PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Introduction to Human Genetics – uncertainties and the financial implications ahead

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INTRODUCTION

Forty years ago the genetic basis of a human disease was established for the first time. This was done by Vernon Ingram in the MRC Unit for Research on the Molecular Structure of Biological Systems, in Cambridge (the predecessor of the Laboratory of Molecular Biology). He showed that sickle cell disease was due to a single amino acid change—a mutation—at a specific position in one of the protein chains of haemoglobin. This was done using certain methods of protein chemistry, then recently developed.

With the advent of more powerful molecular biological techniques, DNA sequencing and cloning, and recombinant DNA technology, genetic defects could be traced much more easily, at the DNA level, and in the last ten years or so the genetic origins of hundreds of diseases have been determined. Many of these are rather rare and not generally known, but genes associated with cystic fibrosis, muscular dystrophy, Alzheimer's disease, breast cancer and heart disease, have been identified. A distinction must be made here between those cases where the harmful mutation in the gene leads inexorably to the disease (as in sickle cell)—a straightforward Mendelian disorder—and other cases where it constitutes a risk factor (as in Alzheimer's disease) and where more than one gene may be involved (as in heart disease). I expect we shall hear more about these distinctions, and also differential susceptibility to disease and to infectious agents, at the Symposium today, and indeed one of its objectives is to provide the terminology and tools needed to understand and evaluate these complex scientific and medical issues.

Now the advances I have mentioned were almost all made by individual researchers pursuing a given disease, and the road to the identification of a gene responsible can be a long hard one. But advances are likely to be much more rapid with the steady flow of information from the human genome projects now being conducted in many countries, to map the genome (that is, to provide signposts or markers) and provide very large runs of actual DNA sequence. This will greatly facilitate the search for the locations and sequences of genes, including those involved in disease.

The immediate effect will lead to more DNA-based diagnostic tests and make them easier, and, through over-the-counter marketing, accessible to the public. Ultimately, when the functions of more genes are known, it will be possible at least in part, to determine the genetic profile of an individual, with respect to susceptibility to disease. The availability of these and related techniques must have a dramatic impact on society, and of course this has not gone unnoticed by the scientists involved in the research. Indeed, the mandate of the US Human Genome Project includes a provision to spend part of the funds on addressing the social impact of human genome research. This is known under the acronym ELSI, which stands for ethical, legal and social implications. Scholarly papers on ELSI have begun to appear, and there are, indeed, chairs on the subject in several US universities, which goes further than traditional medical or bioethics. But it seemed to us in the Royal Society that it is necessary to carry discussion on ELSI to people *professionally* concerned with the changes that the new human genetics will bring to health care, employment, insurance, education and even perhaps the doctor–patient relationship.

This Symposium is intended to be a contribution to that discussion, concentrating initially on the impact of genetic testing on the insurance industry. It provides a forum for debate. Thus, we are pleased that the Institute and the Faculty of Actuaries have joined us in this Meeting. Indeed, this particular meeting arose as a continuation of the City-Science and Technology Dialogue, initiated by my predecessor as President, Sir Michael Atiyah, who has also kindly agreed to chair this session. The organizers of the programme have, however, wisely in my view, broadened its scope, so we shall in fact be engaging with other aspects of ELSI. I am sure the Symposium will arouse the interest of the public as well as that of our legislators. After an initial refusal, the Government finally agreed to the proposal of the House of Commons Science and Technology Committee to set up a Genetics Commission. Let us hope this Symposium will provide some guidance in its implementation.

But, to return to the theme of this Symposium, one might note that obtaining genetic information is not something new in the insurance industry or in employment. A family history and some conventional medical tests do provide this to a limited degree. What has changed, and changed dramatically, is the advent of DNA-based genetic testing coupled with the very rapid expansion in knowledge of gene structure and function in relation to disease, and this is what society has to grapple with today.

Sir Aaron Klug, O.M.
President, The Royal Society

The Faculty and Institute of Actuaries were delighted and honoured by the invitation to share this Symposium, particularly after I learnt that this is the first time the Royal Society has held a joint meeting with a professional body whose members have commercial interests in the City of London.

Those of us who are here are looking forward to a lively discussion over the next two days on this topical subject of considerable public interest.

I would like to remind our members and guests that it is a source of pride for actuaries that we can trace our roots back to the point where they intertwine with the Royal Society at its foundation in 1660. On Wednesday 28 November 1660, twelve men, not without consequence in the world's history, met together to hear a lecture on astronomy from a certain Mr Christopher Wren. After the lecture, because, luckily they were men who had not permitted the serenity of professional success to allay the promptings of intellectual discontent, they came to a resolution, which I daresay had long been an intention, that there should thereupon be founded a scientific society for promoting physico-mathematical experimental learning. Two years later 'The Royal Society of London for improving natural knowledge' gained its Royal Charter and became the enduring archetype of most scientific associations, including our own.

It is of special interest to actuaries that one of those twelve men was Sir William Petty, who was, amongst other things, an economist, demographer, statistician and student of mortality. I have no doubt that if our Institute had ante-dated the Royal Society, Sir William would have been described as an actuary.

The links continued. Many early Fellows devoted time and study to the science of gunnery; actuaries have been students of mortality on the battlefield.

An extraordinary seminal paper published in *Philosophical Transactions* in 1693 by Sir Edmund Halley set about constructing a life table. He proceeded immediately to calculate some specimen present values not only of single-life annuities, but also of joint-life annuities on two and three lives, the compounding of the probabilities for which he illustrated with a two-dimensional diagram and a perspective drawing of a three-dimensional model. Price in 1769 and Gompertz in 1825 also published works in *Philosophical Transactions*, the latter being on the search for a function to express the law of mortality.

The Institute is a mere youngster compared with the Royal Society. We will celebrate our 150th anniversary in 1998 and our Royal Charter was granted nearly 200 years after the society's. As a professional body we differ in some respects from a scientific society. There are three necessary aspects to being a professional man or woman. First, in relation to our own profession, actuarial science is an applied science which is usually applied in the specialist areas of insurance and pensions but has wider applications when we consider that our basic tools are risk analysis and financial modelling. The second element is judgement. We are a practical profession that is required to advise our employers and clients on the best solutions to real problems.

Analysis and mathematics only take us so far. We have to judge how best to make certainty out of uncertainty. These two functions of applied science and judgement can variously be described as the known and the supposed, the factual and the conjectural, the deductive and the intuitive, the rational and the instinctive.

The third element is equally important. We are required to act in the public interest and must therefore live up to high ethical and professional standards. These three elements apply to each individual actuary in his or her daily work but they are reinforced by our professional bodies in the code of conduct and guidance we give our members.

It is hard to think of a better example of the need to use applied science, professional judgement and ethical standards than the subject of genetic testing. The objectives for the actuarial profession are first to ensure that our members are as well informed as possible on the facts and the information coming from genetic scientists and the medical profession so that they can exercise their professional judgement, as we do in other areas, on an informed basis. The second objective is to ensure that our members consider the ethics and fairness which insurance companies must apply, recognizing that actuaries are in a position of considerable influence over these companies. I am not just talking here about mathematical and actuarial fairness. There are social and political issues affecting the public interest that actuaries must consider as well, and in all this, and particularly in the debate at this Symposium, we must distinguish between the trusted professional role which the Faculty and Institute expect our members to live up to, and the commercial role which individual members may express when speaking on behalf of their employer.

The Symposium will be a fascinating two days and we are delighted that it is being held under the joint auspices of the Royal Society and the Faculty and Institute of Actuaries.

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