disease is a *case* or *instance* of a disease entity. The system of disease entities (i.e., nosology) has to fulfill two principles:

1. *Principle of completeness*: every single abnormal or pathological phenomenon or finding, and every case of being ill, is (= must be conceived as) an instance of one disease entity (or multiple concomitant disease entities). Medical theory does not allow for pathological conditions that are not subsumable by at least one disease entity: quasi “ownerless” or isolated pathological conditions outside any disease entity do not exist in reality.

2. *Principle of unambiguousness*: every single abnormal or pathological phenomenon or finding, and every case of being ill, is unambiguously subsumed by only one single disease entity. This task of unambiguous subsumption is the particular task of *differential diagnosis*. As long as there is more than one single disease entity left that might subsume the present case, one has to perform additional diagnostics in order to disambiguate the case. The final, conclusive diagnosis is formed by the one and only disease entity that subsumes the case correctly, completely, and exclusively.

This second principle is not violated by the possible existence of multiple coexistent diseases in the same patient or *multimorbidity*. A patient already suffering from disease entity A may acquire a second disease entity B, and so on. Strictly speaking, the condition of “A plus B” is a third disease entity C different from both A and B because of the causal interactions that inevitably will take place. In simple cases, these interactions may be neglected. But in most cases of multimorbidity, these interactions must not be neglected for diagnosis and treatment, because they form important and sometimes decisive features of the clinical picture. Thus, it is theoretically justified and correct to classify them as cases of discrete, composite, complex disease entities in their own right.

Unfortunately, there is no standard, comprehensive, and complete account of medical nosology in its entirety. The International Classification of Disease (ICD) classifications do not only list genuine disease entities but also signs and symptoms, pathological findings, complex pathological conditions that are not diseases, etc. The proper and binding nosological system is to be found, in *distributed* form, in the guidelines elaborated and published by scientific associations of the special disciplines of medicine, and—hopefully—in the standard, comprehensive textbooks of the specialties. Guidelines and textbooks of this type usually list the genuine disease entities of the discipline and take multimorbid conditions into account.

The conceptual relationships sketched in this section may aptly be illustrated by an example<sup>9</sup>: Suppose a person XY suffers from recurring attacks of *chest pain* precipitated by some bodily activity or psychological stress and lasting several minutes. There are a lot of possible causes of this kind of chest pain. In any case, chest pain is a pathological phenomenon or a pathological condition, but not a disease. Suppose further that this phenomenon of chest pain, after some diagnostic investigation, is classified as *angina pectoris*. Angina pectoris is defined by its particular cause, roughly, as “chest pain due to ischemia of the heart muscle.” But angina pectoris is not a disease either, but a complex symptom. The reason is that there are (at least) two essentially different mechanisms (“pathomechanisms”) that can cause cardiac ischemia: *obstruction* and *spasm* of the coronary arteries. Hence, there are (at least) two distinct diseases that could be present in this case:



atherosclerotic heart disease (AHD, ICD-10 I25.1) or Prinzmetal's angina, also called *variant angina* (ICD-10 I20.1). These both are genuine *disease entities*, at least as far as we know at present.<sup>10</sup> As a result, our patient XY could be suffering from an *instance* of either AHD or Prinzmetal's angina. Lastly, there are rare cases where chest pain, and even angina pectoris, is caused by coincidence of atherosclerosis and spasm of the coronary arteries. Current classification deals with these cases by a two-fold diagnosis, AHD *plus* Prinzmetal's angina. From a theoretical point of view, these cases should be subsumed by a third, conceptually new diagnosis, for example, "complex painful heart disease" or "AHD accompanied by spasm" or something similar.

### Disease Entities as Patterns

The full theoretical description of a disease entity describes the *pattern* or *type* for each natural course of the respective diseases (i.e., instances of the theoretical entity). Logically speaking, a disease entity is a set of possible *alternative* courses; as a predicate in sentences of the form "x has disease entity D," it renders them equivalent to a complex *disjunction* of the form "(x has course D<sub>1</sub>) or (x has course D<sub>2</sub>) or ... or (x has course D<sub>n</sub>)." The descriptions of disease entities in textbooks are explicit formulations of these alternative possible courses, including information about signs and symptoms, frequencies, stages, degrees of severity or seriousness, and types of variation ("variants"), as well as information about the underlying processes and alterations in pathophysiology, pathomorphology, and the corresponding diagnostic findings.<sup>11</sup> Note: diseases and disease entities are particular *pathological conditions*, but the term "pathological" is used here in the *general* sense, including clinical and subjectively experienced signs and symptoms, not in the biologically restricted sense of pathological anatomy or pathophysiology.

### Disease Entities and Kinds of Definitions

If medical terminology and classification are built up in a controlled, strict, and logically correct manner, they include genuine definitions of disease entities in the sense of logic and philosophy of science: genuine definitions must consist of conditions that are necessary and sufficient for the definiendum. In medical language, necessary conditions of disease entities are called "obligatory" conditions; sufficient conditions are called "pathognomonic." Thus, one method of defining a disease entity (method A) consists in specifying conditions that are obligatory and pathognomonic for its presence. Unfortunately, this method of defining is not bound to use only those conditions that are taken to be *essential* in a *medical* (therapeutical) perspective; rather, all conditions that are formally necessary and sufficient will do.

Besides the defining conditions, there may be conditions that are obligatory but not sufficient, and conditions that are pathognomonic—if present—but not necessary. These types of conditions may be very useful in diagnostics, because they often allow for exclusion or proof of the presence of a disease. Thus, there may be *several* distinct *diagnostic criteria* for its presence or absence. But definitions and diagnostic criteria must not be confounded (see below, subsection Disease Entities and Diagnosis).

A second method of defining a disease entity (method B) consists in listing all possible alternative natural courses of this entity, in the form of a complex disjunctive statement as sketched above (subsection Disease Entities as Patterns). This method may be more laborious than the first one but has the advantage of carrying much more information for the reader. Therefore, the method preferred in medical textbooks is this second one. This kind of definition resembles a comprehensive theoretical characterization of the disease entity to be defined, because the reader obtains a condensed overview over all *essential* features that might be expected during the course of a single case of this entity.

To show the difference between definition and diagnostic criteria, the following example may be helpful: “myocardial infarction” (MI) can be defined, according to method A, by “necrosis (= death) of at least one heart muscle cell caused by oxygen shortage.” This definition gives necessary and sufficient conditions for the disease entity MI; any other conceptually and causally independent features of MI, such as pain, fear, arrhythmia (= functional deficiency), or death of the patient, is not mentioned in the definition. But the diagnostic criteria for MI do not directly rely on the definition but on different symptoms, signs, and findings like ECG and blood enzymes that are pathognomonic. Also, for the definition, it does not matter by which particular cause or mechanism the oxygen shortage is brought about. For the presence or absence of MI, it does not matter whether only one single cell or the whole heart muscle is affected by necrosis. But of course these differences between kinds of etiologic factors and between silent infarction and imminent cardiac death are essential and of vital importance for the patient and for clinical diagnosis and treatment.

### Disease Entities and Causal Explanation

If a disease entity is fully understood, its description covers not only signs and symptoms in the courses but also, particularly, the causal structure “lying behind” them: *etiopathogenesis*. Therefore, disease entities are able to form a basis for causal (etiopathogenetic) *explanation* of symptoms and other manifestations or findings. The theoretical description of a disease entity includes or at least sketches explanatory statements like “the morphological alteration *m* causes (‘leads to’) the subjective experience of *s*,” for example, “the constriction of bronchioles leads to the subjective experience of dyspnea.”



## Disease Entities and Dispositions

Disease entities may be, but are not generally, dispositions.<sup>12</sup> Instead, one could say there is a general disposition of the human organism to fall ill that is triggered by *specific* causes of disease to develop a *specific* course of disease that is an instance of that *specific* disease entity. This general disposition was termed “pathibility” by K. E. Rothschuh (1959, 220ff) (a similar term nowadays in medical ethics is *vulnerability*, but here used with respect to *particular* groups of persons). This general disposition of all human beings must be distinguished from

- a. *less general dispositions* that are not universally distributed in mankind but may involve specific risks (“risk factors”) for developing diseases, for example, *low immunity*. Actually, these specific dispositions form (dispositional) disease entities (Case c. below) on a relatively high level of abstraction, because they can co-cause a number of different, more specific disease entities on a lower level of abstraction, for example, *specific infectious diseases*;
- b. *particular dispositional properties* of specific disease entities, for example, the disposition to sneeze after having caught a cold (= viral infectious disease of the upper respiratory tract); and
- c. *specific dispositional disease entities* that are *defined* by a pathological disposition, for example, allergies to specific trigger substances (allergens) like house-dust.

This important distinction may be illustrated by the following examples:

- Every human being has the disposition to *bleed* and lose blood by bodily injury and lesion of blood vessels; this is part of the *general* pathibility and vulnerability of the human organism.
- Persons affected by greater loss of blood may develop *anemia* and be at risk of breathlessness and dyspnea, as a *specific* disposition of the disease entity *bleeding anemia*.
- People suffering from hemorrhagic diatheses, like *vitamin K deficiency* or *hemophilia*, have a disposition to bleed and lose large amounts of blood, because this is a defining property of the disease from which they suffer: hemorrhagic diatheses are specific *dispositional disease entities*.

## Disease Entities and Diagnosis

The defining properties of disease entities form the ultimate basis for distinguishing between disease entities and for final, conclusive proof of diagnosis in *differential diagnostics*. That is to say, they form the ultimate, ideal gold standard for the diagnosis of a disease entity. But in clinical practice, we

mostly use diagnostic criteria different from the defining conditions because, for example, it might be too difficult, too time-consuming, too expensive, or too much burden to the patient if one were to ascertain the presence of defining conditions. Instead, we use causal effects of the defining conditions that verify their presence. For example, if a case of MI is suspected, it is sufficient to ascertain the effects that are verifying evidence of heart muscle necrosis, for example, pathognomonic ECG and lab findings (see above, subsection Disease Entities and Kinds of Definitions).

### Disease Entities and Granularity

Disease entities may be in relationship with one another, particularly the relationships of predisposition and consequence (consecution, complication). Because the members of such pairs of disease entities are different by definition, the pair itself cannot be conceived as one variant form or variant course of one of the two disease entities. The question of whether a given type of course *can and should be* defined as forming a proper disease entity or a mere variant of an already existing disease entity is a question of concept formation in nosology. Concept formation must be carried out in a consistent, univocal manner, satisfying principles of completeness of the system, distinctness and disjunctivity of the concepts, and respecting also the medical meaning and importance of the corresponding entity. To give one example: AHD is a predisposition for MI. But MI is not a mere variant course of AHD, because (1) there are several different predispositions for MI, (2) MI may occur without any predispositional disease entity, and (3) the eminent vital importance of the event of MI justifies its definition as a separate disease entity.

Because disease entities are always *patterns*, that is, *sets of different* courses, it is almost always possible to *subdivide* a given disease entity into subtypes and to *declare* the subtypes proper disease entities, at least in principle. Hence, there is no general, natural limit for subdividing. This infinite subdividability is limited by the requirements of *causal* and *practical* relevance of further subdivision. Nevertheless, there remains a gray area of possible subdivisions. Therefore, the *granularity* of nosology is not totally fixed, and the *exact number* of different disease entities cannot be determined in an unequivocal manner. But note that by subdividing the conceptual structure of nosology is only refined and enriched quantitatively, not changed qualitatively. Thus, what matters ontologically is the structure of nosology and its possible levels of granularity, not its actual extension.

### Disease Entities and Severity of Individual Course

The different courses that are variants of one etiopathologically defined disease entity may be distinguished by their degree of severity (or seriousness). There may even be courses without any symptoms or signs—so-called

*bland, clinically silent, or inapparent* courses. Whether the disease entity is at hand or not is not decided by the degree of severity of its course, but by the existence (and diagnostic proof) of its defining properties. Thus, somebody can be diseased in the medical sense and can “suffer” from a definite disease entity, though he or she does not observe any subjective complaints or symptoms—if the defining properties are given. The existence of different degrees of severity and even of inapparent courses of defined disease entities implies that it would be misleading to conceive and reconstruct the diagnosis of these diseases in a gradualist manner, if this implies *being diseased at all* only to a certain degree or percentage. Instead, the diagnosis may be supplemented with information about the degree of severity of *this instance of the disease entity* (bland, mild, moderate, severe, lethal, etc.).

### Disease Entities and Temporal Characteristics

Disease entities own a general temporal characteristic, that is, a temporal pattern. They may be acute, chronic, episodic, relapsing, recurrent, progressive, exacerbating, undulant, etc. Different instances of one disease entity may vary concerning duration, frequencies, and other aspects of its general pattern. But in different kinds of disease entities, the temporal patterns themselves may differ extremely in shape, length, and degree of variability in the instances. Additionally, we must distinguish between the temporal characteristic of the entire entity and of its individual clinical signs, for example, fever or pain.

### Disease Entities and Pathologicity

Medical terminology uses a *terminus technicus* for the property of being pathological, that is, the noun “pathologicity.” Outside medicine, this term is rather unfamiliar. But the corresponding concept is central and essential in medical theory of disease. The defining property of a disease entity *must be a pathological* condition. The natural course of an *instance* of a disease entity is the whole set of causally connected states and events of the affected organism, from the primary cause to the final outcome, *as far as they are pathological* (in the sense to be explicated below). Therefore, the reconstruction of the concepts “pathological” and “pathologicity” is central for understanding the nature of disease entities.

The claim that defining properties of disease entities must always be pathological conditions does not mean that any single condition in a complex conjunction of defining clauses must *always*, under *any* circumstances, be pathological, even if it occurs in isolation and separately. For example, *osteoporosis* may form part of the definition of a disease entity if combined with further findings such as vitamin D deficiency, corticoid therapy, etc. But osteoporosis might be a normal condition in aging. Thus, osteoporosis by itself and occurring in isolation is not necessarily pathological.

## IV. RECONSTRUCTION OF THE CONCEPT OF PATHOLOGICITY

## The Pretheoretical Intuition and Criteria

The concept of pathologicity can be characterized by a *system of criteria*. These criteria stem from a prescientific, life-world intuition about disease, illness, and abnormality but are refined and rendered more precise in a step-wise process of theoretical clarification. Thereby, they are adjusted to the theoretical, medico-scientific description of the human organism. The last step is formed by a theoretical, scientific criterion, based on the concept of disease entity that may complement and override the pretheoretical criteria. The first and primary step or level of criteria of pathologicity—or, for short, *disease criteria*—may be formulated by five criteria. The basic intuition may be recognized by the following five clauses:

(CR1) A condition of the human organism is pathological if

1. it is immediately lethal or definitely life-shortening,
2. it is a condition of pain, suffering, or other specific complaints (to be enumerated),
3. it is a condition of infertility (incapability of biological reproduction),
4. it is a condition of inability or impairment for living together in human symbiotic communities, or
5. it is a nonuniversal disposition of the organism to develop a condition that is pathological according to one or more of these criteria.

Of course, this basic intuition is in need of a more precise and somewhat technical formulation in order to avoid circularities and misinterpretations. Some refinements and restrictions of application are given below.<sup>13</sup>

Philosophers might ask what the *justification* for the medical system of disease criteria is. My account in this paper is restricted to an analysis and reconstruction of this system in itself, because until now there has been little philosophical attention given to its existence. This task of reconstruction must be distinguished from the task of *explaining* how and why disease criteria are naturally given criteria and not arbitrary conventions. This can be done only in a lengthy scientific explanation of the biopsychosocial genesis and meaning of all criteria, which cannot be given here.<sup>14</sup> Additionally, in order to avoid naturalistic fallacies, this task of *explaining* must be distinguished from the task of *justifying normative consequences* from the medical concept of disease and its criteria. The *norm* that diseases *should* be treated medically, or that ill persons possess a *right* to medical aid and assistance, is a normative claim that, indeed, is in need of *justification*. But this is a matter of ethical and political debate and cannot be dealt with in this paper. Also, the *valuation* of criteria—for example, of early death—is a matter of subjective preferences or cultural values, and different from their meaning and use in medical theory.

### Conditions of Applicability of Pretheoretical Criteria

The criteria (CR1) refer to life conditions that are, at least partially, attributed to the organism and are not exclusively attributable to its environment. The criteria are restricted to life conditions and processes that are biologically autonomous and are independent from the volition and insight of the affected person. Interrelations and interactions of organism and environment, involuntary desires and imaginations, illusions, misperceptions, hallucinations, and delusions are attributed to the affected organism.

The five criteria (CR1) are independent from one another. Each criterion is a sufficient condition of pathologicity. However, they can apply simultaneously to the same case.

There are more preconditions of applicability that may be more or less self-evident from the viewpoint of common sense and medical understanding but may be stated explicitly in order to avoid misinterpretations. Some of them are:

1. CR1 is to be applied exclusively to the *untreated* state and *natural* course of the life condition to be evaluated as healthy or pathological.
2. In evaluating a life condition, the entire range of possible alternative natural states and courses is taken into account. If this range is empty, that is, the condition is *inevitable* (like mortality and natural death), the life condition cannot be judged pathological. The same holds true if the only possible alternatives are *artificial* ones. Of course, the inevitability of a life condition—for example, childbirth pain—must be ascertained regarding all relevant aspects of it, including degrees of intensity, duration, etc. There may be severe pain in childbirth that indicates complications or a hidden disease; hence, a careful differential diagnosis of childbirth pain is indicated.
3. Particularly, the sexual dimorphism and the existence of phases and stages of ontogenetic development, including gravidity and intrauterine life, are natural and inevitable stages, and thus not pathological in themselves.
4. CR1 does not apply to actions of a person, provided that his/her cognitive, emotional, and volitional abilities are not changed pathologically. Note: the pathological restrictions or alterations of volition are themselves *not* voluntary.

### Secondary Pathologicity

All life conditions that satisfy (CR1) are *pathological in the primary sense*. Based on these criteria, further pathological life conditions can be defined in a derived, *secondary* sense. This is done by the following criterion:

(CR2) A life condition that is not pathological in the primary sense is *pathological in the secondary sense* if

1. it is a causal consequence of pathological life conditions (= conditions that are already known to be pathological in the primary sense or pathological in the secondary sense) and
2. its absence is not pathological (and known as being not pathological).

There are some very “special cases” of pathologicity that may be noted explicitly but cannot be discussed here in greater detail: *facultative* pathologicity (or pathologicity *in the tertiary sense*), *ambivalence* regarding health and disease (= a condition that may be protective and detrimental at the same time), *neutrality* regarding health and disease (= a condition the presence and absence of which are not pathological either), and maybe the *paradoxical* pathologicity (“the disease not to be able to be diseased”) (Müller-Eckhard, 1951, 1955). Here are some short examples as a substitute for a detailed theoretical analysis:

- a. *short stature* is a case of *facultative* pathologicity, see below (next section);
- b. *fever* is a case of *ambivalence*, because it can improve the function of the immune system but may be life-threatening if body temperature increases beyond 42°C; and
- c. *the capacity to wiggle the auricles* is a *neutral* life condition.

### The Theoretical Criterion

Disease entities are discovered (as a rule) in clinical practice by observing or recognizing patterns or typical traits in the disease course of individual cases—that is, they are discovered by *pattern recognition*. The discovery must be confirmed by further empirical and experimental research and investigation of the individual cases in order to establish a real etiopathogenetically definable disease entity in its whole underlying causal structure and range of possible variation. When established, a disease entity is added to the corpus of nosological knowledge and used in diagnostics and differential diagnostics.

Disease entities are (clinically) discovered by virtue of their pathological manifestations—that is, pathological in the pretheoretical sense; hence there are always instances that are pathological beyond doubt. But, as stated above (Section III, subsection Disease Entities and Severity of Individual Course), a disease entity, as a pattern of pathological behavior of the organism, may cover a wide range of clinical courses, particularly also mild and inapparent ones. Nevertheless, such minor cases are cases of a disease entity and, hence, pathological conditions. This fact may be used to disambiguate theoretically or clinically doubtful cases of possible pathologicity.

In order to disambiguate doubtful cases, the diagnostician has to examine and prove, whether or not defining or conclusive criteria of the disease entities in question are present. If they are, then a mild, abortive, or inapparent



course of the respective disease entity is present; if not, the case is either a variant of normality—perhaps a so-called nondisease—or medical science may have to discover a new, hitherto unknown disease entity. The latter case may be rare but should not be forgotten at all.

Typical cases that need disambiguation in clinical practice (and theoretical or philosophical discussion) are:

- *Short stature*: cases of short stature may be either statistically normal variants of body height or mild cases of pathological hyposomia, occurring in the context of several growth disorders (= disease entities).
- *Fatigue*: may be a case of normal tiredness or a symptom of mild or latent viral infection (= specific disease entities).
- *Grief*: may be a case of normal mourning or sorrow, or a case of mild or moderate depression, according to the presence or absence of pathognomonic signs of clinical (pathological) depression in the sense of psychiatry.
- *minimal cerebral lesion (MCL)*: many forms of slight neurological, intellectual or emotional weakness, malfunction, or deficit *may be* due to MCL caused by hypoxia during birth, discrete brain infarction, or similar noxae.

There is a borderline and maybe a no man's land between diseases and non-diseases (health/normality) that can be characterized as follows: on the one side, there are diseases that are real, authentic disease entities in the sense explicated here, but exhibit, *in most cases*, a very mild or inapparent course. They must be counted as pathological conditions notwithstanding. On the other side, there are conditions that are not disease entities ("nondiseases") that, nevertheless, may or might require medical treatment or observation. The first kind of such conditions is known as "benign" disease; examples are:

- *warts (verrucae) of the skin*: caused by viral infection (human papilloma virus); in the vast majority of cases, harmless but may proliferate, spread, and impair health and well-being
- *comedos*: caused by hyperkeratosis and obturation of the sebaceous gland; in most cases, harmless and self-limiting but may suppurate and cause pain
- *solitary cyst of the kidney*: caused by imperfect embryonic development of the kidney; in most cases, harmless but may cause compression in case of big size and, in rare cases, may develop complications like hemorrhage or cancerous degeneration.

The second kind of condition is formed by *facultatively pathological states* and *risky variants of normality*; examples are:

- *ribs of the neck* (supernumerous cervical ribs): variations of the number of ribs are found in a small percentage of cases, in most cases without

complaints or pathological findings. But sometimes, cervical ribs may compress nerves and/or blood vessels and cause pain, palsy, or damage of tissue.

- *white skin color*: a genetic adaptation, not pathological or a disease entity like albinism, but may be a disadvantage in tropical climates (increased risk of sunburn, melanoma, etc.)
- *prenatal life/gravidity*: the stage of prenatal life, living in somatic symbiosis with the maternal organism, is an inevitable stage of every human being; but because it implies several risks for the health of both mother and child, it is in need of medical observation and, possibly, treatment.

In order to discriminate between benign diseases and risky normality, the following additional, comparative criteria may help: look at the causes of the condition in question! If there are only causal factors and conditions that are needed for sustaining life and health, there is no disease. If there is a causal factor that is not necessary for sustaining life but is known to be a typical etiological factor in other disease entities—factors like infection, obturation, incomplete development, or externally induced necrosis of cells and tissue—then a proper disease entity is present, though a benign one.

## V. GENETIC DISTRIBUTIONS, VARIANCE, AND THRESHOLD VALUES

A great number of phenotypical traits of the organism show a distribution and variance of its value or expression that is caused by the variance of genetic factors or dispositions. Now, genetic variance and variability are preconditions of biological life and development; they are inevitable conditions even if they lead to inequality concerning advantages and disadvantages for the individuals. It has to be accepted that differences inside this range, if genetically contingent, are inevitable and thus *not pathological*.

Therefore, it may occur that one individual, by genetic variation, bears an expression or value of a property that is the same as that of a second individual, but in the second case, it is caused by disease (and is pathological in the secondary sense), for example, concerning body height or mass. In such cases, the condition of the first individual is never pathological; the condition of the second individual is pathological because its *expected value* is changed *by disease*.

Nevertheless, there are genetic conditions that lead to phenotypical conditions that are definitely pathological (in the primary sense). Insofar as they are sufficient causes or dispositions for pathological (phenotypical) conditions, these genetic conditions are themselves pathological in the primary sense.

The second criterion of CR1 refers to pain, suffering, and a number of specific complaints. There are two kinds of complaints: the first one is always pathological, and the second one is pathological if the degree of the sensation, the quantity of the stimulus, or the intensity of the response of the

organism exceeds a definite threshold value. This threshold value, although in many cases felt intuitively, must be determined empirically for every form of complaint of this second kind. There is no unique methodology for determining thresholds of this kind because of the manifold nature of their causes. Rather, discovering and determining thresholds is a typical topic in physiological, biochemical, and psychological research.

The first kind of complaints—without threshold—embraces, besides the sensation of *pain*, the sensations of *nausea*, *dizziness*, *pruritus* (itching), *dyspnea*, *tinnitus*, *tussive irritation*, and many more. They all involve *suffering*, whether mild or severe; in contrast to that, their absence is never felt as harmful. Their threshold value is zero.

The threshold value of the second kind of complaint is different from zero. The sensations of, for example, fear, grief, lust, and pleasure undergo permanent undulations that are triggered by internal, physiological rhythms and oscillations as well as by the reaction to external events. But there are threshold values that mark the changeover to pathological forms: *angst* and *panic*, *depression*, *frigidity*, and *anhedonia*. To find out the objective threshold value<sup>15</sup> for this changeover, a minute knowledge and thorough analysis of the morphological foundations, physiological regulations, and other etiologically relevant circumstances of the subjective sensation are needed. If it is possible to demonstrate the existence of a temporal regulation or homeostasis that is directly correlated to the sensation and can be disturbed, we have an objective criterion for the existence and value of the threshold. For example, in the sensations of warm/hot and cool/cold, there is a changeover from the excitation of sensory receptors of heat and cold to sensory receptors of pain if a definite degree of (objective) temperature is exceeded.

There are domains of medical knowledge where the objective foundations of many threshold values are not known or not yet fully understood—particularly in psychopathology. Nevertheless, the existence of threshold values is strongly supported by clinical experience. Therefore, clinicians usually rely on scores and indices that form a surrogate for this objective knowledge. Many definitions of psychiatric disorders in ICD-10 and the Diagnostic and Statistical Manual of Mental Disorders IV/V are of this kind. The real thresholds and the real disease entities have to be identified by the ongoing etiopathological research that still may take years or decades.

## VI. NONDISEASES REQUIRING MEDICAL TREATMENT

There are many states and life conditions that are in need of treatment by physicians but are not diseases (disease entities) or pathological conditions. In medical practice, this is a known and accepted fact. But in health policy and ethical discussions concerning health care, this fact seems underestimated, if known at all. Thus, treatment of such conditions is frequently

disguised, for example, as prevention, and is not openly presented as treatment of nondiseases. Sometimes this practice is legitimated by inaccurate versions of the concept of disease. To be sure, the treatment or prevention of the following conditions is not a treatment of diseases:

- discomfort of aging, that is, decreasing abilities and increasing vulnerability caused inevitably by the very process of aging
- inevitable pain, as in childbirth, teething, and menstruation
- gravidity, when there is no medical indication for contraception or abortion
- bodily attributes that are not pathological but elicit negative reactions from other people or society in general
- conditions that form extreme values of a statistical distribution, for example, low values of intelligence or talent
- mental and emotional problems because of difficult circumstances of life

In many of these cases, medical assistance and advice are judged appropriate, if requested and possible. But because they are not pathological conditions, the justification of medical treatment must refer to the *analogy* or *equivalence* between these conditions and genuine pathological conditions, and to some principle of *justice* regarding the right to help and assistance. Here, a clarification by social law and health policy is overdue.

## VII. DISEASE ENTITIES, PSYCHIATRY, AND GRADUALISM<sup>16</sup>

The high tide of antipsychiatry has gone, definitely, even if authors like Thomas Szasz are still under discussion (Szasz, 2003; Schaler, 2004; Szasz, 2008). But psychiatry is still an exception among medical specialties, insofar as most mental disorders are not (yet?) disease entities that are etiopathogenetically explainable. Indeed, most psychiatrists agree that some mental disorders such as major depression and schizophrenia are disease entities or clusters of disease entities in the *clinical* sense. But there are a lot of other disorders that are, at best, clinical syndromes or aggregations of clinical symptoms and signs, lacking sharp boundaries and unequivocal criteria of identity or identification. And what is worse, there may be cases of alleged disorders that, on closer scrutiny, should better be classified as nondiseases such as *social conflict*, *need for help*, *bad habit*, or *problem of everyday life* without fulfilling any criterion of pathologicity. As Thomas Szasz put it: “Bad habits are not diseases” (Szasz, 1972)! But, ironically, Szasz referred to the case of alcoholism; and as we know by now, there are cases of alcoholism that are cases of true pathological addiction, because we know the pathobiochemical mechanisms underlying the alleged bad habit. Alcoholism A is not alcoholism B, and we have to distinguish between voluntarily and

nonvoluntarily, that is, pathologically drinking.<sup>17</sup> On account of insights of this kind, the search for a nosological system of psychiatry that originated in the 19th century is still going on in the 21st century and is stimulating a bulk of debates and controversies.<sup>18</sup> Research in the area of so-called biological psychiatry is aimed at bridging the gap between biological and psychological sciences, between neurobiology and neuropsychology. It aims at the discovery of models explaining mental disorders by integrating genetic, morphological, biochemical, behavioral, cognitive, and emotional factors and respecting the role of social and environmental conditions. Of course, there is still a long way to go, though there are, at this stage, encouraging results.<sup>19</sup> However, there are also voices that advise us to dispense with further search for disease entities. Instead, they recommend the position that there be a continuum between health and disease that allows only for gradual or graduated distinctions, that is, degrees of healthiness and/or diseasedness.<sup>20</sup> This so-called *gradualist* position is based, to some extent, on a general skepticism concerning the concept of disease entity. Hence, gradualist arguments may be critically examined in the concluding section of this paper.

#### Gradualism and Degrees of Severity

In medical theory and pathology, the conceptual distinction between healthy/normal and diseased/pathological is conceived as a qualitative, sharp, and objective demarcation and not as a matter of degree; it is marked by the respective boundaries of the disease entities. *Inside the realm of pathological conditions or respectively the realm of disease entities*, there are graduations, namely, degrees of severity concerning symptoms, manifestations, and courses, including inapparent yet pathological courses. These graduations are consistent with the diagnostic classification of a case as being an instance of a definite disease entity, if only the defining property of this entity is present. But in practical medicine, the exact, etiological diagnosis frequently must be left open, because an etiological oriented diagnostics is judged inappropriate or unacceptable for the patient, particularly in mild cases. Nevertheless, this abandonment of etiological diagnosis because of *practical* reasons is not to be confounded with a *conceptual* vagueness or fuzziness. In addition, some borderline cases of diagnosis are due to insufficient knowledge about etiopathogenesis, especially in psychopathology. In these cases, medical theory is in need of empirical research in order to identify causes and thresholds of disease, not conceptual gradualism.

#### Unequivocal Identifiability of Disease Entities

The concepts “ill/diseased/pathological” and “normal/healthy” in medical pathology are not “family resemblance concepts,” as some gradualists maintain.<sup>21</sup> The central theoretical concepts are the concepts of disease entities. These concepts must be introduced and justified by an exact definition that refers to objectively

determinable *pathological* conditions, and not by family resemblance. Thus, they refer to criteria of pathologicity, as shown above. These criteria are not totally unequivocal if looked at in an intuitive formulation; but in the context of general and special pathology and etiopathogenetic nosology, they become unequivocal. Because the distinction between normal and pathological refers, in the final analysis, to disease entities, it is unequivocal as well.

#### “Natural Kinds” and Indeterminate Granularity of Disease Entities

Are disease entities natural kinds? This question must be returned to the questioner. Until now, nobody has suggested a proper *definition* of “natural kind” that can satisfy minimal preconditions of a scientific, applicable concept. It may well be that “natural kind” is not a natural kind, or—to put it nonparadoxically—“natural kind” may be simply a designation for well-established scientific concepts and classifications. To be sure, there is a broad philosophical discussion concerning the nature of (alleged) natural kinds, and a considerably narrower branch of it that deals with diseases as natural kinds. The latter branch seems to have been triggered or at least strongly influenced by Reznek’s (1987) book *The Nature of Disease*.<sup>22</sup> But before discussing the reality or naturalness of disease categories, a closer look at medical nosology is recommended. There is only one conceptual tool and system that is universally applicable in medical theory and generally binding in diagnosis and therapy—the system of *disease entities*. In this respect, its status is comparable to the status of the periodic table of the elements in chemistry. But there are also some conceptual differences from the periodic table in chemistry.

Disease entities are entities without a fixed, unitary granularity (see Section III, subsection Disease Entities and Granularity). That is to say, disease entities can be defined according to different levels of detail. One disease entity on a high level may comprise a number of disease entities on a lower level. For example, the disease entity “common cold” comprises a lot of disease entities defined etiologically by the kind of virus that causes this special kind of common cold (and there are many kinds of viruses that do that). The reason for this difference from chemistry is simply that diseases, as complex causally structured conditions of the human organism, are much more complicated than atoms. Nevertheless, all kinds of disease entities on all levels of granularity are defined by objective, scientifically established properties. Hence, rather than speaking of “natural kinds,” the whole system, including its methods of distinction and individuation, may be called a *natural system*.

#### Practical Problems Regarding Pathologicity and Degrees

Legal and forensic judgments refer not only to the pathologicity but also to the degree of severity or impairment of a condition. There are three types of situation that entail challenges to law and jurisdiction:



1. If the exact causal situation of a case of disease is not known—generally or individually—then it may be difficult to judge the *severity* of this case. If we do not know the causes, we cannot state a well-founded prognosis concerning the further course and outcome of the disease. The same is true if we do not know whether the disease at hand is causally responsible for a certain (e.g., unacceptable or criminal) behavior of a person *at all*. This problem occurs particularly in mild forms of psychiatric disorders. But in European law and jurisdiction, the diagnosis of a “true” severe psychiatric disorder is a prerequisite for the preventive detention of criminal offenders, thus urging psychiatrist consultants to provide diagnoses even in causally doubtful cases.<sup>23</sup>
2. There are situations in diagnosis where we do not know whether there is a risk at all. This may occur in cases where we know only statistical correlations but not causal relationships between certain circumstances and/or conditions. Hence, it is not possible *in principle* to determine individual risks or risk factors. In medical practice, such cases usually are treated according to a *precautionary principle*, if the *potential risk* is great and the patient agrees, even if there is a considerable probability—but not certainty—for not being at risk. Thus, some percentage of these “patients” is treated, though not diseased or at risk at all! This may be justified by practical reason but perhaps, until now, not explicitly by law.
3. If the condition to be judged is not a genuine pathological one but a case of analogy or equivalence to disease (a nondisease, e.g., aging; see above, Section VI), the hitherto existing legal formulations do not cover it. Hence, they dismiss the needs and rights of people that would be justified by a principle of justice. This, however, is a legal and judicial problem that cannot be solved by weakening, deconstructing, or abolishing the medical concepts of disease and disease entity, but only by clearly acknowledging the practical and ethical equivalence of diseases and (some kinds of) nondiseases.

### VIII. CONCLUSION

If the claim is justified that “disease entity” is the central, key theoretical concept of medicine, then this concept deserves more attention from philosophical analysis. For example, what are the ontological presuppositions and implications of the existence of *theoretical entities* of this kind? What are the exact criteria for distinguishing between a *natural course* of a disease entity and an artificially influenced and altered one? Can there be an exact borderline between *organismic* events and *environmental* causes of disease entities? Where is the real borderline between *free will* and volitions or actions that are specifically altered by different disease entities? What about the existing *theoretical accounts of disease and medicine* that neglect the

existence and role of disease entities? There are a lot of questions and tasks for general philosophy of science, philosophy of the life sciences, and of course philosophy of medicine to address.

## NOTES

1. For prior discussions, see Berghoff (1947) and the collected papers in Rothschild (1975) and Caplan, Engelhardt, and McCartney (1981).

2. See Griesinger (1845, 1–3). Griesinger explains his position at full length in the first chapter of this book.

3. For examples, see the many contributions of Boorse, Reznek, Culver/Gert, Engelhardt Jr., and Nordenfelt.

4. See the collections of Humber and Almeder (1997); Nordenfelt (2001); Caplan, McCartney, and Sisti (2004); Gifford (2011); Rothhaar and Frewer (2012); Schramme (2012); Hucklenbroich and Buyx (2013).

5. See Boorse (1977, 1997); definition in Boorse (1997, 7f).

6. Alas, I cannot dwell on the theory of organism here. The structural and functional organization of organisms as a self-processing network is characterized in detail in my “Organism and Program” (Hucklenbroich, 1986, in German) and, in more abridged form, in Hucklenbroich (1987, 1990, 2009), and Hucklenbroich and Chuaqui (1987).

7. For much more historical detail concerning the conceptual development, see Ackerknecht (1963); Temkin (1963, 1973); and Kiple (1993).

8. Except, of course, for psychiatry.

9. This example is somewhat simplified, because in medical reality, there are more disease entities and more possible causes involved. I have omitted them for convenience. You can find the full account in any textbook of internal medicine or cardiology.

10. But see Section III, subsection Disease Entities and Granularity on granularity.

11. This characterization shows that diseases and disease entities in the medical sense are not to be identified with diseases as defined by Boorse. In most cases, the mere deficiency of a function or functional ability, as in the definition of disease by Boorse, is not a sufficient condition for *defining* a disease entity; neither is it a full *description* of the disease. Medical diseases may, and often do, include functional deficiencies, but these are *manifestations*, that is, parts or symptoms of the whole disease entity. Additionally, there are lots of disease entities that are *definable* without reference to any functional deficiency at all, for example, morphological abnormalities and malformations.

12. Marc Lange has argued that diseases (and, I extrapolate, disease entities) are always and generally *incapacities* and, consequently, special kinds of dispositions or, rather, in-dispositions (in-abilities). But this analysis is far too narrow, omits large portions of medical nosology, falls short of the distinctions given in the text above, and does not adequately cover the conceptual structure of medical theory. See Lange (2007).

13. For more details about the criteria and their application in medical pathology, see my articles—Hucklenbroich (2007, 2008, 2012, 2013) (in German), and Hucklenbroich (forthcoming), *Theory of Disease*.

14. See, preliminarily, the discussion in Hucklenbroich (2013, 46–51) and Hucklenbroich (2014a).

15. In this section, the distinction between *objective* and *subjective* refers to the well-introduced, common methodological distinction between properties that are determined and measured by *inter-subjectively reliable*, scientifically validated methods, and properties that must be determined by reference to the *experiences and utterances* of the proband or patient.

16. For a more detailed discussion of this topic, see Hucklenbroich (2014b).

17. For an illuminating discussion of this distinction, see Heinz (2005, esp. 414ff).

18. See recent surveys and collections, for example, McHugh and Slavney (1998); Kendler and Parnas (2008); Millon, Krueger, and Simonsen (2010); and Kendler and Parnas (2012).

19. See more recent textbooks of psychiatry, like for example, Förstl, Hautzinger, and Roth (2006). An impressive account of the development and actual stage of biological psychiatry is given by Walter (2013). See also Rietschel (2014).

20. See the papers in Keil, Keuck, and Hauswald (2014).
21. See Stoecker (2009) and Keil and Stoecker (2014). Somewhat similar approaches are defended in Pickering (2013) and Schroeder (2013).
22. But according to Reznek, there are no natural criteria of pathogenicity. There is some discussion of Reznek's theory, for example, D'Amico (1995) and the response by Reznek (1995); see also Simon (2011, esp. 108–113). The thesis that diseases are natural kinds is also defended in Sulmasy (2005); Dragulinescu (2010); Simon (2010); and Smith (2012). But all these accounts are in need of explicating the concepts of disease entity and of pathogenicity that are applied or assumed by them.
23. For a detailed discussion, see Kröber (2014).

## ACKNOWLEDGMENTS

I am very grateful to two anonymous referees of this journal, whose helpful suggestions and stimulating questions regarding an earlier draft of this paper I accepted with alacrity. Research for this paper has been funded by the German Research Community (Deutsche Forschungsgemeinschaft DFG) as part of the Research Group "Causation, Laws, Dispositions, and Explanation at the Intersection of Science and Metaphysics" (FOR 1063) and the project "Causes of Disease: Causality and Pathogenesis in Medicine" (Hu 397/6-2).

## REFERENCES

- Ackerknecht, E. H. 1963. *Geschichte und Geographie der wichtigsten Krankheiten*. Stuttgart, Germany: Enke.
- Bateson, G., D. D. Jackson, J. Haley, and J. W. Weakland. 1956. Towards a theory of schizophrenia. *Behavioral Science* 1:251–64.
- Berghoff, E. 1947. *Entwicklungsgeschichte des Krankheitsbegriffes*. 2nd ed. Vienna, Austria: Maudrich.
- Boorse, C. 1977. Health as a theoretical concept. *Philosophy of Science* 44:542–73.
- . 1997. A rebuttal on health. In *What is Disease?* eds. J. M. Humber and R. F. Almeder, 3–134. Totowa, NJ: Humana Press.
- Caplan, A. L., H. T. Engelhardt, Jr., and J. J. McCartney, eds. 1981. *Concepts of Health and Disease: Interdisciplinary Perspectives*. Boston: Addison-Wesley.
- Caplan, A. L., J. J. McCartney, and D. A. Sisti, eds. 2004. *Health, Disease, and Illness. Concepts in Medicine*. Washington, DC: Georgetown University Press.
- D'Amico, R. 1995. Is disease a natural kind? *Journal of Medicine and Philosophy* 20:551–69.
- Dragulinescu, S. 2010. Diseases as natural kinds. *Theoretical Medicine and Bioethics* 31:347–69.
- Förstl, H., M. Hautzinger, and G. Roth, eds. 2006. *Neurobiologie psychischer Störungen*. Heidelberg, Germany: Springer.
- Gifford, F., ed. 2011. *Handbook of Philosophy of Science. Vol. 16: Philosophy of Medicine*. Amsterdam, The Netherlands: Elsevier.
- Griesinger, W. 1845. *Die Pathologie und Therapie der psychischen Krankheiten*. Stuttgart, Germany: Krabbe.
- Heinz, A. 2005. Gesunder Geist – krankes Hirn? Überlegungen zum Krankheitsbegriff in der Psychiatrie. In *Bewusstsein*, eds. C. S. Herrmann *et al.*, 407–25. München, Germany: Fink.
- Hucklenbroich, P. 1986. *Organismus und Programm*. Münster, Germany: Diss. med. (microfiche).
- . 1987. Das Konzept der Selbstprogrammierung in natürlichen und künstlichen Gehirnen. In *Medicinale XVII. Das Gehirn und seine Erkrankungen (I)*, eds. E. H. Graul, S. Pütter, and D. Loew, 115–36. Iserlohn, Germany: Medice.

- . 1990. Selbstheilung und Selbstprogrammierung. In *Zur Biologie der Kognition*, eds. V. Riegas and C. Vetter, 116–32. Frankfurt/Main, Germany: Suhrkamp.
- . 2007. Hauptartikel: Krankheit – Begriffsklärung und Grundlagen einer Krankheitstheorie. *Erwägen – Wissen – Ethik* 18:77–90.
- . 2008. “Normal – anders – krank”: Begriffsklärungen und theoretische Grundlagen zum Krankheitsbegriff. In *Normal – anders – krank? Akzeptanz, Stigmatisierung und Pathologisierung im Kontext der Medizin*, eds. D. Gross, S. Müller, and J. Steinmetzer, 3–31. Berlin, Germany: Med. Wiss. Verl. Ges.
- . 2009. Wissensmodellierung und Selbstprogrammierung. In *Physikalismus, Willensfreiheit, künstliche Intelligenz*, eds. M. Backmann and J. G. Michel, 228–43. Paderborn, Germany: Mentis.
- . 2012. Der Krankheitsbegriff der Medizin in der Perspektive einer rekonstruktiven Wissenschaftstheorie. In *Das Gesunde, das Kranke und die Medizinethik. Moralische Implikationen des Krankheitsbegriffs*, eds. M. Rothhaar and A. Frewer, 33–63. Stuttgart, Germany: Steiner.
- . 2013. Die wissenschaftstheoretische Struktur der medizinischen Krankheitslehre. In *Wissenschaftstheoretische Aspekte des Krankheitsbegriffs*, eds. P. Hucklenbroich and A. Buyx, 13–83. Münster, Germany: Mentis.
- . 2014a. Medical criteria of pathologicity and their role in scientific psychiatry – Comments on the articles of Henrik Walter and Marco Stier. *Frontiers in Psychology*. doi:10.3389/fpsyg.2014.00128
- . 2014b. Disease entities and the borderline between health and disease: Where is the place of gradations? In *Gradualist Approaches to Mental Health and Disease*, eds. G. Keil, L. Keuck, and R. Hauswald. Oxford: Oxford University Press (in press).
- . (forthcoming). *Theory of Disease*.
- Hucklenbroich, P. and A. Buyx, eds. 2013. *Wissenschaftstheoretische Aspekte des Krankheitsbegriffs*. Münster, Germany: Mentis.
- Hucklenbroich, P. and B. Chuaqui. 1987. Thesen und Probleme zu den Begriffen von Ordnung, Information und Emergenz. In *Modelle der Pathologischen Physiologie*, eds. W. Doerr and H. Schipperges, 57–70. Berlin, Germany: Springer.
- Humber, J. M. and R. F. Almeder, eds. 1997. *What is Disease?* Totowa, NJ: Humana Press.
- Keil, G., L. Keuck, and R. Hauswald, eds. 2014. *Gradualist Approaches to Mental Health and Disease*. Oxford: Oxford University Press (in press).
- Keil, G., and R. Stoecker. 2014. Health and disease as thick and vague cluster concepts. In *Gradualist Approaches to Mental Health and Disease*, eds. G. Keil, L. Keuck, and R. Hauswald. Oxford: Oxford University Press (in press).
- Kendler, K. S. and J. Parnas, eds. 2008. *Philosophical Issues in Psychiatry*. Baltimore: Johns Hopkins.
- , eds. 2012. *Philosophical Issues in Psychiatry II: Nosology*. Oxford: Oxford University Press.
- Kiple, K. F., ed. 1993. *The Cambridge World History of Human Disease*. Cambridge: Cambridge University Press.
- Kröber, H. L. 2014. “Unsound mind” as justification for the cancellation of fundamental civil rights. In *Gradualist Approaches to Mental Health and Disease*, eds. G. Keil, L. Keuck, and R. Hauswald. Oxford: Oxford University Press (in press).
- Lange, M. 2007. The end of diseases. *Philosophical Topics* 35:265–92.
- Longo, D., Fauci, A., Kasper, D., and Hauser, S., eds. 2012. *Harrison’s Principles of Internal Medicine*. 18th ed. New York: McGraw Hill.
- McHugh, P. R. and P. R. Slavney. 1998. *The Perspectives of Psychiatry*. 2nd ed. Baltimore: Johns Hopkins.

- Millon, T., R. F. Krueger, and E. Simonsen, eds. 2010. *Contemporary Directions in Psychopathology. Scientific Foundations of the DSM-V and ICD-11*. New York: Guilford.
- Müller-Eckhard, H. 1951. Die Krankheit, nicht krank sein zu können. *Psyche* 5:290–309.
- . 1955. *Die Krankheit, nicht krank sein zu können*. 2nd ed. Stuttgart, Germany: Klett.
- Nordenfelt, L. 2001. *Health, Science, and Ordinary Language*. Amsterdam, The Netherlands: Rodopi.
- Pickering, N. 2013. Extending disorder: Essentialism, family resemblance and secondary sense. *Medicine, Health Care and Philosophy* 16:185–95.
- Reznek, L. 1987. *The Nature of Disease*. London: Routledge.
- . 1995. Dis-ease about kinds: Reply to D'Amico. *Journal of Medicine and Philosophy* 20:571–84.
- Rietschel, M. 2014. Mental disorders are somatic disorders. A comment on Marco Stier and Thomas Schramme. *Frontiers in Psychology*. doi:10.3389/fpsyg.2014.00053
- Rothhaar, M., and A. Frewer, eds. 2012. *Das Gesunde, das Kranke und die Medizinethik. Moralische Implikationen des Krankheitsbegriffs*. Stuttgart, Germany: Steiner.
- Rothschuh, K. E. 1959. *Theorie des Organismus*. München, Germany: Urban & Schwarzenberg.
- , ed. 1975. *Was ist Krankheit?* Darmstadt, Germany: Wiss. Buchgesellschaft.
- Schaler, J. A., ed. 2004. *Szasz under Fire. The Psychiatric Abolitionist Faces His Critics*. Chicago: Open Court.
- Schramme, T., ed. 2012. *Krankheitstheorien*. Berlin, Germany: Suhrkamp.
- Schroeder, S. A. 2013. Rethinking health: Healthy or healthier than? *British Journal for the Philosophy of Science* 64:131–59.
- Simon, J. R. 2010. Advertisement for the ontology for medicine. *Theoretical Medicine and Bioethics* 31:333–46.
- . 2011. Medical ontology. In *Handbook of Philosophy of Science. Vol. 16: Philosophy of Medicine*, ed. F. Gifford, 65–114. Amsterdam, The Netherlands: Elsevier.
- Smith, B. 2012. Diseases, and other clinical natural kinds. Paper presented at the conference on “Gradualist approaches to health and disease,” Berlin, Germany, March 2012.
- Stoecker, R. 2009. Krankheit – ein gebrechlicher Begriff. In *Krankheitsdeutung in der postsäkularen Gesellschaft*, eds. G. Thomas and I. Karle, 36–46. Stuttgart, Germany: Kohlhammer.
- Sulmasy, D. 2005. Diseases and natural kinds. *Theoretical Medicine and Bioethics* 26:487–513.
- Szasz, T. S. 1960. The myth of mental illness. *American Psychologist* 15:113–18.
- . 1961. *The Myth of Mental Illness: Foundations of a Theory of Personal Conduct*. New York: Harper & Row.
- . 1972. Bad habits are not diseases: A refutation of the claim that alcoholism is a disease. *Lancet* 300:83–84.
- . 2003. *Pharmacracy*. Syracuse, NY: Syracuse University Press.
- . 2008. *Psychiatry: The Science of Lies*. Syracuse, NY: Syracuse University Press.
- Temkin, O. 1963. The scientific approach to disease: Specific entity and individual sickness. In *Scientific Change*, ed. A. C. Crombie, 629–47. New York/London: Heinemann (reprinted in Temkin 1977, 441–55).
- . 1973. Health and disease. In *Dictionary of the History of Ideas*, vol. 2, ed. P. P. Wiener, 395–407. New York: Scribner (reprinted in Temkin 1977, 419–40).
- . 1977. *The Double Face of Janus, and Other Essays in the History of Medicine*. Baltimore: Johns Hopkins.
- Walter, H. 2013. The third wave of biological psychiatry. *Frontiers in Psychology*. doi:10.3389/fpsyg.2013.00582