Narratives of Geneticization: Cystic Fibrosis, Diabetes and Schizophrenia

Adam Michael Hedgecoe

University College London

Doctor of Philosophy
ABSTRACT

This thesis examines 'geneticization', which is the process by which genetic explanations for diseases and behaviours become more common and the popularity of these reductive ideas leads to the replacement of alternative, more complex explanations. The assumption for many commentators is that geneticization is a negative process which needs to be highlighted and countered. This thesis critically examines geneticization and reconstructs it as a useful tool for sociological analysis through the way in which genetic explanations are used in medicine, in the case of three diseases: cystic fibrosis, diabetes and schizophrenia. Using discourse analysis of review articles, this thesis constructs different 'narratives' about each of these diseases, and shows how linking a disease to a specific stretch of genetic material alters the classification for that condition. In each case study, I highlight the different discursive strategies adopted to persuade the reader that genetic explanations should be preferred.

In cystic fibrosis (CF), the narrative is one of expansion, with previously unconnected conditions being subsumed under the expanding spectrum of conditions classified as 'cystic fibrosis'. In the case of diabetes, the narrative is one of division, or splitting, with genetic information being used to splinter the disease into a number of sub-conditions. Finally, the narrative in the case of schizophrenia is that of 'enlightened geneticization'. Because of the controversial history of schizophrenia genetics, authors in favour of genetic explanations use a number of different strategies to produce a narrative which appears to acknowledge the role of nongenetic factors in schizophrenia causation, but which prioritise genetic explanations and present schizophrenia as a genetic disease.
ACKNOWLEDGEMENTS

First I would like to thank Brian Balmer and Jon Turney for the help, advice and guidance they have provided over the past four years. They have consistently acted 'above and beyond the call of duty', especially during the early parts of this research, when I was self funding. I am very lucky to have had them as supervisors. Many thanks also to the Economic and Social Research Council who supported part of this work with a Post Graduate Training Award.

Celeste Condit generously sent me pre-publication drafts of several of her articles and helped shape my approach to geneticization in a number of email discussions. Alan Stockdale kindly discussed genetics and cystic fibrosis as did Anne Kerr who also read and commented on a draft of Chapter 4. Many thanks to Professor Sir George Alberti and Professor Harry Keen who both set aside time to talk to me about their experiences of diabetes classification committees. John Waller has read and commented on most of this thesis. His points have always been perceptive and my writing is the better for his help.

Finally, thanks to my parents, who have given me so much support, both emotional and financial, during my studies, and to Sheridan Ward who helped me endure the final stages of this thesis with my sense of humour intact. Even when they did not know what I was doing, they trusted that I did.
Table of Contents

ABSTRACT ....................................................................................................................................................... 2

ACKNOWLEDGEMENTS ....................................................................................................................................... 3

PREFACE ............................................................................................................................................................. 5

CHAPTER 1: GENETICIZATION ............................................................................................................................. 7
  1. THE GENETICIZATION CRITIQUE .................................................................................................................... 7
  2. PROBLEMS WITH GENETICIZATION .............................................................................................................. 17
  3. SHIFTING CONTEXTS: MOLECULARIZATION ................................................................................................. 38
  4. CONCLUSION .................................................................................................................................................. 41

CHAPTER 2: THEORETICAL BACKGROUND ......................................................................................................... 45
  1. THE SOCIOLOGY OF (MEDICAL) SCIENTIFIC KNOWLEDGE ........................................................................... 45
  2. SOCIAL STUDIES OF THE NEW GENETICS ..................................................................................................... 55

CHAPTER 3: METHODS AND METHODOLOGY ..................................................................................................... 64
  1. DISCOURSE ANALYSIS AND SCIENCE STUDIES .......................................................................................... 65
  2. POPULARISATION OF SCIENCE ..................................................................................................................... 80
  3. HERMENEUTICS ............................................................................................................................................. 91

  1. INTRODUCTION ............................................................................................................................................. 107
  2. A BRIEF HISTORY OF CYSTIC FIBROSIS .................................................................................................... 109
  3. THE GENERAL DISCOURSE OF CF .................................................................................................................. 114
  4. CONSTRUCTING CF ...................................................................................................................................... 120
  5. "AND NOT YET A DISEASE": THE 1976 REVIEW .......................................................................................... 122
  6. "AN EXPOSITION OF DETAILED INFORMATION": ANALYSIS OF THE 1996 ARTICLE ....................... 125
  7. WHERE DOES THE NARRATIVE GO FROM HERE? ........................................................................................ 140

CHAPTER 5: DIABETES AND THE NARRATIVE OF DIVISION ............................................................................. 150
  1. INTRODUCTION ............................................................................................................................................. 150
  2. MATERIALS AND BACKGROUND ................................................................................................................... 154
  3. CUDWORTH .................................................................................................................................................... 156
  4. IRVINE ............................................................................................................................................................. 170
  5. EXTENDING THE NARRATIVE ........................................................................................................................ 176
  7. IS DIABETES A GENETIC DISEASE? ............................................................................................................. 183
  8. CONCLUSION ............................................................................................................................................... 190

CHAPTER 6: SCHIZOPHRENIA AND THE NARRATIVE OF ENLIGHTENED GENETICIZATION ..................... 193
  1. INTRODUCTION ............................................................................................................................................. 193
  2. TWIN STUDIES ............................................................................................................................................. 196
  3. ADOPTION STUDIES .................................................................................................................................... 205
  4. MATERIALS FOR ANALYSIS .......................................................................................................................... 214
  5. FEATURES OF ENLIGHTENED GENETICIZATION .......................................................................................... 217
  6. STRATEGIES OF ENLIGHTENED GENETICIZATION ................................................................................... 223
  7. THE APPEAL OF ENLIGHTENED GENETICIZATION ...................................................................................... 244
  8. THE FUTURE OF ENLIGHTENED GENETICIZATION ..................................................................................... 246

CHAPTER 7: REINVENTING GENETICIZATION ..................................................................................................... 248
  1. SYNOPSIS ...................................................................................................................................................... 248
  2. OBJECTIONS ................................................................................................................................................... 249
  3. FILLING IN THE BLANKS: THE CHARACTERISTICS OF GENETICIZATION ............................................. 252

BIBLIOGRAPHY ................................................................................................................................................ 261
This thesis is being completed in the aftermath of the announcement of the sequencing of the 'rough-draft' of the human genome project. Heralded as one of the scientific achievements of this (or any other) century, the Human Genome Project (HGP) will have a long lasting and deeply felt impact. The most obvious area of change, and the apparent reason for this enormous project, is the effect the HGP will have on medicine. But this thesis is not about the effect of the Human Genome Project on medicine, except in a peripheral way. My work looks at how earlier research into the genetics of disease has affected medicine, sometimes in quite unexpected ways, and how we are sometimes unaware of the role that genetic explanations play in how we talk about disease. It does this through focusing on geneticization. This is the process by which genetic explanations for diseases and behaviours become more common and the popularity of these reductive ideas leads to the replacement of alternative, more complex explanations.

The main aim of my research is to analyse the concept of geneticization, and give it more definition and clarity. In addition, I will examine the role of review articles in the construction of facts and the settling of debates within medical science. My final research aim is to confirm the value of discourse analysis as a means of investigating the social and ethical issues of the new genetics. As a methodology, discourse analysis is normally limited to commenting on the science-based effects of how scientists persuade; my research aims to show that it can be as useful in investigating broader social issues as more conventional methods such as surveys and in-depth interviews.

In Chapter 1, I introduce the core topic of my thesis, geneticization, and show its intellectual antecedents as well as explaining why it is of interest to those commentators critical of recent developments in genetics, such as the HGP. I also suggest that it is an idea in need of substantial reworking if it is to be of use in rigorous, productive analysis of the new genetics. I then outline the theoretical background (chapter 2) and methodology for my research (chapter 3), which can simply be described as discourse analysis of medical texts within a broad, social constructionist approach. There then follows the empirical content of this thesis in three chapters looking at the role of
genetics in three different diseases. Cystic Fibrosis (chapter 4) is often seen as a classic Mendelian condition, and a paradigm for genetic testing for disease. My research shows how the discovery of the gene for cystic fibrosis in 1989 changed the classification of this disease, and altered the kinds of patients categorised as having cystic fibrosis. In the case of diabetes (chapter 5), I show how genetic explanations come to be used in a common, complex disorder, and how the different types of diabetes increase in number as result of genetics. My final case study looks at how genetic explanations are used in a condition which is hotly contested, Schizophrenia (chapter 6), and the ground is prepared for the discovery of the gene, or genes, responsible.

The methods used in this research are drawn from the social sciences, yet my own disciplinary background is rooted within philosophy, particularly applied philosophy and medical ethics. In many ways this thesis should be seen as a reaction to the top-down, theoretically heavy approach to medical ethics that dominates current discussions concerning the ethics of genetics. It is partly out of frustration with traditional philosophical methods that I turned towards the social sciences and empirical research (rather than simple supposition) as a way of investigating the role of genetics in medicine. Yet, at its most basic, this research is concerned with ethical questions since disease classifications and the role of genetic explanations in these categorisations can have powerful effects on people's lives.
**CHAPTER 1: GENETICIZATION**

Geneticization is a term with a broad range of meanings which has appealed to a number of critics of the new genetics (Hubbard and Wald 1992, Fitzgerald 1998, Hoedermaekers and Ten Have 1998, Van Dijk 1998, Goodman 1999, Sherwin and Simpson 1999). As used by the sociologist Abby Lippman, it describes a process "in which differences between individuals are reduced to their DNA codes" (Lippman, 1992:1470). It has much in common with other terms such as Rose's 'neurogenetic determinism' or Nelkin and Lindee's 'genetic essentialism', yet despite this wide range of usage, geneticization remains a vague, ambiguous term. In this thesis, I aim to analyse the idea of geneticization, and give it more definition and clarity.

The aims of this chapter are:
- to analyse the term geneticization as used by Lippman and to compare it with alternative concepts;
- present research which questions the validity and strength of assumptions which underpin these ideas;
- produce a 'working definition' to use in my empirical case-studies.

1. **The Geneticization Critique**

To arrive at the central elements of geneticization, I will examine three articles by Abby Lippman: "Prenatal Genetic testing and Screening: Constructing Needs and Reinforcing Inequalities" (1991); "Led (astray) by Genetic Maps: the Cartography of the Human Genome and Health care" (1992); and "The Genetic Construction of Prenatal Testing: Choice, Consent or Conformity for Women?" (1994). All of these articles refer to geneticization, but it is important to note that they do not centre on it. They focus on the...

---


2 With regard to spelling, 'geneticization', 'geneticized' etc. will be spelt with a 'z' since it is a specific term coined by an American author. Other terms, such as 'medicalisation' or 'colonisation' will be spelt with an 's', unless in a quotation.
use of a particular technology (prenatal testing) or metaphor (the map or blueprint). Hence these articles are an attempt to outline various aspects of geneticization, rather than to explicitly explore what the process itself means and what its implications are. This makes the task of presenting what geneticization means harder. In addition, Lippman writes from an explicitly politicised position; either feminist (1991/1994) or a broader, social equality position (1992). This does not detract from these articles. Indeed, part of their appeal and strength comes from the power of the concerns expressed, but the political background to the term geneticization merely provides a context, rather than clarifying exactly what this process involves.

At first glance, the definitions Lippman gives for geneticization vary little between the articles:

- "Geneticization refers to an ongoing process by which differences between individuals are reduced to their DNA codes, with most disorders, behaviours and physiological variations defined, at least in part, as genetic in origin. It refers as well to the process by which interventions employing genetic technologies are adopted to manage problems of health" (Lippman 1991: 19).

- "geneticization [is when] differences between individuals are reduced to their DNA codes, most disorders and behaviours as well as physiological variations are defined as at least in part genetic in origin and the adoption of interventions that employ genetic technologies to manage health is advocated" (Lippman 1992: 1470).

- "Geneticization refers to the ongoing process by which priority is given to searching for variations in DNA sequences that differentiate people from each other and to attributing some hereditary basis to most disorders, behaviours and physiological variations (including such things as schizophrenia and high blood pressure as well as the ability of children to sit still while watching television and of adults to quit smoking)...In this sense, geneticization is a process of colonization with genetic technologies and approaches applied to areas not necessarily—or even apparently-genetic" (Lippman 1994: 13-14).

The first two definitions are for all practical purposes, identical. They both talk about DNA "codes", differences "between individuals" and the extension of genetic based interventions into health. They also both make clear that there are two dimensions to geneticization: the conceptual and the technological. Geneticization involves not just thinking of people in terms of their genetics but also acting on them with genetic technologies. For Lippman, geneticization is not just 'genetic labelling'; it involves how we treat people as well. Another point worth noting is that geneticization is not the same as genetic determinism. It does not require that genetics dominate our lives and rule our
every waking moment, only that "most" conditions be thought of as having, "at least in part", a genetic component. This is not crude, all-powerful genetic determinism that is being described here. As will become clearer from my case studies, it is possible for critics explicitly opposed to genetic determinism to unwittingly adopt a 'geneticized' position.

The two dimensions to geneticization might come into play at this point: we may not think of traits as entirely genetically determined, but one might treat people as if they are. With the explosion of genetic information available as a result of the Human Genome Project (HGP), Lippman's requirements for geneticization could be said to already be present. But there still remains the second half of the equation, the use of genetic based technologies in health. While these types of technology may be present in certain areas of medicine (obstetrics and paediatrics for example) one could argue that we are some way from widespread genetic technologies being used in health care. The fact we are not in the state that Lippman describes as geneticization does not, of course, mean that her ideas are of any less value. It is just that medicine has not reached that stage yet, at least in all its forms. This limited requirement for a genetic component to disease mirrors the fact that a great many more diseases are classed as 'genetic' than would be the case if 'genetic disease' meant a disorder clearly caused by mutation at one identifiable point on the genome (e.g. Huntington's disease):

"Most conditions have a large number of 'causes' and the weight arbitrarily given to any one of them will determine how the condition is classified. This weight will reflect the biomedical as well as the social, political and economic considerations of those who name and assign causes, with power accruing to these diagnosticians and classifiers." (Lippman 1992: 1471).

Lippman's third definition, from 1994, is different, both in its wording, and in the range over which geneticization operates. The most obvious differences: "DNA sequence" for "DNA code"; "hereditary" instead of "genetic" basis for disorders; and the failure to stress health but instead listing two conditions treated as health issues (schizophrenia and high blood pressure) as well as two non-medical behaviours. The first change could be due to a desire to link the idea of geneticization to the Human Genome Project; "sequence" would seem more in keeping with the HGP than code. But she does not mention the HGP by name in this article, and thus it seems an unlikely focus for this
particular phrasing. Perhaps a better reason is that in this article, Lippman is highly critical of metaphors which treat the genome like a "blueprint" or a set of instructions, and diseases as "typographical errors" (Lippman 1994:13). With this the case, the more neutral term "sequence" would seem preferable to the slightly more loaded "code". This change is important, since it marks a new vigilance on Lippman's part to avoid using terms which might inadvertently add to geneticization; in her 1992 article, which is explicitly critical of map and blueprint metaphors in genetics, she freely defines geneticization in terms of "genetic code" (p.1470). The second change, from "genetic" to "hereditary" is less obviously value laden. Hereditary might be a less technical term, but she uses "genetic" elsewhere in the article with no concern about being too technical. Perhaps this change is merely stylistic.

As pointed out, Lippman does not specifically mention "health" as the area into which genetic technologies are expanding; instead, she names conditions which are clearly health related, but which are not obviously genetic. This has the effect of making clear that geneticization is expanding into medical related matters, whilst suggesting that this may not be entirely justified. In addition, Lippman expands the remit of geneticization, by also naming two of those behaviours which although hinted at in the two earlier definitions, are not made specific. Again, she chooses two examples which are (fairly) clearly non-medical, and open to question as to whether they are genetically based. This fully extends geneticization into the area of (non-medical) behaviours, clarifying a position that was only implicit in the earlier definitions. The final sentence of this definition, using the metaphor of colonisation, fulfils the balance present in the earlier two, that of perception and action. The use of genetic technologies to 'colonise' other areas is clearly the complement to the attribution of a "hereditary basis to most disorders", there is again the presence of both conceptual and behavioural, or technological levels. The colonisation metaphor also has implications (commercial drives, the patronisation of the colonised -especially relevant in doctor-patient relations) which mesh well with her concerns in all three of these articles. But this quote also highlights

---

3 although elsewhere in this paper, she tends to avoid using the term.
the moral aspect of Lippman's geneticization. If this process is a form of colonisation, in these post-colonial times, how can it be a good thing?

In addition to the aspects mentioned so far, another theme in the definitions is the divisive aspect of genetics, which Lippman describes as either reducing "differences between individuals" to their "DNA codes" (1991/1992) or giving "priority...to searching for variations in DNA sequences that differentiate people from each other" (1994). The message here is clearly one of solidarity, of not reducing society to individuals, or individuals to their genes. This anti-reductionism is particularly clear in the 1992 article, where Lippman places the use of blueprint metaphors in genetics in the "Cartesian tradition of reductionism", adding to the process of "dismembering 'physical health' itself into separate territories to be divided and conquered" (p.1470). There is an issue here of how Lippman feels we should view the differences between people. Her definitions admit that there are differences (a truism), but it is not immediately clear why viewing such differences in genetic terms is wrong (and the tone that Lippman uses is palpably disapproving). The answer lies, not in the definitions of geneticization she gives, but in the context in which she places such definitions. In two of the articles, (1991/1994), this genetic differentiation is wrong, or at least suspect, because: it allows the construction of new problems for pregnant women (to test or not to test); new ways of condemning them for failing to deal with these problems (the irresponsibility of not being tested); and the extension of certain technologies. In the 1992 article however, Lippman claims that genetic differences are used as an excuse for not intervening in social problems. It is not necessarily that such problems are felt to have a genetic cause, but that concentration on genetics somehow makes such problems too difficult to solve, perhaps by diverting our attention, seducing us with claims of a quick fix. As Lippman wryly notes: "Why is childhood poverty, rather than mapping the genome, considered a 'problem too big for us ordinary mortals to tackle' ?" (Lippman 1992: 1472). So at the conceptual level, geneticization is a means of differentiating between people in a way that is value laden; this differentiation occurs in order to place people in the categories of 'sick' or 'diseased'.

Clearly then, for Lippman, geneticization has the following characteristics:

• A divisive differentiation between individuals on genetic grounds;
• Two levels of effect; the conceptual and the behavioural (how we look at people and how we treat them);
• Rather modest requirements for the extent to which genetics is thought of as determining a disease or disorder, rather than just being causally involved;
• The extension of genetics into health through the use of technology.

Since geneticization is an inherently social process, one cannot divorce it from the social context within which it occurs. Lippman (1991) concentrates on two social factors (gender and class) and shows not only how they shape genetic testing and screening, but also in turn how they are shaped by them. This reflexivity inevitably makes geneticization a far more complex process to investigate than if it were simply 'increased genetic determinism', but in return, lends it greater explanatory power and credibility:

"Life circumstances, broadly defined, establish an individual's place in society. They act, therefore, as powerful restraints on health options from identification of a problem to approaches...to its resolution, and they influence possible options, expectations and responses. These dynamics establish inequalities, the contours/terrain of the society...that will modulate the impact of genetic screening and testing just as the latter may themselves landscape the 'playing-field' and its inequalities" (Lippman 1991: 38).

So perhaps one can add another characteristic of geneticization to those mentioned above:
• Geneticization, according to Lippman, is an inherently social process, and as such affects and can be affected in turn by the social/cultural context within which it takes place, redefining what is taken as social or cultural, and what is taken as natural. The same technologies and attitudes in a different society could have very different results.

Finally, and here I draw on some of Lippman's more recent work, her view of geneticization is as a political process. Geneticization is a political tool, used to raise awareness and stimulate activism around particular technologies:

"The process of geneticization is political because it redefines what we take to be significant differences between people and empowers new people and institutions to make these redefinitions"(Lippman 1998:69).

---

4 "Expansion of prenatal diagnosis techniques...and expanding professional definitions of what should be diagnosed in utero, attest to this technology's role in the process of geneticization" (Lippman 1991:21).
In the light of these features, one criticism of the term geneticization is that it is:

"an overly general description that obscures the fact that contemporary genetics discourse is a permutation of long-standing hereditarian discourses that reflect age-old recognitions by human beings that heredity plays a role in the characteristics of living things" (Condit and Williams 1997: 220).

These authors suggest instead that such a process should be seen in terms of the "medicalized version of hereditarian discourse" (p.221), but it is not immediately clear what advantages such a rephrasing would have. Lippman's articles certainly focus on medical topics⁵ and the fact she does not set her 'case studies' in a broader historical context should not be seen as failure. This is not to deny Condit and William's point that discussion of genetics and biological inheritance did not arrive in the public domain with the advent of molecular biology, but it is to highlight, that for some commentators and critics at least, current developments in the new genetics, and their relationship with medicine and society are both quantitatively and (possibly) qualitatively different to what has gone before.

As I made clear earlier, Lippman herself has distinguished her concept of geneticization from other peoples' ideas. She mentions Edlin's term "genicizing", Yoxen's "construction" of genetic disease and Duster's "prism of heritability". Edlin (1987) describes "genicizing" as the labelling of diseases and disorders as genetic or of "polygenic-multifactoral origin" when there is little or no evidence which suggests that they have any genetic basis. Thus "genicizing" is similar to geneticization in that both allow for diseases to be classed as having an at least partially genetic cause (rather than being wholly genetic). Lippman states that she chose not to use Edlin's term since she wants to 'go beyond' his idea of merely classifying diseases as genetic, to the use and expansion of genetic technologies into health and other areas previously thought of as non-genetic. She makes it clear that this is also the reason that geneticization is different from Yoxen's construction of genetic disease (1982) yet my case studies suggest that

---

⁵ Lippman 1994 for example is exclusively focused on health care technologies (as is Lippman 1998) and is interested in "a number of fundamental concerns related to women's health and health care" (1994:9).
genetic classification can have important impacts on people's lives and that classification cannot be easily separated from more obvious ways of 'doing' things. Perhaps one way of bridging the gap between classifying and doing relies on Lippman's emphasis on power. In her 1992 article, she suggests that, through geneticization, power accrues with diagnosticians and classifiers (Lippman 1992: 1471). This certainly implies a degree of control over patients' lives, yet obvious problems remain with her concept of power itself. Lippman's use seems rather 'top-down' in the sense that power resides with authority figures and is exercised over less-knowledgeable individuals; a Foucauldian perspective presents this as rather simplistic. From this point of view:

"doctors are not considered to be 'figures of domination', but rather 'links in a set of power relations'...it is impossible to remove power from members of the medical profession and hand it over to patients. Power is not a possession of particular social groups, but is relational, a strategy which is invested in and transmitted through all social groups" (Lupton 1997:99).

Paul Rabinow has adopted this perspective when he discusses the concept of 'biosociality' and the way in which patient groups might adopt a genetic perspective as a way of constructing identities (Rabinow 1996b:102-103). As I suggest later, the origins of Lippman's concept mean that geneticization can only be seen in a negative light, and that power can only be applied in a top down, repressive way.

Lippman approves of Duster's concept of the "prism of heritability", the core concern of which is "a way of perceiving traits and behaviors that attributes the major explanatory power to biological inheritance" (Duster 1990: 164, note 2). But only when Duster explicitly outlines the response that results from a particular labelling of a condition as having a genetic cause: "does he begin to incorporate all that I [i.e. Lippman] place under the rubric of geneticization" (Lippman 19991: 19, note 18). This all serves to emphasise the point that geneticization is not only about classifying disorders and behaviours in terms of genetics, but also how we then act on those classifications, how they guide actions and affect other people. This explains why Lippman's articles are not 'about' geneticization in anything other than a tangential sense, why they focus on the technologies and metaphors that stem from looking at the world from a genetic perspective. Rather than just outlining how we classify the world in genetic terms, Lippman seeks to show how this classification affects what we do.
In her discussion of Duster's work, Lippman provides another, slightly more ambiguous view of what geneticization entails:

"Duster captures much of this in describing how prevailing social concerns of our age are leading us to see things through a genetic 'prism'. 'Geneticization' goes further, however, and poses genetics as the source of illumination itself, not merely one of the ways in which it might be refracted." (Lippman 1991: 19)

Even if we remain at the 'conceptual', classifying level of geneticization and compare it to these previously mentioned terms, this description would seem to make geneticization a more basic process than the other definitions. Lippman seems to be saying that these other terms are just concerned with looking at the world in a 'genetic kind of way', whilst her term puts genetics in the position of determining what one can see in the world. This does, however, seem to be far stronger than her other definitions of geneticization; their emphasis is on the power over our actions, rather than our perceptions and classifications. It is not clear whether she intends this analogy to be a definition of geneticization, or merely a counter-point to Duster's prism metaphor. Lippman herself suggests that the best comparison with her ideas could be with medicalisation: "Thus the geneticization of pregnancy is following a trajectory similar to...that described and analyzed eloquently by others studying the medicalization of pregnancy" (Lippman 1991: 41). Later in this chapter, I will address the relationship between geneticization and medicalisation.

Before moving on, I would like to compare geneticization with another alternative term, Nelkin and Lindee's 'genetic essentialism'. This comparison is important since in much of the work criticising Lippman's views, her position is linked with that of these authors. In their book, The DNA Mystique, Nelkin and Lindee analyse the impact of modern genetics on popular culture, and propose a dominant view of genetics in society which they call 'Genetic Essentialism'. There are problems with comparing such a position, based as it is on widespread cultural beliefs, with Lippman's ideas, focused as they are on specific medical technologies and the extension of genetics into health care, but it is possible to outline broad similarities and differences. Genetic Essentialism proposes the gene as a secular, scientific version of the human soul:

"Indeed, DNA has assumed a cultural meaning similar to that of the Biblical soul. It has become a sacred entity, a way to explore fundamental questions about
human life, to define the essence of human existence, and to imagine immortality." (Nelkin and Lindee 1995: 40).

The 'gene' that is the centre of genetic essentialism, is no longer a:

"biological entity...its symbolic meaning is independent of biological definitions. The gene is, rather, a symbol, a metaphor, a convenient way to define personhood, identity and relationships in socially meaningful ways. The gene is used, of course, to explain health and disease. But it is also a way to talk about guilt and responsibility, power and privilege, intellectual or emotional status" (Nelkin and Lindee 1995:16).

Clearly, this makes genetic essentialism broader than geneticization, yet there are striking similarities. Nelkin and Lindee's concept is less well defined than Lippman's, but its main components are:

- A strong form of genetic determinism, where DNA is granted "extraordinary powers of agency and control" over human behaviour (Nelkin and Lindee 1995:196);
- Genetic reductionism, again of a fairly extensive kind (DNA as the secular equivalent to the soul);
- "[E]mphasis on the natural origins of human difference" (p.197), putting marginal social groups at risk of exclusion;
- The stress on 'reproductive control' and technologies.

While these ideas are broader than Lippman's and the emphasis on determinism is stronger, there are similar, complementary, themes running through them. The role of genetic differentiation is again highlighted, as is the importance particular technologies have in strengthening genetic essentialism/geneticization. Genetic essentialism is obviously more deterministic than geneticization, as well as being more reductive. The reality is that they are both used in different contexts; perhaps Nelkin and Lindee’s idea has to be less precise, simply because the subject of their study (popular culture) is so vast and diverse. Lippman, on the other hand, can afford to refine her definition, commenting, as she does, on the narrow confines of medicine (or more accurately, prenatal testing). Perhaps the best approach is to view them as complementary terms, each suited to its own context.
2. PROBLEMS WITH GENETICIZATION

Medicalisation
In the 1970s, a number of commentators grew concerned about the increasing role of medicine in society, a process that became known as 'médicalisation'^. Writers such as Ivan Illich and Irving Kenneth Zola suggested that more and more, medicine was "becoming an institution of social control, nudging aside...the more traditional institutions of religion and law...becoming a new repository of truth" (Zola 1972:487). Such claims are very similar to those made about geneticization by Abby Lippman and other critics of genetics. Clearly, to some extent, she has based her ideas on the work of these earlier writers^7. The aim of this section is to examine medicalisation as a precursor to geneticization, and to suggest similarities and differences which may assist in the analysis of the latter concept. As one might expect, a broad term like medicalisation covers a variety of positions, from the extreme - "The medical establishment has become a major threat to health" (Illich 1990:11)^8 - to milder viewpoints, like those of Renée Fox, who although wary of the extremes that medicine can lead to, is also conscious of the positive role that it has played (Fox 1988). In what follows, I intend to present the 'extremist' case of medicalisation in its fullest form, the criticisms that have been made of such a stance, and the possible lessons that can be learnt for the analysis of the more recent process of geneticization.

The extreme 'medicalisation critique' I intend to examine is derived from the writings of both Illich and Zola. The central theme is that modern western medicine has done little to improve and indeed has often actually been detrimental to, the health of populations. In addition, society has become medicalised, so that it now thinks of most problems and

^6 For another review of medicalisation, see Lupton (1997:95-98).

^7 See Lippman (1991:27 footnote 55): "There is an extensive literature on 'medicalisation'...in which this discussion is rooted and from which it derives its guidance". She then goes on to cite Zola (1972 and 1977). The influence of these authors on her ideas has also been confirmed in personal conversation with Professor Lippman. She also explicitly claims that: geneticization "is likely to be even more problematic than earlier forms of medicalization" (Lippman 1998:70).

^8 Illich's 1990 work Limits to Medicine is the definitive version of his work originally published in 1975 as Medical Nemesis: the Expropriation of health which was revised in the light of comments to produce his later work.
social difficulties in terms of medicine, and solutions in terms of medical treatments. Illich uses the term 'iatrogenesis'⁹ to cover the negative impact of medicine on human health, specifically: clinical, social and cultural iatrogenesis.

Clinical Iatrogenesis concerns the effects (or lack of them) of specific medical treatments. For example:

"The study of the evolution of disease patterns provides evidence that during the last century doctors have affected epidemics no more profoundly than did priests during earlier times" (Illich 1990:23).

And:

"The pain, dysfunction, disability, and anguish resulting from technical medical intervention now rival the morbidity due to traffic and industrial accidents and even war-related activities, and make the impact of medicine one of the most rapidly spreading epidemics of our time" (Illich 1990:35).

Social Iatrogenesis means that: "medical practice sponsors sickness by reinforcing a morbid society that encourages people to become consumers of curative, preventive, industrial and environmental medicine" (Illich 1990:42). Zola explains the process by which this comes about:

"The gradual change of medicine's commitment from a specific etiologic model of disease to a multi-causal one as well as its increasing acceptance of such concepts as comprehensive medicine and psychosomatics has enormously expanded that which is or can be relevant to the understanding, treatment and even prevention of disease" (Zola 1977:52).

To a large extent, social iatrogenesis depends on the particular health provision context a person is in. For example, in large scale medical bureaucracies which induce stress in the individual, the 'process' can be said to be socially iatrogenic (Illich 1990:49), as can the ever-increasing scale of the health budget in most western countries (p.60).

Cultural Iatrogenesis is the final stage, a separate level where:

"the so-called health professions have an even deeper, culturally health-denying effect in so far as they destroy the potential of people to deal with their human weakness, vulnerability, and uniqueness in a personal and autonomous way" (Illich 1990:42).

There is an important role for pain, or suffering, in cultural iatrogenesis which:

⁹ From the Greek; 'iatro' for physician, and 'genesis' meaning origin; hence disease originating with the physician.
"sets in when the medical enterprise saps the will of people to suffer their reality...Professionally organized medicine...has thereby undermined the ability of individuals to face their reality, to express their own values, and to accept inevitable and often irremediable pain and impairment, decline and death" (Illich 1990:133).

While Zola's work is less obviously extreme than Illich's, he is clearly writing in the same vein, focusing on the political and normative strengths of modern medicine (e.g. Zola 1975: 85).

Against Medicalisation

The most obvious criticism of the medicalisation critique is that it is too extreme. Illich seems incapable of making a statement without putting it in the most radical frame, without the use of hyperbole. In 1978, David Horrobin published a blow-by-blow refutation of Illich's claims and I wish to outline some of these points. Horrobin's first point of attack is Illich's tendency to exaggerate: "He seems to be implying that it is better to die early as the result of a stroke than to live a much longer if mildly uncomfortable life as a result of treatment for hypertension" (Horrobin 1978:11). Illich's extreme claims are only possible through a very selective reading of the historical facts involved. For example, he claims that the reduction in death from various infectious diseases has nothing at all to do with medicine or doctors, but depends upon environmental factors such as clean water and sanitation: "For more than a century, analysis of disease trends has shown that the environment is the primary determinant of the state of general health of any population" (Illich 1990:25). Such a claim is true, but ignoring the role of the medical profession in this state of affairs requires a failure of memory:

"Many of the important environmental changes, particularly in the supply of clean water, the safe disposal of excreta and the provision of specific items of diet such as iron and vitamins, were initiated and put into effective use by doctors...A lively interest on the part of the medical profession was almost always important in creating an appropriate atmosphere for advance, even when the eventual causes of the improvement proved not to be specifically medical" (Horrobin 1978:9-10).

Illich's 'selective interpretation' of medical history is also evident in his use of the term 'specific medical treatment' which excludes treatments not given only by doctors. Thus
immunisation, vaccination, anti-malarial drugs and hygiene procedures adopted by midwives are excluded since they do not involve "'medical equipment'" (Illich 1990:29). Although Illich recognises that these procedures were initially started and developed by doctors, they only truly began to reduce mortality "by the incorporation of these procedures and devices into the layman's culture" (Illich 1990:29), and they thus do not really count as medical treatment. Horrobin calls this "the most special sort of special pleading" (Horrobin 1978:10), but the acceptance of such incorporation seems to me even more contradictory than that. Here are procedures that were developed and used by doctors; they gain effectiveness only when they enter the social world, the "layman's culture". This is thus the most blatant form of medicalisation, the introduction and spread of techniques and procedures from the medical profession to the layperson. Surely this is what Illich is trying to oppose. In turn, this position conflicts with Illich's objections to the use of "replacement therapy" (i.e. insulin by diabetics) only a few pages later; surely insulin injections are procedures incorporated into the culture of a specific group of laypersons, i.e. diabetics.

Horrobin's list of Illich's inconsistencies and contradictions last an entire book, and there is certainly not enough space to reproduce them here. What I do want to suggest is that Illich's work is driven by polemic rather than empirical data:

"Although his volume appears to be well documented, a disturbing discrepancy exists between the data presented in many of the works Illich cites in his copious footnotes and the interpretive liberties that he takes with them" (Fox 1988:466).

The most obvious example of this 'interpretive liberty' is Illich's claim that the facts about iatrogenesis are "well repressed" (Illich 1990:23) despite the fact that he relies for much of his data on leading science and medical journals such as the *BMJ*, *JAMA*, and the *New England Journal of Medicine*:

"Most of the evidence on which Illich's polemic is based has therefore been gathered by doctors concerned about the problems of their own profession, and anxious to improve the situation by bringing them into the open...It is exceedingly unlikely that any other profession (certainly not the law) would be as openly self-critical and as careless in the publication of damning evidence" (Horrobin 1978:6).

Much of the exaggeration of the medicalisation critique comes from the fact that it talks about a single entity called 'medicine' and claims that evidence of medicalisation from one
area of medicine (for example mental health), must be true for all areas of medicine, impacting on all parts of society. As Renée Fox has pointed out "Along with progressive medicalization, a process of demedicalization seems also to be taking place in the society" (Fox 1988:477), one example being that homosexuality is no longer classed as an illness by psychiatrists. By regarding all medicine as a single object of study, Illich and Zola lose any sense of subtlety in their criticisms, and open themselves up to the sorts of attack mounted by Horrobin. One example of the blindness to the nature of the role of medicine in society is their belief that the current position of medicine in Western societies is unique, but as Fox points out "in all societies, health illness and medicine constitute a nexus of great symbolic as well as structural importance" (Fox 1988: 472). Anthropologists have carried out a great deal of work into how other societies relate to medicine and disease, and how medicalisation cannot be said to be limited to modern, Western capitalist societies. Indeed, "there are certain respects in which health, illness, and medicine are imbued with a more diffuse and sacred kind of significance in nonmodern than in modern societies" (ibid.).

Many of the failings of the critique stem from methodology, and this has direct relevance with more recent discussions surrounding geneticization. For some, for example in anthropology, it is not that medicalization does not exist, but that it has been analysed in the wrong way:

"I think it is a serious error to simplify and confuse the critique of health and medicine in contemporary society by calling it medicalization. Instead of encouraging this fallacy of misplaced correctness, we need to refine our use of this term and understand medicalization as a complex, multisided cultural and social process. Here empirical studies are crucial....it is essential that we understand medicalization as a most powerful and little-examined contemporary cultural tautology that is best illuminated by actual, detailed ethnographic case studies and systematic rigorous cross-cultural studies" (Kleinman 1982: 47).

Another empirical complaint about the medicalisation critique is its short-term historical viewpoint:

"Critiques by Illich...and others allege a process of expansion of 'the medical' or control by medical professionals. They present a very shallow perspective, usually limited to the United States and to the last few decades [refs.]. The historical scope of an investigation of medicalization needs to be extended back at least to the sixteenth century for a comparison with the premodern paradigm of Greek (or Galenic) humoral medicine that then reigned supreme...In addition comparisons..."
should be made with non-Western traditions to offer understanding of different medical paradigms that 'medicalize'..." (Janzen 1982: 3).

The theme of these objections combines the claim that medicalization is more complex than has been presented by the exponents of the medicalisation critique, that empirically their work leaves much to be desired, and as a result, more work, using varying methodologies is required. Alternative criticisms of the medicalisation critique come from work in the Foucauldian tradition, which casts doubt on the possibility of 'de-medicalisation' and the strategies proposed to allow this (Lupton 1997).

I want to suggest that the current state of the debate surrounding geneticization is open to many of the same criticisms levelled against those promoting the medicalisation thesis twenty years ago. Specifically, I want to argue that: the concept of geneticization is based on a very narrow (and empirically limited) methodology, mainly relying on anecdote and supposition; where the proponents of geneticization are most convincing, it is when they focus on very small areas of interest, rather than addressing the whole of society or popular culture; and there is a great deal of scope, and need, for studies approaching this topic using alternative methodologies.

**Questioning Geneticization**

This section examines the work of Celeste Condit, who in a number of recent publications has cast doubt on geneticization and other associated concepts, such as Nelkin and Lindee's 'genetic essentialism'. In particular, she challenges the claim that the use of deterministic genetic explanations in public is more common now than in the past, or that these explanations are being used increasingly. In addition, she questions one of the main tenets of the geneticization thesis, that the way genetics is described by scientists and the media, has a detrimental effect on the public perception of genetics.

Condit started her research on the assumption that she would confirm the findings of the critics, with whom she shares a general political outlook, which she describes as 'progressive' (Condit 1995: 124). Instead, her research suggests that the critics of genetic...
determinism have consistently over stated their case, for what she suggests are both 'ideological' reasons, and because of poor methodology. The main target of Condit's criticism is *The DNA Mystique: The gene as a cultural icon*, Nelkin and Lindee's wide ranging cultural study of genetics in society. Condit also cites a number of other authors, including Abby Lippman, as targets of her criticism, and in this section, I wish to present her claims, evaluate how convincing they are, and draw conclusions that might influence future study of this topic.

In one study (Condit 1999b), Condit challenges the received wisdom, that using the metaphor of 'blueprint' to describe genes is inherently discriminatory and overly deterministic. She cites concern with this blueprint in Nelkin and Lindee\(^\text{10}\), in Lippman\(^\text{11}\) and Hubbard and Wald\(^\text{12}\). There are two themes to these objections about the use of the blueprint metaphor: first, there is the empirical point that such a description does not accurately describe what genes actually do. It suggests determinism, when genes are not deterministic. Second, such a metaphor *encourages* deterministic interpretations of genetics, in popular discussions of the science: "they identify the 'blueprint' metaphor as one of the significant carriers of this meaning in popular understandings and media representations" (Condit 1999b:172). Such distinctions are felt to encourage discrimination.

Condit's study sets out to test public interpretation of the blueprint metaphor. The particular public she chose was 137 undergraduate students at a southern US university. This choice was partly pragmatic, but she also justifies it on the grounds that:

---

\(^{10}\) There is a section of their book called 'The Blueprint of Destiny': "The popular appeal of genetics -focusing on the 'oracle of DNA', 'the blueprint of destiny'- lies partly in its image as a predictive science" (1995:165).

\(^{11}\) "writers...tend to evoke blueprints...as the predominant metaphor for genes and DNA...[but]...The blueprint is not an appropriate metaphor for human biology...In addition to the reductionism inherent in the blueprint metaphor is a problematic notion of determinism." (1992:1470-1471).

\(^{12}\) "when molecular biologists speak of genes as 'control centers' or 'blueprints', this is testimony to the hierarchical models they use rather than a description of the ways in which organisms function" (1992:64).
"high income, literate persons approaching child-bearing age can be expected to be both major users of genetic technologies and major influencers of public policy, and...they are the most frequent users of print media" (Condit 1999b:172).

The students were presented with one of two different news articles discussing genetics in different lights: either in terms of a 'genetic lottery', or as a 'blueprint'. The results of this study were varied but the main point is that readers of the lottery metaphor saw this discourse\(^\text{13}\) as more deterministic than the 'discourse of medical genetics' that uses the blueprint metaphor. In open ended interviews, only 39 of 137 participants offered deterministic interpretations of genetics, with 58 responses being explicitly nondeterministic. This backs up what Condit describes as:

>a platitude in communication studies, but which is all too often forgotten in more popular discussions of media - that audiences are active readers, who bring their own interpretations and counter interpretations to bear on messages" (Condit 1999b, 172: 8).

Nelkin and the other critics' first mistake seems to be the assumption that everybody jumps in the same direction when presented with the same material.

The 'public' does not necessarily interpret the blueprint metaphor in the same way as the critics do: "audience members saw the blueprint metaphor as relatively open and nondeterministic because they interpreted the blueprint as probabilistic...partial...and as malleable" (Condit 1999b:172). The Oxford English Dictionary defines a blueprint as "A (detailed) plan or scheme; a pattern". In the audience's view "blueprints are simply outlines and plans" (ibid.); "particular features of brick and mortar not only can change a plan, but also can make a substantive difference in the reality of the finished structure itself" (Condit 1999b: 172-173). It may be that this is not the 'correct' (i.e. technical) interpretation of the blueprint metaphor as used by the critics, but correct or not, this is the interpretation of the metaphor used by a large number of Condit's respondents. The critics' position leaves little room for the possibility that such interpretations happen.

This is particularly ironic in the case of Nelkin and Lindee, who explicitly state in the preface to their book: "We assume...an active interaction between text and reader, media and audience. Indeed we stress the diversity of people's interpretations and uses of the gene" (Nelkin and Lindee 1995: ix). This is then followed by a reference to literature on

\(^{13}\) 'Voluntary Hereditarianism' in Condit's terms.
audience reception. But while it is true that Nelkin and Lindee do give examples of the many contrasting, sometimes contradictory, ways in which genetics is presented in popular culture, they do not seem to address the possibility that an audience may interpret something as basic as a blueprint metaphor in anything other than a deterministic way. This undermines the second theme of the critics' objections to the metaphor, that the concept of the blueprint encourages a deterministic view of genetics in the public mind. Such claims from Nelkin, Lippman and others seems to be based on an assumption about how the public interprets particular metaphors, rather than any empirical data.

Another important pillar of the geneticization critique is that genetic determinism, however it is phrased, is on the increase. This may be linked to the Human Genome Project or may be a product of social conditions:

"genetic explanations appear to provide a rational, neutral justification of existing social categories....They are thus a convenient way to address troubling social issues: the threats implied by the changing roles of women, the perceived decline of the family, the problems of crime, the changes in the ethnic and racial structure of American Society, and the failure of social welfare programmes" (Nelkin and Lindee 1995:194).

The point is, that it is getting worse. This belief in an increase is clear in Nelkin and Lindee: "Increasing popular acceptance of genetic explanations..." (p.3); "the popular appropriation of genetics has intensified..." (p.5); "As the science of genetics has moved from the laboratory to mass culture...the gene has been transformed....it has become the key to human relationships...it has become the essence of identity and the source of social difference" (p.198, all emphasis added). In an outline of their work, Nelkin and Lindee write of "the cultural preoccupation with 'bad genes'...[and that] Contemporary narratives often attribute behavior that threatens the social contract to 'bad genes' " (Nelkin and Lindee, 1996: 95). Likewise Lippman's definitions of geneticization require that it is a 'process', and that is increasing over time.

To test the claim that geneticization is getting worse, Condit and her colleagues carried out a review of popular literature, to determine the way in which genetic determinism

---

14 Lippman 1992 starts with an outline of the aims of the HGP and a description of the technologies used (p.1469).
has been portrayed in the mass media, and whether this portrayal has changed over time. The research used the *Readers Guide to Periodical Literature*, to select articles from popular magazines from 1919 to 1995. Fifty articles were chosen from five year blocks (pentades) making up this time period, on the basis of their containing words such as "heredity", "genes", "eugenics", "Defectives" and other such terms. A coding system was then developed to measure the degree and type of genetic determinism featured in the articles, and the articles were coded by three independent paid coders\textsuperscript{16}.

Condit suggests that in this study:

"The general trends indicate that contrary to the claims of the critics, there has not been a significant increase...in the level of determinism in the public discourse about heredity and genetics" (Condit et al. 1998:983).

<table>
<thead>
<tr>
<th>ARTICLES WITH STATEMENTS</th>
<th>1919-31</th>
<th>1945-54</th>
<th>1967-76</th>
<th>1985-95</th>
</tr>
</thead>
<tbody>
<tr>
<td>opposing genetic influence</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8.4%</td>
<td>2.1%</td>
<td>0%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>attributing influence to gene + environment</td>
<td>51</td>
<td>28</td>
<td>41</td>
<td>41</td>
</tr>
<tr>
<td>61%</td>
<td>58%</td>
<td>55%</td>
<td>73%</td>
<td></td>
</tr>
<tr>
<td>attributing influence to gene only</td>
<td>25</td>
<td>19</td>
<td>34</td>
<td>15</td>
</tr>
<tr>
<td>30%</td>
<td>40%</td>
<td>45%</td>
<td>27%</td>
<td></td>
</tr>
</tbody>
</table>

based on Condit et al. 1998:982

Condit also suggests that:

"Change in the type of characteristics that have been attributed to genetic causes has also been in a more progressive direction...there have been statistically significant reductions in attribution of mental characteristics [to genetic causes]...coders found a consistent trend in which fewer statements were made that attributed genetic mental and behavioral characteristics " (Condit et al. 1998: 981).

In addition:

"across time, magazine articles were making more fine distinctions among the relative degrees of genetic influence on different types of conditions. This would appear to represent an increasing sophistication about both the probabilistic character of genetics and the partiality of its role" (Condit et al. 1998:982).

\textsuperscript{15} A full length report of this research can be found in Condit 1999a.

\textsuperscript{16} For a detailed description of the methodology, see Condit et al. 1998.
This would seem to offer empirical evidence opposing the critics’ views, which could be described as not having: "systematically characterized the deterministic components of public discourse about genetics across time, but instead have relied on highly subjective anecdotal impressions" (Condit et al. 1998:979). Lippman escapes much of this criticism since for her, geneticization is less about simple genetic determinism. The increasing role of explanations attributing gene and environment would count, in her definition, as increasing geneticization. In addition, the majority of her criticisms focus on the role of genetic explanations in medical settings; the public representation of genetics is, to some extent, peripheral for her.

This is not to say that Condit regards her approach as foolproof, and there are a number of aspects to her empirical evidence that require mention. First, mass magazines were used because they offer "the largest, most systematic, and most rigorous sample" (Condit et al. 1998: 980) while there are:

"no consistent national indexes for newspapers that span these time periods [i.e. back to 1919], and indexing of single newspapers varies widely...and is relatively recent" (Condit et al. 1998:982).

Problems with other media (such as recorded news programmes and congressional discourse) mean that they were only used to assess how representative the mass media discourse was of broader public discussions (Condit et al. 1998:983). These alternative sources suggest that as a rule, the discourse in newspapers is more deterministic, and that newspapers fail to show the decrease in determinism apparent in the magazine sample (ibid.). This obviously raises questions about how 'influential' different media are, and whether the empirical results that hold true for mass magazines can be used to draw conclusions about other media, where empirical evidence is less available. Condit is aware of these difficulties, but concludes that:

"Taken as a whole, this systematic study of the character and degree of genetic determinism in popular media does not support statements by critics that contemporary attention to genetics represents an increasingly biologistic determinism" (ibid.).

The critics could argue that Condit's study cannot draw conclusions about popular media as a whole, only one segment (and perhaps not the most influential one at that). Condit might reply that even if the other media are more deterministic than mass magazines, all media tend to display the same sorts of patterns in terms of the features attributed to genetic causation (ibid.).
Nelkin and Lindee have objected to this analysis, claiming that this research:

"is an example of the problem of trying to quantitate what is most compellingly understood in qualitative terms. Our study...was not a quantitative study for the precise reason that the counting of such ambiguous and heterogeneous materials provides little insight into the public meaning of science" (Nelkin and Lindee 1998: 662). Unfortunately they do not provide much detail about why counting in such cases is inappropriate. Condit's reply insists that a mixed methodology, both qualitative and quantitative, is the most useful, and that even a qualitative assessment of the same material produces results at odds with Nelkin and Lindee's conclusions (Condit 1998:663). Condit has recently published a book length study combining both qualitative and quantitative approaches (Condit 1999a). When Nelkin and Lindee claim that "The idea of genetic predisposition is often used to explain a common contradiction" (Nelkin and Lindee 1996: 95) there is no attempt to say how often is "often". Although they describe "hundreds of stories in popular magazines, news articles, talk shows, TV programmes, novels and childcare books that define the person as a DNA readout" (ibid.), they fail to show how representative these stories are. There may be thousands of alternative stories, defining the person as a result of a complex interaction of their environment, genes and contingent historical events. Or even extreme behaviourist stories claiming that a person is nothing more than a product of their upbringing. A list of stories tells us nothing about the role they play in our culture, and without any attempt to show the predominance of such stories, the importance of Nelkin and Lindee's analysis is limited. They claim that they "have not compiled quantitative data and do not think it would have been appropriate and meaningful to do so" but fail to elaborate upon the inappropriate and meaningless nature of quantitative data (Nelkin and Lindee 1995: ix); rather than carrying out a "statistical study", they present "an analysis of folklore" (ix). The problem lies not in their analysis, but in the assumption that the folklore that they are analysing is the predominant one in western culture.

A larger problem is that, from within Condit's own position, alternative interpretations of the same data are possible:

"A review of the Readers Guide to Periodical Literature from 1976 to 1982 revealed a 231 percent increase in articles that attempted to explain the genetic basis for crime, mental illness, intelligence, and alcoholism during this brief six-year
period. Even more remarkably, between 1983 and 1988, articles that attributed a genetic basis to crime appeared more than four times as frequently as they had during the previous decade" (Duster 1990: 93).

Duster's study is not outlined in anything like the detail of Condit's, but it does not seem to fit with her conclusions about the apparent steady levels of determinism in mass magazines. One reply might be that Condit's study is far broader, covering a time period almost thirteen times that of Duster's (76 years as opposed to only 6 years), and thus any trends that crop up in Duster's study may in fact be rather localised and minor in the longer term view. Although this is a reasonable point, it is undermined by the fact that the Condit et al. (1998) study is a development of her 1995 work, using a similar methodology, but which looked at only a twenty year time scale, from 1971 to 1991. This produced very similar results to her later study:

"there was no increase in biological essentialism in the public discourse during the period in which medical genetics...began to replace earlier hereditarian [i.e. 1971-1981. Very close to Duster's time period] discourses...In fact, there was virtually no change across time in biologically determinant statements, nor was there an increase in the assignment of biological determinism to behavioral or psychological components" (Condit 1995: 122-123).

Without more information on the methodology used by Duster, it is hard to say whether the apparent incompatibility between these two studies is due to error on the part of one of these researchers, differences in methodology or an underlying problem with quantitative surveys of textual materials. Condit herself has stated in personal communication: "I find the quantitative material on its own to be insufficiently informative, but it has certainly opened my eyes and helped me to deepen my qualitative work in ways I wouldn't have expected." Even if one does not accept Condit's results unequivocally, it is worth noting that both of her studies undermine the received wisdom about aspects of geneticization and genetic essentialism: first that the 'gene as blueprint' metaphor encourages discrimination, second that genetic determinism is increasing in public discourse over time. The results are important for my thesis, not because I will resolve the debate between Nelkin and Condit, but because they underline the fact that geneticization has not been questioned enough.

---

17 Personal Communication 5/12/97.
One conclusion of this debate is that focusing on something as broad and amorphous as 'popular culture' makes analysis hard. As a result, my empirical research will focus on the process of geneticization as it takes place in medicine. I will also be adopting qualitative case-studies rather than broad survey techniques, as a means of clarifying how geneticization takes place. Bearing in mind the above criticisms of Nelkin and Lindee this will mean that I will be limited in making claims about the extent of geneticization across medical practice. It is unlikely that I will be able to say whether medicine is more geneticized now than fifteen years ago. But my approach will allow me to characterise different facets of the geneticization process and compare how it occurs in different conditions.

But just using small-scale case studies is not enough. It is perfectly possible to carry out a detailed analysis of geneticization in one disease, but if the definition of geneticization being used is problematic, then the analysis will suffer. As I have already suggested, Lippman's definition of geneticization is inherently critical of genetic technologies; they are 'colonising' technologies that encourage discrimination. This critical stance is, in large part, due to geneticization's foundations in the earlier process of médicalisation. The way in which the concept of geneticization is constructed and the words which are used to describe it mean that it is difficult to use it in a neutral way. In this section, I will discuss attempts in the literature to use geneticization to analyze two conditions: Breast Cancer and β-Thalassaemia. The aim is to show how the current critique, conceiving of geneticization as a form of médicalisation, limits the possible discussions and hinders satisfying analysis.

**BRCA1: Geneticization and the individual**

In their commentary on the breast cancer genes BRCA1 and 2, Sherwin and Simpson are clear about the negative impact that results from the use of such genetic information. They list "some of the facts about breast cancer which form the starting point of our investigation of the geneticization of a disease which threatens the lives and well-being of millions of women worldwide"(Sherwin and Simpson 1999:121). I wish to challenge the idea that this work provides evidence that breast cancer *as a condition* is currently
subject to geneticization\textsuperscript{18}, and also suggest that the use of geneticization, as it is currently constructed, limits the kinds of debates that can be held about conditions and leads to inconsistencies in argument.

Sherwin and Simpson place our understanding of breast cancer within the 'biomedical model' which they define as how:

"we understand disease as something that affects the body when some internal mechanism becomes disrupted either because of an inborn weakness or flaw or because of some sort of invading alien organism or hostile environment" (Sherwin and Simpson 1999:121).

While they accept that there are some therapeutic benefits to the biomedical approach (Sherwin and Simpson 1999:122) they are "concerned about the ways in which the public as well as the private focus on biomedical solutions tends to interfere with other types of approaches to this (and other) serious public health problems" (ibid.). They worry that "society has yet to respond with appropriate sorts of public health measures...most governments have not provided adequate resources to explore possible environmental, dietary, or social links" (ibid.). This seems odd, since two paragraphs later they complain that "not only are women asked to pay worried and regular attention to their breasts, they are also advised to change lifelong eating habits, develop healthy exercise programs, learn stress management techniques" (ibid.). It seems inconsistent to complain about governments' failure to explore the environmental, dietary and social links with breast cancer, and then bemoan the fact that one needs to put into practice dietary, exercise and environmental changes to avoid breast cancer.

What is also not explained is how these 'external' options avoid re-inforcing the biomedical model, which partly relies on the concept of 'hostile environments'. The idea that environmental effects might cause breast cancer crops up elsewhere in this article (Sherwin and Simpson 1999: 124, 125, 126, 128) yet the authors fail to explain how, if

\textsuperscript{18}ironically, recent research does exist that suggests that public representations of breast cancer (especially T.V. programmes) do focus on genetic explanations (Henderson and Kitzinger 1999). My point is that this is exactly the kind of empirical research required to answer questions about the extent of geneticization in specific conditions. The problem with Sherwin and Simpsons' work is their resolute unempirical approach. For discussion of the need for social science research in bioethics, see: Hoffmaster (1992), Kleinman (1999) and Zussman (2000).
their earlier definition of the biomedical model is accurate, their request for more research into the effect of environmental carcinogens is not strengthening such a model. And this is a problem since "As long as health research is limited to the individualized focus of the biomedical model...the dominant approaches to breast cancer are unlikely to serve women's interest well" (Sherwin and Simpson 1999:128). One solution might be to say that by focusing on environmental factors, one is looking at people in a broad sweep, avoiding the individualization of the biomedical model. Yet a population geneticist looking at the epidemiology of a particular genetic disease could make the same claim. In both cases, individuals are important as soon as one moves into the clinical setting. As soon as doctors begin to talk to a patient, the disease has become individualized. The difference between whether the disease concerned is known to be caused by an environmental factor (discovered by population scale searches for carcinogens) or a specific allele (discovered by population scale searches for a genetic marker) may still be important. But from these authors' analysis, it is not clear how.

Another problem with this article's stance on individualization, is that it silences those people who have found benefit in the BRCA1 test. The authors claim that as a result of biomedicine's individualization of breast cancer, "Many women are easily frightened into a mind-set where they are preoccupied with monitoring their bodies for threatening signs of change" (Sherwin and Simpson 1999:122). They suggest that introduction of the discourse of risk alienates women from the reality of their bodies:

"Those with these mutated genes are told they are at "high risk" of developing breast cancer...what does the term "risk" mean? It represents a statistical difference, but not just any statistical variation. "Risk" is a heavily value-laden term; typically, it connotes fear or anxiety" (Sherwin and Simpson 1999:123-124).

It is hard to incorporate this position with the views of some women who have had the BRCA1 test, and who have had to make decisions on that information. What Sherwin and Simpson fail to highlight is that many of these women know that they are already at risk. The following quotations are taken from two women who were helped by the advent of genetic testing for inherited breast cancer:

"I was a 41-year-old female in a family where four other women first had breast cancer in their mid-thirties to mid-forties....Although I knew that a family history like mine was a risk factor for breast cancer, the source of risk was a nebulous 'genetic predisposition' in my mind'"( Marteau and Richards 1996: 31-32).
Family histories mean that a genetic test can actually be a solution (see for example Lerman et al. 1998). It is not that the BRCA1 and 2 tests are unproblematic. I have written elsewhere about the unethical way in which such tests have been marketed (Chadwick and Hedgecoe, forthcoming). The point is that the discourse of geneticization, as it is currently constructed, does not allow the voicing of such opinions. The failure of the geneticization critique to acknowledge the hereditary nature of much family information has been noted before (Condit and Williams 1997).

Sherwin and Simpson might claim that those women who are helped by the BRCA1 test have 'bought into' the geneticized nature of breast cancer. They do claim that "very little attention is paid to the psychological impact of finding out the status of one's genes" (Sherwin and Simpson 1999:126); this is simply not true. Even the most cursory search of the Medline database\(^\text{19}\) throws up over 100 references to psychological research into genetic testing for breast cancer. There are studies looking at women's perception of risk (Watson et al. 1998, Polednak et al. 1991), differences in opinion between patients and health professionals (Geller et al. 1998), the impact of different therapies on women's fears (Massie et al. 1998, Esplen 1998) and even the differences in attitude between ethnic groups (Hughes et al. 1998). Some, or perhaps all of these studies might support Sherwin and Simpson's position, but by not referring to any of this empirical work they undermine the force of their argument. If what they mean is that 'much research has been carried out, but it is ignored by policy makers' then this too is an empirical claim in need of evidence.

Another example of unsupported claims is: "research funds, both private and public, are primarily directed towards developing further technologies that will bring increased profits to industry" (Sherwin and Simpson 1999:123). This is exactly the kind of statement that requires a reference if it is to be anything other than an expression of opinion. What are the figures for this funding? What is the ratio of public to private? How has it changed over time? The geneticization critique does not make use of this

\(^\text{19}\) Using search terms "psychological" "genetic" and "breast".
kind of information (present in discussions of the commercialization of genetics, for example). The ill-defined, unempirical nature of geneticization as a concept does a disservice to the ideas and motivations that underpin it. There is a need for detailed and rigorous analysis of the way in which genetics affects conceptions of disease and illness. But the extreme, value-laden way in which geneticization is currently constructed makes this harder to do since it already assumes that geneticization is unwelcome and negative.

The clearest example of this is the idea that this article illustrates the geneticization of breast cancer as a disease, rather than the specific, familial version that affects a small percentage of women. The authors' own definition of geneticization states;

"Geneticization is the attitude that the differences among people can be reduced to differences in their genetic makeup; it assumes that most disorders are largely attributable to genetics" (ibid.).

The authors do not show how attitudes towards women with breast cancer (as a whole) have been reduced to genetic differences. Possible evidence of this (newspaper content analysis, reader reception, interviews or focus groups for example) is not cited (see footnote 18). Nor in this article do they present evidence that any other disorder is viewed as 'largely attributable to genetics'. Breast cancer may be undergoing geneticization, but unless evidence is presented, how is one to know? These problems stem directly from the medicalization context from which geneticization is derived. Sherwin and Simpson are limited by their analytic framework. Because their core concept of geneticization is inherently critical of and negative towards genetic technologies, there is no way for them to incorporate alternative positive viewpoints.

β-thalassaemia: Geneticization and autonomy

In their 1998 article "Geneticization: The Cyprus paradigm" Hoedemaekers and ten Have analyse the discourse surrounding screening programmes for β-thalassaemia (Hoedemaekers and ten Have 1998). This recessive blood disorder is very common in Cyprus where over the past 20 years, an extensive screening programme has been built up, testing for the disease and advising patients. Hoedemaekers and ten Have's central claim is that the growth of the β-thalassaemia screening programme in Cyprus has been achieved through overriding and manipulating public opinion towards the disease. I
suggest that starting from the perspective of the geneticization critique, this is the only conclusion one could draw. The concept of geneticization, as currently constructed, does not allow that genuinely autonomous decisions are possible with regard to genetic tests.

Hoedemaekers and ten Have split the history of thalassaemia screening in Cyprus into four parts, with the post 1960s period characterized by the classification of β-thalassaemia as a genetic disease and the introduction of selective abortion as an option for parents (Hoedemaekers and ten Have 1998:277). They describe how public education programmes were set up and how the screening programme was justified in terms of the disease burden on a small society and the impact of β-thalassaemia on families (Hoedemaekers and ten Have 1998:278). They suggest that a new form of medicine, 'genetic medicine', has gained dominance, with an assumption that its goal is the prevention of new thalassaemia patients. This assumption "finds expression in educational strategies which challenge the notion of voluntariness" (Hoedemaekers and ten Have 1998:279). Hoedemaekers and ten Have question whether Cypriot couples really make voluntary decisions regarding prenatal screening and selective abortion. They suggest that far from making these decisions free from external influence, parents in Cyprus are subject to "considerable outside pressure" (Hoedemaekers and ten Have 1998:280) in the form of education about the disease. This 'sensitization' "is a form of (subtle) persuasion, propaganda, or manipulation, with free choice and alleviation of suffering as 'hidden persuaders' " (ibid.). When parents are presented with the option of 'preventing a future sufferer' (i.e. selective abortion) the authors ask:

"what choice do the parents really have? Can we expect them to act autonomously after having been conditioned to avoid a thalassaemic child, either by prevention of conception or by prevention of birth?" (ibid.).

It is not clear what the answer to this question is. The authors themselves do not answer directly, perhaps because there is no evidence to allow an unequivocal reply. They have shown that a thalassaemia education programme was mounted in Cyprus. Couples have increased knowledge about the disease, and the option of selective abortion has been taken up by prospective parents: no numbers are mentioned, but no new thalassaemia cases have been born in Cyprus since 1982 (Hoedemaekers and ten Have 1998:276). The health professionals claim that these couples are making free, autonomous decisions on
the basis of this information. But if one starts from the position of the geneticization critique, then these decisions cannot be free and autonomous, the education programmes must be 'propaganda'. Geneticization is an inherently negative process which occurs:

"institutionally, when genetic expertise is required to deal with problems...[and]...culturally, when genetic knowledge and technology lead to changing individual and social attitudes towards reproduction" (Hoedemaekers and ten Have 1998:275).

The geneticization critique cannot accept that these attitudes are not coerced. They have to be the result of 'manipulation' and 'hidden persuaders'.

The authors complain about health professionals' paternalism but have problems explaining doctors' insistence on patients taking responsibility for their own reproductive decisions which "seems somewhat inconsistent" (Hoedemaekers and ten Have 1998:280). Their solution to this lies in both the general increased emphasis on patient autonomy in Western medicine, and the responsibility that professionals have for policy decisions which reinforce their paternalistic position. They then present examples of how healthcare professionals really do feel responsible for reproductive decisions, none of which are referenced, yet which are presented as empirical evidence. This is typical of the discussions around geneticization; claims are made supported by examples which may or may not be true, since no references are supplied to allow readers to make up their own minds. The authors then confusingly use the fact that individuals (i.e. patients) "are now held responsible for any decision with regard to the use of these genetic technologies" (Hoedemaekers and ten Have 1998:281) as an example of how "public health authorities and screeners cannot avoid responsibility" (ibid.). The authors seem to be implying that genetic technologies have lead health professionals to be more paternalistic by allowing individuals to exercise more of their autonomy. This position is not necessarily inconsistent, but requires more detailed explanation to pick apart the separate threads than is provided here.

Perhaps things would be clearer if Hoedemaekers and ten Have had offered up a definition of what they regard as an 'autonomous' decision in the first place. They suggest that patients cannot make such a decision, since they have been exposed to information and education about thalassaemia. But it hardly makes sense to say that one can only make a truly autonomous decision if one is ignorant of the details of a disease, and of
course Hoedemaekers and ten Have are not implying this. Their position suggests that if the patients had the right information about thalassaemia, then they would be able to exercise their autonomy. The problem is knowing which information or education is right, and how any information Hoedemaekers and ten Have might supply to patients would differ from that currently provided. The authors do not deny that β-thalassaemia is caused by a genetic defect, that it runs in families and that the test for the gene concerned is accurate. The 'propaganda' element seems to lie in the offering of screening and selective abortion, and it is this that underpins the inconsistencies in their argument.

The authors are clearly uncomfortable with the availability of selective abortion in a medical setting. They suggest that: "With the advent of these technologies another step has been taken on the way to institutionalization of abortion" (Hoedemaekers and ten Have 1998:281-282). And that the "integration [of abortion] into medical practice can be seen as another phase in the slowly changing attitudes towards abortion. Its exceptional character is disappearing" (Hoedemaekers and ten Have 1998:282). This change in attitude towards abortion is partly explained by developments in society, both an "increased emphasis on self-determination...[and]...less and less inclination to accept suffering passively if it can be controlled or alleviated in some way" (Hoedemaekers and ten Have 1998:283). The authors' attitude towards abortion is clear in the statement that "The grief and suffering caused by termination of pregnancy is apparently believed to be less intense than the grief of having no children" (ibid.). Yet they present no evidence either way. From their position, coloured by the assumptions that underpin the geneticization critique, it is inconceivable that choosing to not have children could be harder than opting for a termination. Personally I suspect that it depends upon the people concerned and their situation, yet the geneticization critique cannot allow that abortion could be the better decision. One solution to a problem where the 'right' answer is so dependent upon how individuals feel is to allow individuals to make these decisions themselves, but it is precisely the possibility of this autonomy that Hoedemaekers and ten Have are disputing.

Their conservative agenda is apparent when they complain about how respecting autonomy allows the possibility of mistakes being made:
"The great emphasis on autonomous decision-making and free choice with respect to selective abortion creates...at least the possibility that immoral choices can be made. Within the limits of abortion legislation a kind of moral vacuum is created where parents are allowed to take the decision that fit in with their beliefs, attitudes and value-system" (Hoedemaekers and ten Have 1998:285).

Autonomous decision making, which they earlier claimed to be defending against paternalistic healthcare professionals, is now a 'moral vacuum'. It is odd that allowing people to make decisions that 'fit in with their beliefs, attitudes and value-system' is somehow regrettable. The authors then claim that:

"This moral position seems characteristic of the domain of genetic screening and counselling, but is, of course, not universally practised in other societal domains. In everyday life we are usually not allowed freely to pursue our own value-systems" (ibid.).

Such a claim seems to me false. The basis of western liberal democracies is the fact that people are allowed (within limits) to pursue their own value-systems, be they religious, political or ethical. It seems that at its heart, Hoedemaekers and ten Have's position is not opposed to the directive nature of the healthcare professionals' imputed paternalism. In fact, they seem to be proposing a form of paternalism of their own, objecting to the decisions patients are being directed to make, rather than the fact that they are being directed at all. This confused position is, at least partly, a result of the use of geneticization in this analysis. Because of the critical nature of this concept, the authors have to contort themselves into criticising the healthcare professionals' undermining of autonomy. At the same time they themselves object to the role of autonomy in medical decision making. Clearly there is a need to reconstruct the concept of geneticization if it is to be of use in the analysis of health care issues.

3. SHIFTING CONTEXTS: MOLECULARIZATION

As I have already suggested, many of the problems of the geneticization critique stem from the fact that it is derived from and still rooted in the ideas of medicalization. The critical voice of Illich can clearly still be heard in the writings of Lippman, Sherwin and others. Yet the need is now for an analytic concept rather than an activist's rallying cry. It is not that geneticization cannot be used to criticise developments in science and technology, but its current construction, where genetic technologies are a priori wrong,
prevents researchers from carrying out coherent, accurate analysis. One solution is to take geneticization out of the context of medicalization, and shift it towards the idea of molecularization. This has the double advantage of giving a degree of historical background (which geneticization currently lacks) and providing a more neutral perspective than medicalization.

The concept of molecularization has been used by a number of authors to discuss the history of diseases such as sickle cell anaemia (Feldman and Tauber 1997, see also Strasser and Fantini 1998). The editors of a recent historical collection addressing this process define it as: "The identification, production, circulation and uses of molecules in biological research and in the explanation and treatment of diseases" (De Chadarevian and Kamminga 1998:1). Seen in this light, geneticization is merely the latest sub-set in a historical process which has taken place over the past 100 years. Molecularisation has many similarities to geneticization; it works at two levels, the physical and the conceptual:

"First, it is a technical process, in which the complex, refractory stuff of biological reality is broken down into discrete molecular constituents...But secondly, molecularization is also a social and cultural phenomenon, evident in the emergence of a wide range of institutions committed to furthering the process of molecularization in its narrower technical sense" (Sturdy 1998:273).

Like geneticization, molecularization has strong links with industry and how it funds research:

"Molecularization, in the laboratory and the clinic, also had important industrial dimensions. Commercial interests often promoted molecular approaches" (De Chadarevian & Kamminga 1998:10).

The historical perspective on molecularization allows one to step back and see this process in its broader context. It is less overtly critical than the discussions of geneticization although it by no means avoids commenting on the awkward and controversial aspects of molecular science (Paul and Edelson 1998:203).

To illustrate how the context of molecularization can 'fill out' discussions surrounding the role of genetics in disease, let us return to the case of the BRCA1. Sherwin and Simpson's discussion revolved around the idea that the discovery of these genes was a
watershed in the way in which we view breast cancer, and medicine as a whole. Although in keeping with the traditions of the Western biomedical model, they suggest the use of genetic tests for breast cancer is a new and unwelcome development in the individualization of this disease. But the 'genetic model' of cancer is not the first time cancer medicine has focused on the individual and adopted molecular technologies. In his discussion of concepts of viral causation in cancer and their replacement with genetic explanations, Jean-Paul Gaudillière claims that there is more that unites these approaches than divides them:

"By the 1980s...after 30 years of a prosperous life, cancer viruses and cancer vaccines quietly left the stage to be replaced by molecular genetics and the promises of recombinant DNA and modern biotechnology...but...the 'recombinant DNA revolution' of the 1980s was only the most recent among the molecularizations of cancer etiology. Molecularization was not a single process but a series of retrospectively unified 'molecularization practices' which emerged in different places at different times" (Gaudillière 1998:139 and 165).

Seen in this light, the emergence of tests for the BRCA1 and 2 genes is not the revolutionary break that it has been presented as, but more the latest part of a steady process of molecularization. This may not satisfy the critics. The fact that the 'geneticization of breast cancer' can now be set in a richer historical context may not be of interest to those who feel that geneticization is by definition wrong. What it should do though, is suggest that it is possible to reformulate the concept of geneticization in such a way as to be of use in the analysis of science and technology. The definition of geneticization that I wish to use in my empirical research should incorporate elements of molecularization, rather than medicalization, to achieve greater neutrality.

In the case of β-thalassemia, the context of molecularization would blur the differences between the historical phases suggested by Hoedemaekers and ten Have. The third phase that took place in the 1950s when "molecular research revealed that a defect in the formation of globin was the cause of the symptoms" (Hoedemaekers and ten Have 1988:277) would be harder to distinguish from the fourth, genetic phase. Emphasis upon the role of genetic technologies in screening populations would be placed in some form of historical context. From Hoedemaekers and ten Have's article there were clearly screening programmes already in place in Cyprus before the actual genetic defect was identified. By using molecularization, critics would have to specify whether the practices
brought in with genetic technologies are different in kind from molecular screening; and the assumption that genetic technologies are inherently unwelcome will be harder to make.

4. CONCLUSION

I have tried to show that the current concept of geneticization, however useful in raising political awareness and activism, is lacking as a serious analytic tool. Situated within the context of medicalisation, it lacks empirical grounding and clarity. Geneticization can become a useful tool, but what is needed is a more neutral attitude towards this process. It is not that we should avoid criticism of genetic technologies, or blind ourselves to the problems that arise. Its just that going into such analysis with the prior assumption that the use of genetic explanations and technologies is inherently bad prevents a balanced discussion of the pros and cons and an accurate picture of how the process of geneticization takes place.

My attempt to avoid this assumption begins with the reformulated definition of geneticization that I wish to use in my empirical research: 'geneticization in medicine takes place when the disease concerned is linked to a specific stretch of DNA'. At a practical level, this definition allows me to specify particular time-periods of interest, and choose the review articles I wish to analyse. Thus although there are obvious differences in terms of time periods and diseases between the three case studies, comparison is possible, since the materials examined have been chosen on the basis of the same criteria.

My definition clearly places my analysis within the broader process of molecularization; as I suggested earlier, molecularization provides a more neutral context for debates than the medicalisation critique. It thus highlights molecular genetics over other perspectives on heredity. Condit, for one, is critical of such emphasis, but then I am not applying this definition to public perceptions of genetics, but to the discourses in a very small sub-section of the broader public, the medical profession. Whatever the public perception of molecular genetics, medicine certainly regards it as separate and distinct from traditional perceptions of inheritance.
One possible objection from Lippman might be that criticising the concept of geneticization undermines the critique of modern genetics and gives too much ground to those who would push genetic explanations as far as possible. As someone who is broadly sympathetic to Lippman's aims, this is a real concern. But it can be set in context by comparing the position of geneticization with the concept of criminalisation and how it has been used in sociology and criminology. The point of this comparison is not to show that criminalisation operates in the same way as geneticization, or that the same factors drive it, be they sociological, cultural or institutional. It is to suggest that the case of criminalisation provides evidence that you do not need a solid, unexamined analytic concept to say interesting things about social processes. As a sociological concept, criminalisation has been around since the early 1950s and:

"Our understanding of the criminalization process depends on the important case studies regarding laws on theft...juvenile law...alcohol prohibition...marijuana...opiate use...and sexual psychopathy" (Hollinger and Lanza-Kaduce, 1998:313).

Yet despite this wealth of research, "Many theoretical and empirical issues...remain unresolved" (ibid.). Some researchers place the blame for these problems on empirical factors:

"Existing conceptualizations of criminalization tend to neglect the temporal and spatial aspects of criminalization. This is partly because the literature on criminalization is dominated by historically specific qualitative studies that affect criminalization in selected cases" (Grattet, Jenness, and Curry, 1998: 287).

Others lay the blame at the feet of inadequate theoretical considerations: "The criminalization literature reveals no consensus on what criminalization itself entails or means. In fact, very little attention has been paid to the definition of criminalization" (Steury, 1991:335). Yet in claiming that this analytic term is confused, ill-defined and lacking in consensus, researchers are not claiming that it is worthless and should not be used in research. Even the strongest criticism is a plea for more work, not abandonment. When Steury suggests that "Until a more meaningful definition of criminalization is established, support for or refutation of the criminalization hypothesis has commensurably limited value" (Steury 1991: 341), he is not claiming that research should not be conducted on this process. In fact, he is claiming that more work needs to be done; "The analysis presented here is not intended as a test of the criminalization
hypothesis itself. Rather, it is an effort to empirically specify the key term 'criminalization'" (Steury 1991: 336).

Similarly, when my thesis casts doubt on claims about the extent and range of geneticization, I am not rejecting geneticization as an analytic concept. It is rather that, because it has so much potential for helping us to understand the relationship between genetics and society, it needs clarification. Just as Steury is not testing the 'criminalization hypothesis', I am not testing the 'geneticization critique' in terms of how widely it is occurring. The results of my case studies are unlikely to settle the differences between Lippman, Nelkin and Lindee on one side, and Celeste Condit on the other. But they do show what happens when we adopt a specific definition of geneticization. There could be alternative definitions of geneticization. Some might be broader, to take into account general trends in heritability, and others narrower, perhaps not counting a disease as geneticized until its gene has been cloned. The advantage of my definition, which states that geneticization occurs when a medical condition links to a specific stretch of DNA, is that it is largely value neutral. It does not assume that geneticization is necessarily of benefit to medical practice and patients, but neither does it start from the position that geneticization is a priori wrong.

Another objection revolves around the relationship between my stripped down definition and those genetic technologies which are at the forefront of non-scientists' interaction with the new genetics. How does my definition relate to amniocentesis for example? In her detailed, book-length study of prenatal testing and amniocentesis, Rayna Rapp documents the variety of attitudes and problems that surround the use of amniocentesis in detecting (mainly) Down's syndrome (Rapp 2000). This technology has a profound and intense effect on women's lives, and using Lippman's definition, it seems appropriate to say that, for better or worse, these patients are undergoing geneticization\textsuperscript{20}. But

\textsuperscript{20} Rapp herself only uses the term geneticization in reference to broader societal beliefs about differences between individuals. For her it is: "an historically consonant ideology linking individual attributes and social problems as if they could be effectively reshaped or eliminated only in the realm of biomedicine" (Rapp 2000:215). Yet her work ties into Lippman's early use of the term in reference to amniocentesis and other prenatal testing technologies (Lippman 1991 and 1994).
pedantically applying my own definition which focuses on making the link between DNA and a condition means that amniocentesis is not a 'geneticizing' technology, nor can it even be said to facilitate geneticization. Yet technologies such as this are crucial in giving geneticization a widespread social and ethical impact. The disease classification for cystic fibrosis may have undergone geneticization, but it only alters patients' lives when that classification can be accessed through testing technologies. Technologies such as amniocentesis are the conduit through which geneticization enters people's lives, yet the geneticization of diabetes took place, and altered classification systems, independent of these technologies. In this sense my research is exploring discourses and events upstream of such tests, looking at the work that gets done that makes the dilemmas and impacts documented by Rapp possible.

Lippman might claim that my definition is weak and watered down; it lacks the passion and power of her approach. This is true, but I do not want a definition that automatically assumes that genetic technologies are undesirable. A serious sociological analysis of geneticization should not start from the assumption that, as a process, it is regrettable and a negative thing. I hope that my definition still allows me to be critical, and comment on practices that have a negative effect on people's lives, but that such judgements are the result of my analysis, rather than my starting assumptions.
CHARTER 2: THEORETICAL BACKGROUND

1. THE SOCIOLOGY OF (MEDICAL) SCIENTIFIC KNOWLEDGE

Having introduced the topic of this thesis, geneticization, I now wish to place my research within a particular discipline, namely the sociology of science. Over the past twenty years, the various studies of science referred to as the Sociology of Scientific Knowledge (SSK), the 'Edinburgh School' (or 'Strong Programme'), the 'empirical programme of relativism' and actor network theory have had a deep and powerful effect on the history of science (Golinksy 1998) and science and technology studies as a whole (Jasanoff et al. 1995). These schools of thought, which have a largely positive attitude towards social constructivism, presuppose that scientific knowledge itself is a suitable subject for study: how it is generated (or 'constructed'), propagated, and disseminated. All these positions agree that science, and scientific knowledge, is a human activity, and hence is inherently social. These are the grounds for investigating how social factors help produce scientific knowledge.

It would be a mistake to assume that there is total cohesion, or even coherence, among the various approaches that can be linked via social constructivism. For example, as well as non-constructivist critics (such as Laudan 1981) there are those from within this broad approach who criticise aspects of the Strong Programme (e.g. Woolgar 1981a) and, more recently, David Bloor has attacked Bruno Latour's approach to these issues (Bloor 1999). These debates are therefore still current (e.g. Schmaus, Segerstrale and Jesseph 1993), but this is not the place to rehearse them. Of more relevance to this Ph.D. are the debates that have gone on inside medical sociology, which echo much that has taken place in the sociology of science but which should be seen as separate.

Medical sociology has traditionally been seen as a separate discipline, focusing on class and race based health inequalities and, on the sociological aspects of the doctor-patient relationship. But over the past two decades, certainly since Wright and Treacher's The

---

21 For the purposes of this thesis, SSK will act as an 'umbrella' term for the type of research which focuses upon the content of scientific knowledge claims (i.e. non-Mertonian sociology of science).
Problem of Medical Knowledge (1982), those working in medical sociology have become interested in questions about the nature of medical knowledge, and its social construction. This has led to the perception that there are two separate sub-disciplines with greater or lesser overlap: medical sociology and the sociology of medical science (Elston 1997).

Bury vs. Nicholson & McLaughlin

As a way of reviewing the debates in medical sociology over constructivism, I intend to focus on an article by M.R. Bury published in 1986, and the 1987 reply to it written by Nicholson and McLaughlin, which rehearse many of the arguments one finds in criticism and defence of social constructionism22. Bury starts his article by claiming that:

"the number of writings influenced by constructionist precepts has undoubtedly grown in recent years...[and that]...such a trend is developing in medical sociology" (Bury 1986:137-138).

Bury lists the influences on these developments in medical sociology as:

- "Marxian-influenced 'critical theory'...critical social philosophy, particularly that of Foucault...[as well as]...a developing debate within the medical field itself and among wider 'publics' concerning medicine's effectiveness and efficiency" (Bury 1986:139-140).

He suggests that the main features of constructionism in the sociology of medicine are:

- "The 'problematising' of reality...treat[ing] medical knowledge as problematic and as a central issue in analysis" (pp.140).
- "Mediating Social Relations...[where] rather than standing outside of social relations, medicine, not only in its practice, but also in its knowledge base 'mediates' social relations in important respects" (pp.142).
- "Medicine and the neutrality of technique...the technical realm cannot be regarded as neutral...the world of the technical cannot be left to itself in view of the incorporation of significant social and political issues...into its realm" (p.144).
- "The Social Construction of Nature: abolishing 'discovery'...disease categories should not be regarded as signalling the discovery of natural phenomena by the application of neutral and rational methods...claims to the discovery of disease are themselves social events and take place in social contexts" (p.145).
- "The Questioning of medical progress...linear or 'narrative' processes in the history of medicine and in medical progress must be abandoned " (pp.146).

22 Medical Sociologists tend to use the term 'Constructionism'/Constructivist', while Sociologists of Scientific Knowledge tend towards 'Constructivism'/Constructivist'. After Nicholson and McLaughlin (1987:122 Note 1), I intend to assume their semantic inter-changability.
Bury's main objections to constructionism are that:

"little is said in the constructionist literature which faces the problem of accounting for its own perspective and methods. The issue which arises can be simply put: if all forms of knowledge are part of 'discourses' where does that leave constructionism?" (Bury 1986:151).

The fact that constructionism privileges the social dimension over rationality when accounting for types of knowledge:

"places us in a circle from which there appears to be no escape. If rationality cannot be treated as external to social forms, as a means of understanding reality or adjudicating accounts, what methods are available to evaluate books, articles and arguments which put this view forward" (Bury 1986:153).

This is, of course, a version of the classic anti-relativist argument 'if the relativist is right then s/he cannot justifiably convince anyone of the fact'. Bury then moves on from this to the related issue of constructionism's relationship to realism:

"the generative structures of...nature, cannot be totally incorporated into constructionist accounts...social constructionism in the medical sociology field...has largely failed to address this issue, and has weakened its own case as a result" (Bury 1986:153-154).

He then claims that constructionism's relativism undermines existing categories of knowledge, making them dispensable, "for why should one interpretation or construction prevail over any other, if they disclose or discover no aspect of an independent reality" (pp.156). In addition, Bury claims that the intellectual resources drawn on by social constructionism are so varied and diverse as to be incompatible:

"Containing Foucault and Kuhn, for example, under the same roof is quite a task, and it is even more difficult to shelter Foucault and medical writers like Cochrane and McKeown who stand poles apart" (Bury 1986:161).

Realism

Nicholson and McLaughlin's reply to Bury criticises his overly negative assessment of constructionism (Nicholson and McLaughlin 1987:107). They begin their defence by dismissing Bury's objections to constructionism as a heterogeneous approach covering sometimes contradictory positions: "This is of course completely true and may be instantly conceded" (Nicholson and McLaughlin 1987:109). But this is, of course a generalisation for the whole area of social constructionism and:

"existence of a wide diversity of opinion is not proof that everyone is mistaken...Any examination of belief should take care to locate the belief systems
under study precisely to the specific groups and individuals who employ them" (Nicholson and McLaughlin 1987:110).

This underlines Bury's main fault which is to inflate the characteristics of a small sub-set of social constructionism to stand for the approach as a whole. As has been pointed out, in the sociology of science, social constructionism is a very broad church, and by no means all social constructivists agree on how to study science (Atkinson 1995:43. See also Sismondo 1993).

Nicholson and McLaughlin raise objections to Bury's claim that social constructionism "cannot fully acknowledge the importance of input from external physical reality" by suggesting that:

"one need not deny that a photograph of the interior surface of one of the cavities of the brain is a photograph of something which is not wholly an artefact - even if the objects photographed could be named and conceived of differently...even if a medical photograph is itself a conventional representation, the making of which requires years of training and specific socialisation" (Nicholson and McLaughlin 1987: 110 - 111).

Bury has replied to this, claiming that Nicholson and McLaughlin caricature him, and that he:

"find[s] nothing remarkable in the view that medical knowledge is influenced and shaped by social circumstance. What I was pointing to was the limits of 'over-socialised' versions of this approach, where biological realities are completely excluded from the picture" (Bury 1987: 440).

Yet this defence misses one of the points about the role of reality in social constructionism, which is that if one wants to explain differences in human knowledge, the most productive approach is not to focus on reality, since:

"reality is, after all, a common factor in all the vastly different cognitive responses that men produce to it. Being a common factor is not a promising candidate to field as an explanation of that variation" (Barnes and Bloor 1982:34).

In addition, it is never clear in Bury's critique of constructionism when he is talking about characteristics of constructionism as a whole and when he is referring to specific brands of constructionism, as in the conclusion where he claims to have "shown that there are several quite distinct types of constructionism, with varying degrees of friendliness towards each other" (Bury 1986:164). Constructionism's inability to "disclose or

---

23 for example the section called "The main strands of constructionism" (Bury 1986: 140-148), where he distils out what he sees as the defining features.
discover [any] aspect of an independent reality" (Bury 1986:156, line 6) "arises directly from constructionism's relativistic stance" (ibid., line 4). And Bury is quite clear that relativism is one of those "common themes and propositions" (Bury 1986:164) true for all breeds of social constructivism. As Atkinson states:

"There is...absolutely no need for a constructivism to adopt a naive idealism any more than there is for Bury or other critics to endorse a vulgar materialism....a constructivist view does not imply that social actors whimsically conjure reality out of thin air....It is necessary to remind oneself that the 'social construction of reality' does indeed refer to social processes; that it refers to collective acts, not to individual, much less private cognition. It is not a solipsistic view of reality construction. It is sometimes less easy, however, to remind oneself, or critics like Bury, that the collective acts of reality construction are themselves material" (Atkinson 1995:43).

Reflexivity

Nicholson and McLaughlin also take exception to Bury's attack on constructionism's apparent failure to acknowledge reflexivity, summed up by them as "if all knowledge is socially caused, then the beliefs of social constructionists are socially caused, and therefore such beliefs cannot be accorded the status of real knowledge" (Nicholson and McLaughlin 1987:113). In addition to this theoretical point, Bury claims that "social constructionism in the medical sociology field...has largely failed to address this issue [of reflexivity] " (Bury 1986:153) which is at the very least disingenuous. While this might be true for work limited to constructionism in the sociology of medicine, even writing in 1986, one can hardly claim this for SSK at large. Since Bury is quite willing to look outside the sociology of medicine to find examples of what he sees as the iniquities of social constructionism, it seems a little one-sided not to do the same in order to find examples of researchers in SSK addressing the topic of reflexivity. As Nicolson and McLaughlin note "Bloor...[even]...makes reflexivity one of the four essential tenets of his 'strong programme' " (Nicolson and McLaughlin 1987:116). Thirteen years later, some might say that researchers have taken debates surrounding reflexivity in the construction of knowledge to their logical conclusion (see Ashmore 1989 for an example of this).

Nicolson and McLaughlin's solution to Bury's theoretical point is a community-level one:

"work in the sociology of knowledge must be assessed according to the standards of a community of scholars...the fact that sociology of knowledge is socially sustained and collectively scrutinised need not prevent it becoming a very
successful form of knowledge, commanding wide assent" (Nicolson and McLaughlin 1987:114-115).

This idea of reflexivity being developed by a community of researchers arises again in a later article of Nicolson and McLaughlin's, written to continue their debate with Bury:

"Reflexivity, if it is to be a valid part of sociological inquiry, has to be achieved collectively...its principal focus should not be the individual investigator but the scholarly community" (Nicolson and McLaughlin 1988:252).

Relativism

Bury suggests that social constructionism, related as it is to the work of Michel Foucault, leads one into "the abyss of relativism" (Bury 1986:152) where "discourse creates its own objects and is created by them...any 'external' or general level of explanation is suspect" (Bury 1986:154) which in turn leads to a "deeper nihilism...[that]...threatens to follow relativism" (Bury 1986:155). Nicholson and McLaughlin claim that Bury's mistake lies in not recognising the methodological nature of the relativism present in constructivism:

"One is forced to relinquish truth and falsehood as explanatory devices in the sociology of medical knowledge....proper standards of sociological scholarship imply and demand that sociologists of knowledge be methodological relativists" (Nicholson and McLaughlin 1987:117).

This echoes Barry Barnes and David Bloor when they claim that:

"Far from being a threat to the scientific understanding of forms of knowledge, relativism is required by it...It is those who oppose relativism...who pose the real threat to a scientific understanding of knowledge and cognition" (Barnes and Bloor 1982:21-22).

Bury is unconvinced by Nicholson and McLaughlin's defence of 'methodological relativism' claiming that their explanation only serves to show "just how shaky the social constructionist case is" (Bury 1987:440). Their main problem is that they combine the terms 'belief' and 'knowledge'. For Bury, the sociology of belief has been covered extensively by sociologists and thus, if the sociology of knowledge is nothing more than the sociology of belief in a new guise; "the claim by social constructionists to be developing an original approach falls away", with methodological relativism remaining "an unclear proposition" (Bury 1987:440 & 441). Barnes and Bloor would reply that social constructionism does not equate 'belief' with 'knowledge', but that knowledge should be seen as "any collectively accepted system of belief" (Barnes and Bloor 1982:22, footnote 5), and it is that element of collective acceptance which is missing in
Bury's critique. He paints a very solipsistic picture of social constructionism, consistently ignoring that fact that what is interesting about this approach is its focus on the social aspects of human knowledge.

His complaint against methodological relativism being 'unclear' suggests more about Bury's unwillingness to explore the literature of social constructionism than about any actual deficits in this approach. One way to think of the problems faced by the social constructionist is to consider the issue of credibility, in that:

"all beliefs are on a par with one another with respect to the causes of their credibility. It is not that all beliefs are equally true or equally false, but that regardless of truth and falsity the fact of their credibility is to be seen as equally problematic" (Barnes and Bloor 1982:23).

It is this credibility which leads to a belief being collectively accepted, to becoming knowledge, and "regardless of whether the sociologist evaluates a belief as true or rational, or as false and irrational, he must search for the causes of its credibility" (ibid.).

Critics' inability to separate methodological from ontological relativism is still an issue in the debates surrounding SSK\textsuperscript{24}, yet it can be treated as a simple matter of methodology:

"A methodologically inspired scepticism about what we know and how we claim to know it does not necessarily lead to a nihilistic perspective. It is quite wrong to confuse a methodological precept with an ontological position" (Atkinson 1995:44).

By analogy it is quite possible for a biologist to use a form of 'methodological reductionism', analysing an organism by 'breaking it down' into smaller and smaller parts, whilst at the same time being at the fore-front of criticism of the use of reductionism as a guiding principle for biological research programmes\textsuperscript{25}. In the same way, it does not seem at all clear why a sociologist's commitment to methodological relativism should plunge him or her into Bury's abyss of nihilism.

\textsuperscript{24} For example, see Sokal and Bricmont (1998) for an example of this apparent blind spot.

\textsuperscript{25} This is a reference to Steven Rose, who maintains that use of reductionistic strategies in scientific research does not commit one to a belief in overarching reductionism (Rose 1997).
Concluding the Debate

Atkinson states that Bury's ideas are worthy of attention, not for their validity and accuracy (for him, they are mainly "wide of the mark"), but because "they encapsulate many vulgar misconceptions about the sociology of knowledge". In his view, Nicholson and McLaughlin subject them to a "thorough rebuttal" (Atkinson 1995:43). Not, obviously, thorough enough to silence criticism of social constructionism, at least with regard to scientific knowledge, since complaints similar to Bury's have been lodged time and again over the years. There is little one can add from the theoretical perspective that is likely to sway a critic in favour of the constructionist position. What can be presented though are the practical, empirical results of approaching medical knowledge as a social construct, for:

"abstract or theoretical discussion is not the most effective means of demonstrating the heuristic value of social constructionism. The strengths of the approach are best displayed by its deployment in empirical case study" (Nicholson and McLaughlin 1988:235).

The detail of my chosen methodology, discourse analysis, is covered in Chapter 3 of this thesis (see also Myers 1990a), but in brief, my analysis should be seen against the background of the debates outlined above. Although this thesis is not specifically aimed at vindicating SSK, I hope that if the analysis in my empirical work is convincing, then this will 'feed back', and add to the evidence in favour of a constructivist approach to debates in science and technology.

With regard to the terminology in this thesis, the case has been made that both the 'social' and the 'constructionism' should be abandoned by social constructionists. Latour and Woolgar, in their postscript to the second edition of Laboratory Life suggest that the 'social' should be "ditched" since:

"There is no shame in admitting that the term no longer has any meaning. 'Social' retained meaning when used by Mertonians to define a realm of study which excluded consideration of 'scientific' content...'social' was primarily a term of antagonism...But how useful is it once we accept that all interactions are social?" (Latour and Woolgar 1986:281).

And they point out that the 'social in science' is normally associated, by scientists and non-scientists, with: "the seedier aspects of scientific life...tales of scandal and intrigue,

---

of behaviour which fails the usual high standards of scientific enquiry” leading to the suggestion that "sociologists are engaged in some kind of scholarly muckraking" (Latour and Woolgar 1986:19 and 21). Yet if we remove the social, we run the risk of returning to the solipsistic vision of constructionism put forward by Bury. As pointed out earlier, Paul Atkinson warns against this stating that:

"It is necessary to remind oneself that the 'social construction of reality' does indeed refer to social processes; that it refers to collective acts, not to individual, much less private cognition" (Atkinson 1995:43).

This thesis will retain the 'social'.

Paul Atkinson also suggests a way of avoiding the unfortunate connotations of the word 'construction'\(^27\). He proposes to use the term social 'production' instead, the idea being to:

"draw more explicit attention to precisely those socially organised practices...by which facts, findings representations, opinions, diagnoses...are produced and reproduced. The emphasis is thus placed on medical knowledge production as work" (Atkinson 1995:45).

While this is initially an attractive way round the problems associated with the word 'construction', it is not clear that this is anything more than a cosmetic alteration, and that critics' objections will remain the same. At some level, 'productions' (e.g. plays) are as artificial and as human made as 'constructions' (e.g. buildings), and it is not clear why one should be more associated with medical work than the other. Alternative terms such as 'co-production' (Jasanoff 1996), which indicates the simultaneous production of scientific knowledge and social order, have their appeal, but in this thesis, I will keep to the term 'constructionism', maintaining preference for this rather than 'constructivism' for aesthetic reasons, since even within the sociology of science, there seems to be slippage between the two terms\(^28\).

\(^27\) "That term does undeniably carry connotations of mental and individual activity. It does sometimes fail to convey the sense of material transactions with the world" (Atkinson 1995:45).

\(^28\) On a reflexive note, my choice to retain the this term ('Social Construction') is of course a discursive strategy, used to place my research within an already existing body of knowledge and literature. By choosing to avoid less common options, such as 'ditching the social' or 'social production', I am sacrificing what advantage these terms may give me for the secure knowledge that 'social constructionism' places my work on a solid disciplinary footing.
Sociology of Medical Knowledge: the current state of play

Since the debate between Bury and Nicholson and McLaughlin, researchers have steadily promoted the need to adopt the methods and approaches of SSK to the subject of medical knowledge. For example Bartley's 1990 article, "Do we need a strong programme in medical sociology" is explicit in its championing of the SSK approach, describing it as "a bandwagon I would not like the sociology of health and illness to miss" (Bartley 1990:371). In this manifesto, Bartley outlines the 'Strong Programme' approach, as well as the 'Laboratory Studies' method pioneered by researchers such as Latour or Collins, whilst remaining attuned to the different strains of thought that exist in this area of research and the disagreements present (see her endnote 2, p.387). While there might be differences between SSK and the sociology of medical knowledge in application\(^{29}\) the core of the approach is that when groups within medicine make a claim, "that very claim to knowledge becomes a topic for sociological investigation as much as the professional or political activity which is premised upon it" (Bartley 1990:383).

In 1995, Casper and Berg offered another call to arms for medical sociologists to adopt constructionist techniques, and sociologists of science to study medical practice:

"unfortunately for both science studies and medical sociology, 'inclusive' studies of medical practice [focusing on both the content of medical science, and medical situation within which it is used] remain relatively rare. For medical sociologists to ignore the technical content of medical practice is...an unnecessary deprivation...Similarly, sociologists of science, in not looking more expansively at medical practices, deprive themselves of sites at which many current issues and problematics of interest within science studies are at stake" (Casper and Berg 1995: 397-398).

Elston notes this gap between knowledge and practice in her introduction to the 1997 book The Sociology of Medical Science and Technology but she suggests that there has been "some rapprochement between the two sub fields" of medical sociology and the sociology of medical science and technology, with:

"an increasing number of contributions explicitly applying sociology of science approaches to health care...[appearing]...in medical sociology journals...[and]...medical technologies and practice...[figuring]...prominently in key sociology of science journals" (Elston 1997:4-5).

\(^{29}\) "we [i.e. medical sociologists] might often want to start not from the scientists...at all, but from the perspective of a sub-profession or a pressure group or client group" (Bartley 1990:383).
While there are those within medical sociology who still raise questions about the validity of the social constructionist approach\(^{30}\), the impression gained from Elston's introduction, and the book as whole, is that constructionist approaches to medical science are generating productive research questions, and interesting answers. This thesis contributes to this research tradition, on the edge between medical sociology and the sociology of medical science. Although I will be focusing on a traditional SSK resource of scientific texts published in professional journals, one aim is to see how scientific knowledge is communicated to a wider scientific audience, outside of a specific, narrow research community, and how this new knowledge affects one particular part of medical practice, disease classification.

2. SOCIAL STUDIES OF THE NEW GENETICS

If we move outside of the strictly constructionist approach, it is clear that social scientists have approached the new genetics from a variety of different directions. Anthropology comes with a history of research into the effects of new reproductive technologies, such as IVF (e.g. McNeil, Varcoe and Yearley 1990, Strathern 1992, Edwards et al. 1993, Franklin 1997), while in genetics, anthropologists have looked at: differences in attitudes towards prenatal diagnosis and amniocentesis between cultures (Rapp 1993 and 1998) and doctors and patients (Rapp 1990); differences between interest groups in specific disease communities (Heath 1998); and the problems surrounding research into human genetic diversity (Lock 1994). In terms of ethnography, Paul Rabinow has produced two book length studies of how genetic science works in the laboratory (Rabinow 1996a and 1999) as well as a collection of papers reviewing issues in genetics from an anthropological perspective (Rabinow 1996b).

Conrad and Gabe (1999)\(^{31}\) suggest that sociological analysis really turned to issues in genetics, in the 1990s although writing in this area extends back to, at least, the early 1970s (Sorenson 1971, 1973). A great deal of work has focused on aspects of genetic


\(^{31}\) See this reference for a more detailed review of the sociological literature.
counselling including: dilemmas for counsellors (Bosk 1992) and clients (Rothman 1986); and broader issues from the client’s perspective (Lippman 1991, Burke and Kolker 1993, Lippman 1994, Kolker and Burke 1994a/b). Sociologists have also paid attention to differences in attitude towards genetics between professionals and lay persons, both in general (Kerr et al. 1997, 1998a) and with regard to specific disorders, such as schizophrenia (Turney and Turner 2000) and cystic fibrosis (Stockdale 1999). There are a number of papers discussing the role of sociological research into genetics, both at a theoretical level (Lippman 1992, Rothman 1995) and in terms of outlining a sociological research programme (Richards 1993)\(^\text{32}\).

Cutting across these disciplines, several book-length studies have analysed the representations of genetic science in popular media and culture, both as a whole (Nelkin and Lindee 1995, Van Dijk 1998, Turney 1998, Condit 1999) and in specific instances (Franklin 1988, Conrad and Weinberg 1996). The implications of public understanding of genetics for policy makers has been investigated (Kerr et al. 1998b) as has the concept of 'genetic literacy' and the public understanding of genetics (Turney 1995a/b). In addition, several surveys have been carried out to assess the public's attitudes toward, and understanding of, the new genetics (Marteau et al. 1995, Durant et al. 1998).

A number of psychological studies\(^\text{33}\) have been carried out, looking at: dynamics and nondirectiveness of genetic counselling (Michie et al. 1996a, Michie et al. 1997, Armstrong et al. 1998); the effects of prenatal testing on pregnant women (Marteau et al. 1989); patients' understandings of predictive genetic testing (Michie et al. 1996b); and research on the impact of genetic testing for specific conditions (Binedell et al. 1996, Hamann et al. 2000). There is also work on predictive genetic testing in children (Michie and Marteau 1996).

\(^{32}\) A wider review of psychological and social research into the new genetics can be found in Marteau and Richards 1996, especially chapters 3-8, 12 and 15.

\(^{33}\) Review of this literature can be found in: Marteau and Croyle (1998).
My own work enters these debates from a constructionist position to look at how certain diseases become geneticized, and how this alters their classification. Focusing on texts, it might appear that my research is intended to act at the theoretical level, but it should primarily be seen in empirical terms. Although my main aim is to illuminate the theoretical concept of geneticization, the methods and material used root this research in an explicitly empirical tradition. To fill in the theoretical background to my research, I will now focus on the debates surrounding the classification of a disease as genetic, starting with the philosophical debates, and then moving onto more sociological considerations, to show what an STS approach can add.

**Philosophy and disease classification**

Philosophy of medicine has normally concerned itself with questions about what counts as the cause of a disease, what are the differences between diseases and syndromes, and whether diseases are natural kinds or human distinctions. I will briefly review debates surrounding the status of disease entities before moving onto the issue of disease causation (with particular reference to what counts as the genetic cause of a disease).

*Entities or words?*

Under-pinning the relationship between diseases and syndromes is the philosophical debate over the status of disease entities. Are disease classifications setting out value-free differences between real entities, or are they just flexible, contingent and value-laden tools humans use to pigeon-hole the world? To quote Reznick's excellent introduction and review of this topic:

"Do the taxonomic distinctions [between diseases] that we recognize correspond to natural kinds that exist independently of our attempts to classify objects, or do they merely represent convenient ways to code information?" (Reznick 1987:23).

Working through the opinions on the issue of whether disease classifications are discovered or invented, Reznick reaches a position he calls 'Taxonomic skepticism' which claims that disease taxonomies are neither correct or incorrect in terms of correspondence to natural kinds, since there are no natural kinds or divisions between
disease entities: "what at one time may have been classified as a disease entity may later (with increasing knowledge) come to be classified differently" (Reznick 1987:66).

Many who have recently written in this area share Reznick's instrumental, anti-essentialist position, sceptical as it is about the 'reality' of taxonomic divisions. For example, in their introduction to the philosophy of medicine, Wulff, Pedersen and Rosenberg agree with Reznick that "disease classification is the tool which doctors use to pigeonhole professional knowledge and experience" (Reznick 1987:73) suggesting that:

"the history of the classification of disease stresses the point that it is a man-made classification of individual patients...According to this point of view, there are no genera and species of disease, and disease names may be regarded as labels which we attach to groups of patients which resemble each other in those respects which we consider important" (Wulff, Pedersen and Rosenberg 1988:77).

I accept these authors' claim that the most productive attitude towards these questions lies in the middle ground between the Essentialist, with a total reliance upon realism, and the Nominalist's insistence that disease classifications are human artefacts. What is required is a form of moderate nominalism, which has much in common with the relativist position espoused by Paul Atkinson in the first part of this chapter. Acceptance of the existence of material reality does not mean that one has to accept that divisions and distinctions within that reality are free from human subjectivity.

Causes

Since one of the core themes of the idea of geneticization is the role of genes as (at least partial) causes for diseases, exactly what counts as a cause is a serious consideration. The most important thing to note when considering the causes of disease is that what we call a cause, is, to a greater or lesser extent, a decision made independently of a realist position. As Wulff states:

"All events in and outside medicine are determined by numerous factors, and the selection of the cause is not a question of natural science; it depends on our interests which in medicine are often therapeutic or preventive" (Wulff 1984:69).

This plurality of causes exists not just because for every cause, we can trace it backwards in time to other, earlier causes, but also because at any single moment, there are any number of simultaneous causal factors operating on a single event (Hesslow 1984:183).
Of course, diseases are no different from any other event or process in that when we select the cause of any event, it is a choice which reflects our interests (Wulff, Pedersen and Rosenberg 1988: 67).

But although we might be prepared to accept that there is no such thing as any one cause of a disease, does this commit us to the position that all causes are equal, and that there is no way of distinguishing between causes? We are perhaps used to thinking of necessary conditions for an event to take place and comparing them to sufficient conditions, yet this is too crude an analytic structure, certainly in the case of medical causation. For example, borrowing from Wulff (1984), consider a case of meningitis, where a lumbar puncture confirms that the patient has been infected with pneumococci. In addition, this patient has had his spleen removed, and has not been inoculated against pneumococci. It might be tempting to call the pneumococci the cause of the meningitis, yet we cannot view it as a sufficient cause, since if he had been inoculated, or had not had his spleen removed, he is unlikely to have become sick. Nor can we consider the pneumococci to be a necessary cause since there are other viruses and bacteria which infect patients with meningitis. Yet the pneumococci are a necessary cause of this particular case of meningitis. The answer lies in considering all three factors, what Wulf terms a 'causal complex', to be the cause of meningitis; a sufficient but not necessary cause.

Thus the individual factors (the pneumococci, the spleen removal and the lack of inoculation) although not necessary or sufficient as causes of meningitis in themselves, are each a necessary part of this particular causal complex. They are thus each an insufficient but necessary part of an unnecessary but sufficient causal complex; they are each an *inus-factor* (Wulff 1984:170). It is these inus-factors which we normally refer to as the causes of disease, and as has already been noted, since there are any number of such causes for any single event:

"it is a Utopian thought that we should ever be able to map the whole causal network in any one patient...but the clinician may still be able to interrupt the disease process if only he can eliminate one necessary factor in that complex - if only he can eliminate a single inus-factor" (Wulff 1984:172).
If we view the cause of a particular disease as a complex of inus-factors, it becomes even harder to decide whether one can talk about one cause (i.e. inus-factor) being more important than another.

"When a cause of some particular phenomenon has been judged more important than some other condition, it is very tempting to regard this as being somehow inherent in the causal relation itself, as reflecting the 'strength' or 'effectiveness' with which the cause brings about the effect...The fact that what are the 'most important' causes is not something intrinsic to the events entering into the causal relation, but is relative and subject to variation, considerably weakens this realist stance" (Hesslow 1984:191).

It would appear that social factors are relevant, not just when considering whether diseases exist or not, but also when one tries to decide upon the cause of a medical condition. This obviously has relevance if we are interested in diseases which are thought to be caused by genetic factors.

Genetic Causes

The following table is included in Hesslow's 1984 article "What is a Genetic Disease?" and he points out that on the basis of this information, the disease X seems to have a strong genetic influence, certainly stronger than, say, that in diabetes. The more genetic material you have in common with someone who has 'X', the more likely you are to contract the disease.

Percentage frequencies of X in the families of persons with X.

<table>
<thead>
<tr>
<th>Relationship to affected person</th>
<th>Percentage affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unrelated general population</td>
<td>1.4</td>
</tr>
<tr>
<td>Spouses</td>
<td>7.1</td>
</tr>
<tr>
<td>Parents</td>
<td>16.9</td>
</tr>
<tr>
<td>Half-sibs</td>
<td>11.9</td>
</tr>
<tr>
<td>Sibs</td>
<td>25.5</td>
</tr>
<tr>
<td>Nonidentical twins</td>
<td>25.6</td>
</tr>
<tr>
<td>Identical twin</td>
<td>87.3</td>
</tr>
</tbody>
</table>

from Hesslow 1984: 190

34 taken from Stern 1973:672.
The figures for X are those for tuberculosis from forty years before he wrote since:

"Forty years ago almost everyone came in contact with the tubercle bacillus, and
the factor that decided whether someone was to develop the disease was therefore
not the exposure to the bacillus but the individual susceptibility" (Hesslow
1984:190).

The counter-intuitive identity of X relies on the questions one asks, and the objects of
comparison. If one takes people who have been exposed to tubercule baccili as the
normal to compare against, then one gets the table above:

"The genes will dominate if we ask why x got the disease, when y and z did not.
But if we ask instead why x got tuberculosis this year, when he was perfectly
healthy before, the environment may have been decisive" (Hesslow 1984:190-191).
Thus, depending upon the normal to which it is compared, tuberculosis could be viewed
as a genetic disease (see Lomax 1977 for an historical perspective on this). What one has
to pay attention to is the asking of particular questions, which is of course, inherently
social. Diseases can only be viewed as genetic in relation to other diseases. And as the
general theme in the philosophy of classification might suggest, decisions about the
'objects for comparison' for a disease are less about objective reality, and more about
factors external to the disease process, such as social factors.

In her discussion of genetic explanations, Gannet suggests that the reason for selecting
genes as the cause of particular diseases lies in scientific pragmatics; that they are a far
more likely site for medical intervention than broad environmental factors (Gannet
1999). Interestingly, Gannett makes 'geneticization' synonymous with 'genetic disease'
(an error implicit in Philip Kitcher's ideas of 'strong' and 'weak' genetic disease; Kitcher
1996) suggesting that "if we are to make sense of geneticization, it is necessary to
understand the bases upon which traits are labelled 'genetic' " (Gannet 1999:350). But
this overlooks Lippman's specification that in geneticization diseases need only be seen as
'in part' genetic. This is part of the subtlety of her concept, and it is largely missed by
philosophical discussions which are concerned with genetic diseases and simple
determinism. My case studies will show how it is possible to oppose genetic determinism
and simplistic definitions of genetic disease, but still 'buy into' the geneticization of a
condition. The problem with the philosophical discussions of genetic causation is the lack
of any sort of social explanation. If whether Tuberculosis is a genetic disease or not
depends upon the kinds of question you ask, the important thing is to discover how and
why people decide to ask particular questions. Even Gannett's work which nods towards the social in its use of 'pragmatic' reasoning, fails to clearly specify the social factors at play in the classification of disease. This deficit is obviously an area for STS research.

**Sociology of classification**

Edward Yoxen (1982) was one of the first commentators to take a sociological approach to the construction of genetic disease (for historical perspectives, see Rosenberg 1974, Olby 1985). He suggests that the structure of professional medical specialisation and the interests of institutionalised research produce an environment within which genetic explanation can flourish. Peter Conrad claims that part of the foundation for the classification of certain diseases as genetic lies in the residue of nineteenth century germ theory which still exists in medicine today. This substrate encourages the idea that there must be a specific aetiology behind every disease, and leads to easy acceptance of genetic causation in the news media (Conrad 1999).

But alongside the genetic aspect, the role of classification itself needs to be considered. This is the crucial element missing from the philosophical discussions surrounding genetic diseases. Even non-realist positions fail to acknowledge how complex, historically contingent, and powerful the classification systems we use are. And since one of the clearest conclusions of my case studies is that geneticization has a significant impact on disease classification systems, the way in which such systems work is central to my research. In their excellent investigation into classification systems, Bowker and Star pinpoint the power of classification when they suggest that when things are perceived as real, then they have real consequences:

"even when people take classifications to be purely mental, or purely formal, they also mould their behavior to fit those conceptions. When formal characteristics are built into wide-scale bureaucracies such as the WHO...then the compelling power of those beliefs is strengthened considerably" (Bowker and Star 1999:53).

Classification systems are vital in the standardisation and institutionalisation of diseases; in all three of my case studies, formal, institutional classifications play an important role in geneticization. In Cystic Fibrosis and Diabetes, it is the formal classification systems (of the US Cystic Fibrosis Foundation and the American Diabetes Association) which
undergo changes as a result of genetic information. In schizophrenia, because of the state of the geneticization process, the formal classification system (the Diagnostic and Statistical Manual of the American Psychiatric Association) provides the background against which the debates are played out. Through their analysis of a variety of different nomenclatures (including disease classification systems), Bowker and Star reveal how such systems are negotiated by social actors and constructed by a number of different external factors: "classifications, however dry and formal on the surfaces, are suffused with traces of political and social work" (Bowker and Star 1999:49. See also Bayer 1987)\(^{35}\).

The social underpinnings to classification means that most classification systems are compromises. It is very rare that any one side in a debate over categories comes out on top (Bowker and Star 1999:55). This is clear in the case of diabetes for example, where genetic explanations took over 20 years, from their initial introduction into the formal classification system, to dominate and oust alternative approaches. Classification is also the way in which my work can be said, at its core, to be a work on ethics:

"each category valorizes some point of view and silences another. This is not inherently a bad thing- indeed it is inescapable. But it is an ethical choice, and as such it is dangerous - not bad, just dangerous" (Bowker and Star 1999:5-6).

Having outlined the broad disciplinary approach of my thesis, I will now turn to the narrower issue of my methodology (discourse analysis), and how it relates to my chosen materials (review articles).

\(^{35}\) The social is emphasised in the term used by Annemarie Mol to describe the different ways classifying and diagnosing anaemia: ontological politics (Mol 1999).
CHAPTER 3: METHODS AND METHODOLOGY

The aim of this chapter is to introduce the methodology, discourse analysis, used in my case studies, explain how it relates to research in science and technology studies and outline the possible problems that such a text-based method faces. Discourse analysis as a discipline has both a long and a short history. Its roots are in the ancient Greek tradition of Rhetoric, the art of good speaking. The main focus for rhetoric was persuasion, swaying audiences to the speaker's point of view. It was therefore a practical discipline. Over time, rhetoric lost much of its importance as a discipline, and Van Dijk (1985) suggests that the modern origins of discourse analysis lie in the semiotics movement of the 1920's and 1930's, and the structuralism of the 1960's. As a methodological approach, discourse analysis has proved fruitful in a number of areas, for example social psychology (Potter and Wetherall 1987, Billig 1987) or racism studies (Van Dijk 1993). It has also been a major approach in the social studies of science, although it would be wrong to assume that it represents a single coherent position.64

My research applies discourse analysis to review articles in the scientific literature to explore how the geneticization of disease takes place. As a method, this involves three distinct stages. The first focuses on identifying the articles for analysis, and depends upon a solid knowledge of the debates surrounding each of the diseases. From a thorough review of the literature and citations, it is possible to identify review articles which are influential within, or which are representative of specific discourses. The second stage, the actual analysis, entails re-reading the selected articles, paying careful attention to themes and strategies which might play a role in geneticization, particularly if they are repeated in more than one article. Finally, the third stage, writing up, ties the analysis into a coherent description of how these themes construct particular points of view and persuade the reader.

---

64 For a range of different studies, see Law and Williams (1982), Blakeslee (1994), Godin (1997), and Dewsbury (1997).
1. **Discourse Analysis and Science Studies**

Focusing on the words used in science makes a great deal of sense:

"A lot of what scientists can be observed to do is linguistic behavior. They converse with one another as they work, communicating the details of techniques and observations. They spend long hours drafting and redrafting grant applications. They read at length in the relevant literature, before composing, with great care, the papers in which results are reported. When they come together in scientific institutions, they participate in further communicative acts, such as delivering lectures or commemorative addresses, or debating the merits of one another's work" (Golinski 1998: 103).

Some Science Studies researchers have gone so far as to say that the primary purpose of science is the production of words in the form of texts (Latour and Woolgar 1986). But even if one does not accept this, clearly science is obsessed with words, both spoken and written. How can one communicate a great discovery if one cannot speak about it? The importance of language is, of course, an obvious indicator of the social nature of science. Language is therefore problematic for those who would undermine, or at least play down, the role of social factors in scientific thinking and explanation.

I do not intend to carry out a detailed review of the different approaches to discourse analysis in science studies; there are already two excellent reviews in Myers (1990a: 14-34) and Golinski (1997: 103-132). Instead, I will focus on those studies which have direct relevance to, and which serve to define, my own approach of: text based social constructionist research within the empiricist repertoire, with a focus on narratives. As will become clear, my work follows closely that of Greg Myers and should be seen as an attempt to apply his ideas to a practical sociological issue, geneticization.

**The written word**

My research focuses on review articles published in the medical literature. The question of 'why review articles?' will be covered in part 2 of this chapter. For now, the question is simply, 'why focus on what scientists write instead of what they say?' The most obvious answer is that this has been a productive approach in the past. Historians rely heavily on written texts for their research, and the history of science has proved itself the testing ground for many of the ideas that are now commonplace in science studies as a whole.
Golinski (1997) credits Steve Shapin's discussion of Boyle's 'literary technology' with setting the scene for much of the debate that comes after it. In "Pump and Circumstance", Shapin sets out to show that "speech about natural reality is a means of generating knowledge, of securing assent to that knowledge" (Shapin 1984:481). Shapin is interested in how the experience of watching an experiment is extended from a small number of witnesses, to the community at large. Boyle, he claims, was not satisfied that an experiment be witnessed by one man: "If that witness could be extended to many and in principle to all men, then the result could be constituted as a matter of fact" (Shapin 1984:484). To carry out his experiment, Boyle used material technology: an air pump of elaborate design and variable operational reliability. But at least as important as this was the literary technology he used to communicate his results to a wider audience: the experimental report, written to give the reader the impression that they had seen the experiment taking place, what Shapin calls 'virtual witnessing' (p.491). Boyle wrote in such as way that:

"the reader could take it on trust that these things happened. Further, it would be as if that reader had been present at the proceedings. He would be recruited as a witness and be put in a position where he could validate experimental phenomena as matters of fact" (Shapin 1984:493).

The various means by which Boyle achieved this included: reporting experimental failures; modest piece-meal reporting rather than grand system building; confidence on matters of fact.

Shapin ties the formal conventions used in this writing to the larger social context of Restoration England. In his expansion of this article with Simon Schaffer, he shows how many of the political and social debates of the time were mirrored in the way in which experimental evidence was presented (Shapin and Schaffer 1985). The importance of this study to my own work lies not in the details of the literary methods used by Boyle to bolster his position and persuade his audience, but in the fact that scientific texts are open to analysis from a constructionist position. It is possible to show how texts are constructed to produce 'indisputable matters of fact' and how the origins of these facts can be explained in terms of social and political struggles. This focus on the text is reminiscent of Michel Foucault's view of historical documents:
"Traditional historical methods...consider documents to be representative traces of the past through which a historian can discover the underlying truths, or monuments, of the past. To Foucault, however, the documents are the monuments [ref]. The appropriate objects of inquiry for the historian are therefore documents themselves, not the events and continuities of ideas that have generally been assumed to exist somehow behind and apart from documents" (Haller 1998:57).

Critics of textual approaches might complain that although the historian is stuck with writing as his/her main research material, the same is not true for the sociologist. Scientists do so many other things apart from writing. To focus on this one aspect of their life seems perverse. To talk about how scientists do science, one needs to look at them in the laboratory, listen to them as they talk to colleagues. We need to "get behind the written text" (Myers 1990a:5).

Greg Myers defends the use of written texts, not because they are in some way superior to other aspects of social life, but for practical reasons. Written texts have two distinct advantages over other resources: "1. Texts hold still. 2. Texts are portable" (Myers 1990a:6). The stillness of texts means that one can indulge in very 'close' reading. One can read through a written text over-and-over in an iterative fashion, highlighting features that one might miss in the normal reading process. It allows one to link themes running through the same, and across different, texts. A sociologist might reply that one can take the same approach with interview transcripts. They too are permanent and fixed. They can be read carefully and comparisons can be drawn between them. But interview transcripts lack a text's portability. When an ethnographer analyses a conversation between scientific colleagues about a particular piece of machinery, that event is rooted as a local event (Myers 1990a:6). That event has to be recorded and transcribed. Even then, disagreements are possible over muffled words on a tape, and whether individuals actually said what the analyst claims they said. There is always recourse to the tape (if there is one) to settle the argument, but the reader still has to trust in an interviewer's integrity a great deal since "the reader and author of an ethnography do not have access to the same experience" (Myers 1990a:6).

The same is not true for the textual analyst. One needs no faith in a textual analyst's integrity since "When I quote a published text, anyone can go to a library and look up the
same article in another copy of *Nature* or *Sociobiology*. A reader and I can argue about the same thing" (Myers 1990a:6). While a reader and author may disagree over the interpretation of a particular text (dealt with in part 3 of this chapter), if they both have a copy of the article concerned, they both have access to the same experience of reading that particular article.

Some authors have chosen to look at different drafts of an article, to find out how ideas change in relation to criticism and shifting audiences. Myers himself does this when he looks at various drafts of papers sent to journals, referees' comments and editorial correspondence (Myers 1990a: 63-100). My own research focuses on the final, published version of the article. The methodological reason for this is that these articles are the finished product. They are the 'public face' of a particular piece of research, and it is the final articles that are cited, not the earlier drafts. Thus final, published articles play a specific role in the construction of scientific knowledge that other texts do not. Final articles have (almost always) been refereed. If they have been written by a number of people, then the authors have reached enough of a consensus for them all to agree to put their names to it. There is a 'solidity' to published articles. One might disagree with what they mean, but one cannot disagree with what they say. It is there in black and white. This shifts the debate onto the *meaning* of what is written in articles, and away from the actual words contained in the text. While ethnomethodologists claim that we need to get behind the texts to the context within which they operate:

"many of us as researchers find ourselves sitting in front of a pile of written texts, already removed from the scene of production. The usefulness of these [literary] approaches to interaction is that they suggest ways of going beyond the marks on the page to place the text in a larger context, even if we do not have access to the author and readers" (Myers 1991c:324).

**Repertoires**

The second aspect of my approach is that it focuses upon scientists' empiricist repertoire. This stems from the work of Gilbert and Mulkay, who in their 1984 book *Pandora's Box*, examine a controversy in biochemistry through interviewing scientists and looking

---

37 The pragmatic reason is that drafts of articles are hard to get hold of unless you know the researchers involved.
at research papers. Gilbert and Mulkay suggest that scientists use two different 'repertoires', two different ways of accounting for social action and scientific results. The empiricist repertoire is present in both research papers and interviews, and explains events and beliefs in terms of experimental data. It is characterised by absence of social information about the author and his or her personal commitments. This repertoire allows authors to "construct texts in which the physical world seems regularly to speak...for itself" (Gilbert and Mulkay 1984:56). The contingent repertoire is in direct opposition to the empiricist. It refers directly to how scientists' actions and beliefs are affected by external factors, outside of science. In this repertoire:

"scientists' actions are no longer depicted as generic responses to the realities of the natural world, but as the activities and judgements of specific individuals acting on the basis of their personal inclinations and particular social positions" (Gilbert and Mulkay 1984:57).

Greg Myers is unconvinced by Gilbert and Mulkay's work, suggesting that analysis using two repertoires is a "cumbersome tool" (Myers 1990a:29). Even more, "while it is clear enough what the empiricist repertoire involves, the contingent seems to be defined as just everything else" (Myers 1986:600). Gilbert and Mulkay are aware of this possibility, admitting that the contingent repertoire might be seen as "merely a residual category, containing a *melange* of disparate elements". They hope that they show that how contingency is employed as a "coherent discursive resource", in regular ways (Gilbert and Mulkay 1984:61-62). Clearly, Myers is not convinced, but the coherence, or otherwise, of the contingent repertoire is, I suggest, irrelevant to my own work.

The most important thing about the repertoires is *when* they are used. The empiricist repertoire occurs in both interview and formal paper, but the contingent repertoire only in the interview setting. The formalised conventions of scientific writing act to 'strip-away' the contingent elements of scientific discourse, and leave only the empiricist repertoire. This means that by focusing on formal published articles, my work is limited to the empiricist repertoire (Gilbert and Mulkay 1984:40). Myers misses this point when he mistakenly claims that: "Thus the repertoires coexist in the same texts, instead of being found in separate places" (Myers 1990a:28). Even accepting a broad definition of 'text', to include spoken discourse, this summary is only half right. Only in informal (i.e. interviews) 'texts' do scientists employ both repertoires.
Why is focusing on the empiricist repertoire noteworthy? For one thing, it is harder. Although both repertoires are explicitly social, the very nature of the empiricist repertoire makes finding social explanations in formal texts harder. This means that if one can find such social explanations, this is more evidence in favour of sociological explanations for scientific knowledge. This is not the main goal of my research though. Myers' work, which focuses on formal texts rather than interviews, has elegantly demonstrated the socially constructed nature of biological knowledge. My focus on the empiricist repertoire reveals the link between formal, 'neutral' scientific discourse and the effect this has on disease classification and, in turn, patients. It requires scientists to take responsibility for the broader impacts of what they write and publish.

The return of social constructionism

The approach used in this thesis is constructionist. The exact tribal affiliation of my constructionism (Strong Programme, Bath School, Actor-Network Theory) is less of an issue. Since I am relying on Myers for so much of my methodological underpinning, his own position on constructionism is helpful. He adopts a broad, eclectic range of positions, borrowing different aims and beliefs from different authors within science and technology studies (Myers 1990a:34). While this lacks 'ideological purity', if one is interested in the pragmatic use of theory, it allows one to build up a solid foundation for empirical research.

Some aspects of these approaches are ruled out by the use of texts. The Strong Programme emphasises the role of social interests in the production of scientists' beliefs. The nature of authors' interests is hard to discern from a published article, as are any social motivations. This means that my research cannot answer questions such as 'why are some scientists interested in using genetic explanations to expand the definition of cystic fibrosis?' There is some evidence in the texts, mainly focusing on the relationship between clinicians and researchers, but the focus of my approach are 'how' questions. Such as 'how do authors present the geneticization of cystic fibrosis so as to expand its definition?' Other aspects of the Strong Programme are relevant to this research. The need for symmetry in explanations is crucial. Only by adopting methodological relativism
can one make sense of trying to explain how the textual construction of a narrative leads to changes in disease classification. To assume that 'schizophrenia is a genetic disease' and that is why the articles which argue this are so persuasive, is to miss the point. What is of interest is how the concept of 'genetic disease' is constructed to fit the hereditary component of schizophrenia, how that component is itself presented to emphasise genetic factors, and how environmental explanations are sidelined. This means, of course, that it is equally mistaken to assume that genetic explanations for schizophrenia are 'wrong', a likely assumption in the context of the geneticization critique.

This neutral stance opens up discourse analysis, and SSK as a whole, to the charge that it forces its practitioners to 'sit on the fence' on topics of ethical and political importance. Myers is acutely aware of these charges and tries to provide a political justification for his approach (Myers 1990a: 252-259. See also Jasanoff 1996). I am not so concerned about my own work. My aim is use discourse analysis as a tool to tell us more about the process of geneticization. It does not prevent others from attacking this redefined geneticization on ethical or political grounds. But previous definitions of geneticization have pre-judged its ethical status before it has even been defined. My own analysis does present evidence on the social impact of particular narratives and the disease classifications they produce (see chapter 4 and the CF case study). The aim is not to follow through with an in-depth ethical discussion, but to reinforce the fact that disease classification has concrete effects on patients and their families and in turn, on health policy.

What role do texts play in this mid-range form of constructionism? The text is not a clean, pure conduit for scientific facts, shuttling information from the author to the reader. Nor is it a formalised smokescreen, floating between the reader and the facts, which needs to be cut through (Myers 1990a:26). The text is the means by which scientific facts are constructed and exist. Both the conduit and smokescreen positions

---

38 I am aware that this might sound like an attempt to construct a 'value-free' concept of geneticization. This is impossible of course. My point is that current definitions of geneticization are built on the premise that geneticization as a process is morally wrong, and as such tend to be rather circular when used to assess whether geneticization is morally wrong.
suggest that there are 'real' facts the other side of the text. Constructionism shows that
the facts are the text. Since this links to the idea that scientific language is involved in
persuasion, the danger here is that this will be seen as a threat to science (Golinski 1997:
105-106).

Thus we are back at the debate between the realist and the constructionist. By focusing
on language, discourse analysis is right at the front-line of the science wars. Stephen Jay
Gould, while discussing analysis of his own use of rhetoric, criticises:

"[s]cientists...[who]...for the most part simply do not acknowledge that the form
and language of an argument...could have anything to do with its effectiveness"
(Gould 1993: 323).

Gould's reaction to this analysis is essentially positive. This is also the impression given
to Myers by the majority of the scientists that he talked to about his work, who seemed
to have no problem with it. They might not be consciously aware of the nature of
scientific writing, but they seemed quite willing to accept it when pointed out to them. It
was only non-scientists who objected to his ideas about rhetoric in scientific texts (Myers
1990a:248). One has to hold a very limited view of science and scientific writing to
oppose the idea that scientists write to persuade.39

Narratives

In this research, I am interested in narratives:

"the selection and sequencing of events so that they have a subject, they form a
coherent whole with a beginning and an end, and they have a meaning that is
conveyed by the sequence as a whole" (Myers 1990a:102).

Golinski terms this type of research 'narratological hermeneutics' (Golinski 1997:130)40.
The focus is on those elements that construct a story about a particular topic. Much of

39 Even that arch-opponent of social constructionism Alan Sokal declared that one of the things
that sociologists of science should be looking at is the 'rhetoric of scientific articles': in
conversation with Christopher Norris, "Theorists under Attack", Institute for Contemporary Art,
London, 7/7/98. Of course, he refused to accept that methodological relativism was necessary for
such work to carried out properly.

40 For a discussion of the usefulness of narrative in the social sciences as a whole, see Linde
(1986).
Myers' work has focused on the different narratives employed by opposed parties in a scientific controversy (for example Myers 1990: 101-140, 193-246) but he has also shown how narratives operate in the reporting of scientific discoveries (Myers 1990b). Holmes has shown how narratives are constructed by the conventions of the experimental report (Holmes 1991).

There are several advantages for my research to analysing text in terms of narratives. Narratives, by definition, move through time. Since the overall aim of this thesis is to analyse geneticization, a process taking place over time, it is useful to have an analytic framework which incorporates a diachronic element. Alternative concepts, such as discourse, are too static to fully describe the changes that take place in disease classification over 20 years.

In narratives the focus is on the parts that go towards making up the story, rather than the motivations that lie behind them. In his analysis of the controversy surrounding E.O. Wilson's book *Sociobiology*:

"Myers displays the role of competing narrative constructions by declining to choose between the two sides. Adherence to Bloor's symmetry postulate leads him to refuse to assign political or social motives to one side in the dispute...Instead, the focus is on the process of construction by which elements of language are put together into meaningful stories by authors on both sides of the debate...the role (if any) that social interests play in the process remains obscure" (Golinski 1997: 131-132).

By focusing on the narratives of geneticization, is it easier to maintain a neutral position with regard to the ethical rights or wrongs of such a process. This is important since one of aims of my research is to distance geneticization from the idea that it is necessarily an unwelcome (or welcome) process. Thus focusing on the construction of narratives helps achieve both sociological symmetry and an element of ethical neutrality with respect to geneticization.
This neutrality might present problems in my case studies since, unlike Myers, I will not be presenting two, opposing narratives. My work does not focus on controversy. The narratives I present are the dominant ones in each disease, and although there are contributions from those who dispute elements of these narratives, there will be no attempt to put forward alternative perspectives. The conclusions from this might be that the narratives described are a) unavoidable, and b) desirable. These should be resisted. It is not the case that the geneticization of cystic fibrosis necessarily had to happen in the way that it has. Nor is the current classification of cystic fibrosis necessarily the best that could be used, in the sense that there are people who could be better off under alternative systems.

Within each narrative, I claim that various different strategies are used to construct and persuade. The problem with a word like 'strategy' is that it implies a degree of conscious authorial intention which is problematic for a purely textual analysis (see part 3 of this chapter for a discussion). But there are precedents for using it in this sense:

"Foucault's use of the word "strategy" must not be confused with definitions typical of the term, which imply authorial intention. To Foucault, a strategy is simply a theme or theory enveloping and reflecting patterns in the formation of objects, subjects and concepts within a discourse" (Haller 1998:64).

Rhetoric of Science

To clarify the exact nature of my methodology, it might be helpful to distinguish it from alternative, though related approaches. Although Myers freely admits that he is interested in scientific rhetoric, clearly he is less keen on the rhetoric of science as a discipline. Myers' main objections to work in the rhetoric of science seems to echo his complaints about Gilbert and Mulkay's repertoires, in that it uses categories that are too broad to be

---

41 This might be disputed in the case of schizophrenia, but as I hope to show, the controversial elements of this narrative have been smoothed away. Partly as a result of the narrative itself, but also from the failure of its opponents to maintain an effective critique.

42 Whether or not the geneticization of cystic fibrosis, in some form, was inevitable is not clear. I simply dispute that it had to take the form it did.

43 For a similar, 'non-conscious' use of strategy, see Dewsbury (1997).
analytically useful (Myers 1990c:561). In a review of Lawrence Prelli's 1989 book *A Rhetoric of Science: Inventing Scientific Discourse*, Myers states that:

"Prelli treats these categories of *stasis* or *topoi* as facts about the rhetorical world, known by the writers who apply them separately...But what is interesting is just that scientists do not study *stases* and *topoi*....They have not made their rhetorical knowledge explicit in this way...If there are certain stereotypical forms of argument...we must look for their origins elsewhere: to the ways scientists are trained, the structures of their careers, the ways they talk in labs and use their equipment, the ways they are funded and evaluated, the ways they write, rewrite, review, and read their papers" (Myers 1990c:561-562).

Rhetoricians' interest in telling writers what they should do to be successful means that they lack interest in why and how scientific writers do what they do. This complaint about rhetorical analysts putting scientific discourse into ready-made, overly capacious categories is also made about the rhetoric of science as a whole, by Gaonkar (1993:283). Likewise, the failure to look beyond the text to social structures for explanation is a charge levelled broadly by Ceccarelli (1995:106). Myers suggests that:

"a rhetorician like Prelli makes what might seem a rather odd use of sociology. In every case, he takes the example as an account of the rhetorical choices of individual scientists, as if they were choosing from one of his lists, and he leaves out the context of other texts, the expectations of genres, the institutional constraints on reading and writing, and the role of these texts in a social system. Watson and Crick's *Nature* article is described as if it were the first scientific article ever published" (Myers 1990c: 562).

The most influential assault on the rhetoric of science comes from Gaonkar. His 1993 article is interesting not just for the ferocity with which he attacks the rhetoric of science, but also the comparisons he draws with SSK. He suggests that modern trends in rhetoric have reversed the traditional emphasis upon rhetoric as a practical discipline, teaching how to produce persuasive discourse. Instead, modern rhetoric is interested in analysis and interpretation of what has already been written, and is satisfied with that as an end product (Gaonkar 1993:259).

---

44 For a discussion of problems in rhetoric as whole, see Leff (1992).

45 For a more sympathetic review of the rhetoric of science, see Harris (1991).

46 This is the opposite of Myers' earlier objection of course.
Rhetoric of Science (RS) is squeezed between rhetorical studies as a whole, and science studies, to which it is a late-comer, trying to catch up with developments in other methodologies (Gaonkar 1993:267). Yet:

"the differences between RS and SSK are striking and instructive. Although both started roughly at the same time in the 70s, SSK has developed into a complex empirical research program that displays considerable internal variation in theory and methodology, while RS remains little more than an uncoordinated research initiative carried out by a handful of committed individuals" (Gaonkar 1993:268).

Gaonkar criticises the rhetoric of science for failing to have enough self awareness to reflect back on the idea of 'rhetorical', in the same way that SSK has reflected on the nature of the 'social' (ibid.). Partly, this is because of the roots of rhetorical analysis which lie in:

"the positioning of the rhetor as the generating center of discourse and its 'constitutive' power. The rhetor is seen (ideally) as the conscious and deliberating agent who 'chooses' and in choosing discloses the capacity for 'prudence' and who 'invents' discourse that displays an ingenium and who all along observes the norms of timeliness (kairos), appropriateness (to prepon), and decorum that testify to a mastery of sensus communis....The agency of rhetoric is always reducible to the conscious and strategic thinking of the rhetor" (Gaonkar 1993:275).

But it is this focus on the self-conscious rhetor which distances RS from the contingent social and institutional issues that science studies has highlighted. This leads to situations where Charles Bazerman's historical review of the rhetoric of experimental articles can be criticised for:

"presenting a Platonic ideal of a scientific community rather than an historically-contingent, constructivist account of how...the social structure of science has changed and developed. And in this case, Plato is apparently a Mertonian sociologist studying twentieth-century science...for Professor Bazerman, there are people he finds appropriate to call 'scientists' in the seventeenth century, unproblematically doing 'science', and we can even, again apparently unproblematically, distinguish between 'amateurs' and 'professionals' " (Dear 1988:276).

It is not my aim here to criticise rhetoric of science, or the work of individuals within that discipline. Replies to Gaonkar can be found in Gross (1993) or Prelli (1993) and a more neutral commentary on this debate in Fuller (1997). Clearly, one needs caution in accepting Gaonkar's claims. His rose-tinted view of SSK suggests that at the very least, his opinions be taken with care. My aim is merely to suggest that we can make enough
distinctions between the rhetoric of science and constructivist discourse analysis, to accept that the latter can be done without extensive, or even limited, knowledge of the former. Discourse analysis is different enough to not require a grounding in rhetoric.

Reflexivity

Gaonkar suggests that one of the reasons that SSK and other parts of science studies are preferable to the rhetoric of science is because they have shown a degree of reflexivity. Much discussed in the theoretical literature, reflexivity is: "The ability to think about our own assumptions (that is limits)" (Fuhrman and Oehler 1986). Although reflexivity is important for science studies as a whole, it is a particular issue for discourse analysis. If we analyse a scientific text (written or otherwise) to show how it constructs facts and persuades its audience, then communicating our results will involve text to construct facts and persuade our audience. The discourse analyst could be open to the charge of hypocrisy for use of persuasive language, but only if one sees his/her role as essentially 'debunking' the objective nature of science. In this sense, reflexivity is only an issue for science warriors manning their defences against an inaccurate caricature of discourse analysis. And this need not include all practising scientists by any means. Nonetheless, reflexivity still matters in discourse analysis. Fuhrman and Oehler go so far as to suggest that the need for reflexivity undermines discourse analysis as an approach to the social studies of science:

"Reflexivity in science studies must pay attention to the social structures and processes under which knowledge is produced and legitimated; such a focus precludes analyzing texts alone. Important as they are, sociological scrutiny of texts may be a caricature rather than a painting of the larger scientific establishment. Important as caricatures are, they should not be mistaken for a 'Mona Lisa' "(Fuhrman and Oehler 1986:304-305).

Such objections seem to make sense, until one thinks about whether any single method in science studies could reasonably claim to produce a 'Mona Lisa'. Although Gilbert and Mulkay do make polemic claims about the power of their approach (Gilbert and Mulkay

---

47 See Gould (1993) for an appreciative and perceptive reception, by a scientist, of textual analysis of his own work.
1984:13-17) the modest claims of Greg Myers seem far more convincing if only because his reasons for using written texts are practical rather than ideological (Myers 1990a: 7).

Myers himself does address the issue of reflexivity, referring to it as irony. He claims that:

"Discourse analysts take an ironic stance toward scientific texts, but they also take an ironic stance toward texts in the sociology of science, toward all the devices of interpreters establishing an extratextual reality on which to base their arguments" (Myers 1990a: 30).

One solution to the issue of reflexivity is for the discourse analyst to provide a running commentary (perhaps in footnotes) on the analysis being presented, underlining and explaining the rhetorical function of the analyst's text. The problem with this type of writing is that it can tend to narcissism (Fuhrman and Oehler 186:303). The alternative is to embrace reflexivity so fully, that it alters the entire form of one's text. This has led to the idea of 'new literary forms', best exemplified by Mulkay's use of plays and dialogues (Mulkay 1985) or Ashmore's inclusion of a transcript of his Ph.D. viva exam (Ashmore 1989). Although such exercises push the boundaries of the science studies text, they do mean that one focuses more on the form of the text than its content. Often, it is the clever, reflexive structure of such texts that one remembers, rather than what conclusions they draw about scientists and scientific practice. Myers' solution to 'the reflexivity problem' is to set it to one side and I intend to follow this example; acknowledge the importance of reflexivity as a theoretical concern, and avoid it as a practical issue.

I am aware of the rhetorical nature of this thesis. I have analysed and attacked previous conceptions of geneticization to construct a problem needing a solution ('geneticization needs more definition'). My case studies, relying upon the idea of a narrative as a guiding structure, tend to present evidence in chronological order. This emphasises the diachronic nature of the discourse, and thus reinforces my use of narrative. This chapter itself serves the purpose of setting my work within a methodological context, gathering antecedents as supporters, to justify my particular approach. This thesis is rhetorical, it is intended to persuade. But having acknowledged that, I do not think it is necessary to bring it to the reader's attention further, either through footnote reminders, or by rewriting it as a one-act play. The focus of my research is geneticization, rather than primarily being about how scientific texts persuade.
How to choose target articles

One final methodological issue concerns the selection of articles for analysis. I have chosen review articles that play an influential role in the discourse surrounding a particular disease. How does one assess 'influential'? One way is to see how often an article is cited, to see how much impact it has had on debates. For some of the articles chosen, their impact is clear; one of the cystic fibrosis articles has been cited over 700 times since its publication in 1976. This seems a significant number of citations. Yet the problem with using citations as a basis for selection is the variation in citation culture (i.e. the number of citations that counts as significant) between disciplines. In comparison with numbers presented by other authors, it would seem to be a significant article. Yet for two of my case studies my choice of articles, although influenced by citations, also pays attention to what happened next. In the case of both cystic fibrosis and diabetes, the review articles I analyse present new disease classification systems. Historically, these systems were adopted by formal consensus groupings of professionals. These review articles are influential, both because of the number of citations they have received, but also because the narrative constructed within them has had a profound effect on how the diseases concerned are classified.

The case of schizophrenia is slightly different. The reviews analysed are in a leading schizophrenia journal, and have a high number of citations. But the narrative of enlightened geneticization I claim is constructed within these reviews has not yet achieved the dominance of those in CF and diabetes. The articles represent a mainstream of opinion, because of the citations, but also because of the links to I.I. Gottesman, one of the major figures in the field, and the controversy the studies presented in the reviews have stirred up.

48 Phelan, for example claims that a paper with "a total of 226 citations from 1983 to 1995...is one of the most cited papers in the natural science during this period with an Australian author" (Phelan 1999:122).
2. Popularisation of Science

One of the aims of this research is to investigate the role of popular science in influencing disease classifications where the kind of popular science I will look at is review articles in the scientific literature. This might seem odd to the traditional view which sees popularisation as:

"the transmission of scientific knowledge from scientist to the lay public for purposes of edification, legitimation and training...a low status activity, unrelated to research work" (Whitley 1985:3).

I question whether it is possible to draw the line between popular science writing and technical writing. In particular, I hold that review articles may be treated as a form of popular writing, and play a pivotal role in the formation of narratives and the settling of debates.

The continuum of exposition

Those who would distinguish between popular and technical science writing face a problem: where do you draw the line? While theoretically it might sound simple to separate writing for a popular audience from 'proper' science writing, actual attempts to do this in the past have proved fruitless (Hilgartner 1990:524). For example, in the case of medical texts, how does one distinguish between a popular audience and a scientific one? "Do medical doctors constitute a truly scientific audience, or should one reserve that category for active researchers?" (Hilgartner 1990:525). There is no technical text that does not imply some form of popularisation, nor any popular text that does not involve a degree of technicality.

One approach might be to say that only publication of original scientific work, when knowledge was first created, counts as technical writing. Everything else 'downstream' of that is a popularisation. But much work in the sociology of science shows that 'facts' only exist as facts when they are accepted by the community, well downstream of the original article. Myers (1990b) shows how scientific discoveries are only recognised as such when they are recreated in review articles. Only selective hindsight allows such an approach to work (Hilgartner 1990:525-526).
The dominant view of popularisation, what Shinn and Whitley describe as the 'conventional wisdom' position, links closely to traditional realist perspectives on science. It reflects a particular view of scientific knowledge and it involves:

"the tacit presupposition that scientific popularization belongs essentially to the realm of non-science, or only concerns the periphery of scientific activity. According to conventional wisdom, then, scientific popularization is irrevocably separated from the central core of scientific research and thus from the process of knowledge production" (Shinn and Whitley 1985: vii).

Shinn and Whitley propose an alternative vocabulary to the dichotomy of popular vs. technical. They refer to scientific exposition:

"exposition is defined here as a sort of continuum of methods and practices utilized both within research and far beyond, for purposes of conveying science-based information, whether as pure cognition, pedagogy, or in terms of social and economic problems" (Shinn and Whitley 1985:viii).

If we adopt this idea of a continuum, then it becomes easier to see review articles as a form of popular science. They summarise and communicate scientific knowledge to a broader community than just the researchers involved on specific problems. But their role as popularisation does not reduce their importance. Rather, the review article's position on the continuum is unique in terms of the role it plays in pooling references, interpreting information and structuring disciplines.

The importance of popular writing is emphasised in the writings of Ludwik Fleck, who compares the esoteric circle (those scientists at the fore-front of a specific bit of research) and the exoteric, who are those, scientists and lay-men, who are not specialists:

"Take the case of a researcher who creatively approaches a problem and is a "specialized expert" informed in the greatest depth...He constitutes the center of the esoteric circle of the problem. The circle includes, as 'general experts,' scientists working on related problems- all physicists for instance. The exoteric circle comprises the more or less 'educated amateurs.' A contrast between expert and popular knowledge is hence the first effect of the general structure of the thought collective in science. The richness of this field requires that even within the specialized esoteric circle, a sphere of special experts must be distinguished from that of general ones" (Fleck 1979:112).
Thus the relationship between popular and specialist texts is built into the nature of scientific practice. Such a position fits in well with that of Baudouin Jurdant, who claims:

"In other words, popularization of science seems to have an epistemological role to play within science itself...The significance of such a role is that not only should popularization of science be seen as part of science itself, but also that it is a necessary ingredient" (Jurdant 1993:371).

Merging into the Stream of Knowledge

The majority of the texts analysed in this thesis are review articles in scientific journals. They are clearly review articles, either because the journals concerned are kind enough to label them as such, or because they correspond to what one can recognise as the format of such articles. They display a review's "mandatory" characteristic, of reporting no original research (Woodward 1974:369). Review articles are a good choice if one is trying to gain (or present) an overview of developments in a particular area of research. They are also useful because they do things that other scientific articles do not: "a review shapes the literature of a field into a story in order to enlist the support of readers to continue that story" (Myers 1991a:45). A review interprets research papers and findings in order to construct a narrative and knowledge (Sinding 1996:57).

A review is an exercise in rhetoric, since it is intended to persuade readers of a variety of different things: to accept and use the author's claims in the reader's own research, to see the topic as relevant to the reader and thus to ally themselves with the proponents of this particular interpretation of the facts (Myers 1991a:46). In this sense, the review is a recruiting drive. If review articles are exercises in persuasion and recruitment, how do they go about producing their rhetorical effect? After all, they cannot produce some new, previously unpublished finding in an attempt to sway their audience, since the defining feature of review articles is their lack of new findings, their lack of original results (Myers 1991a:45). The review article must use the published literature as its raw material. But as Myers points out, the nature of this material does not mean that nothing new can be said. For although

"At any moment in the development of a field, the past has a canonical shape, recorded in the historical introductions of textbooks, in citations of "classic" articles, in eponymous terms...the present is still a scattering of articles reporting various results with various methods aimed at various immediate problems...The review selects from these papers, juxtaposes them, and puts them in a narrative
that holds them together, a narrative with actors and events, but still without an ending" (Myers 1991a:45).

In terms of discourse analysis, one must look at the ways in which the narrative, this 'moving in a certain direction', is produced. It is the construction of knowledge in review articles that allows certain experimental reports to be seen as 'key' articles. Even the idea of a specific event as the 'discovery' of a particular fact depends upon review articles to organise the claims and techniques in a particular direction (Myers 1990b:104, Sinding 1996). The neglect of review articles and the perception of experimental articles as key is not only present from the viewpoint of the scientist, but also from that of STS. But interest in the social construction of science requires us to look at all forms of scientific writing: "such as reviews, news articles, textbooks and popularizations" (Myers 1991a:70).

What follows next is a detailed presentation of how Myers analyses two review articles to show how they construct their narratives using a specific format of dividing narratives into 'plot' and 'story'. I do not use this method in my own research for just as Myers finds Gilbert and Mulkay's division into the contingent and empiricist repertoires unhelpful (Myers 1990a:29), so I find the use of Plot and Story to be limiting. The distinction between these two categories is, at times, arbitrary and forcing particular themes into one or the other seems unproductive. I present Myers' approach in such detail for two reasons. First, it shows convincingly how important review articles are in reconstructing fields of study and influencing disciplines. Second, it provides a point of comparison to my analysis of review articles, which is less formalised.

**Plot and Story**

Myers suggests that the literary distinction between plot and story is useful in analysing narratives in review articles, where "*Story* is the supposed chronology of events behind the plot...[and] the plot of a review article is what gives it a surface organization...it follows the reader's experience of reading" (Myers 1991a:52). In the two review articles that Myers examines, by Darnell and Crick, the plots are similar ("they move from the discovery of split genes to the evolutionary implications" Myers 1991a:52) while the
stories are different. Darnell's is about a new account of evolution and organisms, while Crick's is about the scientists who discovered this new theory (ibid.).

One obvious way of assessing the plots is to look at the structure of the article, as represented in headings and sub-headings:

"the headings of Crick's article suggests that the plot moves from the experimental data to broader speculations, from sections on the problem in general, to the extent of genes, the kind of molecules affected, and the length of the introns, to the mechanism of splicing, to evolutionary and taxonomic questions. The basis of his plot is to start with statements of facts that seem quite scattered, presented as if in simple lists - lists say, of which genes have been found to have introns" (ibid.).

For Darnell's article, Myers summarises both plot and story in such a way as to make them directly comparable:

"the plot has to do with research and argument among scientists
- Recent experimental results cause a shift in thinking.
- Researchers present two views of when divided genes arose.
- One can propose two ways divided genes aid evolution.
- Researchers present evolutionary reasons for the retention of divided genes.
- Research strategies will change as a result."

"the story has to do with eukaryotic organisms.
- Eukaryotes and prokaryotes arose from a common ancestor.
- Eukaryotes maintained split genes while prokaryotes eliminated them.
- Eukaryotes were able to use split genes to their advantage in evolution.
- Eukaryotes keep divided genes today."

(based on Myers 1991a: 52-53)

Darnell's article is presented as "much more like most reviews" than Crick's which is "atypical in many ways...[an].odd text" (Myers 1991a:47). Myers has stated that atypical texts are useful, since they make apparent those elements of a genre that we normally take for granted, and expose their persuasive function (Myers 1991c:325). The review articles I focus on are, in the most part, typical, without the idiosyncratic style of Crick's writing.
Verb Tenses

Myers suggests that by focusing on plot and story, other issues such as the role verb tenses play become apparent. For example:

"Darnell's article...begins with a present perfect verb, implying a series of events leading up to and including the present moment...then it continues with present-tense statements giving the knowledge that the new research takes as given...[There is then a] move to the past tense at some point [which] signals the story of the work of the researchers, a narrative of human events contingent on techniques, luck, genius, or institutional organization...The return to the present signals the new state of knowledge" (Myers 1991a:54-55).

According to Myers, Crick also uses this verb-tense structure, where "the past tense signifies events in human history...the present tense signifies truths about nature...and the present perfect focuses attention on recent research that is directly relevant to the present" (ibid.). It would seem that the importance of this is less to do with the actual order that the tenses occur in, and more to do with their close proximity to each other. This characteristic verb structure "relate[s] the order of statements -the plot- to the order of narrated events -the story" (Myers 1991a:54) and acts as a signpost to the difference between plot and story.

Referencing

Different uses of references allow Myers to highlight the differences between the two review articles he is analysing:

"Darnell's article has a reference for nearly every statement...72 references in all, so that the pattern of the article is an alternation between the claims of the cited texts and the comments of the review...Although Crick cites more than a hundred articles...his text is not organized around the references as Darnell's is. Most of the references that Crick does give occur in densely packed paragraphs that explore ideas with few references. " (Myers 1991a:55-56).

The most influential sections of Crick's article are where he has the least reference support. The often cited section where he outlines the possible ways for genes to split, contains very few citations itself (Myers 1991a:56). The different use of references highlights the different aims (i.e. Stories) of the two articles. "For Darnell the citations support each step of a complex argument. For Crick they are just the first step from which he begins his own thinking" (ibid.). Myers' point is that Crick and Darnell are trying to do different things with their research articles:
"the style of Darnell's article plays down any sense that he is attempting to enlist support for his own view...[while]...Crick's article...is focusing attention on the process of sorting out findings...he is enlisting support, not for a claim, but for a way of formulating claims" (Myers 1991a:47).

One reason for the differences in the two authors' styles is that they are "famous for different things" (ibid.). They are thus faced with different persuasive needs. Darnell, the experimenter, has to try and use his own laboratory's results without seeming to promote them. Crick, the theoretician, has to sort through the research without having done any of it himself (ibid.). This leads to differences in the 'authorial voice' or 'persona' presented in each article.

Persona
The persona presented to the reader is part of the rhetorical stance taken by the author, but:

"Persona is complicated in both articles because the authors speak for several points of view. Darnell divides the field at the moment into two 'views' that are compared in one impersonal voice...Crick seems to present a more personal voice, but it would be more accurate to say that he presents several voices in contrasting styles" (Myers 1991a:56).

"Darnell begins:
For some years evidence has been accumulating that the messenger RNA...formation in eukarotic cells is substantially different and more biochemically complex than in bacteria...[ref]
We are asked to read the article because impersonal evidence requires a change in impersonal theories" (p.56-57).

"Crick...has an unusual opening:
In the last two years there has been a mini-revolution in genetics. When I came to California...I had no idea that a typical gene (ref) might be split into several pieces and I doubt if anybody else had...[ref]
We are asked to read this article because an important theorist has had his ideas shaken up" (p.57).

Myers points out that Darnell's persona is both "assertive" and "impersonal". He fails to state that the work being described is from his own lab. Names are replaced by footnote numbers, which means that he can present his own work without naming himself in the text. He can maintain appropriate modesty about his own lab's achievements (Myers 1991a:58).
In the case of Crick however, "one is immediately aware of a strongly personal, colloquial, spoken voice" (ibid.), but the situation is in fact more complex, with Crick using "two voices...a kind of dialogue between the Crick who speculates and the Crick who reports (ibid.). The 'reporter' restrains the 'speculator', yet maintains the informality of a post-conference presentation discussion. In Myers' evocative phrase: "This is an article with a mug of beer in its hand" (Myers 1991a:59). Crick's inclusion of 'himself' in the article also allows him to include personal comments from other researchers: "Gilbert has pointed out to me...." or "A reasonable guess, as supposed by Tongewa..." (quoted in Myers 1991a:58 and 59). This 'name dropping' reinforces the impression of Crick as an "important theorist", on personal terms with significant individuals in the field, placing him in a network of the 'great-and-the-good'.

Kinds of Readers

The detail of Myers' analysis extends to pointing out that Crick uses shorter sentences, simpler syntax, and generates cohesion in the text through replacement and substitution instead of repetition and conjunction (Myers 1991a:59). This is because the reader for Crick's article is held to have more background knowledge, and will be able to flick backwards and forwards between statements about split genes and statements about the research. Myers goes so far as to say that "Crick's style is characterized by apparent gaps that can only be filled by a reader with some knowledge of the field" (Myers 1991a:63). While this may be hard work for the reader, Crick's style does have "the effect of including them, implicitly, in the set of intended readers, those familiar with this semantic network" (ibid.). This sense of personal inclusiveness may thus aid reader reception of Crick's article (if one can understand it).

Darnell's style, using complex sentences, manages to make statements and raise possible objections to them in the same grammatical construction. Darnell is trying to make clear that there are only two possible sides to the argument over split genes, and his grammatical structures serve to present two clear views of the evidence. Such a style would be very helpful if, as a reader, you had very little background knowledge. Even the basic distinction between prokaryotes and eukaryotes is laid out. Darnell repeats words and phrases and this "allows the reader to follow the main point through a series
of difficult sentences. The constant topic is part of what gives the sense of exhaustive argument to Darnell's style" (ibid.).

In the end though, it is not that Crick's style is 'better' than Darnell's or vice versa. Both styles serve a specific purpose: "Crick's choices of cohesive devices are consistent with the creation of a sense of discussion, as Darnell's devices are consistent with his emphasis on the logical resolution of two views" (Myers 1991a:64).

*Rhetoric as Recruitment*

Myers claims that his aim is to show how the rhetorical strategies used in review articles construct a story and act to "enlist the support of readers to continue that story" (Myers 1991a:45). He attempts to assess these reviews' effectiveness as recruiters with the use of citation analysis and random examination of citations. He concludes that although:

"A review is typically cited often, but not for long...Darnell's and Crick's articles are both cited a great deal...[though]...in somewhat different ways. Darnell's article is nearly always cited in relation to one issue, the view of evolution he proposes, while Crick's is cited for a variety of general ideas and specific phrases" (Myers 1991a:64). This difference in citation is due, at least in part, to the differences in the stories that the two articles present: "Darnell organises a complex series of narratives around one story of how evolution could have occurred. In Crick's article, the underlying story of the shaking up of the research field is not so easily summarized" (p.64-65).

The two authors' styles are also reflected in the way in which they are cited. With Crick, his influence is such that casual phrases or off-hand remarks can be cited later, while Darnell's influence lies in his inseparable relationship with other researchers with similar ideas at the same time. Both these styles show how: "the successful researcher must have both allies to carry out the program and have his or her individual contribution to this program recognized" (Myers 1991a:68). But the different authors approach the same problem in different ways.

*How to do discourse analysis*

When Myers analyses a text, he focuses on actions:
"I start with some attempt to characterize the social acts involved in a text (such as making a claim, making a criticism, referring to the work of others for support, naming, popularizing), always trying to find an act that is recognizable and that has a name for the participants" (Myers 1993: 256 or see Myers 1992).

But Myers' method is influenced by the fact that he wants to highlight the social in scientific texts. He wants to prove that scientific knowledge is socially constructed, through a careful analysis of scientific texts. What do you do if, like me, you accept the social in the text, but are more interested in the way in which genetic explanations are presented in the text? The specific methodology for this type of discourse analysis only really emerges from the text, when one is actually reading the target article although Myers offers some suggestions in his conclusion to *Writing Biology* (Myers 1990a:247-259). My focus will be on the way in which genetics is presented in the articles (including the approach towards non-genetic aetiological factors) and the way in which things (genes, proteins, diseases) are named. What I intend to maintain though, is the degree of rigour and intensity of analysis which Myers uses on his texts.

**Problems: Myers and Popularisation**

One problem confronts anyone who chooses to carry out discourse analysis in the style of Greg Myers, while setting it within the context of Shinn and Whitley's 'continuum of exposition'. Myers uses the idea of narratives to distinguish between the 'narrative of science' that takes place in technical scientific articles, and the 'narrative of nature' that occurs in popular texts (for example, see Myers 1990a, Chapter 5; Myers 1991b). On the face of it, this dichotomy is hardly compatible with the idea that all scientific texts need to be seen in the same terms, as examples of exposition. But this would be too simplistic a reading of Myers, and neglects his emphasis on the social construction of (all kinds) of knowledge. He is explicitly critical of the:

"tendency to take either articles for popularizations or specialist articles as primary and dismiss the other form as a distortion. Either the popular article is seen as watering down the difficult truths of the professional version...or the professional version is seen as complicating the simple truths of the popular version" (Myers 1990a:141).

Myers points out that if we focus on the way in which texts construct scientific facts, then it is much harder to claim that popularisations 'distort' the proper, technical view. What a popularisation might achieve is the construction of a different scientific fact:
"Even when two articles seem to be about the same research, it may turn out that one is about garter snakes and the other about isolation of a pheromone" (Myers 1990a:143).

This difference is because the popular article[^49] constructs a narrative of nature which: highlights the plant or animal under discussion (the garter snake); removes the presence of scientific activity; applies a chronology; and emphasises the separate existence of nature from science. The specialist article, with its narrative of science, arranges time into a series of simultaneous events, and highlights the structure of the discipline that the research is part of (Myers 1990a:142). Obviously, scientific articles assume a different readership than popular texts. Part of this assumption is displayed in the different ways in which articles link sections of text, what Myers calls 'lexical cohesion' (Myers 1991b). Specialist articles rely almost exclusively on repetition to link passages and produce cohesion. This is only possible because scientific readers have enough knowledge to infer these relations. Popular articles use repetition, but also replacement of terms, conjunctions, pronouns and other techniques:

"readers of scientific articles must have a knowledge of lexical relations to see the implicit cohesion, while readers of popularizations must see the cohesive relations to infer lexical relations" (Myers 1991b:5).

Whitley also stresses the fact that popularisations have alternative meanings from specialist articles on the same topic. He suggests that popularisations can be categorised in terms of:

"the degree to which ordinary, everyday language is used as opposed to an esoteric and technical symbol system...[and]...the degree of formalisation and technical precision used to communicate results. The more they rely on diffuse, discursive means of communications, the lower the degree of formalisation" (Whitley 1985:14).

The point about the continuum view of popularisation is not that 'all scientific writing is the same'. Each genre of scientific writing takes place in a different context, and speaks to a different audience. Of course they will be different. The value of classing scientific writing as exposition rather than separating it into 'proper' specialist texts and 'distorting' popular writing, is that it removes the burden of a hierarchy. There is no right way to

[^49]: In this context, Myers is concerned with an article published in a popular science journal: *Scientific American*. 

90
write science. Rather, we are forced to look at the social context of the text, who it was written for, how it tries to persuade.

Summary

This section of my thesis had two aims. The first was to suggest that rigid distinctions between popular science writing and technical texts are hard to draw, and that a more productive approach is to see all science writing on a 'continuum of exposition'. The second aim was to suggest that review articles are a form of popular-science writing, and that previous studies suggest that they are extremely influential in shaping disciplines and in reconstructing scientists' views of historical events such as discoveries.

These two points support my decision to look at review articles in my case studies. It is these reviews, rather than the experimental reports they draw on, that serve to construct the narratives of geneticization. The experimental results themselves could fit into a number of different narratives, some of them contradictory. But the review articles I analyse use them to construct a narrative which makes it seem as if it is the only possible interpretation.

And the issue of interpretation is the focus of the third part of this chapter. In my analysis of the review articles, I show how an interpretation is constructed; this is itself an interpretation. How can the reader be sure that it is correct? Are there alternative interpretations? If so, how do we choose between interpretations? This is the discipline of hermeneutics.

3. HERMENEUTICS

Introduction
What is hermeneutics? "The simplest answer is that hermeneutics is a tradition of thinking or of philosophical reflection that tries to clarify the concept of...understanding" (Bruns 1992: 1). In current usage, the object to be understood can range from a text to a human action to another way of life. Hermeneutics is relevant to my research because,
Despite its current wide-ranging applications, it has its roots in the close analysis of texts. If research is based on texts, on their interpretation and the attribution of particular meanings to them, then the question arises, how do you know what the author meant?

One of the most influential of modern hermeneutic practitioners, Paul Ricoeur claims that the "primary sense of the word" hermeneutics is "the rules required for the interpretation of the written documents of our culture" (Ricoeur 1979:73). If through discourse analysis one can show that the discussion of a particular condition has become more 'geneticized', how can you prove that this is what the author(s) or participants in the discourse meant? In the rest of this chapter I intend to show that scientific texts are suitable objects for hermeneutical study, that there are issues to do with interpretation and meaning that can be addressed and answered by textual analysis. The issue is not whether the practice of science, in the laboratory or field, involves interpretation. Whether scientists interpret the real world, and if so, how they do that are separate issues and are not addressed here. This part focuses on scientific texts as the written records of science, in much the same way that the original proponents of hermeneutics focused on the scriptures as the written records of religious communities.

In many ways, this definition of hermeneutics as limited to textual issues turns back the clock:

"In the nineteenth century, the old theological and literary ancillary discipline of hermeneutics was developed into a system which made it the basis of all the human science. It wholly transcended its original pragmatic purpose of making it possible, or easier, to understand literary texts" (Gadamer, Truth and Method cited in Bernstein 1983:112).

For the purposes of this research, it is exactly those 'original pragmatic' purposes that I am interested in. An essential difference between older approaches to interpretation and modern (i.e. post-Gadamer) ones is the role of textual meaning, particularly in terms of how it is related to the author's intentions. Modern hermeneutics proposes that the role of interpretation is not to ascertain the author's intention from a text (for meanings do not reside in inaccessible mental processes) but to reveal the subject matter, the 'thing meant'. This leads to the position of never-ending interpretation, and the view that there are as many different interpretations as there are interpreters. Such a position does not help when one is trying to reveal practical rules for analysing texts. Hence the return to
older versions of hermeneutics. To some extent, such a return is justified on the sheer complexity and muddle of definitions that currently surround this topic:

"Hermeneutics has meant so many things over the last two decades, not to mention the last two centuries, or the last two millennia, that any definition must be either vague, partial or misleading" (Szondi 1995: xiii).

**A History of Hermeneutics**

Although the word hermeneutics crops up as the title of one of Aristotle's works, *Peri Hermeneias* (On Interpretation), it is only with the Renaissance and Reformation that it came into existence as a discipline of its own. Protestant reformers proclaimed the 'self-sufficiency' of holy writings and in 1567, Matthias Flacius Illyricus supplied the foundations for Protestant hermeneutics with his book *Calvis Scripturae Sacrae*. Flacius provided two important arguments for those that came after him: just because the scriptures had not been interpreted properly, did not justify the external imposition of an interpretation by the Church. Full and proper hermeneutics could remedy this situation. Second, the scriptures have a coherence and internal consistency to them which requires one to interpret any one section in the light of the whole scriptures. As well as the contributions of the Protestant reformers, additions to hermeneutics came from the disciplines of philology, jurisprudence and philosophy. Enlightenment thinkers such as Christian Wolff and Johann Martin Chladenius used the idea of authorial intent to assist in their interpretation. But for them, such intent is not the indication of an author's psychological state or personality, but relates to how closely the author has stuck to the rules and principles that governed the particular genre or discursive form that the author is writing in (Mueller-Vollmer 1994:4-5).

Friedrich Schleiermacher, who wrote around the turn of the 18th Century as part of the Romantic movement, combined the major trends in hermeneutics and synthesised them into an approach which is still influential today, an approach which held:

"the conception of the organic unity of the work, subscribed to the notion of style as the inner form of a work, and adhered to a concept of the symbolic nature of art which gave rise to the possibility of infinite interpretations. The ancient art of interpreting and explicating texts suddenly appeared in a new and pristine light" (Mueller-Vollmer 1994:9).
From this perspective, it cannot be assumed by a reader that s/he has ever interpreted a text correctly. The act of hermeneutics becomes never-ending, continually requiring addition and revision. Schleiermacher also introduced the idea that understanding was not just a linguistic activity, but a mental, psychological process taking part within the speaker/writer of a text. This led to hermeneutics being seen as a true scholarly discipline, and no longer either a specific body of rules for use by theologians and jurists, or the presentation of material to others, which was restricted to rhetoric.

From this point on, developments in hermeneutics stressed the concept of a comprehensive theory of understanding, rather than practical rules and precepts for the interpretation of texts. Wilhelm Dilthey, who wrote in the mid-nineteenth century, proposed hermeneutics as an 'analysis of human life', influencing Heidegger. He attempted to provide a philosophical foundation for the human sciences, which he insisted should be seen as separate and distinct in subject and methodology from the natural sciences. Although Dilthey viewed language as the "fullest and most complete expression" of our mental life, and the written word as the place where "explication finds completion and fullness" (Dilthey, cited in Meuller-Vollmer 1994:27) his theories stressed the need to interpret 'categories of life', everyday situations in which all human find themselves where they are required to 'understand' what is going on around them, so as to act correctly.

This move away from textual interpretation, to broader consideration of the human sciences, their foundations and how they differ from the natural sciences is visible in the work of those who came after Dilthey. The exemplar of this is perhaps the debate between Hans-Georg Gadamer and Jürgen Habermas following the publication of Gadamer's *Truth and Method - Outline for a Philosophical Hermeneutics* in 1960. However important this trend is, it is of less practical use to research in discourse analysis than the rules and precepts for interpretation developed by jurists and theologians hundreds of years ago. And it is in this limited sense that I will define hermeneutics in the rest of this chapter. This sense of hermeneutics fits with Markus' view (see below), and it is his ideas that will be examined next.
Hermeneutics of the Natural Sciences?

If hermeneutics has traditionally been applied to the humanities and arts, and more recently to the social sciences, the question then arises whether it is also a suitable method of analysis for the natural sciences. In this section, I shall be discussing the article by Gyorgy Markus, "Why is there no Hermeneutics of Natural Sciences? Some preliminary Theses" (1987). The first point to bear in mind is that far from being an opponent of hermeneutics, (and implicitly from his text, social studies of science), Markus views it as a valid method for analysis in the social sciences. His core point in this article, however, is that the way that contemporary natural sciences are constructed means that they are extremely 'hermeneutically naive'; i.e. they are resistant to any form of hermeneutic analysis. This resistance exists despite the best efforts of scholars and academics in other disciplines to analyse the natural sciences:

"Philosophers of science may convincingly destroy the idea of an ideally sharp and unambiguous language of physics; historians of science may discover that in all the great disputes in this field...the adversaries not only regularly misunderstood each other, but these misunderstandings also played a constitutive role...'ethno-methodologists' of laboratory life...can demonstrate that already simple 'experimental reports' are underdetermined...despite all these criticisms, the 'hermeneutical naivety' of the natural sciences persists, because it 'works'. That is, the 'ideology'...of the natural sciences which regards any acceptable scientific text as totally self-sufficient as to its meaning...does succeed because the hermeneutical consequences of a so conceived practice seem to confirm this belief" (Markus 1987:9).

If Markus is correct, then the way natural sciences currently operate precludes any hermeneutics which suggests that a scientific text may carry a 'hidden' or non-obvious meaning, that reading a scientific text involves anything more than just reading a scientific text. In short, he doubts that there is any interpretation involved in reading a scientific text. It is not that Markus is saying that we cannot ascertain the factors (social, political, historical and philosophical) that have led to science adopting this particular stance, but that since it has adopted this stance, we cannot rely on a scientific text to give any help in these alternative analyses of science. We must thus look outside the text.

---

50 Markus is using an idiosyncratic reading of what hermeneutics involves if it is to be restricted to 'just' the text being read. One of the traditional rules for hermeneutic reading requires that the reader know as much as possible about the social, cultural and economic environment within which a particular text was written, in order to make the most accurate interpretation possible.
Martin Eger (1993) has questioned Markus' position and although I agree with much that Eger proposes, I will approach Markus from a different direction. The main thrust of my argument is that Markus misunderstands the nature of the scientific text on a number of levels. He tends to focus on the experimental report as the paradigm of scientific texts, this in turn leads him to draw a distinction between 'proper' science writing and popular texts, which is linked to ideas concerning the professionalisation of the audience of scientific texts.

_Inscribing authors and the norm of depersonalization_

Markus suggests that in science, the author is 'depersonalised' in the sense that "the author inscribed into the texts of contemporary natural sciences is (as a norm) a completely depersonalized one" (Markus 1987:12). The author:

"appears as an anonymous performer of methodologically certified, strictly regulated activities and a detached observer of their results - without any further personal identifying marks beyond possession of the required professional competence" (Markus 1987:13).

So while Markus accepts that natural sciences are, in a proprietary, creative sense, strongly authorial51, the nature of the scientific text acts in such a way as to erase the author's personality from its inscribed surface. This depersonalisation of the text is a result of: the paucity of genres in natural science; the routine, standardised structure of the scientific paper (or more specifically the 'research report'); and the actual style of the research articles which decontextualises the details. It is important to note that the depersonalised author may not occur in every scientific paper, but it is rather a norm, a generic requirement. Such a position is clearly possible, if one agrees with Markus' extremely limited reading of scientific texts, both in the genres that exist in science writing, and the content of such genres: "The 'scientific paper'..., the 'comprehensive textbook' and the 'theoretical monograph' are its [i.e. science's] main literary genres", but these can be boiled down to the 'paper' since it "remains as the nearly sole genre for the

51 "there exist elaborate, highly formal conventions concerning 'name ordering' to recognise each particular author's 'assumed share' in the collaboration's literary outcome. Individual authorship in the above sense plays a pivotal role in modern science, since its social reward...system is firmly anchored in this concept" (p.11).
formulation (or at least public recording) of new scientific results and ideas" (Markus 1987:12).

While this might be the case in terms of original results, in the light of the discussion earlier in this chapter it is not true for scientific ideas. As Myers (1991c) shows, the review article is a genre where new ideas in the form of speculation, are presented. Similarly, the 'drawing together' role of reviews allows new interpretations to be put on data. Markus's position also seems to be extremely impoverished with regard to the range of different genres present in science writing, the most glaring omission being that of 'popular science', which has now expanded into a major area of publishing. Part of this limited view may lie in the fact that Markus seems to be suggesting that science regards (normatively) the main aim of science writing to be the "formulation of new scientific results and ideas". This ignores the equally important (normative) role played by the repetition of scientific results. Without the possibility of recognition, the results put forward in a research paper are of far less value.

In fact, the reason behind the artificial structure and "peculiar, idiosyncratic and highly conventional style" (Markus 1987:12) of the research paper which he comments on has a great deal to do with repeatability of experimental results (Shapin 1984). This need for repeatability is just as much a normative convention of the research paper as the depersonalisation of the author. It undermines Markus' claim that the research paper should be regarded as the canonical genre in science writing since it is the primary source of novelty. A novel result is nothing if it cannot be repeated. Even allowing novelty to take precedence over repeatability, this does not necessarily lead to the prioritisation of the research paper. 'Popular science' texts can also be a way of 'publicly recording new scientific results and ideas'. This, of course, requires that we accept that 'the public' is not one homogeneous group to be addressed by means of the research paper, that for a

52 With due acknowledgement of the limitations of this term.

53 For example, Diamond (1997) proposes a novel thesis concerning the technological differences between ethnic groups. This is a popular text proposing a previously unpublished argument, as is Lovelock (1979), which proposes the Gaia hypothesis.
certain audience (or public), popularisations are the main way of achieving communication.

Before moving onto Markus' discussion of the target audience, I will comment on the two other points he makes to support his claim that the research paper is depersonalised, and hence insulated from hermeneutics. The first concerns the structure of the research paper which he discusses at some length (Markus 1987:37-40). He performs a rather neat hermeneutical analysis of the role the structure of the scientific paper plays in suggesting the:

"idea of scientific progress...is a postulate, the admittance of which is necessary to confer meaning upon natural scientific activities....the requested 'adequate understanding' of a scientific paper, posited by its generic form, demands its comprehension as a contribution to an encompassing, irreversible process of knowing, constantly moving forward" (Markus 1987:39-40).

I would contest that this analysis, accurate as it is, indicates, not just the collective normative viewpoint of what qualifies as a research paper, but also the personal beliefs of the scientists themselves. Some scientists have not agreed with the essentially Baconian, inductivist position presented in the structure of the research paper. For example, Peter Medawar once tried to convince the scientific community to change to a more 'realistic' structure which embodied the hypothetico-deductive method, which he regarded as characteristic of science (1964). The fact that his attempts failed might support Markus' when he suggests that social factors have deeply ingrained structure of scientific texts.

Markus' last claim about texts in the natural sciences, is that they "fix language normatively in the role of a mere instrument of communication" by use of their "restricted vocabulary, pedestrianly straight syntax, the ban on the use of rhetorical and poetic figures and topos, [which] all make the language used....unobtrusively transparent, render the text's linguistic constitution completely opaque" (Markus 1987:15). This claim is the one that, for my research, needs the most debunking. Rather than demonstrate the rhetorical, persuasive nature of scientific texts by performing an example of discourse analysis, at this point I merely want to claim that the rhetoric of science and discourse analysis of scientific texts suggest that scientific texts are not 'just' communicative, they are also persuasive. This rhetorical side to science writing is not just an aberration that
'slips through' the normative rules that Markus is outlining, but a necessary and admitted part of scientific texts. This is important for my own research since I wish to show that the review articles I analysis construct particular narratives about the diseases they discuss, that these narratives perform a persuasive function and serve to help the geneticization of those diseases.

**Intended readers and 'popular science' writing**

"The so-conceived 'intended' reader of contemporary scientific literature is - and solely- the expert professional, working in the same research area to which the work in question pertains....In principle...the audience of natural scientific discourse is restricted to those who can equally participate in its continuation. This social closure of the discourse upon itself; the specialization and professionalisation of its intended/implied public...constitute again a specific feature of contemporary natural science as a cultural genre" (Markus 1987:19-20, all emphasis in original).

What is clear in this position is the belief that the canonical text of the natural sciences is the research report, and it is this type or genre of writing that contains and maintains all the normative standards of science. Having criticised the presentation of the research paper as depersonalised and purely communicative, I now want to suggest that it is also erroneous to suggest that the research paper should be prioritised above other genres in science writing, as the primary text. And rather than suggest that there is another alternative that should take its place, I would refer back to the discussion in part 2 of this chapter and the idea that there are a number of styles of writing in science, each of which is valid and a 'proper' form of science-writing, but each of which has different goals and target audiences. Markus would probably agree with this last point, but would object to the further point that the 'professional' audience is not 'better' than the lay/public readers of science. The institutional history of science writing that Markus is sketching is extremely impoverished in its neglect of the role publicisation of science has in science writing (both modern and in earlier times). Although I will not repeat points made earlier, I will address specific claims made by Markus.

The first comparison he makes is with the social sciences and humanities. Here, he claims:
"Even today the most important and influential scholarly works in humanities and social science regularly find an audience wider than the one comprised of the 'professional experts' in the field. This public is constituted partly by scholars in other disciplines and specialities, partly by the elusive 'cultivated reader' - and it seems to be growing rather than diminishing" (Markus 1987:20).

One could oppose Markus' position on the grounds that he offers no evidence to support this statement, and only mentions in passing a sample of the types of authors he is considering. This could be seen to miss the point. Markus is sketching a broad outline of a situation, and has no need for figures and data. One answer to this is that taken by Martin Eger (1993) when he suggests that there is a 'third genre' between science and humanities writing, that addresses large scale philosophical issues using the form of a popular science text. Eger analyses a selection of such books, drawing out their common themes and hence presenting them as a single, coherent genre. Another alternative, which I wish to suggest, is that such popular humanities books may cross the disciplinary and professional boundaries, not because there is a difference between humanities and sciences, but because they are specifically written to do just that, to be valuable scholarly works and best-sellers. For example see Miller (1984:125) for a description of a historian deliberately aiming to outsell an intellectual rival.

This should serve to remind us that Markus' focus on the 'historical hermeneutics' of the cultural institution of science blinds him to the fact that other cultural institutions (the humanities, social science) are not 'black boxes', but have their own rules, normative forces and social tensions as well as exceptions to those rules. If one adds to that Eger's assertion that there are texts which "are still classed as 'popularizations' " but which also "distil the deeper meaning of scientific advances on fairly broad fronts, calling attention to cognitive implications that bear on human self-understanding" (Eger 1993:187) the weaknesses in Markus' generalisations become apparent. Although it would be inaccurate to represent Eger as accepting that his 'third genre' texts are the same as popular texts, his ideas, and the paucity of Markus' evidence with regard to the differences between the natural sciences and other disciplines open the way for an alternative view of popular science texts.

54 For example, a comparison of the books sales of one of his 'genre-breaking' humanities texts with its citation rates in the Humanities citation index.
The central issue to whether a piece of writing is 'popular' or not, is its target audience, "the reader/addressee prescribed and implied by these texts as their adequate... recipient" (Markus 1987: 19). It is here that an element of incoherence enters into Markus' claims: "The so-conceived 'intended' reader of contemporary scientific literature is - and solely- the expert professional, working in the same research area to which the work in question pertains" (ibid.). Yet this makes many research papers extremely limited in their possible audience, excluding those not working in the same 'research area'. Markus tries to solve this by suggesting that "this research area - and thereby also the circle of recognized addressees- is only defined in a diffuse way. Basically it is pre-given to the author by the existing institutional structure of scientific specialization" (Markus 1987:19-20). Thus 'proper' scientific papers are still restricted to within their institutional divisions.

This makes explanation of journals such as Nature or Science, and more importantly, the kudos associated with publishing in such journals, extremely difficult. If Markus is correct, and the "professionalization of the audience" (p.20) in science is such that the normative rules of natural science writing require addressing "solely...the expert professional working in the same research area" (p.19), then journals such as Nature which publishes "reports whose conclusions are of general interest" or Science and its "items that seems to be of general significance" (Myers 1990a: 75) are aberrant rule breakers, and could hardly be deemed the preeminent means by which a scientist can publish his/her work. That Nature and Science are widely read, valued and sought after as a venue for publishing by scientists across the different 'institutional structures of scientific specialization' should alert us to the fact that Markus is badly wrong. These journals have different standards and needs from other scientific journals\(^5\), yet that does not detract from their standing. They involve more 'popular' (i.e. non-technical writing) than specialist journals (Myers 1990a), but they are hardly 'popular science' in the mould of, say, Scientific American or New Scientist. Yet if they do not fit Markus' conception of a natural science text, under the dichotomy which he uses, they must be placed with

---

\(^5\) For example, articles which are publishable by specialist journals may not be suitable for Nature or Science (Myers 1990a: 41-100).
popular science texts. Markus' view of the natural sciences as professionalised and specialised though accurate\textsuperscript{56} is not the whole story, his view is too intent upon "This social closure of the discourse upon itself" (p.20). Even popularisations of science in the conventional view\textsuperscript{57} can play two important institutional roles in the natural sciences.

First, they are important to the scientists themselves because they produce the 'reality effect', the impression of the unity of science as a single enterprise (Jurdant 1993). This ties into the position that popularisations have, as actual science (see above). The second institutional role that popularisations play relates to external representations of science:

"There is clearly prestige within the research community attached to being asked to speak for one's field, and there is a chance to address a broad audience that includes many researchers and administrators in related fields who would not ordinarily read one's work in specialist journals" (Myers 1990a:145).

Thus there are external, even funding reasons for writing popularisations. These are the sorts of institutional issues that Markus' supposed "historical hermeneutics of cultural institutions" misses; they are also the types of meaning and intention that a hermeneutical reading of science texts can reveal. 'Science texts' here is inclusive of both 'technical' writing and 'popularisations of science'. Some texts may be easier to interpret in terms of institutional issues and gaining publicity for an obscure area of research, and these may be what are described as popularisations. But even those texts which seem to be depersonalised and transparently communicative serve a persuasive function, not as a side effect of breaking the 'normative rules' such texts should ideally follow, but rather by conforming to institutional rules of writing such texts.

**Rules for Reading**

The title of this section refers not to rules which determine what makes a text a member of a particular genre, rather they are about how to read and hence interpret a text, so as to understand its meaning. This is not about the methodology of discourse analysis, but a meta-methodology about how any particular method of analysis -be it discourse, content or psychoanalysis- can produce interpretations that one can consider valid.

\textsuperscript{56} There are after-all professional scientists who work in specialised areas of science.

\textsuperscript{57} i.e. *New Scientist* and *Scientific American*. 
One approach is offered by E.D. Hirsch in his 1967 book *Validity in Interpretation*. Hirsch's book is interesting because, written as it is in the aftermath of Gadamer's *Truth and Method*, it represents an attempt to return to a very old fashioned view of hermeneutics. Although he does not quite return to the unpsychological position of Seventeenth century writers such as Wolff, he does treat with scorn the modern notion that an infinite number of interpretations can be made from any one text, with all being equally valid.

What Hirsch does accept is the 'hermeneutic circle', which stems from the self-confirming nature of interpretations: "Every interpretation labors under the handicap of an inevitable circularity: all his internal evidence tends to support his hypothesis because much of it was constituted by his hypothesis" (Hirsch 1967:166). Despite this problem, Hirsch counts himself among the optimists who believe that one can reach "objectively grounded discriminations between conflicting interpretations - despite the circularities and complexities which bedevil the interpretive enterprise" (Hirsch 1967:169). The solution lies not in hard and fast rules of interpretation (a 'canon' as Hirsch terms it) but in 'the logic of validation'. Such a logic underpins probability judgements about the possible validity of different, competing interpretations. While it is never possible to show that a particular interpretation is undeniably correct, some interpretations are more likely to be correct than others. The "objectivity of interpretation as a discipline depends upon our being able to make an objectively grounded choice between two disparate probability judgements" (Hirsch 1967:180).

The central point of Hirsch's position is that rather than adopting a set of rules and methods which would only be of use in relation to specific genres, the trick is to adopt this 'logic of validation' which requires a reader to propose alternative interpretations, and to test them in the light of probability, excluding those which do not fit the likeliest explanations. As a guide to a method like discourse analysis, such logic requires one to continually asses the probability of any particular interpretation against the alternatives

---

58 Although not in a statistical sense.
that may present themselves. For my work, such assessments would force one to ask whether a genetic explanation is actually being proposed, or whether alternative aetiologies are more probable candidates. As a broad 'rule of thumb', such probability judgements seem sensible. An article by a scientist whose career is based on the idea that schizophrenia is a genetic disease, for example, is more likely to place certain meanings on evidence of environmental influence. Yet Hirsch's attack on the 'infinite interpretations' school of thought lacks power. One does not have to be an extreme post-structuralist to suggest that any one text can have a large number of equally valid interpretations. The empirically grounded reader-response theory explicitly states that different readers will interpret the same text in very different ways (Steinke 1995:434).

The critic and philosopher Stanley Cavell suggests that there are two worries about the interpretation of texts. The first:

"that a critic is reading something into a text...putting something into a text that is not there...as a term of criticism [this] suggests something quite particular, like going too far even if on a real track" (Cavell 1981: 35).

Cavell's solution to this is characteristically forward. Although he appreciates this concern, it is a mark of timidity with regard to texts. "In my experience people worried about reading in...[are]...typically afraid of getting started" (Cavell 1981:35). The trouble with most texts is not that they are 'over-read' but that they are not read enough. Any complaint about reading-in must be made on the basis of individual texts, rather than as a sweeping claim about interpretation as an activity.

Cavell's second worry is that there is more than one interpretation of a text. Again, rather than backing away from this problem, Cavell embraces it, suggesting that it is not that there might be more than one interpretation, but that there must be more than one interpretation. Building on ideas from Wittgenstein, Cavell suggest that when we talk about seeing 'an aspect' of something ("seeing something as something"), two things must be true. One, "There must be a competing way of seeing the phenomenon in question, something else to see it as" and also that "a given person may not be able to see it both ways, in which case it will not be true for him that sees it" (Cavell 1981: 36). Thus, for something to be an interpretation "there must be conceived to be competing interpretations possible, where 'must' is a term not of etiquette but of...grammar,
something like logic" (ibid.). In hermeneutics, the existence of alternative interpretations should not be seen as undermining one’s work. It is an essential feature of what it means to interpret a text. This reflects on how Cavell views a complete interpretation.

"Completeness is not a matter of providing all interpretations but a matter of seeing one of them through. Reading in, therefore, going too far, is a risk inherent in the business of reading, and venial in comparison with not going far enough, not reaching the end" (Cavell 1981: 37).

In each case study in this thesis therefore, I will follow one particular interpretation through to the end, read the text as far as it will go. In a reflexive sense, this means accepting the one’s role as persuader, the fact that one has to be an advocate for one’s interpretation of a text, while acknowledging that the text is itself persuasive.

I have already partially addressed the issue of authorial intent: my use of the term ‘strategy’ to describe the elements that make up a narrative is done without implying authorial intention. It is all too easy, when analysing a process such as geneticization, to attribute intention to the writers one is reading. My interpretations avoid attribution of authorial intent, not just because this is a standard position within hermeneutics, but also because I wish to distance my definition of geneticization from the kinds of moral claims that are made about it by others. I do not claim that the authors of the review articles I analyse are consciously trying to geneticize particular diseases. Nor do I claim that they wish to 'expand' or 'split' disease classifications. I do not have the right sort of material, such as interviews, to make these kinds of assumptions. And these assumptions are, to a greater or lesser extent, irrelevant anyway. I am interested in the effect of these articles on the reader. My interpretations could therefore be dismissed as 'personal' and subjective. It is perfectly possible (or even necessary) that there are many ways to read these articles and that other people might not be able to see my interpretation. But that does not undermine my interpretations. And proponents of alternative positions need to offer their own readings, and follow them through to the end as I do, if they wish to

---

59 The one place where I do indulge in a slight degree of psychological speculation is when I discuss Andrew Cudworth’s classificatory system for Diabetes (chapter 5). This is partly due to the kinds of detailed debates that take place in diabetes literature. It is also due to the great help given to me by Professor Sir George Alberti and Professor Harry Keen.
challenge my interpretations. In the next chapter, I present the first of my case studies, and look at how geneticization takes place in cystic fibrosis.
CHAPTER 4: STATE OF THE ART: CYSTIC FIBROSIS AND THE NARRATIVE OF EXPANSION.

"Compared with polygenic diseases, cystic fibrosis is easy and therefore paints the rosiest picture of what can be achieved by genetic research" (Geddes and Alton 1999:1052).

1. INTRODUCTION

How does geneticization take place in a hereditary disease? That is the question for this case study. The definition of geneticization adopted in Chapter 1 of this thesis - geneticization takes place when a condition is linked to a particular piece of DNA - means that the one can trace the geneticization of cystic fibrosis to a specific date and a specific article. This case study reveals the existence of a narrative in the discussions surrounding CF which expands disease classifications to absorb traditionally separate conditions. The main example of this 'narrative of expansion' in the case of CF is the reclassification of a type of male infertility (called CBAVD) as a mild form of cystic fibrosis. The narrative is such that future absorption of other conditions (for example, pancreatic disease) also seems likely. This reclassification and absorption is explicitly made possible by genetic testing for the CF gene, and is thus a direct result of geneticization.

Eric Juengst predicts one kind of 'nosological expansion' when he suggests that prioritising genetic explanations for disease will lead to all diseases influenced by genetics being classified as 'genetic diseases', and thus an increase in the diagnosis of individuals with genetic diseases (Juengst 2000). The type of expansion present in CF is subtly different from that discussed by Juengst. Instead of diseases being newly classed as 'genetic', this form combines diseases in a spectrum of conditions. Classifying diseases on genetic grounds leads to diagnosis being based on the presence or absence of a particular gene or allele. Yet even in a 'simple' Mendelian disease like cystic fibrosis, the disease mechanisms are such that a genetic diagnosis can have unfortunate consequences for patients and families. Chmiel et al. (1999) discuss the case of a girl who initially presented at their CF centre, aged 2 months, for a second opinion. Some of her relations had been diagnosed as CF-sufferers and both her parents were CF carriers (since CF is a recessive disease, one needs two copies of the faulty gene to develop it). Since they refused prenatal testing on the foetus, it was at birth that they found that the girl had
inherited both faulty versions of the CF gene. It was thus assumed that she would develop the condition in later life.

Despite this diagnosis of cystic fibrosis, the girl remained healthy. Her sweat was collected and found to be normal (one test for CF is to measure levels of chloride ions in sweat). Pancreatic enzyme treatment which had begun when the original diagnosis was made, was discontinued 3 months later with no apparent negative effect on her digestion. The authors point out that although "This child was given the diagnosis of CF based solely on the presence of two mutant alleles...she does not yet meet diagnostic criteria for CF" since she displays none of the clinical symptoms traditionally associated with the disease (Chmiel et al. 1999:825). The reason for this apparent discrepancy is that despite having two copies of CF causing alleles, she probably also carries normally neutral alleles which serve to ameliorate the effect of the deleterious genes. As a result, her body produces enough of the protein that goes wrong in CF (called CFTR) and she has a normal phenotype. As Chmiel et al. point out, "Had this child presented before the discovery of the CF gene, a sweat test may have been obtained...[on the basis of family history]...but the CF diagnosis would not have been made" (Chmiel et al. 1999:825).

One might think that no harm had been done by the CF diagnosis; the girl is too young to understand what has happened and no harmful treatment had been carried out. Yet this would be to ignore the wider, familial effects that diagnosis of a condition such as CF has:

"These parents did not proceed with termination of the pregnancy...[since they did not use a prenatal test]...However, they initially decided against having more children...and were considering methods of irreversible birth control. The patient's father, a career serviceman in the US Navy, accepted a discharge so that his daughter could receive consistent medical care at one CF centre. Because he was then unable to obtain employment for 6 months, the family was forced to seek temporary housing and governmental assistance" (Chmiel et al. 1999:825).

The point of this example is not to suggest that misdiagnosis is a new problem, or one restricted to genetic diseases. Rather, the aim is to raise the question of what counts as

---

60 She inherited the ΔF508 allele from her father, and R117H from her mother.
adequate grounds for diagnosis of CF, and how the authors of the review articles I examine convince others of these grounds.

2. A BRIEF HISTORY OF CYSTIC FIBROSIS

In his 1952 synopsis of CF history, Bodian suggests that we divide the clinical history of cystic fibrosis into three separate phases. In the first, cases of steatorrhea\(^{61}\) were described, which may have been due to CF. Sir Everard Hove (1813), Byron Bramwell (1902 & 1904), John Thomson (1904) and Garrod and Hartley (1912) all described pancreatic symptoms which are reminiscent of cystic fibrosis. In 1919, Passini proved that abnormality of the pancreas was sometimes the cause of steatorrhea, and these findings were echoed by Miller and Perkins (1920), Daffinee (1931) and Parmlee (1935):

> "the general picture described by these authors was of a disease occurring in infants and children, with onset sometimes at birth and sometimes later, in which transient or persistent fatty diarrhoea was always prominent, with wasting and a distended abdomen, accompanied with frequent bronchitis, terminating sometimes in a fatal broncho-pneumonia" (Bodian 1952:4).

The second phase "is that in which attempts were made to organise the cases of steatorrhea into definite groups" (Bodian 1952:4). This revolves around Anderson's work in 1938 which showed that Cystic Fibrosis was a distinct disease entity, with a natural course and symptoms present at birth, which had a tendency to run in families. It was the clarity of this paper that allowed doctors to recognise many previously undiagnosed cases of 'cystic fibrosis of the pancreas'. The third of Bodian's phase's is that in which it was assumed that there is a single basic defect occurring throughout the body which causes CF. Faber (1943, 1944, 1945) proposed that the pathology present in the pancreas was only one manifestation of an abnormality affecting all mucus glands in the body.

We can use Bodian's structure to suggest that there are two more phases which have occurred since 1952. In 1953, researchers made significant discoveries on the electrolyte composition of the sweat of CF patients, paving the way for the development of the

\(^{61}\) Steatorrhea is a form of diarrhoea characterised by high fat content and is a classic clinical symptom of CF.
diagnostic sweat test. The 1960's saw the development of specialised CF clinics in the US and elsewhere, such as in the UK and the Scandinavian countries (Kulczycki 1990:9-10). Starting in 1960, a series of meetings and symposia on CF took place until "After 1970 CF topics and CF symposia took place almost on all continents, representing an integral part of paediatric, medical and surgical meetings" (Kulczycki 1990:10). This then is the Fourth phase, where CF becomes a normal topic of clinical study and professional specialisation, with accurate diagnostic tests and increasingly effective treatments.

The fifth phase is defined in terms of the discovery of the Cystic Fibrosis gene on chromosome 7, and the identification of the protein involved in CF, the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR). The hunt for the CF gene is interesting, not just in clinical terms, but also as one of the first successful examples of reverse genetics. This is where a specific gene is identified without prior knowledge of the protein involved (other examples where this has been used include Huntington's disease and Duchenne Muscular Dystrophy). Since this is felt to be the likely use for much of the information being generated by the Human Genome Project, CF was an important test case (Geddes and Alton 1999). Finally, this research is interesting for its human element: "Even within the highly competitive field of human genetics, the search for the cystic fibrosis gene stands out for the intense nature of the rivalry" (Roberts 1988a:141). The result of this competition was the announcement in September 1989 that researchers had identified the CF gene as a stretch of chromosome 7 (Rommens et al. 1989).

**Clinical Diagnosis**

The clinical diagnosis of cystic fibrosis is based on a number of symptoms affecting mainly the pulmonary system, but also including gastrointestinal problems, defects in the pancreas and infertility in male CF patients.

Treatment for CF includes antibiotics and physiotherapy (to treat the lung infections and clear the airway), as well as large calorie intake (due to both increased effort to breathe
and reduced absorption of calories/proteins). In the most extreme cases lung and/or liver transplants are required.

**Chronic sinopulmonary disease manifested by:**
- Persistent colonisation/infection of the lungs with typical CF pathogens
- Chronic cough and sputum production
- Persistent chest X-ray abnormalities
- Airway obstruction manifested by wheezing and air trapping

**Gastrointestinal and nutritional abnormalities including:**
- Intestinal: rectal prolapse, intestinal obstruction syndrome
- Pancreatic: pancreatic insufficiency, recurrent pancreatitis
- Hepatic: chronic hepatic disease
- Nutritional: failure to thrive (protein-calorie malnutrition)

**Salt loss syndromes:**
- Acute salt depletion

**Male urogenital abnormalities resulting in obstructive azoospermia:**
(adapted from Rosenstein and Zeitlin 1998:277)

The main clinical test used to confirm most suspected cases of CF is a sweat test. This utilises the fact that sodium and chloride levels are abnormally high in the sweat of patients with CF. The sweat test has remained much the same since Gibson and Cooke developed it in 1959; pilocarpine nitrate is driven into the skin by an electric current. This stimulates the production of sweat which collects in gauze or filter paper sealed with plastic over the area. After 30-60 minutes, the gauze is removed, and the amount of sweat collected weighed, before being analysed for sodium and chloride content and concentration. The normal range for a child's sweat chloride level is less than 40 mmol/l. A concentration of over 60mmol/l is abnormal while 40-60mmol/l is equivocal (Birnkrant and Stern 1991).

**Nature of the defect**
Historically, the most obvious symptom for CF was salty sweat. Indeed, this is what the sweat-test diagnosis identifies, and the identification of the gene revealed that the underlying problem in CF is the patient's inability to transfer Chloride ions across cell membranes in secretory epithelial cells, such as the lining of the respiratory airways and
the small intestine. The protein CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) is needed for effective Chloride transfer. The various mutant types of CFTR present in CF fail to operate correctly in a variety of different ways (for example not responding to activation signals, or degrading inside the cell before reaching the site of impact) (Davis et al. 1996: 1232). In normal cells, the chloride channel is opened by a process called cyclic AMP (cAMP)-dependent phosphorylation. This does not occur in the cells of CF patients because the chemicals that stimulate this process (the 'agonists') fail to work. With the chloride channels closed, the transport of sodium chloride and water across cell membranes is disturbed, altering the quantity and composition of the fluids secreted by the epithelial cells (hence the thickened mucus in the lungs of CF patients).

Competitive research

As suggested above, the search for the gene responsible for CF was particularly competitive and, at times, acrimonious\(^2\). There were three main research groups involved in some form of controversy in the search for the CF gene: the Toronto Hospital for Sick Children, the St. Mary's London Group of Bob Williamson and the Hughes Medical Institute at the University of Utah.

At the end of 1984, the Toronto group teamed up with a commercial company, called Collaborative Research Inc. in Boston (which had a large range of DNA probes for tracking down polymorphisms), and quickly produced results. By August 1985, they had identified a probe which was within 15 million bases of the CF gene. Despite the numbers involved, this was a huge step forward, and the Collaborative researchers said that they would carry out the next step, and track the gene down to a specific chromosome. At this stage, the lead researcher in Toronto, Lap-Chee Tsui quickly became frustrated with the company's delays. It was taking them weeks to carry out what should have been a one-week experiment and so he followed up a suggestion from Collaborative that the gene might be on Chromosome 7 by carrying out the experiment himself. His confirmation to Collaborative that 7 was indeed correct soured relations between him

\(^2\) This section is based on Roberts L. 1988a&b.
and Collaborative's lead researcher, Helen Donis-Keller. When their joint results were published at the October 1985 meeting of the American Society of Human Genetics in Utah, no mention was made of the location of the gene on Chromosome 7. The company claimed that this was because they had not definitely confirmed it, but other researchers, both at Toronto and elsewhere, suspected that Collaborative was holding this information back (and obliging Tsui to do so as well) to gain commercial advantage.

The 28 November 1985 issue of *Nature* published three articles locating the gene on Chromosome 7. One was by the Collaborative/Toronto team, but the other two were by Bob Williamson in London and Ray White in Utah. These latter two had acted on scientific rumour around at the time of the October Utah meeting, which suggested Chromosome 7, and carried out their own experiment to replicate the Toronto findings. Of course, since the Toronto group had delayed publication of its results, they risked losing the initiative if their rivals published first. In the end, Collaborative convinced *Nature* to publish their article as well, although Tsui was incensed that Collaborative's secrecy had almost led him to be pipped at the post. In December 1986, White and Williamson identified two markers on Chromosome 7, *met* and J3.11, which were closely associated with CF. This promoted a degree of joint effort between the groups concerned (save Collaborative itself, due to its refusal to share DNA probes). This led to the conclusion that these two markers flanked the gene, narrowing down the region to be searched and producing a test which could now offer 99.9% accuracy for the presence of the CF gene in those families where there was a history of the disease.

The next major controversy came in the 30 April 1987 issue of *Nature*, with Williamson's claim to have identified a candidate gene for CF, present in the space between the two flanking markers. The scientific and popular press heralded this as a breakthrough and it was so convincing that other research groups stopped their own investigations. The U.S. National Institutes of Health turned down research grants to other groups wanting to clone the gene. But by the summer, and a conference in August, tempers in the research community were fraying. With no new information coming out of the London group, Helen Donis-Keller of Collaborative, stung by Williamson's sustained and sharp criticism of her company's policies, attacked him openly. A very public wrangle ensued and by
September 1987, at a genome mapping conference in Paris, Williamson was on the verge of accepting that he had made a mistake. By October, he had admitted that he had been wrong and critics claimed that his genuine enthusiasm for discovery had misled the research community, and set back others' work by months. The final push to identify and clone the gene, eventually called the CFTR-gene after the protein it encodes for, resulted in a trio of articles co-authored by the Toronto team, in the September 8th 1989 issue of *Science*.

The story of the discovery of the CF-gene might seem an ideal topic for research into the way social conditions and personalities influence science, but this chapter focuses on very different material. Rather than the intrigue and competition that surrounds a major scientific discovery or controversy (the high points, or mountains on the rhetorical landscape), my research focuses on the subsequent use of and extension of this discovery, into clinical medicine. The aim of this chapter is to investigate the 'black-box' that CF has become subsequent to the discovery of the gene, to analyse the way genetics in CF is presented and how it is used. The main emphasis will be on the way in which the discovery of the gene responsible for cystic fibrosis has altered CF classification and diagnosis in clinical medical literature.

3. THE GENERAL DISCOURSE OF CF

**United by Pessimism**

One consistent rhetorical feature of the discourse of Cystic Fibrosis is the claim that CF is 'most common', and that it is 'severe' or 'fatal'. These phrases are not restricted to pre or post-1989 accounts, but straddles the discovery of CFTR.

From 1976:

"Cystic Fibrosis is the most frequent lethal genetic syndrome among white children" (Wood et al. 1976: 834);

To 1992:

"Cystic Fibrosis is the most common potentially lethal autosomal recessive disease of Caucasians" (Collins 1992: 774).

What has changed is the fact that the average age for CF patients has increased from 16 in 1976 to 29 at the beginning of the 1990s. Alan Stockdale (1996) has criticised the
representation of the child as CF patient in publicity material for patient groups. Stockdale suggests that the overly pessimistic presentation of CF as a 'child-killer' is a rhetorical strategy: "a very effective method of selling the public and investors on gene therapy research. Cute children with ugly diseases sell" (Stockdale 1996:5). From this point of view, presentation of CF as a frequent lethal childhood disease is a means of raising funds, both by clinical researchers and companies that may be developing tests and treatments.

What is not clear is whether the stress in medical texts on the 'lethality' of CF is for the same reasons. In 1981, A.P. Norman claimed that:

"It is time that we stopped talking in terms of 'the most lethal genetically determined disease'. Some of our most respected colleagues still talk about 'the problems of individuals expected to die in early childhood', and of 'the stricken infant who insists on surviving to adulthood' " (Norman, 1981:86).

Norman's complaint was that the average age of CF survival was steadily increasing. For the mental and emotional well-being of those patients who did survive childhood "it is necessary that we do nothing, nor say nothing that might damage their confidence in themselves" (Norman 1981:87). These complaints are echoed strongly in Stockdale's paper where he quotes an adult CF patient as saying:

"At times I get the feeling from the [CF] Foundation that they want us Adults with CF to just 'fade' away...We are not all little cute children...The Foundation's almost total neglect in aiding People with CF [i.e. adults] in our day-to-day lives is criminal" (quoted in Stockdale 1996:9).

Norman suggests that such discourse is a habit which doctors need to replace with a more modern attitude, while Stockdale presents it as a form of rhetoric used to raise funds. Can these explanations be applied to the use of similar discourse in medical texts?

While there may be an element of stressing the importance of one's area of study (by emphasising the particularly lethal nature of the disease) in the medical texts, it is not clear that a review article in a scientific journal is the place to use rhetoric intended to attract charitable funding. The audience for such emphasis is unlikely to read what are specialised articles (even though they are written for a broad medical audience). The regular way such statements occur in texts suggests another explanation. They often constitute the first sentence of an article, sometimes leading the abstract:
For example:

- "Cystic fibrosis (CF), the most common lethal genetic disease affecting Caucasians..." (Blyth and Farrell 1984:277, abstract 1st sentence);
- "Cystic Fibrosis (CF) is regarded as the most common severe autosomal recessive disorder in the Caucasian population" (Rommens et al. 1989:1059, 1st sentence);
- "Cystic fibrosis (CF) is the most common disease caused by a single gene abnormality within the caucasian population." (Krauss and Rado 1989:334, abstract 1st sentence);
- "Cystic Fibrosis (CF) is a lethal genetic disorder inherited as an autosomal recessive..." (Smith et al. 1989:B17, abstract, 1st sentence);
- "Cystic Fibrosis is the most common lethal single gene disorder in pediatric Caucasians" (Buchwald 1990:1275, 1st sentence);
- "Cystic fibrosis (CF) is one of the most common lethal genetic disorders affecting Caucasian populations" (Santis 1995: 15, 1st sentence).

The use of this phrase has obviously continued since Norman made his plea in 1981. Is it still just habit? Articles which do not start with this standard introduction are usually written for specifically non-clinical audiences. For example, Ianuzzi and Collins (1990), writing in the American Journal of Respiratory and Cell Molecular Biology barely mention CF as a disease entity at all. Their article is a methodological review, explaining how reverse genetics was used to identify CFTR. There is no mention of the symptoms of CF. The authors either assume that the reader knows about CF already (likely given the journal title) or, that they are simply not interested in the information. If one accepts that the first is the case, that Ianuzzi and Collins are aware of their readers' basic knowledge and do not feel the need to state the obvious, why do the authors of these other articles, whose readers are likely to be at least as knowledgeable about CF, start their articles with such basic, formulaic sentences? It seems likely that the readers of the American Journal of the Medical Sciences would be well versed in the genetic nature, frequency and severity of Cystic Fibrosis. What purpose would this very formalised introductory sentence serve? It does not appear to have parallels in articles on, for example, diabetes, but then diabetes has been a long-recognised disorder (certainly since the ancient Greeks), while CF was only identified as a clinical classification in 1936. As Norman recalls, "I can remember in the forties the surprise we felt that such a clear cut and such a fatal condition had not been recognized earlier and the interest there was in the remarkable pathological findings" (Norman 1981:85).
The reason may lie in professional specialisation. Paediatricians, particularly pulmonary specialists, are usually the first to see CF patients since the symptoms tend to present in infancy as affecting the lungs, although the disease itself affects a large number of physiological systems. Even fertility specialists become involved due to the CBAVD infertility which also occurs in men with CF. "CF care used to be dominated by gastroenterologists when GI [gastro-intestinal] complications were less manageable" (Stockdale, personal communication). But because CF patients are such a small proportion of total patients, even paediatric pulmonologists regard CF as of small interest, although the ones that are interested in CF, tend to want to hold onto their patients. CF is too minor a condition (in the grand scale of things) to count as even a subspeciality (ibid.).

The introductory sentence in articles on CF is a discursive convention serving to unite researchers and clinicians in this area, and to mark out the one thing that does unite them, the disease of Cystic Fibrosis. The sentence indicates to the reader, from the outset, that the author has a basic knowledge of what CF is and how important a condition it is to treat. It thus serves to bind a disparate community of different specialisations. Rather than just being a lazy habit, it might be better to see it as a badge of affiliation to an ideal, the need to research this condition. This is perhaps why Ianuzzi and Collins' 1990 article in the *American Journal of Respiratory and Cell Molecular Biology* did not use the formulaic sentence. Its readers are less likely to be interested in the nature of CF as a disease entity, and hence little need to state one's allegiance to a clinical position.

**Overselling the Gene?**

This section will present a sample of the discourse present in the medical literature at the time of the discovery of the CF gene in 1989. One perspective on this claims that the discovery of the CF gene was over-hyped, leading to unreasonable expectations on the part of the media and public:

"The other branch of human genetics that has been something of a disappointment is what is rather optimistically called 'gene therapy'. If we can identify genes that cause disease, why not replace them with good ones? The concept was so simple that about ten years ago it seemed likely that successes would be imminent, yet so
far we have not witnessed a single one. Transferring genes into a new environment and enticing them to behave themselves and do their jobs, with all the sophisticated regulatory mechanisms that are involved, has, so far, proved too difficult a task for molecular geneticists....The over-selling of the enormous amount of activity in this field reflects the naivety of some of the scientists involved, many of whom seem to have lost touch with the real world of chronic illness, and, to some degree, to a pharmacological industry which wants to believe that it will yield quick dividends" (Weatherall 1998:4-5).

It is true that gene therapy is often touted as the most obvious and the most beneficial outcome of human genome research. For example, a recent review of developments in paediatrics for the *BMJ* plainly states that "Gene therapy has become one of the central tenets of medical science" (Pearn 1997:801). Yet a careful analysis of the discourse in the medical literature of the time of the CF gene's discovery suggests that it is too simplistic to propose a one-to-one relationship between expectations and proposals for gene therapy and geneticization. The research raised hopes that full understanding of the underlying defect responsible for CF would soon be achieved, and steps towards an effective cure would be taken. But for any disease with a genetic component, the discovery of the gene responsible would be seen as a breakthrough for possible therapeutics. We should also remember the degree of medical ignorance about the causes of CF that existed prior to the cloning of CFTR: "A little more than 10 years ago most scientists surveying research in CF were pessimistic about the possibility of major advances, given decades of frustration and the inability to understand the basic disease defect" (Collins 1992:779).

Stockdale (1999) has documented some of the overselling of gene therapy that took place in the news media and other non-medical sources, but it is important to note that the scientific discussion of the time was far more cautious. For example, just prior to the September 1989 publication of the gene's exact location and cloning, Buchwald, Tsui and Riordan (all members of the successful Toronto research group) mildly suggested that "it may be possible to show that a given mutant allele leads to a specific clinical outcome, thus improving our ability to provide a prognosis to newly identified patients and perhaps also to indicate the most appropriate therapy." (Buchwald, Tsui and Riordan 1989:L50). They wrote this article for the *American Journal of Physiology* so perhaps its readers might not be so interested in the clinical implications of the CF gene. Yet it still seems
restrained that they make no specific mention of gene therapy in this piece, only of "appropriate therapy".

In an article published just over a year later, Buchwald is slightly more upbeat, though still cautious: "Genetic therapy is an exciting prospect, though at this point in time we have no way of knowing whether it is feasible" (Buchwald 1990:1278). He pins more hope on purely biochemical treatments for the symptoms of CF rather than attempts to change genetic make-up. "In the long run, the therapy that will be most likely to be of benefit for the majority of patients would be that directed at amelioration of the symptoms caused by the defective biochemical step" (ibid.).

Most discussions of gene therapy in the medical literature were expectant and hopeful, but realistic in terms of the hurdles to be overcome:

"....strategies for gene therapy must be developed. It is unclear what must be targeted to which cells and how. Thus, while we marvel at the discovery and enjoy the excitement generated by success in science, there remains a long and equally exciting path to travel before we can move much beyond the symptomatic and prophylactic therapy that results in the majority of CF patients dying in the prime of their productive years. " (Brody 1989:348).

Of course, there are always extremes of reporting. For example:

"One of the most dramatic approaches under consideration is gene therapy.... Beall says that gene therapy for CF will be a simpler matter [than therapy for immunodeficiency diseases]. It will involve retroviruses, but not cell transplantation. The retroviruses will be incorporated into a suspension that will be inhaled and are expected to infect and deposit their genetic cargo, the CFTR gene, into the epithelial cells of the lungs. If the gene is appropriately activated and the CFTR protein produced in adequate amounts, mucus within the lungs should be thinned substantially"(Merz 1989: 1573).

'Overselling' is more evident in the case of diagnostic testing and screening people for the CF gene than gene therapy. Following the cloning of the gene, Merz claimed that:

"Finally, when the CFTR defects responsible for the additional 15% of cases becomes known, prenatal diagnosis will be simplified and carrier screening will be a reality...[And that]...when all forms of the CFTR gene have been deciphered, carrier screening will be feasible for anyone at any time. The most widely discussed approach is one that will involve analyzing the DNA from epithelial cells gathered from a mouth rinse" (ibid.).
Theoretically this is correct, but at that time researchers couldn't foresee what is now widely acknowledged about CF testing, that with over 800 identified CF gene mutations already noted (Geddes and Alton 1999), genotyping with 100% certainty becomes practically impossible. It certainly suggests that in 1989, the idea that "CF screening and treatment are likely to be dramatically altered in coming months" (Merz 1989:1573) was over optimistic. A similarly view of the development of these technologies is present in Scambler 1989 for example.

Following the discovery of the CF gene, the discourse in the medical literature was one of hope, but there was a fair degree of caution as well. It would be misleading to suppose that gene therapy was unanimously heralded as the best use of the new genetic information, and even more misleading to suggest that everyone was claiming that gene therapy was just around the corner. Having presented the positions expressed in the medical discourse surrounding CF both before and after the discovery of the gene responsible and its product, CFTR, I will now focus on the three review articles (1976, 1996 and 1997) to show in detail how this discourse has developed. The disappointments concerning gene therapy and testing might suggest that CF has 'resisted' the effects of geneticization. However I will show how geneticization has had a profound effect on CF sufferers and their families by reclassifying CF along genetic grounds.

4. CONSTRUCTING CF

Method
My research on cystic fibrosis is intended as a 'benchmark' for my other case studies. The reasoning is that if my research is to examine the genetic discourses in complex conditions such as diabetes and schizophrenia, a good starting point is an analysis of the discourse in a disease which has been seen as genetically caused for as long as it has been acknowledged. I will show how discursive strategies construct a narrative around this disease. The narrative identified is the 'narrative of expansion' which describes the changes in CF classification which have taken place since the cloning of the CFTR gene in 1989. The central thesis of this chapter is that CF classification has expanded to
incorporate bordering, traditionally non-CF conditions, into a CF continuum. This reclassification is, in part, due to the discursive strategies used by authors in this area. The result is a narrative which expands what counts as CF.

Materials

The articles that will be analysed in this chapter are three cystic fibrosis review articles: one from 1976 (Wood, Boat and Doershuk); a second from 1996 (Davis, Drumm and Konstan); and the last from 1997 (Stern 1997). The first of these is heavily cited in the literature. Since its publication, the Science Citation Index lists 696 citations (to March 2000), an average of 29 citations a year. There is a consistent level of over twenty citations a year from 1978-1996, with only 1995 dropping below with 15. The citations drop off rapidly after 1996 (28) to 11 in 1997, 5 in 1998 and 6 in 1999. This is presumably because the newer, 1996 article has taken over as the review article of choice. All this suggests that the Woods et al. 1976 article represents a 'canonical' text in the CF literature.

The 1996 article, (Davis et al.) was chosen because it is the direct successor to Woods et al. It is published in the same journal and there were no intervening CF review articles published between 1976 and 1996. Since publication, it has been cited 106 times (to March 2000), which again is a very high rate. Both articles were published in the journal of the American Thoracic Society which started life in 1917 as the American Review of Tuberculosis. By the time of Woods et al. its name had changed (in 1966) to the American Review of Respiratory Disease, and in 1994 it changed its name again to the American Journal of Respiratory And Critical Care Medicine. The journal describes itself as "the primary journal in the field of pulmonary medicine" (Crapo 1993:2), and "the American Review is now an international journal" (Klocke 1992:507). It thus seems a suitable journal to analyse in order to investigate the geneticization CF. Both articles are clearly review articles in structure and content, although the journal adopts the label "State of the Art". State of the Art articles are described in the journal's current advice for contributors as "broad, comprehensive, scholarly works, which are considerably
longer than the other types of review articles [carried in the journal]". They cover more topics than might normally be considered for a review article and for the discourse analyst, they are advantageous for the increased amount of text they contain.

In addition to these two articles, and some contributions from other articles, I will also analyse one other article in detail. This is Stern's 1997 review for the *New England Journal of Medicine*, "The Diagnosis of Cystic Fibrosis". This provides comparison with a review written for a broader clinical audience, and a chance to see how the concepts outlined in the 1996 article might have been incorporated into the discourse surrounding CF. It has been cited 37 times and is thus less 'influential' than the other two, but the fact that it appears in the *NEJM* widely read, generalist gives it a different, broader readership.

5. "AND NOT YET A DISEASE": THE 1976 REVIEW

I chose this article to show how the discussion surrounding CF has changed due to the discovery of the CFTR gene. One can only really assess the impact of geneticization if we know what the narrative was like before the gene was located. Wood et al's article seems to fit the standard CF template noted above. They contain the mantra of the severity of the condition "Cystic Fibrosis is the most frequent lethal genetic syndrome among white children...". But they ameliorate it with details concerning the improved treatment available, "However, increasing survival has resulted in more than 11,000 patients in the U.S. Cystic Fibrosis Data Registry..." (Wood et al. 1976: 834) and go on to list the increasing numbers of patients surviving. The bulk of this article is devoted to outlining the pathophysiology of CF patients, its diagnosis and treatment. This makes its high citation rate into the 1990s all the more impressive. Despite the references and treatments being decades out of date, this article still receives a high number of citations.

---

63 The style guide is available through the ATS website; http://www.thoracic.org/bluecont.html.
Genetics

For a review concerned with a genetic disease, there is very little discussion of the genetics of CF in this article, and much of that is very tentative: "Several pieces of evidence indicate that cystic fibrosis is transmitted as an autosomal recessive trait...It has been proposed that a single mutant allele is responsible for the manifestations of this syndrome" (Wood et al. 1976: 835, emphasis added). The genetics section even discusses the possibility that CF might be polygenic (in the sense of more than one locus being involved) citing evidence that "Recent calculations based on affected first cousins of the proband are consistent with the involvement of either 2 or 3 loci[ref]". This is immediately followed by "Although it is tempting to support a hypothesis of multiple alleles for cystic fibrosis, especially in view of repeated difficulties with detection of a single pathogenic mechanism, enthusiasm should be tempered..."(Wood et al. 1976: 836). This seems to suggest that for a disorder to be caused by many different alleles, more than one locus needs to be involved. The possibility of many different alleles occurring at the same locus, so integral to our post-1989 conception of CF genetics, seems not to have been considered.

As noted, the majority of this article is devoted to discussing the physiological manifestations and clinical approaches to CF with the genetics section covering less than one of the 29 pages of text. The discourse presented is one of symptoms and treatments. Although CF is described as "genetic" there is little or no attempt to offer up a genetic explanation of CF, or of the relationship between genotype and phenotype. The evidence presented on the pathophysiology of CF notes that "Obstruction of exocrine gland ducts or the passageways into which the exocrine secretions are discharged occurs in all...patients with cystic fibrosis" (Wood et al. 1976: 837) and that "Sodium and chloride concentrations in the sweat of cystic fibrosis patients are clearly elevated" (ibid.). But ultimately the authors conclude that "It is difficult to develop a unifying hypothesis for electrolyte abnormalities in cystic fibrosis when these abnormalities vary from one exocrine gland to another" (Wood et al. 1976: 838).

Research into the possible gene product or protein responsible for CF is also covered, with the 1967 discovery of "a factor in the serum of cystic fibrosis patients and their
parents that would disrupt the normal ciliary beat pattern of rabbit tracheal explants" (p.841) yet "no pathophysiologic role has been defined for the presumed factor, and the mechanism by which the 'factor' might alter ciliary activity is not known" (Wood et al. 1976: 842).

Despite the lack of any real mechanism to link the as yet unknown genetic cause (or causes) of CF to the wide variety of physiological manifestations and clinical symptoms present in patients, this article is clearly looking forward to a genetic explanation to solve the mystery. Much hope is pinned on finding and testing for 'the gene product' i.e. what we now call CFTR. In 1976, prior to reverse genetics, the assumption would have been that research would reveal the protein involved in CF prior to the gene itself being discovered. For example, the article considers prenatal diagnosis and carrier testing, but states:

"In the absence of a definitive test for the defective gene products, prenatal diagnosis and heterozygote screening are unavailable. Early enthusiasm for the use of various bioassays for the 'ciliary factor' has been tempered with time, and it is now generally agreed that these 'tests' should not be used for genetic counseling" (Wood et al. 1976: 849-850).

With regard to diagnosis in adults, and the possible problems that can arise with equivocal sweat tests, the article notes that "Although 'factor assays' and other research tools are not helpful for diagnosis in our present state of knowledge, hopefully a specific test for the gene product will become available" (Wood et al. 1976: 850).

Syndromes and Aetiology

This 1976 article lays the foundations for the narrative constructed after 1989. One important element to this is the concepts of syndromes and diseases. In the 1976 article, the authors describe a disease about which very little is known in terms of causation. "No known biochemical or structural defect will account for all the pathophysiologic phenomena of cystic fibrosis. Thus the definition of the disease rests on the clinical findings; cystic fibrosis is a syndrome, and not yet a disease" (Wood et al. 1976: 834, bottom of second column). This is interesting in that it suggests that

- cystic fibrosis is a syndrome;
• clinical definitions are inadequate;
• and that more causal definitions should be sought.

A syndrome is by definition based on symptoms:

"Mere syndromes are, as the name implies, the running together of symptoms and signs. They are a constellation of phenomena without a nomological structure to bind the signs and symptoms in a fashion to provide a model for explanation" (Engelhardt 1981:37).

By this assessment, CF in the 1976 article is definitely a syndrome. The article lists series of symptoms in various organs and physiological systems, some of which may be primary, but many of which may just be secondary symptoms of a more basic defect. The lack of an explanation to bind the symptoms together means that it is not even clear whether CF is caused by one or several defects.

As noted in Chapter 2, the drive towards aetiological explanations over syndromes is a familiar one in medicine. But it is also a factor which allows the development of geneticization. The need for causal explanations and dissatisfaction with symptomatic descriptions makes genetic explanation more attractive. The secondary status given to the syndrome in the quote cited above clearly suggests that this article would give priority to a genetic explanation, if only it had one. Is saying a disease has an as yet unknown genetic cause the same thing as saying that it is geneticized? Whatever geneticization is, it does not seem a suitable term to describe the discourse in the 1976 article. Of course, in terms of my restricted definition, geneticization cannot have taken place in 1976; that is, after all, why this article was chosen. But even by a broader definition, Lippman's for example, the authors of the 1976 article hardly seem to be discussing a disease which could be described as undergoing geneticization.

6. "AN EXPOSITION OF DETAILED INFORMATION": ANALYSIS OF THE 1996 ARTICLE

In this section, I will analyse Davis, Drumm & Konstan's 1996 article, "Cystic Fibrosis" published in the American Journal of Respiratory and Critical Care Medicine. As noted above, this journal had been called the American Review of Respiratory Disease but changed its name in 1994.
"'Review' has become 'journal' in delayed recognition that its soul is original scientific investigation. 'Critical Care' has been added to announce that this important discipline has found a home in the American Thoracic Society (ATS). 'Disease' has become 'Medicine' to recognize the rapidly evolving and gratifying reality that investigations of disease mechanisms are leading to increasingly effective prevention and treatments" (Klocke and Sylvester 1994:2).

The title of the journal has changed to keep up with its readership, yet it still has its roots and interests in pulmonary care. This may indicate a degree of specialist interest, in line with Stockdale's suggestions mentioned above.

**Genetic interventions and evolutionary advantage**

If we are interested in geneticization, then one of the first areas to look at might be those sections which deal with evolutionary explanations for cystic fibrosis. In this article, it lies in the section called 'Heterozygote advantage' (Davis et al. 1996: 1233). Because CF tends to kill sufferers before they have children (and in the case of males, renders them infertile anyway), evolutionary explanations face something of a challenge. Natural selection means that if particular genotypes are selected over time, they must provide individuals with improved survival or sexual selection, which are then passed onto their offspring.

In the case of CF, it hard to see what advantages there are to being a sufferer, and anyway, until twenty years ago few sufferers survived to reproductive age. So why has CF remained in the human gene pool for so long? Although it was clinically identified in 1938, there are ancient German folk sayings which seem to mention a similar condition. The answer lies in the advantages that being a CF carrier (i.e. only having one copy of a CF causing allele) is supposed to bring. The 1996 article describes experiments that suggest that CF carriers have increased resistance to the effects of secretory diarrhoea (as caused by diseases such as cholera). This would give carriers a survival advantage over non-carriers in the event of an epidemic, and explains why the gene still exists. Of course, an adaptionist explanation like this is only one possible example of evolutionary explanation. The article notes that "other possibilities exist such as founder effect and
random genetic drift" (Davis et al. 1996: 1233)\textsuperscript{64}. Thus the article does not propose solely an adaptionist explanation for CF. In fact it is even sceptical, presenting the results of studies which undermine the idea that a heterozygote (carrier) advantage exists in the case of secretory diarrhoea. Yet it is important to note that once geneticization takes place, some form of evolutionary explanation seems likely. If nothing in biology makes sense except in the light of evolution, this is even more true for genetics. By invoking an evolutionary explanation, geneticization can be set within a broader context, that of secure evolutionary biology.

The other obvious point of entry into the narrative surrounding CF is the section 'Prenatal Diagnosis and Carrier Screening' (Davis et al. 1996: 1233-1234). Like the discussion of evolutionary explanations for CF, it is low-key. It does not propose wide spread carrier screening of the general population, or 'over-sell' the accuracy and power of genetic testing for CF.

"In families where an affected member can be examined, diagnostic accuracy [of prenatal diagnosis] is nearly 100%...[but]...Because in CF there is a large number of mutations that occur at low frequency, testing at present can detect only about 90% of carriers" (Davis et al. 1996: 1233). This section concludes that "genotyping can also be useful in patients in whom the diagnosis of CF is equivocal" (Davis et al. 1996: 1234). It is this 'settling' role that gives the CF genetic test its reclassifying power. As we shall see, there is a circular relationship between those symptoms judged to be equivocal, and the use of genetic tests.

This rather low-key view of the potential of genetic intervention mirrors this article's discussion of gene therapy. The section starts by claiming that "CF seems an excellent candidate for gene therapy because it is a single-gene defect..." (Davis et al. 1996: 1245). Yet it concludes with the caution that "formidable practical barriers have been identified" (Davis et al. 1996: 1246). These barriers are increased by the successes that have been achieved using more traditional clinical treatments: "the success of conventional therapy imposes a special burden to do no harm. The slow rate of decline in pulmonary status

\textsuperscript{64} Founder effect is the result of genetics in small, isolated populations, when the genes (good or bad) of the original founders tend to predominate. Genetic drift describes random changes in gene frequencies in a population.
will also make it difficult to prove that gene therapy halts the progression of the lung disease" (ibid.).

**CFTR as protagonist**

Since I am analysing this review in terms of a narrative, it should be possible to discuss its 'central character'. If so, then the protagonist in this article is the protein CFTR, the "biochemical or structural defect" that Wood et al needed to "account for all the pathophysiologic phenomena of cystic fibrosis". This provides a new focus for the review article, and the contents listing for the 1996 article changes accordingly. There are new sections such as 'Structure of CFTR Gene' and 'CFTR Is a Chloride Channel' which are additions one would expect following the discovery of the gene involved in CF and its gene product.

More interesting changes take place in the naming of the clinical sections of the 1996 article. In the 1976 article, Woods et al. have the main section 'Clinical and Pathologic Manifestations' (1976:843) which subdivides into 'Respiratory' (p.843), 'Gastrointestinal' (p.845), 'Genitourinary Manifestations' (ibid.) and 'Sweat Gland' (p.847). In the 1996 article, the approach is very different. The clinical information is contained in two different sections; 'Clinical Implications of Mutations' (p.1232) and 'Physiologic Role of CFTR in Organs Outside the Lung' (p.1237). The clinical discussion is very clearly phrased in terms of the function (or lack of it) of CFTR.

- "At least some of the variability in the clinical presentation of CF is explained by differences in CFTR mutations" (p.1232);
- "In the sweat duct, CFTR is the only channel capable of reabsorption of chloride from the sweat...Because of the sweat electrolyte defect, patients with CF are prone to heat prostration" (p.1237);
- "Because in the gut the only apical chloride channel in most regions is CFTR, defects in CFTR render the individual incapable of secreting chloride...This defect results in severe pathologic disorders" (ibid.);
- "In the liver, CFTR is localized to the epithelial cells lining the biliary ductules...In the absence of functional CFTR, the biliary ductules may become plugged with secretions...obstructive cirrhosis may occur" (p.1238);
- "The pancreas is affected in nearly all patients with CF...the lack of CFTR in its normal sites along the pancreatic ductules and larger ducts leads...to precipitation of protein and plugging of ductules and acini" (ibid.).
The pathogenesis of the lung disease associated with CF is presented in a separate section (Davis et al. 1996: 1239), in large part because "Precisely how the CF electrolyte transport defects give rise to persistent lung infection and inflammation is not clear" (ibid.). All sections of this review focus on the role and action of the protein. In the terminology of Feldman and Tauber, cystic fibrosis has certainly become a 'molecular disease' in this article.

'Syndromes' and Continuums

The hope expressed in the 1976 article was that once the genetic defect responsible for CF was discovered, CF would cease to be a 'syndrome' (a series of connected symptoms with an uncertain cause) and would become a 'disease', with a clear aetiology. Initially, the 1996 article seems to suggest that CF is still a syndrome. It states that:

- "All patients with the clinical syndrome of CF have mutations in both copies of a gene on chromosome 7..." (Davis et al. 1996: 1230);
- "not everyone with two mutant alleles at the CF locus...manifests the full CF syndrome" (ibid.);
- and that "The CF clinical syndrome is nearly unique..." (ibid.).

The point here is that CF is still a syndrome on clinical grounds. These quotations are all in the first section of the article, 'Diagnosis of CF'. Once the next section ('Cloning the Gene') begins, there is no mention of the 'clinical syndrome of CF', but only 'CF'. The effect of this is to confirm the prediction of the 1976 article. Once the gene is discovered (or in this case, presented in the article), CF ceases to be a syndrome and becomes a disease. The terminology of the 1996 article mirrors the chronology of the classification of cystic fibrosis; the CF-syndrome becomes a disease through the introduction of CFTR and the gene that codes for it. This is reminiscent of Woolgar's discussion of the role of sequence in the textual construction of a scientific fact:

---

65 There is a possibility that the two articles use the term 'syndrome' in slightly different ways; the 1976 article in the way described (as a collection of symptoms with no clear cause) and the 1996 one as meaning a disease which manifests itself in a variety of different organ systems. But if this were the case, one would expect consistent use of 'CF syndrome' throughout the 1996 article, especially in those sections that deal with the manifestation of cystic fibrosis in the various body systems. But there is a definite cessation of the use of the term syndrome after the section called 'Cloning the Gene' (p.1230); following this section and its introduction of CFTR into the discourse, there is no further mention of the CF-syndrome.

---

129
"practical expression of, or reference to, a phenomenon both recreates and establishes anew the existence of the phenomenon. In describing a phenomenon, participants simultaneously render its out-there-ness" (Woolgar 1981b:246).

Genetic Elision: CFTR gene = CF Gene

The 1996 article seems to use 'CF Gene' and 'CFTR Gene' as interchangeable terms. Examples of this include the section titled 'Mutations in the CF Gene and the Genetics of CF' which then states that "Since the discovery of the CFTR gene and the ΔF508 mutation, more than 400 other mutations in this gene have been found" (Davis et al. 1996: 1231). This close link between the CF gene of the section title and the CFTR gene discussed in the text implies a degree of interchangeability. Other examples of this slippage include:

- "information on the structure and function of the protein of the CF gene, called CFTR" (p.1229);
- "the nature of the protein encoded by the CF gene" (ibid.);
- "the circumstantial evidence that the CFTR gene is the CF gene was overwhelming" (p.1231);
- "The normal gene for CF...restores the missing cAMP-mediated chloride conductance of these cells [ref]. When the cDNA for CFTR is expressed in heterologous systems, a cAMP mediated chloride conductance appears" (Davis et al. 1996: 1234, emphasis added to all).

This linking of the gene for CFTR with the gene that causes CF means that it is far more likely that any condition associated with mutations in the CFTR gene will be automatically linked to CF, and becomes a candidate for the CF continuum. This running together of CFTR-gene with CF-gene, this 'genetic elision', is to some extent the result of the naming of CFTR- Cystic Fibrosis Conductance Regulator. Any defect in a protein named after a disease will tend to be associated with that disease, rather than a possible alternative classification.

The original intention in naming the protein CFTR seems to have been clarity and avoidance of confusion. In one of the three 1989 Science articles describing the discovery of the CF locus, Riordan et al. state "For the convenience of future discussion and to avoid confusion with the previously named CF protein and CF factor [ref], we will
call the putative CF gene product the cystic fibrosis transmembrane conductance regulator (CFTR)" (Riordan et al. 1989:1071).

Yet the use of 'CF gene' and 'CFTR' in the 1996 article is ambiguous. For example, from the quotations above, "the protein of the CF gene, called CFTR" suggests that CFTR is the defective protein produced when the gene causing CF is present, while "normal gene for CF" could be interpreted to mean 'the most common mutation causing CF'. It actually means the gene that the non-CF population has which doesn't produce the CF phenotype, the 'wild-type'. While such analysis might appear pedantic (the intended audience for this article will know exactly what this shorthand means) such ambiguity does support a continuum of CF diseases, all united by mutations in the same gene, rather than clinical resemblance.

**Representing the continuum**

On page 1233, figure 3 (reproduced below) shows the "CFTR activity and tissue manifestations of CF", and the text that comments on this figure claims:

"The association of specific organ involvement with specific CF mutations, some of which have significant residual CFTR activity, allows us to speculate that there exists a hierarchy of organ sensitivity to deficits in functional CFTR" (Davis et al. 1996: 1232).

The left hand side of the figure lists the tissues affected in CF ("unaffected...vas deferens...sweat duct/airway...pancreas") the right hand side the different degrees of CFTR activity in percentages, with the genotype believed to cause it in brackets. For example 100% protein activity is caused by 'wild type' (wt) protein and 50% by the normal protein of a CF carrier. Terms such as 'R117H', 'G551D', and 'ΔF508' refer to specific CF causing alleles. '5T', '7T' and '9T' do not refer to stretches of the CF gene, but to DNA which regulates it.

---

66 wild type refers to the protein present in unaffected individuals.

67 5T, 7T and 9T refer to regulatory sections for Exon 9 of the CF gene: 'Just 5' to the splice acceptor site of Exon 9 is a tract of thymidines that can vary in number from 5 to 7 to 9 [ref]. The length of this pyrimidine tract affects the efficiency of splicing in Exon 9" (p.1232). These are therefore references to changes in the genes effectiveness.
The central column of the figure is not labelled, but it lists the conditions that are associated with these tissue variations and CFTR activity: "CBAVD" (Congenital Bilateral Absence of the Vas Deferens), "PS CF" (Pancreatic Sufficiency CF), "PI CF" (Pancreatic Insufficiency CF). This diagram, figure 3, is not referenced and is presented as an original contribution by the authors of the 1996 article. It is in fact a development of a diagram in Chillon et al. (1995), a research article which investigated the role of the 5, 7 and 9T variation of exon 9 and its relationship to the CBAVD phenotype.

<table>
<thead>
<tr>
<th>Tissue Affected</th>
<th>CFTR Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>unaffected</td>
<td>100% (wt protein 9T/9T)</td>
</tr>
<tr>
<td>vas deferens</td>
<td>50% normal protein, CF Carrier</td>
</tr>
<tr>
<td>sweat duct/airway</td>
<td>10% (wt protein, 5T/5T)</td>
</tr>
<tr>
<td>CBAVD</td>
<td>5% (wt protein/5-95% inactive mutant)</td>
</tr>
<tr>
<td>PS CF</td>
<td>4.5% (60% CFTR with 15% activity, R117H, 7T)</td>
</tr>
<tr>
<td>PI CF</td>
<td>4% (A455E/Severe mutant)</td>
</tr>
<tr>
<td>pancreas</td>
<td>1% (10% CFTR with 15% activity R117H, 5T)</td>
</tr>
<tr>
<td></td>
<td>&lt;1% (G551D, ΔF508)</td>
</tr>
</tbody>
</table>

Based on Davis et al. 1996:1233
The originality of Davis et al's diagram is the inclusion of information about many other mutations in the CFTR-gene, more detail on the different percentages of working CFTR produced, and the correlation of this data with the phenotypic manifestation of CF in different tissues.

It is not that Davis et al. are introducing a brand new concept ('CBAVD as mild CF') into the discourse of CF, but that they are using new, perhaps more effective, discursive strategies to help them to do so. Their diagram is the next step up from Chillón et al's in terms of information content and persuasiveness.

This 'nosological expansion' is most apparent if one considers the condition of Congenital Bilateral Absence of the Vas Deferens, or CBAVD. This is the cause of the infertility experienced by men diagnosed with CF and is also the cause of up to 1.5 % of all male infertility (25% of all obstructive azoospermia). It is characterised by reabsorption by the body of the male genital tract (Patrizio and Zielenski 1996). Although this had long been recognised as a symptom of CF (it was noted in the early seventies and cited in the 1976 article) it was clear that other conditions, not associated with CF, could also cause CBAVD.

In their 1995 review of genotypic and phenotypic variations for the Annual Review of Genetics, Zielenski and Tsui present a table (p.796) showing "Atypical (non-CF) diseases associated with the CFTR gene", headed by CBAVD, whose "Common manifestations shared with CF" are "absence of vas deferens (bilateral)". This table cites a reference showing that 78% of patients in a study had at least one CFTR mutation. So in this article, CBAVD is a separate 'non-CF' condition, although there is an at least partial association with CFTR mutations. But the 1996 article reclassifies CBAVD. It is no longer an 'atypical' or 'non-CF' disease. Figure 3 presents CBAVD as part of a continuum of CF, ranging in severity and phenotypic expression, but all linked through mutations in the CFTR gene. CBAVD "represents a mild form of CF" (Patrizio and Zielenski, 1996:30). The diagram reclassifies according to mutations in the CFTR-gene. CF becomes a continuum, a number of linked sub-conditions, each of which can be identified via protein activity and genotype. The same series of symptoms are connected by
different faults in the same gene, to form separate conditions (for example Pancreatic Sufficiency CF and Pancreatic Insufficiency CF).

One can see the success of this diagram as a discursive strategy for the narrative of expansion in its reproduction as "table 2" in the 1997 *New England Journal of Medicine* review article by Stern. The text states:

"Although absolute correlation of phenotype with specific genotype is impossible, there appears to be a reasonable correlation (Table 2) between the percentage of normal CFTR function and the presence of disease in various organs [ref]" (Stern 1997:489).

What Davis et al. referred to in their 1996 article as "speculation" has by 1997 become a system "helpful in evaluating a patient whose symptoms suggest cystic fibrosis...but whose sweat test is negative" (Stern 1997:489). The reference for Table 2 in the above quotation from Stern (1997) is to the 1996 Davis et al. review article. This suggests that the causal effect of the discursive strategy used in this article is to construct this narrative, solidify and reify CBAVD as a form of CF, and produce nosological expansion.

Despite the persuasive power of this representation of CF as a clinical continuum, there appear to be certain inconsistencies in the information presented by Davis et al. In the section titled "Diagnosis of CF", having stated that "Cystic fibrosis remains a clinical diagnosis" (Davis et al. 1996: 1229), they claim that "Eventually, all patients with CF manifest lung disease, though it may develop after the time of diagnosis" (Davis et al. 1996: 1229-1230). Yet this contradicts the inclusion of CBAVD in the CF clinical continuum: "CBAVD is also found in the absence of other organ involvement" (Davis et al. 1996: 1232). Surely the whole point of the genetic definition of CF, the inclusion of CBAVD as a 'mild form' of CF, is to suggest that there are patients with CF who do not manifest lung disease. Only 11 lines further on, the authors declare that "Some persons, with 'mild' mutations on both chromosomes, have only congenital bilateral absence of the vas deferens (CBAVD), and no apparent lung or pancreatic involvement" (Davis et al. 1996: 1230). This article seems to be presenting CF, not just as a genetic disease, but as a disease defined in terms of mutations at a particular genetic locus.
The narrative being constructed is one of expansion, allowing the classification of CF to incorporate CBAVD as a mild form of cystic fibrosis. But one of the advantages of thinking in terms of a narrative is that one does not have to accept that the story always goes one way. There are setbacks and defeats in the best narratives. Thus we can appreciate this ambiguity over the CBAVD classification as a facet of a narrative which has to gain dominance over the discourse of CF. As we shall see, articles like Stern's 1997 review confront the debate over CBAVD and turn it to the narrative's advantage.

Flexible Interpretive Strategies

The incorporation of CBAVD into CF should not be seen as straightforward. As Stern states in his *NEJM* review, "Classifying seemingly isolated CFTR-based congenital absence of the vas deferens as a variant of cystic fibrosis is controversial" (Stern 1997:490). Anne Kerr has noted a number of what she terms 'flexible interpretive strategies' which have been used in the research literature to construct CBAVD as a mild form of CF and to overcome this controversy. Although Kerr mainly focuses on original research literature, these interpretive strategies crop up in review articles as well.

The first strategy depends upon the convention that variations in the genetic code can be classed as either 'mutations' or 'polymorphisms'. The former are changes in the code that are seen to produce a faulty protein associated with a particular disease or disorder. Polymorphisms on the other hand are part of the normal variability in the human genome, and do not disturb the protein produced by a gene in any detrimental fashion. Obviously whether a particular piece of variable DNA is a benign polymorphism or a malign mutation is an important consideration if one is screening members of a population for a genetic disease (Kerr forthcoming:15). The CFTR gene has a large number of mutations associated with it and: "Many DNA sequence alterations in the CFTR gene are classified as polymorphisms or benign variations because they either do not appear to have any disease implications or are found on the non-CF alleles" (Zielenski and Tsui 1995:790-791).

The slippage between mutants and polymorphisms is clear in the 1996 article when Davis et al. introduce the idea of 'mild' mutations: "Some persons, with 'mild' mutations' on
both chromosomes, have only congenital bilateral absence of the vas deferens" (Davis et al. 1996:1230). The idea of mild mutation is required since in the previous sentence this article defines CF in genetic terms:

"All patients with the clinical syndrome of CF have mutations in both copies of a gene on chromosome 7, which encodes...the cystic fibrosis transmembrane regulator (CFTR) but not everyone with two mutant alleles at the CF locus on chromosome 7 manifests the full CF syndrome" (Davis et al. 1996: 1230).

This attempt to define CF genetically cannot but be equivocal and qualified. This definition implicitly accepts the unease of fit between what we have traditionally (clinically) recognised as CF, and what the genetic classification of CF recognises.

Kerr has highlighted this lack of corresponding CF mutations on both chromosomes. She notes that in the initial studies of CF and CBAVD, researchers suggested that there were higher than normal frequencies of CF mutations among men with CBAVD. But these patients were all heterozygous, i.e. only carrying one copy of the CF mutation, and hence on a par with CF-carriers (traditionally viewed as unaffected by their status). But "rather than suggesting that CBAVD is akin to CF heterozygosity...[researchers]...argued that CBAVD is akin to compound heterozygosity for CF (two different genes) and that they had yet to find another mutation, on the other chromosome" (Kerr forthcoming: 13).

This approach is needed if one is to forge a link between CFTR-gene mutations /variations and CBAVD. The current genetic paradigm states that CF heterozygotes/carriers remain unaffected by the mutation they carry since the unaffected allele on the opposite chromosome should supply the required protein. But to class CBAVD patients as affected by their single mutation would be to state that carriers are affected by their heterozygosity, and hence to undermine the paradigm. Therefore geneticists require CBAVD patients to have another, as yet unidentified mutation, making them compound heterozygous and thus CF sufferers.

An example of this in Davis et al. (1996) includes the identification of rare, CBAVD linked mutations, and the reclassification of previously benign polymorphisms (in this case the 5T variation on exon 9):
"It was noted that the carrier frequency of the ΔF508 mutation in men with CBAVD is about 0.5, whereas in the general population it is about 0.003 [ref]. Subsequent analyses revealed that a number of these men with CBAVD carry a second CF mutation on their non-ΔF508 chromosome. These CBAVD-associated mutations have significant residual channel activity, although less than wild-type, suggesting these are very mild mutations. More recently, it has been found that many of the men with CBAVD who have only one detectable CF mutation are also carriers of the 5T Exon 9 splice variant on the other chromosome" (Davis et al. 1996: 1232).

This demonstrates the appeal to as yet unidentified mutations and the enlistment of the 5T variant, which is not even part of the CF-coding intron. Kerr's work shows how even an apparently straightforward concept such as the distinction between mutations and polymorphisms is value laden and serves to construct this narrative. By using her ideas in this section, I hope to have shown that discursive strategies she noted in a variety of different articles (research papers, reports, letters and reviews) also occur in the 1996 article I examine. This suggests that the strategies identified in my own research may well be present outside of the narrow range of the review articles I focus on. This reinforces my claim that such articles can be seen as representative of the discourse in a particular disease, and supports the interpretation I make of these articles.

"Classic" CF

The final discursive strategy to be analysed is the idea of "classic" cystic fibrosis. The term "classic CF" does not appear in Davis et al. (1996), but in Robert Stern's 1997 review article in the NEJM. This is a short (5 page) article, focusing specifically on the diagnosis of CF, covering 'Laboratory Tests', 'Correlation of Genotype and Phenotype', and 'Relation of Cystic Fibrosis to Congenital Absence of the Vas Deferens'. Stern refers to Classic cystic fibrosis throughout the article68. It is defined on a clinical basis.

"The traditional diagnostic criteria for classic cystic fibrosis [ref] are still valid: persistently elevated concentration of electrolytes in sweat plus characteristic clinical findings (typical gastrointestinal or pulmonary disease and perhaps obstructive azoospermia)" (Stern 1997:487).

68 Pages 487, 489, and 490 (four times).
It is contrasted with 'atypical disease' (p.487) or 'milder variants' (p.490). This review explicitly classes CBAVD as "the presenting symptom of milder variants" (ibid.). It seems as if the introduction of "classic" and "atypical" as descriptive terms is another discursive strategy to solidify the CF classificatory continuum. While CBAVD cannot reasonably be classed as 'normal' CF, the use of terms such as 'milder variant' and 'atypical' allows it to become at least a form of CF. Thus this article serves to support the nosological expansion constructed by Davis et al. This promotes the position where "All patients with the clinical syndrome of CF have mutations in both copies of a gene on chromosome 7" (Davis et al. 1996:1230). Incidentally, Stern uses the term 'classic' in an unqualified way (i.e. with no quotation marks around it) while Colin et al. (1996), who are sceptical about the value of classing CBAVD as a mild form of CF, refer to 'classic' CF. The presence or absence of such qualification perhaps acts as an indicator as to the position an author takes on the expansion of the CF continuum. Anne Kerr has pointed out to me that discussion in terms of the 'classic case of CF' dates back to the 1940s (Kerr, Personal communication, 28/04/2000), but this does not undermine the way in which Stern uses this phrase in his review article. The fact that others use classic with quotation marks suggest that use of this phrase is, at the very least, open to interpretation.

Stern comments upon the controversy that surrounds the classification of CBAVD as a mild form of CF, as does another recent CF review in The Lancet. Here Rosenstein and Zeitlin mention patients with CBAVD and state that

"Many of these individuals have CF mutations in one or both CFTR genes, or an incompletely penetrant mutation (5T) in a non-coding region...Whether such individuals should be given a diagnosis of CF is still controversial" (Rosenstein and Zeitlin 1998:277).

While in this article there is no further discussion, Stern makes a historical point: "A similar debate, many years ago, about patients with pulmonary disease typical of cystic fibrosis but normal pancreatic function, was settled by the advent of sweat testing" (Stern 1997:490). This lead to the construction of two types of cystic fibrosis, Pulmonary Sufficient and Pulmonary Insufficient CF. This use of historical precedent is a way of incorporating nosological expansion into CF as a normal development of the classification system. And the controversy over CBAVD to be settled by the advent of genetic testing.
Summary

The 1996 and 1997 articles show how the narrative of expansion has been constructed in cystic fibrosis. This had been achieved through the use of a number of discursive strategies:

- Evolutionary explanations.
- CFTR as a protagonist.
- The change from a syndrome to a continuum.
- The naming strategy equating CF gene with CFTR gene.
- The diagram enforcing the nosological expansion.
- Adoption of flexible interpreive strategies.
- The concept of Classic CF.

Comparison with the 1976 article shows just how much has changed as a result of the geneticization of CF. The structure and focus of the review has changed, with all the previously disparate symptoms tied together in a genetic explanatory framework. Although the focus has been on a small sample of review articles, we should remember that they are representative of the research community. It is not that Davis et al. propose a wholly original thesis but that their review of the literature pulls together various ideas and presents them in a discursively powerful format. Nor is it the case that the narrative of expansion is overwhelmingly dominant at the expense of alternative views of CF classification. In the next section, I will present the discussion that is taking place in the CF literature surrounding the genetic reclassification of CF and the resistance to the narrative of expansion.

But first I should note the drawbacks to my particular approach to this topic; they mainly derive from my definition of geneticization, and the materials I have chosen to study. By defining geneticization in purely molecular genetic terms, I run the risk of presenting a distorted history of CF classification. Anne Kerr suggests that she does not:

"think geneticization started with the identification of the gene - I see it more as a process of reform which was certainly bolstered by identification of the gene but I don't think it is as fundamental as you suggest" (Anne Kerr, Personal communication, 28/04/2000).
To some extent this is a dispute over the definition of geneticization, and I accept that the pragmatic definition I use in this thesis has its drawbacks. But at the same time, the discovery of the gene for CFTR did change the discourse surrounding cystic fibrosis. There are considerable differences between the 1976 and 1996 articles, and they seem to stem, in the main, from the introduction of molecular genetic explanations after 1989.

Kerr is also right when she suggests that my research does not highlight the role of different professional groups in disease classification and the "increasingly blurred distinction between research and clinical services" (ibid.). But this is the nature of my research materials (review articles) and this emphasises Myers' point that review articles reconstruct the history of disciplines, removing disputes and emphasising the smooth flow and progress of science.

What is clear from this narrative is the profound effect geneticization has had on cystic fibrosis, even without gene therapy and large-scale genetic screening. The early promise of these technologies and their subsequent disappointing reality to date might lead one to think that the discovery of the gene for CF has been relatively unimportant. What this case study shows is how, through disease classification, geneticization can impact on patients and clinical practice, even in the absence of genetic technologies.

7. Where does the narrative go from here?

As Stern points out in his justification for the new classification system, CF underwent nosological expansion prior to the gene being discovered. CF has expanded before, accepting plain pulmonary disorder as a symptom, leading to Pancreatic Insufficient CF and Pancreatic Sufficient CF. Is the continued expansion of the disease continuum to take onboard CBAVD simply the next stage of a process that has been happening in cystic fibrosis classification, regardless of the molecular genetic evidence? It is quite possible that "the genetic angle develops practices and interpretative strategies which are already present in the field and have been since CF was first defined as a condition in its own right" (Kerr, personal communication, 30/7/98). But geneticization involves a turn towards aetiological explanation, while the sweat test is still just a clinical test.
Imbalances in the ratio between sodium and chloride ions in sweat is still a symptom of an underlying malaise.

When discussing the debate over the reclassification of CBAVD, Stern accepts that "Different diseases can indeed result from different mutations of the same gene". But he justifies the inclusion of CBAVD in the CF continuum on the grounds of clinical pragmatics:

"clinical management, including genetic counselling, requires that physicians regard these patients as being at the extremely mild end of a disease with a very broad spectrum of severity" (Stern 1997:490).

Colin et al. disapprove of the new classification system on the same grounds stating:

"The appropriateness of classifying CBAVD alone within the spectrum of CF remains unclear...In this widening spectrum of CF, a dichotomy is emerging between the perspective of the scientist and that of the clinician and patient. Although the scientists may consider that CBAVD is theoretically part of the spectrum of CF, this definition is not necessarily clinically helpful...we suggest caution in describing CBAVD alone as equivalent to CF in the clinical setting" (Colin et al. 1996:444).

Stockdale (1999) has noted the tension between clinicians and research, and it needs consideration. What benefits were there for the girl discussed in the introduction to this chapter from being diagnosed on genetic grounds? What pragmatic benefits accrue for the infertile man with CBAVD who is told that he now has cystic fibrosis, a condition which is associated with high morbidity and mortality rates? When asking why of the 50 CBAVD men in their study 'reclassified' as having CF, only 18 accepted the offer of free and confidential follow up evaluation, Colin et al. remark that:

"The diagnosis of male infertility appears to be sufficiently stressful for many men that the possibility of making an additional diagnosis, especially one carrying the social stigmatization of CF may be avoided...perhaps, it may be that the concept of having an underlying chronic illness is inconsistent with their personal belief that they are fit and healthy" (p.444).

This point of view suggests CF be diagnosed on clinical grounds. It accepts that the high number of mutations means that a comprehensive genetic test remains theoretical (at least for the moment). It is at odds with the theoretical position which defines CF in terms of having two mutant CFTR alleles and which is the foundation of the new CF
continuum. The use and acceptance of this continuum supports the theoretical position, and as technologies develop which may allow comprehensive testing for large numbers of CF mutations, this theoretical position may gain ascendancy in the discourse of CF. What arises from the analysis of the discourse of CF is not that the expansion of the CF classification system to the current continuum is only indicative geneticization, but that the source of this expansion may be. Expansion does not necessarily mean that geneticization is taking place, but in the case of cystic fibrosis, it is a consequence of geneticization.

One reason why narratives are so useful for discourse analysis is their momentum. As explained in chapter 3, narratives imply the movement of discourse through time. They also imply that this movement will continue unless slowed and stopped. By describing the genetic reclassification of CF as the narrative of expansion I am tacitly claiming that this expansion will continue. In the rest of this chapter, I will explore the debates that surround the continued expansion of the cystic fibrosis classification system.

**Pancreatic Disease**

As one would expect, the reclassification debate has also concerned other, 'bordering' conditions, pancreatitis for example. This section focuses on two recent articles investigating the relationship between CFTR mutations and pancreatitis and the role they play in CF reclassifications. Each of these studies took DNA samples from a number of patients suffering from chronic or idiopathic pancreatitis and compared their genotypes.

One of these, Cohn et al. (1998), contributes to the expansionist position. In their study of 27 patients, the authors found one compound heterozygote (ΔF508/R117H) and two heterozygotes with a 5T mutation on the other chromosome. There were four other patients with CF mutations and three with 5T mutations on one chromosome. This information was presented in terms of overall rate of CFTR mutations: "CFTR mutations were found at 11 times the expected frequency" (Cohn et al. 1998: 654). This is the way in which the early studies on the role of CFTR in CBAVD made the case for

---

69 For example, thorough parallel sequencing technology such as gene-chips.
reclassification (Kerr forthcoming). The one compound heterozygote and two 5T
heterozygotes are described as having "the CFTR genotypes that are most commonly
seen in patients with congenital absence of the vas deferens" (p.656). Cohn et al. claim
that:

"these findings suggest that in this group of patients, abnormal CFTR genotypes
cause pancreatitis as one component of an inherited syndrome affecting multiple
epithelial tissues and that such patients should be examined for congenital absence
of the vas deferens [ref] and sinusitis [ref] which are not typical of pancreatitis"
(Cohn et al. 1998: 656).

This is perhaps as close as one can get to reclassifying these cases of pancreatitis as CF
without actually calling them CF. As an euphemism for CF, 'an inherited syndrome
affecting multiple epithelial tissues' is perfect.

When discussing those patients with no CFTR mutations, the authors adopt a version of
Kerr's 'appeal to unknown mutations'. In this case, it is an 'appeal to untested mutations'.
They point out that the genotyping in their research only looked for 17 of the then 500
known CFTR mutations. Therefore there could be other pancreatitis patients in their
study, beyond the 7 identified, who carry one or even two copies of CFTR mutations.
The finding of only 7 carriers in their sample is a "cautious interpretation" (ibid.). This
position is also adopted with regard to whether any of these seven are actually
compound heterozygotes, with an undetected second mutation.

This is potentially significant for the classification of CF. The lack of evidence
concerning other CFTR mutations means that the authors: "could not determine whether
having one copy of an abnormal CFTR allele (as is found in carriers of cystic fibrosis) is
sufficient to predispose persons to pancreatitis" (Cohn et al. 1998: 657). If CFTR
heterozygotes (i.e. carriers) are deemed to be at increased risk of pancreatitis, then this
erects a conceptual barrier against reclassifying pancreatitis as a form of CF. The
conventional view of cystic fibrosis genetics implies that heterozygote carriers of CF
alleles are not negatively affected by their genome (in fact, they may even benefit in
evolutionary terms). Admitting pancreatitis into the CF continuum would mean accepting
that CF can be caused in heterozygotes.

A partial solution lies in suggesting varying tissue sensitivity to CFTR mutations:
"Our data...suggest that the pancreas and the vas deferens are both relatively susceptible to injury resulting from the reduced CFTR levels...the pancreas differs from the lung, sweat gland, and vas deferens in that it is affected in qualitatively different ways depending on the degree to which CFTR function is impaired" (Cohn et al. 1998:657).

This shows the construction of a continuum of tissue sensitivity and CFTR activity level.

The positioning of pancreatitis as a mild form of cystic fibrosis seems likely, if not inevitable. These authors suggest that since:

"CFTR mutations may increase the risk of pancreatitis after exposure to alcohol or certain drugs...genetic testing to identify patients at risk may be useful and may increase our understanding of the clinical course of these patients and their therapy" (ibid.).

A less expansionist position is in the Sharer et al. article, published in the same issue of the *NEJM*. This reports a study of 134 patients with chronic pancreatitis, where "No patient had a mutation on both copies of the CFTR gene" and 18 had a single CFTR mutation (Sharer et al. 1998:647). The 5T variant was identified in a total of 14 patients, 4 of whom also carried a CFTR mutation. The other 10 were from the non-carrier group of 116 patients. The authors are clear on the relationship between these pancreatic patients and cystic fibrosis:

"None of the 18 patients with a CFTR mutation alone or in combination with a 5T allele met the diagnostic criteria for cystic fibrosis when all the evidence was considered [reference: to Stern 1997]" (Sharer 1998: 647).

Sharer et al. are cautious about comparisons between CFTR-related pancreatitis and CBAVD. Although they add pancreatitis to the list of conditions (which includes CBAVD) in which CFTR mutations are of pathogenic importance, they seem to be aware of the complexities that this might raise:

"There is a fundamental difference between our findings and those reported in patients with congenital absence of the vas deferens...the relation between CFTR mutations and the development of chronic pancreatitis is more subtle...Further studies are needed to explain why chronic pancreatitis does not develop in the majority of persons with a CFTR mutation" (Sharer 1998: 650-651).

While almost everyone (i.e. male) with "classic" CF also has CBAVD, not everyone with CF has pancreatic disorders. These authors make no attempt to suggest that further CF associated alleles might be found on heterozygotes' other chromosome, if only time and money permitted the necessary research.
Consensus statement on diagnosis

These two articles, Cohn et al. and Sharer et al., provoked a response on the letters page of the *NEJM*. A letter criticises Sharer et al. for finding that none of their patients fitted the criteria for CF, and Cohn et al. for claiming that one of their patients had 'atypical cystic fibrosis' (Ren 1999:238). The author states that using the criteria drawn up by a consensus panel of the US Cystic Fibrosis Foundation, two of Sharer et al's patients and Cohns et al's 'atypical' patient have cystic fibrosis. The criteria agreed by the consensus panel are:

- one or more phenotypic features\(^{70}\);
- and a history of CF in a sibling;
- and a positive laboratory test: either a sweat test, nasal potential difference abnormality or a genetic test for two CFTR mutations (Rosenstein and Cutting 1998:590).

In reply Cohn et al. claim that their patient was still on the borderline, even when these criteria are used. Both the nasal and the sweat test results were within normal bounds. The gene test revealed one mutation that normally causes CF (ΔF508 with 9T variant) and one which normally does not (R117H with a 7T variant\(^{71}\)). Therefore the patient was heterozygous and a non-CF sufferer. Despite this, Cohn et al. felt that "the patient's condition was related to an inherited abnormality of CFTR on the basis of his genotype" (Cohn, Silverman and Knowles 1999:239).

Sharer et al's reaction to Ren's comments reveals the concerns present in the cystic fibrosis community. Far from improving diagnosis, the discovery of the CFTR-gene (i.e. the geneticization of CF) has meant that "The definition of cystic fibrosis has become progressively more hazy" (Sharer, Swartz and Path 1999:238). As in the case of CBAVD, there is a tension between clinical practicalities and the genetic reclassification:

\(^{70}\) These include persistent infection with a CF pathogen, chronic coughing, Gastrointestinal abnormalities (such as pancreatic insufficiency) and CBAVD (Rosenstein and Cutting 1998:590).

\(^{71}\) R117H only counts as a CF mutation when combined with the shortened, 5T variant. According to the consensus statement, on its own (i.e. with the normal 7T variant) it does not count as a CF mutation (Rosenstein and Cutting 1998:592).
"Because the phenotypic spectrum that may now legitimately be called cystic fibrosis has become so large, it is unhelpful in the clinical context" (ibid.). Since "the time is right to recognize that the diagnosis of cystic fibrosis is too nebulous to preserve in clinical practice", they suggest a new classification system is needed. This would include:

- cystic fibrosis "disease" which is "the progressive suppurative respiratory tract condition irrespective of other phenotypic features" and
- cystic fibrosis "syndrome" which includes "pancreatic manifestations, congenital absence of the vas deferens, and lesser pulmonary manifestations" (ibid.).

One obvious objection to this is that it misunderstands what 'syndrome' means. We know the aetiological factor behind those CBAVD cases classed as mild CF. It is the CFTR gene. The issue is not what causes these other, non-pulmonary, symptoms of CF, but whether they should be considered as part of the disease called cystic fibrosis at all. The division into CF 'disease' and 'syndrome' merely ducks the issue over what counts as cystic fibrosis.

What is also clear from this discussion is the circularity built into the consensus statement on CF diagnosis. If pancreatitis counts as a symptom and a positive CFTR-mutation test counts as the laboratory test, then the consensus statement casts no light on the wisdom of reclassifying what counts as CF. The consensus statement is strict over what counts as a CF diagnosis, and also sets rigorous requirements for what counts as a CF causing CFTR-mutation. Despite this, it includes on its list of 24 "Mutations that cause cystic fibrosis" (Rosenstein and Cutting 1998:591) alleles such as G551D, which Colin et al. (1996) list as causing borderline sweat tests in CBAVD patients. In this case, is it a CF causing mutation or simply a CFTR-mutation associated with another condition, CBAVD? The fact that CBAVD can be caused by mutations which also cause 'classic' CF means that the best attempts of the Cystic Fibrosis Foundation's consensus panel are unlikely to resolve the issue of what counts as CF. The statement highlights this problem by the presentation of 'atypical' CF (basically chronic sino-pulmonary disease) and admission that "Of particular interest are individuals with congenital bilateral absence of the vas deferens...many of whom have CF mutations on one or both CFTR genes" (Rosenstein and Cutting 1998:590). If someone presented with pancreatitis and had CFTR mutations and a borderline sweat test, the consensus statement would allow that person to be classified as having CF.
Whether or not mutations are classified as CF-causing may provide an interesting means of assessing the degree to which the CF continuum is expanding. For example, in a 1998 study of the relationship between CFTR mutations and forms of male infertility, Kanavakis et al. discovered a novel mutation. This allele, called D565G "has not been detected in >250 CF chromosomes, nor in >100 non-CF chromosomes" (Kanavakis et al. 1998:336) and was found in a patient with CBAVD who had another CFTR mutation on his other chromosome. The question is how to classify this man? He carries a novel CFTR mutation which has not previously been associated with cystic fibrosis. His normal sweat test suggests that he is not obviously suffering from cystic fibrosis. How this mutation is classified in future reviews may act as a marker for the degree of expansion.

Policy Implications of the Narrative of Expansion

I have tried to remain neutral on the question of whether CBAVD and types of pancreatitis should be classified as forms of cystic fibrosis. In part this is because my aim is to detach the concept of geneticization from the conclusion that it is automatically morally suspect. This neutrality is also due to the research tradition of SSK, which requires that the sociologist preserve symmetry when approaching a scientific issue. While 'symmetry' is properly held to be in terms of explanation invoked, I interpret it to also refer to the rights or wrongs of a particular scientific choice. The main choice in this case study is:

"whether all cases of CBAVD as an isolated finding should be uniformly classified within the spectrum of CF or be defined as CFTR associated but distinguishable from clinical CF" (Colin et al. 1996:442).

The answer made in the CF literature is that "CBAVD and cystic fibrosis are extreme forms of a wide nosologic spectrum of conditions that have a common molecular basis" (Chillon et al. 1995:1479-1480).

My case study has shown how this answer was reached, by constructing the narrative of expansion, and extending the CF continuum beyond the bounds of what was traditionally recognised as cystic fibrosis. Why the CF medical community should have adopted this narrative is beyond the scope of this study, although I suggest an examination of the relationship between clinician and researcher may prove informative. As I have shown, there is considerable tension between clinicians who doubt the pragmatic usefulness of
the new geneticized classification system, and researchers who seem to be pushing it. The consensus statement lists four reasons why CF genotyping is desirable: diagnosis, family information, prediction of phenotypic features and "categorization of patients for research protocols" (Rosenstein and Cutting 1998:592). From a research point of view, it makes sense to have clear categories, and to be able to distinguish between patients on unequivocal, genetic grounds. Of course, this does not mean that the meaning of these genetic grounds is unambiguous. But the authors of the statement do not make clear why it is desirable for clinicians to adopt categories required for research.

The choice of what counts as cystic fibrosis has real policy implications. On the personal level, there are those like the parents of the young girl discussed in the introduction to this chapter. Through leaving the Navy to remain in one place they were financially disadvantaged because their daughter was diagnosed as having CF solely on genetic grounds; I am not going to speculate about the psychological and emotional effects of this decision. There are those infertile men, reclassified as CF sufferers, who may struggle with stigmatisation and or insurance difficulties (Colin et al. 1996).

At a broader level, discussion around the setting up of CF screening programmes needs to consider what actually counts as CF. While some authors tout such programmes as one of the most positive results of the geneticization of CF (Geddes and Alton 1999) clearly there are important issues that must be settled before such programmes can be implemented (Grody 1999). One of these is the definition of CF that such research will use. This will in turn play a large part in determining what mutations are actually screened for. Far from being an obscure academic issue, the geneticization of CF concerns concrete points of health policy.

Cystic Fibrosis was the test case for the technologies and concepts that would open up human illness and allow us to treat previously impervious conditions. It turned out to be far more complex than was expected. Presently with 800 mutations (and counting), the geneticization of CF should serve as warning to those who assume that the introduction of a genetic test will automatically introduce clarity and constancy into medical classification. The geneticization of CF is a cautionary tale about responsibility for social
decision-making in medicine. The introduction of the test for the CFTR gene did not remove social decisions from the classification and diagnosis of cystic fibrosis, it highlighted them.

In the next chapter I will show how the geneticization of diabetes produced a quite different narrative to that constructed in cystic fibrosis, a narrative of division.
CHAPTER 5: DIABETES AND THE NARRATIVE OF DIVISION

Diabetes is a mysterious illness
- Aretaeus of Cappadocia (c.81-138 AD)

1. INTRODUCTION

If geneticization in a supposedly 'simple' disease like CF turns out to have such complex consequences, how does this process take place in a multifactoral disorder, where environmental factors also play a role? Diabetes is now the classic, multifactoral genetic disease. It "Has been studied extensively and the disorder has become a paradigm for genetically complex diseases" (Concannon et al. 1998:292). John Bell, Professor of Clinical Medicine at Oxford University states that:

"Almost inevitably evidence of causality leads to a redefinition of disease. This has already been accepted for a number of disorders where phenotypic definitions have been replaced by genetic ones. A good example is provided by the subdivision of diabetes into Type I (juvenile) and Type II (maturity onset). This emanated in large part from the fact that genetic factors (histocompatibility genes) contribute to Type I diabetes" (Bell 1998:618).

The NHS Central Research and Development Committee on the new genetics claims that:

"The ability to redefine common human disease, using genetics to define the biochemical processes responsible for disease, will allow the subdivision of heterogeneous diseases such as hypertension or diabetes into discrete entities... This has already begun in diabetes, where definition of the involvement of HLA genes suggested an immune mechanism in a subset of patients, leading to the subdivision into type I and type II diabetes" (Department of Health 1995:5).

These quotations suggest that genetic information has played a pivotal role in the classification of diabetes leading to what they both describe as the 'subdivision' of diabetes into different 'types'. This chapter looks at the way in which this reclassification came about, how it relates to the geneticization of diabetes and how it illustrates what I call the 'narrative of division'. The quotations above suggest that the division of diabetes into two types (I and II) was an obvious, inevitable consequence of the involvement of specific genes in diabetes causation. As I hope to show, this presents a simplified
perspective on the changes in diabetes classification that started in the late 1970s and which have continued until the present day. I suggest that diabetes is an example of 'geneticization by stealth', where genetic explanations 'sneak' into a disease classification, only to become truly apparent years later. It is not that Bell and the NHS Central Research and Development Committee are wrong in claiming that links to genetic aetiology caused the division into two types of diabetes. It is just that this was not inevitable, and alternative classification systems could have become standard.

Diabetes is an interesting case study because it shows that geneticization can happen to a disease without genetic tests being widely available. Only recently have predictive genetic tests become available for any sort of diabetes, and even then they are only possible in the case of the rare version known as Maturity Onset Diabetes of the Young, or MODY. In the first study of its kind, Shepherd et al. discuss the issues facing a family where the father, Bob, has MODY as has one daughter, Kim, and the possibility exists for presymptomatic testing on the other daughter, 5 year old Jill (Shepherd et al. 2000). The issues surrounding presymptomatic testing raised in this study are important, but my own research precedes debates concerning genetic testing, and shows how geneticization can have an impact on disease classification decades before genetic testing becomes an possibility.

In the medical community, debates concerning diabetes classification are nothing new; the issue of 'what counts as this disease' has long been explicit. One main theme in these discussions is the need for disease classifications to be of therapeutic value to the patient:

"Classification schemes and diagnostic criteria should, above all, be utilitarian. They should help physicians select a management program which is of maximum benefit and minimum harm to individual patients in their offices today" (Genuth 1982:1191).

Yet there is also acknowledgement that different parts of the scientific community need different classifications:

"a classification appropriate to a clinician whose concern is with diagnosis and treatment may well be inappropriate to a basic scientist whose concern is research strategy and experimental design" (Keen 1985:31).

This obviously has echoes of the classification debate in CF, and occurs throughout discussions of diabetes classification. The diabetes medical community were (and are)
acutely aware of the implications of classification. With diabetes being cited as effecting 2-3% of Western populations and with up to one third of all diabetics never being diagnosed (Smallwood 1990:33), how this disease is classified has a serious impact on people's lives.

Nature of the illness

Diabetes Mellitus is an umbrella term for a number of different diseases of glucose metabolism. Broadly, this syndrome is divided into two kinds of disease: the kind that affects young, thin people, which is life threatening and requires insulin injections to treat; and the kind that affects older people, who are often obese, and who do not rely on regular insulin injections for their survival.

In the case of the first kind of diabetes, the body's immune system has destroyed the β-cells in the pancreas, which make insulin. Therefore, when a diabetic's blood sugar rises (after a meal, for example), the body cannot produce insulin which promotes the storage of glucose as glycogen and fat. Symptoms include: thirst, increase in appetite and glucose in the urine. In its search for energy, the body begins to break down fat, producing ketones, a process called ketoacidosis. The build up of ketones in the body can lead to coma and death. Regular injections of insulin allow the body to absorb glucose and the diabetic to survive.

In the second kind of diabetes, the body's cells become insulin resistant (often a result of obesity or fetal malnutrition). Therefore although the body is producing insulin, it cannot produce enough to fully overcome the insulin resistance. Symptoms include: thirst, increased urination, the slow healing of wounds, weakness, fatigue and blurred vision. It can normally be controlled with dietary changes and lifestyle alterations (Smallwood 1990).

Classification systems in Diabetes Mellitus

The condition we currently recognise as diabetes mellitus (DM) has been medically described for over 2000 years, including the recognition that it involves two distinct
'types', one 'quick and thin' and the other 'fat and slow'. In 1875 Bouchart suggested that the terms 'diabète gras' and 'diabète maigre' be used to describe two diseases with different prognoses and classifications. These ideas lapsed in the early twentieth century, as DM was described as a single disease consisting of different stages such as 'brittle'/stable' or 'juvenile'/maturity'.

The idea of DM as a syndrome was emphasised in the late 1940s by, among others, Sir Harold Himsworth, who suggested that it be divided into 'insulin sensitive' and 'insulin insensitive' varieties. Soon after this, R.D. Lawrence proposed that a distinction should be drawn between versions of diabetes mellitus on various grounds such as: primary pancreatic destruction; disturbance of other endocrines; disturbance of fat storage; diabetes associated with obesity without ketosis; and insulin deficient diabetes. He pointed out that the different types seemed to run in different families, leading to a clear clinical divisions in patients: those who require insulin to survive and those who do not (Lawrence 1951:375).

Hugh-Jones was the first to use a numerical classification system for diabetes. In 1955 he drew a distinction between Type 1 diabetes mellitus (where the patient required insulin to survive), and Type 2, where the patients did not need insulin injections and were treated with changes in diet (Hugh-Jones 1955:892). In 1976, Andrew Cudworth revived and popularised Hugh-Jones' 1955 distinction between Type I and Type II DM (Bennett 1985:19). At this point, it is enough to note Bennett's perceptive statement that:

"The move towards a numerical classification of diabetes was clearly driven by the desire to arrive at an aetiological classification incorporating the heterogeneity of Diabetes Mellitus" (Bennett 1985:21).

By the end of the 1970s there was great concern in the diabetes medical community about the classification of the disease:

"types of diabetes were loosely divided into 'juvenile onset' and 'maturity onset', with secondary diabetes, chemical diabetes, borderline diabetes and prediabetes all used in ill-defined ways" (Alberti and Zimmet 1998a:535).

The result of this confusion was the system devised by the National Diabetes Data Group of the American Diabetic Association, which met in 1978. In 1979, it published its definitive recommendations for diabetes diagnosis and classification. This system was
drawn up with the intention of producing clear, mutually exclusive divisions on the basis of simple clinical observations:

- Insulin Dependent Diabetes Mellitus (IDDM) : Type I
- Non Insulin Dependent Diabetes Mellitus (NIDDM) : Type II
- Other Types: from pancreatic disease
- Impaired Glucose Tolerance (IGT)
  - non-obese
  - obese
  - IGT associated with certain conditions/syndromes
- Gestational diabetes

(Based on NDDG 1979)

This classification system was adopted and recommended by the World Health Organisation in 1980, revised in 1985 and a whole new classification process took place at the end of the 1990s.

2. MATERIALS AND BACKGROUND

The focus of this chapter is on two articles written by A.G. Cudworth and one by W.J. Irvine, all from the late-1970s. The two Cudworth articles to be analysed are: "The aetiology of diabetes mellitus" (1976) and "Type I Diabetes Mellitus" (1978). The former was published in the *British Journal of Hospital Medicine* and the latter, as a review article in *Diabetologia*. They have been cited in the BIDS ISI database 25 and 126 times respectively, and thus, while not as heavily cited as the 1996 CF article in the previous chapter, have been acknowledged as influential. My contention is that over the space of these two articles, Cudworth's classification system for diabetes mellitus, specifically that form of diabetes which normally occurs in childhood and which usually requires insulin injections to survive, becomes more and more 'geneticized'. To some extent I am proposing Cudworth as the 'agent of change' in the geneticization of diabetes. This is not a wholly artificial position to take, since he is identified by commentators as the driving force behind the adoption of a numerical system of classification (Bennett 1985, Keen 1986).^72

---

^72 This role for Andrew Cudworth has also been confirmed by Professor Keen in interview, 21/4/99.
The article by Irvine is "Classification of Idiopathic Diabetes", from *The Lancet* of 1977 (thus chronologically between the two Cudworth articles), and it has been cited 106 times. While covering much the same ground as Cudworth, Irvine produces a different classification system, focusing on the role of autoimmunity and pancreatic-islet-cell-antibodies (ICAs). As above, I aim to highlight the discursive strategies used in this article but this time to show that the geneticization of diabetes (implicit in Cudworth's system) was far from inevitable. Alternative classifications, such as Irvine's, were possible. Although this article shares Cudworth's focus on aetiology, its main focus is the autoimmune processes that destroy the active cells in the pancreas, rather than the underlying causative genes.

Building on my analysis of these three articles, and extending it up to current debates surrounding diabetes classification, my research shows that:

- changes in the classification system between the late 1970s and the present day are a result of geneticization;
- current classifications demonstrate the construction of a 'narrative of division';
- this geneticization is explicitly *not* due to our knowing more about the genetics of diabetes now than in 1978. Rather it is due to the way in which language has been used to describe the disease.

**The HLA complex**

The link between diabetes classification and genetics pivots around the major histocompatibility system (HCS; sometimes referred to as Human Leukocyte System, HLS). The HCS is a section of the short arm of chromosome 21; its genes code for Human Leukocyte Antigens, proteins that sit on the surface of cells involved in the immune system. There are a number of different HLA genes in the HCS; those close to each other on a chromosome tend to be inherited together as a unit (called a haplotype). Humans have two HLA haplotypes, one inherited from each of our parents. HLA-nomenclature lists the loci or the gene (D for example), and the subregion (e.g. R) if
known, followed by a number indicating the allele. More modern names include whether
the gene concerned encodes for the α or β chain of the protein molecule (She 1996:324).

From the late 1960s onwards, it was noted that certain combinations of these antigens
seemed to have associations with certain disorders, such as Hodgkin's disease. Studies
such as Singal and Blajchman's (1972) suggested that there is also a relationship with
diabetes, which they describe as "a genetically determined disorder of metabolism in
which inherited susceptibility plays an important part" (p.429). This is the starting point
for the assumption of an association between HLA-genes and diabetes. Although these
studies used only serological tests, to assess the presence of particular antigen proteins,
the stretch of DNA coding for these proteins was already known. Any claim linking a
disease to HLAs, is a claim linking a disease to a particular stretch of DNA.

3. CUDWORTH

A central point of my analysis is that change in Cudworth's terminology from 'Type 1
diabetes' (i.e. Arabic numerals) to 'Type I diabetes' (i.e. Roman numerals) indicates a
change from a clinical classification of diabetes, to a genetic one. At first glance, the
change from '1' to 'I' might seem merely stylistic, but Cudworth uses both of them in the
same article (1978), and with consistency. Of course, the dangers of confusing two such
similar terms is high, and indeed seems to have occurred in the 1978 article73, but this
similarity is, I think, one of the devices Cudworth uses to make his case. By naming his
new classification system in a very similar way to the previous system, Cudworth avoids
the risk of seeming to propose a wholly new means of classifying diabetes (whilst
accepting the risk that confusions may occur). The core of my case is that 'Type I'
diabetes is a geneticized category; i.e. it links the disease to a specific stretch of DNA.

73 On page 289, Cudworth refers to "classical Type 1 diabetics...shown in figure 5". The
accompanying figure 5 refers to "Age of onset distribution for 373 classical Type I diabetics". I
feel it is safe to assume that this is an error and should read "1", since Cudworth frequently, and
consistently refers to 'Type I' as a 'classical' form of diabetes. Similarly, on page 286, he refers to
'an analysis of 40 families with a pair of Type I diabetic siblings...(fig. 4)" yet Figure 4 's
explanatory note states that it represents the "Zygotic assortment of HLA A-B haplotypes in 40
pairs of Type I diabetic siblings". The former is surely correct. (Emphasis added throughout).
It may be important that the errors occur in the caption underneath diagrams rather than the main
text. It may indicate confusion on the part of the typesetter for the diagrams.
To construct 'Type I', Cudworth uses a number of different strategies, some of which are specific to a single article, and some which encompass both of them.

"A satisfactory classification...": 1976 and Type 1

Although the title of the 1976 article is "The aetiology of diabetes mellitus", Cudworth does not propose to abandon clinical classification in favour of an aetiological means of classifying the disease. At least initially, he goes some way towards actually supporting a form of clinical classification. Starting from the position that: "Diabetes is a clinically heterogeneous disorder" (Cudworth 1976:207), Cudworth makes a common complaint about the then current system of classifying the disease:

"the terms 'juvenile onset' and 'maturity onset' are too rigid and should perhaps be discarded in favour of type 1 and type 2 diabetes respectively" (ibid.).

His point is that distinctions based on age are inadequate since there are many exceptions to the 'age of onset' rule. For example, youth onset diabetes "can also occur as the insulin-dependent syndrome of typically abrupt onset at all ages, including elderly" (ibid.) and "Mild diabetes [i.e. type 2] has been reported in children, sometimes referred to as MODY (maturity-onset diabetes in the young)" (Cudworth 1976:207-8)\(^74\). From this clinical heterogeneity, Cudworth concludes that:

"there are two aetiologically distinct forms of the disease determined by differences in age of onset, relative abruptness of onset, tendency to ketoacidosis, and dependence on insulin" (Cudworth 1976:207).

As a result of these differences, he proposes the following classification system:

<table>
<thead>
<tr>
<th>CLINICAL AND AETIOLOGICAL CLASSIFICATION OF DIABETES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary diabetes</strong></td>
</tr>
<tr>
<td>type 1 - juvenile onset or insulin dependent</td>
</tr>
<tr>
<td>type 2 - maturity onset or non-insulin dependent</td>
</tr>
<tr>
<td><strong>Secondary diabetes</strong></td>
</tr>
<tr>
<td>pancreatic disease</td>
</tr>
<tr>
<td>liver disease</td>
</tr>
<tr>
<td>hormone induced (endogenous and exogenous)</td>
</tr>
<tr>
<td>obesity</td>
</tr>
<tr>
<td>drugs</td>
</tr>
</tbody>
</table>

from Cudworth 1976: 207

\(^{74}\) MODY has now been separated off as a particular sub-type of diabetes, caused by MODY-specific genes. See the final section of this chapter.
It should be noted that the table reproduced above cuts across aetiological and clinical boundaries in its classification. Within 'Primary diabetes', the distinction made between types is on clinical evidence (age of onset or insulin dependence). In secondary diabetes, distinctions are causal/aetiological. 'Pancreatic disease' is a cause of Secondary diabetes in a way that 'juvenile onset' cannot be a cause of Primary diabetes. The distinction between primary and secondary diabetes can be seen as both clinical and aetiological.

This cross-classification (which is, after all, signalled by the table's title) makes any comparisons between different variants of diabetes difficult. It is hard to compare items classified aetiological with those classed on clinical grounds. What such a table does do is serve to associate a disease normally classified on clinical grounds with a form of aetiological classification. A second association it strengthens is that between classifications made on the grounds of age of onset and those made in terms of insulin dependence; and in turn between these classifications and the terms 'type 1' and 'type 2'. The objections raised by Cudworth to age-based distinctions are used to favour a type 1/2 distinction, which seems, from the table, to be a shorthand for age based distinctions or insulin dependence. This link is important in the 1978 article where it becomes a means of undermining the classification of diabetes on clinical grounds.

Having outlined this new classification system, Cudworth goes on to describe the work that has previously tried to reveal the genetic component to diabetes. In this section, he lists four previous articles, only to point out the difficulties and faults with each of them. Their main fault is that they try to apply simple Mendelian strategies to describe a highly complex disorder. He implies that the next steps have to be made at the molecular level: "more elaborate statistical methods are unlikely to disclose any new information...better methods are required for identifying the genotype" (Cudworth 1976:208). This leads
onto Cudworth's own work on the HLS. By presenting this chronological progression\textsuperscript{75} of research, Cudworth both sets his own work within a particular context (the search for the genetic basis to diabetes) while allowing him to justify his own research (previous work in this area has failed, a new approach is required). There is certainly nothing novel about this 'appeal to authority', it having been widely noted in a variety of different sciences (Gross 1990:86-87, Myers 1990a), yet that does not detract from its effectiveness.

Cudworth's own work on the genetics of diabetes shows: "a positive association" between the HLA antigens B8 and BW15. Later work also shows a link to B18 so that:

"The relative risk for developing this type of diabetes is increased two to three times in those subjects who type HLA B8, BW15, or B18 positive. In those subjects who possess two of these antigens the risk appears to be additive" (Cudworth 1976:208).

When Cudworth addresses the then current knowledge about the aetiology of diabetes mellitus, he covers the three main factors: genetics, environmental agents, and immunological factors fairly equitably (2½, 2 and 1½ columns respectively). He notes that environmental factors must be important in diabetes aetiology because of:

"the studies in identical twins [ref.] in which it was shown that approximately 50 per cent of twins with insulin-dependent diabetes are discordant for the disease" (Cudworth 1976:209).

He concludes his section on type 1 diabetes with a figure attempting to model how all three of these factors might relate. However vague this figure is, and Cudworth views it as only a "possible unifying hypothesis" (p.214), it does serve to integrate all three factors of the pathogenesis of type 1 diabetes in a way which suggests that all three have an important, even equal, role to play. Much of this is to do with the pictorial representation. Cudworth could have described this hypothesis in the text of the article, but the figure serves to reify the interaction between the various factors and strengthen their individual roles.

\textsuperscript{75} The years of the papers cited are 1933, 1952, 1962, and 1967.
The 1976 article presents Cudworth's attempt to introduce the type 1/2 distinction. He explains why it is preferable to alternative systems (i.e. age based classification) though he has crucially failed to explain how it is *different* from them. He has also underpinned this new classification system with a suggested model for its pathogenesis.

**1978 and Type I**

"Type I Diabetes Mellitus" is ostensibly a traditional review article. It does not include any new, previously unpublished results and it outlines the current state of scientific knowledge about a certain type of diabetes. But it also proposes a novel classification system and prioritises one factor (HLA typing) above others in the classification and explanation of the pathogenesis of diabetes mellitus.

As suggested at the beginning of this chapter, the important point to note in this article is the introduction and use of the term 'Type I' diabetes, in opposition to the 'Type 1' used in the 1976 article. The summary section that starts the 1978 article begins:

"The major genetic susceptibility to insulin dependent (*Type I*) diabetes is determined by genes in the HLA chromosomal region".

18 lines further on, half way through the summary section, Cudworth writes that:
"Certain factors...are associated with a significantly reduced risk...in Type I diabetes" (Cudworth 1978: 281, emphasis added to both).

There is no explanation of the change from 1 to I, and by the time the introduction to the article proper mentions types of diabetes, further down the page, it has reverted to "Type 1 (juvenile onset type)".

Like the earlier article, the 1978 article contains a section on previous attempts to discern the genetic component of diabetes. Though the section is of a similar length to that in the 1976 article (53 as opposed to 42 lines), its referencing is far more extensive. Fifteen separate studies are cited, in comparison to the four in the 1976 article. All of the articles would have been available for reference in 1976, since the latest one cited is 1972. This difference between the articles may be due to the different conventions of the journals concerned; the British Journal of Hospital Medicine cites author and date in the text, with full references in the bibliography at the end of the piece. Diabetologia, on the other hand, uses an endnote system, which means that far more references can be entered into a text, without taking up so much room (though of course the full references are listed at the end of the article concerned).

Whatever the reasons for this difference in referencing between the articles, the effect is to place the 1978 article in a more extensive research context; it seems as if more work is being done on the genetics of diabetes, it makes the idea of a genetic cause for diabetes appear more credible. Of course, all these references could be refuting the concept of genetics in diabetes but the use of citations here puts Cudworth's work within an apparent network of research, strengthening the idea that there is a genetic factor causing diabetes.

The genetic research introduced by Cudworth in the next section ("Studies of the Major Histocompatibility System (MHS) in Diabetes: 1. Genetic and Biological concepts") is presented in a very tentative manner. He writes that "these chromosomal regions probably control difference in immune response...", "such genes may operate in association...", "It is unlikely that...", "and almost certainly..." (Cudworth 1978:282, all emphasis added). Such 'hedging' has been noted by other researchers (e.g. Myers 1990a) and allows authors to introduce ideas which are under-supported by empirical evidence.
This background information is presented in such a way, that Cudworth concludes this section with the very mild suggestion:

"A possible working hypothesis is that genes with a similar role exist in the HLA chromosomal region to produce susceptibility to certain types of diabetes" (Cudworth 1978:283).

Through the next five sections, Cudworth marshals his evidence of the link between certain HLA specificities and some forms of diabetes. One result of this review of a wide range of studies is the 'spread' of HLA-types that become associated with diabetes. In his 1976 article, Cudworth mentioned only 3 that were positively associated with 'type 1' diabetes (B8, BW15 and B18). In the 1978 article, he lists association with 12 HLA genes. He concludes that:

"the studies of the HLA system in diabetes have provided scientific evidence for the existence of genetic heterogeneity which formed the basis of the new classification of the disease, the HLA linked genetic susceptibility operating irrespective of age of onset (Type I diabetes)" (Cudworth 1978:285).

This, then is the new definition of a form of diabetes, or rather a new form of diabetes altogether. Before this definition of Type I, there was no classification of diabetes that exactly matched it. This is not so much a renaming, as an invention of a type. While the 1976 article presented Type 1 as a new classification, a simple glance at the table "Clinical and Aetiological Classification of Diabetes" confirms that type 1 is short hand for juvenile onset or insulin dependent diabetes. The apparent close equivalence between these two classifications is vital for one of the main strategies Cudworth uses to make his case (see below).


77 "An increased relative risk for developing the disease is observed in subjects who are HLA A1, A2, B8, B18, B15, B40, CW3, BF, DW3, DW4, DRW3, DRW4 positive" (Cudworth 1978:281).

78 There is a contradiction here, of course, in that juvenile onset and insulin dependent diabetes are not equivalent terms. Cudworth himself has a section in his 1978 paper: "HLA frequencies in Late Onset Insulin Dependent Diabetes". If juvenile onset and insulin dependence are equivalent, then this translates into "HLA frequencies in Late Onset Juvenile Onset Diabetes".
Type I cuts across previous classification categories, including young and old people within its bounds. The fact that β-cell destruction probably occurs in advance of clinical symptoms and insulin-dependence is merely the end result also implies independence from other classification systems (Cudworth 1978:288).

Tentative to Confident

To some extent, the confident presentation of 'Type I' diabetes is at odds with what has gone before in previous sections. Of particular interest is Cudworth's conclusion that there is an "HLA linked genetic susceptibility". Previous to this point, he has only referred to the idea of genetic susceptibility in a very qualified manner. Throughout most of his text, he relies upon the more neutral term "association", for example: "A stronger association has been demonstrated between 'juvenile-onset' diabetes and the HLA DW3 and DW4 specificities" (Cudworth 1978:284). At the bottom of page 284 Cudworth concludes that the number of associations has led to "a more complete picture of a pattern of 'susceptibility' and 'protection' ", and he maintains this qualified use of 'susceptibility' in the title of figure 2 (Cudworth 1978:285): "Pattern of 'susceptibility' and 'protective' HLA factors in Type I diabetes". Half way down the same column, Cudworth claims his HLA linked genetic susceptibility, with no qualifying quotation marks.

By means of this creeping, step-by-step process, from association to 'susceptibility' to susceptibility, Cudworth constructs the "HLA linked genetic susceptibility", and hence Type I diabetes. This is despite contradictory information that he cites in the two previous sections. In the section "HLA Frequencies in Late Onset Insulin Dependent Diabetes", while the increased relative risk for certain HLAs is similar to that for 'Juvenile-Onset' diabetes, there is "no increase in B18 [one of the genes mentioned in 1976]". But this is defused with the explanation that, "as seen in earlier studies...the presence or absence of significant associations only becomes apparent with larger numbers" (all Cudworth 1978:285).

Similarly, the section entitled "HLA Frequencies in Japanese Diabetics" suggests that in this population, different HLAs are associated with diabetes. Again these results are qualified on the grounds that the samples involved are small, since: "'juvenile-onset'
diabetes is relatively uncommon in Japan" (Cudworth 1978:285). Such contradictions of
his position actually strengthen Cudworth's case; he can rightly claim to have taken into
account contradictory information, but by qualifying it in this way, he can use it to
bolster his case, and move from association to susceptibility.

Environment

Where Cudworth cannot claim to have taken all available information into account is in
relation to environmental factors and immunological associations, the factors that his
1976 article joins with genetic susceptibility to form a model of diabetes pathogenesis. In
terms of amount of space devoted to these two factors, there are obvious differences
between the 1976 article and "Type I Diabetes". Immunological factors, in the form of
studies of islet cell antibodies (ICAs), which played such an important part in the
pathogenesis hypothesis of 1976 are relegated to a minor position. Cudworth discusses
the "distribution of particular HLA B phenotypes in 115 Type I diabetics...in relation to
the persistence of islet cell antibodies" (Cudworth 1978:287). He concludes that while
there is some significant association between certain HLA combinations and ICAs, these
only occur in cases where the diabetes is of "more than five years duration" (ibid.). In
"newly diagnosed cases...there was no evidence of an association between ICA and HLA
phenotypes" (Cudworth 1978:287-288). Thus while some support for ICA typing as a
means of classifying diabetics is offered, it is only in a very narrow band of possible
cases.

Similarly, the role attributed to environmental factors, specifically viruses, is very
different from the 1976 article, which uses animal comparisons and twin studies to
suggest that although "Firm evidence for virus-induced beta-cell damage in man is
lacking...the development or not of diabetes of a co-twin probably depends on chance
environmental events" (Cudworth 1976:209-210). Crucially, the 1978 article, which
dedicates only half a column to the role of environmental factors, uses both animal study
information and epidemiological studies but not the results of twin studies, the
discordance of which were so convincing in support of environmental factors. There are
also less tangible, but equally persuasive aspects to this section, the main one being the
querying of the evidence in favour of a viral factor. The section starts with the sentence:
"It seems likely that environmental factors (? viruses) are operating to trigger the disease" (Cudworth 1978:289). The effect of this peculiar use of a question mark before the word concerned, rather than after, is to make the idea of viruses as a possible factor extremely questionable.

Another reversal takes place at the end of this section:

"Of considerable interest are the reports of an increased incidence of diabetes in patients with evidence of congenital rubella. Five out of 8 cases...[ref]...under the age of 30 years were HLA B8 or B15 positive" (Cudworth 1978:289). Apart from the fact that this means that 3 out of eight (38%) were not positive for HLA B8 or B15, the placing of the HLA information at the end of this structure reduces emphasis on the fact that there is "an increased incidence of diabetes in patients with evidence of congenital rubella". Rather than using this information to suggest that there is a role for viruses as possible causal factors in the pathogenesis of Type I diabetes, the focus on the HLA typing ensures that it becomes a question about the role of HLA (i.e. genetic factors) in diabetes.

The end result of these strategies is the prioritising of Type I diabetes at the expense of alternative classification systems. The essential distinction between the two types of diabetes, made on genetic rather than clinical grounds, is the beginning of the narrative of division. This narrative continues to sub-divide diabetes, leading to the current classification system where 57 distinct types are listed (see below). In the next section, I present in detail the way in which the differences between the two kinds of diabetes are constructed over the space of the two Cudworth articles.

---

79 This preceding '?' is also used in reference to autoimmune processes (p.288), environmental causes of Type I (p.289) and the dominant inheritance of MODY (p.282). All these are facts which he has to acknowledge, but which undermine, or at the very least are peripheral to the construction of type I diabetes as a geneticized category.
How to get from 1 to I

Together they fall

As has been suggested above, one of the most effective strategies in these two articles involves the discrediting of alternative classification systems. If the Type I system presented in the 1978 article is to be believable, then possible alternatives must be reduced in plausibility. This is a two stage process. First, it involves tying an already dubious classification system (age of onset) to the other alternative system (insulin dependence). The second stage involves invoking the evidence against the weak system, reducing its credibility, and that of the linked classification system, against which no evidence need be presented. Over the course of these two articles, no evidence is presented to suggest that insulin dependence is not a perfectly decent and effective form of classification in diabetes. It is only 'guilty by association' with age of onset.

This two-stage process takes place over both the articles, as Cudworth links and then discredits the two classification systems that might rival type I. This linking varies from the obvious (the table from the 1976 article labelling type 1 as "juvenile onset or insulin dependent") to more subtle cases. For example, the 1978 article's first page starts with: "The major genetic susceptibility to insulin dependent (Type 1) diabetes" and moves onto "immune mechanisms in Type 1 ('juvenile onset' type) disease" (Cudworth 1978:281). The section of the 1978 article looking at "Studies in 'Juvenile-Onset' Diabetes" uses data from "323 insulin dependent diabetics with an age of onset of below 30 years" (Cudworth 1978:284), stressing the link between these two different types of classification and, in a way, constructing a variant on 1976's Type 1. While that was just "juvenile onset or insulin dependence", 1978 is presenting Type 1 as 'juvenile-onset' and insulin dependence. Thus there is a step-by step process, from the beginning of the 1976 article which formally joins the two classification systems under the 'umbrella' title of Type 1, through the 1978 article which uses 'juvenile-onset' and insulin dependent as interchangeable subtitles for Type 1, to its the later stages, where the two systems are fully joined together.
The second stage of this strategy involves discrediting age of onset as a form of classification. One noticeable difference between the 1978 and the 1976 is Cudworth’s use of ‘stress’ marks around the terms ‘juvenile’ and ‘late’ onset diabetes in the later article. In fact, when he first mentions age of onset as a criteria for classification, three lines into the 1978 article, he refers to "so called 'juvenile-onset' diabetes" (Cudworth 1978:281). This stress is consistent throughout the article, and not only serves to cast doubt on age of onset as a means of classification but as we shall see, by implication, all clinical criteria. In addition, evidence of conventional wisdom is marshalled against age of onset classification: "It is well recognised..." (Cudworth 1976:207). As has been stated, neither article offers any evidence to suggest the inadequacy of classification based on whether a patient is insulin-dependent or not. The conclusion of the 1978 article starts with:

"Irrespective of age of onset, the major susceptibility to classical insulin dependent diabetes is conferred by genes in the HLA chromosomal region" (Cudworth 1978:289).

It is then assumed that HLA typing should replace any alternative system of classification. The use of the word ‘classical’ obviously has echoes of Stern’s 'Classic CF' (see previous chapter), and seems to serve the same purpose, of indicating an old fashioned, outdated form of classification. Over the space of these two articles, insulin dependence has been inextricably linked with age of onset as a means of classification. With the attack on age of onset, it is assumed that all other clinical classifications (i.e. insulin dependence) are also invalid.

As Bowker and Star make clear, the negotiated, social nature of classification systems means that rarely does any one side in a debate see their preferred classification triumph outright (Bowker and Star 1999:55). Thus despite Cudworth’s attempts to undermine it insulin dependence was still formalised as a category of diabetes classification in the 1979 NDDG system (see below). But his strategy was finally successful, twenty years later, with the final removal of age of onset in the 1997 ADA classification system.

Genetic Heterogeneity

A second strategy that is vital for Cudworth’s reclassification of diabetes is his reliance upon genetic heterogeneity. It is the founding stone of his reasoning for using HLA
typing: "Diabetes is a clinically heterogeneous disorder with different modes of presentation" (Cudworth 1976:207). As before, Cudworth uses a step by step process to introduce his preferred means of classification. He starts his 1976 article with a section entitled "Clinical Heterogeneity" and with the admission that "there are obvious dangers in taking differences in phenotype as a basis for investigating genetic heterogeneity" (Cudworth 1976:207). But having accepted this, he then goes on to assume:

"that there are two aetiologically distinct forms of the disease determined by differences in age of onset, relative abruptness of onset, tendency to ketoacidosis, and dependence on insulin" (Cudworth 1976:207).

This leads him onto his table 1 with its classification of diabetes both clinically and aetiologically. Thus this table, which might at first be thought to offer support for the idea of clinical classifications is rooted in Cudworth's need to redefine diabetes in genetic terms. The link between aetiology and genetics is explicit, best exemplified by a sentence which is almost identical in the two articles:

1976: "Any investigation into the aetiology of diabetes should at first take into consideration the role of genetic determination" (p.207);

1978: "Any investigation into the aetiology or pathogenesis of diabetes...should first of all consider the important role of genetic determination" (p.282).

This does not just place the two articles in the same milieu, but links them in an intimate way. While it is a mistake to see them as two parts of the same conscious plan, it is easy to see that the careful, step-by-step approach adopted by Cudworth over the two articles, might also be more effective if mirrored in the two stage release of his ideas driving diabetes towards an aetiological classification system.

This seems to be contradicted though, in the 1976 article, where genetic heterogeneity is used to support the type 1 classification system:

"This provides strong evidence for the existence of genetic heterogeneity in diabetes and lends support to the concept of type 1 diabetes (independent of age of onset) in which the major susceptibility is HLA linked" (Cudworth 1976:209). But it is important to see that this is in fact the first appearance of Type I diabetes, albeit under the old name. This provides a clear link between the two articles, with the 1978 review expanding upon this suggestion.
Apart from this, Cudworth never makes an explicit attempt in his 1976 article to reclassify diabetes in terms of HLA typing, seeming to be content with the type 1 clinical/aetiological amalgam. It is only in the 1978 article, when he has built up to it, that he can explicitly present Type I diabetes as the logical solution to the confusion resulting from genetic heterogeneity:

"the studies of the HLA system in diabetes have provided scientific evidence for the existence of genetic heterogeneity which formed the basis of the new classification of the disease, the HLA linked genetic susceptibility operating irrespective of age of onset (Type I diabetes) [49, 56]" (Cudworth 1978:285).

The two cited articles, numbers 49 and 56, are both written by Cudworth: the first is a 1976 article with J.C. Woodrow for *Diabetologia* called "Genetic susceptibility in Type 1 (insulin dependent) diabetes"; the second is Cudworth's 1976 article "The aetiology of diabetes mellitus". By using citations, even of his own work, he provides his classification system with an apparent network, a context of research within which it has a secure position.

**Summary**

Over these two review articles, Andrew Cudworth constructs a geneticized classification system for diabetes using a number of different strategies:

- Linking clinical classifications together;
- Undermining *all* clinical classifications through attacking one ('Together they fall');
- Genetic heterogeneity as a research strategy;
- Elision from '1' to 'T';
- Moving from tentative to confident claims
- Undermining non-genetic explanations (e.g. viruses).

These strategies fixed the divisions between the two kinds of diabetes on genetic grounds, and provided the impetus for the splitting of diabetes into sub-diseases: the narrative of division. It is important to note that these articles are rooted in the research literature of the time; they offer up-to-date and comprehensive assessments of the then current state of play regarding genetics and diabetes. The classification systems
constructed are interpretations of this empirical evidence\textsuperscript{80}, a point which I wish to emphasise by presenting Irvine's alternative classification system, which uses much of the same material.

4. IRVINE

Autoimmunity
Irvine's 1977 article, "Classification of Idiopathic Diabetes", is interesting because it explicitly redefines diabetes in terms of autoimmunity and the process of disease. It shows that a genetic reclassification was not inevitable on the basis of the scientific data available at the time, that a non-genetic (though aetiological and splitting) system was a viable alternative.

Like Cudworth, Irvine starts with an expression of dissatisfaction with classifications based on age of onset or treatment; unlike Cudworth, he actually gives reasons against both 'juvenile/adult' and 'insulin dependent/independent' classifications (rather than just the former):

"It is difficult to think of any condition in which the age at onset of clinical features of a disease or the type of treatment required are satisfactory bases for classification" (Irvine 1977:638).

Irvine's classification rests on the relationship between 'juvenile' diabetes and autoimmune diseases such as Addison's disease, thyroid disorders and anaemia:

"the only common linking factor in all the other diseases strongly associated with idiopathic Addison's diseases is organ-specific autoimmunity....By inference, insulin-dependent diabetes is likely to be associated with pancreatic-islet-cell autoimmunity" (Irvine 1977:638).

The pancreatic-islet-cell antibodies (I.C.A.) can then be used to differentiate between people suffering from juvenile/insulin dependent diabetes and others:

"I.C.A is found in similar proportions of insulin-dependent diabetics, whatever the age on onset of the clinical features" (Irvine 1977:639).

This does lead to slightly odd situations such as "These cell mediated reactions were confined to insulin-dependent diabetics including those who had either never received

\textsuperscript{80} Although the empirical studies are themselves also socially constructed.
insulin at the time of study or very briefly" (Irvine 1977:638). This mention of insulin-dependent diabetics who have never received insulin highlights the apparent contradictions of the clinical approaches to classification.

Irvine reaches his classification system, dividing diabetes into Types I and II, on the grounds of presence or absence of I.C.A. The issue of HLA antigens is also addressed by Irvine, but only as a secondary factor, to support his classification based on I.C.A. This is clearly visible in his table III, which although located in the section of his article entitled "HLA studies", classifies diabetes without recourse to these studies at all:

**TABLE III - CLASSIFICATION OF IDIOPATHIC DIABETES MELLITUS**

<table>
<thead>
<tr>
<th>Type I</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main features:</strong></td>
<td></td>
</tr>
<tr>
<td>Insulin-dependent juvenile-onset diabetes</td>
<td>\</td>
</tr>
<tr>
<td>Insulin-dependent maturity-onset diabetes</td>
<td></td>
</tr>
<tr>
<td>I.C.A.-positive diabetics initially controlled by O.H.A()(^{82}) but requiring insulin in subsequent years</td>
<td></td>
</tr>
<tr>
<td>(a) Severe autoimmune/non-viral</td>
<td>(rare)</td>
</tr>
<tr>
<td>(b) Moderate viral/moderate autoimmune</td>
<td>(common)</td>
</tr>
<tr>
<td>(c) Severe viral/non-autoimmune</td>
<td>(rare)</td>
</tr>
</tbody>
</table>

from Irvine 1977:639

This classification system clearly cuts across previous concepts. It defines type I diabetes in terms of the presence of I.C.A. One could see it as explicitly anti-geneticizing, in that it does not clearly distinguish between MODY, (here called "insulin-independent juvenile onset diabetes") and other types of 'type II' on genetic grounds.

---

\(^{81}\) Irvine's paper can therefore be seen as contributing to the *molecularisation* of diabetes

\(^{82}\) Oral Hypoglycaemic Agents.
This prioritisation of autoimmunity over genetics is even clearer when one considers Irvine's "Table IV Characteristics of different types of idiopathic diabetes mellitus" (Irvine 1977:640) (see below). The structure of this table is such that it reinforces and strengthens Irvine's classification system.

- the table emphasises the autoimmune process by placing positive testing for organ specific autoimmunity on the left hand side of the table;
- as one moves from left to right, the table presents more aspects of the autoimmune process, until the sixth column, where the evidence from HLA studies is presented. It is only the tenth and twelfth columns which present information on age of onset and treatment for the types of diabetes;
- the structure also emphasises the difference between the types/subgroups of diabetes. The first sub-group (Ia) receives four ++, two +++ and one -. Ib has three ++, two ++ and two +-. Ic has one++, one + (which is not significant since it is the same as the control population's) and five -. Similarly the "I.C.A. in serum" moves from "Persistent", through "Transient" to "Absent". The effect of these differences is to reinforce the idea of diabetes as two separate types, one of which is subdivided into three sub-groups. The structure acts to reify the heterogeneous nature of diabetes;
- The mention of 'genetic susceptibility is not an example of geneticization as used in this thesis. Irvine suggests that there is genetic susceptibility to autoimmunity and viral infection but there is not an explicit link to a stretch of DNA. He suggests that there might be a link to HLA B8, but is unable to tie it into both susceptibility to viral infection and autoimmune problems (p.640). This might be called a form of geneticization: secondary geneticization?

---

83 There appears to be some confusion over I/I in the table since it uses Type 1 and type II; in the rest of his paper he discusses types in terms of roman numerals. I therefore believe the inclusion of I in the table is a mistake, but have left the error to stand, as presented in the original table.
**TABLE IV - CHARACTERISTICS OF DIFFERENT TYPES OF IDIOPATHIC DIABETES MELLITUS**

<table>
<thead>
<tr>
<th>Type</th>
<th>Organ-specific-autoimmunity including I.C.A.</th>
<th>Viral infection of islets</th>
<th>I.C.A. in serum</th>
<th>Cell-mediated immunity to islets</th>
<th>H.L.A.-B8</th>
<th>Associated clinical organ-specific A.I.D.</th>
<th>Prevalence of adrenal and ovarian antibodies</th>
<th>Prevalence of thyrogastric antibodies</th>
<th>Age at onset of clinical diabetes</th>
<th>Sex ratio F/M</th>
<th>Type of treatment required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a</td>
<td>++</td>
<td>-</td>
<td>Persistent</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>Any age</td>
<td>F&gt;M</td>
<td>Insulin usually from start, but sometimes after some years of control with diet and O.H.A.</td>
</tr>
<tr>
<td>b</td>
<td>+</td>
<td>+</td>
<td>Transient</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>++</td>
<td>++</td>
<td>Any age but mainly &lt;35 years</td>
<td>M=F</td>
<td></td>
</tr>
<tr>
<td>c</td>
<td>-</td>
<td>++</td>
<td>Absent</td>
<td>-</td>
<td>+(^1)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Any age but mainly &gt;35 years</td>
<td>M=F</td>
<td>Insulin (sic)</td>
</tr>
<tr>
<td>Type II</td>
<td>-</td>
<td>-</td>
<td>Absent</td>
<td>-</td>
<td>+(^1)</td>
<td>-</td>
<td>-</td>
<td>+(^1)</td>
<td>Any age but mainly &gt;35 years</td>
<td>F&gt;M</td>
<td>Diet with or without O.H.A.</td>
</tr>
</tbody>
</table>

*Genetic susceptibility to type-II diabetes is different from that to type I and is not related to autoimmunity or to viral infection.

\(^1\)Same as in control population.

A.I.D=autoimmune disease.
Division of diabetes into different types does not indicate geneticization, since such division can be done on clinical grounds. By the same light, Irvine's work could be seen as a narrative of division, but not one based on geneticization since his emphasis is on the autoimmune process. What makes Cudworth's narrative of division part of geneticization is the fact that it is based on genetic difference. Given the variation in symptoms between different diabetics, I think it is quite likely that diabetes would undergo some degree of division, whatever the factor used to draw up categories. What is important to note is that, while division might be inevitable, geneticization was not. Irvine's article clearly shows that at the end of the 1970s, it was possible to draw up a classification system for diabetes which was empirically rooted, convincing but not based on genetic difference.

It is in the final section of his article, "Proposed classification of idiopathic diabetes" (Irvine 1977:641) that Irvine fully outlines what Table IV is leading towards by clarifying the differences between the different subgroups within his type 1 (or I as he means to call it). In keeping with the rest of this article, the distinctions are drawn on the grounds of autoimmunity:

"Subgroups a, b, and c within type-I diabetes are based on the persistence, transience or absence of autoimmunity to islet cells....Autoimmunity is given pride of place in this classification because I.C.A and cell-mediated immunity to islet cells have been clearly described in human diabetes, because there is tangible evidence of the occurrence of other forms of autoimmunity in these patients, and because there is an HLA marker, at least indirectly, for islet-cell autoimmunity" (ibid.).

<table>
<thead>
<tr>
<th>Autoimmunity</th>
<th>Viral Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>rare</td>
<td>common</td>
</tr>
<tr>
<td>c</td>
<td>rare</td>
</tr>
</tbody>
</table>

Classifications of type-I diabetes mellitus

from Irvine 1977:641
From this one can see that the majority of diabetes cases will result from a combination of genetic susceptibility to both autoimmunity and viral infection, as well as the influence of viruses themselves. It is important to note that Irvine is not opposed to genetic studies of diabetes, it is just that he does not think that we know enough about it to classify on this basis. Indeed one aim of his classification system is to: "considerably facilitate the study of the genetics of this type of diabetes" (Irvine 1977:641). The very purpose of this classification system is to assist in identifying of the genetic nature of diabetes:

"The recognition of the different subgroups of patients in type I and of the two genetic susceptibilities that may operate individually or in conjunction with each other within type I, may help elucidate the genetic aspects of this type of diabetes" (ibid.).

Bearing in mind the evidence Irvine marshals in its defence, one has to question why it is that his classification system, which attempts to describe the complex, heterogeneous nature of diabetes in detail, failed to catch on. Perhaps clues lie towards the end of his article where he comments on other classification systems for diabetes:

"Cudworth called juvenile-onset or insulin-dependent diabetes 'type I' and maturity-onset diabetes 'type II'. Bottazzo and Doniach used this numbering system to refer to type Ia diabetes as being possibly due to virus infection, and type Ib as possibly being due to autoimmunity. In my view, this is an oversimplification" (Irvine 1977:641).

Yet in the case of classification systems, is 'over simplification' such a bad thing? As I will show in the rest of this chapter, it was Cudworth's system that was accepted in the formal reclassification that took place in the early 1980s. Irvine's complex system, based on the interaction of antibodies, genetics and viruses, while accurately describing the different forms that diabetes can take, lacks the simple elegance of Cudworth's type I/II distinction, based on the presence, or absence of particular genetic markers. Even though Irvine sat on the committee that drew up the new formalised classification, his was not the preferred system. Why did Cudworth's system succeed, even though, as we will see, efforts were made in the literature to suppress classifications made in terms of type I/II? I suspect, in part, because of its simplicity; as Cudworth notes in his 1976 article: "A simple classification has the advantage of flexibility" (Cudworth 1978:207). And it was the flexibility of Cudworth's system which allowed it to be combined with clinical categories in later classifications, and which made it attractive to use.
5. EXTENDING THE NARRATIVE

Both Irvine and Cudworth produced their work at a time when debates surrounding diabetes classification were taking place within the medical community. One result of these debates were the National Diabetes Data Group (NDDG) of the American Diabetic Association classification of 1979 and the WHO classifications of 1980 and 1985. It is at this point that the geneticization of diabetes became formalised through the official classification system. My claim is that by using Cudworth's Type I/II distinction, the NDDG institutionalised the geneticization of diabetes, and reinforced the narrative of division constructed in the review articles examined. In many ways, this form of geneticization was 'stealthy', and not immediately obvious, but the end result of this are the claims made twenty years later by those such as John Bell and the NHS Central Research and Development Committee: that diabetes is the paradigm of the complex genetic disorder.

When the NDDG discusses what it calls "Type I, insulin-dependent diabetes mellitus", they state that it "is usually characterized clinically by abrupt onset of symptoms, insulinopenia and dependence on injected insulin to sustain life, and proneness to ketosis" (NDDG 1979:1041). They then claim that "Genetic determinants are thought to be important in most patients, as expressed by the associated increased or decreased frequency of certain histocompatibility antigens (HLA) on chromosome 6" (ibid.). Using my working definition of geneticization - geneticization occurs when a condition is explicitly linked to a specific stretch of DNA - this is obviously a key statement, reinforced by the table then presented, showing the "Classification of Diabetes and Glucose Intolerance".

One aspect of this table that is clear, is the large number of possible terms for diabetes (see 'Former terminology'). One can understand the medical profession's exasperation with the classification system, and the feeling that there was a need for this revision.
<table>
<thead>
<tr>
<th>Class</th>
<th>Former terminology</th>
<th>Associated factors</th>
<th>Clinical characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes Mellitus (DM)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin-dependent type (IDDM), Type I</td>
<td>Juvenile diabetes, juvenile-onset diabetes, juvenile-onset-type diabetes, JOD, ketosis-prone diabetes, brittle diabetes</td>
<td>Evidence regarding etiology suggests genetic and environmental or acquired factors, association with certain HLA types, and abnormal immune responses, including auto-immune reactions</td>
<td>Persons in this subclass are dependent on injected insulin to prevent ketosis and to preserve life, although there may be pre-ketoic, non-insulin-dependent phases in the natural history of the disease. In the preponderance of cases, onset is in youth, but IDDM may occur at any age.....</td>
</tr>
<tr>
<td>Noninsulin-dependent types (NIDDM), Type II</td>
<td>Adult-onset diabetes, maturity-onset diabetes, maturity-onset-type diabetes, MOD, ketosis-resistant diabetes, stable diabetes</td>
<td>There are probably multiple etiologies for this class, the common outcome being derangement of carbohydrate metabolism. Evidence on familial aggregation of diabetes implies genetic factors, and this class includes diabetes presenting in children and adults in which autosomal dominant inheritance has been clearly established (formerly termed the MODY type, maturity onset diabetes in the young)...Obesity is suspected as an etiologic factor and is recommended as a criterion for dividing NIDDM into two subclasses, according to the presence or absence of obesity</td>
<td>Persons in this subclass are not insulin-dependent or ketosis-prone, although they may use insulin for correction of symptomatic or persistent hyperglycemia and they can develop ketosis under special circumstances, such as episodes of infection or stress. Serum insulin levels may be normal, elevated, or depressed. In the preponderance of cases, onset is after age 40, but NIDDM is known to occur at all ages. About 60-90% of NIDDM subjects are obese and constitute a subtype of NIDDM: in these patients, glucose tolerance is often improved by weight loss.....</td>
</tr>
</tbody>
</table>

excerpted from NDDG 1979:1042
The desire to bring "order to a chaotic situation in which nomenclature varied and diagnostic criteria showed enormous variations" must have been strong (Alberti and Zimmet 1998b:540). Except of course, although the NDDG classification system cleared away some problems (confusion over age of onset for example[^4]), other difficulties remain, or are even reinforced by it.

The most obvious problem with this classification system is the apparently straightforward combination of aetiological and clinical features; 'IDDM' and 'Type I' are presented as if they are interchangeable. The contemporary state of knowledge about diabetes clearly indicated that this was not the case[^5]. Dissatisfaction with this system of classification was strong. Professor Harry Keen, a member of the NDDG committee, claimed later that:

"Many people use the terms Type I and Type II diabetes interchangeably with IDDM and NIDDM respectively but that is unsatisfactory, both clinically and epidemiologically. Type I, as used, is not so much of a description of a clinical state as of a presumed pathogenic process..." (Keen 1985:38).

One of the most astute analyses of the issues surrounding the problems with this classification system was presented by Peter Bennett who, like Keen, had sat on the NDDG's 'International workgroup to develop a nomenclature and classification system for diabetes mellitus'. Bennett notes that over time:

"there has been a tendency to adopt the terms Type I and Type II diabetes to indicate different etiologies, although the original usage of these terms was a clinical classification to differentiate between insulin dependent and non-insulin dependent disease" (Bennett 1985:17).

He suggests that the popularisation of the Type I/II distinction is mainly due to Andrew Cudworth (p.19) who: "then went on to justify the classification of Type I as a separate

[^4]: Almost all Keen admits about this new system is that changing to IDDM/NIDDM does "little more thereby than giving new and rather more satisfactory names to what had been 'juvenile onset type' and 'maturity onset" (Keen 1986:11).

[^5]: "Although there is a broad parallelism between the 'Type I process' and the 'insulin-dependent state', the two terms, as commonly used, cannot be considered interchangeable synonyms" (Keen 1986:11).
entity by pointing out the then recently established HLA associations" (Bennett 1985:21). Like Harry Keen, Bennett suggests that as a result:

"The NDDG and WHO classification, unfortunately perhaps, implied an equivalence of these terms, yet the authors who initially popularized their usage [ref. to both of the Cudworth (1976 and 1978) and Irvine (1977)] had justified and made the distinction on etiological grounds, rather than on the basis of clinical descriptors as used by the NDDG-WHO classification. On the other hand, the original usage of Type I and Type 2 had been simply a convenient way of labelling the clinical entities of insulin dependent and non-insulin dependent diabetes" (Bennett 1985:25).

What is clear about the discussion surrounding the NDDG and WHO classification system is that Cudworth is the source of both the terms Type I and II, and their explicit link to the HLA complex and genetics:

"Type I was promoted by the late Andrew Cudworth to describe a pathogenesis rather than a clinical state. This arose from the findings that a large portion of youthful onset, insulin-dependent diabetic patients of European origin has histocompatibility antigens coded for at the B locus (B8 and B15) and later demonstrated to be in linkage disequilibrium with the primary correlates DR3 and DR4 at the DR locus...[There was also evidence]...supporting the notion that HLA was not only a genetic marker but also a genetic mechanism for this form of diabetes" (Keen 1986:11).

The geneticization of diabetes was not 'all conquering'. The NDDG maintains the use of insulin dependence as valid grounds for classification. This supports my claim that in neither of his articles does Cudworth actually present evidence against the IDDM/NIDDM categories; instead he relies on their association with age-related categories to undermine them. In part, a wholly aetiological classification system was just not possible in the late 1970s. Too little was known about the causes of even type I diabetes, let alone the aetiologically mysterious type II. This discussion also demonstrates the effects of review articles as a popularising genre within the scientific literature. Cudworth and Irvine's review articles are cited as the cause of the adoption of the type I/II distinction.

---

86 Bennett claims that Hugh Jones coined "Type 1 and 2, as a clinical classification" but that it lay dormant until Cudworth revived it in 1976 (Bennett 1985:19). Bennett mentions that both arabic and roman numerals are involved, but fails to distinguish between them.
I have termed the narrative constructed in the review articles I examine, the 'narrative of division' because of the way in which diabetes splits into a number of subdivisions under the impact of geneticization. Yet, one could object, diabetes was already divided into two separate diseases on clinical grounds, and had been for hundreds of years. Why should I claim that geneticization has fostered this? My point is that geneticization has solidified the division between the two kinds of diabetes, so that they could never again be seen as different varieties of the same condition as they were at the beginning of the 20th Century. By talking about a narrative of division, I am also implying that this process will continue in the future. Genuth predicted this progressive splitting on genetic grounds in 1982:

"Although further subdivision of these two main classes is currently of little clinical usefulness, practitioners should be aware of these evolving concepts as they may soon aid in providing better prognostic information and more assured genetic counseling" (Genuth 1982:1195).


Following the 1979 NDDG recommendations, and the WHO's similar classification (in 1980), there was period during which IDDM and Type I were used fairly interchangeably, as the official classification system implied (Keen 1986:11). The result of this, and the problem with the system already noted in Bennett and Keen's work, is that in the mid 1980s, when the NDDG and WHO reviewed their classification of diabetes:

"Both have recommended that, if the terms Type I and Type II continue to be used, they should shed any pathogenetic implications and be regarded as totally synonymous with IDDM and NIDDM respectively. However, the identification of Type I with the autoimmune pathogenesis has now become so deeply embedded in consciousness that it is unlikely that it will ever divest itself of that implication" (Keen 1986:12; see also Alberti and Zimmet 1998b:542).

But as Keen grudgingly predicted, "despite the exhortations of NDDG and WHO and the force of semantic logic" the use of Type I to imply aetiology did not decline (Keen

---

87 The reference to WHO here is clearly to the 1985 reclassification. There is no reference in the literature to a NDDG reclassification around this time. The most recent NDDG classification, published in 1997, makes it clear that it is a direct 'descendant' of the 1979 paper. I assume that any debate within the NDDG was informal and did not result in a formal position paper.
Cudworth's system, for whatever reason, resisted attempts to replace it with alternative classifications. Thus the NDDG's hybrid classification system, combining clinical and aetiological information, continued until 1997. This is when the next ADA report, "a significant advance for people with diabetes as well as those who care for them" was published (Eastman and Vinicor 1997:1057). One important point to note is that Cudworth's subtle, but vital distinction between Type 1 and Type I (Arabic and roman) was lost in the swirl of classificatory debate. In the intervening years, Type 1 and I were held to be interchangeable. Of course, this does not detract from the geneticization of diabetes. Having constructed a geneticized classification of diabetes, the specific strategy by which this was done (I overtaking 1), is less important and becomes a 'black-box'.

The 1997 ADA report does mention the difference between 1 and I, recommending the "adoption of arabic numerals in part because the roman numeral II can easily be confused with by the public as the number 11" (American Diabetes Association 1997:1184). Thus "We now have Type 1 and Type 2 diabetes again" (Alberti and Zimmet 1998a:535). But like the confusion between 1 and I, this is a cosmetic change. In the 1997 classification 'Type 1' means much the same as Cudworth's 1978 'Type I'. The ADA defines this disease as:

"Immune-mediated diabetes...[which]...results from a cellular-mediated autoimmune destruction of the β-cells of the pancreas...the disease has strong HLA associations, with linkage to the DQA and B genes, and it is influenced by the DRB genes" (ADA 1997:1186).

There are obvious similarities between this latest classification and the system constructed in Cudworth's articles.

In their 1997 report to the ADA, the Expert Committee resisted the temptation to refine the classification system into some form of clinical/aetiological half way house. Such a system would contain two elements: one indicating the clinical symptom, the other the suspected aetiology. Such hybrids could lead to a situation where: "the various phases [of the disease] could be described as Type 1 IGT, Type 1 NIDDM, Type 1 IDDM, etc."

---

88 Professor Keen suggests that the historical roots to his opposition to the use of 'type I/II' lie in the debate between Platt and Pickering concerning blood pressure (Swales 1985).
These combined classification systems were not just the product of the disputes of the 1980s, but are present in contemporary debates. For example, in 1997, Kuzuya and Matsuda suggested that: "the etiology and the degree of deficiency of insulin and/or insulin action should be considered separately, with both incorporated in the classification of diabetes" (Kuzuya and Matsuda 1997:219). It is interesting to note that in their outline of the new WHO classification system, Alberti and Zimmet (who both sat on the WHO and ADA committees) seem more positive about a mixed clinical/aetiological classification, and claim that the proposed WHO classification system would follow Kuzuya and Matsuda's suggestions (Alberti and Zimmet 1998b:542-543).

The ADA report leapfrogs such mixed-classifications to firmly assume aetiology as the basis of diabetes classification:

"It is now considered to be particularly important to move away from a system that appears to base the classification of the diseases, in large part, on the type of pharmacological treatment used in its management toward a system based on disease etiology where possible" (ADA 1997:1183).

It specifically eliminates the use of IDDM/NIDDM as classificatory categories, stating that: "These terms have been confusing and have frequently resulted in classifying the patient based on treatment rather than etiology" (ADA 1997:1184). The result of this is the following classification system:

<table>
<thead>
<tr>
<th>Table 1 - Etiologic classification of diabetes mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Type 1 diabetes (β-cell destruction, usually leading to absolute insulin deficiency)</td>
</tr>
<tr>
<td>A. Immune mediated</td>
</tr>
<tr>
<td>B. Idiopathic</td>
</tr>
<tr>
<td>II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)</td>
</tr>
<tr>
<td>III. Other specific types</td>
</tr>
<tr>
<td>A. Genetic defects of β-cell function</td>
</tr>
<tr>
<td>1. Chromosome 12, NHF-1α (formerly MODY3)</td>
</tr>
<tr>
<td>2. Chromosome 7, glucokinase (formerly MODY2)</td>
</tr>
<tr>
<td>3. Chromosome 20, HNF-4α (formerly MODY1)</td>
</tr>
<tr>
<td>4. Mitochondrial DNA</td>
</tr>
<tr>
<td>5. Others</td>
</tr>
<tr>
<td>[seven more subdivisions (B-H), each containing between 3 and 11 subclasses of diabetes]</td>
</tr>
<tr>
<td>IV. Gestational diabetes mellitus (GDM)</td>
</tr>
</tbody>
</table>

from ADA 1997:1185
This new classification system demonstrates the effects of the 'narrative of division': there has been an explosion of different subtypes of diabetes\textsuperscript{89}; classification is made on aetiological (often genetic) grounds; and further division is expected\textsuperscript{90}. The differences between Type 1 and 2 are drawn in terms of aetiology and underlying genetics. I suspect that Andrew Cudworth would be happy with this new classification system: clinical categories have been removed (though it took 20 years to eradicate insulin-use from the classifications), and HLA typing is used to draw the distinction between different kinds of diabetes.

Would diabetes have divided in this way if 'geneticization by stealth' had not taken place in the late 1970s, and if Type I and II had not been constructed on genetic grounds? Irvine's article shows that similar divisions could have been drawn on the grounds of autoimmunity. But this route was not taken. The reasons for the (eventual) success of Cudworth's geneticized system over Irvine's ICA based classification are beyond the kind of analysis I am doing in this thesis, which simply aims to chart the process of geneticization in different diseases. As suggested earlier, Cudworth's system had the advantage of simplicity; neither had the edge in terms of scientific knowledge since the role of both I.C.A.s and HLA genes was unclear at the that time. Nor it is clear that it could it be attributed to personal preference; Irvine was a member of the NDDG working group, as were Keen and Bennett (neither of whom were fond of numerical classification systems); Cudworth was not.

7. IS DIABETES A GENETIC DISEASE?

As I suggested at the beginning of this chapter, diabetes has become, in certain circles, the paradigmatic case of a complex genetic disease. But this is not to say that such a

\textsuperscript{89} In 1979 there were 9 types of diabetes (types I and II of various kinds), 7 kinds of Impaired Glucose Intolerance (IGT), and Gestational diabetes: a total of 17.

In 1997, the classification includes 57 different types. IGT is now a clinical 'stage' of the disease development rather than a category itself.

\textsuperscript{90} "The task is not complete, however, because the precise etiology process in the majority of patients with type 2 diabetes under the new system remains unknown" (Eastman and Vinicor 1997:1057).
position is unchallenged and unproblematic. Opposition to the genetic view of diabetes in the literature is clear to see. For example, the debate over two possible causes for type 2 diabetes the 'thrifty genotype' and the 'thrifty phenotype' gave rise to the following declaration:

"To conclude that NIDDM depends upon a combination of genetic and environmental factors is as safe as it is unhelpful. It is a truism which relates to every single aspect of the outcome of human life...it is urgently necessary to determine what are the major factors causing the condition rather than minor factors which play a more subtle role in increasing susceptibility. A good example of the distinction which needs to be made is provided by insulin-dependent diabetes mellitus (IDDM). It is undoubtedly true that genetic factors play a role in susceptibility to this condition...Nevertheless it is also clear that the real cause(s) of IDDM are environmental and remain to be discovered" (Hales, Desai and Ozanne 1997:193).

Responding to a review of the molecular genetics of type 2 diabetes, during which genetic knowledge of the disease was described as 'the holy grail', one author notes that:

"There is an epidemic of non-insulin dependent diabetes (NIDDM) in many populations in the developing and newly industrialised world...Rare mutations...are largely irrelevant to the causes of diabetes in this and similar populations. One could draw an analogy with work on genetic markers of susceptibility to cholera in the midst of an outbreak" (Perry 1995:1489).

Another commentator terms such tension between genes and environment, a 'phony war' and claims that:

"Ultimately the role of genes and environment in IDDM will be judged by their clinical usefulness...The ultimate aim of the work on the aetiology of IDDM is not to establish a superiority of genes or environment but to develop their dual role in disease prevention" (Hattersley 1997:148).

This refuge in clinical application has obvious echoes of the debates surrounding cystic fibrosis although it is less explicit that 'researchers' are forcing geneticized classifications on 'clinicians'. The ADA report was written with the explicit intention of improving clinical care, and making diagnosis easier for both doctors and patients. Yet some in the medical community suggest that the nature of modern diabetes research will lead to an increase in the separation between researcher and clinician:

"It is clear to me that we are unable to function as basic scientists and caring physicians at the same time, as ideal as this may have been in the past...[instead]...we must constantly try to incorporate scientific, critical thinking into clinical medicine" (Berger 1996:754-755).

If Berger is correct, then we might expect to see more research lead classifications developing in diabetes. When interviewed, both Keen and Alberti suggested to me that
there was a tension in diabetes classification between the needs of researchers, such as John Bell at the beginning of this chapter, and those of clinicians. This may have slowed down the possible effects of geneticization on diabetes classification, but it certainly did not stop it.

What is important to note is that the debate between nature and nurture is to a large extent irrelevant in considering the effect of geneticization. Lippman is clear that geneticization does not involve explaining all causality in terms of genetics. Simply linking a disease to a gene is enough. My own definition also assumes that a wide degree of causality is possible in a geneticized condition. What seems to have escaped the notice of those who object to studies into the genetic causes of diabetes is that the entire structure upon which the debate takes place, the classification of diabetes as different diseases, is resolutely based on genetic differences. This shows how geneticization by stealth can impact upon disease classification, even entering into the position of those who are opposed to the use of genetic explanations. It also highlights the differences between traditional debates about nature/nurture and genetic determinism, and those that surround geneticization.

One possible objection to my claim that diabetes is now geneticized due to the discursive strategies used to construct the narrative of division, is simply that scientists know more about the genetics of diabetes now. Of course it is now geneticized, but that is because we have a better idea of which genes provide susceptibility to diabetes (at least in the case of type 1) rather than because the of the linguistic strategies used to construct the disease narrative. This objection falls down on the fact that we do not know a great deal more about the genetics of diabetes than Andrew Cudworth did. The ADA in 1997 suggests that: "the disease has strong HLA associations, with linkage to the DQA and B genes, and it is influenced by the DRB genes" (ADA 1997:1186). In his 1978 article Cudworth mentioned association with 2 HLA A genes, 4 B genes (especially B8 and 15) and an number of others, including 4 D genes. All that has happened is that the focus of modern genetic knowledge is narrower than in Cudworth's time (She 1996). In part, this

---

91 See my next chapter, on Schizophrenia, for another example of how critics of genetic explanations unconsciously 'buy into' geneticized positions from which to make their claims.
is because the technology used now is more specific. Instead of serological blood tests to
detect the HLA proteins, DNA sequencing allows direct 'contact' with the genes
themselves (Friday, Trucco and Pietropaolo 1999:9).

The current research focus upon the HLA-D region was suggested by Cudworth in
1978: "the proposed 'diabetogenic' gene(s) may be closer to the D locus than the HLA A,
B, C and Bf loci" (Cudworth 1978:284). Cudworth claims that the 'penetrance' of the
HLA-linked genetic component of Type I diabetes is "25-50%" (Cudworth 1978:288). A
recent review of the genetics of diabetes suggests that "60% of the genetic susceptibility
to type 1 diabetes is conferred by HLA" (Lernmark 1999:1332). One attempt to carry
out a genome-wide screening for Type I susceptibility genes concluded that:

"Other than the well-established linkage with the HLA region at chromosome
6p21.3, there was only one region, located on chromosome 1q and not previously
reported, where the log likelihood ratio (lod) was greater than 3 [and thus showing
linkage]" (Concannon et al. 1998:292).
The conclusions of this article are disputed by another article in the same volume of
Nature Genetics, but as the commentary on these articles notes, about the only thing
these results did agree on is the HLA link (Lernmark and Ott 1998). A meta-level review
of previous studies claims that:

"one common finding was the exclusion of intervals that have an effect nearly as
strong as IDDM1 [the HLA region]. Highly significant linkage for IDDM1 was
revealed in all reports...and no other interval showed such strong evidence for
linkage" (She and Marron 1998:682-683).

Future research will probably reveal more about the genetic basis behind type 1 diabetes,
but at the moment, we know little more than we did in the late 1970s. Certainly any
increased knowledge has not impinged on the classification system, as it stands.
Therefore claims that the geneticization of diabetes over the past 20 years is the result of
increased genetic knowledge are unfounded. Whatever the reason for the geneticization
of diabetes, it must lie outside the realm of our knowledge of genetics.

Just as in the last chapter I used the current debates surrounding pancreatitis and CF to
suggest that the narrative of expansion will continue to expand, so I now wish to
examine the future of the narrative of division in diabetes. I have argued that the current
ADA classification system is a direct result of geneticization, and the steadily increasing
division of diabetes into separate conditions on the grounds of genetics is a consequence of the initial reclassification suggested by Andrew Cudworth. I now wish to suggest that one might predict the possible direction of the narrative of division by analysing one diabetes sub-group, MODY.

**MODY**

In this section, I will examine the classification of the subset of diabetes known as Mature Onset Diabetes of the Young or MODY. This condition:

"is characterized by an age of onset of less than 25 years, the correction of fasting hyperglycaemia without insulin for at least 2 years following diagnosis, nonketotic disease [i.e. no breakdown of proteins and production of ketones], and an autosomal dominant mode of inheritance" (Winter, Nakamura and House 1999:765).

This collection of distinct diseases is interesting for a number of reasons. First, MODY is another example of the way in which particular nomenclature resists removal. Just as the aetiological concept of Type I and II persisted throughout the 1980s (despite the best efforts of the NDDG and WHO to replace them with purely clinical definitions) so the term MODY has been targeted for replacement. Originally coined by Fajans in 1964, by 1979 the term MODY had become:

"diabetes presenting in children and adults in which autosomal dominant inheritance has been clearly established (formerly termed the MODY type, maturity onset diabetes in the young)" (NDDG 1979:1042).

The 1997 ADA classification has a category 'Genetic defects of the β-cell' which "were formerly referred to as maturity onset diabetes of the young (MODY)" (ADA 1997:1187). Despite this, two recent review articles have been entitled: "Molecular Genetics of Maturity-onset Diabetes of the Young" (Froguel and Velho 1999) and "Monogenic Diabetes Mellitus in Youth: the MODY Syndromes" (Winter, Nakamura and House 1999).

The other reason for my interest in MODY is that it is both highly genetic (it is a Mendelian monogenic condition) and classed as 'like' type 2 diabetes (clearly, given its name). Thus: "These monogenic forms of MODY have been used as model systems to
investigate the inheritance and pathophysiology of type 2 diabetes" (Winter, Nakamura and House 1999:782). MODY is "an attractive model for studying the genetics of Type 2 diabetes" (Froguel and Velho 1999:142). MODY may suggest the direction in which the narrative of division and the geneticization of diabetes might go. MODY is an example of the extreme geneticization of diabetes, but it is not significant for that reason. Clearly the MODYs will be extremely geneticized, they are Mendelian dominant disorders where the loci of many of the genes responsible have been identified. The 'group' of the MODYs can be split into six different diseases (MODY 1 to MODY 5 plus MODY X, the unidentified 'other' varieties), the first five of which can be identified according to the gene concerned. What this does is give a very strong example of what happens when geneticization constructs the narrative of division.

Does the classification of MODY tell us anything about the way in which diabetes classification, and the narrative which I claim underlies such systems, will develop in the future? Just as in the case of cystic fibrosis, there is risk in predicting changes in classification system, but this is required, to some extent, by the 'momentum' that narratives possess. The MODYs, particularly MODY 2, which is caused by mutations in the gene for glucokinase\textsuperscript{92}, and the other sub-types (which help regulate gene action) have increased understanding about the biochemical mechanisms responsible for Type 2 diabetes. They also provide a classificatory comparison for Type 1 diabetes, which reinforces its geneticization.

The following table shows clearly how comparison with MODY reinforces the geneticized perspective of Type 1 diabetes. Direct comparisons are made between the dominant genes for the MODYs, and the HLA complex genes in the case of Type 1. This table implies an equivalence between the genes that cause MODY, which act in a Mendelian fashion, and those involved in type 1 diabetes, which are far more complex.

\textsuperscript{92} The protein Glucokinase (GCK) plays a major role in the regulation and integration of glucose metabolism. Impairment leads to a glucose-sensing defect, which increases the threshold of blood glucose required to trigger insulin secretion (Froguel and Velho 1999:142).
## Diagnostic Classification of Youth Onset Forms of Diabetes

<table>
<thead>
<tr>
<th>Type of Disease</th>
<th>Definitive Evidence</th>
<th>Supportive Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute onset, insulin-dependent diabetes</td>
<td>ICA+, GADA+, IA-2A+, IA-2βA+, IAA+</td>
<td>DR3+, DR4+, DQB1<em>0302+, DQB1</em>0201+</td>
</tr>
<tr>
<td>Type 1 diabetes</td>
<td>Family history of early onset, initially insulin-dependent diabetes in two or more generations; later non-insulin dependence</td>
<td>African-American ethnicity</td>
</tr>
<tr>
<td>ADM(^{93})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insidious onset, non-insulin-dependent diabetes</td>
<td>Diabetes onset in proband at &lt;25 years of age</td>
<td>Mutation identified in HNF-4α, GCK, HNF-1α, IPF-1, HNF-1β</td>
</tr>
<tr>
<td>Classic MODY</td>
<td>Family history of type 2 diabetes in two or more generations</td>
<td></td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>Family history of type 2 diabetes in two or more generations</td>
<td></td>
</tr>
</tbody>
</table>

from Winter, Nakamura and House 1999:781

The British Diabetic Association's guidelines on genetic screening suggest that while "Genetic testing of MODY families is thus feasible...genetic screening for identifying individuals at high risk of developing [type 1] diabetes is not helpful" (Avery et. al. 1998). Yet as shown in the table above, the classification of the MODYs can reinforce the geneticization of Type 1 diabetes, and strengthen the narrative of division. And genetic distinctions are not just being drawn within the research literature, but also within clinical discourse. A recent review for the *BMJ* points out that type 1 diabetes in early childhood is associated with heterozygosity for HLA DR3/4, while its onset in older children and adolescents is linked with HLA DR3:

"Whether these groupings represent separate diseases or simply reflect the rapidity with which β cell destruction takes place is unclear" (Mandrup-Poulsen 1998:1221).

\(^{93}\) ADM is 'atypical diabetes-mellitus of African Americans' which is another subtype of type 2 diabetes. Symptoms include onset at less than 40 years, initial symptoms similar to type 1 diabetes, which develops into non-insulin requirements. It is inherited in a dominant fashion.
The effect of the MODY model on the classification of type 2 diabetes is hard to predict. It may be informative about the different ways in which the glucose metabolism can go wrong, and the numerous biochemical pathways involved. It may provide a testing ground for pharmacological products which can then be used to treat the majority of type-2 diabetics (Mandrup-Poulsen 1998:1223). But geneticization and reclassification along genetic grounds is a real possibility when one considers the heterogeneous nature of type 2 diabetes. It is extremely unlikely that it is caused by any one gene. Far more viable is a model where different genes (or markers) are associated with different subtypes of type 2 diabetes; a lot like MODY.

8. CONCLUSION

In this chapter I have shown how diabetes has been subject to geneticization, and the effects this has had on its classification. I claim the geneticization of diabetes can be traced back to research in the mid-1970s, and that the incorporation of genetic information into the classification system was begun by Andrew Cudworth. Through two review articles, he constructed a classification system which reified the distinction between the two kinds of diabetes on genetic grounds, and which initiated the narrative of division. This geneticization was not inevitable at the time; alternative systems, such as Irvine's, were serious options.

The geneticization of diabetes was formalised by the NDDG's classification system, which mixed Cudworth's HLA-based classification with insulin dependence. This hybrid system continued, despite complaints about the HLA link, until the 1997 ADA system, which removed insulin dependence as a category (twenty years after Cudworth suggested its removal) and which strengthened the division between type 1 and 2 diabetes on genetic grounds. Throughout this period, the narrative of division has continued, increasing the number of different types of diabetes.

Further genetic sub-division in diabetes seems likely; it is encouraged by both genetic research and the discursive history of its classification. In the previous chapter, I suggested that the geneticization of cystic fibrosis and its attendant narrative of
expansion were proving problematic for a number of patients who have found themselves reclassified as CF 'sufferers'. There is little evidence that the same can be said for diabetes. There are still debates around the 1997 ADA classification, but these tend to revolve around the figures for blood-glucose level tests and diagnosis of diabetes (see Decode Study Group 1998). The idea that diabetes should be sub-divided is not questioned since: "better subclassification will lead to more precise targeting of specific treatments and eventually to better outcomes" (Wareham and O'Rahilly 1998:359). At the broadest level, the subdivision of diabetes can only be positive; to blur the distinction between type 1 diabetes and type 2, would be to deny some people the insulin they (probably) need to live. But issues do surround when a diagnosis is made; geneticization implies that diagnosis will eventually be made on genetic grounds, when patients are still asymptomatic. There is awareness that, certainly in the case of type 2 diabetes, asymptomatic diagnosis and treatment may not be the ideal option (Goyder and Irwing 1998). A recent report on the disease haemochromatosis suggests that patients' views of medical intervention based on asymptomatic genetic diagnosis are not necessarily positive (Seamark and Hutchinson 2000). Asymptomatic testing is one area of interest in diabetes because:

"Type 1 diabetes is an autoimmune disease with a long preclinical course [ref.], the identification of individuals prior to the onset of the disease process provides a real opportunity for predictive testing and for therapeutic intervention" (Friday, Trucco and Pietropaolo 1999:11).

It is not that such interventions are a bad idea, but it is notable that they should be considered as an automatic application of genetic testing for diabetes. Predictions like these ignore the complex issues that surround the presymptomatic testing for even 'simple' Mendelian diseases. How much more difficult are the choices to be made in the case of a disease like diabetes, which even if one thinks is a genetic condition, is caused by a number of separate genes?

In the introduction to this chapter, I mentioned Shepherd et al's research on the presymptomatic testing of a child for MODY. The authors of this study interviewed an affected family, the genetics specialist and paediatrician involved. They concluded that although:

"each request for genetic testing should be considered individually, we would suggest exploring the four main themes that arose with this family in consultations
with other MODY families considering predictive genetic testing" (Shepherd et al. 2000:257).
The four themes they identified were: the role of autobiographical experience (since many families will have experience with diabetes and this will alter their attitude towards testing\textsuperscript{94}); the motivation for testing (often cited as the reduction of uncertainty); the competing priorities of health professionals and clients in genetic counselling (patients are often seeking a result, while counsellors are concerned with imparting information); and the differing attitudes towards testing in children (and in turn whether parents should have the final say on testing) (Shepherd et al. 2000:256). These results suggest, like much of the psycho-social research into genetic testing for complex disease, that asymptomatic testing for diabetes needs to be approached cautiously. This is important, especially since the authors of this study suggest that focusing on MODY will give insights into genetic testing for type 1 and 2 diabetes (Shepherd et al. 2000:255-256).

The fact that geneticization in diabetes has not produced the same problems as in cystic fibrosis does not mean that such issues will not arise in the future. In comparison, schizophrenia, which I turn to in my next chapter, has proved to be a controversial site for geneticization, even without the development of a genetic test. In fact, even without the undisputed identification of a piece of DNA with the disorder.

\textsuperscript{94} In this case, Bob (the father)'s sister had died from diabetes in her early 30s.
CHAPTER 6: SCHIZOPHRENIA AND THE NARRATIVE OF ENLIGHTENED GENETICIZATION

"It is the relative prevalence of the genetic predisposition to developing schizophrenia compared with the relative prevalence of alleged environmental causes that leads us to prefer calling it a genetic disorder"
(Gottesman and Shields 1976b:447)

1. INTRODUCTION

In contrast to my two previous chapters, this one looks at what happens when geneticization is controversial. Although debates have taken place about the effect of genetic explanation on both cystic fibrosis and diabetes, the discussion has generally been low-key. This is not the case in schizophrenia. This chapter begins with an extensive introduction, outlining the historical debates surrounding the search for 'schizophrenia genes'. These lead onto an analysis of three review articles covering 1989 to 1997 and the narrative I have called 'enlightened geneticization' which attempts to define schizophrenia as a genetic disease, yet at the same time tries to be balanced and avoid the more unfortunate associations with genetic explanations. This is a narrative which, wary of the controversy surrounding genetic studies of schizophrenia, seeks to present molecular research in a cautious, careful way, highlighting problems and ostensibly acknowledging the role of non-genetic factors in disease causation. But ultimately, this narrative constructs schizophrenia as a genetic disease, and undermines non-genetic factors.

Schizophrenia is a devastating illness both in personal and societal terms. One estimate claims that 5.4% of National Health Service in-patient costs, and an annual total of £2.6 Billion, goes into treating and caring for schizophrenics (Schultz and Andreasen 1999:1425). In addition, the suicide rate among sufferers is 10% (Andreasen 1999:645). As a condition, it is characterised by 'disordered thinking', a wide, catch-all phrase which covers impairment of: perception (hallucinations), inferential thinking (delusions), motivation, thought and speech (Andreasen 1999; Schultz and Andreasen 1999). Identifying the underlying causes of schizophrenia therefore has important implications for diagnosis, therapy and health care spending.
In 1988, Sherrington et al. announced the discovery of a locus on chromosome 5 which they claimed indicated susceptibility to schizophrenia. The resulting high-profile media discussion became embarrassing when other investigators failed to replicate these results. It was even worse when the same research team also failed to repeat their earlier findings. Despite much soul searching, it is still not clear what went wrong, and how to explain this unfortunate incident (Kendler and Diehl 1993:276). But it has not stopped research into the molecular genetics of schizophrenia. A recent study has announced the discovery of two genes, labelled Disrupted-in-Schizophrenia (DISC) 1 and 2, linked with schizophrenia in a specific Scottish family (Millar et al. 2000). Whether this result will stand the tests of time, analysis and repeatability that have ended other putative 'schizophrenia genes' remains to be seen. Although this chapter focuses on the narrative constructed around this search, it has an extensive discussion of the pre-molecular genetics of schizophrenia, based on twin and adoption studies. I provide this review, not as a substitute for my own discourse analysis, but to provide a detailed context with which my own work is situated. To a large extent the later discussion surrounding the geneticization of schizophrenia only makes sense in the light of these earlier disputes.

The term 'schizophrenia' was originally coined in 1911 by Bleuler, but his ideas were simply the last in a century's worth of developments including Kahlbaum's 'catatonia' and Hecker's 'hebephrenia' in the 1860s, and Kraepelin's 1896 refinement of 'dementia praecox'. Bleuler's concept of schizophrenia contained four subtypes: the catatonic (excitement and stupor); paranoid (delusions of persecution); hebephrenic (laughter and talking with detachment from external environment); and simple (lethargy and apathy). Subsequently the application of the diagnosis of schizophrenia differed across the world, with different psychological traditions adopting different concepts. By the early 1970s, this had produced a situation where "the syndrome continues to defy a sharpness of definition that would in any way satisfy a scientist" (Patterson & Kaelbling 1972:11-12, 15).

Beyond problems with differences in applying the diagnosis of schizophrenia, disquiet existed over whether 'schizophrenia' was a disease entity at all. In an acerbic article titled "The Unfortunate Concept of Schizophrenia" Lawrence Kubie questioned the over-use
of schizophrenia as a diagnostic term and attacked those who tried to increase the concept's value by suggesting various sub-types of schizophrenia as well as the labelling of individuals as schizophrenic (Kubie 1972:67-69). He questioned whether 'schizophrenia' existed as a disease entity at all\(^{95}\) pointing out that as a concept, it had encouraged the idea that its biological, even genetic, foundations would eventually be revealed (Kubie 1972:66). Similar complaints are still being voiced (e.g. Boyle 1990).

As well as the concept of schizophrenia lending support to the idea of genetic aetiology, there are those critics who claim that the idea of a heritable cause is vital for the concept of schizophrenia as a viable disease entity. For example, Mary Boyle notes how,

"before any empirical literature existed, the belief that 'schizophrenia'...had a genetic basis was apparently strong...[B]efore any attempt at systematic data collection was ever made, the two most prominent users of the concepts of dementia praecox and schizophrenia [Bleuler and Kraepelin] were disseminating the view that whatever phenomena they included under these terms were largely inherited" (Boyle 1990:118).

This argument that, in schizophrenia, genetic causation is an axiom rather than a hypotheses, implies that there is something rather circular about investigating the possibility of a genetic cause for a disease which has to be seen to be genetic to exist as a disease entity at all. As Richard Marshall claims:

"attempts to establish schizophrenia as genetically determined have been pursued with greater or lesser conviction since disordered conduct was first construed as some form of illness...this medicalization process required as a cornerstone the resort to biological explanation, and this, in turn, could only gain scientific respectability if the source of the disorder could be located in genetic transmission" (Marshall 1990:89).

Thus the critics' claim is that the concept of schizophrenia as a disease entity and the idea that it is genetically caused are "mutually reinforcing", each reifying the other and helping to turn it into a valid object of study (Marshall 1990:91).

Criticism of the concept of schizophrenia, and of the idea that it has a genetic aetiology, has not stopped the use of the term in psychiatric diagnosis, its treatment with

\[^{95}\text{Kubie is at pains to stress that he is not questioning the existence of "states of psychotic disorganization" which are wide ranging. Rather, his opposition is to "the current tendency to look upon all of these varied conditions as being...manifestations of a separate subentity among psychosis called 'schizophrenia'" (Kubie 1972:66).}\]
pharmaceuticals and investigation into the means of its inheritance. The wide number of different definitions criticised by Patterson and Kaelbling is now less of an issue, with researchers tending to use the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM), the latest version of which is the 1994 DSM IV. This does not remove ambiguities from the concept of schizophrenia as a disorder, for the selection and categorisation of conditions for inclusion in the DSM are themselves socially contingent and often controversial (e.g. Ritchie 1989). But it has provided a 'common standard' against which to assess the diagnosis of this disorder.

An important issue for my research is whether it is productive to analyse the geneticization of a condition which has always been presented as, to some extent, inherited. There was of course the same problem with cystic fibrosis, solved by comparing the classification of the disease before and after the identification of the gene responsible for it. This is not possible with schizophrenia since no genetic marker has been reliably associated with the condition, let alone the actual gene been cloned. Yet this does give access to the discourse that occurs while such a search is going on, especially in a disease such as schizophrenia where there is so much criticism of the idea of genetic aetiology. The rest of this chapter will first examine the debates that surround the twin and adoption studies carried out prior to the availability of molecular genetic techniques, and then move onto analysis of the discourse of the linkage and association studies which attempt to discover a genetic marker for schizophrenia. As pointed out earlier, this extensive review of debates provides a crucial context within which to set my own analysis.

2. TWIN STUDIES

Comparing identical (i.e. monozygotic) twins is one of the oldest methodologies in genetics research. Luxenburger performed the first twin studies for schizophrenia in 1928 and 1934, not to determine whether there was a genetic component to schizophrenia (which was the general assumption of that time) but to discover whether or not it was transmitted in a Mendelian fashion (Gottesman and Shields 1976a:361). The largest of the early twin studies were carried out by Kallman, Slater and Shields in the 1940s and '50s, and these seemed to confirm the existence of a strong genetic component to
schizophrenia, with pairs of monozygotic twins (MZ) having a much higher concordance\(^6\) rate than non-identical, dizygotic twins (DZ) (Gottesman and Shields 1976a:361). As has become the trend in this area of research, a series of articles then came out criticising the assumptions, methodologies and results of this early twin study work. Those who supported this research tacitly accepted many of the criticisms, changed their research methodologies and continued the studies.

Any review of the debates between proponents of twin studies and those who object to such methods raises continual issues of objectivity and distance. From outside, both sides seem to rely on partial readings, misunderstandings and caustic asides to undermine their opponents' position. Although I do not intend to carry out a full discourse analysis of the debates surrounding non-molecular research (i.e. twin and adoption studies), some detail is required to lay out the background discourse of later articles.

In their 1976 review of genetic studies of schizophrenia, Gottesman and Shields are painfully aware that their position could be misconstrued as ignoring the role of environmental influences in schizophrenia aetiology. They clearly state:

"We...are not the only genetically oriented investigators to acknowledge and to value the part played by external environmental and internal psychodynamic factors in the development of schizophrenia" (Gottesman and Shields 1976a:360).

The core of Gottesman and Shields' section on twin studies is their 'Table 4' which summarises 'Concordance in recent twin studies' (see below). Gottesman and Shields then work through these studies, explaining the background to the research and outlining how they calculated the 'probandwise concordance' from the original studies\(^7\).

<table>
<thead>
<tr>
<th>Pairs</th>
<th>Kringlen</th>
<th>Fischer</th>
<th>Gottesman and Shields</th>
<th>Tienari</th>
<th>Pollin et al.</th>
</tr>
</thead>
</table>

\(^6\) concordance is a measure of the proportion of index subjects whose wife/husband/brother/twin shares a particular characteristic with them. For example, the concordance between blue eyed men who have blue eyed wives.

\(^7\) They took the original studies and identified those pairs where the symptoms approximated those of their own 1972 study (where diagnosis was carried out by a panel of judges having reached a consensus). They then used these pairs to calculate the probandwise rate (Gottesman and Shields 1976a:372).
Monozygotic:

| Pairwise range (reported by investigator) | 25-38% | 24-48% | 40-50% | 0-36% | 14-27% |
| Number of pairs (used for consensus) | 55 | 21 | 22 | 17 | 95 |
| Probandwise concordance (our consensus) | 45% | 56% | 58% | 35% | 43% |

Dizygotic:

| Pairwise range | 4-10% | 10-19% | 9-10% | 5-14% | 4-5% |
| Number of pairs | 90 | 41 | 33 | 20 | 125 |
| Probandwise concordance | 15% | 26% | 12% | 13% | 9% |

Gottesman and Shields 1976a:373

They conclude that:

"there is reasonably good agreement among the recent twin studies of schizophrenia ...[and]...the differences between the classical studies of Luxenburger (1928), Slater (with Shields 1953), and Kallmann (1946) and the current work are less marked than was supposed at the beginning of the 1960s" (1976a:377).

This positioning of modern results within a research tradition is part of the narrative constructed in the reviews I analyse later in this chapter, and lends historical support to the claims being made in those texts. Unless care is taken, it also saddles them with the flaws and deficiencies present in the earlier work.

Criticism of twin studies focuses on a number of different aspects of this research, particularly those related to methodology, underlying concepts, and the presentation of statistical data. While I intend to focus on the debates surrounding pairwise vs. probandwise concordance, and the use of the 'schizophrenia spectrum', other possible problems include sample selection (drawing samples from hospitalised twins biases the concordance rate\(^{98}\)), zygosity determination (accurate blood typing is not extended to whole samples to confirm MZ/DZ status\(^{99}\)) and the diagnostic criteria used in different studies to determine schizophrenia.

\(^{98}\) This problem is avoided in studies such as those carried out in Scandinavia, which access twin registers and then track down twins who are diagnosed as schizophrenic.

\(^{99}\) "Fischer used these tests in only 39 percent of pairs, Gottesman and Shields in 50 percent and Kringlen in 71...The problem of establishing zygosity is confounded by the fact that subjects included in a research sample may actually be dead at the time the research is carried out" (Boyle 1990:123).
Concordance rates: pairwise and probandwise

Looking at the table above, one can see that there is considerable difference between the pairwise concordance rates offered in the original studies, and the authors' re-analysis of this data, presented as 'probandwise concordance'. Each rate provides an answer to a different question, with the pairwise method asking 'in what proportion of pairs are both schizophrenic', and the probandwise 'in what proportion of the probands (i.e. those schizophrenic twins discovered in the original search for subjects) is there a schizophrenic co-twin'? (Boyle 1990:131).

The following example shows how each rate is calculated from the same subject group. Suppose an investigator reviews a hospital's records to find schizophrenics who are also twins. Of 100 pairs, s/he finds 30 cases where both twins are diagnosed as schizophrenic. This gives a pairwise concordance of 30% (30/100). Of those 30 concordant pairs, 10 of them were discovered independently, i.e. they were not traced as the co-twin of a schizophrenic, but were discovered in the original 'sweep' of the records. Therefore, in terms of index cases of a genetic study (those cases found independently of each other), there are not 100 probands, but 100 plus the extra 10, i.e. 110. The proband rate is therefore (30+10)/110 = 36.4%. If all 30 of the concordant pairs were discovered independently in the first sweep, the proband rate would rise to (30+30)/(100+30) = 46.1% (Marshall and Pettitt 1985:7).

Such calculations, which increase the concordance rate, have been attacked by critics of twin studies, one of whom suggests that: "It is difficult to avoid the impression that statistical manoeuvres are being employed with the aim of increasing the heredity indices" (Marshal 1990:107). An exasperated Gottesman and Shields claim that:

"The proband method is not a device thought up by wicked geneticists to make a condition appear to be 'more genetic' than it really is by the unwarranted double counting of pairs" (Gottesman and Shields 1976a: 400).
They suggest that rather, it is a reduction of the case-wise rate, which is yet another way of calculating concordance (see below). Gottesman and Shields claim that since the probandwise rate is a reduction of an even higher one (the casewise rate) the twin studies researchers are acting responsibly (Gottesman and Shields 1976b:450).

But this does not clarify Marshall and Pettitt's claim that in 1972, Gottesman and Shields were quite happy with the simple pairwise rate which: "has the merit of simplicity and it is the only rate based on the raw number of pairs observed" (Gottesman and Shields 1976a: 400)\textsuperscript{100}. Yet by 1982, they had analysed all twin studies with both pairwise and probandwise rates presented, emphasising the drawbacks of the pairwise rates. Marshall and Pettitt muse that "Perhaps future publications might omit...[pairwise rates]...altogether" (Marshall and Pettitt 1985:6). Correctly, as it happens; the 1987 article co-authored by Gottesman lists a summary table of "Pooled European family and twin studies of schizophrenia 1920-78" which defines cases simply in terms of 'probands' (Gottesman, McGuffin and Farmer 1987:29).

In turn, Gottesman and Shields are not above imputing an external motive to their critics, claiming that the "investigators least interested in 'pushing' a genetic argument are those who do not report their data in proband wise fashion", although this is an admission that they themselves are interested in pushing a genetic argument (Gottesman and Shields 1976a:373). One should not assume that the use of the probandwise rate is necessarily underhand (c.f. Marshall 1990). For example Mary Boyle's critique of this method admits that:

"At first glance, the use of a 'counting twice' method might appear suspect. It is, however, not so provided certain sampling requirements are met and the appropriate conclusions are drawn" (Boyle 1990:132 emphasis in original).

In the case of an exhaustive search of a population for original subjects, where every person who was a twin and diagnosed as schizophrenic was found, then every subject would have been located independently and would count as a proband. In these circumstances, if 100 twin pairs were again produced, in 30 of which both partners were diagnosed as schizophrenic (but of course each 'discovered' independently of his/her

\textsuperscript{100} This is from the statistical appendix the 1976 article, which in turn is reprinted from Gottesman and Shields' 1972 monograph.
twin), then the concordance rate would again be \((30+30)/(100+30) = 46.1\%\). But this rate is the *casewise* rate, which answers the question 'how many cases in the sample have a schizophrenic co-twin?' (Boyle 1990:132). When *all* cases are found independently of each other, then the probandwise and casewise rates are identical.

Yet this independence of ascertainment is one of the issues attacked by critics. Gottesman and Shields state that probandwise rates are only viable "where independent ascertainments of affected individuals had been recorded" (1976a:400), and Neale and Oltmans note that probandwise rates are only suitable "if the probability of ascertaining an index case is independent of the condition of the co-twin" (1980:182, cited in Boyle 1990:132-133). Boyle suggests however that the required independence of reporting is highly unlikely in the case of identical twins. How likely is it that if both co-twins in a MZ pair are acting 'strangely' and one is reported, the remaining twin has the same chance of being reported as an unconnected individual (Boyle 1990:133)? She points out that age and the geographical mobility of populations play an important role in such reporting since if both twins are living together, or are in the same vicinity, then the chance of them both being reported (and thus ending up as index cases in twin studies) is increased.

Gottesman and Shields counter the critics' focus on the imperfect nature of the sampling methods employed in twin studies with the claim that:

"Schizophrenia research ought to be avoided by those individuals who cannot readily tolerate ambiguity and uncertainty" (Gottesman and Shields 1976a:389). Their message is that the twin researchers are grappling with the messy, problematic real world, while the critics are prone to retreat towards platonic truths to defend their position. Yet in many ways, by discussing issues such as geographic mobility, Boyle is introducing complex and 'messy' reality. The difference is that the twin researchers are prepared to ignore ambiguity in order to attain results, while critics feel that this amounts to dishonest interference with research.

The debate over pairwise and probandwise rates highlights the role that choice of statistics plays in determining results; Marshall elegantly shows this when he reverses the twin studies' usual focus on concordance and looks instead at discordance. Using the
imaginary figures from the example of pairwise/probandwise rates (30% and 46%, see above), Marshall applies the same statistical changes to the 70% discordance rate initially achieved and argues if all 70 discordant probands were discovered independently, then the probandwise rate for discordance would be 82%\(^{101}\):

"Here we have an example of how the same original data could be used to support an extreme environmentalist or an extreme hereditarian position, simply by the introduction of the probandwise method" (Marshall 1990:106).

It is not that Gottesman and Shields are wrong to use the probandwise method of calculating the concordance rates for the twin studies, but that one should see the use of such methods as part of the construction of schizophrenia as a genetic disease, and the geneticization of this condition.

One might claim that because the concept of schizophrenia and the concept of schizophrenia-as-a-hereditary-disease are so inter-mingled, the acceptance that there is an unproblematic clinical entity called schizophrenia commits one to a geneticized position:

"It is worth noting that no twin researcher apparently doubts the validity of the concept of schizophrenia...a naive reader of the studies...would receive the impression that neither the concept nor the business of inferring it presented any serious problems" (Boyle 1990:125).

This idea of a 'prior assumption' of heritability is clear in Gottesman and Shields' discussion of testing various different criteria of schizophrenia used to make their diagnoses:

"We asked which concepts of schizophrenia preserved and maximized the difference in concordance rates between MZ and DZ pairs...we found that either too narrow or too broad a concept of schizophrenia eroded the MZ-DZ contrasts - too narrow lowered the MZ rate to the value of the DZ rate and too wide raised both the MZ and the DZ rates to dilute an indicator of 'biological specificity', the ratio of the MZ:DZ concordance rates" (Gottesman and Shields 1976a:375).

The assumption seems to be that narrow criteria are too narrow and broad criteria too broad because they reduce the support for the genetic causation of schizophrenia. Since from this perspective schizophrenia is obviously heritable, any criteria which undermine this conceptualisation are automatically invalid. This interpretation is perhaps too harsh on Gottesman and Shields; they might be seen as implying that, having acknowledged that there is an environmental component to schizophrenia causation, they set out to find

\(^{101}\) \((70+70) / (100+70) = 82\%\).
the genetic component. The best way to do this is to use the definition of schizophrenia that provides the best genetic description of the disease.

Schizophrenia Spectrum

One continual point of criticism of twin studies is that their practitioners do not limit themselves to including those twins who are clearly diagnosed as schizophrenic, but also include in their figures 'borderline' diagnosis of 'schizophreniform', or 'schizophrenia-like' conditions. This use of broad criteria increases the possible number of probands and thus adds to the level of the proband rate. But it is too simplistic to claim that broad criteria are simply used to inflate the probandwise rate. For example Gottesman and Shields' avoid wide criteria in calculating Kringlen's probandwise rate (Gottesman and Shields 1976a:373). The use of broad criteria serves (and is served by) the idea of schizophrenia existing as part of a wider spectrum of disorders, which does itself have a significant genetic aetiology. Boyle suggests there are two problems with such a schema. The first, mundane but important, is that there is no agreement about the bounds and criteria of such a spectrum. There is no way of knowing how to compare two different twin studies, since their definitions of what it might mean to appear in this spectrum may not overlap (Boyle 1990:130). The second problem is conceptual, and Boyle draws a comparison with diabetes to illustrate her point:

"There have been a number of studies of concordance for diabetes in MZ and DZ twins...[ref]...These however have looked at concordance for signs and symptoms or for signs and not simply at concordance for loosely defined symptoms. If we found a twin pair where one had an abnormal response to a glucose-tolerance test, sugar in the urine, severe thirst, weight loss, tiredness, and so on, while the other had recently lost some weight or sometimes felt 'a bit tired', it would be absurd to call them concordant for diabetes in the absence of signs in the second twin and because weight loss and tiredness are so overdetermined. But this is exactly how twin researchers have proceeded [in schizophrenia] but without, of course, the pretence of any phenomena in the proband twin which would merit the term 'sign' " (Boyle 1990:130).

The use of the schizophrenia spectrum based on symptoms also ensures that investigators assume that any similarities in the behaviours of two twins must be caused by the same

---

102 Thanks to Brian Balmer for pointing this out.
factors (Boyle 1990:131). Gottesman and Shields seem ambivalent towards the idea of a schizophrenia spectrum; they base their probandwise calculations on broad (but as noted, not the broadest) criteria. Yet when discussing the "so-called schizophrenia spectrum" and its relation to a polygenic theory of inheritance, they outline their own preference for a 'threshold model' of causation lamenting that:

"Most other schizophrenia researchers have not chosen to differentiate between threshold and continuum [i.e. spectrum] models, even if they support a polygenic view over a monogenic one" (Gottesman and Shields 1976a:375-376).

This arms-length approach to the idea of a schizophrenic spectrum fits well with the idea that if the defining criteria for schizophrenia are 'too broad', one runs the risk of eroding the distinction between MZ and DZ concordance rates, and thus undermining the role of genetic aetiology. Yet at the same time, conditions bordering schizophrenia on the spectrum can also be seen as heritable, and their inclusion in concordance rates supports the genetic position; a careful balancing act. The spectrum crops up in my own analysis as one of the strategies used in the narrative of enlightened geneticization constructed in the discourse surrounding the molecular genetics of schizophrenia.

One important question concerns the fact that even if one accepts the twin studies' concepts, methodology and statistics, there still seems to be a large gap between a concordance rate of 45% (Kringlen's results for example) and the idea that schizophrenia should be viewed as a genetic disease. On one level, critics are justified in their concern since Gottesman and Shields also discuss genetic transmission in terms of heritability. The heritability of a characteristic or trait "is the proportion of all the variation of a trait in a population that is accounted for by the genetic variance", where the variances, both environmental and genetic "are not universal properties of a trait but depend upon which population of individuals is being characterized and under which set of environments" (Rose et al. 1984: 97).

Gottesman and Shields translate MZ concordance into heritability:

"with a population prevalence for schizophrenia of about 1.0 percent, the expected MZ concordance rate is only 13 percent when the heritability is 50 percent and only 37 percent when the heritability is as high as 80 percent" (Gottesman and Shields 1976a:377).
In other words, one does not need a high concordance rate to achieve high heritability. Kessler challenges this use of heritability on a number of technical grounds and points out that heritability scores vary with the model of inheritance being proposed (with polygenic models producing the highest scores). He concludes that Gottesman and Shields:

"use of heritability estimates is more in the service of convincing the reader that there are major genetic inputs in the liability to schizophrenia than in producing meaningful information" (Kessler 1976:435).

Not surprisingly, Gottesman and Shields suggest that Kessler has misinterpreted them (1976b:450).

This would seem to confirm the critics' objections that twin researchers over-emphasise the genetic contribution to schizophrenia (Marshall 1990:104). Yet Gottesman and Shields themselves admit that "While environmental factors may contribute only about 20 percent...to the variance of the combined liability to developing schizophrenia in the whole population, they will be critical in determining whether the individual with a high genetic risk breaks down" (Gottesman and Shields 1976a:378). Gottesman and Shields bolster their balanced, enlightened position with regard to the role of environmental factors in schizophrenia causation; "It may bear repetition that both the genes and the environment...are each necessary but not sufficient for developing schizophrenia" (Gottesman and Shields 1976a:389).

3. ADOPTION STUDIES

The most obvious objection to twin studies is the fact that similarities between MZ twins may not just be due to their having the same genome, but also because they have been brought up in similar environments. The first defence against this is the inclusion of the figures for DZ twins to allow comparison with a pair of twins raised in a similar environment, but there is some evidence that MZ twins share greater environmental similarities (such as wearing the same clothes and having the same friends), especially during childhood (McGuffin and Martin 1999:38). The most common solution to this problem is to separate environmental and genetic factors by using adoption studies, a form of research described by Gottesman and Shields as "the straw that broke the
environmentalist's back" (1976a:364). There are three main types of adoption study which focus on:

- the biological and adopted relatives of a group of schizophrenic adoptees;
- the children of schizophrenic mothers who were adopted ('adopted-away' studies);
- and the adopted children of non-schizophrenic mothers one of whose adoptive parents had been diagnosed as schizophrenia ('cross-fostering')\(^\text{103}\) (Boyle 1990:139).

The original US schizophrenia adoption studies were carried out by Heston in the mid-1960s, but the main focus of the critics' attacks were the 'Danish-American Adoption Studies' carried out by US researchers such as Rosenthal, Kety, Welner and Wender, using raw data from Denmark. Denmark is a fertile source of information for these types of studies due to its excellent, extensive records of all adoptions agreed by the state, including biological mother (and father where known), adoptive parents, and general records on geographic mobility. In addition, as was useful in the twin studies, hospital records are also excellent, noting admissions to psychiatric hospitals and diagnoses (Boyle 1990:139).

**Schizophrenic Adoptees as subjects**

These studies, in which Kety was senior author (Marshall 1990:108), were aimed at discovering whether the biological relatives of schizophrenic adoptees have a higher rate of schizophrenia than the norm, despite the lack of a common environment. The methodology involved in the first of the reports from these studies (Kety et al. 1968) drew subjects from Copenhagen adoption records between 1924 and 1947. Cross-referencing with psychiatric records produced the 507 sets of records which were then examined by two Danish psychiatrists. The first, who knew the purpose of the study, rated the subjects as 'definitely schizophrenic', 'probably schizophrenic' and 'definitely not schizophrenic'. The second psychiatrist, who did not know the aims of the study, provided a summary of the subjects' records giving information such as symptoms, age of

---

\(^{103}\) These studies are few and far between since adoptive parents are routinely screened, and thus subjects for this type of study are rare. Since the main objections to the results of these studies are methodological, I will not be reviewing them here. For details, see Boyle (1990:155-157).
onset and probable diagnosis. This summary was then sent to Kety and Wender in the US, who made their own separate diagnoses of the subjects. When all three psychiatrists (the first Danish and the two US) agreed on the diagnosis of schizophrenia, the adoptee became a subject of the study and those unanimously declared not schizophrenic were dropped. Disagreements were settled by another summary of records being drawn up by the first Danish psychiatrist, and where unanimity was again reached, the adoptee was included as a subject. Then the investigators tracked down both the biological and adoptive relatives of the subjects, and gathered psychiatric information on them from Psychiatric Registers, police and military records and the Mothers' Aid organisation. (Boyle 1990:139).

The main results of the 1968 study are the fact that 8.7% of the biological relatives of index (i.e. schizophrenic) adoptees had been assigned a diagnosis within the schizophrenia spectrum used in this study. The figure for control subjects was only 1.9% (Boyle 1990:141). The conclusion drawn was of a strong role for hereditary factors in the aetiology of schizophrenia. Later studies in this series (Kety et al. 1975) supplemented the review of relatives' records by interviewing relatives, to improve diagnosis, but similar results were attained. As well as problems relating to the schizophrenia spectrum, objections to this interpretation of these results focus on a number of different areas, ranging from the type of home the adoptees were placed in\(^{104}\), the failure to distinguish between first and second degree relatives (Lidz and Blatt 1981:427-428) and the rather flexible interpretation of the word 'interview' in the later studies in the series\(^{105}\).

---

\(^{104}\) Rose et al. (1984: 223) claim that in 24% of the index cases' adoptive homes, an adoptive parent had been in psychiatric hospital, while not one adoptive parent of a control case had been similarly admitted.

\(^{105}\) By contacting the Danish psychiatrist who carried out the interviews, Rose et al. determined that many of the relatives concerned were dead, so a 'pseudo-interview' was drawn up, based on hospital records, with the psychiatrist imagining the relatives' responses to questions (Rose et al. 1984:224).
Adopted-away children of a schizophrenic parent

These studies, which have either Rosenthal or Wender as their senior authors (Marshall 1990:109) are concerned with finding out whether the children of schizophrenic parents, who are then adopted, are more likely to be diagnosed as schizophrenic despite growing up in a different environment from their biological parents. These studies drew on the same pool of adoptees as Kety et al. with records being cross-referenced to find people who gave up children for adoption and who had also received a psychiatric diagnosis. Again, researchers summarised records and made a diagnosis. For the 1968 study they gathered information about the children of each of the 56 index-parents selected, producing 155 adopted subjects, 39 index and 47 control (i.e. their biological parents had not received a psychiatric diagnosis) (Boyle 1990: 151-152). They gathered further subjects in later sweeps and the results of this study were published in a series of articles: Rosenthal et al. 1968, Rosenthal et al. 1971 and Haier et al. 1978.

The role of the 'schizophrenia spectrum'

As in the case of the twin-studies, much of the critics' attention is focused on the 'schizophrenia spectrum' which is used in the adoption studies and the assumption that conditions on such a spectrum are related to each other genetically and to schizophrenia itself. With regard to my own discourse analysis of more recent articles presented later in this chapter, it is enough to again note the fact that the strategy of the schizophrenia spectrum plays an important role in modern geneticization.

As in her criticisms of twins studies and the analogy with diabetes, Boyle suggests that if the types of comparisons made on the schizophrenia spectrum were repeated in other areas of medicine, then there would be serious cause for concern. The adoption researchers:

"appear to have fallen into the same trap as have twin researchers, of assuming that just because some relatives show behaviours which seem vaguely similar to those of the index subjects, then they must be 'suffering from related disorders'...If their strategy were to be used by...cancer researchers, we should hardly consider them justified in including in a 'cancer spectrum' biological and adoptive relatives who had ever complained of nausea, abdominal pain, or of passing blood or even of 'growths' such as warts, bunions or cysts" (Boyle 1990:143).
The 'schizophrenia spectrum' used in the original adoption studies classified diagnoses under a number of headings ranging from 'chronic schizophrenia', through 'homosexual panic' to 'Uncertain borderline or latent schizophrenia' (see below).

### Diagnostic classification system used in adoption studies: 'The schizophrenia spectrum'

| A. | Definitely not schizophrenic |
| B1 | Chronic or process schizophrenia |
| B2 | Acute schizophrenic reaction, including schizoaffective psychosis, possible schizoaffective psychoses, acute paranoid reactions and homosexual panic |
| B3 | Borderline or latent schizophrenia, including pseudoneurotic, borderline and ambulatory schizophrenia; questionable simple schizophrenia; psychotic characters; and "sever schizoid individuals" |
| C  | Inadequate or schizoid personality |
| D1 | Uncertain chronic schizophrenia |
| D2 | Uncertain acute schizophrenia |
| D3 | Uncertain borderline or latent schizophrenia |

In their 1968 study, Kety et al. classed as subjects those adoptees diagnosed within the B, D and C categories. By 1975, they had discovered by analysing their data that the C category failed to distinguish between the biological relatives of the index and control subjects; thus the C category was dropped. Boyle suggests that this is:

"like a researcher who hypothesises that men are more intelligent than women but who refuses to accept as a test of intelligence any task on which men and women perform equally well" (Boyle 1990:148).

Another example of the flexible nature of the schizophrenia spectrum is given by Rose et al. when they discuss the case of a woman who in 1968 was diagnosed with an 'inadequate personality' (then inside the spectrum, in category C). By 1975, 'inadequate personality' had been removed from the spectrum, but a personal interview diagnosed the woman as a case of 'uncertain borderline schizophrenia' which was inside the spectrum (D3). Rose et al. then discovered through correspondence with the Danish psychiatrist
involved, that the woman had in fact committed suicide several years before, and he had only performed a 'pseudo interview' on her. The final irony is that the woman had twice been admitted to hospital with manic-depression, which is categorically not included in the schizophrenia spectrum. Rose et al. wryly note:

"We can only marvel that the American diagnosticians...[without ever seeing her]...were twice able to detect...that she really belonged within the shifting boundaries of the spectrum" (Rose et al. 1984:224).

Damaging as this case is, one should note that it is not representative of the adoption studies; or at least, one can assume that if it were, the other cases would have been brought to light by Rose et al., Boyle and Marshall. The critics of adoption studies clearly want the reader to extrapolate from this one example, and assume that the whole concept of the schizophrenia spectrum is likewise unsafe.

The topic of manic-depression also arises in Lidz et al's 1981 critique of the adopted-away studies. They claim that the data for schizophrenic parents were corrupted by the inclusion of parents who had been diagnosed, not with schizophrenia or any other spectrum disorder, but with manic-depression, which, as Boyle claims, Kety et al. specifically excluded from their spectrum diagnoses. Lidz et al. suggest that perhaps some manic-depressives were initially included in the study to provide another comparison to add to the control adoptees. But when a relatively large number of the children of manic-depressive parents were diagnosed on the schizophrenia spectrum, the investigators assumed that there is an inherited 'core' which is the same for both schizophrenia and manic-depression. Thus of the 76 index adoptees in the combined 1968/1971 series, 24 were those whose parents were either manic-depressive, or of an uncertain diagnosis (Lidz et al. 1981: 1064). Lidz et al. claim that "the study could no longer properly be termed a study of adopted-away offspring of schizophrenic parents" (Lidz et al. 1981:1064). If one subtracts the manic-depressive parents and their spectrum children from the study, then the difference between index and control groups is no longer statistically significant (Lidz et al. 1981:1066).

Boyle (1990:148) quotes Kety et al. as stating "Manic-depressive illness was never thought to be in the schizophrenia spectrum by us". Unfortunately, she fails to make clear which of 5 possible references she is citing.
The schizophrenia spectrum also allows overlap between the 1968 results and those of 1971; there can be considerable difference between the results presented for each part of the study, but since they are united by the spectrum, all the results can be presented together. This was the case with the 1971 results, which combined the original 1968 figures with later research. In their critique, Lidz et al. 'tease out' the additional results in the 1971 article by subtracting the numbers for the 1968 research from the 1971 (combined) figures (Lidz et al. 1981:1065). As Lidz et al. point out, "Not a single one of the 37 adoptees in the 1971 half of the series received a diagnosis of schizophrenia or even a definite diagnosis of borderline schizophrenia" (p.1066). The main problem with this objection, as a defender of the adoption studies writes, is that it "seems to assume that if the second half of data collected in a study does not closely resemble the first half, a 'failure...to replicate' has occurred" (Grove 1983:999). This is not necessarily the case, of course, since the two articles can be seen as part of the same study, with publication of preliminary results being followed by more 'rounded' ones.

Interestingly, Lidz et al. do not object to the concept of the schizophrenia spectrum in principle, but rather their point is that they are not convinced of a genetic relationship between the disorders on the spectrum. They conclude that: "the usefulness of the concept of genetically determined 'schizophrenia spectrum disorders' seems dubious when it encompasses 17%-25% of a control series" (Lidz et al. 1981:1067).

Gottesman and Shields claim that as well as showing that certain alleged environmental factors are neither necessary nor sufficient to produce schizophrenia, adoption studies "provided a bonus by reawakening interest in the so-called schizophrenia spectrum" (Gottesman and Shields 1976a:366). Reviewing the current (1976) view of the schizophrenia spectrum, they compare it to the different versions which appear in the adoption studies literature. Gottesman and Shields are critical of some of the conclusions drawn by the adoption researchers. For example, commenting on suggestions that acute schizophrenia is aetiologically distinct from chronic and borderline schizophrenia, they are cautious:

"Lest their [Rosenthal, Kety et al.] conclusion be taken more seriously than it deserves...The problem of where to place the acute...in our taxonomy is one of long standing and will require more research before we can reach an informed conclusion" (Gottesman and Shields 1976a:367).
Gottesman and Shields do not reject the concept of the schizophrenia spectrum outright, preferring to see it developing over time towards a more accurate representation of how schizophrenia relates to other mental disorders. They note that "while once manic-depressive illness was thought to be in (Rosenthal et al. 1968 and 1971), now more sensibly, it is excluded (Rosenthal 1975)" (Gottesman and Shields 1976a:367).

One alternative to this 'consistent' progressive view of the spectrum is the fact that it is flexible, and can be manipulated as and when it is needed. For example, one could draw such a conclusion from Lidz et al. who, commenting on Rosenthal, note that in the 1968 study, manic-depressive parents were included as indexes, but by 1970\textsuperscript{107}, Rosenthal was extremely dubious about linking schizophrenia with manic depression, concluding that manic-depression and schizophrenia were distinct and different disorders (Lidz et al. 1981:1066). By 1971 of course, with the second half of the adopted-away study, he was again prepared to link schizophrenia with manic-depression, before finally relenting in 1975. This gives the impression of the spectrum as a flexible construct, altering as circumstances require, to fit the genetic hypothesis. Gottesman and Shields fail to mention the 1970 change in position, and can thus suggest that although Rosenthal's view of the schizophrenia spectrum had changed, it had consistently moved in the same direction.

Within the context of the narrative of 'enlightened geneticization' constructed in the schizophrenia reviews, there is a noticeable disparity between the critics of the adoption studies and more well disposed reviewers such as Gottesman and Shields. The critical reviews of the Danish-American adoption studies (Boyle, Lidz and Marshall) focus on the early articles, while Gottesman and Shields are more concerned with later writings. This is a pattern that is repeated in later reviews, where links to previous research are required to bolster and support later work, but the errors and faults of early reports must be avoided. Gottesman and Shields pay only a cursory attention to individual articles within the adoption studies series, presenting information in terms of summaries. It

stands out that Gottesman and Shields, writing in 1976, give comprehensive synopses of adoption studies research published as late as 1975108 while the critics, writing in 1981 (Lidz, Blatt and Cook, 1981) or 1983 (Lidz and Blatt, 1983), 1984 (Rose et al.) or 1990 (Boyle, Marshall) focus on the early reports from 1968 or 1971. One might think that later reviews would be more likely to cover later articles, but one possible reason for this time lag is suggested by Gottesman and Shields: "As the Danish adoption studies of schizophrenia have progressed, modifications have evolved in the original views about the schizophrenia spectrum" (1976a:367).

If one wanted to identify aspects of the adoption studies to criticise, the best place to look would be the earlier articles, before the researchers' concepts had 'progressed'. Although they wrote before any other critiques of the adoption studies had been published, it is quite clear that Gottesman and Shields were aware of the kinds of attacks that would be levelled against this work. In their introduction to the adoption studies Gottesman and Shields launch a pre-emptive strike, noting that "Perfectionism is the last refuge of the skeptic, and no amount of purified data can pierce that defense" (Gottesman and Shields 1976a:364). This echoes other comments made (re: twin studies) by these authors that the critics can always retreat to pedantic details, while the genetic researchers have to deal with the messy, ambiguous real world.

**Closure of the debate**

When the next *Schizophrenia Bulletin* review article came out in 1987 (Gottesman, McGuffin and Farmer 1987), the authors claimed that since the 1976 review "The controversies surrounding the causal factors continue unabated" (p.23). They cite a number of critiques including Lidz et al. 1981 and Rose et al. 1984109. Yet when they come to the sections on twin and adoption studies, there is no mention of the critics, let alone a discussion of their objections. This is because this review turns towards "The most prominent trend in the past decade...[the]...creative and sophisticated recycling and

---

108 see for example, Gottesman and Shields 1976a:364-365.

109 although it is listed as Lewontin, Rose, and Kamin 1984.
reanalysis of the hard-to-collect family, twin and adoption studies” (p.28). This apparently renders any earlier criticisms redundant. Just as the proponents of twin studies look back at the earliest research (e.g. Kallman) and admit its methodological flaws, claiming that newer studies are improved, so the authors of this review can defuse the detailed critiques of more recent twin and adoption studies, by focusing on reanalyses that have been performed since those critiques were written. Unless the critics update their arguments and address the newer studies, they run the risk of being seen as anachronistic. Why should one pay attention to detailed criticisms of twin and adoption studies published in the 1960s and 1970s when the latest studies cited by Gottesman, McGuffin and Farmer are from the mid-1980s? This discrepancy becomes clear in the first of Portin and Alanen's 1997 articles, in which the sources of their criticism of adoption studies are from 1976, 1983 and 1984, while the latest Danish American adoption study they cite is from 1994 (Portin and Alanen 1997a:2). Their position with the twin studies is better in that, although they list Rose et al. (1984), they also refer to two more recent critical reviews (1990 and 1993).

Closure is achieved with a steady growth of updated information rather than with a single piece of irrefutable evidence. If the critics were to successfully cast doubt on the genetic studies in schizophrenia, then a continual process of review and criticism would be required. Even Boyle and Marshall's 1990 reviews rely heavily on previous critiques, with little attempt to address more recent research. Closure comes, at least in part, because the critics fail to update their attack and address newer studies.

4. Materials for Analysis

The reasons for such detail in this preliminary section are twofold; first, the debates over twin and adoption studies clearly lay the foundations (and rehearse some of the discursive strategies) for the narrative present in recent schizophrenia literature, which I have termed 'enlightened geneticization' (see below). Second, because the current state of molecular research is such that no definite candidate marker has yet been identified, later reviews rely for much of their authority on twin and adoption studies. How a review article treats the debates and controversies surrounding this research is one way of accessing the authors' attitude towards the geneticization of schizophrenia.
The articles selected for analysis in this case study are all drawn from the journal *Schizophrenia Bulletin*, which is published by the US National Institutes of Mental Health. This journal specialises in publishing schizophrenia review articles rather than any original research so it is a rich source of material. The articles chosen for this analysis focus on the molecular aspects which qualifies them for the definition of geneticization being used in my research—i.e. that there is a link between the disorder and a stretch of DNA. This therefore excludes two review articles from this journal which have already been mentioned: Gottesman and Shields (1976a) and Gottesman et al. (1987). The first focuses exclusively on population genetic approaches to schizophrenia, and the second, although interesting in its updated coverage of the debates over twin and adoption studies and its review of the possible genetic models for schizophrenia, only mentions molecular approaches (namely 'genetic markers') at the very end.

The three articles for analysis are subsequent reviews of the genetics of schizophrenia published in the *Schizophrenia Bulletin*:

- McGue and Gottesman (1989) "Genetic Linkage in Schizophrenia: Perspectives from Genetic Epidemiology" (68 citations);
- Kendler and Diehl (1993) "The Genetics of Schizophrenia: A current Genetic-Epidemiologic Perspective" (169 citations);

All three of these articles have been highly cited, Kendler and Diehl's 1993 review in particular. They represent the dominant themes in schizophrenia genetics (though this is not necessarily the dominant approach in schizophrenia research) as a whole. The first of these articles focuses on molecular approaches to the genetics of schizophrenia; it has very little to say about the actual techniques that could be used to find the gene 'for' this disease. Although it mentions genetic linkage in the title, it is not concerned with the

---

^110^ All citations from the BIDS ISI database.
Kendler and Diehl's 1993 article is heavily cited in the literature, and introduces many of the molecular techniques and methods used in schizophrenia genetics. It is certified by the journal as an 'official' schizophrenia genetics review, but the fact that there is no discernible difference in the narrative in this article confirms that all three act as valid representations of discourse current in schizophrenia genetics.

Again, while the last of these articles is not a typical Schizophrenia Bulletin review article\textsuperscript{113}, its appeal lies in the fact that it:

- is co-authored by Irving Gottesman, which provides continuity with one of the other 'target' articles and, of course, the two earlier review articles (1976 and 1987) and;

\textsuperscript{111} Genetic Linkage studies use the fact that genes are often located near a specific, identifiable marker on the chromosome. The gene and marker tend to be inherited together, so families tend to have similar patterns of markers. Linkage studies use families with a high proportion of schizophrenics in them to identify markers which are unique to these pedigrees, and which might therefore indicate the presence of a gene contributing to schizophrenia.

\textsuperscript{112} writing in 1993, Kendler and Diehl refer to Gottesman, McGue and Farmer (1987) as "the previous review" (p.265).

\textsuperscript{113} It comes from the 'At Issue' section of the journal which "contains viewpoints and arguments on controversial issues...[which]...may not meet the strict editorial and scientific standards that are applied to major articles" (Moldin and Gottesman 1997:547).
provides a 'prospective' (albeit personal) view on the role that the genetics of schizophrenia will play in the future, and thus provides an interesting perspective on how enlightened geneticization may develop.

Its focus and the fact that it is co-authored by Gottesman make it an interesting addition to the narrative. It repeats and reinforces many of the elements of the narrative and provides interesting predictions as to how schizophrenia genetics may develop and be applied in the future.

Unlike the two previous chapters, my analysis in this case study does not focus on the effect of geneticization on disease classification. In large part, this is because it is not possible to say that geneticization (in terms of my working definition) has taken place in schizophrenia. What these articles construct is the narrative that occurs in a disease where genetic explanations are presented as appealing, but where the use of such explanations is fiercely resisted by critics.

5. Features of Enlightened Geneticization

The aim of the discourse analysis that follows is to show that the narrative that predominates in schizophrenia genetics is one of 'enlightened geneticization'. The central theme to this narrative is the presentation of current genetic thinking as reasonable, non-extremist and accepting of a role for non-genetic factors in schizophrenia causation. The term 'enlightened' has been adopted from the 1987 review article by Gottesman, McGuffin and Farmer who state in the abstract that they intend to:

"review a sample of the highlights relevant to enlightened genetic thinking, i.e., a broad diathesis-stressor framework with multifactoral causation assumed and with provision for the epigenetic interaction of psychosocial as well as neurobiological factors" (Gottesman, McGuffin and Farmer 1987:23).

The idea of such enlightened thinking is particularly intriguing in the light of criticisms raised against current genetic research into schizophrenia which is sometimes described as 'simplistic' (e.g. Portin and Alanen 1997a/b). Thus for me the idea of enlightened geneticization is half-ironic in that the concept criticised by Lippman and others for encouraging discrimination is an unlikely candidate for that most liberal of notions, enlightenment. As I will show, researchers present this narrative as genuinely enlightened, in a political sense. At the same time, although the review articles analysed
do not baldly state that schizophrenia is a genetic disease, the narrative subtly constructs schizophrenia in such a way that alternative, non-genetic aetiologies are not presented as viable options.

The difference between such a position and 'crude' genetic determinism is illustrated by the following example. In a letter replying to Lidz et al.'s critique of the adopted-away studies, Wender claims that:

"Each of these studies, using different approaches, has produced results that have to date demonstrated only the action of genetic factors in the etiology of the schizophrenias. None of these studies has produced data consonant with the hypothesis of psychosocial contributions to etiology of the schizophrenias" (Wender 1981:1393).

It is not uncharitable to view Wender as claiming that only genetic factors contribute to the etiology of schizophrenia. In comparison, Gottesman and Shields' claim is not extreme:

"the burden of proof has shifted from showing that genes are important to showing that environment is important even though adoption studies cannot prove that environment is unimportant" (Gottesman and Shields 1976a:367).

Such a challenge does not deny the relevance of environmental effects, it merely requires evidence of such factors, in the same way as, it is claimed, adoption and twin studies provide evidence for inherited factors. The point is that the narrative of enlightened geneticization is constructed in such a way as to deny non-genetic factors the possibility of making a serious contribution to schizophrenia aetiology.

Thus, there is far more to the narrative of enlightened geneticization than calling schizophrenia a 'genetic disease' and proposing a 'gene for' schizophrenia with little role for environmental influence. For example, the final section of the 1989 article, 'Discussion and Conclusion' (McGue and Gottesman 1989:460-462), acts as a detailed description of the narrative of enlightened geneticization. Divided into three sections, it emphasises the fact that:

"Nobody has ever been able to demonstrate statistically that a single major gene accounts for a large share of the overall risk for schizophrenia...Approaches

---

114 The first half of this statement might be saying that the adoption studies were only designed to assess genetic factors, but the claim that none of the data from these studies is at all in accordance with the environment making contributions to the aetiology of schizophrenia would seem to belie that.
premised upon the hypothesis that schizophrenia is a unitary single gene disorder run counter to a vast amount of empirical research that suggests otherwise" (McGue and Gottesman 1989:460).

The final part of this section warns that:

"Environmental influences play an essential role in the etiology of schizophrenia. In the rush to molecular biology, it would appear shortsighted for psychopathologists no longer to consider why it is that among two individuals, both of whom inherit a genetic diathesis, one will go on to develop the disorder while the other will not" (McGue and Gottesman 1989:461).

Such openness about the limitations of the purely genetic approach are a mark of enlightened geneticization as is apparently highlighting the potential role of environmental factors in schizophrenia aetiology:

"The pathway from gene product to behavioral expression is obviously long and presumably provides many opportunities for environmental modulation as well as moderation by other biological, physiological, and behavioral systems" (McGue and Gottesman 1989:461).

But this statement starts with the gene product. All the environment can do is alter the degree of its effect. The cause lies in the genes.

The fact that the narrative presents a complex, multifactoral version of schizophrenia with a role for environmental influence should not hide the fact that in a more subtle way, it also:

• ensures that schizophrenia can only be considered in terms of some necessary genetic aetiology (even if it is not sufficient);
• strengthens the supporting role that the twin and adoption studies play in this narrative by presenting them as achieving closure and;
• suggests that the variety of different possible environmental factors should be seen against a 'genetic baseline' which is the only single necessary condition for causation.

This final point, links with Gottesman and Shields' (1976b) claim that the 'diathesis-stressor' model which they suggest implies that schizophrenia is a genetic disease. In their reply to critics of their 1976 review, Gottesman and Shields state that:

"Our emphasis...is on a large and rather specific genetic 'something' interacting with nonspecific, rather universal, environmental factors" (Gottesman and Shields 1976b:447).
For them, these grounds suggest that schizophrenia should be called a genetic disorder because of the "relative prevalence of the genetic predisposition to developing schizophrenia compared with the relative prevalence of alleged environmental causes" (ibid.). Their proposed 'threshold' model of schizophrenia has the effect of introducing genetic causation as the basic explanation of the condition. However valued the environmental contribution is, it is much harder to define rigorously, and thus the main causal factor should be seen as genetic. Hence schizophrenia as a genetic disease. The 'diathesis-stressor' or threshold model has remained constant in schizophrenia genetics and is represented by the idea of an environmental 'trigger' for schizophrenia which is also present in geneticists' verbal discourse about schizophrenia (Turney and Turner 2000).

But again it must be stressed that enlightened geneticization is not simplistic genetic determinism. In their 1997 review, Moldin and Gottesman reject the idea that the environment has no causative role in the schizophrenia stating:

"[i] Environmental factors are clearly of importance in the etiology of schizophrenia. Unfortunately, [ii] no specific factor has been found to trigger schizophrenia in many or most cases. Our best leading candidates...are nonspecific and idiosyncratic. [iii] These factors are more likely to be implicated in the course of illness, rather than in its distal etiology" (Moldin and Gottesman 1997:554, numbers inserted)

One can see the following aspects of the narrative:

[i] the acceptance of environmental factors;
[ii] the nonspecific, ungeneralisable nature of these factors and in this case;
[iii] the additional fact that these environmental factors are not part of schizophrenia's real (i.e. distal) causes.

In discussing the narrative of enlightened geneticization, it is all too easy to characterise the authors of these reviews as malicious conniving genetic determinists, or even worse. Just as the critique of médicalisation tends towards characterising doctors as oppressive, so considering geneticization might suggest similar things about geneticists. This should be resisted. The narrative is called enlightened not just because it acknowledges (at the surface level at least) the role of non-genetic factors, but also because it can be genuinely enlightened in a political sense. In the 1997 review, Moldin and Gottesman present a
number of "Common Misconceptions and Current Realities". They answer the misconception "Individuals with schizophrenia should not reproduce; prevention of reproduction will lead to the eradication of schizophrenia" with the statement that:

"Given that there is an imperfect relationship between genotype and phenotype...there is unlikely to be a way to predict with great certainty who will or will not become affected with schizophrenia" (Moldin and Gottesman 1997: 555, emphasis in original).

The use of uncertainty of prediction in this statement undermines, or even contradicts comments made earlier in the same article, about the "enhancement of diagnosis" and even gene therapy that will result from advances in knowledge of schizophrenia genetics (Moldin and Gottesman 1997:552). Yet this contradiction is unavoidable because however ironic 'enlightenment' might seem in this narrative, it is a genuinely liberal discourse, which does not sit comfortably with the authoritarian position expressed in the italicised misconception above. The concepts of improving diagnosis, aiding genetic counselling and gene therapy are all part of what Philip Kitcher has called Utopian Eugenics (Kitcher 1996:205-219). This is the idea that individuals and couples, through exercising their autonomy, will achieve eugenic results without the coercion and paternalism of earlier, darker eugenic programmes. To accuse the authors of these articles of promoting old fashioned eugenic views, just as claiming that they push simple genetic determinism, is nonsense. Yet there is an uneasy balance to keep; awareness of the dark side of genetic determinism is perhaps why this narrative ostensibly admits the role of environmental factors in schizophrenia aetiology. Letting the environment have a role keeps the old eugenics at bay, yet the narrative is constructed in such a way to deny non-genetic factors decisive control. This political role reflects Kerr et al's findings about how genetics professionals draw discursive boundaries around their work to present themselves in a positive light (Kerr et al. 1997). Perhaps it is also where the political element of Lippman's vision of geneticization intersects with my own. Lippman sees geneticization in political terms: her 1996 article is entitled "The Politics of Health: Geneticization Versus Health Promotion". My own definition distances the process from politics, but accepts that geneticization can have political implications.

There is a moderation in the narrative of enlightened geneticization, which is demonstrated in Kendler and Diehl's 1993 article. The authors state that: "Center stage has shifted from traditional family, twin and adoption studies to linkage analyses of
"high-density" families" (Kendler and Diehl 1993:461). They then suggest that psychiatric geneticists can be split into three groups according to their reaction to these new techniques: those who believe that the diagnostic and aetiological complexity of schizophrenia "renders such a simple approach useless" (Kendler and Diehl 1993:462); those who have adopted the opposite view, embrace the new technology and dismiss family, twin and adoption studies as "antiquated...and ready for the dustbin of history" (ibid.); and those who have taken the middle ground and regard molecular techniques as the latest in a number of different approaches. Unsurprisingly, the authors place themselves within this last group, highlighting their reasonableness, balance and perspective. It is interesting to note that there are no references cited for the extremists on either side. This view is even "long-held" by the authors, and while they appreciate the impatience of many in their field to bring to bear "these glamorous new technologies", they feel that "a balanced research plan for this devastating illness should include both traditional and gene-mapping approaches" (Kendler and Diehl 1993:462). Taking the middle ground between two extremes is a very obvious (though none the less effective) strategy to present this research as reasonable and balanced.

In the final section of the 1993 review, 'Conclusions and Future Directions', Kendler and Diehl outline several of the elements that make up this narrative: the straightforward use of twin and adoption studies which "continue to confirm...the major etiologic role played by genetic factors" (Kendler and Diehl 1993:278)\textsuperscript{115}, the call for moderation which characterises this article\textsuperscript{116}; and the need for realistic expectations with respect to the outcomes of molecular research.

"It is critical that we avoid premature disillusionment with linkage studies of schizophrenia...If there are many genes, none of which has any more than a small effect on liability, then current methods and projected sample sizes are almost certainly inadequate and will yield negative or unreplicated results" (Kendler and Diehl 1993:279).

\textsuperscript{115} Alternatively: "The aggregate results from twin and adoption studies allow us to conclude with some confidence that genes that influence liability to schizophrenia exist somewhere in the human genome" (p.279).

\textsuperscript{116} "we caution against prematurely abandoning the more tried and true methods of psychiatric genetic research" Kendler and Diehl 1993:278.
The need for patience on the part of researchers is echoed again in the last paragraph of the review which, while discussing the potential role of the large numbers of genetic markers being made available, states: "this approach, if allowed sufficient time to mature, could yield truly unprecedented insights into the etiology of this disorder" (ibid.). Having sketched in the themes of narrative of enlightened geneticization, I will now present in more detail the strategies used to construct it.

6. Strategies Of Enlightened Geneticization

Unlike the other case studies in this thesis, in this chapter I adopt a thematic rather than chronological approach. This is because with three articles to analyse, one runs the risk of repetition if chronology is used. Instead, I will present the different strategies used throughout all three reviews, to construct the narrative of enlightened geneticization.

These strategies can be broadly separated into:

- the use of history;
- genetic modelling;
- responsibility and caution;
- the schizophrenia spectrum.

The Use of history

This strategy looks back to the twin and adoption studies to provide proof of the genetic component in schizophrenia aetiology and hence the justification for molecular research. The problem for those concerned with molecular genetic approaches to schizophrenia is that there are "features of schizophrenia that represent challenges to the design of linkage studies" including the fact that:

"analysis of twin and family data has consistently failed to identify a single major gene effect upon schizophrenia risk...[and]...environmental influences appear to play an essential role in the etiology of at least some forms of schizophrenia" (McGue and Gottesman 1989:453).

This is a typical statement of enlightened geneticization. The limitations of the current genetic information (from the twin studies etc.) are made clear and the important role of environmental influences is pointed out. But there is also another level at which this position operates. Whatever the deficiencies of the twin and adoption studies, according
to this narrative they do provide hard evidence of the role that genetic factors play in the aetiology of schizophrenia. At the same time, environmental factors are usually classed in terms of being 'non-specific' and hard to identify; unless one or two specific environmental influences can be identified then the role of environmental factors, while accepted, cannot be given priority. As Gottesman and Shields make clear in 1976, from this perspective, schizophrenia is a genetic disease (1976b:447). The irony is that the narrative of enlightened geneticization is not so strict about the identifiability of genes. A single gene model is not a credible explanation for schizophrenia aetiology, yet the lack of a single genetic cause is not counted as a weakness.

As an example of the role historical perspective plays, the 1989 review presents the epidemiologic data from research which summarises twin and family studies and includes a table which:

"gives estimated life time risks...for developing schizophrenia among the relatives of schizophrenic probands pooled from systematic studies undertaken in Western Europe since 1920" (p.454).

<table>
<thead>
<tr>
<th>Familial relationship</th>
<th>% Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offspring of 2 Schizophrenic parents</td>
<td>36.6</td>
</tr>
<tr>
<td>Monozygotic twins</td>
<td>44.3</td>
</tr>
<tr>
<td>Dizygotic twins</td>
<td>12.1</td>
</tr>
<tr>
<td>Siblings</td>
<td>7.3</td>
</tr>
<tr>
<td>Offspring of 1 Schizophrenic parents</td>
<td>9.4</td>
</tr>
<tr>
<td>Half siblings</td>
<td>2.9</td>
</tr>
<tr>
<td>Nieces or nephews</td>
<td>2.7</td>
</tr>
<tr>
<td>Grandchildren</td>
<td>2.8</td>
</tr>
<tr>
<td>First Cousins</td>
<td>1.6</td>
</tr>
<tr>
<td>Spouses</td>
<td>1.0</td>
</tr>
</tbody>
</table>

based on McGue and Gottesman 1989:454, Table 1.

There is no attempt to explain how the large number of different studies with varying methodologies were combined to produce this table. Nor is there any description of the fact that the early twin and family studies are normally treated with extreme caution, since even the strongest exponents of twin studies now admit that the lack of controls
and non-blind status of the investigators renders many of the early results doubtful. Readers are merely referred to two other articles where the compilation of the data is explained (McGue and Gottesman 1989:454). There is no mention of the debates surrounding twin and adoption studies; as presented here, any controversy over the role of genetics in the aetiology of schizophrenia has reached closure. This is an example of the way in which review articles reconstruct the history of a discipline, to present a smooth unruffled image (a similar process took place in cystic fibrosis). The authors state that "the MZ twin concordance rate is substantially less than 100 percent and thus...environmental factors...play a significant role" (ibid.). But the role as presented is almost that of 'background noise' since the environmental influence "obscures the mechanism of genetic transmission, resulting in continued debate as to whether schizophrenia is a single gene disorder" (ibid.).

In the 1993 article, the authors again review family, twin and adoption studies. The discussion of the first of these follows the same pattern of the debates in the introduction to this chapter; early family studies are introduced which suggest that "schizophrenia consistently and substantially aggregates in families" (Kendler and Diehl 1993:262). But these studies were methodologically flawed (in this case nonblind, without controls and without organised diagnostic criteria) and objections were raised. Subsequent studies are carried out which repeat the earlier studies under more rigorous conditions. They produce largely the same results suggesting that:

"the earlier first-generation family studies were substantially correct in concluding that schizophrenia strongly aggregates in families. Their findings were not systematically biased by nonblind or unstandardized diagnostic practices, the absence of control groups, or an overly broad classification of the disease" (Kendler and Diehl 1993:264).

By constructing the debate in this way, the narrative gains the benefits of historical precedence, without having to accept the faults and weaknesses of the early research (see above). This gives the narrative strong historical 'roots' in population genetics but also clears the early researchers of the kinds of accusations of bias and ideology that critics of the genetic approach often raise against them.
The 1993 section on twin studies is short (about one column in length) since "The last 10 years have seen relatively little twin research in schizophrenia" (Kendler and Diehl 1993:264) and they give the results of the only study to have been completed since the previous official *Schizophrenia Bulletin* review[^1]. The results of this study are felt to be:

"toward the upper end of the estimates obtained from previous twin studies...[but]...Overall, the results from this study are reassuringly similar to those obtained from previous studies [ref] in suggesting that genetic factors play a major role in the etiology of schizophrenia" (Kendler and Diehl 1993:265).

One of the references cited here is Gottesman and Shields (1966), which seems an old reference for a review article which is meant to be presenting the most up-to-date information. Of course, the use of such a reference adds to the idea that the results from twin studies are an accepted and approved form of evidence and have been for some considerable time. This is thus another form of the 'use of history' strategy. The authors also state that the single study reviewed:

"is also consistent with previous twin studies in suggesting that familial environment makes little or no contribution to the liability for schizophrenia" (Kendler and Diehl 1993:265).

This comment is in keeping with the narrative of enlightened geneticization which, while admitting the role that environmental factors play in schizophrenia aetiology, does not allow such factors to be generalised, identifiable and predictive.

With regard to adoption studies, Kendler and Diehl discuss two papers which appeared since the previous review. One is a replication of the Copenhagen studies (Kety 1987) and the other is work carried out in Finland by Tiernari (1991). The Kety study repeated the Copenhagen methodology, applying it to adoptees outside the capital, identifying 42 schizophrenic adoptees and their relatives whose records were then searched, blinded and reviewed. In addition, they also reviewed personal interviews with the adoptees and their relatives. In both these studies, researchers found significantly greater levels of schizophrenia[^2] in the biological relatives of adoptees than in the adoptive (Kendler and Diehl 1993:265). There is no mention of the doubts that were raised by Lidz and his


[^2]: defined to include chronic, latent and uncertain types.
colleagues, Rose et al. or the more recent work of Boyle and Marshall. The authors do not state whether the newer studies led by Kety have addressed the methodological concerns raised by the critics; if not, then exactly the same points could be made about these more recent studies. Simply avoiding the issue allows the authors to present the adoption results (like the twin studies) as uncontroversial and the debate as having reached closure.

The authors of the 1997 review start with a clear statement of their position:

"Family, twin and adoption studies conducted over the past 30 years have provided very strong evidence that both genes and environment play a role in its [schizophrenia's] etiology" (Moldin and Gottesman 1997:547).

This is easy to recognise as the 'mantra' of enlightened geneticization. The first section is, as tradition demands, on "Studies of Familial Transmission", laying down the historical roots of the latest genetic research:

"data from more than 40 family studies spanning seven decades of research consistently show that risks to different relatives of affected individuals are in fact significantly greater than the population risk" (Moldin and Gottesman 1997:547). Citing an average MZ concordance rate of 46%, the authors note that since this is "significantly less than 100 percent...[it]...implicates the role of nongenetic factors" (Moldin and Gottesman 1997:547). This is followed by archetypal enlightened geneticization when discussing the heritability scores for schizophrenia gained from twin studies. Moldin and Gottesman note that the two scores (89% and 74%) are "without contribution from the common environment" and that the nongenetic contributions are likely to be the result of "idiosyncratic environmental events" (Moldin and Gottesman 1997:548). Such a discussion fits neatly into the diathesis/stressor model maintained by the narrative in these reviews; the acceptance of environmental factors is only possible if they are not regular and predictable. This section concludes with a review of the possible models of inheritance that are supported by the empirical data stating that:

"A polygenic (multilocus) model has been supported consistently...[and]...it is clear that a single major locus does not account for a large proportion of the familial aggregation of schizophrenia" (Moldin and Gottesman 1997:548).

**Genetic Modelling**

This section shows how the strategy of genetic modelling is used in these articles to undermine non-genetic causes and allow strong, single gene models some role in the
narrative, despite empirical evidence to the contrary. In the 1989 article, McGue and Gottesman review the single gene concept (the so called generalised single locus model, or GSL), describing it as the oldest and most prominent hypothesis in the genetics of schizophrenia (McGue and Gottesman 1989:454). The attraction of the GSL lies in its economy and the fact that its simplicity would make molecular searches for the gene involved much easier (McGue and Gottesman 1989:455). Unfortunately, as they also point out, "the GSL model has repeatedly failed to account for the observed pattern of familial risk in schizophrenia" (ibid.). To demonstrate this point they present a graph which compares lifetime risk of developing schizophrenia among relatives of sufferers as a function of the proportion of genes shared with the proband. This striking image shows the linear relationship represented by the GSL model alongside the empirical data, which is exponential, as is the line for an alternative explanatory model, the MFT (see below). This divergence from the empirical data makes it extremely unlikely that the GSL is an accurate explanation of the genetic aetiology of schizophrenia. In addition, the low penetrance of the gene required by the GSL model is at odds with the "relatively large MZ twin concordance rate" (McGue and Gottesman 1989:456) which is of course still "substantially less than 100 percent".

In their next section, the authors focuses upon the 'Multiple Gene Models' of which two are presented: the multifactoral threshold (MFT) and the mixed models (meaning mixed major and polygenic causation) (McGue and Gottesman 1989:456). With the MFT, "genetic factors are assumed to be polygenic" meaning that:

"a large number of genes, each of small and equal effect, combine additively with the effects of other genes and environmental factors to influence schizophrenia liability" (McGue and Gottesman 1989:456).

Under this model, schizophrenia happens when "an individual's combined liability exceeds some threshold value along the unobserved liability continuum" (McGue and Gottesman 1989:456). The concept of a 'threshold' to schizophrenia liability was favoured over a straight continuum model by Gottesman and Shields in 1976 (p.376). McGue and Gottesman claim that the MFT model successfully accounts for patterns of familial risk, producing the characteristic exponential risk function seen in schizophrenia. But they admit that "there is a general reluctance to accept the MFT model as an explanation for the transmission of schizophrenia" (McGue and Gottesman 1989:456).
The reasons for this are not intrinsic to the model itself, but are contingent factors, namely the lack of identified specific genes and environmental factors which might contribute to the liability, and the fact that:

"strict polygenic inheritance...would likely preclude, for the near future, attempts at identifying single gene effects on schizophrenia risk through molecular genetic approaches" (McGue and Gottesman 1989:456).

Neither of these objections undermines the MFT in any real sense. The MFT allows for co-existence with:

"a single major gene whose effect upon schizophrenia risk is large relative to the effects of other (poly)genes...[In addition]...rare single gene disorders that give rise to schizophrenia...[and]...a tractable MFT model of a limited number of polygenes (3, 4, or 5) each with a 'subcomponent effect' on schizophrenia" can be fitted into the MFT (McGue and Gottesman 1989:456-457).

The strength of this strategy is that it allows one to remain committed to the MFT model, which is empirically strong but hard to investigate, while justifying molecular research into schizophrenia since there are a number of other co-existing varieties of schizophrenia which are easier to investigate. The mixed model presented as an alternative to the MFT is not supported by the authors (McGue and Gottesman 1989:457).

The authors note that there is a popular division between familial versions of psychopathology, and sporadic forms (where there is assumed to be no inherited component, with causation due to environmental factors), and present information which undermines this assumption. Using MZ twin rates from a study by Fischer they suggest that:

"Relatively low rates of schizophrenia are expected among the offspring of discordant MZ twins if discordance among the genetically identical parents is due largely to environmentally induced phenocopies" (McGue and Gottesman 1989:459-460)\textsuperscript{119}.

The assumption is that the difference between the identical twins is because one has a wholly environmentally induced type of schizophrenia (hence phenocopy) while the other, not exposed to the same environmental factor, does not develop it. And neither do

\textsuperscript{119} Phenocopies are conditions similar to schizophrenia but which arise from a different cause, for example drug misuse.
the children of either twin, since the cause of the schizophrenia is environmental rather than genetic. McGue and Gottesman then present the following table:

"Schizophrenia and schizophrenia-like psychosis in off-spring of discordant twins"

<table>
<thead>
<tr>
<th>Parent status</th>
<th>Number</th>
<th>Affected</th>
<th>MR%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monozygotic sample</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected twin</td>
<td>14</td>
<td>1</td>
<td>10.0±9.0</td>
</tr>
<tr>
<td>Unaffected twin</td>
<td>24</td>
<td>4</td>
<td>17.4±7.7</td>
</tr>
<tr>
<td>Dizygotic sample</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected twin</td>
<td>13</td>
<td>1</td>
<td>8.3±7.6</td>
</tr>
<tr>
<td>Unaffected twin</td>
<td>52</td>
<td>1</td>
<td>2.1±2.1</td>
</tr>
</tbody>
</table>

Note- Affected gives the total number of offspring affected with either schizophrenia or a schizophrenic-like psychosis. MR gives the estimated lifetime morbid risk of being diagnosed as schizophrenic.

from McGue and Gottesman 1989:460

McGue and Gottesman admit that the small size of the sample limits the conclusions one can draw, but suggest that that data in this table support the concept of a widespread genetic component to schizophrenia, even when it is not expressed (McGue and Gottesman 1989:460). The offspring of both the MZ twins have a similar rate of schizophrenia (represented in the MR column), and both rates are comparable to the risk to the offspring of a schizophrenic parent (9.4%). The rates for the offspring of the DZ twin are significantly different, with the children of the affected twin having a higher risk than those of the unaffected (McGue and Gottesman 1989:460).

The authors draw the conclusion that this is because:

"the expression of schizophrenia depended upon both an inherited genetic diathesis, which was transmitted regardless of whether the diathesis was phenotypically expressed, and exposure to environmental stressors, to which the twins are differently exposed" (McGue and Gottesman 1989:460).

In many ways this is a restatement of Gottesman and Shield's (1976) point, that the construction of this 'genetic baseline' presents the genetic liability to schizophrenia as the main requirement for schizophrenia aetiology. Although the environmental stressors are needed for schizophrenia to develop, it is the genetic diathesis which is ever-present, just needing the correct trigger. Alternative phrasing, with the environmental stressors occurring in cases where there is not the requisite genetic 'background' but having their effect when it is present, is not presented. One should also note that such results, while
they might serve to explain discordance in MZ twins, do not account for 'spontaneous' schizophrenia, unless it is implied that it is merely a less common version of the familial genetic factor. The authors seem to assume that what holds for schizophrenia in twins also holds for schizophrenia in single persons (but then that is one of the underlying assumptions of twins studies as a whole).

In their 1993 review, Kendler and Diehl review the likelihood of schizophrenia being caused by a single gene, concluding that "schizophrenia differs from the classic Mendelian disorders in at least four crucial ways". These differences are: the lack of full penetrance; the existence of phenocopies; schizophrenia's relative frequency (and heterogeneity); and the lack of distinct diagnostic boundaries between affected and unaffected individuals (Kendler and Diehl 1993:271). The distancing of schizophrenia from Mendelianism avoids accusations of simplification and ignorance of empirical reality. To subtly construct schizophrenia in terms of geneticization, one has to distinguish it from less sophisticated visions of genetic disease.

The authors follow this discussion of schizophrenia as a single gene disorder with a section outlining segregation analysis\(^{120}\) (including the work by McGue and Gottesman 1989) suggesting that although the results are "rather inconclusive", most evidence supports some form of multifactoral model since "it appears unlikely that the distribution of schizophrenia is due to the effect of a SML\(^{121}\) (Kendler and Diehl 1993:271). Yet however strongly schizophrenia is constructed as a multifactoral (or mixed) genetic disorder, a back door is always left open to allow single major genes some role in its aetiology:

"lack of evidence for schizophrenia should not be interpreted as strong evidence against the possibility that such 'major' genes exist in a subset of families" (Kendler and Diehl 1993:271).

---

\(^{120}\) Segregation analysis uses large pedigrees or families of affected individuals, but looks at the disease phenotype, rather than genetic markers involved.

\(^{121}\) SML = 'Single Major Locus' model of disease inheritance. Synonymous with McGue and Gottesman's GSL.
This strategy acknowledges the empirical reality and complexity of schizophrenia genetics and the limitations of the methods of molecular analysis used to investigate them. It also permits continued investigation using the same techniques. The authors have presented information suggesting that schizophrenia is not inherited in a Mendelian fashion, yet they admit that the main method used to investigate the molecular genetics of schizophrenia is linkage analysis which "was developed originally for simple Mendelian traits" (Kendler and Diehl 1993:271). If one expects solid, wide-ranging information on the molecular genetics of schizophrenia, then one is apt to be disappointed (as the rest of this review article shows). But if one is seeking some form of genetic association with schizophrenia, then one solution is to use linkage analysis but allow for the existence of a rare, Mendelian version of the disorder. Such a strategy enlists the results of genetic research without them having to refer all instances of schizophrenia.

When Kendler and Diehl discuss the concept of the genetic baseline, they address Tienari's 1991 study which is the largest adopted-away study conducted, and which presents information which at first glance seems "highly significant" (Kendler and Diehl 1993:265). Of the 361 families looked at (index and control) there were 15 psychotic adoptees. Of these, 13 (of 178) were offspring of schizophrenic mothers, and 2 (of 178) were of control mothers. But these adoptees were diagnosed as psychotic rather than strictly schizophrenic; only 7 of the 13 index adoptees were actually schizophrenic\(^\text{122}\), with both the control adoptees being diagnosed as schizophrenic. The authors state that "the prevalence of schizophrenia is also significantly greater in offspring of index mothers...than in offspring of control mothers" (Kendler and Diehl 1993:266-267). The obvious question concerns the relevance of the rate of psychosis to the schizophrenia rate. It would suggest that there is a link between general psychosis and schizophrenia, and is a presentation of the schizophrenia spectrum in all but name (see the discussion earlier in this chapter). The issue of the spectrum was not raised in the 1989 article but it is discussed directly by Kendler and Diehl, and as at the beginning of this chapter, its

\(^{122}\) of the others, 2 had schizophreniform disorder, 2 had delusional disorder and 2 had bipolar illness (Kendler and Diehl 1993:265).
importance in the debates surrounding twin and adoption studies is mirrored in its role in the molecular debates. The main importance of the Tienari (1991) paper is that:

"This adoption study has also examined the role of familial-environmental factors in the etiology of schizophrenia and found a substantial correlation between the functioning of the adoptive family and the psychiatric outcome in the adoptee" (Kendler and Diehl 1993:266).

Such a finding resists the narrative of enlightened geneticization because it presents an identifiable, repeating environmental factor and contradicts data from twin studies already covered earlier in the review which claimed that "familial environment makes little or no contribution to the liability for schizophrenia" (Kendler and Diehl 1993:265). The most obvious way to defend against such findings is simply to cast doubt upon their validity by reversing the cause-effect implied in the correlation:

"However, most of the families were evaluated when the adoptees were well into adult life. Thus this observed correlation...could also be due to disturbed adoptees creating disturbed families" (Kendler and Diehl 1993:266).

This kind of 'throw away' dismissal is reminiscent of many of the objections to the twin and adoption studies, and shows how both sides in a scientific controversy adopt similar strategies (cf. Myers 1990a:214-238 on the use of irony in the Sociobiology controversy).

In Moldin and Gottesman's 1997 article, the section "Gene-Environment Interaction" suggests that the environmental factors that might increase liability to schizophrenia "include nonspecific stressors, obstetrical complications and illicit drug use". But they moderate this by claiming that "the predictive power of these factors for a schizophrenia phenotype...is low" (Moldin and Gottesman 1997:548). When addressing the results achieved by Tienari and colleagues in the Finnish adoption studies Moldin and Gottesman, like the previous review, admit that this research "found evidence for gene-environment interaction" (Moldin and Gottesman 1997:548). The type of environmental factor which was found to be important was "Communication deviance in adoptive parents based on projective test results" but the authors dismiss this as "a nonspecific environmental factor commonly found in many families". The summary of the Tienari results is phrased as "genes controlling sensitivity to the environment" (Moldin and Gottesman 1997:548). This reinforces the idea of a genetic 'baseline' in schizophrenia, with the environmental factors, nonspecific and vague, merely layered on top.
Finally, this section debates possible models relating to genetic and environmental risk factors. First, the 'additive model' supposes that increases in risk from environmental stressors affect those with high and low-risk genotypes alike. In short, environmental and genetic risk factors operate separately (Moldin and Gottesman 1997:548). The alternative model, 'genetic sensitivity', specifies genetic control of the sensitivity to environmental risk factors; those with higher genetic risk are more sensitive to environmental factors. This second model offers a reduced role for environmental factors in comparison to the 'additive' one, which allows a degree of independence for non-genetic factors; there is always the possibility that a multitude of environmental stressors could cause schizophrenia in a genetically low risk individual. But the 'genetic sensitivity' model ensures that environmental stressors are only of relevance when high-genetic risk is also a factor. Moldin and Gottesman cite research into depression which follows this model, but admit that there is no evidence for either of these models in the case of schizophrenia, since "a careful assessment of putative environmental risk factors...has not been done" (Moldin and Gottesman 1997:548). Despite this lack of evidence, the authors clearly prefer the second, genetic sensitivity, because:

"Such a model will likely permit a more accurate understanding of the etiology of schizophrenia, in which genetic and environmental risk factors interact in a complex way" (Moldin and Gottesman 1997:548).

Such a model also limits the role of these environmental factors in a way the first, additive model does not. The use of the comparison with depression clearly depends on the schizophrenia spectrum for credibility.

**Responsibility and Caution**

As one of the strategies used, caution deflects criticism of the narrative, that it is over-enthusiastic and guilty of genetic hype. In the 1993 review article, the section on linkage analysis is a detailed and persuasive account of the difficulties faced by those looking for a putative genetic marker for schizophrenia. The authors "again emphasize the special challenges". Schizophrenia cannot be seen as a "simple disorder" (Kendler and Diehl 1993:271), making linkage studies "qualitatively and quantitatively more difficult" (Kendler and Diehl 1993:273). The qualitative changes are required because the method has to be altered to be effective and quantitatively because of the sheer size of the
samples required in such a complex case. Kendler and Diehl present their 'Table 5' which suggests the numbers of subjects needed to produce reliable results.

<table>
<thead>
<tr>
<th>Penetrance</th>
<th>0.5</th>
<th>0.6</th>
<th>0.7</th>
<th>0.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>47</td>
<td>43</td>
<td>40</td>
<td>34</td>
</tr>
<tr>
<td>0.9</td>
<td>61</td>
<td>56</td>
<td>51</td>
<td>44</td>
</tr>
<tr>
<td>0.8</td>
<td>76</td>
<td>71</td>
<td>64</td>
<td>56</td>
</tr>
<tr>
<td>0.7</td>
<td>99</td>
<td>93</td>
<td>84</td>
<td>73</td>
</tr>
<tr>
<td>0.6</td>
<td>137</td>
<td>126</td>
<td>114</td>
<td>99</td>
</tr>
<tr>
<td>0.5</td>
<td>196</td>
<td>180</td>
<td>160</td>
<td>140</td>
</tr>
<tr>
<td>0.4</td>
<td>300</td>
<td>277</td>
<td>246</td>
<td>213</td>
</tr>
<tr>
<td>0.3</td>
<td>522</td>
<td>483</td>
<td>434</td>
<td>370</td>
</tr>
<tr>
<td>0.2</td>
<td>1106</td>
<td>1045</td>
<td>922</td>
<td>794</td>
</tr>
<tr>
<td>0.1</td>
<td>4359</td>
<td>3824</td>
<td>3550</td>
<td>2994</td>
</tr>
</tbody>
</table>

Note: $\alpha$ is the proportion of families in which the schizophrenia-predisposing gene is linked to the marker.
(based on Kendler and Diehl 1993:272)

This table shows the intuitively obvious trend that the higher the penetrance (i.e. the stronger the gene's effects), the fewer the number of families required to detect linkage.

The figure $\alpha$ is inversely proportional to the degree of heterogeneity present in schizophrenia. The optimistic view that schizophrenia is homogeneous (i.e. single gene, $\alpha=1$) with 60 percent penetrance means that only 43 families (301 individuals)\(^{123}\) would be required to ascertain linkage (Kendler and Diehl 1993:272). But, assuming the same penetrance:

"More likely, the single most common gene responsible for schizophrenia is present in only 50 or 30 percent of high-density families, so that required samples would amount to 180 families (1,260 individuals) or 483 families (3,381 individuals)"
(Kendler and Diehl 1993:272).

Should the heterogeneity of schizophrenia be even higher, with the most common gene accounting for only 10 or 20 % of these families, then "sample sizes required to detect linkage by current methods may be unobtainable with realistic resources" (Kendler and Diehl 1993:272-273). Similar sample sizes are required if one assumes that each high-density family has a small number of genes (four or five) instead of just one (Kendler and Diehl 1993:273).

\(^{123}\) Assuming an extended family of seven.
The authors then run through the history of linkage analysis in schizophrenia and discuss the case of the alleged chromosome five linkage. Following the observation that a young man and his uncle, both diagnosed schizophrenic, also had a form of distorted facial features, analysis showed that they each had a chromosome 5q11.12-q13.3 trisomy. As a result:

"In 1988, Sherrington et al. reported linkage in seven high-density pedigrees...between schizophrenia-related phenotypes and two DNA markers in the region of the 5q trisomy" (Kendler and Diehl 1993:273).

This study was striking for a number of reasons:

- the pedigrees were very large and of extremely high density for schizophrenia;
- there was very strong evidence in favour of the linkage between the DNA markers and the phenotype;
- the evidence was strongest when a broad diagnosis was used (including phobia, depression and alcoholism) and finally;
- the strong linkage was found in all of the pedigrees, implying more homogeneity than expected (Kendler and Diehl 1993:273-274).

Kendler and Diehl then present a table, which lists 45 other studies subsequently carried out, 11 of which looked at the same area of the genome. "Attempts to replicate this finding have been uniformly negative" (Kendler and Diehl 1993:274-275) including new studies carried out by the same research team that reported the initial results. The authors ask:

"How can we explain the initial strong positive evidence of linkage, followed first by uniformly negative results in all independent studies and then by an inability of the original investigators to replicate their own work?" (Kendler and Diehl 1993:276).

Having assessed, and rejected, the various kinds of error that could have led to this result the authors are forced to conclude that "we remain in the unsatisfactory position of having no adequate explanation for this puzzling and discouraging series of events" (ibid.).

What purpose does this discussion serve in the narrative of enlightened geneticization? There is a certain over-eagerness on the part of the authors to highlight the problems and mistakes in the molecular genetics of schizophrenia. Such 'over cautious' strategies work
at two levels. The first denotes responsibility and reasonableness on the part of the authors. In tune with their claim to be outlining a 'third way' between the extremes of the molecular pessimists and evangelists, such responsible strategies accept how difficult the molecular investigation of a complex disorder such as schizophrenia is. They deflect claims that the authors are 'hyping' the prospects of linkage results too much (cf. the debate over the CF gene) and not accepting the mistakes that have been made in the past. By 'coming clean' on the problems with the 5q13 trisomy, the authors present this review as a sober, solid and objective piece of work. The second level at which these strategies work is more prospective. By setting the hurdles so high, no one should be surprised if linkage results are not forthcoming for a great deal of time. With the problems of such studies openly acknowledged, this strategy prevents critics of this research from claiming that 'no results' means that there are 'no stretches of DNA that can be associated with schizophrenia'. This is clear in the conclusion to this section:

"no replicated positive findings have yet emerged from efforts to locate individual genetic loci that influence the liability to schizophrenia. This is not surprising, nor should it be too discouraging" (Kendler and Diehl 1993:277).

In 1997, when Moldin and Gottesman address linkage studies (Moldin and Gottesman 1997:548-551), they spend over one side explaining the specifics of the level of proof required to suggest linkage. Such proof is expressed as a logarithm of the odds (LOD) ratio of that linkage occurring, with the criterion for Mendelian disorders set at a lod of 3. This score means that the observed data are 1,000 times more likely to occur if there is linkage, than if there were none (Moldin and Gottesman 1997:549). But schizophrenia is not a Mendelian disorder, and the authors point out the apparent contradiction upon which linkage studies for polygenic disorders are based:

"Despite the inability of the single locus model to explain the familial aggregation of schizophrenia, investigators have conducted traditional linkage studies under single locus model assumptions" (Moldin and Gottesman 1997:548-549).

The contradiction is heightened if we consider the 'use of history' strategy that suggests that schizophrenia is genetic because of the family, twin and adoption studies. Yet it is these same studies which produce the models proving that schizophrenia is not a single locus model and thus cannot be adequately investigated using linkage analysis. Avoiding this contradiction requires a higher standard of proof from the linkage studies of
polygenic disorders than one would need with Mendelian ones. Thus Moldin and Gottesman adopt a scoring system devised by Lander and Kruglayak which describes a lod score of 1.86 as "Suggestive", 3.30 as "Significant" and 5.10 as "Highly Significant". They then assess actual linkage studies by these criteria, and find them lacking. The abstract to this review states that "the strongest evidence implicates chromosomes 6 and 8, but these linkages are not yet confirmed" (Moldin and Gottesman 1997:547). This an apparent understatement since in the article itself, Moldin and Gottesman agree that the chromosome 6 has "the strongest evidence thus far for linkage in schizophrenia" but also that correction of these results for different models had reduced their strength (Moldin and Gottesman 1997:550).

In addition, "Nonreplications of chromosome 6 linkage have been reported" (reference to four studies) and "the markers implicated [sic] by the studies reporting suggestive evidence...lie within a very large chromosomal region that contains many genes" (ibid.). As for chromosome 8, which was also mentioned in the abstract, two studies gave evidence classed as "suggestive" for linkage, but the results from one of these would be down-graded to "less than suggestive" if corrected for "multiple transmission and disease models". There has also been at least one nonreplication study for this region (ibid.). Summarising the results for these two regions, the authors conclude that "the magnitude of the statistical evidence and the existence of nonreplication demonstrate that these are clearly not confirmed, convincing findings" (ibid.). As for the rest of the genome, "Reported linkages to other chromosomes (3, 5, 9, 20, 22) are less compelling" (Moldin and Gottesman 1997:551).

The presentation of such a large amount of negative evidence is perfectly in keeping with the narrative of enlightened geneticization. The concept of genetic causation in schizophrenia is insulated from doubt by the 'fall-back' position that the twin and adoption studies show that there is a strong genetic component in schizophrenia aetiology. Since the debate on these studies has, for these authors at least, reached closure they never have to question this fact. This support means that Moldin and Gottesman can move from what might be seen as depressing linkage results to outlining
the US National Institute of Mental Health's 'Genetic Initiative'. Launched in 1989, this aims to:

"create a national resource of demographic, clinical, and diagnostic data, as well as DNA extracted from immortalized cell lines, that would be available to the scientific community" (Moldin and Gottesman 1997:551).

The implication is that access to the large numbers of subjects that such a resource will give will produce linkage analysis results. It is not the methodology that is flawed or the assumptions underpinning it, but only the numbers of subjects that research has used.

Moldin and Gottesman briefly review association studies (see next section for explanation) without presenting any results from this research, and move onto the section "Advances in Genomic Technology" (Moldin and Gottesman 1997:551-552). Again there is no presentation of results directly related to schizophrenia. Instead the authors outline "a new revolution in molecular genetic techniques" that will help the large scale analysis of the genome (Moldin and Gottesman 1997:551). One example is that of parallel sequencing using DNA arrays or genechips. Another is "New robust statistical techniques that rapidly extract inheritance information provided by many genetic markers and permit estimation of disease gene location" (Moldin and Gottesman 1997:552). They even cite "the successful cloning of a lamb from the cells of an adult sheep" explaining that:

"Large numbers of identical copies of animals for genetic studies may be generated more efficiently and used to develop epigenetic and neurodevelopmental models of processes aberrant in schizophrenia" (Moldin and Gottesman 1997:552).

The speculative enlistment of these cutting edge technologies advances the narrative by implying that molecular results for schizophrenia genetics have almost been achieved despite the limitations of "traditional linkage studies"; these new techniques will lead to advances. This has echoes of the comments in the 1987 review on linkage studies that, despite the obvious difficulties of studying a complex non-Mendelian disorder:

"there is considerable optimism about the future usefulness of such markers in detecting major gene effects and resolving problems of heterogeneity in schizophrenia" (Gottesman, McGuffin and Farmer 1987:41).

As mentioned earlier, Moldin and Gottesman are concerned that 'misconceptions' surrounding the genetics of schizophrenia be exposed and corrected. In the section
"Minimising Misconceptions" (Moldin and Gottesman 1997:553-554) they discuss the "false step in the path of discovery" that was the 1988 chromosome 5 result, stating that it was "welcomed with considerable optimism and insufficient scientific criticism" (Moldin and Gottesman 1997:544). One of the reasons they give for this acceptance is "because localization of a locus was 'confirmation' that schizophrenia was in fact a 'biological' and not a 'psychosocial' disorder" and thus undermines the stigma associated with having schizophrenia (ibid.). The reason for the quotation marks in this statement are not clear. Perhaps the most likely explanation is to cast doubt on the idea that there is any useful distinction to be made between genes and social causes. This is in keeping with the enlightened position which is firmly in favour of polygenic, multifactoral explanations, and for which old fashioned nature/nurture distinctions are too crude. It also casts doubt on the idea that linkage analysis provides 'confirmation' of anything. This may be a cautious warning about the strength of such studies in the case of complex disorders, but it can also be seen as a reinforcement of the original twin and adoption studies. For many of the researchers in this field, the earlier, non-molecular work has already confirmed the biological nature of schizophrenia causation. They don't need molecular results to confirm what, for them, is already a fact.

This caution is repeated when the authors put forward proposals for avoiding embarrassing mistakes (like the chromosome 5 affair): they recommend the use of multiple markers for any one chromosomal region; maintenance of a "healthy skepticism about initial linkage reports"; the need for low-key publicity about non-confirmed results; and rigorous peer review for published results. Finally, they press for continued education about linkage analysis and psychiatric genetics for science writers and other disseminators of information, so that the public to lawmakers can "become informed consumers and critics" (Moldin and Gottesman 1997:554).

Return of the Schizophrenia Spectrum

The schizophrenia spectrum played a major role in the early, non-molecular research into schizophrenia genetics. Its role in modern research is as important as that in twin and adoption studies and is most explicit in Kendler and Diehl's (1993) article. Following their review of the family, twin and adoption studies, the authors turn to the section
called "Boundaries of the 'Schizophrenia Spectrum' ", where they test four different hypotheses on the transmission of schizophrenia:

- only liability to typical schizophrenia is transmitted;
- liability to schizophrenia and schizophrenia-like personality disorders is transmitted;
- liability to all nonaffective psychosis (e.g. schizoaffective disorder, delusional disorder and atypical psychosis) is transmitted and;
- liability to all psychiatric illness is transmitted (Kendler and Diehl 1993:267).

Reviewing work in this area, the authors state that levels of schizotypal personality disorders and paranoid personality disorders (SPD/PPD) are higher in relatives of schizophrenics than in controls, proving the second hypothesis, namely that: "family liability to schizophrenia can, at least in part, express itself as a predisposition to a certain set of schizophrenia-like personality traits" (Kendler and Diehl 1993:267). There are some doubts over the third hypothesis (liability to nonaffective disorders), but:

"The preponderance of the evidence...supports the validity of the third hypothesis that the family vulnerability to schizophrenia may manifest itself...as a predisposition to more broadly defined psychosis" (Kendler and Diehl 1993:269).

The authors do not support the final hypothesis, that "the risk for all major forms of psychopathology ought to be increased in relatives of schizophrenia" (ibid.). The "familial liability to schizophrenia appears to be neither extremely narrow nor extremely broad" and thus the concept of the schizophrenia spectrum is reified (Kendler and Diehl 1993:270). The construction of the spectrum is carefully worded, and throughout this section, the authors use the term 'familial liability' rather than 'genetic liability'. The two are clearly distinct since earlier in the review, the authors state that:

"Family studies suggest that schizophrenia strongly aggregates in families. Twin and adoption studies continue to suggest that genetic factors account for most of this familial aggregation" (Kendler and Diehl 1993:266, emphasis added).

Therefore, genetic and family effects are not one and the same thing. This makes perfect sense, especially in the light of the results of the Tienari study. Of the seven studies used to examine the second hypothesis ('liability to schizophrenia and schizophrenia-like

---

124 It also has echoes of Gottesman and Shields' definition of schizophrenia so that it was neither too wide nor narrow to exclude genetic evidence (1976a:375).
personality disorders’), only two are adoption studies while the remaining five are family studies; and family studies do not provide the sort of information with which to separate genetic from environmental effects.

Clearly this discussion does not present evidence that supports a genetic basis to the schizophrenia spectrum, but it may encourage this interpretation. One example of this is in the discussion of the second hypothesis, where it is stated that:

"the familial liability to schizophrenia is expressed, at least in part, as a predisposition to a set of schizophrenia-like or schizotypal personality traits" (Kendler and Diehl 1993:266).

The use of the word 'predisposition', a word often preceded in the literature by the word 'genetic', could easily imply an inherited factor linking these disorders to an extent which might not be supported by the family and adoption studies. At the beginning of this section, the authors state that "An accurate definition of the affected phenotype is crucial in any genetic investigation" (ibid.), and that is what this section is, an exercise in accurately defining the schizophrenia phenotype. It then continues, that it is helpful "to use genetically informative designs to determine" associated disorders. In addition, "Such an endeavour is also of interest because it can provide insights into the nature of that familial liability and hence into the etiology of schizophrenia itself" (ibid.). This section could be seen to blur the meaning between the words 'family liability' and 'genetic predisposition' so that the former stands as a shorthand for the latter, potentially reinforcing the concept of the schizophrenia spectrum as a genetic entity.

By presenting the concept as neither the narrowest nor the broadest possible hypothesis, the authors present the spectrum as a balanced, reasonable proposition (in much the same way that their view of the use of molecular methodology was presented as between two extremes). The next section starts by asking: "If schizophrenia is strongly influenced by genetic factors, the next logical question is, What kind of factors?" (Kendler and Diehl 1993:270). This implies that the previous section presented evidence that genetic factors play an important role, strengthening the slippage from the familial factors to genetic ones.
The next section of the 1993 review addresses the alternative molecular methodology of 'association studies'. While linkage focuses on the cosegregation of genetic markers and disease phenotype within a family, association studies examine large numbers of unrelated disease sufferers and compare the frequency of individual genes (Kendler and Diehl 1993:277). One obvious advantage of an association study is that it is far easier to find large numbers of individual schizophrenics than it is to find high-density schizophrenia families. Since association studies are looking for specific genes (or alleles) rather than the larger areas of genome covered by linkage analysis, they are reliant upon linkage disequilibrium and the close location of the target alleles on the genome. Thus association studies are limited to 'candidate genes' which are suspected of playing some form of aetiologic role in schizophrenia. For example, studies have found association with the porphobilinogen deaminase (PBGD) gene which causes a form of porphyria, a mental disorder which has a number of similarities to schizophrenia (Sanders et al. 1991). But linkage analysis for this gene has shown that between 60 to 80 percent of high-density families do not carry it, so the evidence is equivocal (Kendler and Diehl 1993:278). Association studies provide another means by which to investigate the genetics of schizophrenia, but they also support enlightened geneticization, in that they neatly complement linkage analysis by offering a form of investigation which doesn't involve multiplex families, which relates the genetic research to actual diseases.

Again we can see the importance of the schizophrenia spectrum in this narrative. It is far easier to see association studies contributing to schizophrenia research if the whole concept of schizophrenia genetics is built of the idea that 'bordering' diseases share a genetic aetiology (although it should be noted that porphyria is not normally included in the schizophrenia spectrum). The introduction of association studies means that diseases such as porphyria, which were normally described as schizophrenia 'genocopies' now become an important research resource (Propping 1983:4). This technique allows the enlistment of diseases normally excluded in discussion of schizophrenia, highlighting the position of the phenocopies, still excluded from schizophrenia classification.
7. The Appeal of Enlightened Geneticization

The subtle nature of the narrative of enlightened geneticization is clear if we consider criticism of molecular genetic research and how it often seems to miss the point about the recent discourse of schizophrenia genetics. In her 1990 critique, Boyle mentions linkage analysis, and is typically acerbic about the chromosome 5 results, particularly secondary reporting of them (Boyle 1990:158). She notes that in the discourse used, the:

"conflicting results reflect the complexity of the search and the possible heterogeneity of 'schizophrenia'...[and that]...the twin and adoption studies...have been uncritically cited in support of the belief that schizophrenia has a genetic basis" (ibid.).

Both these points are valid, and contribute to the narrative as has been shown in this chapter. Boyle's criticisms of the simplification of linkage results by the media (in this case a Nature editorial and commentary: Lander 1988) would probably be shared by Moldin and Gottesman who make clear their doubts about non-experts' abilities to handle the complex nature of this information.

Portin and Alanen, in their second critique of schizophrenia genetics (Portin and Alanen 1997b), spend two sides (pages 74-75) reviewing association studies between schizophrenia and specific, identified markers (especially Dopamine genes) and suggest that, as yet, there is no strong evidence for association with any specific marker (Portin and Alanen 1997b:75-76). This is perfectly in keeping with the narrative. Their review of "Studies involving the whole genome or large parts of it" cites many of the same studies as Moldin and Gottesman and leads to the conclusion that "it appears that the hypothesis of a single major gene as a risk factor is unlikely" which, as they note, is "in agreement with the viewpoints expressed previously by many psychiatric geneticists" (Portin and Alanen 1997b:76). Here they cite four papers, two by McGue and Gottesman, one of which is the 1989 review article. Portin and Alanen suggest that Lander and Kruglyak's requirement of a lod score of equal to or greater than 3.6 is a prerequisite to suggest significance in linkage; Moldin and Gottesman make it the requirement for serious consideration in their review\(^\text{125}\). They suggest that schizophrenia phenotype diagnosis is

\(^{125}\) Although both Portin and Alanen and Moldin and Gottesman cite the same article, the latter use the lod score of 3.30 to denote significance, which is more accurate. The lod score of 3.6 is mentioned by Lander and Kruglyak, but refers to siblings and half siblings only rather than full family studies (Lander and Kruglyak 1995:244, table 1).
ambiguous, that the disorder may in fact be "a heterogeneous group of diseases rather than a single disease" and that "The use of over-simplified hypotheses of genetic aetiology of schizophrenia...have lead to reductionistic research strategies and goals" (Portin and Alanen 1997b:77). All these are uncontroversial for the narrative of enlightened geneticization.

Portin and Alanen conclude by stating that they "favour an integrative approach to the study of schizophrenia" and that "there is a need for holistic perspectives" in schizophrenia research. But it is the last sentence of the article which displays the weakness of their critique: "However reductionistic views still prevail in the field" (Portin and Alanen 1997b:77). These authors have failed to make clear what the 'reductionistic views' are. They claim that their conclusions regarding the paucity of molecular results are in agreement with 'many psychiatric geneticists' and this is not controversial. Their descriptions of the limitations of molecular linkage analysis are, if anything, less powerful than Moldin and Gottesman's or Kendler and Diehl's, if only because they have less space to devote to it. Even their preference for a multifactoral model with "many non-specific minor genes which act together" over a oligogenic one (where "two or three genes together lead to a predisposition to schizophrenia") is perfectly in tune with the narrative of enlightened geneticization (Portin and Alanen 1997b:76). Although the tone of Portin and Alanen's article suggests that they are aiming to challenge a dominant, reductionistic position in psychiatric genetics, the information they use and the assumptions they accept unquestioningly suggest that they are also using this narrative.

Part of the strength of the narrative of enlightened geneticization then, is that it appeals to those who ostensibly oppose its core theme, the dominant role of genetic factors in schizophrenia causation. Boyle does not accept the constraints of the narrative, but this is mainly because her opposition to genetic research in schizophrenia is simply a small part

---

126 It is ironic that to support this point Portin and Alanen cite a paper co-authored by McGuffin who in a 1994 article suggests that schizophrenia is solely caused by genetic factors and that any apparently environmental input is actually due to random variations in gene function and structure (McGuffin et al. 1994).
of her broader opposition to the idea of schizophrenia as a coherent disease category. This co-option of opponents is similar in many ways to debates about the genetics of diabetes, where all participants, even those who are opposed to genetic explanations for diabetes causation, use a classification system which is geneticized.

8. The Future of Enlightened Geneticization

I have claimed that the narrative of enlightened geneticization is the dominant story told about genes and schizophrenia. It is not clear that it is dominant within schizophrenia discourse as a whole. Any reading of the clinical literature on this disease suggests that there are large gaps which are inadequately addressed in these review articles. The presentation of schizophrenia as a developmental disorder is largely ignored, as is research into the medical imaging of schizophrenics' brains (Schultz and Andreasen 1999). Perhaps this lack of a 'bigger picture' is understandable; these reviews are explicitly focused on the role of genetics in schizophrenia aetiology. Yet the failure to put genetic explanations within a broader framework is perfectly in keeping with the narrative of enlightened geneticization, which avoids detailed, specific non-genetic causes if at all possible.

The success of the narrative of enlightened geneticization is dependent upon scientific results. At the moment it simply maintains the idea that schizophrenia can be (and should be) seen as a genetic disease. But how long could such ideas be sustained without empirical evidence? Although the narrative has built-in expectation of delay as one of its strategies, with competing stories challenging for supremacy (the neuro-developmental one for example), it is not clear that the narrative of enlightened geneticization has indefinite license to persuade. Of course, what counts as adequate 'empirical evidence' in support of the narrative is contestable. What lod score would count as indicating linkage? How many families do researchers need, to gather enough genomes to compare? It seems unlikely that in a disease with a history of such controversy surrounding genetic explanations, geneticization will be accepted without resistance.

If schizophrenia is geneticized 'properly' -i.e. a link made to an identifiable piece of DNA-is there any way of telling whether it will resemble cystic fibrosis or diabetes in its
classification? Will it expand or will it divide? The apparently heterogeneous nature of schizophrenia genetics might lead us to expect a number of different genes, all of which have different effects and interact differently in different people. It seems likely that schizophrenia would divide into various subtypes. The effect of such geneticization on patients is hard to judge. The instinctive assumption that the 'gene for schizophrenia' will automatically lead to stigmatization of sufferers needs to be resisted (Turney and Turner 2000). Such research may in fact release families (and particularly parents) from the 'blame' of causing the onset of schizophrenia but despite caution about assuming stigmatization, Turney and Turner note that:

"At present, schizophrenic individuals have a wide range of attitudes to the diagnostic label for their condition...Many [schizophrenics] share the attitude that the label is, in some degree, negotiable. They may well feel that this negotiability is lost if the diagnosis is backed with a genetic warrant. Some will then conclude that their fate is inescapable, and that science has painted them into a diagnostic corner" (Turney and Turner 2000:20).

The geneticization of schizophrenia is, in ethical terms, currently an unknown quantity. What is needed is far more research into the effect of geneticization on patients, not just in terms of changing disease classification and material situation (e.g. insurance or job status), but also in personal socio-psychological terms.

\[127\] Of course the ground is already laid for this with the schizophrenia spectrum encompassing so many different symptoms.
CHAPTER 7: REINVENTING GENETICIZATION

What conclusions can we draw about the process called 'geneticization'? What lessons can we learn from examining the diseases that have undergone this process? What are the broader implications of this research, beyond interest in the new genetics, in Science and Technology Studies as a whole? At the outset of this thesis, I stated my research aims which were: to analyse the concept of geneticization, and give it more definition and clarity; to examine the role of review articles in the construction of facts and the settling of debates within medical science; and finally to confirm the value of discourse analysis as a means of investigating issues in science and technology.

1. SYNOPSIS

This thesis started from a position of empirical doubt. I introduced the concept of geneticization, its similarities to other terms (such as genetic essentialism) and suggested that it had become part of the conventional wisdom for many who write on the new genetics and society. Using the work of Celeste Condit, I then highlighted the empirical and theoretical difficulties of the geneticization critique, including the need to relocate it within molecularization. I gave examples of how other authors have used it and the problems of their approach. Finally I suggested that if the concept of geneticization was to be of real use in the social studies of genetics, further research was required to detail: how it worked as a process, the variations across diseases and the impact of the process on medical discourse. I then set out to show how this might be done.

In my discussion of the theoretical background (chapter 2) of this thesis, I placed my research within the context of both the sociology of medical knowledge, and traditional philosophy of medicine. Then followed a discussion of methodology (chapter 3), which reviewed debates surrounding discourse analysis and the rhetoric of science, the role of popularisation and review articles in scientific exposition, and the issues and difficulties surrounding the interpretation of written texts. In the case studies that followed (chapters 4, 5 and 6) I presented what I have labelled 'narratives of geneticization'.

248
In cystic fibrosis, we looked at variations in the medical discourse either side of the discovery of the gene responsible for CF. The narrative had changed from a clinical discussion of the treatment to a review focused on the reclassification of the disease along genetic grounds. Different strategies were employed to construct the CF continuum and the 'narrative of expansion' that acts to draw in neighbouring conditions and reclassify them as cystic fibrosis, on the strength of genetic information. Finally I discussed the impact that this reclassification has had on a number of patients.

The diabetes case study focused on the work of Andrew Cudworth in the late 1970s. It presented an analysis of two of his review articles that attempted to reclassify diabetes along genetic grounds. This attempt was only partially successful as a reclassification since it took another 20 years before the clinical classification of diabetes officially stopped. But as a form of geneticization, it succeeded, linking the condition diabetes to a specific stretch of DNA. This chapter continued by tracing the path of the 'narrative of division' constructed here into current clinical usage.

The schizophrenia case study differed from the previous two in that despite the best attempts of molecular geneticists, no firm link has yet been made between this condition and a specific piece of DNA. But the 'narrative of enlightened geneticization' constructed around schizophrenia shows what happens when controversy attaches to geneticization. By a detailed review of previous debates in schizophrenia research, I presented the strategies which have constructed a narrative where non-genetic influences are subtly undermined and schizophrenia is reclassified in terms of genetic causation.

A number of conclusions can be drawn about geneticization from this empirical research: geneticization is heterogeneous; it can occur to hereditary diseases and by stealth; geneticization is driven from research rather than clinical need; and it can affect clinical practice without the introduction of a genetic test. But before I deal with these conclusions in detail, I will address possible objections to my research.

2. Objections
The most obvious complaint about my research is that although my 'problematisation' of geneticization is based on the fact that it is not clear how broadly this process is
occurring, this thesis does not settle the debate between Lippman and Nelkin on one side, and Celeste Condit on the other. Yet to raise this as an objection is to miss the aims of my research. As I pointed out in chapter 1, since I chose to study diseases causally linked to particular genes and hence already 'geneticized' (even if tenuously in the case of schizophrenia) my research cannot assess the scope of geneticization across medicine. In my research, I was less concerned with 'how widely is geneticization happening' and more, given a rigorously worked out definition, 'how does it happen?' The case studies show that there is a difference between the way that geneticization takes place in cystic fibrosis and diabetes, and the way in which it is happening in schizophrenia. This admission of difference matters. It is the first step on the way to using geneticization as an analytic tool.

Before making broader claims about geneticization and beyond, there is a need to defend my approach from a number of other objections. Some of these come from among those who analyse the role of genetics in society. Those researchers who have adopted the geneticization critique as a framework for analysing genetics may object to my research on a number of grounds. First, they may be unconvinced by the narratives constructed in each of the case studies. I cannot defend my interpretations other than to point critics at the review articles they are drawn from, and ask for alternative narratives. Each narrative was drawn from significant texts that are easily available for analysis, and the onus is on those who are unconvinced by the stories I am telling to present more convincing alternative explanations. As I suggested in chapter 1 with the example of criminalisation, the examination and redefinition of a concept does not mean that it is invalid. My research does not undermine critical use of the concept of geneticization or the aims of such work. I see my case studies as adding depth and colour to an otherwise sketchy concept, but not undermining the value of that concept or the work that has gone before. Work on criminalisation suggests that acknowledging the difficulties and criticisms of a concept does not necessarily invalidate it. It is perfectly possible to complain about the under-defined nature of criminalisation while at the same time accepting its validity as a research tool and a means to generate future research: "Future research should sort out the circumstances under which the routes to criminalization involve different factors" (Hollinger and Lanza-Kaduce, 1998: 326-327). The same is true of geneticization.
**The realist objection**

From another standpoint, some brands of realist would take exception to the mid-range constructivism that my research has at its core. My position suggests that differences between disease classification, and how geneticization occurs, are only due in part to the genetics of these diseases. They are also caused by the social, institutional and (most pertinently for my work) discursive differences that are unique to each condition. Why does cystic fibrosis expand and diabetes divide? Why do schizophrenia researchers employ a narrative of enlightened geneticization to defend their use of genetic explanations? The reason lies in the way in which scientists try to persuade others that their approach to particular diseases is the right one.

A realist might state that the differences between disease classification systems are a result of the differences between the genetic causes of the diseases. Cystic Fibrosis is a monogenic disorder, the 'classic' case of a recessive Mendelian disease. Diabetes is far more complex, and apart from some rare subtypes (the MODYs) can in no way be seen in Mendelian terms. The genetic component to CF causation is a single locus and a variety of different alleles; expansion seems an obvious result. The genetics of diabetes involves a number of different alleles at a number of different loci, seemingly far more amenable to division.

Yet wider comparisons quickly undermine this argument. True, it is easier to make a case for expanding a disease classification where the cause is a variety of different mutations at the same place. But clearly such diseases also undergo division. Muscular Dystrophy is a case in point. That both Duchenne and Becker varieties of muscular dystrophy are caused by different alleles at the same locus has been known since 1984 (Roland 1998). Although Becker MD is usually described as a 'milder form' of muscular dystrophy, it is clinically and nosologically distinct from the more severe variety, Duchenne (Kingston et al. 1984). If genes fix nosology then Becker muscular dystrophy would have long since ceased to exist, absorbed by the nosological expansion of Duchenne. The fact that this has not happened, that this allelic heterogeneity still exists, forces the realist to rely on social explanations. For example 'expansion is the norm, prevented in this case by
external, contingent factors. This is not a situation that sits well with strong realist claims. Even within the bounds of strict realism, the realist is confronted by the fact that allelic heterogeneity is not restricted to diseases such as Duchenne and Becker which are broadly similar in their symptoms. In other cases, "allelic mutations of the same gene result in totally different syndromes" (Roland 1998:124). To suggest that sharing the same gene locus implies a shared disease classification is to ignore the medical evidence. To strictly reclassify along these 'genetic realist' lines, would require a significant upheaval of current medical classification systems. These differences seem more a case of different scales, quantitative rather than qualitative. The CF locus is 250 kilobases long. It is not a single point on the genome, but a stretch of DNA. Different mutations at different points along this stretch cause CF (however it is defined). The loci for diabetes are on chromosome 6, a stretch of DNA. The differences are only of scale.

**Why not 'types' of geneticization?**

What follows are the conclusions that can be drawn about geneticization as a process, based on the three case studies. I am not suggesting that there are different types of geneticization. I am merely 'sketching in' different facets of one process. While it might be tempting to claim that in cystic fibrosis there is a 'expanding type of geneticization', and in diabetes a 'dividing type of geneticization', it is not clear that the evidence supports such categorical divisions, or that such distinctions are analytically helpful. What is clear is that within each of the case studies, a different narrative can be constructed, about a different disease, highlighting different aspects of the same process. This is part of the value of using the concept of 'narrative' to analyse discourse; it does not require that there are no alternative, competing descriptions of a topic. Indeed, with each narrative focused on a particular disease, one should expect that there will be differences.

**3. Filling in the blanks: the characteristics of geneticization**

**Geneticization is heterogeneous**

In the light of my case studies, this is, perhaps, an obvious point. But the initial writings on geneticization (from Lippman and others) are not at all clear whether this process was
anything other than monolithic and homogeneous. Claiming that it is complex, disjointed and varied has important consequences for the future study of geneticization. It allows the researcher to focus on how geneticization operates in individual situations and conditions, permitting depth of description. It also makes broader study harder, since drawing conclusions across disparate conditions will become difficult. Of course, the straight-forward definition of geneticization I use does not preclude quantitative surveys, which aim at discovering how many conditions have been 'geneticized' in the past five years (for example). But as I have shown in this research, the problems lie less in whether a condition has been subject to geneticization. Rather, given my definition, my interest has been in how that process has occurred, and how claims on its behalf are made and rendered persuasive. And this is harder to discern from a survey.

**Geneticization occurs to hereditary diseases**

This is another obvious point, but there is a distinction between hereditary diseases and geneticized ones. Clearly, the classification system for the hereditary disease cystic fibrosis underwent change in the light of molecular genetic information. Geneticization altered this disease, even though it was already thought of in terms of Mendelian genetics. This highlights the need to see geneticization in the broader context of molecularization. The changes in CF classification make sense in terms of linkage with the protein molecule CFTR and the numerous alleles responsible for changes in its structure and function. If we do not see geneticization as part of a broader historical movement towards molecular explanations, then the changes in the classification system become more opaque. They are more likely to be brushed away with the excuse that: CF has always undergone classificatory changes. There was once a debate about intestinal disorders as symptoms. Then they too were absorbed into the CF continuum (for example, Stern 1997). This suggests that rather than emasculating geneticization as a tool for critiquing genetic technologies the context of molecularisation allows it to criticise those changes that are genuinely harmful by disadvantaging patients, both financially and socially.
Geneticization can occur by stealth

It is important to note that despite my criticism of the initial ideas surrounding geneticization, there are elements that are highly accurate, if a little under-defined. One of these is Lippman’s point that geneticization does not have to involve wholesale genetic determinism to have its effect. This is clearly the case in diabetes. The effect of genetic information on classification discussions in the late 1970s was significant. It reified the division into at least two diseases, it edged out classifications based on age-of-onset, and put pressure on other clinical classifications, such as insulin dependence. The fact that victory over the clinical was not declared until the late 1990s should not diminish our view of how effective the geneticization of diabetes has been. It has redefined how diabetes is viewed in the clinical and research setting. It has altered membership of that group of people known as ‘diabetics’. It has also redefined what counts as a genetic disease in the clinical and research setting, by providing an example for those who preach the need to understand the genetics of complex diseases. The narrative of division is now the standard way to talk about diabetes.

Geneticization is driven from research rather than clinical need

Although geneticization intervenes on the clinical plane through disease classification, it derives its impetus from the concerns of the research community. Such tensions that do exist over this are usually not explicitly acknowledged in the review articles examined; only one of the CF review articles openly discussed this (Stern 1997). In the case of diabetes, the tensions only really came apparent in conversation with senior clinicians involved in the debates surrounding classification. In schizophrenia, complaints about research driven perceptions of disease do arise, most obviously as part of Rose, Lewontin and Kamin’s broader critique.

Geneticization affects clinical practice (classification) without introducing a test

This relates to the idea of ‘geneticization by stealth’ but clearly reflects upon the claim of the original geneticization critique, that the process introduces new technologies into the clinical encounter. Perhaps the geneticization critique has focused on the clinical use of technologies because the early empirical work that inspired Lippman was on the effect of
technologies on pregnancy. The idea of geneticization thus gained a technological ‘bias’ in its concerns, heightened by the fact that it clearly focuses, not just on how we talk about people but also what we do to them. This emphasis on the ‘doing’ side of geneticization leads us to expect that as a process, it will open the door to particular technologies and encourage their use in a clinical setting. It may be that in the future, genetic testing technologies will become common-place in the clinical encounters of cystic fibrosis, diabetes and schizophrenia. But to focus on this is to ignore how changing talk about diseases already effects what happens to people. The classificatory changes wrought by the introduction of genetic aetiologies have definite impact upon those people who are subsequently reclassified. To reclassify someone as now suffering from a particular genetic disease (e.g. CBAVD patients as suffering from CF) is to change their life, either in terms of their self perception, or in terms of their health insurance rating. It does something to them.

For this reason, it seems sensible to begin to erase the distinction earlier conceptions of geneticization drew between how we talk about people and what we do to them. We need to broaden our view as to how geneticization affects peoples’ lives as a whole, rather than becoming too focused on the arrival, or delay, of specific technologies. The geneticization that occurs ‘upstream’ of the clinical situation can have just as significant an effect on people’s lives. Technologies are good ‘rules of thumb’ as to the presence of geneticization in particular circumstances, but they should not lead us to assume that geneticization lies in the availability of genetic tests or gene therapy. The 1998 British Diabetic Association guidelines on genetic testing for Type 1 diabetes concluded that due to the complexity of factors, “Genetic screening for Type 1 DM...cannot be currently recommended”. Attempts to identify high risk individuals were described as “not helpful” (Avery et al. 1998: 643). But the lack of viable genetic screening for diabetes has not stopped it undergoing over twenty year’s worth of geneticization.

**Geneticization in a controversy moves from implicit to explicit claims**

In comparing diabetes with schizophrenia, one can see how geneticization differs between a condition in which such a process is relatively uncontroversial (diabetes) and one where the controversial nature of the claims being made shapes the entire narrative.
There are other obvious differences of course. Diabetes underwent geneticization in the mid-1970s when the association with the HLA genotype was made. Schizophrenia currently hovers on the cusp, with all links to specific stretches of DNA contested, and no firm correlation established. Yet despite this, my analysis shows how the narrative constructs schizophrenia in terms of genetic causation, using historical results, undermining non-genetic explanations, and presenting itself as a restrained, moderate approach. These steps are required because of the intense criticisms levelled at studies into the genetics of schizophrenia. Diabetes researchers were under no such pressure, so the narrative for this disease is quite different. The narrative of division present in diabetes is explicitly focused on disease classification; in schizophrenia, the debate has yet to get that far. Although the schizophrenia articles do discuss the nature of the schizophrenia spectrum, there is no attempt to push the debate further and propose a reclassification of the disorder along genetic grounds. Clearly the current view of schizophrenia genetics, with its wide selection of different genes all contributing aetiologically, displays the potential for classificatory division as in diabetes. One might look out for strategies from the narrative of division, except this would be to assume that if such a narrative were to develop in schizophrenia, it would do so in the same way as it did in diabetes. It is hard to claim that this must be the case. There is no reason to expect that if the classification of schizophrenia splits into sub-diseases at some stage in the future, that the same discursive strategies will be used as those in the reclassification of diabetes twenty years ago. As noted above, the controversial nature of schizophrenia has meant that its narrative has taken a very different shape to that of either CF or diabetes.

Geneticization as a narrative

A broader issue to consider is of geneticization itself as a narrative. Throughout this thesis, the focus has been on the narratives of geneticization, which are essentially about particular diseases. Although my concern is with the process as a whole, the focus of this research has been those conditions that undergo the process of geneticization. But above and beyond stories about diseases, there is the question of what sort of story do they tell about geneticization itself? If we view geneticization as a narrative, what sort of narrative is it? At one level, we can talk about an idea, defined in the early 1990s and arising out of empirical research and feminist theory; about how this idea was used until
it was challenged and subject to analysis; and about how it subsequently came to be described in a number of different ways. Yet this account conforms only to what Myers designated as 'plot', the surface order of events in sequence (Myers 1991). But what is the 'story' of geneticization about? As explained in chapter 3, I have not used the story/plot distinction in this thesis, and perhaps an alternative way to broaden our thinking about geneticization is in terms of a meta-narrative. The research in this thesis adds colour and depth to a concept that has until now been under-described. However many articles there are decrying the geneticization of breast cancer or detailing the role geneticization plays in Cypriot society, what fails to come across is the nature of the process itself. My meta-narrative of geneticization is one of increasing character. It is a narrative about revealing the different facets of a previously one dimensional process.

An important point is whether the narratives of geneticization I present are really there in the texts I analyse, or are fictions imposed to aid interpretation. At one level it does not matter since the importance of the narratives lies in what they tell us about geneticization and this is not dependent on their status. I have tried to remain true to Stanley Cavell's advice (from chapter 3) that what matters with interpretations is seeing them through as far as they will go. There are alternative interpretations (narratives) that can be made of the articles I analyses; this is necessarily true. But my interpretations have been seen through with rigour and detail, and as such they are meant to be persuasive. The narratives are true since they are made up of claims, themes and concepts present in the texts. They are fictions in that there are other orderings of these excerpts which might tell different stories.

**Broader Conclusions**

*Review articles as popularisation*

One of the aims of this thesis was to explore the idea that we should see scientific review articles as a form of popularisation, and in turn explore the role that such popularisation can play in scientific debates. The analysis of the case studies shows how the articles studied conform to the genre of review articles. They do not present new findings and they offer broad, sweeping overviews of particular disorders. In terms of Shinn and Whitley's continuum of scientific exposition, the review article edges towards the
popularisation end (Shinn and Whitley 1985). Yet the fact that review articles are popularisations does not detract from their influence on scientific discourse. It was in review articles that the CF continuum was constructed, reclassifying CBAVD as a form of Cystic Fibrosis. It was in review articles that the reclassification of diabetes along genetic grounds took place, and where schizophrenia was constructed as a genetic disease despite the lack of physical evidence tying the condition to a specific gene. The role of the review article in interpreting the empirical evidence, marshalling the arguments and undermining the opposition, is crucial. It is not that research articles fail to do these things; research articles are not intended to do these things. It is only in the review article that authors gain the space and license to enlist a wide range of sources to support their interpretation. Review articles serve to reconstruct the history of a discipline or disease, smoothing out irregularities such as controversies and errors, and present science as smooth progression. Review articles are widely read by specialists and those outside of particular disciplines, and thus provide a large platform to broadcast one's position. The research in this thesis shows the role of review articles in supporting a particular scientific position, and in turn thus makes a case for the importance of popularisations in scientific discourse. Popularisations do not just make known a view which is already widely held in the scientific community to the broader publics. Popularisations can also act as the means by which these views are constructed.

**Narratives and discursive strategies**

A secondary aim of my research was to extend the use of Myers' type of discourse analysis, and to apply it to a process such as geneticization which has broader social implications beyond scientific concerns. At a simple methodological level I have shown the value of this approach and how it highlights factors which are of ethical concern (how medical science constructs disease), but which tend to be over-looked in traditional philosophical discussions of the new genetics. Discourse analysis focusing on texts should be added to the armoury of researchers interested in the social and ethical implications of genetics.
I have also shown how looking at scientific debate in terms of narratives brings out themes that consistently run through a discourse over time. I have taken the analysis one step beyond Myers' goal, which was to prove the socially constructed nature of scientific facts, and have shown how a process such as geneticization is in turn constructed. This research has shown how useful narratives are as a way of thinking about scientific discourse. They allow one to present a variety of its aspects without suggesting that they do not form part of a unified whole. The three narratives of geneticization presented in this thesis overlap with each other, contradict each other (expansion vs. division) and are certainly not exclusive. By talking about the diseases in terms of narrative, one can convey the fact that these disease classifications move through time, that they are not static and immobile.

I have also used the idea of 'discursive strategies' to show how each narrative of geneticization is constructed. As noted in chapter 3, one problem with a term like 'strategy' is that it implies a degree of conscious thought behind it. It thus becomes embroiled in the issues that surround interpretation and author intentionality. As in Greg Myers' work, I hope that my own research has avoided the issue of author intentionality, although not solved it. My research is open to the criticism that I have not proved that my interpretation is the one intended by the authors. For example, I have not 'proved' that I.I. Gottesman intends to present schizophrenia as a genetic disease, only that review articles written by him (and others) tend to do this. I cannot prove that Andrew Cudworth wanted to geneticize diabetes and reclassify it along genetic grounds. He is dead; interviewing him is not an option. But having spoken to people who knew him when he was working, I do not think that this is an unreasonable interpretation. Perhaps if, like Greg Myers, I had access to my authors' first drafts, rejected articles and funding applications, I would be able to tell a different story. But such speculation is irrelevant to my research. I have chosen to focus on the written, published record, the texts that are finalised and non-negotiable. I have chosen to show how disease classifications are constructed in the finished article. What the authors wanted to say is not especially important. What matters to my research is what they did say. In this context, the idea of discursive strategies does make sense. Divorced from authorial intentionality, they are a useful tool to analyse texts.
Future research

My work opens up a number of possible future directions for research. Further comparative case studies can be carried out, looking at other conditions and seeing how geneticization takes place. Interesting examples might be PKU, the muscular dystrophies and alcoholism. Away from strictly medical discourse, another area of research might be to look at how the narratives I have outlined in the thesis are communicated to the broader publics. What are the factors affecting the up-take of geneticized classification systems by the newspapers and other media?

A sceptic might cast doubt on how widely geneticization will take place across medicine, and suggest that the three diseases studied in this thesis are the exception rather than the rule. One reply to this is to point them in the direction of a new technology which the pharmaceutical industry is claiming will become common-place in the clinical encounter: pharmacogenomics. This is the study of the genetic differences between people that lead to variations in drug effectiveness, speed of action and even adverse reactions. The pharmaceutical industry expects that sooner or later, many drugs will be prescribed on the basis of a genetic test, to determine the dosage and nature of the drug required. This is already possible in the case of cancer (Shelling 1997), Alzheimer's' disease (Andersen et al. 1999) and asthma (Drazen et al. 1999). One theme that is strong in recent agenda setting articles on this topic (e.g. Roses 2000, Wolf, Smith and Smith 2000) is the way in which pharmacogenomics will redefine diseases in terms of the genes which cause them, rather than the phenotypic signs and symptoms. Pharmacogenomics is one way in which geneticization of disease may become common place. This is therefore an important area in which to apply the ideas that have been developed in this thesis.
BIBLIOGRAPHY


Anderson et al. (1999) "Current and Future Applications of Pharmacogenomics" New Horizons 7(2):262-269


Avery et al. (1998) "British Diabetic Association Guidelines on Genetic and Immune Screening for Type 1 Diabetes Mellitus" Diabetic Medicine 15:643

Bartley M. (1990) "Do we need a strong programme in medical sociology?" Sociology of Health and Illness 12(4):371-390


Chmiel J.F. et al. (1999) "Pitfall in the Use of Genotype Analysis as the Sole Diagnostic Criterion for Cystic Fibrosis" *Pediatrics* 103(4):823-826


Concannon P. et al. (1998) "A second-generation screen of the human genome for susceptibility to insulin-dependent diabetes mellitus" *Nature Genetics* 19:292-300


Condit C. (1999b) "How the public understands genetics: non-deterministic and non-discriminatory interpretations of the 'blueprint' metaphor" *Public Understanding of Science* 8:169-180


Conrad P. "A mirage of genes" *Sociology of Health and Illness* 21(2):228-241


Conrad P. and Weinberg D. (1996) "Has the gene for alcoholism been discovered three times since 1980? A news media analysis" *Perspectives on Social Problems* 8:3-24


Cudworth A.G. (1978) "Type I Diabetes Mellitus" *Diabetologia* 14:281-291


Department of Health *The Genetics of Common Diseases: A second report to the NHS Central Research and Development Committee on the new genetics* (London: HMSO)


Docter J.M. (1981) "Unmet challenges in Cystic Fibrosis" in Warwick W.J. (ed.) *1000 Years of Cystic Fibrosis; Collected Papers presented at an International Conference on Cystic Fibrosis at the University of Minnesota* (Minneapolis: University of Minnesota)

Drazen et al. (1999) "Pharmacogenetic association between ALOX5 promoter genotype and the response to anti-asthma treatment" *Nature Genetics* 22: 168-170


Franklin S. (1988) "Life Story: the gene as fetish object on T.V." *Science as Culture* 3:92-100


Froguel P. and Velho G. (1999) "Molecular Genetics of Maturity-onset Diabetes of the Young" *Trends in Endocrinology and Metabolism* 10(4):142-146


Geller G. et al. (1998) "Decision-making about breast cancer susceptibility testing: how similar are the attitudes of physicians, nurse practitioners, and at-risk women?" *Journal of Clinical Oncology* 16(8):2868-2876


Hugh-Jones P. (1955) "Diabetes in Jamaica" *The Lancet* October 29:891-897


Jurdant B. (1993) "Popularization of science as the autobiography of science" *Public Understanding of Science* 2:365-373


Keen H. (1985) "Limitations and problems of diabetes classification from an epistemological point of view" pp.31-46 of Vranic M., Hollenberg C.H. and Steiner G.
(eds.) Comparison of Type I and Type II Diabetes: Similarities and Dissimilarities in Etiology, Pathogenesis, and Complications (New York and London: Plenum Press)

Keen H. (1986) "What's in a Name? IDDM/NIDDM, Type 1/Type 2" Diabetic Medicine 3:11-12


Kerr A. (forthcoming) "(Re)Constructing Genetic Disease: the clinical continuum between cystic fibrosis and male infertility" Social Studies of Science


Kety S.S., Rosenthal D., Wender P.H., Shulsinger F and Jacobsen B. (1975) "Mental illness in the biological and adoptive families of adopted individuals who have become schizophrenic. A preliminary report based on psychiatric interviews" in Fieve R.


Kingston et al. (1984) "Localisation of the Becker muscular dystrophy gene on the short arm of the X Chromosome by linkage to cloned DNA sequences" Human Genetics 67:6-17


Lawrence R.D. (1951) "Types of Human Diabetes" *British Medical Journal* February 24: 373-375


Lerman C. et al. (1998) "What you don't know can hurt you: Adverse psychologic effects in members of BRCA1-linked and BRCA2-linked families who decline genetic testing" Journal of Clinical Oncology 16(5):1650-1654


Lock M. (1994) "Interrogating the Human-Diversity Genome Project" *Social Science and Medicine* 39(5):603-606


Medawar P. (1964) "Is The Scientific Paper fraudulent ?" *Saturday Review* 49 (1 August 1964)

Merz B. (1989) "Capture of Elusive Cystic Fibrosis gene prompts new approaches to treatment" *Journal of the American Medical Association* 262(12):1572-1573


Millar J.K. et al. (2000) "Disruption of two novel genes by a translocation co-segregating with schizophrenia" *Human Molecular Genetics* 9(9):1415-1423


Myers G. (1990c) "Sociology of Science Without the Sociology" Social Studies of Science 20:559-63


Myers G. (1992) "'In this paper we report...': Speech acts and Scientific facts" *Journal of Pragmatics* 17:295-313


National Diabetes Data Group (1979) "Classification and Diagnosis of Diabetes Mellitus and Other Categories of Glucose Intolerance" *Diabetes* 28:1039-1057


Norman A.P. (1981) "Cystic Fibrosis and Normality" pp.85-89 in Warwick, W.J. (ed.) *1000 Years of Cystic Fibrosis; Collected Papers presented at an International Conference on Cystic Fibrosis at the University of Minnesota* (Minneapolis: University of Minnesota)


Propping R. (1983) "Genetic disorders presenting as 'schizophrenia'. Karl Bonhoeffer's early view of the psychoses in the light of medical genetics" *Human Genetics* 65:1-10


Roberts L. (1988a) "The Race for the Cystic Fibrosis Gene" Science 240:141-144


She J. (1996) "Susceptibility to type I diabetes: HLA-DQ and DR revisited" Immunology Today 17(7):323-329


Sheppard D.N. and Ostedgaard L.S. "Understanding how cystic fibrosis mutations cause a loss of Cl- channel function" Molecular Medicine Today July 1996, pp.290-297

Sherrington R. et al. (1988) "Localization of a susceptibility locus for schizophrenia on chromosome 5" Nature 336:164-167


Sorenson J. (1973) "Counselors: A self portrait" *Genetic Counseling* 1:29-34


Stern C. (1973) *Principles of Human Genetics* (San Francisco: Freeman)


Weatherall D.J. (1998) "How much has genetics helped?" *Times Literary Supplement* January 30, pp.4-5


Woolgar S. (1981a) "Interests and Explanation in the Social Study of Science" *Social Studies of Science* 11:365-394


Zola I.K. (1975) "In the name of health and illness: on some socio-political consequences of medical influence" *Science and Medicine* 9:83-87

Zola I.K. (1977) "Healthism and Disabling Medicalization" in Illich I. (ed.) *Disabling Professions* (Marion Boyers)
