The clinical benefits of molecular medicine

Many clinicians seem to feel that, while molecular and cell biology are extremely exciting areas of basic biological research, the practical fallout that has come from these new fields, despite a lot of hype on the part of the scientists, has not altered clinical practice very much. But perhaps this should not surprise us too much. After all, Robert Koch announced the discovery of the tubercle bacillus in the 1880s. It was immediately assumed by both the medical world and the public that a cure for tuberculosis would follow overnight, an expectation that was taken up with enthusiasm by the press of the time, both in Great Britain and Germany. In the event, it was to be nearly 70 years before Selman Waxman announced the discovery of streptomycin, and chemotherapy for tuberculosis became a reality. It is a recurrent theme throughout the history of medical research that there is usually a considerable lag period before developments in the basic sciences have a major clinical application.
When viewed in historical perspective, molecular medicine has not done so badly, particularly when we remember that it is only about 15 years since the first human gene was isolated.

Apart from some of the early successes of the biotechnology industry, the most important practical application of DNA technology in the clinical world has been for the diagnosis and control of genetic diseases. DNA analysis is being applied to increasing numbers of single gene disorders and is now being used in the clinic for the prenatal detection of many of the most serious diseases of this type. In the case of the inherited haemoglobin disorders, the diseases to which these techniques were first applied, it has had a major impact on the numbers of new cases and has led to their population control in many countries. In the long term, carrier detection and prenatal diagnosis will become an option for parents at risk for having children with most of the important single gene disorders. Reports are already appearing of the first applications of gene therapy, and not just for inherited diseases. Surprisingly, this new approach seems likely to have its earliest successes in the cancer field.

Like so many areas of modern medicine, this new field is driven by technical advances. A major development, which is completely revolutionising genetic diagnosis is called the polymerase chain reaction, a technique which has already spawned several offspring. Essentially, it allows minute amounts of DNA to be amplified over a very short period of time and hence makes it possible to carry out carrier detection or prenatal diagnosis within a day or less. The DNA can be obtained from sources as unpromising as ancient bones, old pathological specimens, dried blood stains and hair roots. The power of this method is well illustrated in the paper by Cox et al. from Cambridge in this edition of the Journal. Here it was possible to make a genetic diagnosis from a small fragment of a necrotic liver that had been obtained by post mortem needle aspiration.

The polymerase chain reaction has applications right across medical practice. For example, it can be used for making genetic diagnoses from a few cells obtained from ova after in vitro fertilization, identifying genetic diseases within a few hours from small DNA samples including, remarkably, cells of fetal origin in the maternal circulation, identifying infectious agents, and defining mutations in cancer cells from a variety of different tissue sources. It can also be modified for rapid sequencing of genes and for isolating genetic markers for linkage analysis. In its short lifespan it has already changed the face of molecular medicine.

In the last few years there has been remarkable progress towards an understanding of the molecular basis of monogenic disorders and in the application of this knowledge for their population control. There has also been progress, albeit slower, towards the identification of some of the genes involved in susceptibility or resistance to some of our common killers, notably heart disease, hypertension, diabetes, and dementia. Remarkable insights have been obtained into the molecular basis of cancer and there have been some genuine success stories in the biotechnology field, in the generation of both diagnostic and therapeutic agents.

Overall, molecular medicine seems to be living up to its early promise. But don't expect too much too quickly. Recently, Victor McKusick has estimated that we will know the complete sequence of the human genome by 2015. Exciting though this prospect is, this information will not, as has been suggested by one molecular biologist, tell us everything about Man. We will, in effect, simply know the anatomy of our DNA. We shall then have the daunting task of finding out how the whole thing works. The potential of this knowledge for medical practice may be enormous. But in thinking about when it will all hit the clinic we should not forget Koch and tuberculosis, or, for that matter, William Harvey and modern cardiology.

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