The context and content of the human genome project and the American eugenics movement: An analytical, case study approach

by

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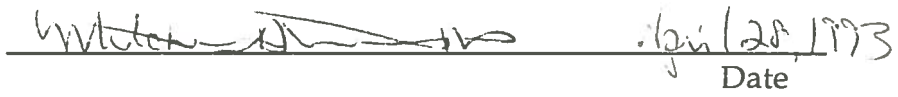

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This thesis is dedicated to the women in my family, without whom I would not be in a position to produce it, and who continually encourage me to look forward and not back.

To Rosie, a tower of strength and enduring source of inspiration.
To Mom, who proves every day that life is a kinetic process.
To Jessie, my best friend and confidante.
To Louisa, who teaches me more about myself than she'll ever know.

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Chapter One:

Introduction

Throughout history humankind has struggled to understand itself, its inner and outer worlds. Introspection takes many forms and occupies many media. Perhaps no form of introspection so compels and so eludes us as that which is concerned with our own existence, our own place in the world, that which defines our humanness and yet our own individuality. Theology, philosophy, anthropology, biology, psychology, and many other fields devote themselves to such study, but self-examination pre-dates the academic center. One common form of introspection involves our heredity, our posterity.

That like breeds like has been observed throughout the ages, and used for human benefit. Daedulus was perhaps the first geneticist. When he crossed a bull with a human he created the terrifying minotaur, a creature with the cunning of a man and the ferocity of a beast. In the Old Testament, Jacob manipulated his herds, and reaped the benefits of darkly colored sheep. Neither of these men understood the nature of the hereditary substance, yet each used it to his advantage.

Conceptions of the exact nature of the hereditary substance vary throughout history. The early Greeks believed in the inheritance of acquired characteristics. This concept gave way to the theory of pangenesis in the fifth century, B.C.E., a theory which postulated that semen forms throughout the body of both males and females, and travels to the testes of the male for storage.[1] Theories of vitalism also endured for many years. These concepts suggested that an inner force was responsible for the transmission of life from one generation to the next; this force was transmitted in the semen.

The invention of the compound microscope marked a new era in theories of heredity. Viewers saw microscopic humans--*homunculi*--in their fields of view, and hypothesized these represented pre-formed humans

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[1]Pollock, MR.

waiting to develop. Higher-resolution microscopes allowed those in the eighteenth century to see that human components were not pre-formed, but in fact developed from the substance of the egg.[2] Further delineation of the hereditary substance continued for hundreds of years until, in the middle of this century, scientists proved the hereditary material to be a molecule called deoxyribonucleic acid (DNA), found in the nuclei of cells.

The discovery of DNA laid many age-old controversies to rest, but generated as many new ones as it resolved. It is a misconception to assume, however, that controversy over research in the area of genetics only began with the discovery of DNA as the hereditary substance, or even with Mendel's discovery of the laws of inheritance. In fact, such controversy has existed throughout the ages. In this century, we witnessed two major episodes of controversy over genetics, first during the eugenics movement from the turn of the century through the 1930s, and second, today with the human genome project.

Our current controversies over genetics take aim at the human genome project, an American and multi-national initiative to map and sequence the entire human genome, or all the DNA in a human cell. In the United States, the National Institutes of Health (NIH) and the Department of Energy (DOE) jointly fund the project to the tune of $200 million per year for all fifteen years of the project. Now in its third year of funding, the project hopes to systematically discover all disease genes in the human genome, their nucleic acid sequences, and the function of their protein product. Those involved in researching the genome predict the application of such knowledge would be revolutionary in medicine. Others decry the project as a reenactment of our mistakes with eugenics earlier in the century.

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[2]Wagner, RP, pages 3-4.

Eugenics is a word coined in 1895 by the Englishman Francis Galton, a cousin of Charles Darwin. He defined the word, which literally means *to be well-born*, to encompass all social functions which humans could bring under their control in an effort to guide the advancement of the human race to new heights and achievements. The eugenics movement began in England, but quickly spread to the continent and to the United States where it enjoyed popular support for many years. Eugenicists, or supporters of the theory of eugenics, who came from all walks of life, wished to draw social behaviors such as marriage and mating under their control, fearing that if such activities were not controlled, the human race would deteriorate. They were particularly concerned with the apparent increase in the numbers of mentally and physically unfit, and the rate at which they claimed these groups reproduced. Eugenicists were equally concerned with the eugenically fit who were thought to be abandoning their responsibility to society by not having enough children.

The eugenics movement receives short shrift in the popular literature of today which often paints a picture of a movement full of racists and fringe elements. In reality, the eugenics movement was a complicated and complex social movement which was a product of its times. By the 1930s, however, the times had changed, the science had changed, and eugenics failed to keep pace. The 1930s also saw the culmination of Germany's eugenics movement, the mass killings of the "unfit." The 1930s thus saw a precipitous decline in the popularity of eugenic theory and practice.

Eugenic theory and methods find increasing press again today, popping up commonly in discussions of the human genome project. Those who oppose the project often invoke the eugenics movement, linking the two in infamy. Those who support the project dismiss such claims as readily as

those who oppose it put the allegations out. It is true that certain similarities exist between the two efforts. What would a closer examination reveal, however? Does the eugenics movement deserve the treatment it gets in today's literature? Does the genome project reflect a similar mindset to that of the eugenics movement? These questions are important in both a contemporary and an historical perspective.

One subgroup of the genome project, the working group on the Ethical, Legal, and Social Implications (ELSI) of the HGP, solicits grants exploring the connection of the eugenics movement and eugenic theories to the genome project. They state that investigating the "uses and misuses of genetics in the past and the relevance to the current situation," including "the eugenics movement in the U.S. and abroad,"[3] is "of particular importance."[4]

Many people have explored such a relationship between the genome project and the eugenics movement. Daniel Kevles is an historian of eugenics, and his book *In the Name of Eugenics*, published in 1985, is the standard by which other works on eugenics are judged. Kevles' published his book before the genome project was born; nonetheless, he deals with the relevance of advances in molecular biology to the eugenics movement. He often refers to the "songs of deicide" sung by geneticists and eugenicists as they proselytize for their secular faith (that of eugenics and genetics), but Kevles suggests that "the melodies of deicide have not enabled contemporary men and women to remake their imperfect selves. Rather, they have piped them to a more difficult task: that of establishing an ethics of use for their swiftly accumulating genetic knowledge and biotechnical power."[5] Kevles

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[3]U.S. Congress. House, 1988, page 69.
[4]*Ibid*, page 67
[5]Kevles, DJ, 1985, page 301.

concludes that it is in the area of ethics that we learn the most powerful lessons from eugenics.

Later works and authors deal more directly with the issue of the eugenic implications of the genome project. George Annas, Director of the Law, Medicine and Ethics Program of the Boston University Schools of Medicine and Public Health, clearly expressed his concern for the genome project in his *Reproductive Genetics and the Law*, urging that the public and scientific community "resist...a eugenic agenda."[6] Annas[7], along with several other authors, also discussed the eugenic implications of the genome project at the meeting of the New York Academy of Medicine. These discussants included Dorothy Nelkin, who warns that the genome project, though ostensibly allowing individuals an expanded freedom of choice, actually is as socially coercive and restrictive as the eugenics movement was.[8] Garver and Garver, two geneticists, strongly warn against the increasing eugenic power associated with increased ability to specifically test for genetic disease.[9] Troy Duster, sociologist at the University of California at Berkeley, suggests in his book *Backdoor to Eugenics* that the project opens the door once again to a strictly biological view of human variation and behavior, that it represents a misplaced emphasis on genetic rather than environmental influences just as the eugenics movement had.[10] Those involved in the genome project also speak to the issue of eugenics. James Watson, head of the National Center for Human Genome Research at the National Institutes of Health, dismisses any similarity between the genome project and the eugenics movement.[11]

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[6]Annas, G and Elias, S, 1987
[7]Annas, G, 1992.
[8]Nelkin, D, 1992.
[9]Garver and Garver.
[10]Duster, T.
[11] Watson, JD, 1992, page 323.

However, with a few notable exceptions, works and comments comparing eugenics to the genome project are flawed in several ways. First, most works simplify one or the other effort to such an extent that their conclusions have no integrity. Garver and Garver seem to miss the point of the genome project. Watson underestimates the depth and breadth of the eugenics movement, referring to it as an effort to sterilize prostitutes in the 1920s and 1930s.[12] Such dismissive efforts do not contribute to an educated discussion of how the two are similar, how they are different, and what we can learn from eugenics that will help inform contemporary conflicts with the genome project. Second, most use such general language and ask such general questions of the two movements that at times the studies seem to compare apples to oranges, or end up writing only in generalizations.

This paper is an effort to look more closely at the relationship between the genome project and the eugenics movement. It will attempt to do so by using a different approach than that used by other investigators. First, it will use a case study approach, focusing in on one disease. By picking one disease, the paper is able to ask very specific questions of the eugenics movement and the genome project, making sure to compare oranges to oranges. In addition, the case study approach provides a narrowness of focus which seems to be missing from many other investigations. The last advantage to a case-study approach is that it brings the implications of both efforts down to a personal level; instead of having to speak in generalities, a case study allows for discussion of very specific and real issues--which will affect very real people--in a more concrete way.

The disease on which the paper will focus its investigation of the genome project and the eugenics movement is schizophrenia. Schizophrenia

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[12]Ibid. Page 323. *Los Alamos Science*

is a mental disorder which often comes on in adolescence or young adulthood and is characterized by a recurring and remitting psychosis with intervening periods of chronic symptoms and lower than average social functioning. There is no inherent intellectual deficiency incumbent with the disease, though cognitive impairment often follows the ravages of the symptoms. Schizophrenia is characterized by a higher than average incidence among first degree relatives of people with the disease, but no clear or consistent pattern of inheritance is present. Schizophrenia is commonly referred to as a "multi-genic" disease, meaning it likely has more than one gene associated with it, and more than just genes associated with it as well.

I chose schizophrenia as the case study for a variety of reasons. First, the genome project hopes to improve particularly the outcome of those with multi-genic disorders, including heart disease and schizophrenia,[13] so it is a disease which the HGP has specifically named as one they hope to learn more about. Second, like all mental diseases, schizophrenia stigmatizes those who come near it: affected people and their family members. As such, the social attitudes toward people with schizophrenia play an important role in the way in which people with the disease are allowed to function in our society, and what roles they are allowed to play. The disease is vulnerable particularly to the social constructs around it, and since the genome project and the eugenics movement raise controversy primarily (though by no means exclusively) because of their social implications, it seems important to focus on a disease which sways with the social tide. Third, schizophrenia is a disease which to this point has eluded researchers' attempts to define and detail its dysfunction. Thus, the genome project may make great strides in the basic understanding of the disease itself, its etiology and pathology, not just its

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[13]National Research Council, pages 27 and 45.

inheritance. Fourth, it represents a particularly tricky disease for genome project researchers and eugenicists alike because of its seeming multiple causes and modifiers, as compared to a straight genetic disease. Thus, schizophrenia represents one of the most difficult diseases which the genome project and the eugenics movement address, and learning something about schizophrenia under these two efforts will have broader applications than a more cut-and-dried disease.

The paper will examine the relationship of the eugenics movement to the genome project, using schizophrenia as a case study, utilizing a varied approach. Chapter Two uses a strict historical method, relying almost exclusively on primary sources from the 1920s and 1930s. In this chapter, the paper explores the social, scientific, and professional forces which combined to give eugenics the prominence it enjoyed during the 1920s and the infamy it gained during the 1930s. The chapter represents a thorough-going investigation of what the eugenics movement really involved, and what controversies surrounded it during its own era.

The case study approach is maintained during the historical chapter, though for a variety of reasons, its integrity may be breached at times. First, during the 1930s and particularly the 1920s, confusion about the disease remained prominent, and the ability to distinguish it from other psychoses was minimal. Second, eugenicists, as will be explored thoroughly in that chapter, refused to accept that schizophrenia was distinct from any other mental disorder, including pauperism and epilepsy. All these diseases were felt to be on a continuum with each other, grouped as the mentally "unfit." Thus, eugenic discourse of the times often refers only to mental disease or deterioration, not specifically to schizophrenia, or dementia praecox, as it was still often called during that time.

I hope that Chapter Two will present the reader with a cogent picture of the eugenics movement and its multiple complexities, in contradistinction to the more simplistic pictures painted by both the detractors and supporters of the genome project.

Chapter Three explores the eugenic roots of the field of human genetics, and provides a brief historical sketch of the field of genetics after the Second World War. Out of these advances in understanding of genetics that the genome project became a feasible reality. I explore the technical and structural aspects of the genome project are explored in the chapter.

Chapter Four can be seen as parallel to Chapter Two, but in a contemporary time frame. The recent nature of the project precludes any historical perspective on the project, and as a product of its own times, the chapter is likely filled with cultural biases. Nonetheless, the Chapter explores, as in Chapter Two, the social, scientific, and professional context in which the genome project functions. Contemporary controversies in schizophrenia research are explored as they relate to the project, and the social context of the person with schizophrenia is once again investigated. Some of the ethical issues which the project brings out are discussed as they relate to schizophrenia. A variety of opinions and points of view are expressed in the chapter, again in an effort to highlight the complexity of the project and redress any prior efforts at oversimplification which may exist in the literature.

The final chapter, Chapter Five, includes a discussion and some conclusions. The Chapter explores the appropriateness of the comparison between the genome project and the eugenics movement, and what relationship they might more accurately have. In addition, the chapter addresses the question of why people are drawn to make such comparisons,

drawn to invoke eugenics in discussions of the genome project. Finally, some suggestions are made as to what the eugenics movement can teach us about the genome project and its applications, and what both efforts teach us about ourselves.

I hope that through the paper, the reader will gain insight into the historical context of our current concerns over the genome project, and that through such insight, we may be able to achieve the most difficult of all types of introspection: that of looking at our own fears and our own mortality and imperfection.

Chapter Two:

The American eugenics movement and schizophrenia between the wars

> The fifth patient, a teacher, twenty-four years of age (Frieda G.), was somewhat depressed by her work, felt herself a failure, tried to commit suicide. When restrained by police and given a sedative by her physician she thought that her sisters had wanted to compromise her sexually with the police, that the physician had given her poison to kill her, that everybody was against her. She passed through various phases of distressed over-activity and of silent under-activity. In the hospital she talked of vague sinister happenings, appeared suspicious of poison, talked in a religious strain. When transferred to a state hospital she was mute, untidy, grimaced, gesticulated, and for some time she was dirty, unresponsive and vacant in appearance. One month after this she began to improve rapidly, and two months later she was able to go home, but made a poor adjustment and was readmitted to the hospital; there she was very difficult to manage and would attack the nurses. After a few months the patient seemed to make a good recovery, left the hospital again, and within the year she married.[14]

Frieda had schizophrenia, a disease characterized by a relentless and progressive psychosis, often beginning in the teen-age years or young adulthood. Fearing that Frieda would pass her "defect" on to her children, in the 1920s and 1930s the organized eugenics movement in the United States targeted Frieda and others like her in their negative eugenics campaigns. They sought to segregate her from the rest of society or sterilize her; they effected legislation which kept groups of people suspected of having a high rate of schizophrenia from immigrating to the U.S. In the 1920s, the medical and scientific communities, as well as the public, largely embraced these eugenic efforts, and the genetic theory of causation of schizophrenia which was the basis for the theories. The acceptance that eugenic ideology received in the 1920s reflected the times. Scientific management of industry, society, and evolution reigned supreme in the 1920s. Psychiatry searched for legitimacy within medicine and embraced the medical model of mental

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[14]Campbell, pages 78-9.

illness. American society bristled with possibilities after asserting itself in the Great War. All these contributed to the popularity of eugenics in the 1920s. The stock market crash in 1929 marked a shift, and the 1930s saw a marked decline in the popularity of organized eugenics and eugenic measures, again reflecting the changing times. The New Deal era displayed, more so at least, an ethic of inclusion and tolerance; scientists and doctors, like people in general, shifted their view of the genetic theory of schizophrenia to a wait-and-see attitude. Popular concerns shifted from domestic improvement to economic necessities and international politics. A closer examination of 1920s and 1930s America will reveal the way eugenics rose and fell in the U.S., and will illuminate our current struggles with genetic improvement of the human race via the human genome project.

1920s: Rise of American eugenics

American society blossomed after the Great War, and as eyes turned to domestic concerns, eugenic ideology found welcome support. The U.S. impressed the world as a dominant force during the war, and back home urbanization increased. The lower classes filled the factories doing repetitious work for long hours, while the upper classes smiled at their good fortunes. A burgeoning new middle class managed the workers. Everyone knew his place, as social classes resembled castes. Volunteerism surged, and social welfare agencies, funded by the wealthy philanthropists, tended to the sick and needy; child labor laws protected the young from exploitation. America thrived during the time after the war.

As much as American society boomed after the war, eugenicists prophesied a downhill course without their sterilization, segregation, and immigration measures aimed at the mentally "defective." "Incapacity of

mind will not merely prevent advance, (it) will inevitably lead to retrogression" of society, said prominent eugenicist A.F. Tredgold in 1927.[15] Eugenicists saw only one route to solving the problem, "and that is by the biological road, by the way of eugenics."[16] Eugenists suggested that their road led to a veritable utopia. "Around the year 1975, barring wholly unpredictable catastrophes such as a universal epidemic of black influenza that may shatter civilization, the United States will come more nearly to the ideal aristocracy of talent which Plato dreamed than any previous civilization has," said Chase.[17] To eugenists, the choice between degeneracy and Platonic utopia was clear; society could achieve utopia only by managing and controlling its output of people.

Eugenic measures were in fact Tayloristic attempts to manage society in the present and the future in the same way that scientific management of industry dominated the 1920s workplace. Efficiency stood out as the goal of industry during the 1920s. Taylorism made its way into all social niches, and, according to eugenicists, people with schizophrenia hardly contributed to the efficiency of the State. In a time when "efficiency and standardization are our slogans,"[18] people with schizophrenia were inefficient and deviant. Eugenists declared the need to take evolution into their own hands and direct it in the best and most productive way. Dean Inge underscored the relation between scientific management of people and evolution and national success when he said, "We in the twentieth century feel more strongly than our grandfathers did in the nineteenth that the test of a nation's welfare and value in civilization is not the extent of its territory or the volume of its trade, but the

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[15]Tredgold, 1927, page 2.
[16]Bond, page 183.
[17]Chase.
[18]Diller, page 495.

kind of men and women it produces."[19] Eugenicists did not want the U.S. to produce people with schizophrenia. Eugenicists felt that America had to guide its own population destiny if it was to maintain its standing in the world, and part of guiding its own destiny meant breeding out people with mental diseases. The 1920s saw an acceptance of these eugenic ideas; they fit the 1920s ethic.

In the mid-1920s, eugenicists and psychiatrists defined mental diseases differently, each group's characterization reflecting its own goals and viewpoint. Historian of science and eugenics, Daniel Kevles, highlights the discrepant views of eugenicist Charles Davenport (director of the Eugenics Record Office, the research arm of the American Eugenics Society, from 1910-1934[20]) and prominent psychiatrist Smith Ely Jelliffe. Eugenicist Davenport maintained a *lumping* position. The lumpers felt that all mental derangements were on a continuum with one another. Eugenicists, as lumpers, did not differentiate between any sub-types of mental defect. Schizophrenia, manic depressive psychosis, criminality, pauperism, epilepsy, and feeble-mindedness were just different manifestations of the same defect: bad heredity. Speaking to that position, A.F. Tredgold, a very prominent member of the American Eugenics Society, typifies the eugenic position on mental disorders as being "but different manifestations of one and the same underlying cause," namely, "devitalization of the germ cell."[21] The lumping model fits with Davenport and Tredgold's viewpoint and goals. They were interested in eradicating mentally unfit people all along the continuum; which particular condition any one person had did not matter from the

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[19]Inge, D.
[20]Mehler, page 329.
[21]Tredgold, pages 2-3,5.

eugenic point of view because Davenport and Tredgold (and others) considered all of the defects to be "unfit" and worth eradicating.

In contrast to the eugenic viewpoint, splitting more accurately describes the psychiatric viewpoint which was aimed at the individual, and most psychiatrists were splitters. Psychiatry as a professional body was not interested in vague groups of "mentally fit;" it was concerned with individuals with disease, and as such, the specific condition that any one person had was important. To Jelliffe and other psychiatrists, the distinctions between the various conditions constituted the substance of the research in their field. Psychiatry was in its descriptive phase during the 20s, and its conceptions of mental problems reflected that professional phase in which psychiatrists attempted to describe mental diseases in the same way that other doctors described medical conditions. Dr. Eugen Bleuler, a very prominent Swiss psychiatrist, originally defined schizophrenia in the teens. He took apart the older disease category dementia praecox, ascribing various traits to the schizophrenic psychoses. This restructuring reflected a renewed interest in distinguishing the various mental diseases just as other doctors had done for physical medicine. The splitting model was mired in the medical model of mental disease. Psychiatrists in the 1920s asserted that the diseases with which they were concerned were as discrete as any physical disease, and psychiatry was as important and valid as any other medical specialty.

Although Bleuler published volumes of detailed descriptions of schizophrenia, and the medical community accepted it as a disease entity unto itself, they knew very little of the *biology* of schizophrenia in the 1920s. The Association for Research in Nervous and Mental Diseases devoted its entire 1925 meetings to current research on schizophrenia. Scientists presenting a wide variety of papers in an attempt to expand the

understanding of schizophrenia as a medical disease. Dr. Theophile Raphael, for instance, presented the results of his investigation into body type in schizophrenia. During the 1920s many doctors thought that body type was a "constitutional" given, just as some diseases were "constitutional" (for instance tuberculosis). Raphael concluded that the most common body-type people with schizophrenia displayed was the "linear cast of habitus, with a relatively small narrow face and head and a long, narrow, shallow and less capacious type of trunk."[22] Dr. Marjorie Fulstow presented her investigation into the weight of the heart of schizophrenics as compared to "normals," again, a form of basic anatomical research which doctors had performed on people with physical diseases for decades. She found that the hearts of men with schizophrenia weighed on average 331 grams, and women's averaged 287 grams; this did not represent any deviance from the average weight of the heart in the population at large.[23] Other scientists presented the results of their investigations into toxic[24], metabolic[25], endocrine[26], or infectious[27] abnormalities in schizophrenia, all with the purpose of placing schizophrenia firmly within the pale of medical science. Dr. Charles Dunlap presented the results of his researches into the pathology of schizophrenia, that is, the microscopic basis of the disease. Dunlap commented early in his paper that finding such pathology would confirm the *medical* nature of schizophrenia, that "the mind is sick, and the brain diseased."[28] Dunlap reports, however, that no specific pathology was present, that when comparing brain specimens from people with schizophrenia and healthy people, there were no

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[22]Raphael. p.115.
[23] Fulstow, M.
[24]Gregory, page 177.
[25]Bowman, page 262.
[26]Bowman, page 262; Lewin, page 390.
[27]Meninger, K, page 182.
[28]Dunlap, C, page 371.

discernible differences. Researchers at the conference attempted to ascribe specific biological attributes to schizophrenia, as Bleuler had done for psychological attributes, but their results were often equivocal or even contradictory. While conference attendees had hoped that the conference would allow "noteworthy addition(s) to our knowledge of the difficult subject of schizophrenia,"[29] Dunlap spoke for others when he said that many of the results "obscured what was already obscure enough."[30]

Investigations into the hereditary nature of schizophrenia in the 1920s were as equally equivocal and contradictory as the biological investigations, and it was upon these investigations that eugenics based its claims. Many studies suggested, and most eugenicists assumed, an hereditary etiology for schizophrenia. The hereditary studies fell into three categories: twin studies, adoption studies, and pedigree analyses. In twin studies, researchers (who included both eugenicists and non-eugenicists) identified one twin with the condition under study, in this case schizophrenia. They would then examine the other twin to determine whether he or she was also schizophrenic. The per cent of twins, overall, who agreed in the presence of a trait is called the *concordance rate.* Concordance rate estimates the degree to which heredity determined schizophrenia. Researchers acknowledged that one problem with their twin studies in the 1920s was that there was no sure way of distinguishing identical from fraternal twins.[31] Identical twins have identical genetic endowment, while fraternal twins are no more closely related than other siblings. If schizophrenia was strictly genetic, the concordance rate of identical twins should be 100 per cent; that for fraternal twins would be lower since their heredity is not identical. Adoption studies attempted to discern

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[29]Kirby, GH, page xix.
[30]Dunlap. page 376.
[31]See, for instance, Parker.

the effects of heredity as compared to environment, but again results varied. In adoption studies, researchers followed the children of known schizophrenics after they were adopted into "normal" homes. If a child did not get schizophrenia then environment could be said to determine schizophrenia; if a child did get schizophrenia even in a normal home, then heredity would be implicated as the main determinant. Finally, in pedigree studies a researcher would identify someone with schizophrenia (the "proband"), and trace his or her descendants and antecedents for evidence of schizophrenia or other mental defect. They gathered their evidence either by interview (with living family members), or by word-of-mouth (for living or dead family members). The famous cases of the Jukes[32] and Kallikaks[33] were pedigree analyses.

The American Neurological Association criticized all of the family-type studies at the time for having several basic flaws,[34] but eugenicists persisted in using the studies as their main source of evidence for the hereditary theory. First, there was very poor standardization between studies. In adoption studies, for example, no attempt was made to control for age-at-adoption. In addition, the Association criticized all of the studies for using small, biased samples. They also deemed biased the diagnosis of schizophrenia in siblings or other family members. The Association especially criticized the pedigree analyses as using poorly-collected data; the data concerning antecedents of probands were particularly faulty, according to the Association, because they relied on incidental information. The Association claimed this type of evidence consisted of "gossip," and they ascribed no scientific merit to it.[35]

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[32]Dugdale.
[33]Goddard.
[34]American Neurological Association.
[35]American Neurological Association, page 618-619.

Despite their many flaws, the studies generally supported some hereditary effect, but they did not agree on the extent or nature of this hereditary effect. This disagreement caused a controversy between eugenicists and other scientists and doctors. Eugenicists did not care that the *exact nature* of the hereditary defect was obscure; all that mattered to them was that the character was hereditary. Studies which did not differentiate schizophrenia from any of the other mental problems showed a high degree of inheritance of mental defect, and supported a dominant mode of inheritance.[36] Studies which accepted only schizophrenia in a family member as evidence of inheritance showed a lesser effect, supporting a recessive mode of inheritance.[37] The contradictory nature of the results, however, had different effects on eugenicists as compared to other scientists. Eugenicists, just as they were not interested in discerning the various types of mental disease, yet they were also not dissuaded from their course just because research had not discerned the various types of inheritance. The predominant feeling among researchers in the 1920s, however, was one of marvel at the power and mysteries of genetics, and optimism that its secrets would be revealed.

By the end of the 1920s, however, the mystery of schizophrenia had not been unraveled, and treatment for the disease was generally ineffective. Because scientists did not know the specific cause of schizophrenia in the mid 1920s, psychiatrists and neurologists aimed their treatments at the symptoms, not at the cause of the disease. They achieved questionable results. Electroshock and insulin shock therapy[38] were popular ways of treating schizophrenia. Doctors felt that the shock to the brain incumbent with these methods brought schizophrenics out of the catatonic or melancholic state in

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[36]Rudin, 1930.
[37]Barrett.
[38]Schuster, page 5.

which many schizophrenics functioned. Some doctors gave mercury treatments, as they had for neuro-syphilis. There really was no basis for mercury therapy, and results were poor. Templeton infected patients with malaria, hoping that the fever incumbent with malaria would cure the schizophrenia.[39] Carroll and his co-workers induced aseptic meningitis in schizophrenic patients under the same rationale as Templeton.[40] In addition to these physical therapies, the talking therapy (psychoanalysis) gained prominence in the United States during the 20s, and many analysts attempted to cure schizophrenia using psychoanalytic techniques,[41] exploring the internal conflicts of the schizophrenic patient. Of all the therapies in usage, psychotherapy seems to have benefited the most (or done the least harm), but psychiatrists and neurologists at the time agreed that the treatment for schizophrenia was dismal.[42]

Because treatments for schizophrenia were so ineffective during the 1920s, preventive and social control measures of schizophrenics--including eugenic measures--remained a priority of psychiatrists and neurologists, as well as eugenicists. These measures included segregating schizophrenics--especially reproductive-aged women--from the rest of society.[43] Institutionalization remained standard for most schizophrenics. While both psychiatrists and eugenicists wanted this type of social control, eugenicists also used the cost of maintaining schizophrenics in public institutions as a means of achieving popular support for their measures and ideas. Some families could house their schizophrenic relatives at home, and so those remained in the community; though Pollock suggests these community-

[39]Templeton.
[40]Carroll.
[41]Hinsie.
[42]Beaton.
[43]Bard.

living schizophrenics add to a "considerable number," he claims that "no accounting of these has ever been made."[44] Schizophrenic children often lived in group homes for the mentally defective, such as the Taunton State Home in upstate New York.

Eugenicists wanted to sterilize reproductive-aged schizophrenics as well. In the mid 1920s eugenists campaigned for legalized sterilization of mental defectives. Eugenicists charged that sterilizing schizophrenics (and other mental "defectives") would reduce their numbers in the next generation. In addition, it would keep those unfit to raise children from reproducing. In other words, sterilization would carry the double advantage of reducing both the bad germ plasm and the number of bad parents, according to eugenic doctrine. However, evidence suggested a majority of schizophrenics were born to parents who were themselves mentally well, suggesting that sterilizing only the mentally sick might not have a large effect.[45] Even Tredgold, an avid eugenist, argued that sterilizing only the mentally diseased would not have a strong effect on the next generation. Tredgold suggested that widespread eugenic education was the way to effect a reduction in the birth rate of mentally-defectives.[46] Thus even within the organized eugenic movement people disagreed as to what to do about people with schizophrenia.

At the same time that psychiatry and neurology struggled with the etiology and treatment of schizophrenia, so did they have pertinent internal struggles which related to eugenics. Psychiatry was splitting off from neurology during the mid 20s, and the issues pertaining to this break impacted upon schizophrenia and eugenics. Psychiatry in the 1920s searched

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[44]Pollock, 1939.
[45]Scott.
[46]Tredgold, Pages 10-11.

for its own identity and for validity within both the medical community and the community at large. The acceptance of mental diseases as biological--rather than spiritual or psychological--phenomena put mental diseases decidedly in the realm of medicine, and within medicine, in the realm of psychiatry. These biologically-minded psychiatrists found the eugenic theories of heredity of mental disease very appealing because it gave their profession both legitimacy and a field of research.[47]

At the same time that psychiatry in the mid 1920s embraced the biological hypothesis of mental disease, thus staking their territory within medicine, so did many psychiatrists embrace Freudianism and psychoanalysis. The Freudians did not necessarily agree with the eugenic ideas of heredity of mental diseases. In contrast to the hereditarian-minded psychiatrists, their perspective was a developmental one. They proposed that internal psychic conflict, derived during childhood, lay at the root of schizophrenia.[48] These environmental hypotheses ran counter to eugenic theories, but did not convince the majority of psychiatrists, and certainly not eugenicists. Thus, in the 1920s, the exact cause and biological nature of schizophrenia were unclear, and seemed to follow ideology, not fact.

In the 1920s eugenic arguments and programs were in the forefront of the popular and political scene, and by 1924 eugenicist Harry Laughlin, superintendent of the Eugenics Record Office, wielded tremendous power in the United States Congress. As the official eugenics expert to the U.S. House of Representatives Committee on Immigration, Laughlin "played a major role in the passage of the 1924 law,"[49] a highly exclusionary immigration reform act. The House based the Johnson Immigration Act of 1924 on

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[47]Kevles, page 53.
[48]Amsden.
[49]Mehler, page 182.

eugenic principles, and the Act was the major political achievement of the eugenics movement. Frank Babbott, president of the American Eugenics Society in 1927, commented on Laughlin's contribution to the immigration legislation in his address at the annual meeting in June, 1927. He said the legislation would not "have come so soon or so permanently if it had not been for the demonstration that men, like Dr. Laughlin, have been able to make to the Committee on Immigration."[50] Laughlin declared that white foreigners from Eastern and Southern Europe were of "inferior stock" as compared the Northern and Western Europe, and so sought to restrict these from immigrating to the US. He also sought to prevent all non-whites, no matter the country of origin, from immigrating. Laughlin claimed that the inferior stocks had a higher incidence of criminality, disease, and mental illness; they were of lower intelligence; they could not (and should not be allowed to) assimilate.[51]

Other data, available at the time, conflicted with Laughlin's, though the congress allotted only thirty minutes on the last day of the hearings to such opposing data and views.[52] [53] Horatio Pollock was the director of the Statistical Bureau of the New York State Department of Mental Hygiene, and he contributed most of the statistics available on incidence and prevalence of mental disease in New York and the United States. Pollock found, for instance, that the incidence of schizophrenia in people from Sweden (a nation favored in immigration) was 29.4 per one hundred thousand population, while the incidence in "Jugo-Slavia" (a nation disfavored in immigration) was 20.5 per one hundred thousand population.[54] Ireland,

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[50]Babbott, page 93.
[51]Laughlin, 1920.
[52]Barkan, E, page 98.
[53]Garver and Garver.
[54]Pollock, 1926.

another favored nation, had an extremely high rate of schizophrenia, Pollock putting it at 31.9 per hundred thousand. Laughlin claimed America would degenerated under the influence of these "inferior stocks;" healthy, law-abiding, sane white Americans would have to pay to support the sick, criminalistic, mentally defective immigrants. These arguments won over the House in 1924, and the immigration quotas remain in effect to this day.

Eugenicists won over many scientists and doctors as well, but instead of xenophobic propaganda, eugenicists exploited the specific fears and desires of the scientific and medical communities. Playing on the helplessness with which psychiatrists and neurologists treated schizophrenia, eugenists posed the rhetorical question, "Is it not better to prevent schizophrenics from being born?" Eugenicists also played on biologists current obsession with genetics. Mendel's Laws of inheritance, rediscovered in 1900, gave a mechanism for heredity, and scientists, in the mid 1920s, thought heredity to be the source of heretofore unexplainable phenomena, such as schizophrenia. The eugenicists' intense support of the genetic theory appealed to scientists who were themselves interested in the new genetic theories. Perhaps the strongest weapon that eugenists used to attract support within the scientific community, however, was their framing of genetics as a new religion, of which the biologists were the messiahs. Eugenicists attributed great social power to biologists, which they frankly lapped up. "To those who can read the signs of the times," wrote eugenicist C.J. Bond, "it would seem that we have arrived at the beginning of a new stage in human history--namely the biological age."[55] In this "new age" biologists and medical people were the most worthy and valuable; they led the way to the future of the United States. But in October, 1929, the United States took a detour from its utopian future.

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[55]Bond, page 717.

The stock market crash, and the panic that followed, changed American society forever.

The Depression: A Turning Point for Eugenics

The upheaval and despair of the Depression led to a restructuring of society along lines less favorable to eugenic theory. The panic and depression which followed the crash reduced many previously-wealthy people to poverty, and the impenetrable social system, so firmly steeped in economic prosperity, cracked. Unemployment skyrocketed. Despair prevailed. The boundaries between the social classes seemed to blur. Whereas before the Depression, the eugenically-minded, like biologists Davenport and Laughlin, described those in the lower classes as being destined to remain there--recall that Davenport considered pauperism to be a genetically-determined trait--now people accepted that environment and happenstance played at least a partial role in determining a person's place in society.

The Depression helped change psychiatrists' view of the mentally ill, again along lines less favorable to eugenic theory. During the Great War psychiatrists defined a new clinical syndrome called "Shell Shock" which soldiers came down with in response to the intense stress of the war. A similar sort of syndrome occurred during the Depression, as people who had formerly functioned at a high level broke down under the extreme economic stress. Psychiatrist Douglas Thom, writing in 1932, described the shift in the way psychiatrists looked at the mentally ill. Whereas before the Depression, eugenicists and others had claimed that the mentally ill were a distinct group of people, separate from the mentally well, now psychiatrists conceived of the mentally sick as being on a continuum with the mentally well. The new theory suggested that the mentally ill differed only in *degree*--not in *kind*, as

the eugenicists had suggested--from the mentally well. In addition, psychiatrists suggested that within each person lay the silent potential for mental disease, that all people have an individual threshold of stress beyond which they crack and develop mental disease. Horatio Pollock, director of the Statistical Bureau of the New York State Department of Mental Hygiene, said of different people's reactions to the economic stress of the times, "Strong personalities or those trained to overcome obstacles will survive such unfavorable conditions but others, finding the struggle too great, have recourse to a neurosis or may develop dementia praecox."[56] [57] Pollock's comment suggests that some mental illness could be an unconscious coping response to extreme stress. These new theories represented major ideological shifts away from the conception of mental illness held before the war, and maintained until the Depression. These new conceptions of mental disease emphasized environmental factors in disease etiology more than genetic factors. Genetics maintained a place in the etiologic story, perhaps in setting the individual threshold, but now had to share the spotlight.

In the 1930s, eugenic ideas generally went counter to those which psychiatrists proposed during the Depression, and the popularity of eugenic principles waned among both the lay public and the scientific and medical communities. The public suffered, and saw people suffering, and felt empathy. Whereas before the Depression many eugenicists gained popular support by pointing the finger at the social welfare system and declaring it anti-eugenic and a waste of money, now more people understood hardship first-hand and tolerated the cost to themselves of helping others. Many

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[56]Pollock, 1930, page 230

[57]Dementia praecox is an earlier name for schizophrenia. It was not until the 1940s that the term schizophrenia appeared exclusively in the literature; during the 1920s and 1930s both terms appeared synonymously.

people no longer accepted the eugenic assertion that social welfare worked contrary to evolution and thus reduced the quality of human breeding stock. Another element to the waning popularity of eugenics during the Depression era was that the social decay which eugenicists had forecasted had seemingly come to pass, but it clearly had nothing to do with genetics or eugenics. Finally, the public had other things on its mind, such as surviving, and vague ideas about societal improvement through selective breeding did not compel the populace as much as concrete ideas about finding a job. The intolerance of the 1920s, in which eugenic ideology found a comfortable home, was substantially swept away in the 1930s, replaced by a more accepting society.

During the Depression, while much of the lay public acquired a new sense of tolerance and empathy toward the mentally ill, they also acquired an acute understanding of the cost in dollars needed to support people with schizophrenia. Pollock, of the New York State Department of Mental Hygiene, estimated the annual cost of administering and maintaining the mentally ill in hospitals in the state of New York to total $52 million. He estimated the cost of care for community-living mentally ill to be $330 million for the whole United States.[58] These added to a staggering sum, which eugenists continued to claim through the 1930s, could be avoided in the future by implementing their measures. In addition to the cost to society, schizophrenics suffered loss of taxable income because of their illness. In New York state alone, actuarial tables showed that schizophrenics lost more than $40 million in lifetime earnings.[59] This lost income meant they did not contribute to the tax base, and in fact did not contribute to the economy at all in a positive way. These were not new costs; these were costs that society had

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[58]Pollock, 1939.
[59]Pollock, 1939.

always borne. The Depression, however, amplified these costs because so many were out of work and struggling themselves, and having to support people who (some claimed) had never and would never contribute anything back became intolerable to many.

In the 1930s, eugenicists tried to use the cost of supporting people with schizophrenia to their advantage, but these economic arguments largely failed. Eugenicists such as C.J. Bard argued that "instead of eliminating or preventing the birth of weaklings, we now do more in caring for the health and education of the defective than we do for the normal."[60] He further claimed that "even the ordinary citizen is becoming seriously concerned by the increasing weight of the burden which he is being called upon to bear in providing for the support of the inefficient, unproductive, and defective members of society."[61] Birth control advocate Mabel Boydon warned that money spent on schizophrenics and other mentally diseased people contributed to their survival and increased their likelihood of reproduction, thus ensuring more schizophrenics in the next generation. She decried the social welfare policies as doing away "with many of the natural factors which tended to favor survival of the fittest."[62] Public assistance for schizophrenics, then, not only went to support the "socially unfit" and economically unproductive, but in fact meant a continuing burden on future generations, resulting in an increase in the incidence of schizophrenia. This is an argument we will come across again in our discussion of treatments for schizophrenia in the 1990s. Clarence Campbell, a prominent eugenicist underscored this point when he said: "Economic conditions go far to

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[60]Bard, page 183.
[61]Bard, p. 184.
[62]Boyden, page 61.

determine differential reproduction and differential survival, which in turn will go to determine the biological quality of the succeeding generation."[63]

But Bard, Campbell, and Boyden's views, shared by other eugenicists, did not have the popular support they claimed. Historian of eugenics, Barry Mehler, suggests that the psychiatrist Thom's view more closely represented the popular view when Thom wrote, "The time is at hand when physical factors and economic situations must be stressed in relation to mental instability, and such material relief as can be found must be offered to those in need."[64] This area represents another situation in which eugenic ideology, embraced in the divisive society of the 1920s, fell on deaf ears in the 1930s, an era which (in contrast to Bard's claims) embraced further involvement of government in all areas of society.[65]

Just as eugenicists were alarming people about the increase in schizophrenia, the state of New York did see a small increase in the incidence of schizophrenia between the years 1924 and 1933, which psychiatrists claimed was negligible. The years between 1924 and 1929 showed an average of 18.2 people hospitalized for schizophrenia per 100,000 population; from 1930 to 1933, the number hospitalized for schizophrenia averaged 20.1 per 100,000.[66] Epidemiologists Landis, Carney, and Page attributed the small increase to a shift in schizophrenics from the home to the hospital, due to increased economic pressures at home. People who formerly provided for their schizophrenic family member could no longer afford it, so they ended up in the state hospital. They did not support the notion that there was an increase in actual incidence of the disease.[67] Myerson agreed saying, "Although the

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[63]Campbell, page 69-70.
[64]Thom, page 574.
[65]Allen, GE, 1989.
[66]Landis and Page.
[67]*Ibid.*

problem of mental disease and defectiveness is enormous, there is no new social or biological urgency."[68] Although Myerson and Pollock (who was in charge of following such admittance trends) made their statements about the negligible increase in hospital admittance, eugenicists largely ignored these expert opinions, and continued to try to alarm the populace that rates of schizophrenia would continue to increase without eugenic measures to eliminate those with this genetic disease.

By the 1930s, the genetic basis of schizophrenia was no more certain than it had been in the 1920s, leaving many scientists with lingering doubts. Rudin, the pioneer of hereditary research in mental diseases, had assured scientists at the First International Congress on Mental Hygiene in 1930 that "it remains only a matter of time to discover ... stern and definite laws, complicated as they may be, for the ... hereditary insanities."[69] But in the 1930s, the genetics of schizophrenia remained as foggy as ever. In fact, it appeared that the more research that was done, the foggier and more complex the picture appeared. Franz Kallmann published his treatise, *The Genetics of Schizophrenia* in 1938, and in it he describes how much less complicated the genetic situation was in the 1920s, with the contemporary notion that traits were either recessive or dominant, simple or complex. In the 1930s, more complicated theories had developed having to do with such things as "penetrance" and heterogeneous inheritance. These newer conceptions of genetic theory were far more complex than those in the 1920s, and the genetics of schizophrenia was no less complex than any other disease.[70] Eugenicists were not put off by the complexity of schizophrenia genetics, but the noted psychiatrist and neurologist Abraham Myerson rejected as

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[68]Myerson, 1935.
[69]Rudin, 1930.
[70]Kallmann.

premature eugenists' certainty of the genetic theory. He stated at the First International Congress on Mental Hygiene in 1930 that "when somebody speaks to us about dementia praecox or schizophrenia as if it were something definitely understood, as if it were a well-organized, biological character, he is misleading us."[71] Rudin countered, saying that although research on the heredity of schizophrenia remained remedial, "even this beginning has offered plenty of positive results, a sufficient number anyhow to justify putting them into practice right away."[72] However, the blind enthusiasm which many writers showed in the 1920s shifted to a wait-and-see skepticism in the 1930s. Biologist JP Scott typified this new viewpoint when he said, "Admitting the inconclusive nature of most data on human heredity, the whole feasibility of negative eugenics rests upon this question of fact."[73]

1930s: Downfall of American Eugenics

In the same way that doctors and scientists shifted their attitudes on the certainty of the genetic theory of schizophrenia, so did many in the 1930s shift their attitudes on the necessity of eugenic measures. Many wanted to know, like biologist J.P. Scott, whether the supposed-increase in schizophrenics and other mental defectives "actually produced deterioration of the human race"[74] before he would "trust (the eugenicist) to guide us either up the evolutionary tree or into the sociological soup."[75] H.J. Muller, a prominent geneticist and socialistand future Nobel Laureate, also sneered at eugenics (as it was being practiced by mainstream eugenicists) as social progress. He decried the fallacy of eugenics as being for the social good. Far from being

[71]Myerson, 1932, page 490.
[72]Rudin, 1930, p. 174.
[73]Scott, page 262.
[74] Scott, page 261.
[75]Scott, page 262.

revolutionary, he described the way eugenics in fact promotes the status quo in its affirmation of capitalistic exploitation, because "capitalism leads to an entirely false sense of eugenic needs."[76] Writing 1932, Muller expressed the feeling that the economic upheaval itself would act to break down the barriers between classes and races, and only in the newly equalized system can eugenics actually take the form of social progress. Scott described himself as "a sceptic (sic) and a scientist," as he decided to wait for facts.[77] This was an identification which many in the 1930s shared.

The New Deal era of the 1930s, and its community ethic, provided fertile soil for challenges to the eugenic assertion that people with schizophrenia had no value in society. Myerson asked the question, "Who shall say who is a useful person? In a capitalistic society a communist can scarcely be declared a useful member of the social life of the state. In a Bolshevik society the capitalist falls at once into the class of the useless."[78] Myerson was not a socialist, but merely pointed out the temporal nature of "value" as applied to people. Myerson pointed out that his list of the valuable members of society would likely differ from someone else's list, suggesting that the basis for valuation is itself a subjective matter.[79] Muller, the socialist geneticist, agreed with Myerson when he said that only in an equalized system can "we...properly judge, from a truly social point of view, what characters are most worthy of a man, and what will best serve to carry the species onward to greater power and happiness in a united struggle against nature, and for the mutual betterment of all its members."[80] Myerson and Muller both point out the degree to which a person's value has as much

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[76]Muller, page 46.
[77]Scott, page 261.
[78]Myerson, 1935. p. 455.
[79]Myerson, 1935, page 455.
[80]Muller, p.45.

to do with the assessor, and the social context in which valuation takes place, as it does with a person's skills and contributions. Both suggest that what some consider valuable others do not, and what some consider valuable today might tomorrow be worthless. The ambiguity of who is useless and who holds value did not discourage eugenists. "We may not know exactly which human beings are the most desirable, but we certainly know which are the least desirable,"[81] said pediatrician and eugenicists Charles Herrmann in 1934. In the 1930s, however, the climate was such that Herrmann held the outlying view; his judgment belonged to a different age than the 1930s.

The progressive social agenda and climate of tolerance which permeated the New Deal era after the Depression clashed with the stringent ideology of exclusion and division embodied by eugenics. Eugenic ideas appeared to many in the 1930s to be extremist, though perhaps the ideas themselves had not changed since the public and the scientific community embraced them just ten years earlier. Certainly, the United States and the world had changed since the blissful post-war days of the early twenties. Perhaps the eugenics movement itself also became more extreme in the thirties. As membership in the eugenic societies fell off, and attendance at conferences dropped to one tenth that of the prior decades, those who remained active, such as Harry Laughlin, were eugenics' staunchest supporters and its most extreme members.[82] The American Eugenics Society now embraced not just *voluntary* sterilization for those affected with mental disease and carriers, but *mandatory* sterilization for both groups. Myerson was chairman of the American Neurological Association's Committee for the Investigation of Eugenical Sterilization in 1936. Writing in that capacity,

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[81]Herrman, page 564.
[82]Allen, GE, 1989.

Myerson lambasted the stringent sterilization laws which the organized eugenics movement so supported. He described these laws as "extreme" and as "approaching mania." He saw them as a "threat to civilized life."[83] The tables had clearly turned, as only ten years before, eugenicists held the civil high ground, claiming to be guiding civilization to its zenith under eugenic measures. The combination of shifting societal values and shifting eugenic policies led to an overall decline in the popularity of the organized eugenics movement in the 1930s.

Along with shifting social and economic values, the international situation affected the popularity of eugenics as well. The Germans, long in the forefront of eugenic thinking and research, had begun the largest-scale eugenics campaign in history, a campaign that would later be known as the Holocaust. As eugenical pediatrician Charles Herrmann reflected at the time, "It is unfortunate that the Germans undertook their eugenic program at this time, for as they had done so many ruthless things it was concluded that they might [try] to rid themselves of the descendants of those whom they considered their enemies."[84] Eventually, eugenics became bound up with genocide, and the image was not appealing to most Americans. Doctors felt particularly sensitive in this area because of the prominent role of physicians in the Nazi campaigns.

Many doctors, scientists, and lay-people sought to separate themselves from the organized eugenics movement in the 1930s, and by 1935 organized eugenics retained only a fraction of its previous following. Only 347 people attended the Third International Congress on Eugenics in New York City,[85] whereas only ten years earlier thousands attended. Early in the thirties,

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[83]Myerson, 1935, page 454.
[84]Herrmann, page 560.
[85]Cook, R.

economic concerns dominated the mindset of the country. Later in the thirties, the deteriorating situation in Europe and the Pacific consumed the collective conscience. Eugenics scored a distant last place in a ranking of important societal concerns which sociologist Victor Gruelach conducted in 1938.[86] There are a variety of reasons for the eugenic movement's decline in popularity, in addition to those mentioned above. From the nadir of American civilization in the Depression, people saw society rebuilding around them, but with an ethic of tolerance, not exclusion. This new ethic clashed with that of eugenics. Certainly the social, economic, and political currents which were central to the embracing of eugenics in the 1920s were equally critical to the rejection of organized eugenics in the 1930s, as historian of science Garland Allen suggests.[87] However, factors within the movement itself also contributed to its downfall. Eugenists' arguments aged; historian Barry Mehler says that the American Eugenics Society made "very little substantial change in major policy and orientation" between 1923 and 1935.[88] Eugenists' promise of detailed knowledge of an hereditary etiology for schizophrenia, and other diseases, never solidified. Their prediction of the increase in schizophrenia didn't bear up to scrutiny. The degeneration of civilization materialized in the form of a major economic upheaval having nothing to do with who did, or did not, have children. Studies conducted in the mid 1930s proved there was no difference in incidence of schizophrenia among native-born as compared to foreign-born whites as long as testers used proper techniques.[89] In all, American society changed directions during the 1930s, and eugenic arguments and policies failed to keep pace.

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[86]Gruelach, VA.
[87]Allen, GE, 1989, pages 885-889.
[88]Mehler, Page 139
[89]Landis and Page.

Eugenicists at the time recognized that support for their policies was waning in the 1930s and a debate emerged in the late 1930s as to whether eugenics was, in fact, dead in the United States. Robert Cook, editor of the *Journal of Heredity*, considered the notion that eugenics was "half-baked" in a paper which he read at the Third International Congress on Eugenics in 1938. He concluded that this criticism was in fact at least partially true, as evidenced by the poor showing at the conference.[90] In response to a letter written to the *Journal of Heredity* from a "layman" suggesting that eugenics was "dead," H.F. Perkins (then-director of the American Eugenics Society) suggested that the relative inaction of eugenics was, in fact, a normal phase for the movement.[91] C.C. Little countered that eugenics was not dead, but "sleeping."[92] Leon Whitney, of the American Eugenics Society objected to both declarations. He asserted that eugenics was "neither dead nor sleeping;" soon "there will be plenty of followers as those of us who are interested in eugenics know, there are plenty of leaders as well."[93] Thus within the organized eugenics movement it appears there was confusion about its vitality. Whether the movement was "dead," "sleeping," or just plain waiting for someone to follow, its popularity was down, and these efforts represent the first open acknowledgment of that fact.

But whatever the diagnosis at the time, we know today that eugenics did not altogether die off. Allen and Kevles describe the eugenics societies during the 1940s-1980s as small but energetic foci of eugenic activity. Recently there has been a renewed interest by some in promoting eugenic policies aimed at increasing the intelligence of the American population.[94] Today, the

[90]Cook, R.
[91]Perkins, page 149.
[92]Little, page 149.
[93]Whitney, page 150.
[94]Andrews, 1990.

field of genetic counseling provides what must be considered eugenic information to the cacogenic: potential parents of potentially defective potential offspring. Diane Paul, a historian of eugenics and genetics, considers genetic counseling the modern "education" branch of the eugenics movement.[95] The field of human genetics took up the research division of eugenics, and today boasts the Human Genome Project. The HGP promises to identify all the genes, and all genetic diseases, both for basic science purposes and to add more information to genetic counseling. Ultimately the HGP hopes to provide gene therapy for the genetically sick; in the meantime, it hopes to provide more information to families at risk for having children with genetic diseases, maybe resulting in elective abortion. In certain respects, the HGP can't help but resemble the eugenists' efforts at human improvement. Modern writers hold up such superficial comparisons as red flags, warnings to scientists not to tread too far into the realm of genetic improvement. But while the eugenics movement hoped to advance civilization to new heights, the HGP hopes only to advance the individual to new health. Nonetheless, important comparisons can be made between the two movements, and such a comparison will undoubtedly prove fruitful. Myerson said in 1930 that society should wait to act "until we get to the point where we know just where in the genetic line-up the genes are located for any character."[96] Today we can see a day when we will have that knowledge. The question remains, then, what will we do with that knowledge? Can our experience with eugenics inform those decisions? We will take on these questions later in the paper.

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[95]Paul, D, Feb 15, 1991.

[96]Myerson, 1932, page 490.

Chapter Three:

Historical roots of human genetics

A brief look at the historical roots and ultimate path of human genetics may prove fruitful to our discussion of the current link between eugenics and the genome project. Contemporary comparisons between the human genome project and the eugenics movement usually revolve around similarities in content, a theme which will be explored later in the paper. Aside from applications, however, the genome project has historical links to the eugenics movement. Exploring such historical links may prove illustrative in our future analysis. Such an historical sketch follows.

Although contemporary geneticists shun eugenics as a distortion of their science, and those in the genome project reject the eugenics movement as unrelated to the HGP, there are clear historical links between the two fields. During the 1920s and 1930s, eugenicists considered eugenics and genetics to be the applied and experimental arms, respectively, of the same science. Abraham Myerson, the respected neurologist, took offense. He said of the two fields in 1935,

> Everything that comes along labels itself "science." Science is more than the scientific approach. A man may approach the problem of inheritance of human qualities scientifically, but he, as yet, and mankind, as yet, are unable to be scientific about the subject. A long history of perhaps a hundred years of scientific approach is needed before a science of eugenics can develop.[97]

The field of genetic counseling also grew out of eugenics, according to historian of genetics, Diane Paul. She describes the first genetic counseling clinic at the Dight Institute in Minneapolis, left to the University by eugenic benefactor Charles Dight.[98] A third link between the two field lies in the infamous support many of the early geneticists gave to eugenics, including Thomas Hunt Morgan and his students, Nobel Laureate Herman Muller,

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[97]Myerson, A, 1935a, page 466.
[98]Paul, D, Feb 15, 1991.

Sturtevant, and many more. In contrast, later, developments in genetics were partially responsible for the ultimate downfall of eugenics.

The end of an era

The Eugenics Record Office at Cold Spring Harbor closed its doors in 1938, ending the era of eugenics in the United States. The Carnegie Institution of Washington separated itself from the people and organization it had funded for so many years. With the fall of eugenics came the fall of human genetics as a valid field of study and research. Human genetics would be forever tinged with the scent of eugenics. The number of university positions reserved for human geneticists, which had ballooned during the heyday of eugenics, shrank considerably; research funding, once an endless flow from philanthropic and public sources, dried to a trickle.[99] Human geneticists quickly switched their research interests to other organisms, or competed ruthlessly for the few remaining positions in human genetics.

Many geneticists joined the large group of researchers already investigating maize, bacteria, and *Drosophila* (fruit fly) genetics. These organisms held many advantages over humans as a source of study. First, their generation length was considerably shorter than humans, fruit flies reproducing as often as every two weeks. Second, their matings could be controlled, unlike humans, whose mating style was not conducive to experimental observation, let alone manipulation. In all, non-human organisms proved to be much more useful for experimental genetics.

The shift from human to non-human genetics represented more than just the drying up of funding sources. It marked the definite, permanent shift of genetics from a descriptive field to genetics as the quantitative and

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[99] Allen, GE, 1986.

experimental field we now know. This experimental side of genetics was not new to the 1930s. Research on *Drosophila* and maize genetics had been underway for decades, though it had not achieved the same popular prominence as human genetics and eugenics.

In fact, advances brought about by basic genetic research and by population genetics played a definite role in bringing down the sister field of eugenics, and with it human genetics. The new field of population genetics used mathematics and statistics to model populations of organisms with certain genetic characteristics. Using population genetics techniques, particularly the Hardy-Weinberg Principle, derived simultaneously and independently by the two men in the teens, population geneticists were able to show that in order for an allele, representing a recessive or dominant trait, to be bred out of the population completely (the goal of negative eugenics, you recall), thousands of generations would have to elapse. The principles of population genetics showed beyond a shadow of a doubt that positive and negative eugenic measures would in no way have the immediate effect which eugenicists had claimed. While eugenicists ignored these contemporary arguments, many geneticists in the 1930s could not, and spoke out against eugenics.

Drosophila genetics also proved to be a source of evidence against eugenics with its promulgation of mutation theory. Mutation theory, developed from experiments with radiation, suggested that genes are capable of "mutating," or changing, from normal to abnormal and back. Mutation theory provided further evidence that the simplistic view held by eugenicists about the value of positive and negative eugenics had little basis in reality. If mutations were constantly happening, then one could hardly conceive of eliminating genes just by sterilizing those who express them. As we saw in

the previous chapter, the vast majority of people with schizophrenia were born to well parents. Mutations (along with the incomplete penetrance of the disease) accounted for such a situation. The evidence contradicting eugenicists' claims was great.

Department of Defense gets into human genetics

Two things happened during the Second World War, however, which brought human genetics back into popular and scientific consciousness: atomic weapons and mustard gas. When the United States dropped the bomb on Hiroshima, Japan on August 6, 1945, then two days later on Nagasaki, the specter of human genetics reappeared. It was not long before scientists realized the devastating effects radiation had on the survivors of the nuclear attack. The long-term effects, including effects on future generations, would continue to be felt for years to come. Mustard gas had also been seen to have effects on the genes of victims.[100] Although both of these chemical effects were known during the war, their military nature made them top-secret until after the war was over.[101] The post- World War II era saw an expanded interest in research into genetics, using an experimental model. Once the war was over, the United States Department of Energy (DOE) took over research on the genetic effects of radiation. This marked the first time a federal agency took on genetic research. DOE would continue this research for decades to come.

Advances in knowledge of basic genetics ("classical" genetics) came rapidly during the 1940s. A debate still raged in the 1940s as to the exact nature of the hereditary substance. One camp held that the hereditary

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[100]Auerbach, Robson, and Carr.
[101]Auerbach.

substance was physical matter, probably having to do with chromosomes. Another camp, led by Bateson in England, felt the genetic substance was invisible, not matter. Several pieces of evidence came out during the 1940s giving evidence to the former theory. Avery, Macleod, and McCarty published their classic paper in 1944 which suggested that DNA was the genetic substance; they performed their experiments on Pneumococcus, attempting to discover the mechanism of transformation whereby one strain of Pneumococcus "transformed" into another. Their paper, "Studies on the chemical nature of the substance inducing transformation of pneumococcal types," gave evidence to the camp which suggested that chromosomes were in fact the substance of heredity, evidence which was hard to dispute. Charlotte Auerbach and her colleagues published their classic paper, "The chemical production of mutations" in 1947, again giving evidence to the chromosomal camp. After all, how could physical mutagens, like chemicals, have any effect on a non-physical gene? All but a few skeptics embraced the chromosomal theory of inheritance by the end of the decade.

The 1950s: age of genetic discovery

The final acceptance of chromosomes as the hereditary substance still left many questions unanswered, however. What part of the chromosome was responsible for the information-carrying capacity of genes? Many people thought it was the proteins bound tightly to the DNA. At the time, DNA was thought to be a repeating tetra nucleotide, a molecule which could hardly be seen to provide specific and variable information required of the genetic substance. This controversy led to the search for the structure of chromosomes.

In 1953, with one X-ray crystallographic analysis, James Watson and Francis Crick laid that controversy to rest. They discovered that DNA was in fact not a repeated tetra nucleotide, but was composed of two anti-parallel chains of four nucleotides arranged in any order. The whole molecule was coiled as a double-helix. Far from the repeated tetra-nucleotide which had been earlier reported, the new structure of DNA could be easily seen to have information-carrying capacity; to be different from gene to gene. It could be the genetic substance. Avery, Macleod, and McCarty's work, viewed with skepticism for nearly ten years, could now be whole-heartedly embraced.

The structure of DNA is an elegant case in biology where *form* and *function* are intimately linked, and discovering the form led to a rapid understanding of many of DNA's functions. The anti-parallel arrangement allowed a picturesque view of how DNA could replicate itself, each strand separating, acting as a template for the other, then rejoining. The specific-binding of nucleotides--guanine only binds across to cytosine, and adenine binds only to thymine in what is known as Chargaff's rule--meant DNA could replicate true. It also gave substance to the theory of mutation. Mutation could be seen as being the switch from one nucleotide for another, or adding or deleting nucleotides. What was once purely theoretical now had a rational, in fact elegant, representation in reality.

Watson and Crick's discovery of the structure of DNA in 1953 marked the end of the era of classical genetics and ushered in the era of molecular biology and molecular genetics. In 1956, Tjio and Levan correctly counted the number of chromosomes to be 46 in the human. (The number had been thought to be 48 for years due to poor visualization techniques and confusion over the X and Y chromosomes.[102]) By 1959, three chromosomal aberrations

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[102]Levan, 1978.

were known to cause human diseases: Trisomy 21 caused Down Syndrome; 45 XO caused Turner's Syndrome; 47 XXY caused Klinefelter's Syndrome. Although techniques for visualizing chromosomes were very rough, and resolution poor, hopes were high that as these improved, the number of human diseases ascribable to a particular chromosome would increase.

The 1960s: Linkage analysis takes off and the code is deciphered

Isolating specific genes or diseases to particular chromosomes did improve in the 1960s, thanks to improved techniques for linkage analysis. Linkage, the association of two genes or traits (i.e., non-segregating traits) was first described by J.B.S. Haldane in 1915. By 1959, however, only three pairs of linked traits were known in humans. In 1967, Renwick and Bolling introduced a computer program for linkage analysis, allowing for the rapid development of rough linkage maps. The number of known genes also increased rapidly in the 1960s. Victor McKusick published the first edition of his classic book *Mendelian Inheritance in Man* in 1966, describing 1,487 different genes. *Mendelian Inheritance in Man* is today available as an on-line data-base with over 4,800 entries.[103]

The final link between proteins and DNA was soldered in the mid 1960s when the entire translation of the genetic code was presented at the Cold Spring Harbor Symposium in 1966. The code defined which three nucleotide bases coded for which one amino acid. This decoding marked the culmination of the one gene, one enzyme hypothesis which had been proposed fifty years previously by the English geneticist Garrod, and developed more fully in 1941 by George Beadle and Edward Tatum[104] in their

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[103]Much material from this section was taken from Guethlain.
[104]Beadle and Tatum.

work on the yeast *Neurospora*. Beadle and Tatum's work also revealed the nature of "inborn errors of metabolism," again providing a medical model for a molecular biology system. The beauty of Beadle and Tatum's work rests in part with their sophisticated choice of organism, a yeast. Yeast can reproduce asexually, and as such have a haploid karyotype, unlike sexually reproducing organisms which are diploid. These special characteristics of yeast allowed Beadle and Tatum to manipulate the environment and perform very sophisticated experiments and analyses. Their results have been hailed as some of the most compelling and revolutionary in biology.

Techniques in molecular biology continued to advance at a rapid rate in the 1960s, allowing for further understanding of genetic processes in humans. Linn and Arbor[105], and Meselson and Yuan[106] described the first restriction enzymes in 1968. These enzymes selectively cleaved DNA molecules at sites displaying certain sequences, leaving lengths of DNA which represented the distance between these sites. By digesting the DNA from different organisms and comparing the lengths of the fragments which result from this digestion, researchers could for the first time directly compare human DNA to that of other organisms. Differences in the lengths of fragments between either different individuals of the same species, or individuals of different species, are called "restriction fragment length polymorphisms" or, "RFLPs." RFLP analysis showed the degree to which the DNA of the individuals compared was similar or different, and indicated that human DNA had many polymorphisms with no apparent link to any disease state. The genetically aberrent, apparently, could not be distinguished by virtue of mental or physical traits.

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[105]Linn and Arbor.
[106]Messelson and Yuan.

The 1970s: sequencing and cloning are born

A genetic map can be made from these restriction fragments using a techniques known as "Southern blotting." This techniques was developed by E.M. Southern in 1975. First, the restriction fragments are separated from each other by gel electrophoresis, in which the DNA pieces are embedded in a gel to which an electrical field is applied. The fragments migrate at different rates down the gel depending in their size and charge. After the fragments are separated from each other (but still embedded in the gel), a piece of paper is laid on top of the gel, and some of the DNA from each of the spots diffuses onto the paper. At this time, a "probe" or strand of DNA complementary to the one we're looking for, is introduced into the paper, sticking to the spot which has its complementary fragment. The probe is marked by a fluorescent marker, so when illuminated appropriately, the spot with the piece we're interested in shines bright. We can then transpose the spot on the paper to the corresponding spot on the gel, and we have the piece of DNA we're interested in. The Southern blot technique has become central to much of contemporary genetic analysis.

Also central to contemporary genetic analysis are the sequencing techniques developed in the mid 1970s. The Maxam and Gilbert[107] method and the Sanger[108] method of determining the order of nucleotide bases, both introduced in 1977, allowed for higher resolution of genetic maps than had been possible using just linkage and restriction enzyme analysis. The following year, the first library of human genome fragments was announced,

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[107]Maxam and Gilbert.
[108]Sanger.

the natural result of the advances in mapping and sequencing which had come in the years preceding it.

In 1978 Maniatis announced a new technique to clone segments of human DNA, allowing researchers to study human gene fragments more readily. The result of the enhanced ability to study human genomic fragments brought about by restriction analysis, sequencing and cloning, was the announcement in 1983 that the gene for Huntington's disease had been localized to chromosome 4.[109] The age of modern medical genetics had begun.

The 1980s: the age of modern medical genetics

Electrophoresis and RFLP analysis were aided by the discovery of new techniques for cloning large segments of DNA.[110] Scientists could then take a gene and clone it instead of having to extract DNA from large numbers of cells. The cloning techniques held special significance for human geneticists because they allowed for the production of large numbers of human genes, an impossible task up to that point. The year 1987 also saw the development of the Polymerase Chain Reaction (PCR).[111] PCR was a technique by which short regions of DNA could be amplified very easily and quickly. Both the cloning and PCR paved the way for easier use of human material for research. Whereas before the new techniques, huge cell cultures had to be kept alive in an effort to harvest human DNA, an ethically problematic activity, now human DNA could be easily and quickly "grown" in the lab. The new abundance of human DNA for research purposes had the desired effect of increasing research energies and funds for human genetics.

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[109]Gusella et al, 1983.
[110]Burke, DT; Carle, GF; and Olson, MV.
[111]Saki, *et al.*

The Human Genome Project is born

By 1985 research in human genetics was advancing at such a rapid pace, with new technologies being developed to allow research to forge ahead even faster, that Robert Sinsheimer convened a human genetics conference at the University of California at Santa Cruz. The Santa Cruz Workshop proved to be the intellectual birth-place of a large-scale effort to map the human genome.[112] Though that specific task was never directly brought up the Workshop, as scientists conferred and exchanged information it became clear that such a project was feasible, and would prove fruitful. A detailed description of the events leading up to the momentous project is beyond the scope of this paper; however, Thomas Lee offers an excellent story in his *The Human Genome Project: Cracking the Genetic Code of Life*, and interested readers are referred there for more extensive accounts of the events in the middle and late 1980s which culminated in the HGP.

Helen Donis-Keller published a linkage map of the entire human genome in 1987[113], rough as it was. The time seemed right for a coordinated effort which would further resolve the Donis-Keller map, and maybe add more maps. Later in 1987 the DOE expressed its interest in such a large-scale project. Dating back to the 1940s, the DOE had been conducting genetic research, and saw the mapping project as a way to identify mutations in survivors of the atomic bombings and their offspring. In 1983, the DOE had created Genbank, a huge DNA sequence data bank, at Lawrence Livermore National Laboratory in Livermore, California. Its laboratories at Los Alamos, NM and in Livermore and Berkeley, California were especially suited to a

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[112]Sinsheimer, R.
[113]Donis-Keller, H. *et al.*

large-scale project, having been used for the large-scale nuclear energy research for which they had been designed.

The National Institutes of Health (NIH), the nation's leading health research institution, expressed interest in the project in early 1988. The Congress created a new center for genome research (the National Center for Human Genome Research, NCHGR), and appointed James Watson (of Watson and Crick fame) as the first director. The divisional status for the human genome has broad funding implications. The NCHGR is virtually an Institute of the NIH, and as such has autonomy both in terms of the research it conducts and in terms of funding. The NCHGR does not rely on another agency within NIH for funding, but rather gets its funding directly from Congress, one-third coming through DOE and two-thirds from NIH.

Many nations followed the lead of the US, establishing initiatives to map and sequence the human genome, or that of another organism. To date, however, the United States is the only country that has named mapping and sequencing the human genome a national goal. Italy began its program in 1987[114], the United Kingdom in 1988[115], followed by the European Community in 1990[116]. The USSR started its program in 1988-89[117], only to have the summer coup put it on ice. Japan began its initiative in 1991.[118] UNESCO joined the fray in 1990[119] acting as an advocate for researchers in third world countries. Instead of international competition, the countries involved envisioned multinational cooperation, and in 1988 the Human Genome Organization (HUGO) came into being.[120] Founded by medical

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[114]Dulbecco, R.
[115]United Kingdom, 1990.
[116]European community actions, 1991.
[117]Bayev, AA.
[118]Swinbanks, D.
[119]Grisolia, S.
[120]Bodmer, W.

geneticist, Victor McKusick, HUGO aims to be an international clearing-house for information on the various human genome projects and a means of addressing cross-national and cross-cultural issues brought up by the HGP. HUGO is also funded multi-nationally.

The ethic of international cooperation has never become completely realized, however. Conflicts arose about the sharing of information and technology, commercial considerations (e.g., some countries allow patenting of gene sequences while others do not), and not least, differences of opinion over ethical issues.[121] These remain difficult issues to deal with.

As head of the NCHGR, Watson defined seven areas which receive funding and attention. These seven areas are: 1) mapping and sequencing the human genome; 2) model organisms; 3) Informatics (data collection and analysis); 4) ethical, legal, and social implications; 5) research training; 6) technology development; 7) technology transfer. Each area gets a different percentage of the budget, has working groups and advisory committees, and sets five-year goals.

Mapping and Sequencing the Human Genome

The human genome consists of 23 pairs of chromosomes, which are themselves comprised of genes (approximately 50,000-100,000 in total) and other stretches of DNA, sometimes called, "junk DNA" because of its apparent lack of function. The majority of DNA in the human genome is in fact so-called "junk DNA." All DNA is composed of repeating nucleotides (also called "bases"). Chromosomes are arranged in a double helix, so that one strand of DNA bases matches to another strand which runs anti-parallel to the first. The bases on each strand lie opposite each other in a particular

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[121] Aldhous, P.

arrangement so that Adenosine always lies opposite Guanine, and Cytosine always lies opposite Thymine. The HGP is concerned with creating physical and genetic maps of the chromosomes, and in sequencing the chromosomes.

Sequencing DNA, then, consists of determining the order of the four nucleotide bases in a chromosome, or in a gene. Because the sequence of DNA determines the sequence of amino acids in a protein, sequencing information can be used to learn about protein structure and function. Knowing the sequence of a particular gene would also help determine carriers of mutations for that gene, and might aid in synthesizing gene products for therapy, or identifying what gene product is associated with a particular gene. The committee on mapping and sequencing the human genome is concentrating its current efforts on reducing the cost of doing sequencing from approximately $2 per base pair down to fifty cents per base pair. Only if the cost of such an effort can be lowered to this extent will the funding levels be adequate to achieve the desired long-term goal of sequencing the genome.[122]

Sequencing is genetic mapping at the highest resolution. Genetic mapping is the process of determining the relative position of genes, genetic landmarks, or base pairs on the chromosomes. Linkage analysis is one form of genetic mapping in which a gene or a trait is associated with a particular chromosome, or region on a chromosome, or with another trait. This form of mapping took place as early as the beginning of the century when hemophilia and red-green color-blindness were both associated with male sex. The genome project hopes to map every gene to a particular site on the chromosome.

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[122]U.S. Congress. House, 1988, page 16.

The HGP has instituted a new method of communicating about mapping in their "sequence Tagged Sites," or STS[123]. Sequence Tagged Sites are short stretches of DNA with unique nucleotide sequences. Genes can be mapped with reference to these STS, providing a universal reference point, providing all labs use the sites. The NCHGR instituted the use of these STS as a way to facilitate multi-national communication about mapping. In effect, the STS system provides a common "language" with which researchers can communicate. The committee on sequencing and mapping included STS in their five-year goal of completing a "fully connected human genetic map with markers spaced an average of 2 to 5 centimorgans apart." They hope to identify each marker by an STS.

Physical maps are different from genetic maps, in that they measure the distance on the chromosome (in units of length, for instance base pairs) between two markers. For instance, restriction fragment length analysis leads to a measure of distance between two restriction sites. The STS system facilitates communication about physical maps as well, and the committee on mapping and sequencing the human genome hopes to have STS maps of all human chromosomes by the end of 1995, each STS separated by 100,000 base pairs.[124] Mapping allows for detection of carriers of genetic diseases, translocations, or other genetic effects.

Model Organisms

In addition to mapping and sequencing the human genome, the HGP also encompasses the mapping and sequencing of certain other organisms. The use of these model organisms allows for comparison of human and non-

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[123]Olson, et al.
[124]U.S. Congress. House, 1988, page 14.

human material, important for studies of evolution; the available of such comparative data also allows for an animal model to be developed for various genetic diseases. In addition, the data allows for experimentation and investigation into regulation and control of genes, features which are likely to be common to all DNA carrying organisms, thus relevant to human disease and health. The organisms include bacteria (*Escherichia coli*), fruit fly (Drosophila melanogaster), yeast (*Saccharomyces cerevisiae*), worm (*Caenorhabditis elegans*), and the laboratory mouse.

Each of these organisms plays a strong role in the history of genetics, with the possible exception of the worm. Early experiments in genetics centered around *E. coli* and yeast, as described earlier. *Drosophila melanogaster*, the fruit fly, was instrumental in understanding mutation and mutagenesis. The mouse genetic map has proven to be an irreplaceable model for human genetics. Their inclusion in the HGP seems a fitting recognition of the role they have played in bringing us to the point where such a project is feasible.

Informatics

Informatics refers to the collection and analysis of data. The collection, storage, and distribution of data fall under the rubric of informatics, and without efficiently addressing these issues, the HGP would likely crumble under the weight of its own data, no useful information coming out at all.

Research Training

The Human Genome Project is a labor-intensive machine, and as such, an adequate supply of researchers is needed to keep the engine rolling. Training, then, becomes an imperative if this long-range project is to

continue. The research training program allots money for pre-doctoral and post-doctoral fellowships. It is this aspect of the HGP--that of training a generation of young scientists--that garners some of the most profuse criticism of the entire HGP. Some people feel that training young scientists to engage in monotonous and repetitive research (a type to which mapping and sequencing certainly belong) will drive the brightest and most creative minds away from biology, and will restrict young professors' ability to obtain funding for non-genome project endeavors.[125] However, many would argue that most experimental science consists of repetitive and tedious elements.

Technology Development

Technology development is crucial if the HGP is to complete its goals on time (fifteen years) and on-target ($200 billion). For these goals to be met, new technologies in the fields of computing, mapping, sequencing, etc. need to be developed in an effort to reduce the time and cost of the project. Estimates of the time and cost of various phases of the project depend on such technology development, and have that development factored in to the estimates of cost and time. For instance, the goal of sequencing the genome in the proscribed length of time requires that the cost of sequencing be reduced by 75 per cent, and that totally automated sequencing be developed in order for the task to be accomplished within the time and money allotted.[126] If such development does not occur, other goals will have to be revised.

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[125]Rechsteiner, 1990 and 1991.

[126]U.S. Congress. House, 1988, page 16.

Technology Transfer

Technology needs to be transferred between the HGP researchers and industry if the fruits of HGP labor are to be realized. Once a gene has been identified as causing a disease, the gene product identified, and the gene sequenced, industry needs to develop the tools needed to put that information into practical use. For instance, if a gene should be found for schizophrenia, industry might be encouraged to develop a screening test for schizophrenia. Without such transfer of information, the HGP is all theory, not the concrete tool for the advance e of medical science it is touted to be.

Ethical, Legal, and Social Implications

In addition to practical problems, social and ethical risks and dilemmas abound in the genome project. Much has been said and made of the ethical considerations brought up by the genome project. The NCHGR is itself concerned with these issues, and devotes between three and five per cent of its annual budget to exploring the area of Ethical, Legal, and Social Implications (ELSI). George Annas, of the Boston University Schools of Medicine and Public Health, retorts that "this amount doesn't show much respect for ethics, law, and public policy."[127] He goes on to point out, though, that

> at 3% of the budget, funding [for ethics] could be $90 million over fifteen years. This is more than has ever been spent on bioethics in the United States...And even the annual budget right now is more money than is being spent on all the other bioethical issues put together.[128]

The ELSI Committee identifies four main areas as falling under its purview: 1) addressing and anticipating "the implications for individuals

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[127] Annas, 1992, page 126.
[128] Annas, 1992, page 128.

and society of mapping and sequencing the human genome;" 2) examining the "ethical, legal and social sequelae of mapping and sequencing the human genome;" 3) stimulating "public discussion of the issues;" 4) development of "policy options to assure that the information is used for the benefit of the individual and society."[129]

In light of these mandates, the committee pursues a variety of activities. The committee wants to "stimulate research on the issues through grants." The Committee will also attempt to "redefine the research agenda" in ethics through workshops, papers, lectures, etc. The Committee wants to "solicit public testimony" through town meetings.[130] In addition, the Committee feels educational materials are necessary for all age levels. One particularly challenging area has been fostering "international collaboration" in the area of ethics. Ethics is an acutely culturally-driven phenomenon, and deriving a common HGP ethics across various cultures has been a challenge already.[131]

The working group has outlined what it sees as the main ethical issues which the project brings up. They conclude that the main issues have to do with confidentiality, prenatal testing, informed consent, and screening and testing. The results of many of the investigations supported by the new funding suggest that the genome project itself raises no ethical issues, that it is only the application of such knowledge which poses problems.[132] Ethicist Marga Vicedo, though agreeing with such an assessment, comments,

> We have to admit, nevertheless, that is it impossible to separate the HGP completely from the use that people will make of the data it gathers. On the one hand, there is not a sharp distinction

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[129]U.S. Congress. House, 1988, page 21.
[130]*Ibid.*, page 21.
[131]Aldhous, P., page 507.
[132]Vicedo, page 255.

> between basic and applied research that allows us to say that the HGP is only basic research. On the other hand, even if such a distinction were possible, it would not be applicable in this case.[133]

The genome project and its applications are inextricably linked. This situation exists both because of the nature of the program and because those in the genome project itself have linked the two in an effort to sell the project. The HGP now must pay the price of having to deal with the ethical issues its applications bring on.

We have talked in general terms about the genome project and its ethical implications. The following chapter looks at the genome project as it specifically relates to schizophrenia. By examining the specific ways that the genome project impacts upon people with schizophrenia, we can address the charge of, Eugenics!

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[133]Vicedo, page 261-2.

Chapter Four:

The human genome project and its implications for schizophrenia

> Emilio is a 40-year-old man who looks ten years younger. He is brought to the hospital, his 12th hospitalization, by his mother because she is afraid of him. He is dressed in a ragged overcoat, bedroom slippers, and a baseball cap and wears several medals around his neck. His affect ranges from anger at his mother--"She feeds me shit... what comes out of other people's rectums"--to a giggling, obsequious seductiveness toward the interviewer. His speech and manner have a childlike quality, and he walks with a mincing step and exaggerated hip movements. His mother reports that he stopped taking his medication about a month ago, and has since begun to hear voices and to look and act more bizarrely. When asked what he has been doing, he says "eating wires and lighting fires." His spontaneous speech is often incoherent and marked by frequent rhyming and clang associations.
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> Emilio's first hospitalization occurred after he dropped out of school at 16, and since that time he has never been able to attend school or hold a job. He lives with his elderly mother, but sometimes disappears for several months at a time, and is eventually picked up by the police as he wanders the streets. There is no known history of drug or alcohol abuse.[134]

Emilio and his mother illustrate several salient aspects of the illness schizophrenia, that is, both the medical and experiential aspects of the condition. From a medical standpoint, he expresses auditory hallucinations, a chronic relapsing and remitting course, bizarre behavior, and loose associations, and an adolescent age of onset. From a social standpoint, he has never been able to hold a job or attend school and still lives with his elderly mother (who seems to be his sole source of support) in the community. He presents now with an acute exacerbation of his schizophrenia, probably due to discontinuation of his medicine. The human genome project, now in its third year of funding, hopes to make discoveries which remedy both the social and medical aspects of Emilio's disease.

As we have seen, the human genome project is the largest coordinated research effort in the history of biology, and the largest such effort in the

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[134]Spitzer et al, page 137.

world today. The HGP has been called "biology's moonshot,"[135] and achieving its goals--the mapping and sequencing of all the DNA in a human nucleus--requires an unheard-of (in biology) expenditure of resources, economic and otherwise. Those promoting the project claim their results will "revolutionize medicine."[136] They feel that their approach represents the most efficient and cost-effective way of achieving the desired results. They claim "the blueprint of humankind"[137] that results from the project will give humans "freedom."[138]

What do these claims imply for patient Emilio and his mother? What can they and others like them hope to gain from the project? What do they fear of the project? What do they want from the project? The answers to these questions are far from simple, and reflect the culture and the times in which the questions are asked and answered. A closer view of the culture of schizophrenia, the culture of the genome project, and the intersection of the two will provide a clearer understanding of the HGP and its implications for schizophrenia, obviously, but also for other multi-genic disorders of which schizophrenia is just one. In addition, it will allow a closer examination of some of the pitfalls and complications of the genome project. Ultimately, it will provide a basis from which we can look at eugenics, and compare the two efforts.

The genome project plans to take a multi-stepped approach to improving the diagnosis and management of genetic diseases, areas where there is much room for improvement. Technically, two or three main steps are involved. Remaining with our case study of schizophrenia, first, they

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[135]Shoop.
[136]Mapping the human genome, page 45.
[137]Shapiro, R.
[138]Baltimore, D., 1992, page 320.

plan to identify the genes for the disease and their chromosomal locations. The second step involves determining the sequence of nucleotide bases which comprises each of the genes. A third step may be taken in which researchers study the genes in one of the animal models associated with the genome project. At this point, each of these steps is theoretical, as no genes for schizophrenia have as yet been identified.

Scientists hope the three steps of mapping, sequencing, and modeling succeed, as such success would lead to a variety of advances in the diagnosis and management of schizophrenia and in the basic understanding of the disease. Again, such diagnosis and management involves several steps, the implications of each will be addressed below. First, successful mapping and sequencing might result in specific diagnostic tests for the symptomatic person. Second, scientists could develop screening tests for the asymptomatic (including pre-conceptive, prenatal, and post-natal screening). Third, discovering the biochemical nature of the disease would allow development of specific drug therapies to treat schizophrenia. Fourth, the sequence information which geneticists decode could facilitate somatic cell gene therapies. Fifth, germ-line gene therapy would allow for parents to opt to eliminate the disease genes from their sperm and eggs, thereby eliminating the risk of transmitting the disease to their children. In turn, each of these changes has effects of its own, which will be explored below.

DIAGNOSIS

The genome project hopes to develop genetic tests for schizophrenia which would aid in the diagnosis of the disease, one which has long been a diagnostic headache, dating back to the 1800s. Before that century, people with mental illness were kept in jails or driven from town to town.

Diagnosis of schizophrenia or any other mental illness was not an issue, as the mentally ill were social outcasts, and their conditions not thought to be medical. Beginning in the nineteenth century, however, the mentally ill were increasingly drawn into the social fold and cared for in new institutions. The new insane asylums enabled doctors to observe people with schizophrenia longitudinally, and contrast their disease course with those of other diseases, like syphilis which also produced psychiatric symptoms. Thus, descriptions of the natural history and clinical course of schizophrenia, precursors to diagnostic criteria, began to appear in the literature in the early 1800s. By the end of the century, many prominent psychiatrists had thus described the major psychiatric illnesses. Kraeplin originally described dementia praecox (precocious dementia) in 1895. Dementia praecox would later be restructured under a new name, schizophrenia. When Kraeplin published his work, however, it was ground-breaking. He described various kinds of dementia praecox, associating certain historical, longitudinal, and symptomatic features with each type of dementia praecox, which were in turn associated with a particular prognosis.

In 1905 the Swiss psychiatrist Eugen Bleuler restructured Kraeplin's nosology, finding that the association of the various types of dementia praecox which Kraeplin outlined were not closely linked to a specific prognosis and were difficult to diagnose. Bleuler emphasized not the clinical course of the sub-types of schizophrenia, but thorough and detailed descriptions of the symptoms associated with each of them. Kraeplin's had been a schema designed to assess *prognosis*, Bleuler's to assess *diagnosis*. Bleuler renamed the disease category, *schizophrenia*, from the Greek, meaning *a splitting of the mind.*

Contemporarily, diagnostic issues continue to be a problem, impeding modern research and assessment, and advances in this area would represent a major achievement of the genome project. Current diagnostic criteria for schizophrenia are strictly clinical, and are culturally-dependent. Studies have repeatedly shown that many of the symptoms of schizophrenia overlap with those of bipolar disease (or manic-depressive psychosis), with which schizophrenia is often confused diagnostically.[139] In Britain, for example, bipolar disease is diagnosed far more frequently than in the United States, where schizophrenia is diagnosed more often. Studies have shown that the difference in diagnostic rates does not reflect a real difference in incidence, but rather a diagnostic bias toward bipolar disease in Britain and toward schizophrenia in the U.S.[140] The new diagnostic criteria in the Diagnostic and Statistical Manual, Third Edition, Revised (DSM III-R) have greatly mitigated the country-based, regional, and individual biases by providing strict diagnostic guidelines, which most countries are now using.[141] However, a universal genetic marker or markers for the disease would help eliminate cultural biases in the diagnosis of schizophrenia.

In a related area, the development of genetic tests for schizophrenia would possibly reconcile another diagnostic debate centered around schizophrenia, that of the "schizophrenia spectrum" disorders. The "schizophrenia spectrum" is a conceptual tool which links schizophrenia to other diseases with which it is affiliated clinically, but marked by a more severe and chronic course. The other diseases in the spectrum are schizotypal personality disorder, schizoaffective disorder, and schizophreniform psychosis. These disorders are linked to each other symptomatically, differing

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[139] Pope, HG, Jr. and Lipinski, JR, Jr.
[140] Solovay, MR, MA Shenton, and PS Holzman.
[141] American Psychiatric Association, 1987.

in the duration and intensity of symptoms, and in some cases, by the nature of the symptoms themselves. The relationship between these diseases has been a mystery for years. Are they related etiologically? Are they related only in the final common pathway? Are they related to each other at all? There are theories on all sides of the fence. Some people feel that the diseases are linked to each other etiologically, differing from one another by their intensity. For instance, if the "spectrum" hypothesis was accepted and a viral etiology discovered, the difference between the spectrum disorders might depend on when the viral infection took place (e.g., if an in utero exposure took place, the child would develop schizophrenia, but if the exposure took place as a child, only schizoid personality disorder would result. Researchers are hopeful that the HGP will potentially resolve the issue of whether they are in fact etiologically related to each other, and if so, in what way. Resolution of this issue would be a major achievement of the HGP and would constitute a significant advance in the area of psychiatric research.

Aside from posing research problems, diagnostic issues have widespread clinical implications which the genome project might resolve. First, current diagnostic criteria require a longitudinal view of the patient; no diagnosis of schizophrenia can be made, according to the DSM-III-R without a six month history of the patient's symptoms. Such criteria are used to differentiate schizophrenia from an acute manic episode, from other psychoses, and from other diseases within the schizophrenia spectrum. The diagnosis has treatment implications, however, and putting off a diagnosis or treating presumptively poses problems. If the genome project was able, then, to develop tests for the disease which could identify those with the gene(s) for schizophrenia in an acute episode, appropriate physicians could commence appropriate treatment right away.

SCREENING

Screening tests represent possibly the major achievement and major threat of the genome project. "Screening" usually refers testing of asymptomatic people, as opposed to diagnostic tests which were discussed above. The two tests may in fact be one and the same, and so the modifiers, "screening" and "diagnostic" refer not to any particular type of test; they refer only to a clinical setting in which the tests are performed. Genetic tests don't require that scientists actually understand the function of the genes involved; they need only know the sequence which is aberrant and its chromosomal location. With these two pieces of information, molecular biologists develop a genetic probe to look for the anomaly. Because schizophrenia is thought to be multi-factorial in origin, these tests would have to cover all the etiologic bases in order for them to be accurate. If certain genetic causes of schizophrenia are as yet unidentified, testing for "the gene for schizophrenia" will produce false negatives. In contrast, as many genes have incomplete penetrance (that is, not everyone with the genotype has the phenotype), the tests would also identify those with the anomaly but who have not or will not develop schizophrenia. Screening tests can be administered to fetuses, newborns, children, or adults, each with its own implications and repercussions. Applied to schizophrenia, each of these settings provides new controversies and resolves others, as will be seen below.

Fetal screening for schizophrenia, if positive for the presence of disease genes, would result in three possible outcomes. First, the pregnant woman could decide to continue the pregnancy and give birth to a child who never develops the disease. Schizophrenia is commonly thought to be incompletely penetrant, so the latter situation is not at all unlikely. On the other hand, the

woman could continue her pregnancy and give birth to a completely normal child who later in life develops schizophrenia, likely as an adolescent. The third eventuality is that the woman decides to terminate her pregnancy. Each of these three options carries its own ethical concerns and practical considerations.

Carrying a pregnancy to term after discovering any genetic defect enables the parents to prepare for the coming child. When the disease gene which has been detected is schizophrenia, however, special considerations apply. There is no way of knowing which children with the genes will develop the disease. These modifying factors are commonly thought to be environmental in origin, and the genome project will serve no purpose in determining the nature of environmental influences. Thus, at birth, all parents know is their child has a gene or genes which predispose to schizophrenia. Do they tell the child? Do they separate themselves from the child because of its "time bomb" quality? Social functioning of people with schizophrenia depends on their level of functioning before the disease presented itself.[142] Will "knowing" modify parental behavior in the direction of decreasing or increasing the social functioning of the child? These questions are unanswerable because the parameters are totally unknown, and the very nature of the questions presupposes that parents don't all act the same. These questions are very important in the case of schizophrenia, however, where issues of stigmatization remain important ones in the lives of those with the diseases and their families.

Is aborting any simpler, though? As the genome project was being conceived and sold to congress, and during its first two years of funding, the White House, the Supreme Court, and a vocal minority of the populace

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[142]Africa, B and Schwartz, SR, page 204.

actively challenged a woman's right to abortion. Under the new political conditions, such a right seems secure. However, the prior situation pitted two federal endeavors at odds with each other, and represented a major conflict within the White House. Despite a new political atmosphere, the conflict over abortion remains intense in our society. Roy declares that abortion gives the genome project "eugenic power."[143] He suggests that use of such power is valuable in that it "relieve(s) parental and familial distress," but goes on to say that "we cannot reasonably ignore the eugenic power delivered by these prenatal diagnostic methods and the information they provide."[144] But is fear of eugenics reason enough to restrict families' choices? James Watson, head of the National Center for Human Genome Research at the NIH says no: "To say that parents must perpetuate things which bring only agony upon themselves and their offspring appears to me to be terribly immoral."[145]

Screening in newborns and children brings on many of the same issues, namely, when and why does the child get told of results? If the child is told, does he or she see himself as a social pariah? Stigmatization clearly is at work in these arguments. What is the purpose of testing an asymptomatic child except as a preparatory measure? Do schools have the right to require testing of children and adolescents just as they require medical examination for admittance? The questions of confidentiality and required testing can be decided by a court of law; each family must resolve the other issues individually.

Asymptomatic adults may get screened as a pre-conceptive measure, to assess risk of passing on any genes for schizophrenia which the parent may

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[143]Roy, page 21
[144]Roy, Page 21.
[145]Watson, JD, 1992, page 323.

carry. Such language is reminiscent of eugenic language in the 1920s and 1930s which described the *cacogenic, parents of potentially defective offspring.* Extreme eugenicists thought these people ought to be sterilized; mainstream eugenicists thought they ought to voluntarily restrict their procreation. Here lies a major difference between the two eras, however. Eugenicists thought they could tell who the cacogenic were, that they could be identified on the basis of physical or mental characteristics and educated. The genome project makes clear that everyone is cacogenic; that we each likely carry multiple genetic diseases in the recessive state. No proscribed course of action can take place, or be expected to take place. The fundamental difference in the power of the science today makes the situation simpler (no assumptions have to be made over who is cacogenic), but more complex at the same time (everyone is cacogenic!).

Controversies over the implications of screening and testing are not peculiar to the genome project. David Galas, head of the genome project for DOE agrees, saying,

> There are no *new* problems. Issues concerning privacy, confidentiality, and discrimination will become much more pressing once the genome project generates the tools to diagnose genetic diseases presymptomatically. The *basic* problems, however, are not new--they will simply be exacerbated.

Leon Rosenberg, a noted medical geneticist and physician, offered a look back at times when similar ethical arguments were posited as come up in contemporary discussions of screening and testing. Rosenberg recalls,

> In the 1960s the issue was newborn screening for genetic disease. To clinical geneticists like me, such screening was a means of early diagnosis, to be followed by effective treatment aimed at preventing serious consequences as in screening newborns for phenylketonuria and putting them on a low phenylalanine diet in order to prevent the mental retardation which is the critical and regular outcome of the untreated disorder. But such

> newborn screening raised for some the issue of stigmatization, discrimination, and prejudice. For others, consequences as dire as genocide were forecast.[146]

To say that these issues are not new, however, is not to deny that they are important and will have expanded importance once the genome project produces results. In addition, neither David Galas nor anyone involved in the genome project would suggest that the issues have been resolved, no matter how old they are.

Rosenberg refers to "stigmatization, discrimination, and prejudice...[and] genocide," and these same issues surface in contemporary discussions of genome project-generated screening and testing for schizophrenia, though often surface in complicated ways. Several differences exist between the potential situation with schizophrenia and that which Rosenberg describes above for phenylketonuria (PKU). First, Rosenberg refers to "effective treatment aimed at preventing serious consequences" of PKU. No such preventive treatment exists for schizophrenia, and none is likely to be available until many years after tests are available, if we follow the model of most genetic diseases. When testing for PKU came out, pediatricians understood the importance of dietary therapy. No such prevention is available for schizophrenia. Second, Rosenberg refers to the "critical and regular outcome" of PKU, namely, mental retardation. Again, schizophrenia does not follow a predictable disease course, and is not completely penetrant. Thus, no uniform statements can be made about a fetus (or newborn) that screens positive for the disease. These examples illustrate that while the ethical arguments are not themselves new, they do represent a new presentation of older concerns, concerns which are highlighted in the case of schizophrenia.

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[146]Rosenberg, LE. Page 113-4.

It is perhaps in the area of stigmatization that schizophrenia stands out most from screening tests for so many other diseases. The genome project's working group on the Ethical, Legal, and Social Implications (ELSI) asks what the "impact of knowledge of genetic variation on the individual" will be, "including issues of: stigmatization, ostracism, labeling, individual psychological responses, including impact on self image."[147] In applying these questions to the disease schizophrenia, it should be immediately apparent that these are sensitive areas. Schizophrenia is a disease which stigmatizes all those who come into direct or familial contact with it. The fact of stigmatization is true for most mental diseases, and distinguishes mental illness from somatic illnesses which are often judgment-neutral. Discovering ways to test for the presence of the genetic defect associated with schizophrenia would likely identify those with the genetic anomaly, but who lack overt symptoms of the disease, as schizophrenia is commonly thought to be incompletely penetrant (that is, not everyone with the anomaly has overt disease). Learning of such carriage could be quite alarming and problematic for many people. Being associated with a disease which carries so much social baggage could lead the identified carrier to feel labeled and stigmatized even without the disease itself. Thus, the development of screening tests for the genes involved would only broaden the reach of such social scarring.

On the other hand, humans, like all other living creatures, have a wide array of genetic polymorphisms, a fact that has been known since RFLP analysis developed in the late 1970s. The genome project will increase the awareness that such a polymorphic state exists, and thus may in fact reduce the stigmatization associated with genetic diseases, or with schizophrenia. Everyone is likely to carry at least one and probably many recessive genetic

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[147]U.S. Congress. House, 1988, page 68.

disease genes, so perhaps exact knowledge of such carriage will reduce the stigmatization associated with such diseases.

Rosenberg's recollection is useful to illustrate another point as well. Many of the ethical questions raised about the genome project require the slippery slope hypothesis for their rationale, as did the threats of "genocide" to which Rosenberg refers. However, as he points out, America began its long trek up the slippery slope many years ago and has yet to slide down. The genome project certainly provides an expanded potential for abuses, but, at least in the ethical arena, provides very little in the way of new concerns. Those who invoke the slippery slope assume we cannot be trusted not to abuse or misuse information gained; that once we embark upon the journey to genetic changes, we will not be able to resist making such changes; nor will we be able to stop ourselves from calling these changes "improvements."

In fact James Watson, head of the National Center for Human Genome Research has already begun using such language when he discusses the importance of keeping state controls away from decision-making in genetic counseling. "No one should be allowed to prevent us from improving our own individual lives and the lives of our children," he says.[148] It is true that schizophrenia is a disease which terrorizes those it affects, and reducing or eliminating the terror would definitely be seen as an "improvement" by those affected. So while genetic "improvement" may raise more than a few eyebrows, and may extend our goals to improvements that are not related to disease but rather to cosmetic or behavioral realms, for schizophrenia, at least, the description seems apt.

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[148]Watson, Los Alamos Science, page 323.

TREATMENT

Pharmaceutical Intervention

Aside from providing diagnostic and screening tests, the HGP projects it will provide specific information needed to create drugs aimed at schizophrenia and its particular defects, whatever those may be. Such therapy would be welcomed by those with schizophrenia (and their families and health care providers), as current drugs, though far superior to those of the 1920s and 1930s, remain only partially helpful, and often leave serious side-effects. Anti-psychotic drugs, also called neuroleptics, have greatly improved the outlook for many of those with schizophrenia. May's group found that neuroleptic drugs bring about, within weeks, a remission of acute psychotic symptoms in ninety per cent of those experiencing an acute break.[149] The way in which these drugs ameliorate the symptoms of schizophrenia is not entirely known. Most such drugs fall into two categories: Phenothiazines (for example, Chlorpromazine) or Butyrophenones (such as Haloperidol, or Haldol®). These drugs help abate an acute psychotic episode, but also clearly help prevent further relapses, reduce chronic symptoms (such as a thought disorder), and improve the functioning of the ill person. Another, distinct drug is Clozapine, a new pharmaceutical whose mode of action is unknown. Clozapine shows some success in cases in which neuroleptics have failed.[150]

These drugs are fraught with side-effects, however, including many permanent and disabling ones. Tardive dyskinesia can be a side-effect of long-term usage of neuroleptic agents, often occurring after such agents are withdrawn for some reason, though rarely it occurs after short term use. It is a motor disorder characterized by uncontrollable movements of the face (lip-

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[149]May, PRA et al.
[150]Kane, J., *et al.*

smacking and grimacing) and body (writhing and flailing of the arms and torso). Neuroleptic malignant syndrome is another side-effect of these drugs, one that is acutely life-threatening. Clozapine has been shown to cause a life-threatening agranulocytosis (a loss of one cell line in the white blood cell series), leading the manufacturer to require weekly blood testing in order to receive a prescription. Luckily these serious side-effects are not extremely common. However, the fact remains that since the true neurochemical nature of schizophrenia (or any other psychosis) is not yet known, the drugs currently available are not pointedly aimed at the neural pathway imbalance that causes schizophrenia.

The genome project, if it is able to provide information leading to development of new drug therapies, would fill a major void in the current treatment options which are all aimed at symptoms of dysfunction rather than causes of such. Such cause-specific treatment as the HGP will enable represents a major departure between the HGP and the eugenics movement, where treatment was not a goal or even an issue. In fact, as you recall, eugenicists actively lobbied against increased treatment for those with schizophrenia, as such treatment was seen to increase the level of social functioning and possibly the reproductive rate as a result. Eugenic therapy was aimed only at curing society of its infestation with schizophrenics, not treating schizophrenia.

Somatic Cell Gene Therapy

Somatic cell gene therapy refers to the insertion of a functional gene into the nuclei of cells which normally express the dysfunctional gene, in this case, the genes for schizophrenia. Somatic cell gene therapy for schizophrenia, then, would likely involve the nerve cells of the brain, as

these are likely to be the cells whose dysfunction or dysregulation causes the symptoms of schizophrenia. Somatic cell gene therapy is currently used for a small number of children with a very rare form of congenital immune deficiency called Severe Combined Immune Deficiency. It is not underway on any larger scale anywhere in the world, and remains almost exclusively experimental in nature.

This form of therapy, once again, departs from that espoused by the eugenics movement. Gene therapy is often referred to as curative, since the dysfunctioning gene is compensated for by the presence of the inserted functional one. Thus, people treated with gene therapy could be totally normal, yet carry the disease genes in their germ cells (egg and sperm) only to pass it on to their children. Once again, gene therapy, as with drug therapy--or provision of social services in the 1920s and 1930s--allows the propagation of those with the disease gene, producing a dysgenic effect on the gene pool, a highly non-eugenic act.[151]

The potential benefits of the HGP are not without practical pitfalls, however. First, half of the genome has already been mapped without sign of any gene for schizophrenia, so discovering such genes may prove to be more difficult than the project coordinators had thought. Second, the leap from discovering a gene or genes--should that happen--to designing treatments based on the known product is a leap of faith, one not always borne out in practice. For instance, the gene for cystic fibrosis has been known for many years without any therapeutic advantage coming from such knowledge up to this point. The situation with Huntington's Chorea has already taught us that the leap from mapping a gene to a chromosome is not always quickly followed by exactly locating the gene and sequencing it, as in the case of

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[151]Fraser,GR.

Huntington's such a leap took ten years to complete. In addition, the genome project's sequencing endeavors have been put on the back burner until the cost of such efforts is brought down by 75 per cent.[152] Lowering the cost will require the development of new sequencing technologies, including increased reliance on automation.

GERM-LINE GENE THERAPY

Technically, germ-line therapy follows the same logic as somatic cell gene therapy, but introduces the functional gene into the reproductive cells of the body; in doing so, germ-line therapy acts not as a treatment for the person on whom it is performed, but rather a preventive measure for that person's future children. Substitution of the functional gene "cleans" the genome of the disease. Because such procedures leave permanent legacies to future generations, and are thus fraught with controversy, germ-line therapy has been disallowed in the United States.

Although germ-line therapy is a strictly hypothetical endeavor in the U.S., it nonetheless brings up several salient questions that arise in discussions of eliminating the gene for schizophrenia from the population. Many people feel that schizophrenia confers a selective advantage to those with the gene but who do not overtly manifest the disease. In order for schizophrenia--a disease which confers reduced fertility and, thus, evolutionary fitness on those who manifest it--to be maintained in the population at the constant rate of one per cent prevalence, (the argument goes) those who carry the gene but are not affected must be endowed with a higher than average fitness. Many have suggested that such an advantage may be enhanced creativity, as evidenced by the great number of artists and

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[152]U.S. Congress. House, 1988, page 21.

musicians felt to be suffering from the disease (van Gough, Michelangelo, Mozart just to name a few). Some have suggested, dating back to the nineteenth century, that *genius* may be a side-product of the schizophrenia gene(s). By eliminating schizophrenia are we eliminating creative genius?

UNDERSTANDING OF SCHIZOPHRENIA

The genome project will undoubtedly make major strides in our understanding of schizophrenia, whether the project is successful in finding genes for the disease or not. Schizophrenia has long been a mystery. Early theories did not equate mental illness with medical problems; rather they reflected spiritual states. More recently, we have seen how those in the 1920s and 1930s conceived of schizophrenia. The 1950s saw a resurgence of psychogenic models of schizophrenia in which "schizophrenogenic" mothers were seen as the causative agent of the disease. This particular theory lived a short but painful life. The 1970s saw the anti-psychiatry movement, and some people suggested that schizophrenia was in fact not a disease, but was a rational response to an irrational world. Theories of the 1980s and 1990s reflect many of the same theories which held sway during the eugenics movement. These theories, and the research that supports them, is discussed below. As will be seen, there is no one theory of schizophrenia, and controversy still reigns supreme, controversy which the genome project might help dispel.

Research abounds in the field of schizophrenia, though as in the 1920s and 1930s, controversy still exists as to whether the disease is caused by: a virus (either *in utero* or childhood exposure); a toxic exposure (again *in utero* or in childhood); a developmental disturbance; or a genetic anomaly. Evidence exists in favor of and against all of the hypotheses. Another way of

looking at the disorder schizophrenia is to determine the final common pathway which defines the disease, rather than the causative agent. For instance, the "dopamine hypothesis" is a very popular hypothesis of schizophrenia.[153] In this theory, schizophrenia results from excessive neuronal release of the neurotransmitter dopamine, a molecule present in all people and related to epinephrine and norepinephrine. Someone with excessive or inappropriate release of dopamine would have the symptoms of schizophrenia. However, the dopamine hypothesis is not particular to any one etiology; one could have a congenitally-excessive release in a genetic etiology, or an acquired excessive release in a viral etiology. Therefore these two schemes for looking at the disease are not mutually exclusive.

The viral hypothesis is an old one, dating back to the previous century. Today the putative agents include retroviruses[154] (which have also been causally identified in both AIDS and cancer) and cytomegalovirus (CMV). These are both DNA viruses, and researchers suggest that the virus integrates its own into the DNA of the host, thereby allowing the infected cell to be improperly regulated. It is postulated that the affected cells are in the central nervous system, and that they alter the regulation of neurotransmitter secretion in the ill person. For instance, if a virus inserts its DNA at the regulatory site of the gene for Tyrosine Hydroxylase, an enzyme which catalyzes one step in the synthesis of dopamine, dysregulation of such synthesis would result. As there are many enzymes in the pathway leading from tyrosine (an amino acid) to dopamine (a catecholamine), there are many insertion sites which could interfere with proper regulation of dopamine. The evidence for the CMV hypothesis, at least, is not particularly strong.

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[153]See, eg, Heritch et al.

[154] See, for example, Coggiano, MA, *et al.*

Moises and colleagues isolated cytomegalovirus (CMV) post-mortem from the temporal lobe of one person with schizophrenia; no CMV was isolated from control brains. They conclude that CMV may be responsible for a few sporadic cases of schizophrenia, but that it does not play an etiologic role in the vast majority of cases.[155]

In addition to these viral theories, some researchers suggest that the disorder may result from an *in utero* exposure to the influenza virus. Mednick and colleagues found in a retrospective study that the incidence of schizophrenia was increased in cases versus controls of fetuses exposed to influenza epidemic in the latter two thirds of gestation.[156] The study design does not allow for proving of causation, but the authors do suggest that further investigations are warranted.

Developmental theories of schizophrenia suggest that the disease results from incomplete or aberrant development in any of several areas. Poor development of "the self" has been proposed by some as an etiology for schizophrenia. The theory suggests that the schizophrenic break occurs in adolescence so often because that is the time when individuation becomes so important. A child's development within the family has also been implicated as a source of disease. Lidz[157] found certain patterns of family dysfunction to be prevalent within the families of those with schizophrenia; Wynne[158] found the nature and content of communication between family members to be limited and contradictory in families of those with schizophrenia, and postulates that this type of overt and covert miscommunication may underlie schizophrenia.

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[155]Moises., *et al.*
[156]Mednick et al
[157]Lidz T and Fleck S.
[158]Wynne, LL.

Several other factors have been associated with increased incidence of schizophrenia. Month of birth definitely confounds the study of schizophrenia in children exposed to influenza in the third trimester because there is a higher incidence of schizophrenia among people born from January to April,[159] the same time as the flu season. This increased incidence in winter is seen in the Southern Hemisphere, as well, during the months corresponding to their winter. Urban life has been consistently associated with increased incidence of schizophrenia for the past hundred years. Pollock[160] found such associations during the thirties, and most recently, Torrey and Bowler[161] have once again confirmed such an association. Low socioeconomic status is consistently associated with increased incidence of the disease[162] as well, though some believe this is an effect of schizophrenia rather than a pre-existing condition.

Genetics has repeatedly and consistently been shown to play a causal role in schizophrenia. Early on it was noted that schizophrenia occurred more frequently in family members of those affected than in the general public.[163] Later, twin studies showed that schizophrenia was more common in the monozygotic (identical) twin of an affected person than in other brothers and sisters. The concordance rate for monozygotic twins ranges between 30 and 70 per cent in various studies.[164] Adoption studies again lent support to a genetic theory, as they showed adopted-away children of mothers with schizophrenia had a higher incidence of the disease than the general population, or than the other children in the new home.[165]

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[159]Africa, B and Schwartz, SR, page 207.
[160]Pollock, 1925.
[161]Torrey and Bowler.
[162]Africa, B. and Schwartz, SR., page 207.
[163]See Rudin, 1930, for example.
[164]Africa, B. and Schwartz, SR., page 208.
[165]Kety, SS. et al., 1971.

Recently, genetic investigations have taken the form not just of family studies, but of inquiries into the molecular genetics of schizophrenia. When Franz Kallman published his treatise on genetics of schizophrenia in 1938, it was instantly the classic text on the subject, and remained so for three or four decades. Only in the 1970s and 1980s did research on the genetics of schizophrenia surpass that which Kallman had written. Starting in the 1970s, researchers began applying the newly developed techniques of electrophoresis, linkage analysis, RFLP analysis, HLA markers, and other molecular genetics techniques to the study of schizophrenia genetics.

Several genetic hypotheses have been generated from these studies. In 1988 Bassett and colleagues published a preliminary communication describing the co-segregation of a partial trisomy of chromosome five and schizophrenia in an uncle and nephew.[166] Their observation resulted in a massive effort to map a "gene for schizophrenia" to chromosome five. In that and the following years, more information came out about tracking schizophrenia to that chromosome, often with conflicting results. Some researchers found confirming evidence of such a linkage[167] while others evidence refuted the hypothesis.[168]

The controversy over chromosome five illustrates one of the primary problems with all research on schizophrenia, a conceptual problem. Early on, schizophrenia was conceived of as *one* disease, with *one* etiology, whether it be genetic, social, infectious, etc. Schizophrenia is now conceived of as being a heterogeneous disease; that is, researchers now feel that there are several ways of the disease that we call schizophrenia, and each etiology is associated with a different means of transmission. This new theory contradicted the

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[166]Bassett, et al page 799
[167]Sherrington, et al
[168]Kennedy, *et al.*

unitary theory of schizophrenia which stated that all those with the disease shared one etiology. As a result of the unitary concept, research often was inconclusive.

The shift in the concept of schizophrenia from a uni-factorial disease to a multi-factorial disease allowed researchers to think about schizophrenia in new ways, but meant that care needed to be taken in doing research about the *diseases* schizophrenia. The story of chromosome five also illustrates this last point nicely. In December of 1988, almost one year after Bassett and colleagues came out with the original theory, Iacono, Bassett and Jones discovered that a certain kind of measurable eye movement co-segregated with schizophrenia and chromosome five. The eye movements--called smooth pursuit--can be measured in anyone by having the subject follow an illuminated dot on a sinusoidal path. Normal subjects are able to smoothly track the moving object. The Kennedy study suggests that chromosome five schizophrenia is associated with an impaired ability to complete smooth-pursuit eye movements. They conclude that screening people for this measurable trait will aid in research because people with chromosome five schizophrenia could be separated from those with other etiologies for their disease.

Members of the schizophrenia community have reacted with cautious optimism to the potential new discoveries coming from the HGP or other such genetic efforts. Kennedy and his group remind us, "It is important in this time of exciting advances in molecular genetics of psychiatric disorders to pay attention to the uncertainties present in the new methods." He defines four areas of uncertainty including errors, assumptions, variability, and bad luck.[169] Shultz and Pato point out another reservation when they suggest that "the gene for schizophrenia has not been discovered as yet, as the

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[169]Kennedy, JL *et al*, 1989, page 388.

popular press would have us think."[170] Nevertheless, researchers do see that the *potential*, at least, is great. Kennedy and his group highlight that potential when they say, "These myriad complexities and potential pitfalls no doubt provide fuel for the skeptics and naysayers. Nonetheless, investigators of the genetics of schizophrenia must forge ahead."[171]

MAGNITUDE OF THE PROBLEM

These issues--diagnostic, screening, therapeutic, preventive, and research issues--take on great importance in schizophrenia because of the magnitude of effect the disease has in our society today. Schizophrenia directly affects approximately one per cent of the population of the United States, totaling over two million people. Eighty thousand new people are diagnosed with schizophrenia in the United States each year, an annual incidence of four per ten thousand.[172] Schizophrenia indirectly affects far more people than just those with the disease, however. The disease profoundly impacts upon the families of those affected. Schizophrenia extracts emotional, social, physical, and financial costs on all those within reach of the disease. Today, long-term hospitalization for schizophrenia is not the standard of care in the US, leaving most people with schizophrenia in the community, either living with relatives, in group homes, individually, or on the street. Federal, state, and local governments, and private insurance companies bear some, but not all, of the financial costs associated with schizophrenia. Families and communities bear the burden of emotional, social, and much of the financial costs. These social, emotional, and financial costs behoove us to do something to allay them.

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[170]Shulz and Pato.
[171]Kennedy *et al*, page 389.
[172]Preface.

Economic Costs of Schizophrenia

Just as in the 1920s and 1930s the economic costs of schizophrenia impacted upon how those in the scientific, lay, and eugenic communities viewed and acted toward people with schizophrenia, so does the economics of schizophrenia impact upon those communities today. In order to explore the issue of monetary cost in schizophrenia, the Division of Mental Health of the World Health Organization (WHO) sponsored a conference in conjunction with the Association for Research into the Costs and Assessment in Psychiatry (ARCAP). The conference, held in Venice, Italy in 1990, brought together economists, psychiatrists, and other health care providers in an effort to increase communication between the groups, and to encourage more rational decision-making in the area of resource-allocation and public policy as it relates to schizophrenia. The WHO and ARCAP effort marked the first time such an attempt had been made to jointly effect policy decisions.

The financial costs associated with schizophrenia are of two types: "direct costs" and "indirect costs."[173] *Direct costs* include such factors as the cost of treatment (including drugs, psychotherapy, electroshock therapy); nursing costs; cost of maintaining people with schizophrenia on supplemental security income or disability; costs of housing in group homes or hospitals; costs of case management; costs of federal, state, and local support to mental hospitals. *Indirect costs* are losses associated with the disease, an estimate of "what might have been." These costs include: lost productivity for the ill individual; lost income; shortened life span. Indirect costs are usually assessed with reference to the affected person only, but as we

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[173]Rice, DP; Kelman, S; Miller, LS; and Dunmeyer, S.

shall see later, the families of affected individuals bear a great burden in paying their share of direct and indirect costs.

Indirect costs are calculated using actuarial tables which take into account the affected individual's sex (men are valued at a higher rate than women), race (Caucasians are valued higher than those of color), socioeconomic status, and other factors. A value is then ascribed to the person's life, assuming they had been able to live it schizophrenia-free. The monetary value of lost productivity and shortened life are then determined. This method may seem strange, and Gavin Andrews rightly points out that this is a "concept repugnant to many who argue that life and suffering cannot be measured in monetary terms."[174] However, such a system is used routinely for a variety of calculations, including arriving at malpractice settlements and assessing the utility of targeted funding for certain health programs. It is worth remembering, however, that the costs of schizophrenia are vast, and not limited to economics.

In contrast to indirect costs, direct costs can be calculated rather obviously. Mental health allocations by the federal government (not including costs for substance abuse) totaled $39.3 billion in 1985, of which McGuire reports that "by far the most costly illness was schizophrenia." Rupp estimates that the total cost of mental illness (including direct and indirect costs) summed to $103.7 billion for the same year,[175] though data for schizophrenia alone were not available. In 1975, the total cost of *schizophrenia* in the US (including indirect and direct costs, and costs paid by all payors) added to $131.5 million, which Andrews points out is half the cost of myocardial infarction (heart attack), "even though schizophrenia is twelve

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[174]Andrews, G, p 389
[175]Rupp, page 401.

times less common than myocardial infarction."[176] Clearly, the costs are devastating to society, and are rising at roughly five times the rate of rise of the Gross National Product.[177]

Complicating the economic picture is the fact that like so many other Americans, those with schizophrenia are often uninsured or underinsured, a situation which frequently leads to undertreatment, and thus increased overall cost of care (as those who are undertreated eventually cost society more than those treated with the standard of care).[178] Historically, Rupp points out, most of the mentally ill were cared for in publicly-funded institutions. With the rise in employer-based insurance policies in the 1950s and 1960s, private insurance companies increasingly took over the care of mentally ill dependents of employees, concentrating on acute psychiatric care. When Medicaid entered the picture in the 1960s, those poor mentally ill gained coverage from that public institution (with mentally ill elders gaining coverage through Medicare, though this older age group contains very few, if any, people with schizophrenia owing to the decreased life expectancy associated with the disease).[179] However, as we shall see, these policies and programs often fail to meet the needs of those with schizophrenia.

Rupp estimates the number of uninsured mentally ill (meaning no private or public insurance) to be 300,000. She includes in this number people who may have insurance for other medical conditions, but who receive no coverage for either in-patient (17.3% of the privately insured) or out-patient (28.6% of the privately insured) mental health services.[180] Rupp defines *under*insurance to be not enough mental health coverage for the degree of

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[176]Andrews, G, page 390.
[177]McGuire, 1991, page 386.
[178]Rupp, A, 1991, p 401.
[179]Rupp, A.
[180]Rupp, A, page 402.

illness. The Bureau of Labor Statistics (BLS) published a report in 1989 documenting the fact that private insurance companies often restricted the number of days allowed in a mental hospital (averaging 30-60 per year) more than those allowed for a physical illness (averaging 120 days, with unlimited days allowed by many carriers).[181] Other plans put the cap on lifetime benefits for mental health services lower than that for physical illness. Ninety-five per cent of plans limited out-patient services in some way (or ways), including limiting the number of visits allowed or the total annual expenditure.[182] Even Medicare and Medicaid limit coverage in this area.[183] The result is that many insurance policies and public programs fail to meet the mental health care needs of those with schizophrenia.

One outcome of uninsurance and underinsurance in the United States is that many of those with schizophrenia don't receive chronic out-patient treatment, and thus, enter the health care system in an acute psychotic crisis at which time the costs more than outweigh the cheaper, out-patient treatment costs. These costs are financial--long-term stays in in-patient facilities cost more than out-patient visits which may have prevented the need for admission--but also extract emotional and physical costs from the ill person and his or her family. Some evidence suggests that as the person with schizophrenia suffers more and more acute breaks, somehow their neural pathways become "burnt out" and the post-crisis functioning deteriorates further with each such break.[184] Social functioning may also decrease after such an episode because, as Moscarelli and Capri suggest, at the point of acute

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[181]Bureau of Labor Statistics.
[182]Rupp, A.
[183]Taube, CA; Goldman, HH; Salkever, D.
[184]Africa, B. and Schwartz, SR, page 204.

psychotic crisis, "the symptoms may be so dramatic that they result in a stigmatization of the patient"[185] and the family.

Another consequence of uninsurance and underinsurance is that families take on more and more of the financial and care-taking burden of the individual with the disease, like Emilio's mother. For parents, the losses could be measured as "lost retirement" or "lost freedom," as many people with schizophrenia require continued parental support throughout their lives. Franks found in her survey that parents (average age 61) of people with schizophrenia spent on average 66.5 hours per week in the care of their child. Such care included housekeeping duties like washing and cooking, recreational activities planned for the patient, chauffeuring the child around, and other activities. In addition, her survey group, mostly middle and upper-middle class white people from Massachusetts, spent what amounted to "virtually all" of their discretionary income on the ill child, who in her group was between 20 and 39 years of age.[186]

While the Human Genome Project may, after many years, improve the outlook for those with schizophrenia, it may also have the untoward outcome of increasing the numbers of uninsurable people. Dorothy Nelkin, who carries a joint appointment in the School of Law and the Department of Sociology at New York University, has strongly suggested that any screening tests developed for schizophrenia will lead to insurance companies demanding testing for potential purchasers, and those testing "positive" for schizophrenia will be ineligible for insurance, or will only be able to purchase insurance that excludes mental health services. Thus, in the short run, the project may add to the problems faced by the schizophrenia community.[187]

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[185]Moscarelli and Capri, page 368
[186]Franks, DD.
[187]Nelkin, D., page 141.

However, the genome project's ELSI group is looking closely at the issue of who gets access to genetic information.

We have seen that schizophrenia extracts a great toll in the United States. It requires a large expenditure of public funds for health care, social services, and incarceration. It extracts an immense personal toll, depriving those afflicted of their lives, their livelihoods, their minds. Schizophrenia demands almost as much from the families of those afflicted in the way of personal freedom, money, and energy. Schizophrenia is in every way a costly disease. We have also seen how our ways of dealing with the disease and those with the disease does not effectively address the issues above. Treatments don't always work, have serious side-effects, and allow chronic symptoms to persist. Insurance doesn't always cover the services needed. Diagnosis is problematic.

The genome project hopes to redress some of these deficiencies by providing effective treatments, possible preventive measures, and diagnostic accuracy. But for as many problems as the genome project solves, it raises just as many dilemmas and ethical concerns. Should testing be provided for schizophrenia before a treatment is available? Should insurance companies, schools and employers be allowed to require testing? Does eliminating schizophrenia mean eliminating creative genius? Does selective abortion of affected fetuses imply "eugenic power," as Roy claims?

Roy is not the only one who makes claims of eugenics when describing the genome project. The question remains, however, whether these claims of eugenics are valid. After looking at both the eugenics movement and the Human Genome Project, it is to this question that we now turn.

Chapter Five:

Eugenic implications of the human genome project: Where did we come from and where are we going?

We have seen how the eugenics movement targeted those with schizophrenia in a particular way: that diagnostic issues were unimportant; that uplifting society was paramount to emancipating individuals from a person living horror. We have also seen how the genome project targets schizophrenia, the disease. We know that those promoting and partaking in the genome project hope to find treatments for the disease, to develop diagnostic tests and screening tests which will allow parents to selectively terminate affected fetuses or prepare for the birth of a child who might develop schizophrenia. We have seen that the HGP claims it is interested in emancipating individuals from the legacy of genetic disease. We have seen some connections between this contemporary effort and that of the 1920s and 1930s, but we have also seen discrepancies. We have seen the historical relationship of eugenics to human genetics; what is the contemporary relationship between the two?

An age-old conflict resurfaces

The twentieth century has seen a revolution of science and technology, propelling American society to a position where we can gain more and more insight and control over ourselves and our surroundings. Typifying this shift in the relationship with our environment is the genetic revolution. The rediscovery of Mendel's Laws at the turn of the century marked the beginning of the genetic revolution, setting into motion the experiments leading to discoveries in classical genetics, then human and organismal genetics. The second half of the century ushered in the era of molecular genetics and modern medical genetics. The genetic revolution marked the shift from a common-sense acceptance of the old adage "like breeds like" to a more sophisticated understanding of why that adage is usually true, and why

sometimes it is not. Today, as we close out the century, we find ourselves one step further along the path of increased genetic knowledge, pursuing the decoding of the entire human genome.

We also find ourselves in the midst of an often-vitriolic debate over the human genome project. Opponents object to the project on practical, financial, and ethical grounds. Proponents argue that the genome project will revolutionize medicine. Most people lie in between, feeling both fascinated by the project and scared of its potential uses and abuses.

Although these conflicted feelings are currently aimed in the direction of the genome project, it is important to recognize that such conflict is not peculiar to the HGP. In fact, the genome project brings up few new issues and fears; rather, it allows for old issues and fears to stir anew. Leon Rosenberg, Dean of the Yale University School of Medicine and a clinical geneticist, remarks that historically, "Every significant application of genetics toward humankind and human disease has been met with enormous interest and equally enormous controversy."[188] Thus we can see that genetics has always evoked a double response in our society: one of awe and one of fear. This combination of awe and fear has been seen throughout history, from the ancient Greek geneticist, Daedulus, who crossed a man and a bull to create the terrifying Minotaur, to recent history, where genes were the slaves of Mengele, to modern times, where the human genome project claims to uncover the "Holy Grail of biology."[189] As a society, we are in awe of the beauty and simplicity of the units which allow the continuance of the long-dead to the now-living and of the now-living to the future-living. At the

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[188]Rosenberg, LE, page 113.
[189]Gilbert, W, 1991.

same time, we live in fear that those same units *define* us, and in defining us, eclipse us.

Genes command the dual responses of awe and fear because of our conflict over the meaning of genes, and the meaning of life. If genes are the determinants of life--after all, only the living and the dead have genes--then we may solve the mystery of life when we solve the mystery of genes. This represents a *reductionistic*viewpoint: who we are is reduced to the genes within our nuclei. Genes allow us insight into ourselves as individuals, our ancestors and descendants; they are tools for self-examination at the most minute level. But a reductionistic viewpoint carries other meanings as well. As George Annas, Director of the Law, Medicine, and Ethics Program, Boston University Schools of Medicine and Public Health, warns: "Human beings are more than merely a collection of their genes, and it is dangerous to see them as such, because when we see them as a mere collection of genes we start thinking that we can do things to human beings that we would not otherwise do."[190] In fact such objectification of human beings has been used throughout the ages when one group of people wishes to oppress another for its own purposes, for instance during the slave trade and in the Nazi regime, to name two heinous examples, when Africans and Jews, respectively, were effectively portrayed as not quite human so that their enslavement and obliteration would not be viewed as inhumane. David Galas, head of the HGP for the DOE dismisses the reductionist argument. He said in an interview for *Los Alamos Science*, a publication of that National Laboratory, that he has

> seen some of the [ELSI grant] proposals submitted to the DOE by the academic community, and in my view, many of them are

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[190]Annas, G, 1992, page 129.

> unnecessary and rather off the mark. For example, I read one proposal aimed at studying the implications of the Human Genome Project for reductionism. Reductionism is a perfectly fine thing to study, but the Genome Project is not anymore reductionist than the rest of biology.[191]

Certainly Galas is correct to point out the HGP did not invent reductionism. He "rather misses the mark," however, in dismissing its importance to the project and its role in creating fear of the project.

In contrast to reductionism, we can also envision our genes in a deterministic way. In this way, genes form our present situation: what we can do, who we can be; and the converse: what we cannot do and who we cannot be. In a deterministic mindset, who we are springs from our genes. Charles De Lisi, a leading proponent of the genome project encourages such a view when he calls the genome the "blueprint of the species."[192] However, David Galas, head of the genome project for the DOE rejects the cries of determinism as being due to genetic ignorance. "Often, without the benefit of a solid background in genetics, people tend to adopt the attitude of naive genetic determinism, that there are good genes and bad genes or that genes alone control behavior."[193] However, unlike his assessment of reductionism, Galas goes on to say that "those misunderstandings have been around a long time, and we have to start dealing with them."[194] Both determinism and reductionism make us uncomfortable because they interfere with our idea of free will; they make us feel that our genes have power over us.

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[191]Galas, David, 1992, page 178.
[192]Schapiro, R.
[193]Galas, D., 1992, page 179.
[194]Galas, D., *Ibid*, page 179

Power relations

If genes hold power, then those who hold the genes--the geneticists--hold tremendous power: power to define, describe, change, and maybe create life. David Roy suggests that geneticists hold true power in our society because "real power accrues to those who know not only *that* a given state of affairs obtains but also know *how* to change that state of affairs."[195] We may wonder, Are geneticists helping us to understand ourselves? Are they creating new life? Are they controlling us? Are geneticists good or evil? In this century, we have had a difficult time answering these questions.

Roy claims that we not only confer power to those who bestow technology, but to those who have "ideas, visions, (and) plans" for the future. He goes on to say that these ideas, visions, and plans

> depend on an ability to define. Those who know how to define have access to considerable power over many things and over human beings. This is no less true of those who set about defining what could be, and it is more true for those who can successfully define what should be.[196]

It seems clear that this latter ability to "define what should be" is one point at which the Human Genome Project diverges from the eugenic efforts in the earlier part of the century. Motivated sometimes by genuine interest in improving the human condition, sometimes by a personal agenda, and often by racist dogma, those in the eugenics movement were supremely concerned with "what should be." They envisioned a Platonic utopia resulting from their endeavors; their goal was societal improvement through individual and group actions. In contrast, while those promoting the HGP claim the project will "revolutionize medicine,"[197] there is no reference to utopia in

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[195]Roy, D, page 15.
[196]Roy, D, page 16
[197]National Research Council, page 45.

any genome project publications. Instead, the rhetoric of the genome project centers around "what could be" for those in reach of genetic disease, but scrupulously avoids discussion of "what should be." Be that as it may, the project clearly assumes that people will act on increased knowledge and, as Watson puts it, allow parents to avoid the "gene that brings total and absolute agony upon [their] descendants."[198]

However, not everyone believes that contemporary geneticists and the genome project blindly embrace the individual choice which differentiates *should* from *could*. Dorothy Nelkin finds that genetic testing will increase our ability to identify genetic deviants, and in so doing, will promote conformity. Nelkin highlights this point when she describes the culture of genetic screening:

> Sanctioned by scientific authority and implemented by medical professionals, tests are an effective means of manipulation; for they imply that decisions are implemented for the good of the individual. They are, therefore, a powerful tool in shaping individual choices in ways that conform to institutional values.[199]

Under Nelkin's analysis the applications resulting from the genome project are comparable to the eugenics campaign earlier in this century in their being means of social control. One might say that eugenicists were mainly interested in controlling people with schizophrenia because they are behavioral deviants; in contrast, the genome project hopes to control people with schizophrenia because of their genetic deviance. However, once again, such a tendency is not peculiar to the genome project; instead, Nelkin feels it is peculiarly American. She claims that in America, as part of our national identity, we are obsessed with information, with data, with technology.

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[198]Watson, JD, 1992, page 323.
[199]Nelkin, D.

Nelkin refers to such a tendency when she describes the American "actuarial mentality" in which "accumulation of data is...an important feature."[200] These tendencies leave us particularly vulnerable to such potentials as the genome project offers.

Nelkin's analysis illuminates another aspect of the debate around the genome project as well. Current attacks on the HGP as being a eugenics effort center around concerns that people will be forced to be tested for schizophrenia (or other genetic diseases) and will be compelled to abort. However, Nelkin correctly points out that the threat with the genome project is not that the public will be forced to accept new genetic screening tests, but that they will demand to have access to them.[201] In fact many biotechnology companies are already stockpiling DNA samples from people who want genetic testing as soon as such tests are available.[202] As a 1991 editorial in Nature suggested,

> At least two different, and apparently contradictory, influences are at work [with reference to genetic screening]. First there is the business of the use of personal genetic information to calculate people's risk of calamity later in life. Second, there is the eugenic inclination stemming from people's wishes that their descendants should be genetically as well-endowed as possible.[203]

In the genome project, in contrast to the eugenics movement, it is the individual who is likely to press for more genetic information rather than an external force imposing such knowledge and actions on the individual.

However, under Nelkin's analysis, end result of social control is very similar between the two time periods. Eugenicists firmly believed that if people with schizophrenia or other genetic diseases were educated as to the

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[200]Nelkin, D, page 136.
[201]*Ibid.*
[202]*Op cit.*
[203]Who needs a genome ethics treaty? page 591.

importance of them not reproducing then they would act accordingly. In modern times, Diane Paul[204] describes how the field of genetic counseling took over the "education" branch of the eugenics movement, and it is with genetic counselors that the post-testing education will take place for those with a gene for schizophrenia. Modern genetic counseling, however, does not involve suggesting or requiring action, merely informing and educating the client as to the likelihood of disease. So while eugenics may be the progenitor of genetic counseling, its means of achieving social control are far more subtle, and do not necessarily represent the direct aims of the genetic counselor, or the state.

Those involved clearly do not support the view that their endeavors are a form of social control, nor do they agree that they resemble those of the eugenics movement. James Watson, Director of the NCHGR, directly addresses this question in an interview for Los Alamos Science, a publication of the Los Alamos National Laboratory at which much of the genome research occurs. Watson says,

> Eugenics is supposed to be a bad word we sort of equate with Hitler. It says we are trying to determine or change the nature of the human germ plasm. The most repulsive aspect of the eugenic efforts in this country and, in particular, in Germany is that eugenic choices were made by the state, often on the basis of very incomplete knowledge...[W]hen we saw what happened in Germany, we decided that eugenics was extremely bad. On the other hand, to say that you can't really make choices to eliminate a gene for Duchenne's Muscular Dystrophy, to say that you want to perpetuate that gene for your descendants, is to be *mad*.[205]

To Watson, the central issue differentiating the genome project from eugenics is who makes the decisions. The end may be the same (attempted

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[204]Paul, DB, Feb 15, 1991, page 1. See also Fraser, FC.
[205]Watson, 1992, page 323.

elimination of disease genes), but as long as the individual makes the choice, Watson is assured. Nelkin would not agree that individuals really are left to make their own decisions.

While Watson may be correct in pointing out one of the major differences between the eugenics movement and the genome project--that of individual choice--he clearly oversimplifies the eugenics movement. To say that eugenics is a "word we sort of equate with Hitler" is to fall prey to the same trap which many opponents of the project fall into, to compare the project to a version of the eugenics movement which did not exist. Why are we so obsessed with eugenics?

Obsession with eugenics

Anthropologist, Paul Rabinow describes the current dialogue around eugenics and its connection to the HGP as being one of *nostalgia*, a phenomenon which he sees as culturally "significant."[206] Webster's defines nostalgia as: "A longing for something far away or long ago or former happy circumstances."[207] The eugenics movement can hardly be considered "happy circumstances," and yet the definition seems to apply. The eugenics movement was something we can all look back at, feel indignant about, and be ashamed of. Geneticists look back at it with other feelings as well, ones of embarrassment that the heroes of their field partook in the activities, that in fact their field was born out of eugenics, though perhaps Watson is not aware of this fact.

The problem with taking the position that everything eugenic is bad, and therefore that anything resembling eugenics is bad, is that it is an

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[206]Rabinow, P.
[207]Guralnik, DB.

untenable stance to defend. Those who long for eugenics so that they can reject it long for a movement which did not exist. As with the genome project today, those living at the time of the eugenics movement struggled with the ethical issues the measures brought up; they weren't sure the motivation was in the right place. They thought some groups might be targeted specifically because of their race or their ethnicity, or their social status. They weren't sure what to do about carriers. They weren't sure the diseases eugenics targeted were in fact genetic. They did not claim to know everything about genetics. They admittedly knew very little of schizophrenia. Things were not cut-and-dried; things were not simple in the 1920s and 1930s. All this is not to say that eugenics was *good*. It is only to say that such terminology cannot accurately be applied to such a complex network of issues. An entire social movement cannot be summarized by asking or answering the question, "Was it *good*, or was it *bad*?"

However, a deeper question begs to be asked. Why do we long for something that repels us? From our late twentieth century vantage point (already rejected as biased), eugenics harkens a time when good and evil were clearly separated from each other; when the line between them was broad, distinct, did not waver or blur in any region. Eugenicists in the twenties and thirties, for their part, struggled with many of the same moral and ethical issues we struggle with today, but in hindsight, their tactics were appalling, their theories embarrassing and simplistic. In other words, we can easily take the position that everything eugenic was wrong, bad, and ignorant, despite the fact the eugenics *the real movement* was far more complicated than this retrospective view suggests.

We feel no such comfort in our position on genetic engineering today. Is genetic screening *good* or *bad*? The complicated nature of the debate is

discouraging. There does not seem to be an answer to the questions the genome project, or other genetic engineering tools, poses. The fact is, if we cannot take an absolute position (*e.g.*, the HGP is the panacea of modern medicine) we cannot feel that we understand what is happening, or be sure that we have taken the right stance. Vicedo also decries the tone of the debate when she says that too often, "The debate about the social implications of the new technologies in genetics [is] set up in terms of global acceptance or rejection."[208] She claims this is "not a fruitful way to pose the question, because both the potential benefits and the potential risks of the HGP are enormous."[209]

The result of all this discussion of whether the genome project is good or evil, whether it is the salvation of the human race or its downfall, is that the real issues brought out by the project are clouded. The subtlety of the project gets lost in the bold and blatant discussions which have gone on. Apparently this situation is not new. Hans Jonas said in his 1974 volume *Philosophical Essays, From Ancient Creed to Technological Man* that our fears of genetic engineering should be not "of its malevolent abuses which, with some watchfulness, one can hope to control, but of its most benevolent and legitimate uses which are the very stuff of its active possession."[210] By concentrating on the "malevolent abuses," those who cry, "Eugenics!" (including Watson) distract us from our work.

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[208]Vicedo, M, page 261.
[209]*Ibid.*
[210]Jonas, H, page xvi.

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