# Chapter 2

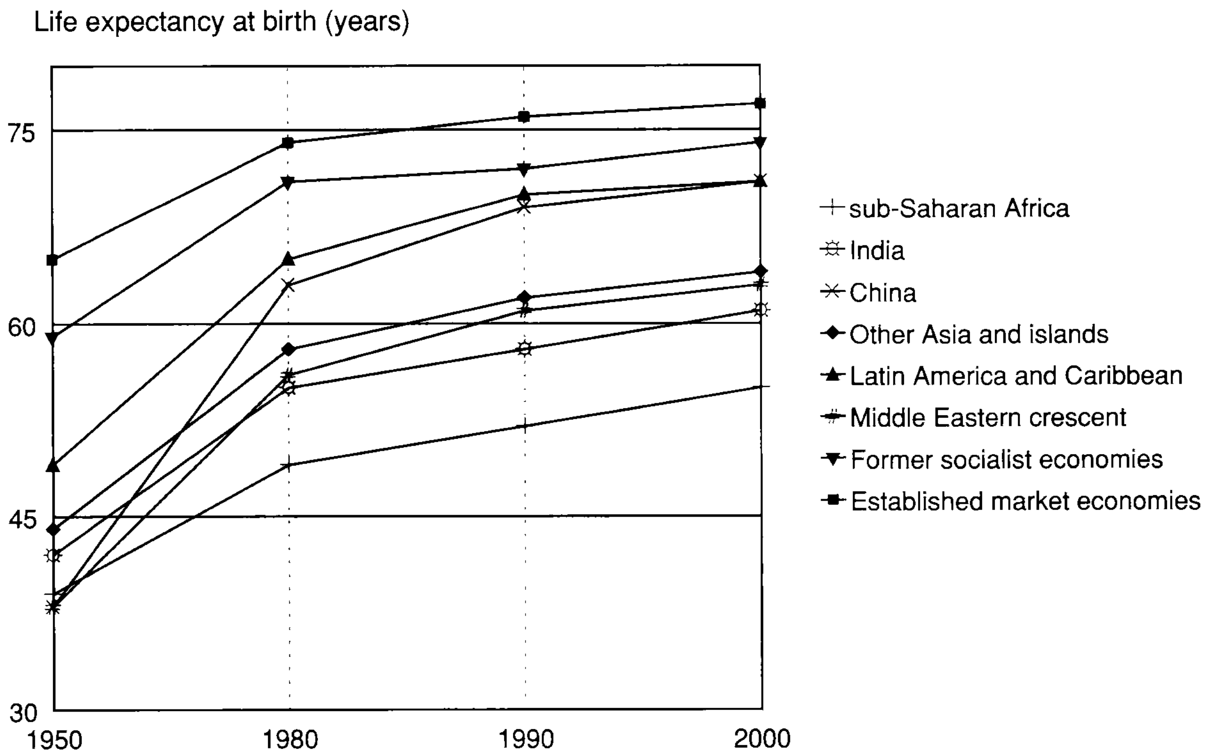
## Why invest in health research? Historical experience and the promise of science

The health of the world's peoples has improved more in the past four generations than in the whole of their history. In China in 1950, the odds that a child would not live to reach school age were as high as one in three. For those children's children, just 30 years later, the odds had fallen to about one in 15, and they are expected to reach one in 28 by the year 2000 (World Bank 1993).

The scale and pace of the change are unprecedented. In the middle-income and low-income countries overall, life expectancy at birth has risen sharply from 40 years in 1950 to 63 years in 1990 (Figure 2.1) and the trend is still upwards. Even in sub-Saharan Africa, where the improvement has been slowest and smallest, the gain has been greater over the past four decades than it was over a comparable period in Europe in the 19th century.

The reasons for the dramatic improvement are complex. The rise in per capita incomes through the 20th century has been closely linked to the rise in life expectancy, with the steepest increases occurring at the lowest income levels (Figure 2.2). As people's incomes grow, they are able to buy more food, live in better housing and reach a higher level of education. And as a population grows more affluent, the proportion of people with access to safe water and better sanitation increases. All of these consequences of higher income have helped to improve health. But income growth alone cannot explain all of the improvement. As Figure 2.2 shows, the life expectancy of people in every income bracket has shifted steadily upwards over the past century so that a given income buys better health now than it did at equivalent levels 30 years before. Therefore, other factors must help to explain the trend since 1900.

**Figure 2.1 Trends in life expectancy, 1950–2000**




*Source:* World Bank 1993:203

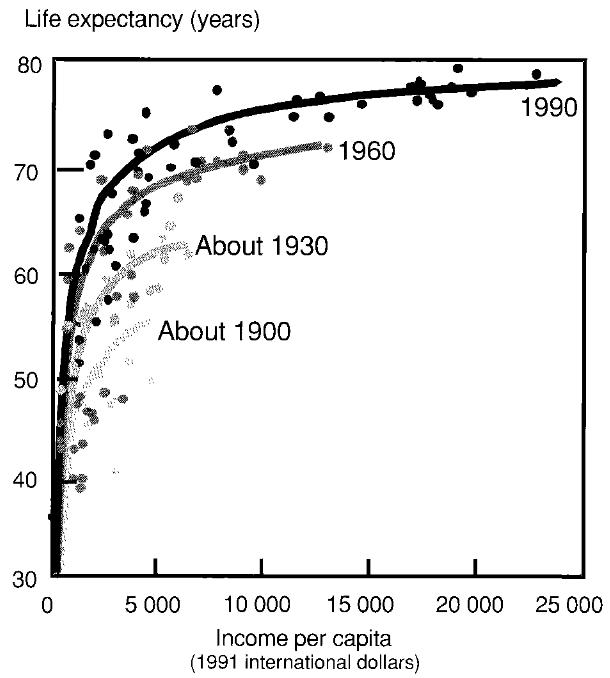
## 2.1 The scientific underpinnings of past health improvement

One vital—and perhaps underestimated—factor has been the impact of scientific research. Research has led to tangible improvements in two ways: by bringing knowledge that people use daily in their homes to maintain their health, and by producing direct technical interventions such as vaccines, treatments and public health measures.

### *2.1.1 Everyday knowledge as a product of research*

The importance of household knowledge for health may only now be gaining recognition. On the basis of studies of the U.S. census for 1900, Preston and Haines (1991) have shown that neither household income nor education made much difference to children's chances of survival until scientific knowledge about the sources of ill-health became available. The work of Pasteur, Koch and others from the 1850s onwards established the germ theory of disease and, as people began to understand about infection towards the end of the 19th century, the differences in child mortality between affluent, educated households with access to that knowledge and poorer, uneducated households without it widened sharply. The implication is that the educated households were able to acquire and use the new knowledge more rapidly to adopt healthier behaviours, such as boiling water for infants, washing their hands regularly, and quarantining sick children. These actions strongly enhanced their chances of survival.

**Figure 2.2 Life expectancy and income per capita for selected countries and periods**




Note: International dollars are derived from national currencies by assessment of purchasing power, not by exchange rates. This measurement returns relatively higher incomes for poorer countries.
*Source:* World Bank 1993: 34. Also see Table 30 in this source for a fuller explanation of the derivation of per capita income.

Studies of present-day populations support the idea that people are more likely to be healthy if they have access to accurate information. In many low-income countries today, the strongest determinant of children's survival is their mother's level of education, even after the household's income and access to health services have been taken into account. In general, educated women are more likely to limit their family size, and children born into smaller families have better survival chances than those born into large ones. Educated parents are more likely to make the best use of health information to adopt safe behaviours, avoid unsafe ones and seek the help of health workers when their children are unwell. Studies in high-income countries also suggest that, while income remains a strong determinant of health, access to information may also play an important role. Immigrants, for example, who may be disadvantaged by language differences, tend to suffer poorer health irrespective of their income level; and even where access to health services is not restricted because the services are provided free, inequalities in the health of households persist.

### *2.1.2 Technical interventions*

Research has also brought technical interventions such as vaccines, drugs, diagnostics, public health tools such as water treatment methods, therapeutic equipment, and algorithms for clinical procedures, whose impact on health has been profound. In many sub-Saharan African countries, child mortality has fallen steeply over a period of little economic growth, suggesting that these technological interventions must account for a large part of the improvement. Safer water supplies and improved sanitation, themselves the products of research, have reduced the spread of diarrhoeal disease, especially in urban areas. Vaccines against a handful of common childhood diseases have played a particularly significant role: without them, it has been estimated, the total burden of disease in children under the age of five would rise by almost a quarter. Improved education has also played a major role in health improvement, largely because it has enabled people to make good use of the preventive and therapeutic interventions available to them.

A brief review of the history of research over the past century shows how information has increasingly been applied to achieve better health. The greatest of the tangible advances since the 1880s has been against communicable diseases, beginning with the demonstration of the microbial origins of infections. From this discovery flowed two main approaches to treating infection: chemotherapy and immunoprophylaxis, or the use of vaccines.

The great flowering of chemotherapy dates from the late 1930s with the production of the sulphonamides, the outcome of a pharmaceutical company's research, and then penicillin, discovered earlier by Fleming and developed by Florey and Chain in academic laboratories within the public sector. Subsequent discoveries have also come from varied origins, with both streptomycin and cephalosporin originating in university laboratories and other antimicrobials emerging from the private sector. During the Second World War, the benefits of this research were powerfully demonstrated when antibiotics and antimalarials transformed the prospects and the morale of the Allied troops, bringing a sharp reduction in the proportion of losses that were due to disease compared with those due to enemy action.

The development of vaccines against human diseases began 200 years ago with Jenner's inoculation against smallpox. The past century has seen the introduction of effective vaccines against polio, diphtheria, pertussis, tetanus and measles which now reach eight out of ten children worldwide. Newer vaccines, for example, against *Haemophilus influenzae* and hepatitis B, are also gaining more widespread use.

Beyond the assault on communicable diseases, there have been many more tangible benefits of R&D. Anaesthesia has evolved from a relatively crude process to become a highly sophisticated technology. With the discovery of insulin the effective treatment of diabetes began; with X-ray, the first of the scanning technologies, which is now complemented by ultrasound, positron emission tomography and magnetic resonance imaging, non-invasive diagnosis became possible for a wide range of conditions. Since epidemiologists established the link between tobacco and lung cancer in the 1950s, governments have gradually introduced policy changes to restrict smoking and millions of individuals have chosen to quit the habit. The development of hormonal contraception has given women greater control over their fertility, and the treatment of diarrhoeal disease has been revolutionized by oral rehydration therapy. The development of the randomized clinical trial has enabled physicians and researchers to assess the efficacy of interventions in a rational manner. Meta-analysis of many trials enables researchers to detect the benefits—and disadvantages—of interventions whose effects are comparatively modest but which may be of great importance in the treatment of common diseases.

Health research goes much further than the biomedical sciences, however. Researchers in health economics and epidemiology have developed measures of the cost-effectiveness of interventions that enable governments and other authorities to plan the best use of health care resources and, at a much broader level, integrate health into their development policies. Health policy research has been instrumental in enabling governments to improve safety standards and increase efficiency. For example, studies have demonstrated the effects of taxing alcohol on reducing the rate of motor-vehicle crashes and investigated the potential of different incentive systems to encourage physicians to use cost-effective treatments. Health services researchers have begun to answer important questions about the most effective approaches to treatment for a wide range of conditions—such as whether community care is appropriate for severely mentally ill patients in specific settings, or which routinely provided obstetric interventions are actually beneficial. Such research has also demonstrated that programmes of primary health care and nutrition in poor rural areas can be highly cost-effective in reducing infant and child mortality. Systematic reviews of clinical research, such as those now being produced by the Cochrane Collaboration, and the dissemination of research findings to practitioners, are enabling health workers to base their practice on evidence.

Behavioural research has also led to improvements in health care. For example, in Kenya and Ghana researchers learned that parents often believe that their sick children's convulsions are caused by spirits. Rather than seek treatment for malaria—the likely cause—they seek charms from traditional healers. The studies have prompted health workers to produce information and education packages for women to enable them to make more informed choices about treatment. Research into the behaviours and beliefs of health care providers has helped to show why, for example, health workers sometimes miss opportunities to immunize children, physicians sometimes prescribe inappropriate treatments for diarrhoea, and general practitioners sometimes fail to administer aspirin immediately after diagnosing acute myocardial infarction. These findings have resulted in better training for health workers and, ultimately, better services to patients and greater efficiency.

## 2.2 The value of research and the fundamental science base

While the impact of research on health is relatively well known, its economic value to society may be less widely appreciated. Data from the United States demonstrate that many products of R&D, such as vaccines and treatments, have produced significant savings by averting disease, reducing health care costs and enabling greater productivity (National Institutes of Health 1995). The fluoridation of water is estimated to save US$ 4 billion a year in the United States by averting the costs of treating dental caries. The vaccine against *Haemophilus influenzae B* is estimated to save that nation US$ 400 million a year. Research into drug addiction has resulted in treatment programmes that for every US$ 1 invested in them bring a return of between US$ 4 and US$ 7 in reduced drug-related crime, criminal justice costs and theft. When savings related to health care are included, total savings can exceed costs by 12 to 1. Research has also helped to reduce the costs of alcohol abuse, a major risk factor for disease and injuries worldwide which costs the United States alone an estimated US$ 98.6 billion per year in lost productivity, treatment, damage to property and crime. After researchers demonstrated that an increase in the minimum legal drinking age in the various states of the United States from 18 to 21 would reduce the number of road-traffic incidents and related fatalities significantly, all states imposed a minimum age of 21 years, saving up to US$ 600 million per year.

There have been few analyses of the payoff from specific R&D investments, and the lack of data on resource flows is striking. However, where data exist, they suggest that very high returns are possible. For example, a sputum test for *Pneumocystis carinii* pneumonia, an important opportunistic infection in HIV disease, was developed through R&D that cost around US$ 440 000. The test is now estimated to save about US$ 50 million per year in the United States by overcoming the need for more expensive invasive diagnostic procedures. Also in the United States, studies have confirmed that it is not necessary to screen all the nation's donated blood for HIV antigens—a much more expensive and laborious process than the routine screening for antibodies to the virus that is practised currently. The studies, which cost US$ 500 000, enabled the Federal government to save up to US$ 49.4 million per year by avoiding the purchase of a costly antigen test kit.

But besides these economic gains, research brings another kind of wealth to society. The culture of research has provided a rational, knowledge-based framework for progress in health. Both medical practice and health policy have been the prey of ineffective remedies and fashions in policy for centuries, and a scientific framework has provided as much for eliminating the irrational and ineffective as it has for developing new ways to improve health. At the heart of that rational framework lies the fundamental science base—the underpinning of all the knowledge, products and practical applications that have emerged since the 19th century.

The development of vaccines, recognized as one of the most cost-effective of all medical interventions, provides an informative example of the role of fundamental science in the development of practical medical interventions. From the end of the last century until the middle of this, vaccines were produced by identifying the pathogenic agent, inactivating it by formaldehyde or attenuating it by prolonged culture. These almost entirely empirical procedures yielded vaccines for smallpox, polio, measles, BCG, pertussis, diphtheria and tetanus. Today it may be argued that the easy vaccines have been made, and that far greater understanding of the complexities of pathogenesis and the mechanisms of immunity will be required for many vaccines in future.

Modern molecular biology has provided a powerful set of methodologies and a new approach to developing vaccines. But the foundations of this new biology were basic scientific inquiries that were totally unrelated to practical application. In the words of Robert Oppenheimer: "It is a profound and necessary truth that the deep things in science are not found because they are useful; they are found because it was possible to find them" (Rhodes 1986). The original questions that led to the key findings could not, at face value, have appeared less relevant to practical applications, and were often ridiculed by politicians (see Box 2.1).

Clearly, strategic and applied research depend critically on the continuing pursuit of fundamental knowledge. Without that knowledge, no matter how important the practical problems society would like to have solved, there may be no tools to solve them. Lord Porter has argued that "there are only two kinds of science—applied science, and not-yet-applied science" (Lord Porter, personal communication to the Committee). The familiar linear model of science, which begins with the very "basic" and moves steadily towards the "applied" is no longer accepted dogma. Today, a real reciprocity between fundamental and more applied science has emerged. For example, clinical studies of people with immunologic disorders and cancers have led to fundamental insights into the immune system and regulation of normal cell growth and development. And basic inquiry into fundamental biological questions has continued to yield practical products, including drugs and vaccines. Interdisciplinary connections will be increasingly important in all of science as the pace of discovery and the amount of available information grows, but most particularly in biomedical sciences.

## 2.3 Looking ahead: research tools for the future

Because opportunities arise from unanticipated experimental findings, it is impossible to predict with any certainty what the major breakthroughs in science will be over the next two decades. Nevertheless, there are a number of developments that are likely to be critical to the direction that biomedical science will take. Some are research technologies; others are conceptual and experimental advances in biology. A few of these are discussed briefly here. The list is by no means comprehensive, but it should provide a sense of the possible consequences of new knowledge to improve the productivity of the R&D enterprise itself.

### *2.3.1 Technologies for health R&D*

- **Recombinant DNA technology.** This has made it possible for scientists to manipulate genes in the test-tube and within cells and living organisms. It is now possible to identify, amplify, clone and mutate many genes from lower organisms, and some from humans. The techniques for gene amplification allow scientists to produce millions of copies of a gene in a matter of hours, and have led to effective and affordable new diagnostics. The proteins encoded by genes can be produced and harvested in bulk, enabling scientists to understand their structure and biological activities. This technology is rapidly becoming more affordable and is already available to many middle-income countries and some low-income countries.

- **Structural biology.** Now that even rare proteins can be produced in large quantities, researchers can crystallize key biological molecules and determine their structures. From the structure, scientists can learn the molecular basis for the biological activity of the protein or enzyme and, using computer modelling techniques, design drugs with specific characteristics to mediate that activity.
- **Combinatorial chemistry.** In the past, the discovery of new drugs was a labour-intensive and nonrational process that involved screening thousands of compounds over a period of months or years, and then making derivatives from lead compounds. With this method, pharmaceutical companies could test at most several thousand compounds a year. By a new process, companies and even smaller research units can synthesize up to 1000 new derivatives in a week. Rather than manipulate specific chemicals, the process makes random derivatives, then active compounds from within the pool are selected by sophisticated biological assays. This technology makes it possible for many more compounds than before to be tested for biological activity both quickly and relatively cheaply. It will almost certainly increase the capacity of the pharmaceutical industry in developing countries.
- **Computer and data analysis technologies.** The rapid development of faster computers and the sophisticated software available to individuals with personal computers has revolutionized the analysis of medical and scientific data and information. Databases containing information on genes from humans and microbes are available to anyone with a personal computer, a modem and a telephone. International links enable countries to share data for analysis of the efficacy and effectiveness of medical interventions, and to study vaccines and drugs in post-marketing surveillance. Powerful data analysis technologies have enabled scientists to conduct meta-analyses of clinical trials and epidemiological surveys that determine the importance of particular risk factors in diseases.
- **The communications revolution.** E-mail, the Internet and dedicated health telecommunications services, such as SatelLife, are enabling growing numbers of researchers to access and share informa-

## Box 2.1 Fundamental questions that brought unexpected health benefits

Fundamental research is driven not by health need, but by curiosity. Yet without it, many health problems could not have been addressed. Here are three examples of apparently "irrelevant" questions that biologists have asked—and found out more than they expected to from the answers.

- "Do bacteria have sex?" If evolution were to derive only from random small mutations, it would be difficult to see how complex traits and organisms could ever have evolved, since most mutations are clearly deleterious. The work of Lederberg established that it is possible to exchange genes and whole pieces of chromosomes in bacteria, and led to an understanding of recombination as a rapid evolutionary mechanism. The process can be observed, for example, in the rapid transfer of some markers for antibiotic resistance across genera. Not only has this discovery been vital in understanding the basis of antimicrobial resistance, but it has also led to the development of recombinant DNA technology and provides the knowledge base for the biotechnology industry.
- "Do tumour cells inhibit the specialized functions of differentiated cells?" Köhler and Milstein were concerned with discovering whether tumour cells suppress normal, differentiated cells, such as the white cells of the immune system, and prevent them from performing their usual functions. In learning that the answer was, generally, yes, they also discovered that when tumour cells of the lymphoid series are fused to antibody-producing white cells, antibody production is not inhibited, and the antibody-producing cells become immortalized. The resulting antibodies, known as monoclonal antibodies, derive from a single cell that can be grown to infinite number. Today, they are used worldwide for diagnostics and for protein purification.
- "Why are some bacteria 'immune' to infection by particular phages?" A number of physicists in the 1940s believed that biology was an exciting new scientific frontier, and to obviate the enormous complexities of studying living mammals, chose instead to study the simplest possible organisms, viruses called phages that infect only bacteria. From that work came the discovery of restriction enzymes that cut DNA, the molecule that carries genetic information, at very precise locations. This has led to the possibility of cloning defined pieces of DNA containing genes of interest for health research, and to DNA fingerprinting, which is useful in molecular epidemiology and studies of genetic traits.

tion regardless of their location. The technology will improve the opportunities for countries to coordinate epidemiological information, such as surveillance networks for infectious diseases. Research journals are also beginning to publish their papers on line and an increasing number of scientists use electronic peer review (see Box 2.2). Physicians and surgeons are beginning to use communications technology to consult each other for information and advice, for example in diagnosing complex or rare conditions. A digitized image, for example from a CT scan, may be transmitted electronically from the treating physician to another thousands of miles away for comments. While so far such technologies have had little impact on the health needs of people in low-income countries, their promise for geographically remote and medically underserved populations in both rural and urban areas is now gaining increasing recognition. The technologies also offer the prospect of distance learning and continuing training for health care providers and health managers. With the costs of international telephone calls expected to fall in the near future, the information revolution may be expected to gather pace in low-income countries.

### 2.3.2 Promising areas of biomedical research

Since the 1970s, biomedical research has moved forward rapidly and the outlook for the future suggests that this pace is likely to continue. Here, we focus on three areas of research whose outcomes are expected to help address important health problems.

- **The Human Genome Project.** This international collaborative effort aims to map and sequence all human genes and understand their functions. The genome contains between 50 000 and 100 000 genes, of which scientists so far know the function of only about 3 000. One-third of these have already been associated with disease. The project is a key investment for, with growing knowledge of human genes and of the complex interplay between genes and environment, it will become possible to predict the probability that an individual will develop a particular disease over that person's lifetime. This may enable more effective strategies for disease prevention and risk aversion. As well as studying human genes, researchers are mapping and sequencing the genomes of several other organisms, including some that provide useful models for studying development. There is now grow-

### Box 2.2 A peer review network for biomedical science

The future of international health and medicine may be shaped by two recent innovations: a global revolution in electronic communication, and a worldwide extension of organized processes of scientific self-criticism for evaluating medical science and practice. Through critical peer review, experts in a particular field (peers) assess the validity and merit of research produced by others in the field. This process of self-criticism and quality assurance has been thus far based in medical journals. While there are thousands of journals, the extent to which they use peer review varies. Research published in peer-reviewed journals helps shape the clinical decisions made by physicians and other health professionals, the kinds of therapies and technologies used, and the strategies adopted by nations to promote health and prevent disease. A science of peer review is emerging at the same time that new communication technologies have extended the reach of information and reduced the costs of its dissemination.

The potential impact of the digital information age on the science and practice of medicine, and particularly on extending the culture of science through the practice of peer review, is well recognized by organizations that promote health internationally and by medical journals. In many regions a scientifically robust medical profession is maturing or just emerging. Participation in self-critical scientific dialogue and peer review promotes a professional culture in medicine that may be as important to sustainable improvements in clinical practice and public health as the delivery of medical education, technology and supplies. Access to the world medical literature and identification with peer review (as a journal reader, author or reviewer) may contribute substantially to increasing professional self-identity and the development of professional institutions and culture. Decreasing scientific isolation by bringing more scientists and clinicians into the world biomedical community is key to achieving change.

A consortium of medical journal editors, led by the *Journal of the American Medical Association* and the *British medical journal*, in partnership with Project HOPE, a nonprofit nongovernmental organization, are now planning a global dissemination of biomedical information through new technologies. This effort was launched at a meeting in Bellagio, Italy, in April 1995 that brought together editors of major medical journals from the high-income, low-income and middle-income countries. A lasting system of communication between medical scientists and practitioners across national boundaries and diverse cultures, based on access to peer review literature and publishing but evolving to other telemedical and tele-distance learning applications, is envisioned. The goal is to improve worldwide access to biomedical peer review systems and information and the practice of peer review in all elements of health care from research to clinical care. The next major step will be a Congress on Global Biomedical Communication to be held in Prague in 1997 to launch a worldwide electronic biomedical peer review network.

ing interest in sequencing the genomes of important disease-causing organisms as a step towards understanding the molecular basis of pathogenesis. Such studies should provide urgently needed information, for example, about potential new targets for antimicrobial drugs and about potential immunogens for the design of new vaccines.

- **Developmental biology.** The power of molecular biology and genetics have begun to reveal clues to the fundamental question in developmental biology: that is, how are the events that lead to the development of specialized organs within a complex individual programmed into the single cell of the fertilized egg? Using simple model organisms that can be readily genetically manipulated—a small roundworm and the fruitfly *Drosophila*—many of the early functions of the developmental programme are now becoming clear. For example, scientists can now understand the development of the eye and other organs, and the determination of head and tail, in terms of molecules produced by specific cells at a precise time in development. The ability to make mutations in these lower animals that mimic human genetic diseases will allow a much greater understanding of the nature of these diseases and allow more rapid research on interventions to prevent or ameliorate them.

  In the course of these fundamental studies on development, researchers have learnt that alterations in many genes critical for normal development can lead to a genetic imbalance that in turn triggers the development of cancer. From these fundamental studies, they have identified a number of oncogenes—mutated or altered genes that are aberrantly expressed in specific human tumours. Scientists have continued to elucidate the role of these oncogenes in the complex web of normal development, learning how changes of even just one amino acid in the proteins they encode can start the neoplastic process. Such work is likely to result in new diagnostic tools for detecting cancer cells at an early stage, and it could lead to new therapies to prevent or correct the aberrant and unregulated growth of cells.

- **Neuroscience**. The human brain remains the ultimate intellectual challenge for biomedical research. But in recent years, studies of its mechanisms have begun to bear fruit. From molecular genetic studies in model organisms, scientists are discovering genes that are critical to neurological development. Fundamental questions about, for example, the ways in which particular nerves home to particular anatomical regions, or how different kinds of stimuli and neurotransmitters evoke responses from specific nerves, are becoming amenable to experimental study. Already knowledge of signalling neurotransmitters and their receptors has led to the development of drugs that are playing an increasingly important role in the treatment of mental illness. Studies using scanning technologies have, for the first time, provided physical evidence of biochemical changes in the brain related to vision, thought and emotion. While it is premature to anticipate what the practical consequences of this knowledge will be, it is anticipated that new treatments and preventive therapies for neurological and psychiatric diseases, such as Alzheimer disease, will be among them. The search for practical responses and affordable preventive strategies for neurological and psychiatric diseases has acquired a new urgency in the light of the worldwide projected epidemic of these diseases.

The question of paramount importance, however, is to what extent these technologies and the knowledge that they are yielding will be engaged to address the health problems of people in low-income and middle-income countries, who make up four-fifths of the world's population. In some respects, there are grounds for optimism. Recombinant DNA technology and monoclonal antibodies are just two examples of advances that have enabled the development of highly cost-effective diagnostics in low-income countries; and combinatorial chemistry is, as we have argued, likely to lower the costs of drug screening dramatically. As these technologies become more widely available, their impact is likely to increase.

But there are also grounds for serious concern. In 1992, no more than 5% of the total spent on health research worldwide was devoted to problems that overwhelmingly burden developing countries. Assessments of R&D spending for this Report have revealed stark imbalances in the allocation of research resources, with some of the most important sources of global disease burden—such as diarrhoeal disease or childhood pneumonias—receiving less than half of one per cent of all health research funds (Annex 5). As we show in Chapter 7, there is also disturbing evidence that even the meagre share of funds that are allocated to the health problems of low-income countries may now be declining, due mainly to shrinking budgets for bilateral official development assistance from the governments of the established market economies. It is of concern, too, that investment by the pharmaceutical industry in R&D on antimicrobials has declined in recent years. If the dividends of research are to be shared equitably by the world's populations, intensive work lies ahead. The challenges of coming decades will not be met unless resources are used rationally and equitably to serve the health needs of the majority. Indeed, given the scale of these challenges, there is a risk that some of the gains of the past could be jeopardized. A key responsibility for researchers and investors in health research is to improve the collection and dissemination of data on the important sources of disease burden and the relative distribution of resources into R&D. With more informed decision-making about the priorities for health research, countries can hope to consolidate the health improvements of the 20th century and achieve new progress in the 21st.

## 2.4 Chapter summary

Life expectancy has risen steeply throughout the 20th century. While rising incomes and education have been key factors in the massive health gains of recent decades, health research has also played an important, and possibly underestimated, role. Health research has brought knowledge that people can use to adopt healthier behaviours and technological solutions such as vaccines, drugs and treatment algorithms for a range of pressing health problems of the low-income and middle-income countries. Advances in biology and in the technologies of research promise further advances in future. But in order to hold on to the improvements of the past and to build on them in future for the benefit of all populations, investors must maintain a strong science base and build assessment of global health needs into their decisions about resource allocation for strategic and applied research.