GENETIC CARRIER STATUS AND THE CONTEXTUAL REALITY OF GENETIC DISEASE: A CONTRIBUTION TO URAM GENOME STUDIES

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INTRODUCTION

Technological advances often press us to redefine action-mandating concepts and language through complex social, political, and economic processes that collectively determine what has been dubbed the 'technological imperative'. The reverse is also true: redefinition of concepts may also operate through complex social, political, and economic mechanisms in ways that shape and guide the direction of technology through shaping public beliefs and expectations.

1.1 *Redefinition of Death*

In recent years we have witnessed such collective revisions in our understanding of death. At present, a whole-brain criterion of death is prevalent. Its acceptance is related to the fact that advancing technology has made possible large-scale organ transplantation, and this criterion enables the harvesting of vital organs from donors better than other criteria. It remains to be seen whether a further revision, to a higher-brain death criterion, will be essayed under the pressure of an insufficient supply of organs, or whether future technological advances will provide sufficient alternatives through more efficient use of available human organs, use of xenografts, or manufacture of cloned organs to relieve the perceived scarcity.

The stunning advances in reproductive technology have caused us to reexamine our traditions and values regarding the sale of gametes, the use of 'rented' uteruses, and pre-conception adoptions of children gestated by 'surrogate' mothers. Intensive care technology allows us to maintain individuals suffering from multiple system failure through application of high-technology substitutions for failing organs, confronting us with questions of the value of life *per se,* where the quality of life has sunk arguably to a merely subsistence level. Our very language becomes scientized under the imperatives of technology, and families of gravely-ill loved ones are faced one day with a relative having tubes exiting every orifice, who is unresponsive to their calls and yet is still warm, and care givers urging hope, and the next day the same phenomenal appearance of a warm, unconscious loved one but with the diagnosis of 'brain dead' and the care givers reporting that all support systems will shortly be turned off. Thus, technology has conscripted our categories: 'alive' and 'dead', 'parent of' and 'child of' are no longer matters of judgment of ordinary folk, but are under the control of technicians and their instruments.

1.2 *The Technological Imperative*

I proceed in this paper from the fundamental assumption that there is a point in resisting surrender to all the tendencies urged on us by the imperatives of technology and scientization, a point that falls short of wholesale rejection of technology. How we should

proceed in controlling our responses to technological imperatives depends on the fundamental values we decide to serve and preserve, values which are constantly shaped and reshaped by the dynamic interaction of democratic deliberation and choices of individuals and groups. The role of the philosopher in this deliberative process consists in paying attention to concepts and definitions, involves reflection on ways in which language determines action, and has to do with assembling, in association with sociologists of knowledge and language, data that might serve as indicators of directions in the linguistic and conceptual revision which we have collectively undertaken.

Reflection on the natural history of language creates the possibility of a critical assessment and deliberate choice of the directions of conceptual change, providing a possible counter to the dehumanizing consequences of unchecked technological advance. For, how we use language determines, in a fundamental manner, our ways of valuing humans and envisioning them in the world. In other words, how we use language is constitutive of Ultimate Reality and Meaning.

The specific conceptual and linguistic question to be addressed below is whether heterozygous carriers of cystic fibrosis and other single locus disorders, or presymptomatic carriers of late-onset disorders such as Huntington's Disease, should count as 'diseased individuals'. (A 'heterozygous' individual has one rather than two copies of the gene of concern, thus can 'carry' the gene to the next generation without manifesting symptoms). As I will indicate below, there is an initial implausibility about calling someone diseased who has no occurrent symptoms. But, the presumed predictive power of genetic diagnosis, touted almost weekly by the public press as the genetic basis for various identifiable, human conditions, gives rise to the temptation to classify individuals who are carriers of such traits as diseased, as flawed individuals. It is this tendency that I want critically to evaluate in this paper.

My remarks here are an outgrowth of work done in several research groups at the Hastings Center of Society, Ethics and the Life Sciences, first in the late 1970s and more recently in the early-to-mid 1990s. My task was to assemble and evaluate competing characterizations of relevant terms, such as 'disease' and 'individual'. In this process, I first retreated to a description and evaluation of ways in which we classify entities and processes. Because the fundamental methodology of this paper rests on a choice between competing classification schemes, I begin by reviewing those options, and later defend that choice. Which option we choose makes a significant difference in the ultimate view we have of the human being.

2. CLASSIFICATORY SCHEMES

2. *Two Types of Taxonomy*

2.1.1 Essentialist Taxonomy

The essentialist, or natural-kinds scheme of taxonomy, holds that, in the order of the world, we can identify nested levels of entities. These entities are organized in ways that are explained by reference to their essential natures. As Aristotle explained in his *Metaphysics*: 'We have knowledge of any given thing when we know its essence ... The

individual and the essence, then, are one and the same thing, and it is not accidentally that they are so' (Bambrough, 1963, p. 88). Further, essential natures are to be understood in a reductionistic way in terms of component systems of entities and the laws which govern their operations. Each level of analysis proceeds through a recharacterization of the given level in terms of entities at a 'lower' level, together with their laws.

The goal of essentialist taxonomy development is to mirror in language the nested layers of natural kinds, so that our understanding of a natural kind, such as the human person, should seek to approximate nature with explanations of one level (the whole person) in terms of natural kinds at another level (organs and tissues and their processes). This level, in turn, yields to explanations at the cellular level, and so on through sublated levels of natural kinds (e.g., components of cells, especially chromosomes and genes; molecules, atoms, components of atoms, and so forth; Laszlo, 1978).

Essentialist taxonomy carries with it the baggage of reductionism. For example, the emergence of qualities not explicable by reductive analysis becomes progressively incomprehensible as the reducing level is progressively more fully specified. Further, it carries with it the assumptions of scientism: that the result of taxonomic analysis is objectively true, to be universally applied to all individuals within its intended domain, and, below the level of whole-person behavior, value-free (Schuster, 1992; Popper, 1979).

2.1.2 Pragmatic taxonomy

The second view of taxonomy construction is atheistic or, at least, agnostic about natural kinds. Following the felicitous characterizations of Lewis Carroll, it has been called the 'Humpty-Dumpty view of language': words mean what we want them to; what matters is to be their master. This is the pragmatic, post modern view of language: language and its meanings are human constructions, made for human purposes and to serve human values. There are more-or-less felicitous ways of constructing language according to the ways in which we think and speak about persons and their problems. An important question always to ask in considering a taxonomic shift is: 'What's to be gained, and lost, by that shift'?

2.2 *Relationship between the Two Taxonomies*

Both views would acknowledge that taxonomy has important consequences. The Natural Kinds view, however, sees capture of objective truth to be the driving value and objective; whereas, the Humpty-Dumpty view is pragmatic in thinking that taxonomy ought to be in the service of human interests, and may even doubt that the notion of objective truth, divorced from human interests and evaluations, is desirable or even possible. While I am sketching here a meta-sociology of language, what must be stressed is that, as language is used in ordinary speech and thought, not only are both types of taxonomy at work, but one or the other may dominate in a given institution, tradition, or theory.

Let me illustrate by tracing one way in which the evolution of the concept of 'genetic disease' interacts with a common view of the beginnings of a human life to produce a term heavily laden with the potential for stigmatization.

2.2.1 An Essentialist Conception of Genetic Disease

A movement down the natural kinds ladder, through levels of cause-and-effect explanation, is what we mean by 'reductionism'. To call a disease 'genetic' signals a reductionist slide to a level of nested natural kinds at which level many believe lies the individual human identity. The individual's genetic substrate or genome coincides, in other words, with his or her identity. The late bioethicist and theologian Paul Ramsey has written:

> Genetics teaches us that we were from the beginning what we essentially still are in every cell and in every generally human attribute and in every individual attribute (Ramsey, 1970).

Ramsey here articulates the view which many, whether religious or not, have accepted, namely that their individual identities are set by, and to be thought in terms of, their inherited characteristics, which genetic science equates with their genomes.

To speak of a 'genetic disease', then, is to speak of a defect in one's essence, in the fundamental substrate that connects one's body through time back with one's existence before birth, and not just from the point of conception. Graft Ramsey's articulation on to talk of genetic disease, and the slide from 'individual with a disease' through 'individual with a genetic disease' to 'individual with a diseased genome' to 'diseased individual' becomes powerfully persuasive. On this identification of the individual's identity with the individual's genome, we cannot sensibly speak of preventing or curing (in the sense of eliminating) a genetic disease (through gene replacement, genetic engineering, or provision of missing gene products), but only of preventing genetically diseased individuals through abortion, or selection of germ cells or of embryos, or of eliminating genetic disease from future generations through sterilization, artificial insemination, or artificial ovulation. For, individuals don't *have* genetic diseases like they have infectious diseases; at the level of essentialist analysis, they *are* genetically diseased, where that '*are*' expresses identity, not possession or predication.

2.2.2 A pragmatic conception of genetic disease

The Humpty-Dumpty, pragmatic approach to taxonomy, by contrast, encourages us to think first about the consequences for the interests of real, specific humans, situated in their social, ethnic, religious, and professional roles and institutions, and, second, of certain ways of speaking about their diseases. Third, it discourages the universal application of value-laden terms like 'disease' to individuals as having similar 'essential characteristics' because such terms, being value-laden, embody values which are functions of the life plans and preferences of people situated in their very different contexts and environments.

The pragmatic approach has a basis in social constructionist theory (Lewontin, 1984; Yoxen, 1984) and in phenomenological-hermeneutical philosophy. As Gadamer has argued, the scientific method will not deliver us from the personally and culturally shaped context in which our understanding of the world is located to some ultimately

value-free standpoint from which we can see 'things-in-themselves' (Gadamer, 1997, p. 447; Polkinghorne, 1983, p. 225).

Pragmatic taxonomies capture an underlying understanding of what we mean when we speak of 'the' cause of a disease or event. Clearly, in some cases, the designation of something as, for example, *the* cause of death, involves identifying one of a number of possible candidates, where that designation, in turn, reflects some particular interest.

Take, for example, the case of the suicide of an unmarried college student from a conservative family who, upon discovering that she was pregnant, was jilted by the father, then lectured scornfully by the physician who rebuffed her tentative queries about an abortion, was cut short by a roommate preoccupied with her exams, and who, finally, jumped off the Golden Gate bridge while motorists jeered at her:

> (a)ny of several of the conditions surrounding her could plausibly be pointed to as the cause . . ., in that we can point to a number of necessary conditions in the sequence of events that led up to her death . . . which, had they not happened . . ., would have rendered the set of prior conditions insufficient to bring about the effect; depending on where our interests lie, we will cite some one or more of these as [the] cause[s] of her death. The coroner may list drowning as the cause; a policeman may list the cause as suicide by jumping off the bridge; various sociologists and psychologists with varying research interests may point to the seduction and abandonment, the coldness of the physician, the alienation from the parents, the preoccupations of the roommate, or even the jeers and passivity of the drivers on the bridge as the event or events responsible for her death. The idea of cause as we most commonly employ it embodies the concept of human interest, in that it is in large part [our interests] that will determine which of several possible candidates for the cause of an event we will so identify (Hull, 1979, pp. 74–5).

As Michael Scriven put it in a seminal paper in 1962: 'A cause is a non-redundant member of a set of conditions jointly sufficient for the effect ..., the choice between the several candidates that usually meet this requirement being based on considerations of context' (Scriven, 1962, p. 15).

Freed from an essentialist notion of causation, the pragmatist determines causal language on the basis of its utility with respect to a set of values. And, if the pragmatist is humanistic and particularistic in those values (rather than, say, capitalistic and aiming at profit maximization), great care will go into deciding whether the balance of utility for the individual identified as having a genetic disease is greater than with some other etiological characterization.

3. GENETIC DISEASE

As a prelude to illustrating these points, let me review some of the facts about our two sample 'genetic diseases', Cystic Fibrosis, and Huntington's Chorea.

3.1 *Cystic Fibrosis*

Cystic Fibrosis (CF) is the most common of the fatal autosomal recessive diseases in

Caucasians. It is characterized by irreversible prenatal pancreatic damage with a resultant deficiency in pancreatic enzyme secretion in about 85% of CF patients, who suffer from a consequent malabsorption of protein. Heavy mucus secretion in respiratory tracts is associated with a proneness to respiratory infection. Typically excessive salt content of the sweat, while usually not of clinical significance, has provided the basis for standard diagnostic tests for many years. Up to 20% of affected newborns suffer bowel obstructions, with the liver frequently being affected in later life.

The World Health Organization issued a 'Report of a Joint WHO/ICF(M)A Task Force on Cystic Fibrosis' in Leningrad and Moscow on the 29th of November, 1990. In it, the facts of the genetic basis for this disease are identified.

> This disease is caused exclusively by mutation of a single gene, is inherited in autosomal recessive fashion, and is the most common such disorder in populations of Caucasian origin. Although very considerable progress has been made during the past 50 years in its clinical management, with a corresponding improvement in the mean life expectancy in developed countries from a few months to a few decades, it remains incurable. ... Consequently, attention has been given to the possibility of screening for carriers of the defective gene – who represent up to 5% in some populations – so that they may be given appropriate genetic counseling. ... Whereas it was previously possible to identify carriers only when they became parents of affected children, in recent years those carriers who were more distantly related to CF patients could often be identified by means of genetic linkage techniques (World Health Organization, 1990, p. 4).

Now, carriers distantly related to CF patients can be discovered by direct genetic testing of the single individual. Family linkage analysis is no longer necessary. Life expectancy has increased in persons living with CF from the few months or years of the early reports of the disease to two or three decades due to advances in clinical management, including the ability to detect individuals with it in utero or prior to full manifestation of symptoms. Ironically, as mean survival time has increased in this population, so has the incidence of diabetes mellitus.

A natural question to ask from an evolutionary perspective is, 'Why should such a dreadful disease occur, and persist at the levels it has in affected populations?'. The explanation of the occurrence and spread of such a disorder is, of course, speculative, but it will provide us with some additional, salient facts relevant to the question of our paper.

Darwinian evolutionary explanation holds that mutations arise spontaneously and are selected for or against in terms of their survival value. As with Heraclitus, the notion of 'change' is very essential to the Darwinian view of the world. Natural selection of mutations is determined by the environmental conditions in which individuals live; if these conditions change, selection may be modified, or even reversed. Survival value is thus contextual. That is, it is value for individuals possessing that mutation in a particular context. One would thus expect that a widespread trait, such as that for CF, would convey some significant benefit to account for its being selected. We know, for example, that the gene for sickle cell anemia confers, in a single occurrence of the gene, a

significant reduction in susceptibility to malaria (Angier, 1994). A similar resistance is conferred by G6PD deficiency, or Favism (Bodmer, 1976, pp. 260, 321). So, one might envision the gene for sickle cell anemia proliferating in a population in which malaria is endemic: the survival of carrier offspring due to malarial resistance selects for the gene despite the high fatality rate of the one child in four who inherits the double dose and is thus susceptible to severe sickle cell anemia.

Not surprisingly then, the single gene for CF conveys a high degree of tolerance to cholera, possibly by a partial phenotypic (displayed) expression in thickened secretions of the newborn, countering the diarrhea and consequent dehydration characteristic of the disease (Gabriel, New York Times, 1994).

3.2 *Huntington's Chorea, or Huntington's Disease*

Huntington's chorea is a lethal degenerative disease caused by a single gene. The name comes from the first person to identify it as a heritable syndrome, and from the Greek root for such words as 'choreography', meaning 'to dance'. Symptoms typically begin between ages 30 and 50. Minor motor discrepancies are progressively followed by increasingly severe loss of fine movement, then of major movement control until the sufferer becomes bedridden. In the later stages of the degeneration, emotional and cognitive functions become involved with characteristic shrieking, mirthless grinning and laughter; death occurs 10 to 20 years after the onset of symptoms.

While we might be tempted to speculate about the possibility of a positive effect of the gene for Huntington's Disease, at least one author reports that presymptomatic people carrying the lethal allele produce more offspring than unaffected individuals. So the gene confers a population benefit at the individual's expense, which is different from heterozygote carrier states of sickle cell disease and cystic fibrosis where carriers receive personal survival advantages as well as conveying population benefits (Fins, 1991). It should also be noted that Huntington's Disease is one of a class of conditions called 'trinucleotide repeats' that need not manifest themselves in their bearers unless the repeat length has reached a certain threshold size, which tends not to happen with the earlier generations having the mutation. Thus the genetic state need not be detrimental, and, in fact, need not manifest itself, though in many of the patients showing up at the doctor's door, because of affected relatives, there is a likelihood that if they do bear the Huntington's gene, the repeat size (which genetic testing can now measure) will have passed the critical threshold for Huntington's Chorea manifestation (Cummings, 1997, pp. 206, 277–79).

One final exploration of a concept, that of disease, is necessary before we begin to draw together the threads of our story to answer our question about the status of carriers and asymptomatic individuals.

4. THE CONCEPT OF DISEASE

In Hull (1978, 1979), I pointed out that the genesis, or root, of the concept 'disease' involves a dis-ease on the part of the patient. Subjectively this may be expressed in terms of abnormal and unwanted feelings, but not every disease manifests in occurrent

disvalued feelings; 'disease' may also be applied to abnormal states or functions of the body the results of which are disvalued by the patient. The irreducibly subjective and frequently teleological character of the concept may be illustrated by noting that we do not speak of infertility as a disease in celibates or those who have been voluntarily sterilized, but we define infertility in a couple wanting children in terms of their 'inability' to 'achieve' pregnancy during a year of unprotected intercourse. In the latter case, infertility is a dis-ease simply understood in terms of a lack of ease in intended procreation. Infertility in a couple not desiring to procreate, but interested in sexual relations, would not be the cause for complaint but for celebration.

4.1 *The First Shift: From Disease to Syndrome*

Partly under the influence of clinical medicine and its interests in classification and treatment, the concept of disease has undergone a causal shift. This shift has occurred in two steps: first, through the redefinition of 'disease' in terms of 'syndrome', that is, a set of associated symptoms and signs, with the association to be understood both through frequent joint occurrence, and through the hypothesis of a common cause for such concurrent symptoms and signs.

It is interesting to note how we proceed from a more or less purely phenomenalistic sense of 'symptom', as in 'Doctor, I don't feel well'. 'What are your symptoms'? to a progressively abstracted sense of the term, by which we speak, for example, of elevated temperature as 'a symptom of suspected infection'. Clearly, the possibility of infection is being posited as causally related to the symptom, reflecting our knowledge that fevers have many causes.

4.2 *The Second Shift: From Syndrome to Cause*

The second step occurs when the term 'disease' is shifted from the syndrome to an actual causal mechanism. Medicine distinguishes between 'merely' treating the symptoms, and avoiding or curing the disease by preventing or removing the underlying cause of the syndrome (Scadding, 1996, p. 594). And, now that we are able to identify the presence of the gene for Huntington's chorea before the onset of the syndrome, we come to speak of its carriers as diseased long before they manifest symptoms.

The hypothesizing of a genetic cause on grounds of pedigree may not be sufficient for this shift: Bodmer and Cavalli-Sforza wrote in 1976 that

> Huntington's chorea is a severe and rare disease with a late age of onset ... In many of the pedigrees in which a patient with this disease is found, one of the parents of the patient has the same disease. In others, a parent died well before the usual age of onset and so *might have had the disease, had he or she lived long enough* (Bodmer and Cavalli-Svorza, 1976, p. 72 – emphasis mine).

Here, a distinction between having the disease and the onset of its symptoms seems struggling to emerge, but has not yet done so.

However, now that it is possible to confirm reliably that one will have the symptoms in one's future, we have already come to speak of the possibility of diagnosing the

(presence of the) disease prior to the onset of its symptoms, signaling that 'disease' is now being applied to the genetic substrate of the disease and not to the onset of the syndrome.

5. SHOULD ASYMPTOMATIC CARRIERS OF THE GENE FOR HUNTINGTON'S DISEASE, OR HETEROZYGOUS CARRIERS OF THE CYSTIC FIBROSIS GENE, BE SAID TO BE DISEASED?

The question of whether individuals who currently lack symptoms associated with a disease are dis-eased would normally be regarded as involving a conceptual confusion but for the predictive power of the diagnosis. For, if to be diseased fundamentally involves 'dis-ease', and an individual lacks a normally necessary condition for the presence of a disease, such as abnormal or distressing symptoms involving either an increase in discomfort or a loss in a desired functional capacity, it is nonsense to speak of such an individual as diseased.

However, if one can now know, on the basis of factors already present, that one's future predictably contains such severe complaints that their occurrence is 'only a matter of time', or that one's children will, with a certain degree of likelihood, suffer severe medical problems as a result of one's genetic transmission, the question of whether one is diseased arises meaningfully. For, to be diagnosed as diseased in some way evokes dramatic changes in one's socialization and life goals that fall in a radical way outside of the normal patterns of healthy life.

Worst-case scenarios galvanize us into action when they become more than merely logical possibilities. The diagnosis of an active disease prompts actions to curb the spread of the disease if infectious to minimize or avoid its symptoms, and, where possible, to eliminate its causes. It provides a powerful excuse from the responsibilities normally associated with health in a social setting. And it imposes special burdens of care and accommodation on family, friends, employers, and the insurers of the bearer of the diagnosis. Since diagnosis of carrier status of an asymptomatic individual predicts a probable future in which similar personal and social disruption will take place in a manner relatively free of further contingencies, the appellation of 'diseased' to such individuals involves a powerful and tempting extension of the concept.

It is important to note, however, the contextual character of the predictive import of a diagnosis of carrier status. For a confirmed celibate, being a heterozygous carrier of the cystic fibrosis gene has no negative predictive value, in that there will be (absent, for example, offspring resulting from a rape or from one's role as a gamete donor or from the change in the fundamental option in favour of celibacy) no individual created at risk for transmission of the disease. Similarly, for a carrier of CF married to a non-carrier, there is (all else being equal) no negative predictive value associated with the status of carrier. And, for a carrier married to a carrier where one or both are sterile by choice or naturally sterile and comfortable with the fact, there is no negative predictive value associated with carrier status. In fact, one can imagine contexts (e.g., the prospect of becoming a missionary or health worker in a region with endemic cholera) in which there is a positive, personal, predictive value associated with the status of carrier, as

well as reproductive value for the prospects of one's offspring surviving to adulthood. In all such cases, and others as well, it would be not only pointless but conceptually confused to call such individuals 'diseased' solely on the grounds of their carrier status. For, given certain simplifying assumptions I have made about expression of the afflicting recessive gene in the heterozygous or carrier state, there is no lack of ease, no 'dis-ease' which any of our cases will ever experience that would ground the root meaning of the concept.

By contrast, a couple intending and able to have their own biological children and who are both heterozygous carriers of the gene for cystic fibrosis are, on my analysis, reproductively diseased: their reproduction will not be easy. On average, without special measures, 25% of their children will be affected by a disease which their parents have given them. Even so, the enormous variation in phenotypic expression of the CF gene does not predict impaired pulmonary function for every child having two alleles, allowing for substantial phenotypic variability as a result of environmental and unrelated genetic factors (Hamosh, 1993; Castaldo, 1996, p. 73). It is true, however, that their lives will be negatively affected for a substantial period of years, and that the future of other members of their family, their friends, their employers, and their insurers will be affected by the combination of their carrier status and their reproductive objectives. It would be appropriate for them to consider extraordinary measures: the possibility of using donor gametes; the possibility of employing reproductive technologies to preselect against afflicted children through fertilization of carrier ova with carrier sperm, or against implantation of embryos with both alleles. If their carrier status is known in advance of marriage, it might be appropriate for them to seek other mates, individuals with whom neither will have such reproductive disease.

Contexts in which being an asymptomatic 'carrier' of the Huntington's chorea gene would have no negative predictive consequences are difficult, but not impossible, to imagine. Carriers with between 30–35 triplet repeats, according to surveys and published studies, will not manifest Huntington's Disease, but individuals with greater repeat lengths will be at risk (HDSA, 1997, p. 7). The latter represent the major proportion of persons assessed to have the Huntington's gene. Having no interest in children or ability to have children would relieve such a carrier of a substantial portion of the negatively valued, predictable consequences of that status. One who knows he or she will die before the earliest point of onset of the symptoms (a convict on death row, or one who has made commitment to a suicidal mission) lacks any negative personal consequences of that status. Indeed, possession of the status of asymptomatic carrier for Huntington's chorea might prompt one to undertake meaningful risks normally avoided by an individual with the prospect of a long and healthy life.

On the other hand, most carriers of the gene for Huntington's chorea do face, and if they know of their status, contemplate, very negative predictable futures. Reason would seem to dictate that, for them, certain activities (e.g., undertaking the long preparation for a career such as neurosurgery) ought to be avoided. In these individuals, the status of one who has a disease might well galvanize appropriate responses to a future that is far more determinate than that of most.

6. CONCLUSION: THE VIRTUE OF PRAGMATIC CLASSIFICATORY SCHEMES

There seems to be strong reason from the discussion above to prefer the contextually sensitive pragmatic scheme of classification to the essentialist approach. Pragmatic approaches generally render classifications of individuals as diseased or not diseased in terms of the benefits of such classifications. Because human contexts, goals, and situations vary so much, it seems pointless to burden all with a common genomic pattern with a classification based on that pattern. One is diseased or not depending on the intersection of purposes and possibilities, and a one-sided scheme that looks at only one dimension of the person is bound to miss this richness.

By contrast, essentialist thinking locates genetic disease's cause in the genetic substrate – the individual's genome. If one individual is genetically diseased by virtue of possession of a certain allele or pair of alleles, then that individual is essentially flawed, as are all individuals with those alleles. The matter of variance in phenotypic expression may be finessed as due to accidental factors, but the essence of the individual – the genome – is what bears the essential flaw. Genetically diseased individuals are thus essentially flawed individuals. So, the imperfections of carriers of the CF gene are only a matter of degree, for carriers bear flawed genes, and, as with other similarly flawed individuals, are at risk of creating children with terrible handicaps. Individuals bearing the gene for Huntington's chorea are diseased from conception, for it is just a matter of time until their inherent flaws will be expressed, barring accidents.

I believe I started personally to reconsider my own essentialist thinking when I learned that estimates are that we each, on average, carry seven lethal recessive genes. By essentialist taxonomy, we are all flawed, all diseased. The term, under such conditions of application, loses its power to discriminate between those who deserve special consideration and those who do not. Essentialism, at least in this context, is a self-defeating taxonomy, in that taxonomies are intended to support judgments whereby individuals may be treated appropriately in light of their differences. Pragmatism, on the other hand, not only offers relief from the constricting categories of essentialism, but it also stimulates our interest in controlling our concepts and their linguistic vehicles.

Aristotle had a sense of this when he distinguished between the substance of a thing, or what the entity is, and terms he called 'accidental attributes' which are asserted of a subject and indeed can apply to many different subjects. In his *Metaphysics,* which I cited earlier, Aristotle insisted on considering a 'well person' as both 'a man' and 'a healthy man', the reason being that the man's *healthiness* arises out of its opposite, *illness*, which are both accidental attributes of the man (Bambrough, pp. 91, 188–89). The realm of exploration of what man is beckons for a comprehensive answer, and in this paper we have looked at various candidates such as genes and the environment, both physical and social. In so doing, we hope to have spread some of the wisdom realized by Aristotle. The concept of what we ultimately are, genes being part of us, is not the same as words like 'disease' we use to describe what we are. Such designations can change, depending on the context, which is inseparably bound up in the same reality of which our genes are a part.

Humpty-Dumpty was right: Words should mean what we want them to; It is just a matter of who is to be master.

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