

The new genetics: a challenge to traditional medicine

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Eugenics and the origins of medical genetics

In developed Western countries many chronic constitutional diseases have a genetic basis [1]. In British Columbia, one in 20 individuals are affected by genetic disease by the age of 25 and perhaps 60% in a lifetime [2]. In Britain, 14,000 infants with serious defects are born each year and many more men, women and children are at risk of being carriers of these or of later onset genetic disorders. The fear of having conceived an abnormal child leads to the unnecessary abortion of normal fetuses, and sometimes to life-long anxiety and unnecessary childlessness among those who erroneously believe themselves to be at risk. In Britain the National Health Service (NHS) has provided a uniquely favourable environment for tackling these problems by encouraging the development of medical genetics in which clinicians and laboratory scientists collaborate closely. But this happy state was not easily achieved, nor is it necessarily permanent.

Anthony Wohl in his book *Endangered lives* [3] describes the conditions of squalor and early death common in Milroy's time, and the sanitary revolution, social legislation and eventually the NHS which produced remarkable improvements in the health of the population. These improvements were opposed by proponents of social darwinism [4,5], who included Darwin himself:

... Thus the weak members of civilized societies propagate their kind . . . hardly anyone is so ignorant as to allow his worst animals to breed. [6]

They would deny medical advances and beneficial social legislation to the masses because it was judged expedient to allow the weak and sick to die. Eugenics appeared to offer a 'scientific' and more humane answer to these problems. Francis Galton, the father of eugenics, claimed that:

... what Nature does blindly, slowly and ruthlessly, man may do providently, quickly and kindly [7].

It was believed in Galton's time that the 'degeneration of the race' was due to hereditary medical and

social ills including stunting, feeble-mindedness, tuberculosis, alcoholism, criminality and prostitution. Eugenics sought by selective human breeding to eliminate undesirable, and propagate desirable social and personal characteristics. Kevles [8] gives an excellent account of the history of the eugenics movement which enjoyed considerable popularity in Britain until the Second World War. Support for eugenics came from many influential people. These included Arthur Balfour, H. G. Wells, Bernard Shaw and the Fabians, Marie Stopes, Winston S. Churchill and Beveridge, whose report provided the basis for the NHS. As recently as 1939 there were attempts in Britain to legislate for the mass sterilisation of those suffering from, or believed to be carriers of, mental deficiency, mental disorder or grave physical defect, including blindness [9].

In the USA, eugenic theories led to Davenport's Eugenics Records Office with its 'scientifically' trained personnel to ferret out human hereditary data by making house-to-house surveys and by scrutinising the records of prisons, hospitals and institutions for the handicapped. The information was intended as: 'a sort of inventory of the blood of the community', which would become '... a purifying conflagration some day'. More ominous legislation in many US states led to enforced sterilisation and segregation of the feeble-minded and others deemed socially undesirable. The ultimate corruption was in Nazi Germany where eugenics and social darwinism led directly to the truly 'murderous science' described by Benno Muller-Hill [10].

By 1945, classical eugenics in Britain was discredited because of revulsion against the Nazi holocaust, but also because many of its scientific tenets were shown to be invalid. Eugenics addressed social and environmental problems as though they were hereditary while disregarding the individual right to free reproductive choice, or even to life and liberty. The rejection of coercive eugenics is international as shown by Wertz and Fletcher [11] in their survey of the attitudes of nearly 1,000 medical geneticists in 19 nations.

Foundations of clinical genetics

Archibald Garrod effectively founded medical genetics with his study of alkaptonuria [12] in which mendelian rules of inheritance were applied to human inborn errors of metabolism, J.B.S. Haldane, R.A. Fish-

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er, Lancelot Hogben and others defined human and population genetics. Lionel Penrose's studies of mental retardation dispelled lingering eugenic views. J.A. Fraser Roberts, Cedric Carter, Victor McKusick and many others established a firm scientific base for clinical genetics using mendelian principles and meticulous empirical data invaluable for counselling couples for the recurrence of genetic and congenital disorders. After the 1939-45 war a clinic for genetic advice was established at the Hospital for Sick Children, Great Ormond Street, London. This was followed by similar clinics in other hospitals in many parts of the world, and genetics emerged as a clinical specialty.

What are the specialist roles of clinical genetics?

Improvements in technology and greater public awareness have encouraged the growth of multidisciplinary genetic services with rapid improvements in cytogenetics, prenatal diagnosis and molecular genetics. Planning these services has involved, in Britain, the medical Royal Colleges and the professional associations [13-20]. Genetics has developed as a specialty characterised by precision of diagnosis (or recognition when this is not possible), accurate risk estimation, empathic and full disclosure, confidentiality and non-directive, non-coercive counselling [21,22], and with an educational role made urgent by rapid technological innovation (Table 1).

Non-directive genetic counselling

It is perfectly possible for genetics to aim for the prevention of serious disorders without coercion. Indeed the professional in clinical genetics aims to inform and support the client (a poor word, but marginally better for healthy individuals than the clinically patronising term 'patient') and is therefore more concerned with client satisfaction than with prevention, although the two goals in practice usually coincide. The skill and empathy with which clients are informed may be a powerful factor in their later decisions concerning parenthood, prenatal diagnosis and abortion. Whether the decision the client makes is consistent with the counsellor's unstated opinion is less relevant than that

Table 1. The specialist roles of clinical genetics

1. Specialist diagnosis, eg of genetic disorders of all types and of dysmorphology
2. DNA and cytogenetic laboratory liaison
3. Risk calculation
4. Non-directive genetic counselling
5. Establishing and running genetic family registers
6. Teaching medical genetics to undergraduates and post-graduates
7. Research, including the development and evaluation of new techniques for clinical use and advice to others on genetic research

the client should have understood the options available and chosen without coercion. Since the currency of clinical genetics is information, the most important components of genetic audit are those that measure the content, accuracy and style of communication, rather than a crude count of abortions procured.

Long-term support: genetic family registers

Medical genetics deals with whole families at risk of genetic disease, in contrast to most other specialties which concentrate on affected patients. For this to be done effectively, currently healthy but 'at risk' relatives consent to their names being recorded confidentially to allow counselling and rapid access to new scientific developments. Of particular value is the reassurance of long-term contact and support available from trusted professionals who are well known to the families. The register employs, for this purpose, clinical co-workers (specialist nurses, non-medical genetic counsellors and social workers) who undertake home visits where many relatives can be counselled once the diagnosis and counselling strategy have been determined by consultant clinical geneticists. The genetic register team encourages preconception counselling to avoid panic testing in pregnancy, and by co-ordinating the work of obstetrician, ultrasonographer, laboratory and family doctor, it greatly facilitates prenatal diagnosis when this is requested by the patient. As children grow up, those at risk are offered counselling and are not forgotten. The register helps to rationalise the long-term follow-up of patients with chronic genetic disease who tend otherwise to attend many outpatient clinics in a haphazard manner [23-26].

Laboratory genetics in the NHS

Diagnostic chromosome services are available in every health service region in the UK, with effective quality assurance schemes supported by the Department of Health [27]. The Department of Health has also encouraged the introduction of molecular genetics into the health service by funding Special Medical Developments (SMD) in Manchester, London, Cardiff and Scotland [28-30].

A formal independent audit of the application of molecular genetics in SMDs was commissioned by the Department of Health and has been reported [31,32] and its success was recognised by an interim report from the DHSS [33] which concluded that:

... recombinant DNA techniques can be applied effectively to increase the precision of diagnosis and risk assessment of carrier states in single gene disorders... these applications allow important decisions of individuals and families at risk to be better informed, enabling them to achieve more favoured birth outcomes. . . the effectiveness of services now introduced in the SMD centres testifies the soundness of arrangements made for their delivery. These arrangements therefore provide a basis from which more comprehensive services may evolve.

Manpower and services

The findings of a survey by the Royal College of Physicians of London (1991, in press) are of vigorous growth of molecular genetic laboratory services such that all but one UK region has set up a laboratory. In contrast, there has been only limited growth of clinical manpower to cope with the consequent increase in clinical workloads. For example, there are only 156.83 whole-time equivalents clinical staff (medical and non-medical) in Britain associated with genetic centres, representing 2.75 staff per million population. Of those, 0.66 per million are consultant geneticists and 0.37 are doctors in training grades.

The organisation of regional genetic services in Britain

In 1987, four medical Royal Colleges (Physicians (London), Pathologists, General Practitioners and Obstetricians and Gynaecologists) made a joint statement to the Department of Health calling for the co-ordinated development of genetic services. They recommended that clinicians, scientists, genetic nurses and others should work together 'under one roof' to offer an integrated service and specialist training. In reply, ministerial statements confirmed the Department's commitment to the regional organisation of genetic services. In Scotland, the Home and Health department was equally responsive, leading to the formation of a consortium for the co-ordinated development of molecular genetics in Aberdeen, Dundee, Edinburgh and Glasgow. Thus, immediately before the National Health Service and Community Care Act 1990 a national framework of regional genetic centres appeared to have been firmly established (Table 2).

Genetic services after the NHS and Community Care Act (1990)

The reform of the National Health Service heralds radical changes in funding both existing services and new developments in genetics. Although resources will still come from general taxation, they will now be allocated to contracts by health authorities after they have themselves assessed the health needs of their resident populations. The emphasis is on improved quality of care and value for money, with new audit and management systems to monitor quality, keep accounts and reimburse providers. Because the reforms emphasise preventive medicine and quality of care, they should favour the development of clinical and laboratory genetics and offer the opportunity to negotiate with general managers and with directors of public health criteria for assessing population needs. Equally, geneticists must audit the quantity and quality of their work since acknowledged disparities between need and provision will suggest planned growth. Genetic services will be better able to survive and develop in this new environment if they understand the health authorities'

Table 2. Medical genetics in the NHS in early 1990

1. Chromosome laboratories with quality assurance in every region.
2. A national network of biochemical genetic laboratories.
3. Many regions have well developed molecular genetic laboratories.
4. A few regions have set up effective genetic registers co-ordinated by the clinical geneticists, and linked to the DNA laboratories.
5. Most regions have some form of regional strategic plan for genetics and most have some form of regional genetic committee or task group to advocate integrated services 'under one roof' as recommended by the joint statement from the medical Royal Colleges.
6. Following centrally funded evaluation, this pattern of service was endorsed by the Department of Health, and more details of existing and planned provision were expected following the Department of Health executive letter (EL (88) P/195).
7. The number of consultants and trainees in clinical genetics is rising and every region has some provision for general genetic clinics linked to the genetic laboratories.

responsibilities and the need for appropriate data with which to negotiate service agreements.

Genetic service needs of resident populations

The genetic service needs of the resident population of a district health authority, influenced by age, ethnic, maternity and other modifiers, will depend on:

1. The population prevalence of relevant disorders;
2. The diagnostic and support measures available;
3. Beneficial outcomes to achieve the optimum improvement in health.

Whether district health authorities purchase genetic services from regional genetic centres will require an unambiguous definition of the specialist roles of genetic services (Table 1). The decisions made by health authorities will be greatly influenced by the cash available, value for money and evidence of beneficial outcomes. These issues are being addressed by a working party of the Royal College of Physicians.

Audit of genetic services

There is urgent need for a simple, standardised data set measuring the quantity, quality and cost of genetic referrals and laboratory tests. Only genetic centres that can adequately document their work will maintain their current services and achieve well evaluated new developments. A joint approach by all clinical genetic and laboratory services in the region will be important to preserve the integrated nature of the service. Genetics will have special problems in resource management because of the non-standard hospital records usually held within genetics departments (for enhanced confidentiality) which contain information

on many relatives over several generations. These specialised records are rarely serviced by hospital records departments and have not generally been included in Körner returns. Clinical genetic workloads are thus under-reported while secretarial and clerical support is generally inadequate because of the rapid increase in referrals. Furthermore, no standardised computer system has been agreed for clinical data storage.

Clinical genetic workloads

No national data are available on numbers of patients and families referred to genetic centres although it is certain that these are expanding rapidly as a consequence of technical advances and greater public awareness. Predictions of population based workloads from the British Columbia Department of Health study [2] found that 5% of the population developed genetic disease by age 25, and 60% in a lifetime. Using the lower figure, in the UK there are more than 18,000 genetic patients (and many more relatives at risk) for every clinical genetic worker. Since clinical geneticists are too few to deal directly with this workload, it will be necessary to look for other recruits amongst the 32,000 family practitioners, nearly 14,000 consultants in hospital specialties and nearly 3,000 consultants in Public Health (Department of Health data (WTE) for England and Wales (1989)).

Genetic anticipatory care and GPs

The 32,000 general practitioners in Britain are responsible for primary and continuing care and outnumber all other medical groups. They are therefore uniquely well placed to deal with families with genetic disorders as well as with individual patients. In *A new kind of doctor* [34] Tudor Hart, himself a general practitioner, suggests that molecular biology:

... is going to give us weapons that act upon causal mechanisms in very large numbers of people, rather than the primitive strategy of salvaging advanced disease. . . [but this] . . . will require personal continuity. . . with patients fully able to share in decisions about their lives, which even more than now will depend on intelligent assessment of conflicting probabilities rather than dogmatic positive assertions. . .

The message conveyed is the expected cost-effectiveness of anticipatory care of the currently healthy compared with the traditional patching-up medicine and surgery.

Genetic skills and non-geneticists

Even recent medical graduates from many medical schools will have received little verified genetic teaching as found by the Royal College of Physicians report on undergraduate medical genetic education [35]. Hours of formal preclinical genetic teaching varied from two in Edinburgh to 66 in Leicester, with a mean

of 20 hours. Teaching was of largely unknown clinical relevance and it was impossible to document the extent of genetic teaching given informally by paediatricians and others, but there was a mean of only 5.6 hours of timetabled clinical teaching while scheduled visits by students to genetic clinics were reported from only half of 28 British medical schools.

The report also gave the results of a survey (in late 1989) of 240 UK physicians, paediatricians, obstetricians, psychiatrists and preclinical teachers in which the majority expressed strong support for teaching of genetics and that non-geneticists should have a sound understanding of the relevance of genetics in clinical practice.

National confidential genetic enquiry into medical services (GEMS)

Improvements in undergraduate and postgraduate education are unlikely to be rapid and other means have to be found to alert general practitioners and non-geneticist consultants to the needs of patients and families for accurate information. A national confidential enquiry is planned by the Royal College of Physicians of London whose aims are explicitly educational, concentrating on the need to ensure that those at risk of genetic disease are adequately informed but are not coerced. The enquiry is concerned with the quality of information available to individuals at risk of genetic disorders and whether the information and genetic services offered have been adequately documented in hospital and family practitioner records. The enquiry is not concerned with laboratory quality control. The disorders to be studied will involve a wide range of clinical specialties in order to maximise the educational value of the enquiry. Although it may not be possible to involve all clinical staff, effective reporting will alert and inform many who have not participated directly.

The methodology will concentrate on a manageable small number of clinically memorable events involving serious genetic disorders which have either recurred within families or apparently not been detected by generally available screening procedures. The enquiry will consider counselling, screening and prevention of disorders of infants and also of late onset genetic diseases, including inherited cancers. The proposed strategy is prospective and would involve scrutiny of new diagnoses involving marker disorders for factors which might have allowed prediction and, if appropriate, prevention, eg family history, maternal age, screening during pregnancy etc.

It is fundamental for the purposes of the enquiry that genetic counselling should be non-directive and should neither advocate nor reject abortion as a means for genetic prevention. To be effective, the enquiry will require co-operation from professionals and this can only be obtained if the enquiry is also non-censorious and confidential. Thus no report will

be traceable to individual patient, doctor or hospital, and no approach to patients will be required for the enquiry. The enquiry will investigate the extent to which individuals are adequately informed and counselled of their genetic risks so as to permit the individuals themselves to make their own most suitable parenthood decisions and to decide for themselves whether they wish to accept pregnancy screening and prenatal diagnosis.

Molecular genetics in the future

Weatherall [36] has explored the clinical implications of molecular genetics generally, while McKusick [37] and Friedmann [38] have described the strategy to map and sequence the human genome and its implications for clinical medicine. Holtzman [39] has reviewed the major public health issues involved. This new genetics will have an impact on all specialties and its significance cannot easily be exaggerated, with effects probably as great as the introduction of antibiotics. The application of these techniques will make possible widespread carrier detection and pre-natal diagnosis and this will inevitably lead to proposals for general pregnancy screening, as has happened since the cloning of the cystic fibrosis gene [40]. Although selective abortion of fetuses found to be affected will remain an important option for some time, fetal therapy at the molecular level will increasingly be possible [41]. Fetal diagnosis may be anticipated by preimplantation tests, and perhaps true prevention of congenital abnormalities. Treatment with gene products and perhaps with somatic cell gene therapy will become commoner. Predictive tests may become possible for high susceptibility to common diseases, as may workplace tests to identify individuals who are unusually susceptible to toxins and other industrial hazards. Table 3 summarises some of these developments and the problems that may arise.

Ethical issues

Some of these developments will create serious problems of ethical acceptance. For example, proposals for germ line gene therapy and genetic engineering for eugenic purposes are unacceptable and will be resisted strenuously. Widespread screening and registration of those at risk will pose serious problems of confidentiality because genetic tests frequently require the co-operation of several or many relatives and professionals. In particular, the pre-symptomatic detection of harmful genes for untreatable disorders (eg Huntington's disease) will provoke dilemmas of disclosure within families. Some individuals will have a legitimate interest in such information (family members at risk themselves and involved health care workers) but the interest of others (insurers, employers) may not be to the subject's advantage. There are also possible areas of discrimination when those shown to be susceptible

to genetic disease seek work, insurance and education. Individuals at risk of Huntington's disease already have difficulty in obtaining life insurance and, when successful, only with loaded premiums. When individuals have their expected working life reduced by genetic susceptibility, will employers take them on with full pension rights, and will universities allocate precious places to genetically susceptible students?

Future challenges

Unlike classical eugenics which was scientifically flawed, molecular genetics has irresistible scientific validity and has great potential for improving the health of the population. Eugenics was used for purposes which we now perceive as inhumane and was closely allied to social darwinism epitomised by the sentiments of the Victorian Liberty and Property Defence League which called for more. . . 'self-help versus state help. . .' [42]. These sentiments resonate in the modern world of market forces, value for money and reducing public expenditure. The accumulating power of molecular genetics will encourage preventive and pro-active medicine, surely the logical preferences of governments who wish to minimise the cost of health care. However, patients will still suffer

Table 3. Potential advantages and disadvantages of DNA testing

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- 1. Adults**
 - a. Carrier tests for all major genetic disorders when the human genome is mapped.
 - b. Predictive tests for high susceptibility to common diseases (cancers, heart disease, diabetes).
 - c. Workplace tests to identify individuals who are unusually susceptible to toxins and other industrial hazards.
 - d. Clinical treatment with gene products and human somatic cell gene therapy.
 - 2. Reproductive biology**
 - a. Widespread prenatal diagnosis for genetic diseases including general pregnancy screening beyond current strategies for neural tube defect and Down syndrome.
 - b. Fetal therapy, including at the molecular level.
 - c. Pre-implantation tests to supplement prenatal diagnosis by chorionic villus sampling or amniocentesis.
 - d. Genetic research on the human pre-embryo.
 - e. Germ line therapy and genetic engineering for eugenic purposes are unacceptable.
 - 3. Problems of confidentiality**
 - a. Some interest that is legitimate (family members, health care workers).
 - b. Because genetic tests frequently require the co-operation of several or many relatives, secrets will be hard to keep.
 - c. The pre-symptomatic detection of harmful genes (eg Huntington's disease) will provoke dilemmas of disclosure within families.
 - d. The interest of others (insurers, employers) may not necessarily be to the subject's advantage.
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from preventable disease and will require conventional treatment from acute services. There will always be individuals who accidentally or deliberately miss the bus. Clinicians must be vigilant if they are to avoid a progressive reduction of resources devoted to therapeutic medicine based on the visionary hope of the removal of disease analogous to the Beveridge optimism of 1942–1947; this anticipated a rapid decline in costs as diseases were cured following the introduction of the National Health Service. Optimism should be tempered by observing the large number of individuals who continue to smoke in the face of irrefutable evidence of harm. This shows how difficult it may be to obtain compliance when changes in personal habits are required.

Doctors must be prepared for dealing with these challenges, or others will, but not necessarily with the same philosophy of the individual worth of every patient. Doctors must have relevant technical knowledge and willingness to share responsibility on equal terms with related professions. But they must also resolutely retain ultimate responsibility for clinical care and have a powerful voice in shaping future strategies.

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References

- Sorensen TIA, Nielsen GG, Andersen PK, Teasdale MA. Genetic and environmental influences on premature death in adult adoptees. *N Engl J Med* 1988;318:727–32.
- Baird PA, Anderson TW, Newcombe HB, Lowry RB. Genetic disorders in children and young adults: a population study. *Am J Hum Genet* 1988;42:677–93.
- Wohl, Anthony S. *Endangered lives: public health in Victorian Britain*. London: Dent, 1983.
- Masterman CFG, ed. *The heart of empire: discussion of problems of modern city life in England*. 1901. Reprinted, Gilbert BG, ed. Brighton, 1973.
- Farr, quoted by Wohl AS. Ref.3, p 331.
- Darwin, Charles. *Descent of Man and selection in relation to sex*. London, 1871.
- Galton, Francis. *Essays in eugenics*. Eugenics Education Society, 1909.
- Kevles DJ. *In the name of eugenics: genetics and the use of human heredity*. Penguin Books, 1985.
- Trombley, Stephen. *The right to reproduce: a history of coercive sterilisation*. London: Weidenfeld and Nicolson, 1988.
- Müller-Hill, Benno. *Murderous science*. Oxford University Press, 1988.
- Ethics and human genetics: a cross-cultural perspective*. Dorothy C Wertz, JC Fletcher, eds. Springer-Verlag, 1989.
- Garrod's inborn factors in disease*. Charles R. Scriver, Barton Childs, eds. Oxford Monographs in Medical Genetics. Oxford: Clarendon Press, 1989.
- Emery AEH, Brough C, Crawford M, et al. A report on genetic registers: based on the report of the Clinical Genetics Society working party. *J Med Genet* 1978;15:435–42.
- Ferguson-Smith MA, Benson PF, Brock DJH, et al. *The provision of services for the prenatal diagnosis of fetal abnormality in the United Kingdom*. Report of the Clinical Genetics Society working party on prenatal diagnosis in relation to genetic counselling. London: Eugenics Society. Suppl 3, 1978.
- Fitzsimmons JS, Baraitser M, Davison BCC, et al. *The provision of regional genetic services in the United Kingdom*. Report of the Clinical Genetics Society working party on regional genetic services. London: Eugenics Society. Suppl 4, 1982.
- Johnston AW (Chairman) and others. Training of medical geneticists. (Medical Genetics Sub-Committee of the Paediatric Specialty Advisory Committee of the Joint Committee on Higher Medical Training: Comment.) *J Med Genet* 1978;15:260–1.
- Harris R, Emery AEH, Johnston AW, et al. *Role and training of clinical geneticists*. Report of the Clinical Genetics Society working party. London: Eugenics Society. Suppl 5, 1983.
- Clinical Genetics Society Working Party Report. *Guidelines on medico-legal aspects of medical genetics*. Discussion document prepared by the Clinical Genetics Society, 1989.
- Yates JRW, Malcolm S, Read AP. Guidelines for DNA banking. Report of the Clinical Genetics Society working party on DNA banking. *J Med Genet* 1989;26:245–50.
- Connor JM (Chairman) et al. Report of the Clinical Genetics Society working party on medical audit in clinical genetics. In preparation.
- Harris R, Wertz DC. Ethics and medical genetics in the United Kingdom. Ref.11 pp 388–418.
- Harris R. Genetic counselling and the new genetics. *Trends Genet* 1988;4:52–6.
- Read AP, Kerzin-Storarr L, Mountford RC, et al. A register based system for gene tracking in Duchenne muscular dystrophy. *J Med Genet* 1986;23:581–6.
- Craufurd D, Dodge A, Kerzin-Storarr L, Harris R. Cautious uptake of presymptomatic testing for Huntington's disease. *Lancet* in press.
- Elles RG, Read AP, Hodgkinson KA, et al. Recombination or heterogeneity: is there a second focus for adult polycystic kidney disease? *J Med Genet* in press.
- Littler M, Harper PS. A regional register for inherited cancers. *Br Med J* 1989;298:1689–91.
- ACC report/services and quality assessment. 1989.
- Harris R, Elles R, Craufurd D, et al. Molecular genetics in the National Health Service in Britain. *J Med Genet* 1989;26:219–25.
- Meredith AL, Upadhyaya M, Harper PS. Molecular genetics in clinical practice: evolution of a DNA diagnostic service. *Br Med J* 1988;297:843–6.
- Brock DJH, Johnston AW, Faed MW, et al. (Scottish molecular genetics consortium: Aberdeen/Edinburgh/Dundee/Glasgow). A consortium approach to molecular services. *J Med Genet* in press.
- Rona RJ, Swan AV, Beech R, et al. Demand for DNA probe testing in three genetic centres in Britain (August 1986 to July 1987). *J Med Genet* 1989;26:226–36.
- Beech R, Rona RJ, Swan AV, et al. Genetic services in the context of DNA probes: what do they cost? *J Med Genet* 1989;26:237–44.
- Special Medical Development in Clinical Genetics. Interim report: *Clinical effectiveness in the service context*. Medical Division CDPNM DHSS, 1987.
- Hart JT. *A new kind of doctor: the general practitioner's part in the health of the community*. London: Merlin Press, 1988.
- Harris R, Johnston AW, Harris H, Young ID. *Teaching genetics to medical students*. Royal College of Physicians report, 1990.
- Weatherall DJ. *The new genetics and clinical practice*, 2nd edn. Oxford University Press, 1985.
- McKusick VA. Mapping and sequencing the human genome. *N Engl J Med* 1989;320:910–5.

- 38 Friedmann T. Opinion: the human genome project—some implications of extensive 'reverse genetic' medicine. *Am J Hum Genet* 1990;**46**:407–14.
- 39 Holtzman NA. Recombinant DNA technology, genetic tests, and public policy. *Am J Hum Genet* 1988;**42**:624–32.
- 40 Riordan J, Rommens JM, Kerem BS, *et al.* Identification of the cystic fibrosis gene: cloning and characterisation of complementary DNA. *Science* 1989;**245**:1066–71
- 41 Harrison MR, Golbus MS, Filly RA, eds. *Unborn patient*, 2nd edn. Orlando, FL: Grune and Stratton, in press.
- 42 Liberty and Property Defence League. See Wohl AS. *The eternal slum: housing and social policy in Victorian London*. 1977, pp 231–3.

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