# Chemical dissection and the ethics of preclinical science

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## Summary

It is my contention in this paper that the bioethical landscape is closely linked to the model of health and disease with which we work, as scientists or as medical practitioners. The Human Genome Project is the logical extension of the dissection process, which has constituted the history of medical science.

It is already revealing an ethical minefield which may result in harming the very people we seed to serve. Adoption of more holistic models of health and disease would counter the reductionist drift into eugenics, and would place thepratice of medical science more humbly within a wider context, as the servant of the patient, rather than as the sole arbiter of health and social acceptability.

### Résumé

*Il* est dans mon objectif de montrer combien les problèmes de bioéthique sont liés à la situation de la santé et de la maladie à un moment déterminé. En fait, la génétique est la suite logique de la science de la dissection qui est à la base de notre médecine actuelle. C'est en soi déjà une mine de problèmes éthiques.

L'approche globale de la santé et de la maladie risque d'entraîner un réductionisme inquiétant et une dérive vers l'eugénisme. Il s'agit donc d'adopter une attitude plus réservée et plus au service du malade et surtout ne pas se placer en arbitre de sa santé.

In order to access the dominant paradigm which informs medical science in our time, I propose first to examine the history of pathology.

The development of scientific pathology since the Enlightenment has necessarily followed the invention of ever more sophisticated techniques of investigation. The serious study of disease first employed anatomical dissection as its main method, elevating the importance of the post-

Gordon McPhate MB, ChB, MA, MTh, MSc, MD University of St Andrews, School of Biological and Medical Sciences, Bute Medical Building St Andrews, Fife KY16 9TS, Great Britain mortem examination, and yielding a scheme of morbid anatomy which was both descriptive and deductive.

This activity is essentially a comparative one, identifying the 'abnormal' by comparison against the reference frame of the 'normal'. Such comparison of the real with the ideal recalls the Theory of Forms of Plato's philosophy, and relies upon the conviction that anatomical and physiological knowledge are fundamentally important for the study of medicine ; and in the seventeenth century the impetus and support for this view largely came from the members of the newly established Royal Society. Support for this approach was not without challenge. The very respected physician Thomas Sydenham insisted that clinical experience, freed from a theoretical framework of knowledge, was the real tutor of Medicine for the practitioner. For him, only those observations made in a specific case were relevant, and yielded the facts of the case, which in turn would give rise to hypotheses about the case. The only medical school for Sydenham was the apprenticeship to life itself! Sydenham doubted the ability of a systematic approach to Medicine which would consistently make connection between causes and effects, such that remedies might be rationally prescribed (1).

Of course, the comparative approach prevailed, and with the advent of microscopy interest turned away from the appearances of body organs and parts in disease, towards the organisms that cause disease, and the responses of body cells to disease. In the nineteenth century the bacteriology of Koch and the cellular pathology of Virchow were founded on the new method of microscopy, a natural extension of anatomical dissection.

The subsequent history of pathology has continued to be informed by the comparative approach, but has been marked by a shift away from anatomical dissection towards chemical The mechanisms of disease dissection. processes are probed by chemical methodologies and techniques, at the ultimate molecular level of biological organisation. The chemical analysis of body fluids has generated chemical pathology, which in a comparative manner helps clinicians distinguish between disease and nomality, and purposes to identify a range of reliable and specific disease markers. The powerful combination of animal models of disease with chemical techniques has generated both experimental pathology and immunology.

The progress of pre-clinical science is well imaged in a painting by Gerrit Dou, which hangs in the Kunsthistorisches Museum in Vienna. It is entitled Der Artz, "the Doctor". Here the physician is not at the bedside of a patient, but rather in a kind of laboratory, attended by an onlooking acolyte. Here the physician is in search of understanding and wisdom, depicted as a consecrating priest at the altar of medical discovery. Discarded at the side of the altar is the well-worn and now unnecessary missal of an anatomical text; but in the central position is an elevated chemical retort flask. From patient to laboratory; from anatomy to chemistry.

But in our own time the progression of pathological investigation, by means of chemical dissection, has led to the analysis of human DNA and has brought about a true molecular pathology. The Human Genome Project, which seeks to map the whole human genome, the whole human blueprint, has been described as biology's Apollo Moonshot . It represents the Holy Grail of a grand unified theory of human disease. And the theory is simpy stated: 'errors' in the genome are either predictive of disease or are directly causative of it.

The diagnostic basis of chemical dissection of DNA is no different from anatomical dissection of the body, requiring a simple check of the deviation of the individual patient from the established 'normal' or 'normal range' and thus identifying disease. Again, it is essentially a comparative process, bringing us to the threshold of a mechanistic, determinist and materialist approach to the diagnosis and treatment of patients.

The Comparison Model of Health and Disease has much to commend it and it has been the presupposed framework within which the science of pathology has developed, and indeed within which the whole of medical science has developed. It relies upon clear definition of the 'normality' of the individual as established by reference to the gold-standards of anatomy, physiology, biochemistry and DNA. It is objective and analytical, following well-established chains of cause and effect. Essentially the comparison model is a definition of disease by means of error detection, in which the real is compared with the ideal, the imperfect with the perfect. For each disease marker or variable under study it ultimately locates every patient either on, or outside, a frequency distribution of the population by which normality is defined.

The Comparison Model of Health and Disease predisposes us to favour a particular ethical stance in relation to the practice of medicine. The simplistic view of disease which emerges is a physical one and an individual one. It becomes increasingly easier mentally to 'reduce' human beings to molecules. Indeed the greatest moral danger of the comparison model is reductionism: insofar that psychology is reduced to behaviour, and behaviour is in turn reduced to physiology, and physiology is reduced to biochemistry, and biochemistry is finally reduced to molecular genetics.

No-one is a more brazen exponent of reductionism than Sir Francis Crick who has said this in a now infamous declaration :

'You, your joys and your sorrows, your memories and your ambitions, your sense of personal indentity and free will, are no more than the behaviour of a vast assembly of nerve cells and their associated molecules.'

A reductionist chain can be discerned in the history of pathology. Morbid anatomy was superseded by histopathology, which in turn was superseded by chemical pathology and then by molecular genetics. Ideas of 'progress' in medical science effectively deny the continued importance of mechanisms and understanding at the higher levels of biological organisation, and assert the supreme value of study at the molecular level alone. The pattern of research grant awards in medical science mirrors this 'progressive' attitude.

At the extremes, psychology and morbid anatomy may be regarded as 'nothing but' the outworkings of molecular genetics. Therefore, most significantly, unwanted behaviour and disease are to be understood simply as disordered genes and DNA errors : that is the stark conclusion of the "nothing buttery" advocate! (2) (3).

The endpoint of the process of convergence which I have described is the arrogantly conceived and commercially motivated Human Genome Project itself, which will bring to focus the ethical problems of the mechanistic, materialist determinism which is the thesis of the card-carrying reductionist ; which thesis is inimical to any concept of human dignity still regarded by many as the only proper basis for the practice of Medicine itself.

Pertinent here are the newfound concerns of the co-author of the medical genetic revolution, James D.Watson :

7 have spent my career trying to get a chemical explanation of life, the explanation of why we are human beings and not monkeys. Still, I sometimes find myself moved to wonder, is it ethical for me to do my job ? A kind of backlash against the Human Genome Project has cropped up from some scientists... The acquisition of human DNA information has already begun to pose serious ethical problems... For that reason, we are putting more than 3 percent of the Genome Project money into an Ethics Program ; and we will put more into it if we find that it needs more'. For behind the reductionist stands the awesome spectre of Eugenics; such that culture defines Pathology, and the distinction is blurred between Gene Therapy and Gene Improvement!

The "comparison" model of health and disease, and the reductionism which has emerged from it, has produced a blinkered understanding of the complex mystery of human being. The philosopher of science, Peter Medawar, urges that the scientific enterprise is only valid and successful within its own sphere of operation, and that it ought to be humbly aware of its own limitations: that there are certain kinds of worthwhile metaphysical and teleological questions relating to the reality and truth of the human condition which Science is not competent to answer. For example, attempts to define and study human personhood or human consciousness are doomed to failure, because these conceived states of being relate at least in part to metaphysical questions outside the proper remit of science (4).

A realistic humility about the limits of Medical Science will recognise that objective study cannot elucidate or negate the reality of the subjective and its possible importance in the disease process.

The Human Genome Project will make us all sick, or potentially sick in one way or another. It will brand the human condition as essentially pathological. II will explode the myth of normality: the ideal that perfectly structured and perfectly functioning human beings actually exist.

Although the comparison model of health and disease has achieved much through anatomical and chemical dissection, and has been the dominant paradigm for medical education, it is not without increasingly serious rivals. I wish to focus on two of these, but in preface let me emphasise that in both models coventional medical science still has a central place : but ultimately it cannot provide the total view or provide all the answers !

The "contextual" model of health and disease places the individual in the context of a life-cycle and of a culture and of a community; recognising the fundamental importance of relationships, and the influence of the environment. The "contextual" model is an holistic one, so that 'health' is defined in terms of physical, mental and social well-being. Some might wish to add spiritual well-being. In this model, patient communication is every bit as important as the measurements of the medical scientists.

Within medical education at the present time, there is a perceptible paradigm shift away from the "comparison" model towards the "contextual" model; a shift which has recently been endorsed and accelerated by publication of the recommendations document Tomorrow's Doctors, by the General Medical Council. Connectedness, not normality, is the key to health.

Finally, I wish to draw attention to a model of health and disease suggested by the work of the medical philosoperGeorgesCanguilhem, which I will call the 'Homeostasis Model' (6).

Again, this model is in part a subjective and holistic one. Its keynote is 'adaptability in the face of crisis': such that 'health' is defined in terms of the ability to respond and adapt to disturbance, whether arising internally or externally, whether affecting physical or mental or social well-being. Thus sickness might be seen as an opportunity to demonstrate health, rather than as the effect of disease; and a severely disabled person might be legitimately defined as healthy! In this model resilience, not normality, defines health. Our medical professional obsession with normality is well illustrated from the text of the successful play Equus in which a troubled psychiatrist tries to understand and treat a troubled teenager who has blinded some horses for no apparent reason. The psychiatrist has a dream in which he sees himself as a Greek High Priest who slaughters young victims at a sacrificial altar, in order to appease the God of Normality. The dream convinces him that it is the priesthood which is sick, and that the medical model based on normality is wrong.

In conclusion, I draw attention to another painting representing Medicine humbled by the mystery of what it means to be human. It is by Frans Van Mieris and also hangs in the Kunsthistorisches Museum in Vienna. It is officially entiled Der Besuch Des Arztes, 'The Doctor's Visit'. But its intended title Liebeskrank or 'Love-sickness' is much more revealing!

A physician is shown taking a woman's pulse whilst on a domiciliary visit: the physician looks efficiently dispassionate; whereas the woman looks up at the doctor with either the exhaustion of sickness or of emotion. The reductionist physician taking the woman's pulse may conjecture autonomic dysfunction of hyperthyroidism, but the wise holistic physician may discern romantic attachment rather than sickness. Indeed he himself may be the cause of her apparent illness!

The two paintings I have referred to must be yoked together if Medicine is to be practised humanely in our time. The Science and Art of Medicine must remain mutually interdependent, and neither one can remove the need for the other. At one time, the same physician could be found in the laboratory and at the bedside; symbolising in his person the inextricable connection between the Science and Art of Medicine This is no longer so, and as a result the inextricable link is under threat. In the face of human illness, Science cannot banish Art and the ethical imperative with respect to patient care and medical action stalks the Laboratory as much as the Clinic.

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