Introduction

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This book is written with you in mind. Bioethics is not something necessarily esoteric. When you and your loved ones encounter modern medicine and modern care facilities, you meet directly what C. P. Snow articulated as the "Clash of two cultures." Scientific culture and human values culture compete for our loyalties daily, but never more so than when we or someone we care for becomes seriously ill or is dying, and needs the assistance of the health care system.

In the personages of physicians, nurses, social workers, therapists, admitting clerks, nursing home administrators, case managers, and all the others we encounter individuals who not only aim for the best interests of the sick, but also represent the scientific culture of modern medicine. Due to the rapid rise of scientific and technological advancement everywhere, and especially in medicine, enormous changes must take place, willy-nilly, in our human values culture, as we call it, whether we like those changes or not. Furthermore, science and technology require rethinking cherished values about the moral status of animals, children, the dying, the mentally compromised, and even those who are healthy and must support the medical care system. Rethinking these cherished values is important because they lead us to examine even more profound assumptions about ourselves. These profound assumptions we can call "second-order" considerations, questions such as what counts as a person either when we have frozen embryos in storage or in parents with advanced Alzheimer's disease, what is personal identity, can animals actually have rights, is there a moral difference at all between animals and humans, what will happen to social values if we try to alter the gene pool, how should we treat

"marginal" people, are there duties that cut across generations, and what about the environment in all this?

When we begin to root around in these questions, we enter the realm of what we call "third-order" considerations as well. These lead us to question what sort of ethical system we ought to employ: can we use the virtues we were taught, is a rights-based or principle-based ethics best, are there inalienable rights that must never be violated, do ends justify the means, should utilitarianism be used to resolve conflicts, is there some other ethical theory that might be better, are we to hold conflicting theories together like a collage, using whichever works at the moment (this is called Post-modernism)?

We do not need a degree in medicine, philosophy, or theology to grapple with these issues. After all, what Plato or Aristotle might have to say on any of these topics is interesting, but does not determine to any great extent what behaviors we exhibit as our grandmother slowly loses her edge, or as a child is born prematurely and must be placed in an intensive care unit, or as we invest in the stock of a private nursing home corporation, or as we survey dogs in a pound that, if not chosen by a family, may wind up being used in cardiology research.

In other words, when we confront the medical culture in our daily lives, we are involved in bioethics. We participate in the decisions that mesh our values with those of scientific culture. It is these decisions that are more important than theoretical reflection, since they shape our understanding of other values, and, by doing so, shape us as well.

Our book is called *Birth to Death: Science and Bioethics* because we trace current challenges to our values by biological discoveries in science and in medicine from before birth, through genetics, to our deaths, sometimes despite medical technology! These current challenges are collected in sections, most of which have three chapters. All chapters are written by experts for educated readers. Each combines a sketch of the most recent advances in the particular field, say understanding fetal growth and development, with details about how the newest scientific and technological understanding of human growth, development, aging, and eventual decline challenge our ethical and moral principles, social frameworks, and public policy about the subject of the chapter. Accordingly, the chapters contain ideas from the past, concepts of the present, and future challenges. In this way, you can gain both an enthusiastic update of the most recent thinking in biology and bioethics as well as glimmers of subsequent challenges we all may face in the future. The concerns of bioethics and the way you confront these issues will be faced every time you talk about them with friends or read them in the newspaper or see them on television. Preceding each chapter is a short Editors' Summary of the chapter so you can determine the major points of the chapter ahead of time.

The first chapter in a section describes the past, present, and future of a current

scientific advancement that challenges our values. For example, we include sections on the following: genetics, which explores a fundamental basis of disease that will ultimately change the way we treat sick people; reproductive technologies, which allows us almost God-like powers over the creation and manipulation of life; newborn intensive care, which rescues children some people think are nature's mistakes; organ transplant technology, which causes problems in objectification and ownership of organs; geriatric science, which can help people live longer and with a greater quality of life; on life-prolonging technology that sometimes is used inappropriately on the dying; research on animals to benefit human beings, which causes controversies for the moral status of animals; and finally environmental science, which has a greater and greater impact on human health and well-being and increasingly requires our attention.

Each of these short sketches about the scientific advancements mostly during this century is followed by ethical commentaries. Sometimes these commentaries represent opposing views on a critical subject engendered by scientific advancement, e.g. arguments for and against using animals for medical research, arguments for and against euthanasia and physician-assisted suicide[1]. At other times, the ethics chapters reflect on complementary issues, such as ethical issues arising from caring for premature children, and then ethical issues in caring for children in general, and their increasing moral status during the past half-century, or an ethical examination of a number of issues created by increasing longevity, and a complementary chapter about how we should treat people with Alzheimer's disease, or two different views about how we might go about buying and selling organs for transplantation. All the chapters have been commissioned by the editors as fresh contributions. Several were adapted by the authors from earlier work. There is one exception. Leon Kass' contribution on "Why doctors must not kill" appears with only minor changes from an original that was published elsewhere. We included his contribution because it so strongly contrasts with other points of view expressed in the section on euthanasia.

Only the most fundamental disagreements are highlighted, so that you may come away from the book with a mind uncluttered by minor academic trivialities. We have included a List of Contributors that provides the names and addresses of all the contributors to this volume, in case you would like to contact any of them. Most chapters contain a short selection of Further Reading for your convenience, should you wish to delve further into the issues.

At the end of the book you will meet us again, where we will encapsulate the most critical issues raised by all the scientific advancements covered in the book. Right now it gives us great pleasure to thank all of our experts for their time and devotion to this project, for it is hard to collect one's thoughts about complex matters in so short a space, and write them clearly for a general audience. In

editing we tried hard to maintain the author's style and interests accompanied by the clearest possible prose. Hence, the pathways taken by the chapter authors are those they chose themselves, knowing the difficulties they left behind in their choices. Nonetheless, it is like having at your fingertips the opinions and positions of noted experts in a variety of health care fields about extremely important issues. As a matter of course, then, this book could not be comprehensive, but it is suggestive of the enormous range of concerns we all must face together as we move into twenty-first century.

We wish to thank Robert Harington, PhD, at the time Comissioning Editor for the Life Sciences at Cambridge University Press, for suggesting this book to us, and encouraging its development, Tim Benton, PhD, later Popular Science Editor of Cambridge University Press, Doris Thomasma and Maggie Hall for their help in editing and corresponding with our contributors. Special thanks, too, for Patricia Marschall for her care in catching details in the final manuscript. Finally, our gratitude extends beyond limits to Sandi Irvine, our copyeditor, and Robbin Hiller, our research assistant in the Medical Humanities Program. They both spent many hours making the text as accurate and readable as possible. Thank you all!

NOTE

1. "Physician" is used throughout this book in the sense of "doctor". It does not exclude surgeons although specialties are usually specified.

GENETICS

Genetics: A scientific sketch

KAREN DAWSON

EDITORS' SUMMARY

Karen Dawson, PhD, adroitly summarizes the nature of genes, the history of their discovery, and their impact on human diseases. She discusses the differences between diseases that may be caused either by numerical abnormalities (in which more genes are present than is normally the case) or structural abnormalities (in which genes are transformed, altered or misplaced). Mapping the human genome is only the first step in understanding where the estimated 100 000 genes might be. We are also interested in the role and function of each gene. Some discoveries about this point have already been made, leading to the possibility of gene therapy for diseases such as cancer and cystic fibrosis. Because of the complexity of genetic interaction, and genes and environmental influences, many challenges about treating up to 3000 genetically based diseases still exist.

From the time we are born, and at different times throughout our lives, we are the recipients of comments such as: "You really look like your mother," "You behave just like your grandfather," and so on. What these comments really are is an acknowledgment that we are showing our genetic inheritance, or our *heredity*, either in our appearance or in our temperament. Classical genetics is the study of these patterns of inheritance. Modern genetics is concerned not only with understanding these patterns of inheritance but also with understanding the answer to the questions of "why?" and "how?" these patterns of inheritance occur.

The beginning of genetics

Genetics is not a long-established science when compared with, say, physics or chemistry. Its beginnings as a systematic study can be traced back to the work of an Austrian Augustinian monk and botanist, Gregor Mendel, in the 1860s, who discovered that the transmission of characteristics from parents to offspring depended on a set of biological elements that behaved in a predictable way. These biological elements were later to become known as genes.

The implication of Mendel's discovery was largely overlooked until about 1900 when various scientists around the world demonstrated that inherited characteristics – the genes within each cell – were carried on structures known as chromosomes. The number of chromosomes for a given species was shown to be constant, although there was a wide variation in the number of chromosomes in the cells between different species. The chromosome number for a species was also shown usually to be an even number, with half of the chromosomes coming from the sperm, or male gamete, and the other half coming from the egg, or female gamete.

The chromosomes of a species were shown to undergo a longitudinal division at the time of cell division when the organism was involved in growth. It was also shown that the chromosomes underwent a special cycle of reduction division in the formation of the male and female gametes that would participate in sexual reproduction. This special division is essential to maintaining the constant chromosome number over the generations for any sexually reproducing species.

As members of the human species, we share these features of genes and chromosomes with the many other sexually reproducing animal species. Our species has a chromosome number of 46; the chromosomes vary in size and occur in pairs; 23 of these chromosomes are inherited from each of our father and mother. In the human karyotype, an arrangement of the chromosomes in a cell constructed from a photograph, it can be seen that there are 22 chromosome pairs, the autosomes, and two sex chromosomes that are the same in a female (i.e. XX) or different in a male (i.e. XY) (see Figure 1).

The beginning of genetics provided us with some knowledge that is used widely in medicine today.

Detecting chromosomal abnormalities

Sometimes problems can occur in the formation of the sperm and egg that combine to form a new generation. It is possible to detect these errors as chromosomal abnormalities in the fetus before birth, using karyotyping and prenatal diagnosis techniques such as amniocentesis or chorionic villus sampling (CVS).

Chromosomal abnormalities can be of two main types: changes in chromosomal

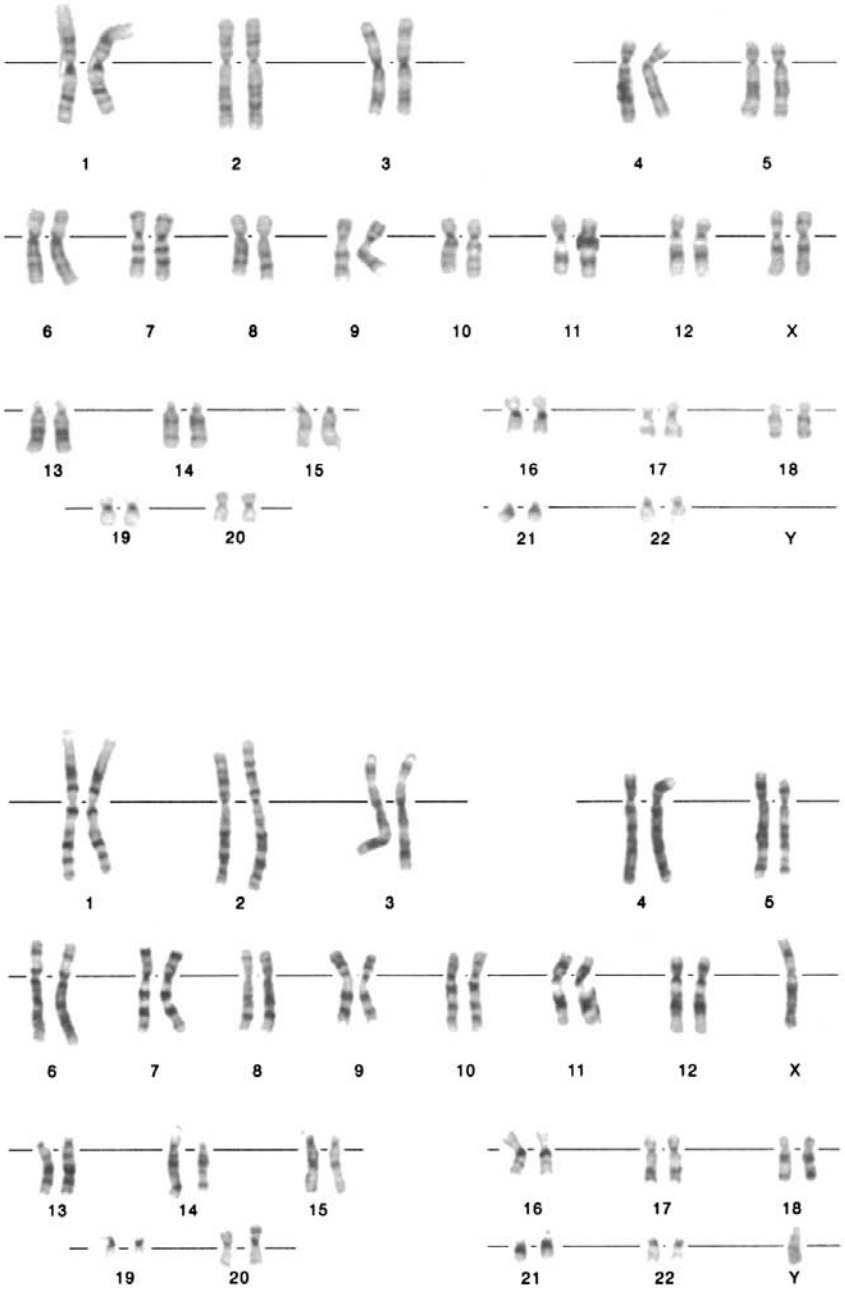

Figure 1. Chromosomes of the human female (XX) (*top*) and male (XY) (*bottom*) arranged in a karyotype.

number (numerical abnormalities) or changes in chromosomal structure (structural abnormalities) and the abnormality can involve either the autosomes or the sex chromosomes.

Numerical chromosomal abnormalities

Numerical chromosomal abnormalities can be either an addition or a reduction in the normal chromosome number. Numerical abnormalities in autosomes that are compatible with life tend to be additions to the chromosome number.

The most common chromosomal abnormality of the autosomes that can result in a live birth can be found in people with Down syndrome. These people have 47 chromosomes, with three copies of chromosome 21 being present instead of the usual two. Hence this disorder is sometimes also referred to as trisomy-21.

Down syndrome can result in both physical and mental handicaps in a child, and there is no known cure. Its incidence is strongly related to the age of the mother at the time of conception, increasing as maternal age increases. It is believed that the chromosomes in the egg cell become less likely to separate properly during gamete formation as a women gets older. The incidence of Down syndrome in relation to maternal age is presented in Table 1.

For a female, numerical chromosomal abnormalities of the sex chromosomes can be either an increase or a reduction in chromosome number. About 1 in 2000 girls are born with Turner syndrome, the loss of all or part of an X-chromosome. There are often only 45 chromosomes in the karyotype of girls affected by Turner syndrome. The effects of this abnormality are that the girls are short in stature and have delayed sexual maturity.

For a male, changes in sex chromosome number that are compatible with life are limited to increases in chromosome number. The most common of these conditions is Klinefelter syndrome, where the male has an extra copy of the X-chromosome, i.e. XXY. This disorder, estimated to occur in about 1 in 2500 males, can have serious effects on fertility.

Structural chromosome abnormalities

Structural chromosome abnormalities can result from a small part of a chromosome being deleted or duplicated, or part of a chromosome becoming translocated (attached) to another chromosome. Whether these changes will result in an abnormality largely depends on the amount of chromosomal material involved and whether or not the change results in the net gain or loss of genetic information.

Table 1. *The chances for women of different ages having a live-born baby with Down syndrome or some other chromosomal abnormality*

Mother's age at expected date of delivery	Chance of having a live-born baby with Down syndrome	Chance of having a live-born baby with another chromosomal abnormality
35	1:384	1:179
36	1:307	1:149
37	1:242	1:124
38	1:189	1:105
39	1:146	1:81
40	1:112	1:64
41	1:85	1:49
42	1:65	1:39
43	1:49	1:31
44	1:37	1:24
45	1:28	1:19

From: *1993 Directory of Genetic Support Groups and Genetics Services Australia & New Zealand. Canberra: New South Wales Genetic Education Program.*

The development of biochemical genetics

The study of the biochemical effects of genes can be dated from the work of British physician Archibald Garrod in 1902. He studied a human disease, alkaptonuria, and concluded that this disease was inherited and resulted from a blockage in the metabolic pathway that led to urea being excreted as a final breakdown product in the urine. What Garrod had demonstrated was that abnormal gene products such as enzymes – the proteins that control metabolic pathways – can cause a blockage at a definite point in a metabolic pathway. He also showed that similar blockages in different pathways could result in diseases such as albinism, cystinuria and porphyria. The gene was now known to have both a structure and a function. This knowledge has been crucial in the diagnosis and treatment of many single gene disorders, genetic disorders that result primarily from a defect in one gene, today.

Understanding the genetic code

In 1953 genetics took a giant leap forward in understanding what genes were and how they functioned. James Watson and Francis Crick discovered the structure

of the genetic material – deoxyribose nucleic acid, more commonly referred to as *DNA*. DNA was shown to be a double helix molecule that was composed of only four paired chemical bases – guanine (G), cytosine (C), adenosine (A) and thymine (T). For each gene, the genetic code is read in triplets, sequences of three bases at a time to yield messenger RNA (ribonucleic acid), which is then translated within the cell to produce a protein that participates in biochemical pathways within the organism.

It is differences in the order of these bases that determine the differences between pieces of DNA, and hence the differences in the composition of the different proteins produced. An insertion, a deletion or a change in any base in a specific piece of DNA – a mutation – can disrupt the production of a protein usually coded for, stop the protein from being produced, or upset the normal function of the protein produced.

A gene can consist of hundreds of thousands of base-pairs of DNA. Special techniques have been developed to enable the position of a particular gene to be determined on a chromosome (i.e. mapped) and the precise sequence of a gene to be determined. These techniques are the basis of the most ambitious research project yet to be undertaken by geneticists (see next section).

The Human Genome Project

In 1990 scientists began work on a controversial large-scale internationally collaborative project to map and sequence the entire human genetic complement or genome. The human genome consists of 300 000 000 base-pairs of DNA that are estimated to contain about 100 000 genes. There are two major goals of the Human Genome Project: first, to create a physical map of the chromosomes that comprise the human genome; and, second, to define the function of each of the genes present on each chromosome.

The first goal of the project has almost been completed due to the amazing developments that have occurred in sequencing techniques and the number of scientific teams that have been contributing data to the project. The achievement of the second goal of the project will be more time-consuming than the first, but also will be potentially more valuable because it will provide more medically useful information. It will change the way we treat many human illnesses.

Understanding the sequence of the bases in human genetic material is the essential first step in understanding the genetic basis of inherited diseases and chronic illnesses, and the future possible development of the prevention, diagnosis or improved treatment of these diseases.

Application of the knowledge coming from the Human Genome Project has already yielded some of these benefits. For instance, it is now possible to diagnose