Issues in human genetics

UNIT 4

European Initiative for Biotechnology Education

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The European Initiative for Biotechnology Education (EIBE) seeks to promote skills, enhance understanding and facilitate informed public debate through improved biotechnology education in schools and colleges throughout the European Union (EU).

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MATERIALS

Contents

World Wide Web

Few areas are developing as rapidly as biotechnology. So that they can be revised and kept up-to-date then distributed at minimum cost, the EIBE Units are published electronically.

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With this software, you can view or print the EIBE Units. In addition, you will be able to 'navigate' around and search the documents with ease.

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Dorte Hammelev (Frederiksberg HF Kursus, København, Denmark), Wilbert Garvin (Northern Ireland Centre for School Biosciences, The Queen's University of Belfast, The United Kingdom) and John Schollar (National Centre for Biotechnology Education, The University of Reading, The United Kingdom) arranged and ran a multinational workshop in which the materials in this Unit were tested. EIBE would like to thank them and the teachers from Denmark, Eire and Germany who took part and gave many helpful comments on the draft materials. The workshop participants were:

From Denmark: Lisbet Leonard; Lene Tidemann; Mario Bro Hassenfeldt; Greta Grønqvist; Jytte Jørgensen; Tine Bing; Per Vollmond; Anker Steffensen.
From Eire: John Lucey; Michael O'Leary; Bruno Mulcahy; Tim O'Meara; Tom Moloney; Brendan Worsefold; Frank Killelea.
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INTRODUCTION

About this Unit

This Unit comprises a rôle play about human genetic diseases, with supporting educational resources. These materials have been devised by practising teachers and educationalists from several European countries, brought together with support and encouragement from DGXII of the European Commission, under the auspices of EIBE, the *European Initiative for Biotechnology Education*.

The EIBE materials have been extensively tested in workshops involving teachers from across Europe.

This Unit is designed to stimulate debate in the classroom. The implications of medical genetics and screening are wide-ranging and profound. Some of the more frequently-raised concerns will be examined. The quality of the discussion will be enhanced by the teacher's own knowledge and understanding of the issues involved.

An introductory section provides some background information on basic human genetics and recent developments in molecular genetics and medicine.

The remainder of this Unit is a rôle play centred around three serious inherited conditions: Cystic fibrosis; Duchenne muscular dystrophy and Huntington's disease.

Many important moral and social questions can be raised regarding the application of scientific and technological knowledge to human genetics.

Issues that could be explored using this Unit include:

- individual privacy and the confidentiality of genetic information;
- how can we draw a distinction be drawn between health and illness ?;
- what, in the context of human genetics, is *normal* ?;
- the application of prenatal diagnosis;
- termination of pregnancy (abortion) and the alternatives;
- reproductive technologies and human molecular genetics in different cultural contexts;
- medical genetics and disability rights.

Among the questions raised by the application of human gene therapy are:

- Who should be given the treatment first? (e.g. people on the verge of death, for whom there is no other hope; the youngest and fittest, who will have time to recover if things go wrong; those for whom existing treatments do little or nothing to alleviate their symptoms.)
- Were it possible to do so, should doctors be allowed to alter characteristics such as intelligence or physique?
- Should we ever permit germ-line therapy, which could affect future generations?
- Who, or what sort of organisations, should regulate and supervise gene therapy?
- What disciplinary action should be taken if the rules are broken?

All of the above (and other) points are of direct relevance to the students as future citizens and possibly as future parents. Teachers have an important duty to address these issues fairly.

Where appropriate, the materials in this Unit should be supplemented by additional resources, especially from organizations that support people whose lives are directly affected by serious genetic conditions. Several of these are listed in *Appendix 3*.

The classroom activities in this Unit were devised by Wilbert Garvin, Director of the Northern Ireland Centre for School Biosciences at the Queen's University of Belfast, with advice from Dr Lorraine Stefani. Comments on this Unit are very welcome and should be sent to:

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BACKGROUND INFORMATION

Genetic disease

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Cells, chromosomes, genes and proteins

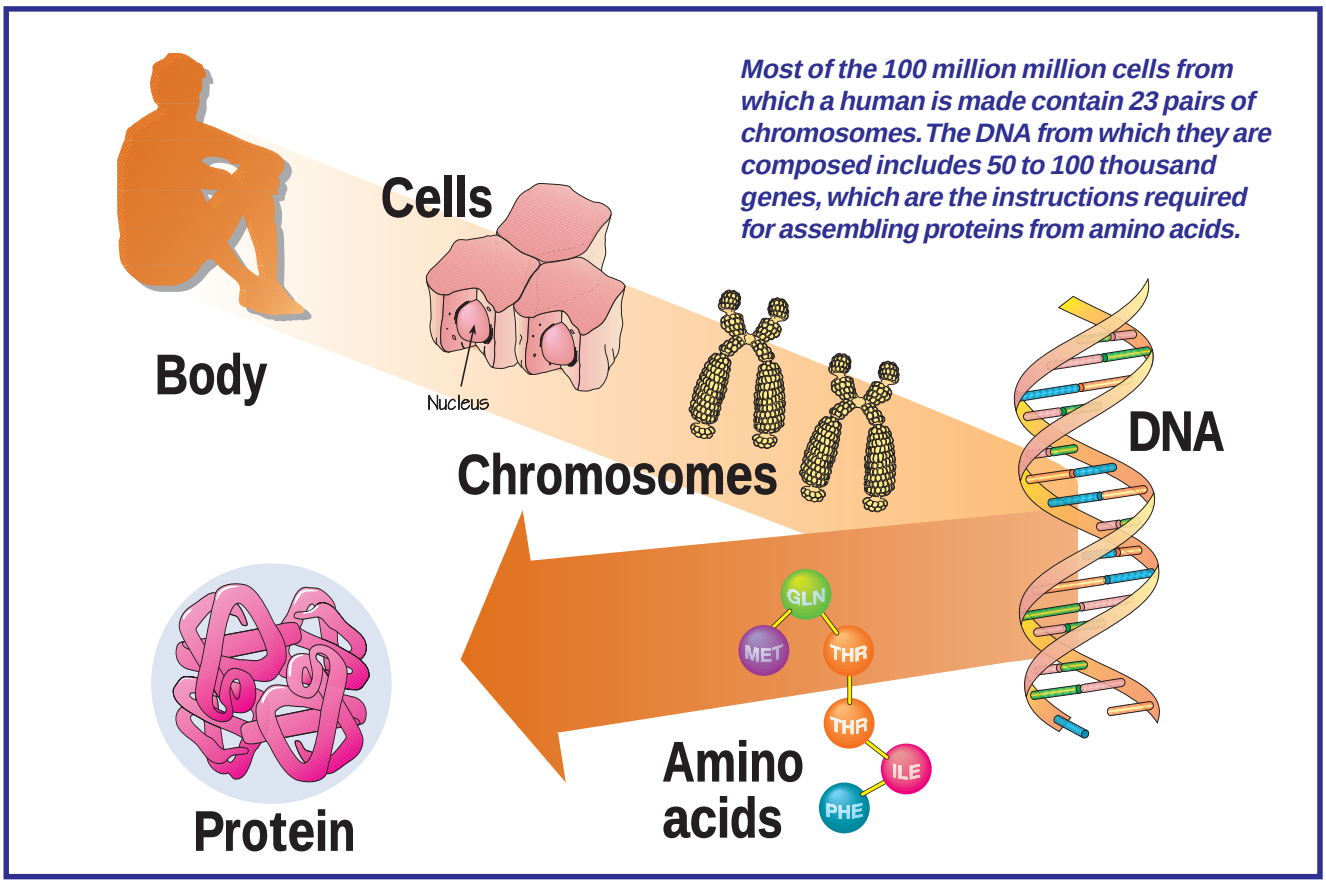
Humans are made from about 100 million, million cells. Within most of these cells are 23 pairs of *chromosomes*. One of each pair comes from each of our parents. The chromosomes are made of *DNA* (deoxyribonucleic acid) and *protein*. Particular sequences of information in the DNA are called *genes*. Genes provide the information necessary for the production of proteins. Recent estimates suggest that human beings have between 50 and 100 thousand genes.

All inherited characteristics are controlled by genes. Sometimes a single gene is associated with a particular feature, so it is possible to talk about a gene 'for' that feature. For example, there is a gene 'for' each of the different enzymes that enable you to digest your food. More often, however, our visible characteristics are the result of many genes working together and interacting with their surroundings. Features such as intelligence and height for example, result from such complex interactions.

Different forms of genes

Each gene can come in alternative forms, called *alleles*. Say, for example, that there was a single gene governing eye colour. There might be one form (or allele) that leads to blue eyes, another allele for brown eyes, one allele for green colour and so on. For all genes we inherit two alleles, one carried on each of the pair of chromosomes we have received from each of our parents. Some alleles are *dominant* and their effects are seen regardless of the nature of the other allele on the accompanying chromosome. Other alleles are *recessive* and their effects are only seen when both chromosomes carry an identical form of the gene.

Variation in genes arises naturally by random mutation. Some mutations can be damaging while others have no obvious effect. In some cases they can bestow benefits. For instance, there are several genes involved in the production of haemoglobin, the oxygen-carrying pigment that is found in red blood cells. One Olympic Gold medallist, a Finnish cross-country skier, has an allele that gives him a higher level of haemoglobin in his blood than most people. This means that he (and others in his family) find endurance sports easier than the average person does.



What is genetic 'disease'?

About 4 000 diseases in humans are thought to result from changes to single genes. Most of them are rare, but many cause severe suffering and often lead to an early death. Although individual genetic diseases are quite rare, the total number of people affected is significant — roughly 2% of all live births every year. At present there is no effective treatment or cure for most of them.

Most genetic disorders are maintained in the population by both the passage of genes from parents to offspring and by the steady input of new mutations. However, not all genetic disorders run in families. Some changes to the DNA or the chromosomes arise during the formation of the sex cells (eggs and sperm) or in the early development of the foetus. One example is Down's syndrome, which causes mental retardation, below-average stature and other changes. It usually arises from an error during cell division (meiosis) leading to the child having 47 chromosomes instead of 46, one of them (chromosome 21) being duplicated.

Because genetic 'diseases' cannot be 'caught' like infectious diseases, some people prefer to make this distinction clear by calling such diseases 'syndromes' or 'dysfunctions' — but there is no commonly-accepted term for genetic changes of this type.

All of the diseases caused by changes to single genes have clear patterns of inheritance, which means that it is often possible to predict the chances that someone will inherit a particular condition. Three main patterns of inheritance are involved.

1. Recessive conditions

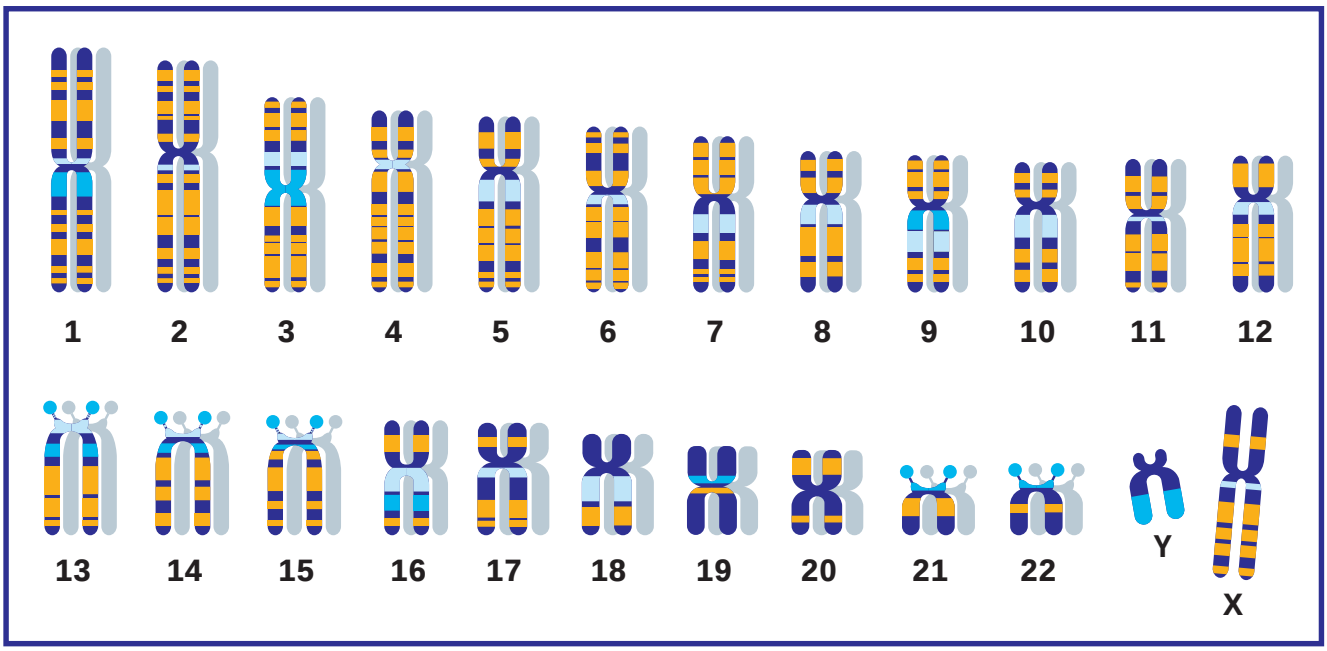
Some disease-causing alleles are recessive: to be affected a person must carry two identical forms of the gene. For example, sickle cell anaemia occurs when someone receives *two* copies of a certain form of one of the haemoglobin genes. However, because the altered form of the gene is recessive, those people who inherit just one copy of it are unaffected — the mutant allele is dominated by its partner on the other chromosome. In some situations people with one sickle cell allele can even be at an advantage, because they are less susceptible to malaria than people with two 'normal' alleles.

People with a single copy of a particular recessive allele are sometimes called 'carriers', because although they are unaffected personally, they can still pass on the allele to their children. These children will not suffer the disease unless they have also inherited a similar allele from the other parent.

Below: Most human genes are packaged into 23 pairs of chromosomes.

Virtually all cells contain a full set of chromosomes. Two major exceptions are mature red blood cells (which have no chromosomes) and the sex cells (eggs and sperm) which carry only one set of 23 unpaired chromosomes.

Men have an X and a Y chromosome; women have two X chromosomes. After staining with various dyes, each chromosome reveals a unique pattern of bands.



Sickle cell anaemia

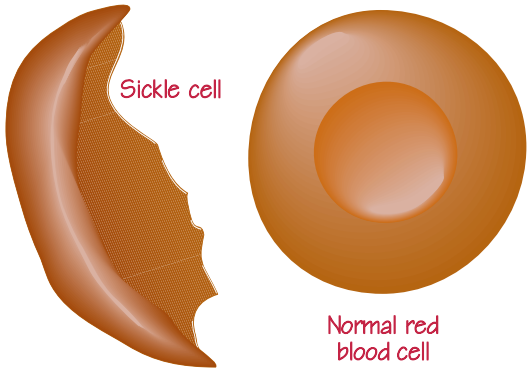
One of the commonest genetic diseases is sickle cell anaemia. People who are affected by the disease have red blood cells that alter their shape when the oxygen concentration becomes low. These sickle-shaped cells often burst open or clog the small blood capillaries, starving the tissues of oxygen and causing the affected person to suffer mild to extreme pain. Additional complications can arise, especially during exercise.

In 1949, the U.S. chemist Linus Pauling traced sickle cell anaemia to a specific change in the structure of haemoglobin, the red oxygen-carrying pigment in the blood. When he examined the molecular structure of haemoglobin from sickle cell anaemia patients Pauling found that it differed from 'normal' haemoglobin.

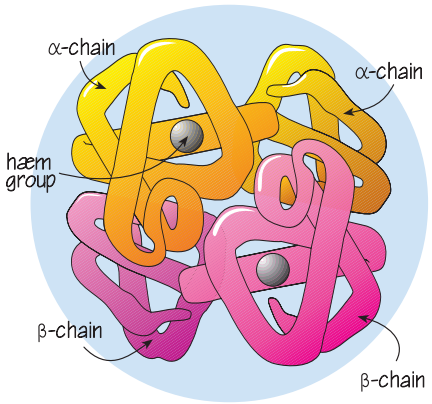
Adult haemoglobin is constructed of two α-globin chains, each 140 amino acids long, and two β-globin chains, each with 146 amino acids.

The sole change in the abnormal haemoglobin was the replacement of one amino acid, glutamic acid (glu) by valine (val) at the sixth position in the β-globin chain.

Red blood cells



Haemoglobin molecule



β-globin proteins

'Normal' amino acid sequence

val — his — leu — thr — pro — glu — glu —···

Sickle cell amino acid sequence

val — his — leu — thr — pro — val — glu —···

2. Dominant conditions

If a disease is caused by a dominant allele, a person has only to inherit one copy to have the disease. If any of that person's children receive the affected allele, they will also inherit the disease and have a 50% chance of passing it on to their offspring.

A particular problem with diseases caused by dominant alleles is that if they do not develop until later in life, parents may unwittingly pass them on to their children.

One such condition is *Huntington's disease*, which is characterised by the progressive development of involuntary muscular movements and dementia, from the mid-thirties onwards. Huntington's disease is discussed in detail later in this Unit.

3. Sex-linked conditions

Among the 23 pairs of chromosomes that all humans have, one pair is connected with the person's gender or sex. Females have two similar X chromosomes whereas males have one X and a smaller Y chromosome. Recent research has shown that a single gene on the Y chromosome determines gender: without this gene, females develop. Other genes that have nothing to do with sex are also carried on the X and Y chromosomes. Such genes are sometimes described as 'sex-linked'.

Genetic disorders that are caused by changes to the X chromosome, although rare, are more common in males. They are often described as X-linked. For example, an allele that can cause red-green colour blindness is carried on the X chromosome. Females are

very rarely affected by this condition, because the offending allele (if present) is usually masked by ordinary gene (allele) on the accompanying X chromosome. Males, however, have no second X chromosome, so stand a greater risk of being red-green colour blind.

4. Multifactorial conditions

Individual disorders caused by changes to single genes are comparatively rare. Far more common are those conditions which arise from the interaction of many genes.

Predicting the pattern of inheritance for these conditions and disentangling the influence of genetic and environmental factors (such as smoking, diet, stress, or exposure to certain chemicals) is only in its infancy. The hope is that people who are 'at risk' can be identified and advised to avoid 'environmental' factors that might lead to the development of disease. The worry is that employers, insurance companies or others who do not understand the relative contribution of the genetic component may overreact and discriminate against affected individuals.

Finding disease-causing genes

Linkage analysis, based on the extent to which particular characteristics tend to be inherited together, allows the positions of mutant alleles responsible for certain inherited conditions to be located on the human chromosomes. The technique requires several generations and large numbers of individuals, and is thus much more difficult when applied to humans than, say, to fruit flies or pea plants. Nevertheless, many genes have been located in this way and their DNA sequences determined. This makes it possible to produce corresponding *gene probes* that allow conclusive identification of those who carry potentially harmful genes.

Many other disorders, whose genes have not yet been isolated, have been mapped to their approximate locations in a chromosome. These genes too can be identified by using gene probes, although with less certainty. One recent success involved Huntington's disease, a devastating condition that usually appears between the ages of 30 and 50 and leads to uncoordinated limb movements, mental deterioration and death. In 1983, Jim Gusella and

Some of the 4,000 known genetic conditions. Mendelian conditions (recessive, dominant and X-linked) follow a clear pattern of inheritance, whereas it is less easy or impossible to predict the occurrence of sporadic and multifactorial conditions.

Mode of inheritance	Disease/ condition	Main features	Time of onset of symptoms
Sporadic	Down's syndrome	Range of mental retardation, etc.	Birth
	Klinefelter's syndrome	Defect in sexual differentiation	Birth
Autosomal recessive	Cystic fibrosis	Wide range of complications due to excessively thick mucus secretion, especially in the lungs/digestive system	1–2 years
	Phenylketonuria	Mental deficiency	Birth
	Sickle cell anaemia	Chronic anaemia/infections/painful or haemolytic crises	6 months onwards
	Tay-Sachs disease	Deafness/blindness/seizures/spasticity	3–6 months
	Thalassaemias	Severe anaemia/skeletal deformity	Six months onwards
Autosomal dominant	Familial hyper-cholesterolaemia	High cholesterol level leads to early coronary heart disease	20–30 years
	Huntington's disease	Involuntary movements/dementia	35–45 years
	Polycystic kidney disease	Cysts in liver/pancreas/spleen/kidney	40–60 years
X-linked	Haemophilias	Failure of blood to clot. Bruising and excessive bleeding after injury	1 year onwards
	Duchenne muscular dystrophy	Muscle wasting	1–3 years
	Lesch-Nyhan syndrome	Mental retardation/self-mutilation	Birth
Multifactorial (often with a high genetic contribution)	Asthma	Difficulty breathing	Birth
	Coronary heart disease	Arteries become narrowed, can lead to heart failure	Middle age

colleagues at the Massachusetts General Hospital, Boston, reported that they had pinpointed a marker gene close to the Huntington's disease allele on chromosome 4. Then, in 1993, following a decade of painstaking research, they and collaborators at other U.S. centres and the University of Wales College of Medicine in the UK announced the precise position of the Huntington's allele.

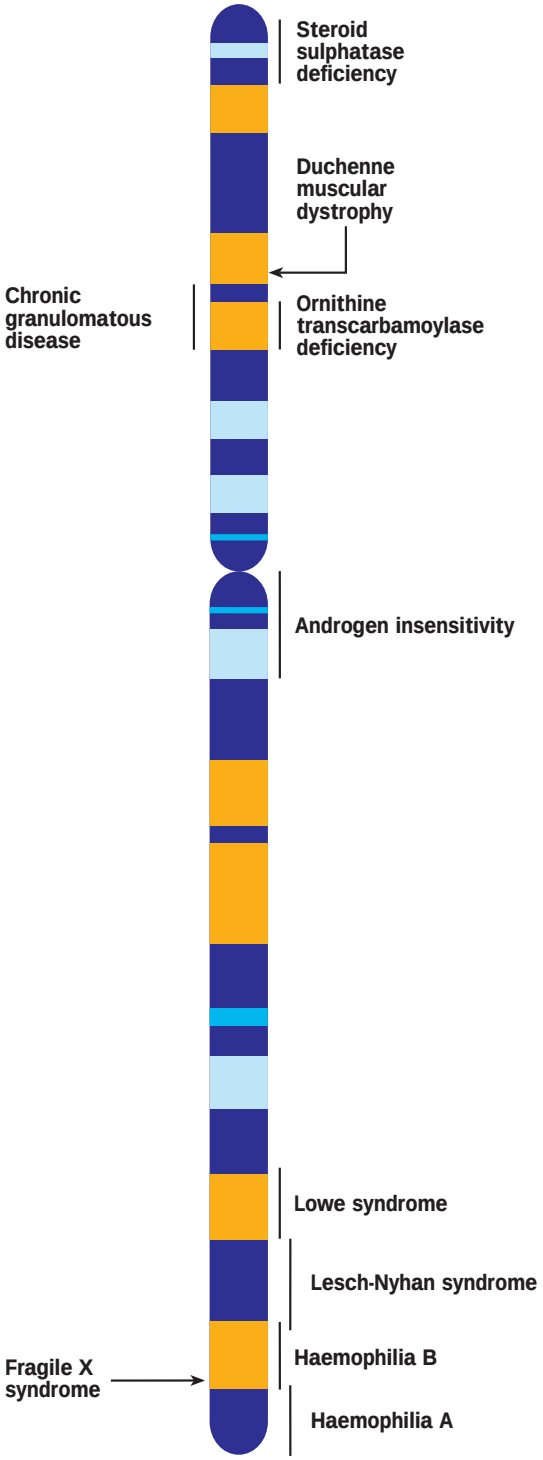
While these were major advances which helped in screening for the disease, they also created a dilemma. In the past, children of a person with the disorder, who have a 50% chance of developing the condition, simply had to wait until middle age to see whether they were to be afflicted. Now they can choose to be tested — but may then have to cope with the news that they face this horrendous disease later in life.

Like Huntington's disease, many other genetic disorders are serious and distressing conditions that cannot be cured or even treated directly. Identification of the genes concerned raises the possibility that scientists may be able to find out precisely what causes the condition, by determining the protein produced by the gene and discovering its effects. It also helps in the development of screening tests, whether applied to the unborn foetus, to 'test-tube' embryos or adults.

Screening and counselling

Genetic screening identifies those individuals who carry alleles that may lead to disease. Genetic counselling provides individuals and couples with advice about the conditions, the risks of having children who will be affected, the severity of the disorder and the options available. This allows potential parents to make informed choices: whether or not to have children, or to avoid the risk of having affected children by choosing the option of using donated eggs or sperm, or to continue normally but to terminate pregnancies if prenatal tests show that the foetus is affected.

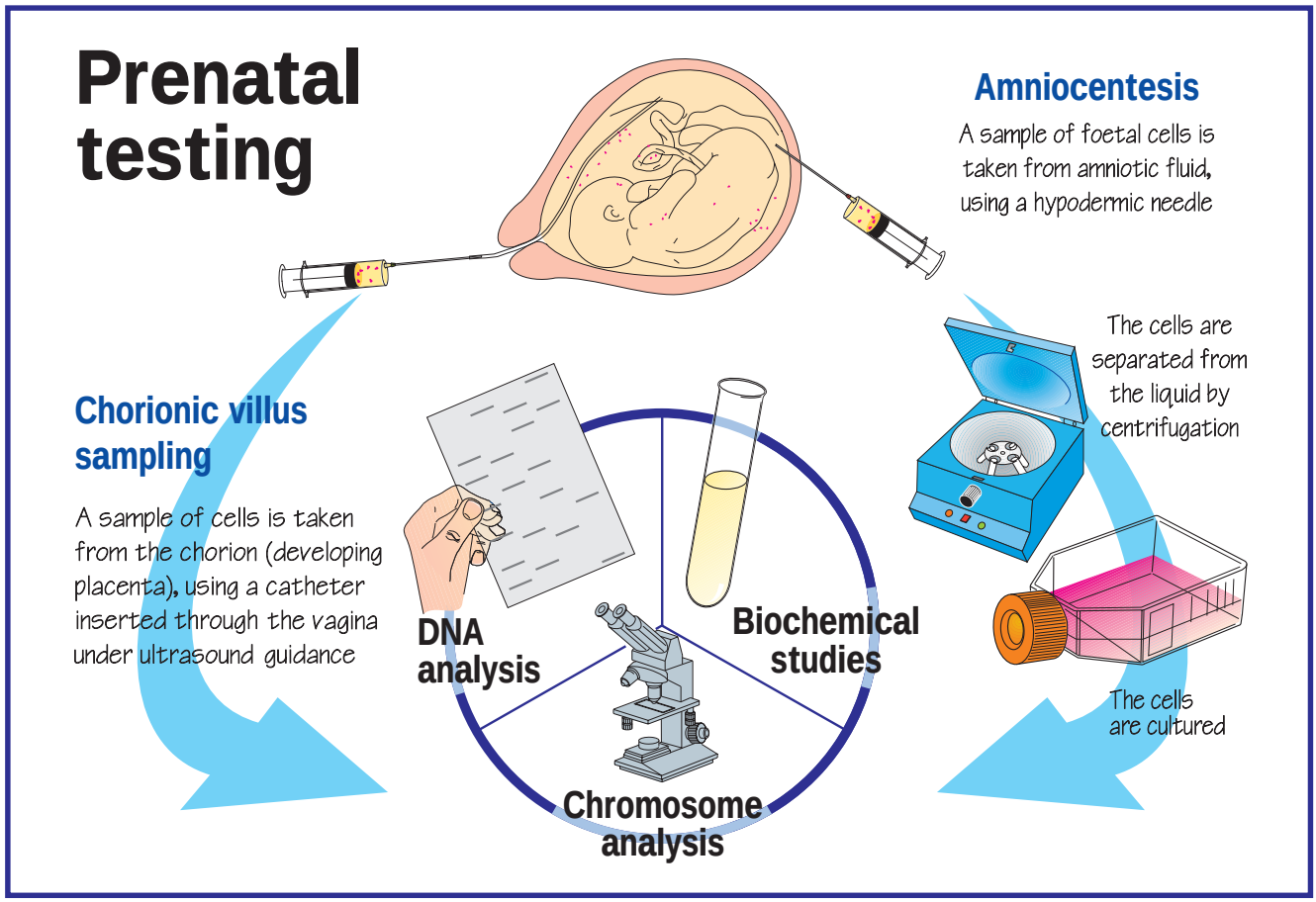
Among the issues associated with screening, prenatal testing and counselling are who should be screened, when, and for what conditions? What educational backup is necessary to ensure that all those who are affected fully understand the results of tests and their implications? A further complication arises because genetic conditions may affect relatives of the individual who is directly affected, so it may not be easy to apply normal rules of medical confidentiality.



A 'genetic map' of a human X chromosome, showing the relative positions of some of the 350 or so genes which can lead to various disorders that are located there.

The width of the line alongside the drawing reflects the precision with which the location of the gene is currently known.

The bands are caused by the differential uptake of various stains that are used to make the chromosome visible.



Screening in early pregnancy

There are currently two approaches to treating genetically-based diseases. The first, which is already reducing the burden of suffering caused by disorders such as cystic fibrosis, is to locate the gene responsible for such a condition, or at least a closely-linked marker gene; to screen foetal cells early in pregnancy for that marker; and thus to prevent disease by terminating a pregnancy. The second is to screen early embryos produced outside the body to test for the gene or gene marker, and to implant one of the embryos that does not carry a defective allele.

Prenatal diagnosis is usually offered when a family has a history of a disorder caused by a single gene or inherited chromosomal abnormality, when a couple already have an affected child, or when the parents are comparatively old (and therefore more likely to give birth to a child with Down's syndrome). It can provide results that either reassure the parents or give them evidence upon which to make a decision.

Amniocentesis is carried out from 10 weeks' gestation. A small quantity of amniotic fluid is taken through a needle from the amniotic cavity and amniotic cells (shed from the skin of the foetus) are cultured and their chromosomes examined to confirm or exclude conditions such as Down's syndrome.

Chorionic villus sampling, introduced more recently, has the same purpose. Chorionic villus comes from the developing placenta, and is removed directly through a needle. Most centres carry out chorionic villus sampling after 10 weeks. Because the cells are derived from the fertilized egg, they nearly always provide a reliable guide to the genetic constitution of the foetus. But both techniques have a disadvantage, because they increase the rate of miscarriage slightly.

Coelocentesis, reported in 1993 by a team at King's College School of Medicine and Dentistry, London, promises to facilitate screening before 10 weeks. In this procedure, cells are taken from the coelomic cavity which surrounds the amniotic sac. The new technique, although relatively untried as yet, is thought to present significantly less risk to the safety of the unborn child than either amniocentesis or chorionic villus sampling.

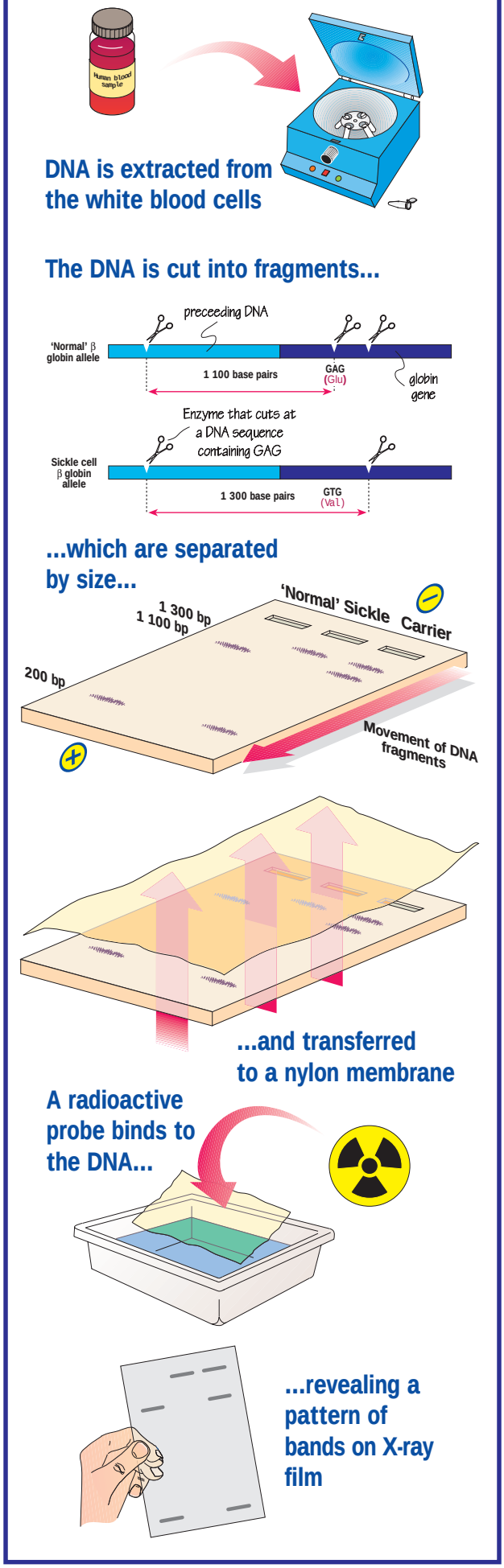
The sex of a foetus can be determined by these methods. Although parents could exploit the results to choose the sex of their offspring for non-medical reasons, the principal purpose is to help them decide what to do if the mother is likely to give birth to a child affected by a condition determined by one of the sex chromosomes. In certain disorders with genes carried on the X chromosome, for example, knowledge of the sex of a foetus is useful when a more specific test is not available.

Screening for haemoglobin disorders

The World Health Organisation forecasts that by the year 2 000 approximately 7% of the world's population will be carriers of the most important haemoglobinopathies. These are serious conditions, caused by a failure of the haemoglobin in red blood cells to carry oxygen to the tissues in the normal way. They are the commonest of all human genetic diseases. As there is no satisfactory treatment, prenatal diagnosis and the detection of carriers will remain the principle means of combating these disorders in the foreseeable future. In some cases, such as sickle cell anaemia, an abnormality in the structure of the haemoglobin molecule is to blame. Thalassaemias, in contrast, occur when one or more of the four globin chains comprising the molecule are produced at a diminished rate, leading to an imbalance in their proportions. Over 90 different mutations have been found to cause one such condition, β-thalassaemia.

Southern blotting (named after its inventor Ed Southern) is one simple test which illustrates the diagnosis of a condition such as sickle cell anaemia. First, DNA is extracted from the patient's white blood cells. This is then exposed to an enzyme that recognises the site coding for the glutamic acid (glu) that is present in normal haemoglobin but replaced by valine (val) in sickle cell haemoglobin. The resulting mixture of DNA fragments are separated by size, and treated with a probe for the normal gene.

If the patient's haemoglobin is normal, the enzyme splits it into two fragments, each containing part of the gene. The probe DNA binds to each of these, and because the probe has been made slightly radioactive the two fragments can be detected as two black bands on a photographic film. If the haemoglobin is the sickle cell variety, it is not cut by the enzyme, and only one black band appears.



Considerable progress has been made recently in the diagnosis of haemoglobinopathies, much of the work being pioneered by Sir David Weatherall and colleagues at the John Radcliffe Hospital, Oxford. These advances in genetic diagnosis have followed earlier techniques that identified abnormal forms of haemoglobin in red blood cells, obtained by passing a needle into the placenta or umbilical cord. Although these methods were effective (resulting in, for example, a marked fall in the birthrate of people with β-thalassaemia in Greece), they could not be used until late in the second trimester of pregnancy.

Focusing on genes, rather than on the haemoglobins they produce, the newer approaches can be adopted before blood cells are available for sampling. The first such advances, in the late 1970s, were made using amniocentesis early in the second trimester. In due course, the first successful diagnoses of DNA in chorion villus, sampled late in the first trimester, occurred during the early 1980s. In some cases, when a specific gene probe is available, prenatal diagnosis is relatively simple. In other cases, more complex methods have to be used.

Pinpointing the cystic fibrosis gene

In 1989, researchers at the Hospital for Sick Children, Toronto, and the universities of Toronto and Michigan announced that they had located the mutant gene responsible for cystic fibrosis (CF). This was a triumph for Lap-Chee Tsui and his co-workers in their use of elegant but nevertheless laborious techniques. Beginning by studying members of families with the disease, they used linkage analysis to locate the gene on chromosome 7 (in 1985), and then painstakingly homed in on the gene itself.

The Toronto discovery led quickly to the development of a gene probe specific for the CF mutation. As well as being used in affected families, this seemed likely to be taken up quickly as the basis for major screening programmes in whole populations. These hopes were dimmed, however, when the newly-identified mutant gene was found in only about three quarters of CF patients. Subsequent identification of further mutations (over 450 are now known) has made it possible to identify 85–95% of carriers, depending on racial and ethnic background. This begins to make population screening seem more feasible.

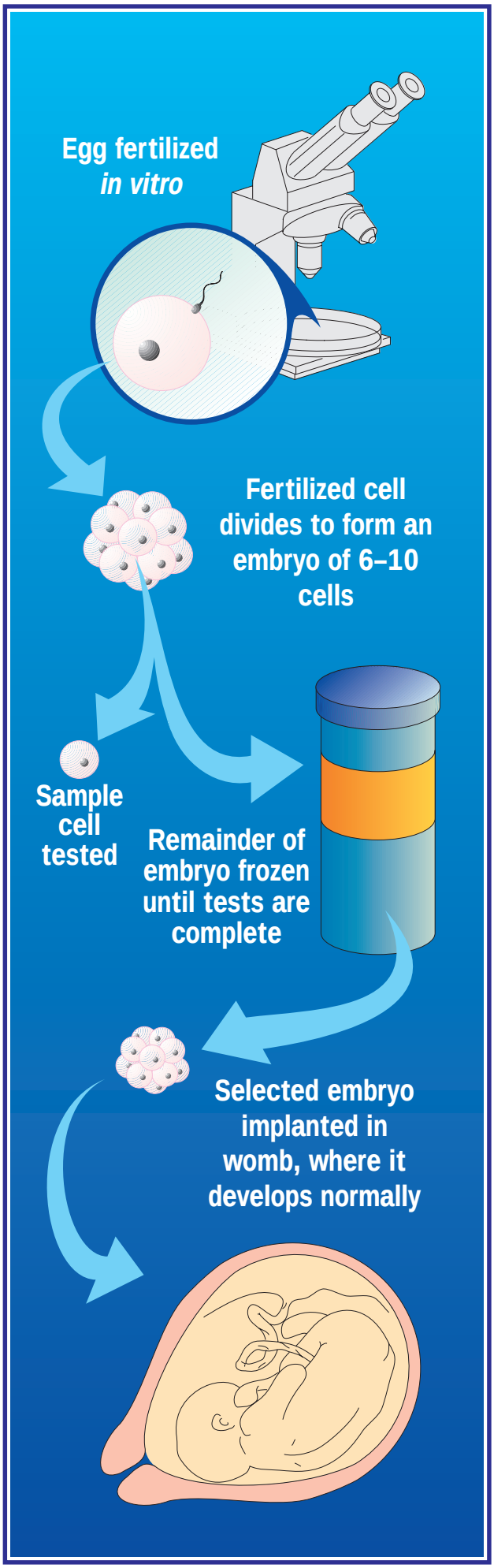
Preimplantation diagnosis

Recently, genetic screening was extended to embryos produced by *in vitro* fertilization — by adding spermatozoa to egg cells growing in laboratory glassware. This method of producing embryos was originally developed to allow certain infertile couples to have 'test tube' babies. Now, however, a healthy embryo can be identified and reimplanted in the woman, who is then assured that her pregnancy is free of any risk from that particular inherited disorder — and indeed several different conditions.

First, Robert Winston and colleagues in London reported that they had been able to take single cells from very early (6–10 cell) embryos and then to sex them by examining specific DNA markers on the Y chromosome. Their aim was to help couples with a history of an X-linked condition. Removal of the individual cell did not damage the rest of the embryo. Although this technique could not guarantee the birth of a healthy boy, it could ensure that the mother received a female embryo. It could also prevent unnecessary abortion: for certain X-linked conditions, all male pregnancies would be terminated following sex determination by amniocentesis or chorionic villus sampling, although half of these would be unaffected.

Winston, together with Bob Williamson and other collaborators, has also used this approach to screen for CF and Duchenne muscular dystrophy. Initially, their targets were gene markers close to the mutation responsible for cystic fibrosis, and part of the sequence coding for dystrophin, which when mutated causes Duchenne muscular dystrophy. Such tests should facilitate screening for other than X-linked conditions (for example, CF) and also permit the implantation of male embryos unaffected by X-linked traits such as Duchenne muscular dystrophy.

Right: Preimplantation diagnosis. A sample (biopsy) is taken from the early embryo at the 8 cell stage. While the sample cells are tested, the remainder of the embryo is stored — to be implanted should the tests show that it is free of serious genetic disease. Since the cells of such early embryos are undifferentiated, the removal of one cell does no harm, and subsequent development proceeds as normal.



Principles of gene therapy

Until recently, it was only possible to suppress the symptoms of inherited disease. Only a small proportion of those affected were thus able to lead fully active lives.

Gene therapy is the repair or replacement of disease-causing genes or the introduction of functional alleles alongside dysfunctional ones in living cells. In this way doctors hope to treat inherited diseases effectively for the first time. Gene therapy has been given the go-ahead by governments in several countries and although this work is still in its infancy, the results of some early trials are encouraging.

In all of the tests to date, functional genes have been introduced alongside the dysfunctional genes in affected individuals (hence this work is currently limited to treating conditions caused by recessive alleles). An alternative would be to alter a malfunctioning gene to correct its erroneous message. Although this appears at least as difficult as the replacing of a faulty gene, genetic sequences have been modified in several different types of mammalian cell cultured *in vitro*.

Whatever the technique adopted, the functional alleles have to be inserted into (or modified within) cells in the affected tissue. This is clearly a much simpler prospect for a tissue such as blood or bone marrow, which can be removed, treated in the laboratory and re-injected, than for tissues such as liver, lungs or brain. In the treatments so far, genetic material has been ferried into the body cells by specially-tailored viruses or encased in fatty droplets called liposomes.

All of this treatment has involved only the body cells of the affected person (*somatic gene therapy*). No attempt has been made, nor has approval been given for genetic modification of the sex cells — eggs and sperm — or the embryo (*germ-line therapy*). Modification of this type could affect future generations. At present, germ-line therapy is considered unacceptable, since so little is known about its possible consequences and hazards. For example, it may not be desirable to remove carrier potential from the population, since in some circumstances apparently deleterious alleles may be beneficial.

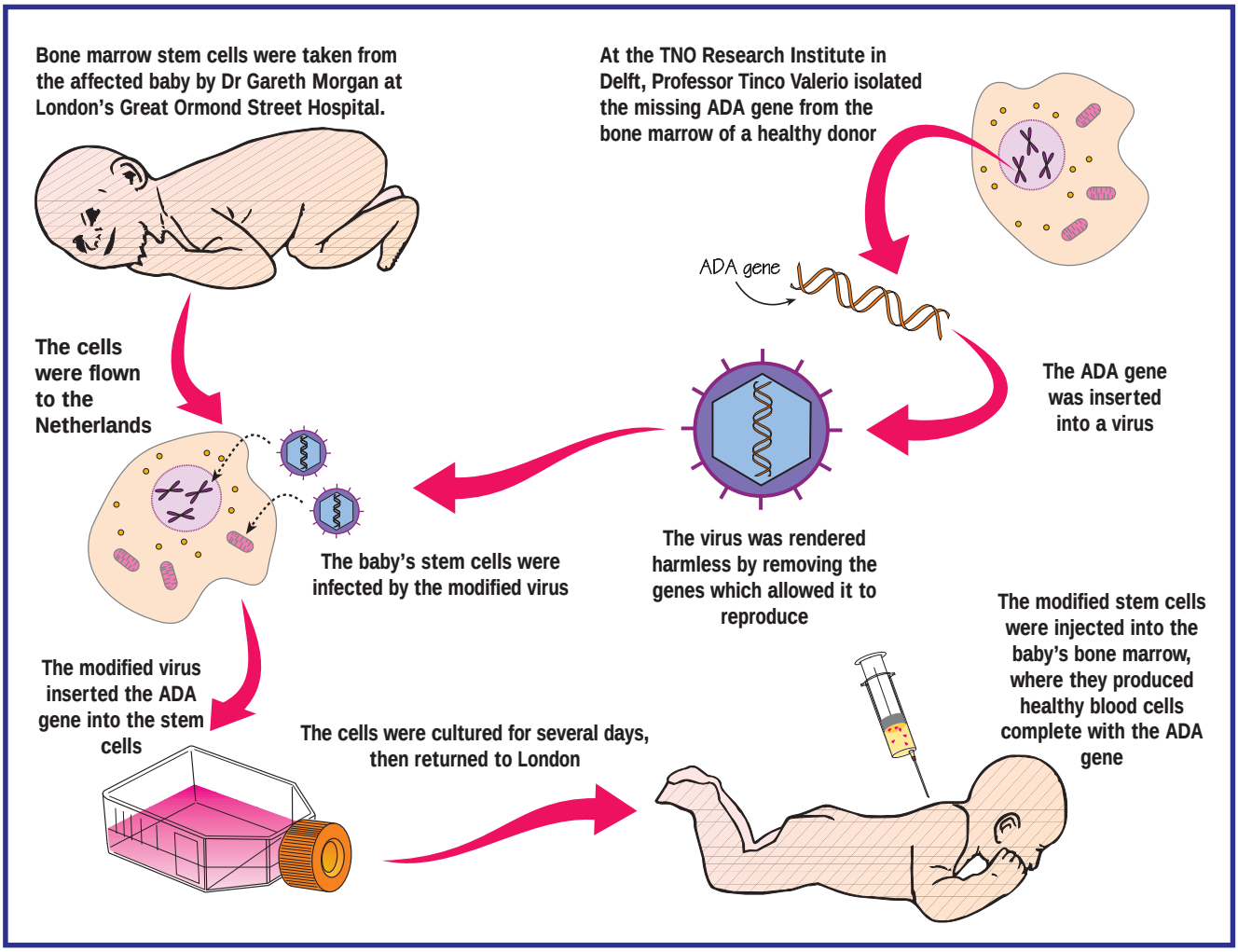
First steps in gene therapy

The first tangible moves towards gene therapy centred on four very different conditions. In 1993, researchers at Oxford and Cambridge in the United Kingdom announced that they had restored normal function to cells in the lungs of mice with artificially-induced CF. They did so by squirting into the lungs copies of a gene called CFTR encased in liposomes (tiny globules of fat). The liposomes fused with the animal's cell membranes, allowing the DNA to pass through into the cells and thus correct the defect. Trials with humans began shortly after, and some success in dealing with the symptoms of CF has been reported, although this therapy is not a cure.

In the second advance, researchers inserted a normal gene into certain white blood cells from a patient with leucocyte adhesion deficiency, a rare genetic disorder that leaves victims exposed to recurrent, life-threatening infections. Using a virus as the vector, they introduced a normal allele to compensate for the abnormal one responsible for the condition. The allele was expressed, causing the cells to behave normally. There are now hopes of transferring the gene into stem cells (where the white cells are formed), leading to the formation of a new population of normal white cells.

The third approach has been pioneered by French Anderson and colleagues at the National Cancer Institute and National Heart, Lung and Blood Institute in Bethesda, USA. The long-term aim is to optimize the treatment of cancer by using certain of the patient's own white blood cells, together with interleukin-2. This is a natural substance which stimulates growth of the white cells that attack what they recognise as foreign tissue. The researchers took white cells from patients suffering from advanced melanoma and then used a virus to introduce into the nuclei of the cells a gene conferring resistance to a particular antibiotic. This enabled them to

Below: Gene therapy to combat Severe Combined Immunodeficiency (SCID) was carried out in Italy in 1991 and in the following year, at London's Great Ormond Street Hospital, with the help of colleagues from the TNO Research Institute in Delft. The treatment involved the replacement of a missing gene for an enzyme (ADA). The gene was placed in the stem cells of the bone marrow, so that blood cells derived from them would produce ADA.



monitor the survival and behaviour of the cells when reinjected back into patients. This preliminary experiment is now being followed by efforts to enhance the tumour-destroying capacity of white cells, by giving them genes to overproduce a potent protein called tumour necrosis factor.

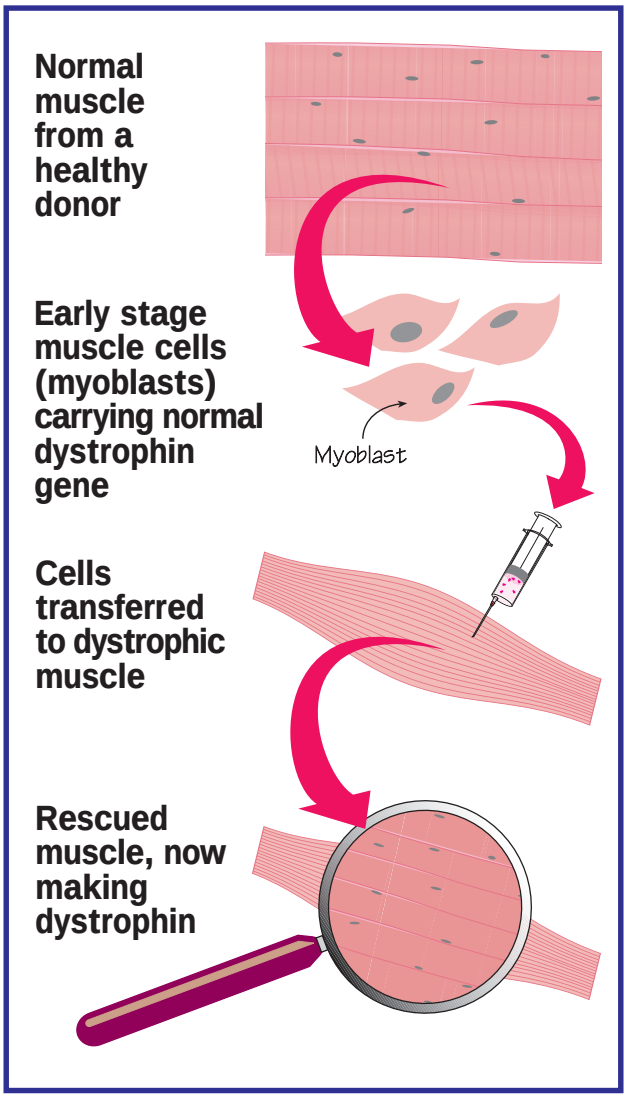
A fourth target is severe combined immunodeficiency disease (SCID), a rare disorder affecting about 40 children worldwide each year. In nearly half the patients, the gene for the enzyme adenosine deaminase (ADA) is defective, preventing the immune system from defending the body against invading microbes. Efforts to combat the condition by taking a patient's white blood cells, introducing a normal gene coding for the enzyme, and then retransfusing the cells, began in the USA in 1990. More advanced treatment, using modified stem cells — and thus removing the need for repeated transplants — began in Italy in 1992 and with help from doctors in the Netherlands, in the United Kingdom a year later.

Potential targets for therapy where diseases arise from single genes include: other immunodeficiency diseases; hypercholesterolaemia (replacing a receptor protein); haemophilia (Factors IX and VIII); phenylketonuria (where the enzyme phenylalanine hydroxylase is missing); Hurler's syndrome (involving an enzyme called α-iduronisase); thalassaemias and sickle cell anaemia (where the β-globin gene is faulty).

Cell therapy

Cell therapy involves injecting cells from a donor who is unaffected by a particular disease at an appropriate site in a person who has the disease. Cells can also be taken from someone who is affected by the disease, genetically modified in culture, then returned to the patient.

A trial of cell therapy to combat Hurler's syndrome was announced in France in April 1995. Doctors at the Institut Pasteur in Paris plan to 'transplant' a copy of a missing gene for an enzyme into skin cells taken from six babies who are affected by the disease. The modified cells will be bound together with collagen, then reimplanted into the peritoneum (the body cavity that contains the gut and other organs). It is hoped that the implanted cells will secrete α-iduronisase, an enzyme without which the babies would suffer from severe damage to organs, bones, nerves and brain and eventually die in early childhood.



Above: How cell therapy might be used to alleviate the symptoms of Duchenne muscular dystrophy.

In Duchenne muscular dystrophy (DMD), where the cells do not produce the protein dystrophin, healthy muscle cells might be cultured and then injected into the patient's muscles. Since the injected cells would contain normal copies of the dystrophin gene they would produce enough dystrophin to prevent further degeneration of muscle fibres. This sort of treatment may prove to be the only route in the foreseeable future for treating DMD, as the dystrophin gene is too large to 'transplant' by current genetic techniques. Cell therapy could also provide a means of treating diseases such as cancer and AIDS, and managing chronic conditions like diabetes.

INSTRUCTIONS

Using these materials

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This activity involves rôle-play and aims to inform students about three serious genetic diseases (Cystic fibrosis, Duchenne muscular dystrophy and Huntington's disease).

Students adopt the rôle of potential parents who are carriers of inherited diseases. As parents they have to make important decisions, which are agreed between the partners. This introduces the task of making informed decisions about several issues, including: having children, prenatal diagnosis, termination of pregnancy and other choices that are now becoming available.

The exercise can foster an awareness that scientific developments must be viewed within wider social, ethical and political contexts. It should also help students to learn more about their own and others' values and attitudes, and help them to develop communication skills and confidence.

This activity is not meant to be definitive. It lends itself to modification according to the depth of information that it is necessary to convey to the students. Teachers may wish to add to or replace the genetic diseases mentioned in this Unit with others they consider to be more appropriate for their own students e.g. sickle cell anaemia.

Dealing with sensitive issues

It would be prudent for teachers to find out whether any members of a class or their close friends or relatives are affected by serious genetic conditions before starting the work in this Unit. This must be done with sensitivity.

One approach would be to ask the class whether anyone is familiar with the inherited conditions mentioned in the Unit and to investigate further if necessary. Alternatively, use the questionnaire in the Unit, the answers to which may indicate if anyone is affected personally. Consider whether to discuss some conditions at all and if so, be prepared to proceed with caution and sensitivity.

Some students may wish to talk in confidence about inherited conditions in people they know. Groups may need to be managed to develop an atmosphere of non-judgemental acceptance and trust.

Aims

To increase awareness amongst teachers and their students:

- about the nature of and the effects of some inherited conditions;
- of the new technologies involved in locating the genes involved, prenatal and carrier testing;
- about some of the issues that arise from developments in human genetics.

Advance preparation

Students should read and understand the *Briefing notes* about the three genetic diseases described in this Unit.

Teachers should prepare to act as a source of information and to deal with the issues that may arise during this activity. Teachers should be aware that people in their classes or their relatives may be directly affected by the conditions described (see *Dealing with sensitive issues*).

Organisation

A minimum of 60 minutes should be allowed for this activity, in addition to the preparatory work.

Materials

Required by each class of students

- Sufficient *Genetics cards* (in male and female pairs) for all the students involved (from the photocopy master in this Unit)
- Sufficient copies of the *Worksheets* and *Briefing notes* for each student (from the photocopy masters in this Unit)

Optional

- *Background information* from this Unit
- Resource materials from various associations and groups (see *Appendix 3*)
- If they are available, video recordings explaining Cystic fibrosis, Duchenne muscular dystrophy and Huntington's disease might prove useful.

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Procedure in brief

1. Do whatever *Advance preparation* is necessary.
2. Give out the *Genetics cards* to individuals. Allow the students to organise themselves to work in pairs.
3. Give out *Worksheet 1*.
4. Give out the *Briefing notes* and use the other resource materials as appropriate.
5. Give out *Worksheet 2*.
6. Show video recordings if they are available and appropriate.

Extension

For biology students in particular the genetics and the DNA technology involved may be extended to relate to other parts of the curriculum. (The *Background information* in this Unit may be useful here.)

Procedure in detail

The accompanying *Genetics cards* should be photocopied onto coloured card so that they are colour-coded e.g. Card 1 on blue, Card 2 on pink, Card 3 on green. Each card states whether it refers to a male or female, and has details of predisposition to three serious genetic diseases.

Each participant selects a card at random from a shuffled deck (ensure that the correct number of cards is in the deck in suitable pairs). You can arrange things so that females are given female cards and males male cards — but this is not always feasible or necessary.

Participants are then invited to find a spouse (husband or wife) — someone with the same colour (and number) of card as themselves, but of the opposite sex (as specified on the card).

Once the 'parents' are settled they are given *Worksheet 1*. This instructs the 'parents' to examine and compare their cards to find out if they are 'at risk'. Note: The cards have been designed so that *every* couple will be at risk of having children who are affected. Card 1 for Cystic fibrosis, Card 2 for Duchenne muscular dystrophy and Card 3 for Huntington's disease. These diseases have been chosen to represent a range of modes of inheritance and to raise a variety of issues associated with genetic disease.

Participants should be told that *Briefing notes* on the diseases are available for consultation so that they can answer the questions on the worksheets.

The cards

There are male cards and female cards of each colour:
No. 1 – Blue cards – CF = Cystic fibrosis;
No. 2 – Pink cards – DMD = Duchenne muscular dystrophy;
No. 3 – Green cards – HD = Huntington's disease.

Worksheet 1

The couple has to decide which genetic disease their children might suffer from and the probability of this occurring.

Cystic fibrosis

Only if both parents are carriers are the offspring likely to be affected .

Duchenne muscular dystrophy

If the mother is a carrier then there is a likelihood of the sons being affected.

Huntington's disease

If one of the parents is affected then the offspring are at risk of developing the disease.

Worksheet 2

Once the 'parents' have identified that they are at risk of having children who might suffer from one of the genetic diseases and have found out that these diseases can be passed on to future generations, they are asked to make a number of decisions. The teacher should try to avoid making any decisions for the 'parents'. Instead, the teacher should adopt the rôle of a facilitator, providing information when it is asked for.

Students should be encoraged to think through the problems and to write down their reasons for making particular decisions, using the information that is available to them.

Decision 1

Even if a couple chooses not to have children at this stage, they should continue to Question 2. The *Briefing notes* should help here.

Decision 2

The 'parents' then have to discuss all the possibilities and to place these in rank order - this encourages them to seek information and to think carefully about possible courses of action.

Again the teacher should resist the temptation to make any value judgements. The 'parents' should be encouraged to make decisions by themselves.

Decision 3

The third decision the 'parents' have to make is whether or not they are going to have a prenatal diagnosis. Even if they decide not to take this test they should continue the exercise, imagining that they did agree to a test and that it was positive. They then have to decide what to do next, considering all the options with care. Even if they agree to an abortion they should continue to consider all other possibilities and place these in rank order of preference.

Finally the 'parents' should consider other diseases with a genetic component, or very mild conditions, to try to find out if their decisions differ from those of the serious conditions considered previously.
At all times the 'parents' should be encouraged to write down the reasons for their decisions.

Confidentiality between the 'parents' should be respected at all times.

If more time is available, or particular 'parents' complete the exercise more quickly than others, give them the opportunity to consider one or both of the other disorders by giving them another set of cards and worksheets.

Try to provide sufficient time for discussion with each group of 'parents'. When run successfully, this Unit stimulates discussion around related topics such as embryo research, surrogate motherhood, the problems associated with applying a wider range of diagnostic tests, and what should be considered as 'abnormal' as more and more probes become available.

It is advisable to have a debriefing session, however short, to round things off and return to normality.

Photocopy these cards onto coloured card for use in the rôle play. Each participant will need a card.

CARD 1 : MALE	
CF	CARRIER
DMD	NORMAL
HD	NORMAL

CARD 1: FEMALE	
CF	CARRIER
DMD	NORMAL
HD	NORMAL

CARD 1 : MALE	
CF	CARRIER
DMD	NORMAL
HD	NORMAL

CARD 1: FEMALE	
CF	CARRIER
DMD	NORMAL
HD	NORMAL

CARD 1 : MALE	
CF	CARRIER
DMD	NORMAL
HD	NORMAL

CARD 1: FEMALE	
CF	CARRIER
DMD	NORMAL
HD	NORMAL

Photocopy these cards onto coloured card for use in the rôle play. Each participant will need a card.

CARD 2 : MALE	
CF	NORMAL
DMD	NORMAL
HD	NORMAL

CARD 2 : FEMALE	
CF	NORMAL
DMD	CARRIER
HD	NORMAL

CARD 2 : MALE	
CF	NORMAL
DMD	NORMAL
HD	NORMAL

CARD 2 : FEMALE	
CF	NORMAL
DMD	CARRIER
HD	NORMAL

CARD 2 : MALE	
CF	NORMAL
DMD	NORMAL
HD	NORMAL

CARD 2 : FEMALE	
CF	NORMAL
DMD	CARRIER
HD	NORMAL

Photocopy these cards onto coloured card for use in the rôle play. Each participant will need a card.

CARD 3 : MALE

CF	NORMAL
DMD	NORMAL
HD	AFFECTED

CARD 3 : FEMALE

CF	NORMAL
DMD	NORMAL
HD	NORMAL

CARD 3 : MALE

CF	NORMAL
DMD	NORMAL
HD	AFFECTED

CARD 3 : FEMALE

CF	NORMAL
DMD	NORMAL
HD	NORMAL

CARD 3 : MALE

CF	NORMAL
DMD	NORMAL
HD	AFFECTED

CARD 3 : FEMALE

CF	NORMAL
DMD	NORMAL
HD	NORMAL

Cystic fibrosis

UNIT 4

European Initiative for Biotechnology Education

BRIEFING NOTES

Cystic fibrosis (CF) is a serious inherited condition which affects mainly the lungs and digestive system, leading to recurrent chest infections and poor absorption of food. It is one of the commonest genetic diseases among people of European origin.

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Frequency

In the United Kingdom about 1 in 2 000 births are affected by CF, which means that about five babies are born every week with this condition. At any one time about 6 000 people in the United Kingdom have CF. On average, three people die every week in the United Kingdom because of CF.

Symptoms

Not every person is affected to the same degree; for some the symptoms are less severe than others. CF causes thick, sticky mucus to be produced in the bronchi. This becomes difficult to cough up so that recurrent lung infections like pneumonia occur. Each bout of infection leaves the lungs slightly more damaged than before and the person's health deteriorates. Vigorous chest physiotherapy (to remove the mucus) and treatment with antibiotics helps to control the infections.

The pancreas becomes blocked by the sticky secretions and fails to produce digestive juices in adequate amounts, leading to chronic diarrhoea, poor weight gain and ill health. Males are infertile because of abnormal mucous secretions in the vas deferens. The loss of chloride ions in the sweat can be severe enough to cause heat stroke in warm weather.

Hereditary basis

This condition is caused by a single gene, which was localised to chromosome 7 in 1985. A protein encoded by the gene regulates the movement of chloride ions in and out of cells. One form of this protein does not work properly so that the secretions that are produced are thicker and stickier than normal. If you have one copy of a faulty allele and one copy of the normal allele you remain healthy but you are a carrier. Roughly 1 in 25 people of European origin carry one copy of a CF allele.

If both parents are carriers and contribute a copy of a CF allele then their child will have CF. If one parent contributes a copy of the normal allele and the other parent contributes a copy of a CF allele then the child, like the parents, will be a carrier of CF but will not show any signs of the condition.

Every time two carriers of CF have a baby the chance on average that he or she will have CF is 1 in 4; the chance of being a carrier is 2 in 4; and the chance of having no CF genes is 1 in 4. These risks apply at each pregnancy — they do not change the more pregnancies you have. CF affects girls and boys in equal numbers.

Early symptoms

All babies in the United Kingdom have a sample of blood taken when they less than a week old. The sample is tested for signs of several diseases which in some health authorities will include CF. About 1 in 10 babies born with CF are very ill in the first few days of life with an obstruction of the bowel. If the test suggests that the baby might have CF then a sweat test is given. In the 1950s it was recognised that children with CF have more salt in their sweat than normal so the sweat test measures the amount of salt in the sweat. If the salt level is very high then the child has CF. Other early symptoms are a troublesome cough, repeated chest infections, prolonged diarrhoea or poor weight gain.

The cause

In 1989 the CF gene was identified. A large number of mutations (about 450 are known) can occur which alter the structure of a large protein called the *Cystic Fibrosis Transmembrane Conductance Regulator* (CFTR) which carries

chloride ions across the membrane of cells lining the lungs and digestive tract. The altered protein doesn't do its job properly, so that too much chloride ion is secreted.

Predictive tests

For most carriers of CF (about 75% of those affected in Britain) the cause is the same — a mutation called ΔF508. It is now possible to follow the CF mutation in families. A test has been developed which identifies who is a carrier, or for prenatal diagnosis. This is usually carried out during the first third of pregnancy (the first trimester) at between ten and twelve weeks using chorionic villus sampling (CVS). A small sample of the developing placenta is removed and sent to the DNA laboratory for analysis. The results are then compared with those of the parents. If the tissue from the foetus has only CF alleles, then the child will have CF at birth. Most prenatal diagnoses have been carried out for couples who already have one child with CF.

Primary care

This is designed to keep the lungs as healthy as possible. Physiotherapy helps to clear the sticky mucus from the lungs; breathing exercises and regular physical exercise also help. Physiotherapy is normally done twice a day. Chest infections are prevented and treated with antibiotics. As children get older the problems increase. To date there have been several successful heart-lung transplants in CF sufferers.

The future

85% of CF carriers can easily be identified. In some places all pregnant women are being offered a CF carrier test as part of a pilot scheme. If the mother is a carrier, the husband will also be offered a carrier test. Such a programme has the potential of reducing the incidence of CF in the population.

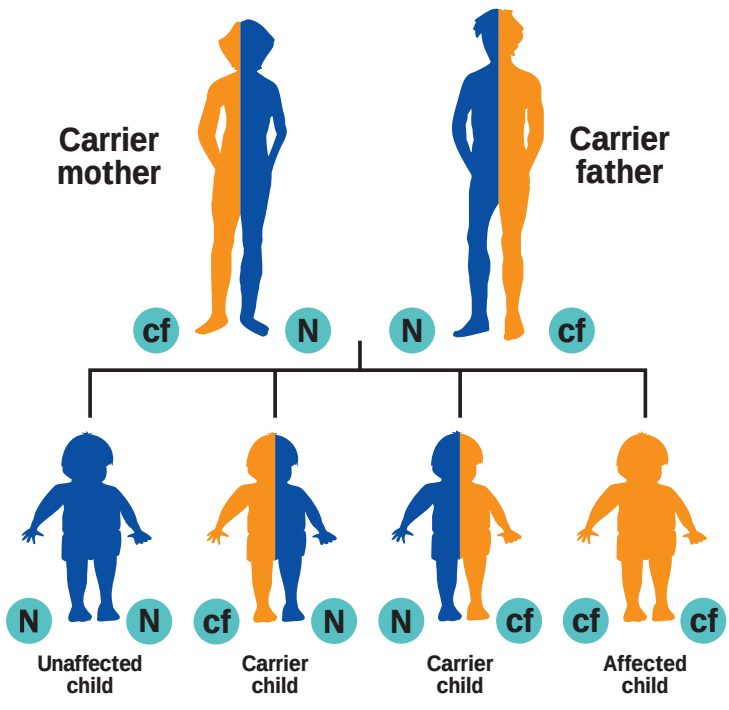
A recent development is the genetic screening of very early stage embryos resulting from *in vitro* fertilization. Those embryos which will not develop into CF children are selected for implantation into the mother who then undergoes a normal pregnancy. Further experimental work is at present being directed towards detecting CF genes in the eggs before fertilization.

Is research leading to a cure for CF? Now that the gene has been located and the function of the protein that is affected is beginning to be understood, scientists are trying several new approaches. New genetic techniques are being used to make better drugs — there will soon be new pancreatic supplements available made using human genes, and also human DNase which loosens the mucus in the lungs. Other scientists are using the human CFTR gene to make protein which will be introduced directly into lungs of patients. Gene therapy is another technique where a normal copy of the CFTR gene is put into the cells lining the lungs to restore normal function.

Inheritance of Cystic fibrosis

(Autosomal recessive)

N= dominant 'normal' allele
cf= recessive CF allele



Duchenne muscular dystrophy

UNIT 4

European Initiative for Biotechnology Education

BRIEFING NOTES

More than 20 conditions can be called muscular dystrophies since they affect muscle cells, causing them to break down. In the United Kingdom several thousand children have some type of MD and about half of these are boys with Duchenne Muscular Dystrophy (DMD). It is so called because it was first described by the French neurologist G.A.B. Duchenne in 1858.

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Frequency

DMD is one of the most common and severe disorders caused by a single gene. It affects about 1 in every 3 000 males born. Girls are affected only extremely rarely.

Symptoms

During their first few years of life infants appear normal but then a gradual, relentless weakening of the muscles begins in early childhood. Infants may be late in starting to walk and they have problems connected with walking. Between the ages of 3 and 7, as the disease progresses, they become more and more clumsy and have difficulty walking, running, climbing stairs and getting up after a fall. At this stage doctors can usually diagnose the disease by means of chemical tests (creatine kinase, an enzyme, is usually present in large amounts in the blood of those affected) or by a muscle biopsy. Muscle weakness gets progressively worse and in most cases contractures develop in the ankles, knees and hips. This means that the muscles get shorter because they are not used, causing the joints to become stiff and tight. By the age of 10 or 12 most boys with DMD are unable to walk. They have to use a wheelchair, and after this their arms grow slowly weaker. Pushing their own wheelchair becomes impossible, so they become dependent on others (or an electric wheelchair) for mobility. Sitting and lying down become difficult and uncomfortable because of the stiffening in the lower body. As the muscles get weaker and weaker, the breathing muscles eventually become affected. Boys with DMD therefore have a shortened life expectancy because they find it difficult to recover from chest infections. All attempts to find out why the childrens' muscles suffered breakdown were unsuccessful. There are about 10 000 proteins involved in the development and function of muscles and the vast majority of these remain unstudied. Biochemists could not find any difference between normal muscle and that from DMD sufferers.

Hereditary basis

This disease is caused by a recessive allele on the X chromosome. With extremely rare exceptions, only boys are affected.

Daughters receive one X chromosome from their mother and one X chromosome from their father while sons receive the X chromosome from their mother and the Y chromosome from their father. In females the normal allele on one of the X chromosomes masks the DMD allele on the other X chromosome, so that the individual is not affected but is a carrier of the condition. In males there is no equivalent allele on the Y chromosome to mask a DMD allele on the X chromosome.

Daughters have a 50% chance of being unaffected or being carriers; sons have a 50% chance of being unaffected or affected. With each pregnancy therefore, a couple in which the female is a carrier has a 25% chance of having an unaffected daughter, a 25% chance of having a carrier daughter, a 25% chance of having an affected son, and a 25% chance of having an unaffected son. The 50% risk does not

mean that exactly half of the sons will get the disease if the mother is a carrier of the DMD allele.

If there were four sons, then none, one, two, three or even all four could be affected. It is also possible for DMD to appear for the first time in a family in which there is no history of the disease — this is due to a genetic mutation and occurs in about a third of cases.

The cause

In 1987 the gene responsible for DMD was isolated. It is located on the short arm of the X chromosome and is the largest gene yet discovered. Some 60% of boys with DMD show a piece of the gene deleted. The protein that it encodes is named dystrophin, and forms part of the structure of the tissue that surrounds muscle fibres.

Predictive tests

At present it is possible to identify from the family tree which women are at risk of being carriers. A combination of creatine kinase and DNA tests allow the great majority of such women to be either identified as carriers or given a strong reassurance that the risk is very low.

The condition can be diagnosed at about the 10th week of pregnancy using DNA studies performed beforehand on all the necessary members of the family. These can give precise information which allows the status of the unborn baby to be identified when its DNA is studied e.g. by a chorion villus biopsy (CVS). If this is not possible, the sex of the foetus can be determined by amniocentesis at about 16 weeks — but this will not show whether the male is affected or not.

Primary care

Primary care can be provided by:

- Family members
  good general health, regular active exercise and not being overweight to maintain muscle strength;
- Physiotherapists
  early identification of contractures and spinal curvature to allow effective and preventative treatment using special exercises;
- Occupational therapists
  special equipment to maintain independence;
- Surgeons
  surgical treatment for contractures and spinal deformity may be considered.

The future

In 1990 the first stages in the development of cell therapy took place and small-scale human experiments began in boys affected by DMD. In 1991 the first stages in the development of gene therapy took place. A copy of the gene coding for dystrophin was inserted into cultured cells, and these were shown to be capable of manufacturing dystrophin. The search for a treatment and an eventual cure continues.

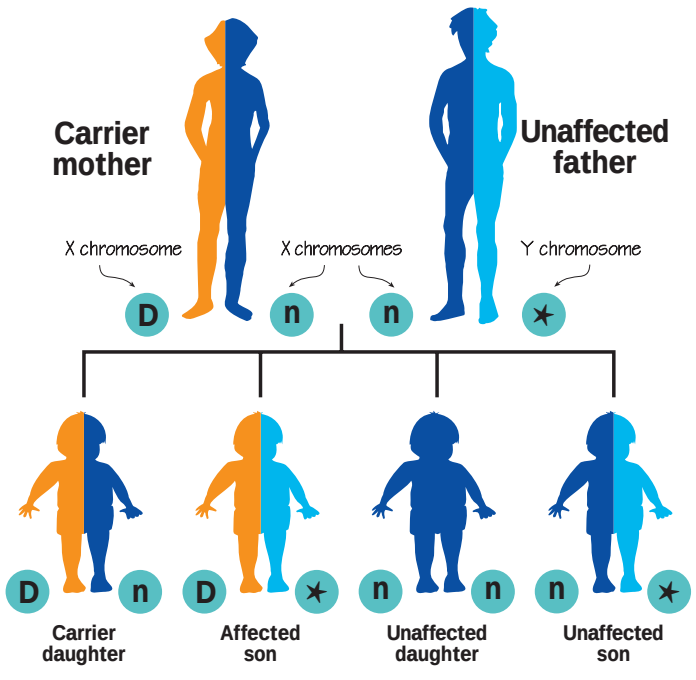
Inheritance of Duchenne muscular dystrophy

(X-linked)

n= 'normal' allele on X chromosome

D= DMD allele on X chromosome

✶= no allele on Y chromosome



Huntington's disease

UNIT 4

European Initiative for Biotechnology Education

BRIEFING NOTES

In 1872 George Huntington, a 22 year-old American doctor from Long Island, New York, presented his scientific paper '*on Chorea*' to the medical academy in Middleport, Ohio. The paper, the only one Huntington ever had published, appeared later in the *Medical and Surgical Reporter of Philadelphia*. He accurately described the inherited nature of a disease as it passed through the generations of several Long Island families. The disease was later named after him as Huntington's chorea (a term meaning purposeless movements) — today it is more commonly called Huntington's disease (HD).

An important feature of HD is that the symptoms do not appear until the person approaches or reaches middle age; usually years after he or she has borne children. In the past people with HD did not live long enough for the disease to have much effect on them. Nowadays the single allele responsible for the disease has more time to express itself.

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Frequency

About one in every 2 700 people are born carrying the allele that causes Huntington's disease. However, as the onset of the disease is late, only about one in 10 000 has the disease at a given time. Both males and females are affected equally.

Symptoms

Huntington's disease is caused by the gradual destruction of brain cells, particularly in those parts of the brain known as the basal ganglia and the cerebral cortex. By some mechanism as yet unknown, the gene, which for years remains inactive, begins to take its toll. Once brain cells die they can never be replaced. The gradual destruction of brain cells causes symptoms which are similar to, but more pronounced than, the normal process of ageing. Early signs of the illness, which start around 35–45 years of age, are mild and increase very slowly and gradually with a change in the person's usual behaviour; they become depressed and moody, have unreasonable outbursts of anger, or have unusual jerky, fidgety movements and a tendency to be clumsy or to fall down.

Over the years the symptoms become more severe. Walking is increasingly difficult, the person suffers from dementia, loss of physical control and wasting of the body. The disease usually lasts for about 10–20 years after which time death occurs, often from secondary infections, heart failure, pneumonia or choking. HD has been called the 'most demonic of diseases' and in the past, many stories of demonic possession and witchcraft may have stemmed from the behaviour of Huntington's sufferers.

Hereditary basis

In 1968 it was discovered that Huntington's disease followed the pattern of a dominant allele — if either parent has this allele then each son and daughter has a 50% chance of inheriting HD and they are said to be 'at risk'.

The 50% risk factor does not mean that exactly half of the children will inherit the disease in a family where HD is known to be present. Each individual child stands a 50% chance at the moment of conception of inheriting HD. This could mean, for example, that one child in a family of four children will develop HD, or two may inherit it, or three, or perhaps all four or none. Huntington's never 'skips a generation'. If a parent with HD has a child who escapes the disease, then that child cannot pass on the risk to any of his or her children: all people who are unaffected are free of the disease-causing allele.

Predictive tests

In the past a person known to be at risk from HD had to live until middle age without showing any sign of the disease before his or her children could be sure that they (and their children) were free from risk. In 1983, 'markers' close to the HD allele were located on chromosome 4 — people who inherit these markers are likely to inherit the HD allele as well. In different people, even from the same family, different forms of the markers can be identified. Predictive tests based on these markers can be used, although the test will not work for every individual who is at risk. In the near future tests based on the detection of the HD allele itself will become available.

Difficulties with HD

The hereditary nature of HD makes the prospect of starting a family particularly difficult. Many individuals who are at risk have already established families before they learn about HD or fully understand the nature of it. Some who fully understand HD and its hereditary implications may choose to have children; others may decide not to have children of their own in order to avoid passing the disease on to another generation. Through counselling the full implications of the genetic characteristics of HD should be discussed and all the alternatives available should be considered. For those affected by HD, over time the marriage relationship will alter and the partner with HD will be less of a friend, companion and lover — this adds personal grief to a complex situation for all concerned. Other important worries about HD are in relation to insurance, employment, mortgages and so on.

Primary care

Primary care can be provided by:

- Occupational therapists
  assess what help and/or home extensions are needed to help the patient;
- Physiotherapists
  can help patients to reduce difficulties with balance and physical co-ordination;
- Speech therapists
  give advice on methods of maintaining communication skills;
- Public health nurses
  help with bathing, dressing, skin and basic care;
- Community psychiatric nurses
  advise the family on patient's behavioural or psychological problems.

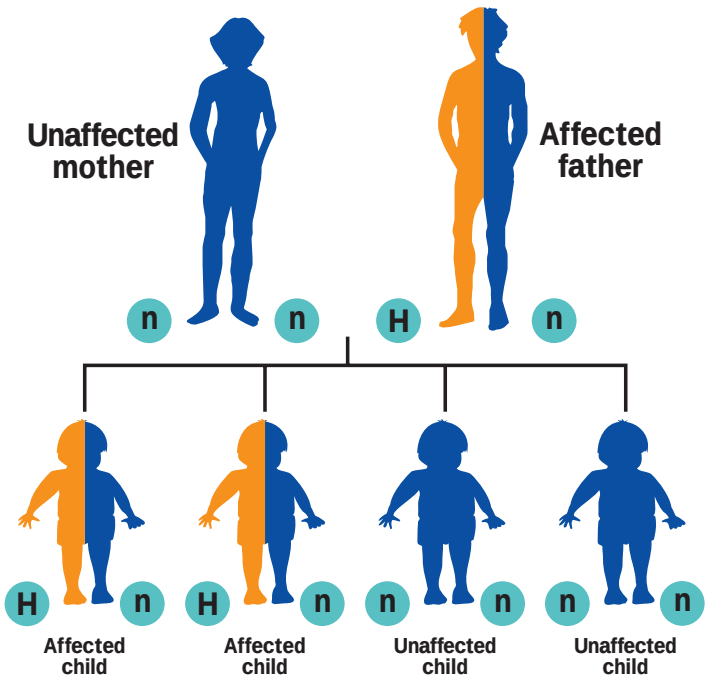
The future

In 1993, the exact location of the HD allele was pinpointed. It will only be a matter of time before the structure of the HD gene is worked out. Then it will be possible to determine which protein is affected. Treatment of this disorder might then be achieved by administering this protein to alleviate the condition — this may be possible using cell therapy techniques. Eventually gene therapy might alleviate the symptoms of or prevent Huntington's disease.

Inheritance of Huntington's disease

(Autosomal dominant)

H= dominant HD allele
n= recessive 'normal'



Worksheet 1

1 You have selected a male or a female card of a particular colour and number. Do not be concerned if it is not the correct sex!

2 Look for a partner, that is, someone who has a card of the same colour as yours but the opposite sex (on the card). For the duration of this simulation you are now husband and wife!

3 Turn your cards over and set them side by side. Each card contains information from genetic screening tests regarding your inheritance for one of three severe genetic diseases — CF = Cystic fibrosis, DMD = Duchenne muscular dystrophy and HD = Huntington's disease.

From this information do you, as parents, think that you are you at risk of having children who will suffer from CF, DMD or HD?
Explain your reasoning.

4 Now read about the relevant disease from the briefing notes.

Work out the reasons why your children might suffer from this genetic disease and what the chances of them being affected are.
Find out as much information as possible about the disease, what treatments are available etc. Ask for help if you need it.

Worksheet 2

1 Having identified the genetic disease in your 'at-risk' family and found out as much as you can about it, try to make the following decisions, which must be agreed upon by both partners. Ask for further information if you need it.

DECISION 1 **Will we have any children?**
Give reasons for your decision.

2 Whether or not you have decided to have any children, assume that you have decided that you do want children. Examine the sheet *'GENETIC DISORDERS: prevention and cure'*, and ask for any help if you need it.

Consider the various options that are open to you e.g. to have children in the normal way, to adopt children (rare nowadays), embryo selection, *in vitro* fertilization by donor, surrogate motherhood, abortion etc.

DECISION 2 **Discuss all the possibilities and place them in rank order of preference (most preferred first).**

3 No matter what your decision in 2 was, imagine that the female partner has just found out that she is pregnant.

DECISION 3 **Will we have a prenatal diagnostic test?**
Give reasons for your decision.

CONTINUED OVERLEAF...

Worksheet 2 (continued)

4 Imagine that you have decided to have a prenatal diagnosis test and that the result is positive — your child will definitely suffer from CF, DMD or HD.

DECISION 4 **Decide what options are now available and what you would do. Once again, give reasons for your decision.**

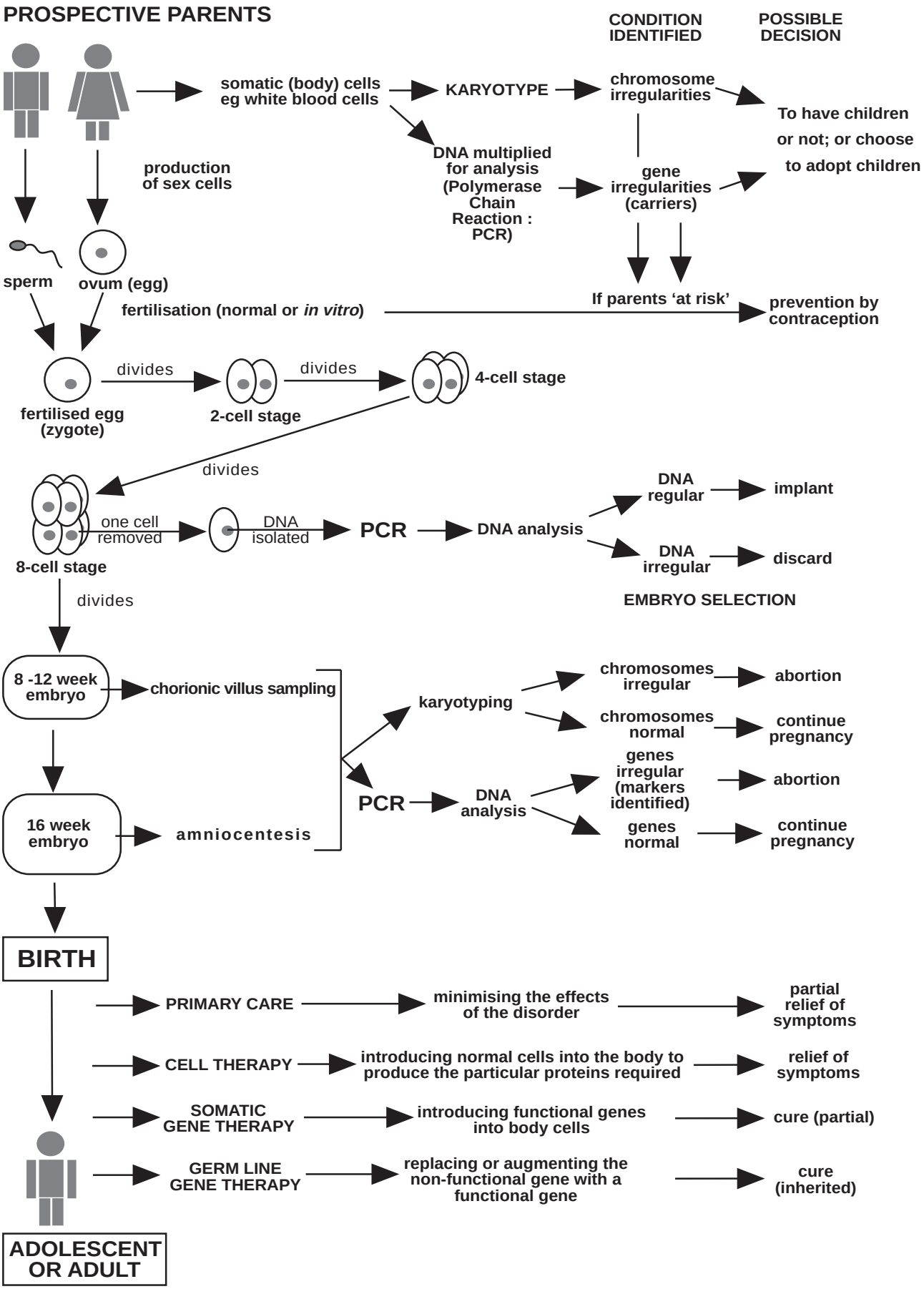
5 No matter what decision you made in 4, imagine that you decided to continue the pregnancy.

DECISION 5 **Look again at all the information, but this time consider carefully the treatments that are available at present, or might be in the future e.g. primary care, therapeutic drugs, organ transplants, cell therapy or gene therapy etc. Try to rank them in order of preference.**

6 The situation above considered a very serious genetic disease. As we learn more about the genetic predisposition to more and more diseases e.g. cancer, heart disease etc. decisions such as those above might become more commonplace (and in some cases, more difficult).

DECISION 6 **Would the decisions that you made above be different if the disease under consideration was: heart disease; diabetes; schizophrenia; cancer; or flat feet?**

Genetic disorders : prevention and cure?



Appendix 1

Eugenics

UNIT 4

European Initiative for Biotechnology Education

EUGENICS

Some people associate developments in modern human genetics with the type of eugenics that occurred in Nazi Germany. Such anxieties are probably unjustified, but there is a need for wider public debate and education to put current developments into perspective and to ensure that abuses do not occur in the future. For this reason, some historical information about the eugenics movement and associated issues has been included here. This treatment is of necessity, superficial; those who are interested should consult the references listed both here and in *Appendix 3*.

★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★

In the late nineteenth century Francis Galton, a mathematician and younger cousin of Charles Darwin, suggested that human beings might be 'improved' in the same way as varieties of plants or farm animals. He coined the word 'eugenics' to describe this process.

Galton's ideas quickly became popular and eugenic research establishments were set up throughout the world. The first eugenicists were encouraged by the newly-rediscovered work of Mendel, which focused on characteristics in plants that were controlled by single genes. Most of the early geneticists were seduced by the ideas of the eugenicists. They tried to explain human characteristics, including temperament and intelligence, in terms of the inheritance of single genes. From their statistical studies of families, researchers claimed to have identified genes governing behaviours such as *'holding a grudge'* and *'pauperism'*. One prominent American eugenicist even searched for a gene for 'love of the sea' (this he believed, would be common amongst naval officers!).

While behaviour was difficult to assess, intelligence, apparently, was not. Tests of 1.75 million American army recruits during World War I seemed to show marked differences in innate ability between those from various countries. Charles Davenport, director of the Eugenics Record Office at Cold Spring Harbor on Long Island, New York, feared that an influx of eastern and southern Europeans would make the American population *"darker in pigmentation, smaller in stature, more mercurial... more given to crimes of larceny, kidnapping, assault, murder, rape and sex-immorality."*

The IQ 'evidence' helped to persuade the US Congress to pass an Immigration Restriction Act in 1924, limiting entry of people from southern and eastern Europe. Tragically, this law kept out an estimated six million people, many of whom were fleeing persecution by the Nazis. Today, the IQ tests' cultural bias (in favour of white, middle class, northern Europeans) and the unfair manner in which they were administered seem obvious (see for example, Gould, 1981).

In the first decade of this century, surgical procedures permitting human sterilization were perfected. Before the advent of antibiotics, a significant proportion of operations led to further complications and even death, but the new surgical techniques were welcomed by the eugenicists. By 1931 compulsory sterilization laws had been passed in 31 of the United States of America. These laws applied to *'hereditary defectives'*, including *'drug fiends'*, *'epileptics'*, *'drunkards'* and *'diseased and degenerate persons'*. The families of the unemployed who were drawing money from social welfare were also encouraged to accept voluntary sterilization. Although the laws were never enforced comprehensively, by January 1935 some 25 000 people had been forcibly sterilized, nearly half of them in California.

During the 1920s and '30s many prominent people of widely-differing political persuasions advocated compulsory sterilization of certain groups. Towards the end of his life the socialist playwright George Bernard Shaw wrote (with deliberate irony, one assumes) *"If we desire a certain type of civilization, we must exterminate the sort of people who do not fit into it... Extermination must be put on a*

scientific basis if it is ever to be carried out humanely and apologetically as well as thoroughly".

In 1910, when he was Home Secretary, Winston Churchill opined "*The unnatural and increasingly rapid growth of the feeble-minded and insane classes constitutes a national and race danger which is impossible to exaggerate. I feel that the source from which the stream of madness is fed should be cut off and sealed off before another year is past.*" Churchill's comments were considered so inflammatory, especially in the light of subsequent events, that they were not made public until 1992.

Despite the enthusiasm of some people, proposals for sterilization were fiercely rejected in Britain, The Netherlands and several central European countries. Marie Stopes, a member of the Eugenics Society in the United Kingdom, advocated family planning through contraception instead. However, throughout northern Europe, particularly in Scandinavia, sterilization was widely practised. The socialist K.K. Steincke (who is accredited with founding the Danish Welfare State) justified this action as follows: "*When the liberty of the individual is detrimental to the common good it must recede, especially when this liberty will lead to immeasurable suffering of future generations.*"

The worst extremes of the eugenics movement occurred in Nazi Germany. Funds were poured into eugenic research institutes by the Nazis in an effort to find scientific backing for their racist policies. Influenced by the American model, the Nazis passed their own 'racial hygiene' law in 1933. By 1945 about 2 million young Germans had been forcibly sterilized — most of them were between 15 and 17 years old. Compulsory sterilization was soon to be supplemented by systematic mass murder of the mentally and physically disabled and eventually, by the horrors of the death camps.

During the 1940s, scientific opinion started to turn against eugenics. The Nazi atrocities had much to do with this. In addition, evidence from conventional plant and animal genetics was beginning to reveal the complex nature of inheritance. The eugenicists had neglected polygenic characteristics — those characteristics, such as height, which are controlled by the interaction of many genes. Eugenicists, influenced by notions of class and race, also failed to take adequate consideration of cultural, economic and other influences on human development. Beckwith (1993) has also identified the key rôle that the eugenicists played in making their subject appeal to the general public (especially in the United States), which helped to secure political support for their cause. By the time geneticists began to speak out openly against the abuse of their field, it was too late (Crew *et al.*, 1939).

To some extent, the modern researcher still bears the stigma of the irresponsible scientist. As Beckwith (1993) states: "*The image of the scientist as someone who carries out ill-considered experiments, often with claims of benefits to humanity, is one of the most common representations of scientists in film and fiction. Less common is the image of the scientist who takes action to prevent damaging results of scientific discoveries. ... Scientists were among the most vocal spokespersons asking for bans or restrictions on nuclear weapons in the 1950s and 1960s. In the 1970s, a group of molecular biologists called successfully for a moratorium on recombinant DNA research until the potential health hazards were fully addressed.*"

In recent years, especially since the advent of the Human Genome Project, there has been a resurgence of genetic determinism (see for example the analysis by Lewontin, 1993). A positive sign is that a significant proportion of the funds for the Human Genome Project have been allocated to ethical, legal and social implications of the research. If developments in modern genetics are to benefit rather than harm people there must be an awareness of the lessons of history amongst the scientific community and society at large.

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Additional information

(see Appendix 3 also)

Crew, F.A.E. *et al.* (1939) Men and mice at Edinburgh. *Journal of Heredity* 30 371–373.

Beckwith, J. (1993) A historical view of social responsibility in genetics *BioScience* 43, 327–333.

The racial state. Germany 1933–1945 by M. Burleigh and W. Wipperman (1991) Cambridge University Press, Cambridge. ISBN: 0 521 39802 9.

The mismeasure of man by S. J. Gould (1981) Penguin, London. ISBN: 0 14 02 2501 3.

The doctrine of DNA. Biology as ideology by R.C. Lewontin (1993) Penguin Books, London. ISBN: 0 14 023219 2.

Murderous science. Elimination by scientific selection of Jews, gypsies an others, Germany 1933–1945 by B. Müller-Hill (1988) Oxford University Press, Oxford. ISBN: 0192615556. [Out of print]

Müller-Hill, B. (1993) The shadow of genetic injustice. *Nature* 362, 491–492.

Postgate, J. (1995) Eugenics returns. *Biologist* 42, 96.

Appendix 2

Cultural contexts

European Initiative for Biotechnology Education

Cultural contexts of genetic screening and counselling

The field of clinical genetics is expanding rapidly. New methods of detecting genetic abnormalities offer the potential to identify and to change what might be considered undesirable traits.

Many people welcome these developments as part of medical progress and wish to seize the opportunities they promise. Some other individuals and groups voice their dissent, though often for different religious or secular reasons.

Fundamental anxieties surrounding the use of genetic technologies regularly involve concern over the sanctity of life and the integrity of nature. Disquiet over the possible threat to the rights of the embryo, foetus, women and the disabled repeatedly act as foci of concern.

However, on the whole, it is probably both too simple and unproductive to place people in 'for' or 'against' camps when considering the issues involved. The often complex factors such as, the technique used, the form and severity of the disease, the wider social context, and not least, the individuals and families concerned with the decision-making processes, deserve a more sensitive analysis.

Some points that are pertinent to the current debate around genetic screening programmes are outlined below.

The rights to knowledge, refusal, privacy and confidentiality

The geneticist's aims for screening for genetic disorders include the prevention of disease and the utility of offering informed choice about reproductive decisions. Yet, past experience of some programmes show that they have led to discrimination and stigmatisation against identified carriers of certain traits (Markel 1992).

For instance, in the 1970s a screening programme for sickle-cell anaemia in the U.S. and for thalassaemia in Greece have both had adverse, albeit unintended consequences, on the screened population. In Greece, once identified, carriers were sometimes isolated, socially ostracised, and considered to be undesirable marriage partners. In the U.S, many African-Americans were stigmatised by their carrier status by being denied health and life insurance, employment opportunities, and even acceptance into the US Air Force Academy.

The screening procedures described were meant to be beneficial to the population screened, but in fact, caused various forms of distress to the people identified as carriers. Clearly, technical capability is a necessary but insufficient means for carrying out *successful* screening programmes. Social implications may need to be more carefully thought out and should be integral to any screening programme.

Networks of support

A genetic counsellor in the U.S. (Walshvockley, 1991) has raised the need for adequate counselling to back up the rapid rise in demand created by the new technologies. She explores how knowledge of carrier status can result in negative psychological consequences and/or have detrimental practical results. By drawing on examples of the newborn, children offered for adoption and those identified as carriers of cystic fibrosis, Walshvockley demonstrated the far-reaching effects such programmes can create in their wake.

These problems centre on the right of refusal, the right to knowledge, the right to privacy and the right to confidentiality. The question of who should make these decisions becomes problematic as concern rises over the growing recognition that many questions cannot be reduced to expert opinion when they overspill into the social arena.

Adequate counselling

Good counselling as part of an accompanying social response to the thrust of genetic screening techniques is advocated. Ideally, the counsellor should give clear and undirected information to a woman whose choice should then be supported. Yet this is difficult to achieve in practice (Birke, Himmleweit, Vines, 1990).

Billings argues for equitable civil rights, equal access to health care, the right to work, optional rather than mandatory screening, and discussion of the processes of discrimination and stigmatisation. Speaking from his experience as a clinical geneticist he concludes that genetic counselling is not always successful (Billings 1991)

A renaissance of eugenics?

This perennial issue is frequently seen to be pertinent to the debate. When considering the eugenic potential inherent in the combined use of the new reproductive technologies and genetic engineering, Holtzman writes: *"To avoid a renaissance of eugenics... interferences with individuals procreative choices... every effort should be made to preserve the autonomy of the individuals in deciding whether or not to be tested."* (Holtzman, 1992)

The British Medical Association (1992), similarly noted fears that the power to control our genetic constitution could also give rise to a new eugenics. They stressed the need to clearly keep in view, the distinction between diagnosis and treatment of disease and the selection of desirable traits.

However, although this may present a laudable principle it suffers from problems. Historical and cultural definitions of what constitutes a 'desirable trait', tends to be a moveable target. This is germane to the application of gene therapy, particularly to germ-line therapy.

Conclusion

Though by no means comprehensive, the above indicates that technical capability is only one factor of genetic screening programmes. Human gene technology is not merely a medical matter, it is embedded in social, political, economic and ethical contexts. Different screening programmes will always have distinct consequences for individuals and perhaps for populations, which may not always be immediate, predictable or intended.

New opportunities for screening and preventing disease therefore, present a challenge to meet them with tolerant, sensitive and adequately-funded social policies.

References

Billings, P.R. (1991) The context of genetic screening. *Yale Journal of Biology and Medicine*. 64 (1) 47-52.

Tomorrow's Child. Reproductive Technologies in the 90s by L. Birke, S. Himmelweit, G. Vines (1990) Virago Press, London.

Our genetic future. The science and ethics of genetic technology. British Medical Association (1992) Oxford University Press, Oxford.

Holtzman, N. The diffusion of new genetic tests for predicting disease. *FASEB Journal.* 6 (10) 2806-2812.

Markel, H. (1992) The stigma of disease: Implications of genetic screening. *American Journal of Medicine.* 93, 209-215.

Walshvockley, C. (1991) Counselling issues in genetic screening. *Yale Journal of Biology and Medicine.* 64 (3) 255-257.

Appendix 3

Additional resources

UNIT 4

European Initiative for Biotechnology Education

Books

Unless otherwise indicated, these are popular accounts intended for a general readership. Where one is available, a paperback edition is referred to.

Our genetic future. The science and ethics of genetic technology Anonymous (1992) Oxford University Press, Oxford. ISBN: 0 19 286156 5. *Report for the interested lay reader, produced by the British Medical Association.*

The book of man. The quest to discover our genetic heritage by Walter Bodmer and Robin McKie (1994) Little, Brown and Company, London. ISBN: 0 316 90520 8. Hardback. *Popular account of the genome project by the former director of HUGO, the Human Genome Organisation.*

Wonderwoman and superman. The ethics of human biotechnology by John Harris (1992) Oxford University Press, Oxford. ISBN: 0 19 217754 0. Hardback. *An academic discussion of ethical issues.*

Genetics and society by Barry Holland and Charalambos Kyriacou (Eds.) (1993) Addison-Wesley, London. ISBN: 0 201 56515 3. *A collection of short papers, by scientists, describing some of the developments that raise wider concerns.*

Exploding the gene myth by R. L. Hubbard and E. Wald (1993) Beacon Press, Boston. ISBN: 0 8070 0419 7. *A critique of biological determinism, the genome project and much of the biotechnology business.*

Genetics for beginners by Steve Jones and Borin van Loon (1993) Icon Books, London. ISBN: 1 874166 12 9. *A cartoon presentation of genetics.*

The language of the genes. Biology, history and the evolutionary future by Steve Jones (1993) Flamingo, London. ISBN: 0 00 654676 5. *A highly acclaimed popular account of human genetics.*

The code of codes. Scientific and social issues in the human genome project by Daniel Kevles and Leroy Hood (Eds.) (1992) Harvard University Press, Massachusetts. ISBN: 0 674 136462. *A broad, balanced collection of articles by scientists and non-scientists.*

The doctrine of DNA. Biology as ideology by R.C. Lewontin (1993) Penguin Books, London. ISBN: 0 14 023219 2. *A series of short articles that are critical of biological determinism.*

The new human genetics. How gene splicing helps researchers fight inherited disease by Maya Pines (1984) U.S. Department of Health and Human Services. *A concise and authoritative guide to basic molecular genetics, with particular reference to human genetic disease and the genome project. (National Institute of Health Publication Nº 84-662).*

Genethics. The ethics of engineering life by David Susuki and Peter Knudtson (1989) Unwin Hyman, London. ISBN: 0 04 440623 1. *Despite the title, predominantly a popular account of the techniques of modern biotechnology, with an attempt to identify some general 'ethical' principles.*

The new genetics and clinical practice by David J. Weatherall (1993) (3rd edn.) Oxford University Press, Oxford. ISBN: 0192619055. *Authoritative reference for a medical/scientific readership.*

Perilous knowledge. The human genome project and its implications by Tom Wilkie (1993) Faber and Faber, London. ISBN: 057117051X.

Exons, introns and talking genes by Christopher Wills (1992) Oxford University Press, Oxford. ISBN: 0 19 286154 9. *Popular account of the genome project.*

Born imperfect by Richard West (1993) Office of Health Economics, London. *Slim, yet comprehensive and authoritative booklet describing inherited diseases and some of the issues raised, especially for the medical community: don't be put off by the title. Available from: Office of Heath Economics, 12 Whitehall, London, SW1A 2DY. (Booklet Nº 110, Price £5.00).*

Educational materials for schools

Genes, diseases and dilemmas Anonymous (1993) Hobson's Publishing, Cambridge. ISBN: 1 85324 898 3. Sponsored by the Association of the British Pharmaceutical Industry. Booklet aimed at 16-19 year-old students (not necessarily those who are studying biology). Includes questions for debate and a teacher's guide.

SATIS 16-19
Unit 87: Cystic fibrosis.
Materials for classroom use, aimed at 16–19 year-olds. Available from:
The Association for Science Education, College Lane, Hatfield, Hertfordshire AL10 9AA. The United Kingdom.

Mapping and sequencing the human genome: Science, ethics and public policy by M.A.G. Cutter, *et al* (1992) Biological Sciences Curriculum Study / American Medical Association. This package contains classroom activities and case studies. It is available from:
BSCS, 830 North Tejon Street, Suite 405, Colorado Springs, Colorado 80903-4720. United States of America.

General

General information about modern genetics and some of the issues associated with it is available from:

The British Medical Association
Tavistock Square
London
WC1H 9JR
Telephone: + 44 (0)171 387 4499

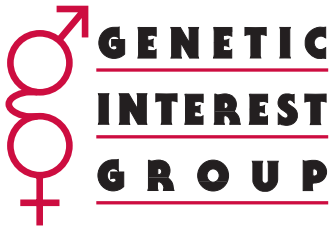
The Medical Research Council
20 Park Crescent
London
W1N 4AL
Telephone: + 44 (0) 171 636 5422

The Nuffield Council on Bioethics
28 Bedford Square
London
WC1B 3EG
Telephone: + 44 (0)171 631 0566

The Information Centre
Wellcome Centre for Medical Science
183 Euston Road
London
NW1 2BE
Telephone: + 44 (0)171 611 8722

Support organisations

There are numerous organizations that support those directly affected by serious genetic conditions. Some of these fund medical research, and all are a valuable source of up-to-date information about the conditions. Although many of them produce magazines, booklets and leaflets these support groups are small charities and they are generally run by volunteers. Teachers and students should bear this in mind should they request information.



In the United Kingdom, there is an 'umbrella' organization which represents the interests of over 100 charities set up to support those affected by genetic disease. This is:

The Genetic Interest Group
Farringdon Point
29–35 Farringdon Road
London
EC1M 3JB
Telephone: + 44 (0) 171 430 0090

The individual organizations that deal with the conditions mentioned in this Unit are:

The Cystic Fibrosis Research Trust
Alexandra House
5 Blyth Road
Bromley
BR1 3RS
Telephone: +44 (0) 181 464 7211

The Muscular Dystrophy Group of Great Britain and Northern Ireland
Nattrass House
35 Macaulay Road
London
SW4 0QP
Telephone: + 44 (0) 171 720 8055

The Huntington's Disease Association
108 Battersea Road
London
SW11 3HP
Telephone: + 44 (0) 171 223 7000

Appendix 4
Human genetics questionnaire

UNIT 4

European Initiative for Biotechnology Education

HUMAN GENETICS

In August 1993, *The Daily Telegraph* newspaper in London commissioned a national poll of the population's attitudes towards various issues associated with human genetics. 1 024 people over the age of 16 were surveyed. The questions and results of the poll are given here.

A blank questionnaire is supplied, so that it may be photocopied and used by students. Note that although Question 7 refers to abortion, an increasing range of options is now becoming available, so that in the future this may not be the only choice. (see *Background information*).

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Question 1
How knowledgeable do you consider yourself to be about genetics? (Tick one box only.)

Response	% of respondents
Very knowledgeable	5
Reasonably knowledgeable	42
Not very knowledgeable	34
Not at all knowledgeable	20

Question 2
Some diseases run in the family. A particular person may not suffer from that disease but may pass it on to their own children. Before having a child would you (and your partner) be willing to take a test to discover whether you are going to pass on a crippling or fatal disease to your child?

Response	% of respondents
Yes, but only to discover whether I might soon show symptoms of the disease	12
Yes, for my child's sake	47
Yes, so I know where we both stand	25
No	11
Don't know	1

Question 3
Suppose you have a strong chance of contracting heart disease at the age of 40. If doctors diagnosed this when you were 21, would you want them to tell you? (More than one answer accepted.)

Response	% of respondents
Yes, because I have the right to know	56
Yes, but only if I could adjust my life to reduce the risks	39
No	11
Don't know	3

Question 4
Do you believe that it is right to select or alter the genes for specific hereditary characteristics in the next generation of children? (More than one answer accepted.)

Response	% of respondents
Yes, to relieve suffering or disability	51
Yes, to prolong the life of someone otherwise destined for an early death	29
Yes, to breed socially useful behaviour	4
Yes, to remove socially undesirable characteristics	7
No, all of these are wrong	35
Don't know	7

Question 5
Doctors may soon be able to treat some inherited fatal diseases, such as cystic fibrosis, by a process of transplanting genes to repair the body's own processes. How willing would you be to accept this treatment if it would save your life? (Tick one box only.)

Response	% of respondents
Very willing	70
Somewhat willing	17
Not very willing	3
Not at all willing	4
Don't know	6

Question 6
Insurance companies could use genetic information from a blood test to target their policies, for instance by ensuring that only those who will develop a disease will pay a higher premium. Employers could screen the workforce, for instance to ensure that those at risk of cancer are not taken on to work with chemicals. In what circumstances should insurers and employers be allowed to have access to genetic information?

Response	% of respondents
Whenever they consider it necessary	8
Only when the individual is known to be carrying the gene for a serious disease	10
Only so long as a government-appointed body monitors the way the information is used	9
In no circumstances at all	68
Don't know	8

Question 7
Faulty genes can cause diseases such as muscular dystrophy and some cancers. If genetic tests on your unborn child showed that it would suffer from a crippling disease at the age of 16, as a parent what would you do? (Tick one box only.)

Response	% of respondents
Choose abortion	38
Take no action and hope that a treatment would be developed	24
Take no action because I consider abortion to be unacceptable	14
Don't know	23

Questionnaire

★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★

Question 1

How knowledgeable do you consider yourself to be about genetics? *(Tick one box only.)*

Very knowledgeable ❑
Reasonably knowledgeable ❑
Not very knowledgeable ❑
Not at all knowledgeable ❑

Question 2

Some diseases run in the family. A particular person may not suffer from that disease but may pass it on to their own children. Before having a child would you (and your partner) be willing to take a test to discover whether you are going to pass on a crippling or fatal disease to your child?

Yes, but only to discover whether I might soon show symptoms of the disease ❑
Yes, for my child's sake ❑
Yes, so I know where we both stand ❑
No ❑
Don't know ❑

Question 3

Suppose you have a strong chance of contracting heart disease at the age of 40. If doctors diagnosed this when you were 21, would you want them to tell you? *(More than one answer accepted.)*

Yes, because I have the right to know ❑
Yes, but only if I could adjust my life to reduce the risks ❑
No ❑
Don't know ❑

Question 4

Do you believe that it is right to select or alter the genes for specific hereditary characteristics in the next generation of children? *(More than one answer accepted.)*

Yes, to relieve suffering or disability ❑
Yes, to prolong the life of someone otherwise destined for an early death ❑
Yes, to breed socially useful behaviour ❑
Yes, to remove socially undesirable characteristics ❑
No, all of these are wrong ❑
Don't know ❑

Question 5

Doctors may soon be able to treat some inherited fatal diseases, such as cystic fibrosis, by a process of transplanting genes to repair the body's own processes. How willing would you be to accept this treatment if it would save your life? *(Tick one box only.)*

Very willing ❑
Somewhat willing ❑
Not very willing ❑
Not at all willing ❑
Don't know ❑

Question 6

Insurance companies could use genetic information from a blood test to target their policies, for instance by ensuring that only those who will develop a disease will pay a higher premium. Employers could screen the workforce, for instance to ensure that those at risk of cancer are not taken on to work with chemicals. In what circumstances should insurers and employers be allowed to have access to genetic information?

Whenever they consider it necessary ❑
Only when the individual is known to be carrying the gene for a serious disease ❑
Only so long as a government-appointed body monitors the way the information is used ❑
In no circumstances at all ❑
Don't know ❑

Question 7

Faulty genes can cause diseases such as muscular dystrophy and some cancers. If genetic tests on your unborn child showed that it would suffer from a crippling disease at the age of 16, as a parent what would you do? *(Tick one box only.)*

Choose abortion ❑
Take no action and hope that a treatment would be developed ❑
Take no action because I consider abortion to be unacceptable ❑
Don't know ❑

★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★

Thank you for completing this questionnaire.