European Journal of Surgical Oncology 1999; **25**: 540–544

BIMILLENNIAL HISTORICAL REVIEW

Part IV. The 20th century: the maelstrom of progress

D. A. Rew

Southampton University Hospitals, UK

'The last decades of the 19th century were occupied with the detailed study of the morphology of tumours, the separation of the varieties of disease, the elucidation of histogenesis and the writing of the natural history of malignant diseases. The twentieth century opens as the experimental era. . . . It seems likely to become noteworthy as the period of specific aetiological investigations which promise to widely separate many neoplastic diseases formerly held to be closely related. It may, thereby, prove to be the era of successful therapeutics and prophylaxis.'

JAMES EWING, *Textbook of Neoplastic Diseases.* Philadelphia: W.B. Saunders, 1919.

Introduction

The closing months of the 20th century provide an opportunity to reflect upon a remarkable period of change in society, science and technology, and their influence upon our more specialized interests in surgery and oncology. Life has been evolving on Earth for some 3000 million years. Our recognizable ancestors emerged some 10 million years ago, and recorded human history extends back some 10, 000 years. The passing of 1999 is insignificant on biological and evolutionary timescales. And yet, the past century has seen a flowering of human achievement in the sciences, in technology, in medicine, in industry and commerce, unprecedented in the evolutionary history on the planet. We are privileged to witness this chronological milestone of a tempestuous and tumultuous century of disorder and change.

The intellectual climate

Rapid change is now an integral feature of Western scientific and technical life. Change and diversity, once the anathema of stable society, is now the nutrient upon which it thrives. We are thus primed to challenge the orthodox and to expect the unexpected. We are trained to use the scientific method in our dealings with the world, aided by immediate access to huge quantities of data upon which to build our ideas. Paradoxically, unlike the case in earlier centuries, this century has not been marked by cataclysmic changes in the process of scientific thought. Changes have been more those of rate, scale and degree. Changes which once took centuries to bring about are now effected in years and decades.

We may nevertheless discern some important general trends in modern scientific thought. Religion now exerts a lesser grip on the Western creative mind. The Darwinian explanation of man's place in the natural order has been consolidated by the elucidation of the genetic code, by the mechanistic explanations of biology and reproduction, by the lonely images of the Earth from the early space missions, and by pictures of the cosmos from terrestrial and interplanetary probes, and the Hubble telescope.

Europe's cauldron of conflict between nation states and between political ideologies is cooling. Society increasingly stresses the rights and the importance of the individual over the state, with the late ascendancy in Europe of democratic liberalism over totalitarian philosophies and systems. The growing accountability of the state and of the institution to the individual finds many resonances in law and medicine, and is having a profound influence on the social environment in which we practise surgery.

We may not be able to discern for many years to come the truly great and lasting influences upon science and society in the 20th century. The many architects of the nuclear, aeronautical, silicon, biotechnical and space ages, though individually obscured by the sheer volume and multiplicity of events and technologies, will live on through their influence on future generations. Mathematics is one example. Einstein's theories of general and special relativity may match the celestial achievements of Galileo, Copernicus and Newton. The mathematics of computing and the workings of the universal calculating engine, devised by Charles Babbage (1792–1871) in the previous century, found fruition in the electronic computer and in the works of men such as Alan Turing.

The electronic computer will be perhaps the most lasting influence and gift of the 20th century to the future. It has profound consequences. The speed at which complex

0748–7983/99/050540+05 $12.00/0

calculating tasks can be undertaken and at which data can be displayed offers a whole new dimension to the testing of creative ideas. New scenarios and hypotheses can be modelled and concepts can be displayed in hitherto impractical ways. Progress in computing thus facilitates intellectual advance through the manipulation of rapidly incremental knowledge.

Advances in communication

The century which has twice given us total war in Europe, the concentration camp and the atomic bomb, has given us the many beneficial technologies. These have produced social, intellectual and economic emancipation, and longer, healthier lives for millions of people. Modern technologies are now wholly integrated in our working and resting lives. Communications and transport systems, which are almost entirely the product of 20th century technology, have brought about a dramatic compression of time and space. The mobility of persons and peoples has been transformed by the pneumatic tyre, by the bicycle, by the ocean liner, the railway, the motor car, the aeroplane and the spacecraft.

The telephone, the radio, the television, the satellite and latterly the Internet have heralded new forms of mass and personal communication. The public media, including newspapers, magazines, books, radio and television, have been hugely influential in altering public awareness and understanding of health and disease. The technology of communication has also changed professional practice in the medical sciences. Easier travel has allowed the rapid exchange of ideas, methods and processes, leading to a transcontinental harmonization of professional standards and systems. In scientific publishing the expansion of specialist medical journals has been largely a 20th century phenomenon. More recently we have seen opportunities in the use of the Internet for the enhancement of scientific exchange.

Professional institutions

Many great medical institutions from earlier times have survived the 20th century, while others have emerged, particularly in the New World. Other important institutions include the cancer charities which raise and distribute funds, and the national and international professional associations and societies which enhance professional development.

Universities, postgraduate, private and commercial Research Institutes have also benefited from the growth in wealth, such that we now have an immense international pool of technical and research resources upon which to draw. Universities and Institutes of Higher Education are now found in most towns and cities in Europe. There has been a shift from classical to technical and scientific education. This has created the intellectual environment in which rapid technical progress could take place. Policies of universal education have created a much broader knowledge base in the general population, which translates into a greater understanding of health and disease. The expanding and systematic education and professionalization of medicine and the allied health sciences has created a large pool of educated individuals to support the health services.

Hospitals and cancer institutes

The general increase in wealth has permitted a huge investment in the infrastructure of health-care delivery, such that all significant population centres in Western Europe now have access to fully equipped and staffed primary care and hospital units. There has been an effective dissemination of skills from specialist centres to provincial hospitals. The 19th century trend towards consolidating cancer treatment in specialist units has also been maintained. We now have a range of specialist cancer hospitals in major centres throughout Europe, supporting cancer units and individual clinicians in district hospitals, with a more even dispersal of professional skills outside the principal cities. Clinical practice is becoming more standardized, thus providing consistent treatment and the opportunity for better comparisons of clinical results and outcomes.

The life sciences

The growth in scientific research has led to progressive subspecialization in all forms of science and technology. We are hard pressed to catalogue and analyse the exponential growth in scientific data and knowledge. Our understanding of cell, tissue, organ and whole body physiology has been progressively refined to reveal the detailed workings of all the major organ and endocrine systems, translated to clinical disciplines such as cardiology, neurology, respiratory, renal and hepatic medicine, and endocrinology.

Cell and molecular biology have refined the analysis of the tissue, cell, organelle and genome ultrastructure and function, helped by a range of specialized instruments, which include the transmission, scanning electron and confocal microscopes, and all the techniques of biotechnology. Biochemistry has extended 19th century chemistry to the structure and function of biological molecules. The discovery of the structure of DNA in 1953 by Watson and Crick[1] was built upon many advances in biochemistry and X-ray crystallography. Molecular biology has spawned a host of further discoveries, including the monoclonal antibody[2] and the function and regulation of genes, and has allowed the ongoing sequencing of the human genome. It has also allowed new techniques in reproductive biology, including the genetic modification of cells, the cloning of animals from somatic cells, and antenatal genetic diagnosis. Microbiology has revealed the mechanisms of sepsis and the nature of viruses.

Anatomy and embryology have been refined to the cellular and subcellular levels. We know a great deal more about the microanatomy and ultrastructure of tumours. Much progress has been made in understanding the processes of regulation of cell differentiation, and about the control and the behaviour of the normal and of the abnormal cell. The concept of the cell cycle[3] created a framework of order with which to interpret and analyse the life cycle of cells and tissues, and with which to investigate its regulation. The understanding of normal and abnormal tissue growth dynamics has been aided by the discovery of apoptosis as a key cell regulatory process. However, we are still far from understanding the full subtlety and complexity of the remarkable process of embryogenesis, nor the processes of dedifferentiation which appear to contribute to neoplasia and tumour behaviour.

Organic chemistry has made a major contribution to medicine. Pharmacology is almost entirely a subject of the 20th century. Discoveries have included antibiotics, receptor antagonists, steroids, contraceptives, and cytotoxic drugs. The discipline is now merging with molecular biology, with the growth in interest in techniques such as gene and immunotherapy. Materials science and the technology of plastics has also had a major bearing on surgical practice, facilitating intravenous fluids, endoscopes, cannulae, and catheters, for example.

Surgery in general

The application of the scientific process to experimental surgery, to new theories, models and operative techniques, is an important legacy of the 19th century, which has contributed to the current status of clinical surgery. Among surgeons who have won the Nobel Prize for medicine and physiology in this century, for example, are Kocher (for thyroid surgery), Banting (for insulin), Huggins (for oncology) and Murray (for transplantation). The two World Wars and many lesser conflicts have profoundly influenced several generations of modern surgeons and forced the pace of many developments in trauma management, reconstruction, antisepsis, physiology (fluid volume management and transfusion) and antibiotics. Many surgical disciplines, such as surgery of the brain, heart, thorax, liver, abdominal viscera and gastrointestinal tract, are largely of this century alone. It would be impractical to select for special mention from the huge numbers of individuals who have contributed to the advancement of surgical oncology in so many ways and in so many fields in the past century.

Surgical instrumentation

Conventional surgical instrumentation has evolved steadily over the century, but would be largely recognizable to our predecessors. Other disciplines have been transformed by technical advances in instrumentation. The fibre-optic light source has illuminated the aerodigestive and urological tracts. Laparoscopic techniques have had a significant impact on general surgery, if not on cancer surgery, in the past decade. Surgical technique has also been assisted by a number of technical developments, including diathermy and materials technology, with products such as sutures and meshes, and reconstructive prostheses. Laser knives, virtual reality and remote operating remain in the realm of experimentation.

Peri-operative care

Advances in pre- and post-operative care over a spectrum of disciplines have hugely reduced the risk and extended the scope of major surgery. Technical advances have included antibiotics, antisepsis and sterilization, blood transfusion, parenteral nutrition, anti-coagulation, while practices have vastly improved in physiotherapy, nursing care, and the allied health professions. Safe and effective anaesthesia, anaesthetic agents and monitoring equipment have been the key to the development of all complex surgery. Intensive care skills and facilities contribute to the management of complex cases and to the reduction of operative morbidity.

Cancer

Cancer is generally a disease of later life. It has come to prominence in the past 100 years because of the significant increase in life expectancy in the Western world. This is largely consequent upon better public health and hygiene measures, sanitation and mass vaccination, improvements in food supply, housing and public education rather than to medical advance. We also recognize tumours which are a consequence of modern human activity, such as tobacco consumption, the use of asbestos, and exposure to high dose radiation sources.

The diagnosis of cancer

The facilities for pre-operative diagnosis of disease have changed radically from the turn of the century, when clinical skills and experience were the bedrock of diagnosis. Diagnostic radiology has progressed from its crude beginnings to computerized axial and magnetic resonance imaging, and to angiography. The sciences of biochemistry, haematology, microbiology, histopathology, immunology and genetic analysis are all largely of the 20th century. Fibre-optic endoscopy and minimally invasive technologies such as laparoscopy have added to diagnosis and to treatment.

Cancer treatment

In the past century, the discipline of surgical oncology has come to prominence. Although much has changed, the treatment of solid tumours provides as much a challenge now as it did a century ago. The philosophy of cancer surgery has become progressively more conservative over the century, where compatible with safe and adequate removal of the primary lesion, and with the recognition that it is often the biology of the disease rather than the radicality of the surgery that determines outcome. Conversely, advances in many related fields have opened up many organs to hitherto impractical forms of radical cancer surgery, including gastrointestinal, hepatic, gynaecological and thoracic surgery.

Responsibility for the surgery of cancers had been ill-defined until modern times. It has fallen within the remit of generalists and specialists alike. Progressive specialization in surgery has altered practice throughout the century. The separation of general and orthopaedic, gynaecological, urological, vascular, cardiac, thoracic and neurological surgery, for example, is now being reflected in a much more specialized subdivision of responsibility for cancer subgroups. Even more important than craft specialization is the recognition of the importance of a multidisciplinary medical approach to cancer management. Surgery alone, however well radically or meticulously practised, will often fail to cure patients of their cancers. Good outcomes often depend upon effective integrated cancer practice. Thus, paradoxically, having at last carved out a professional niche of immense influence by the mid 20th century, surgeons are now relinquishing their individualist pre-eminence in favour of the integrated approach to treatment.

The principal forms of adjuvant cancer therapy, radiotherapy and chemotherapy, have evolved over the century. In one century, radiotherapy has emerged as a separate discipline and treatment modality. The discovery and the harnessing of particulate and electromagnetic radiation to therap was a major advance. The applications of radium (Marie Curie, 1895) were widely explored in radium institutes across Europe in the first half of the century, before being superceded by directional beam radiotherapy in its various forms in the mid 20th century. It has evolved through a period of great optimism to a more guarded assessment. We now understand the radiobiology of tumours, the nature of fractional killing of populations of cells and of cell survival and repopulation during treatment, and the biology of neovascularized and hypoxic tissues. We recognize the side-effects of treatment and the limitations of directional ionizing radiation on the whole body and upon mobile viscera. Many visceral tumours remain unsuitable for radiotherapy, whether through biological resistance, mobility or proximity to sensitive structures.

A wide range of powerful anti-cancer drugs emerged following the discovery of the cytotoxic effects of the nitrogen mustards of military notoriety. The therapeutic utility of most cytotoxic agents still remains limited by a high incidence of systemic toxicity and morbidity. The optimism and promise of the new therapeutic concepts emerging from molecular biology and biotechnology, for example gene and immunotherapy, have yet to translate into effective treatments.

Methodical clinical data collection predates the 20th century. However, methods of data collection, of data handling, of data transmission, of statistics and of data analysis have transformed clinical trials, cancer research and cancer epidemiology. The presentation and publication of scientific data has become less anecdotal and more systematic in modern times.

Social attitudes to cancer

A change has occurred in social attitudes to the mass, institutionalized provision of public health care. No one model of health care provision is ideal, but in general terms there has been a movement towards universal, institutionalized access to 'cradle to grave' health care in Europe. The dissemination of knowledge and public awareness of cancer has changed the relationship between clinician and patient, demanding a more informative and informed approach by the surgeon, and an acute awareness of media and medicolegal issues and of public opinion on clinical matters. The changing relationship between surgeons and patients, new expectations and new social attitudes, to risk, to the law, and to the media, impose new levels of complexity upon professional practice. The environment in which cancer patients are treated has also changed immensely over the century. Palliative and terminal care, quality of life issues, the hospice movement, public information and education play a major role in modern treatment strategies.

Conclusions

The dramatic economic, scientific and technological changes of the 20th century have profoundly influenced the material and intellectual environment in which we practice medicine and treat cancer. The foundations of our heady progress were carved out at a more leisurely pace but in a much harsher social and intellectual climate over the past 2000 years. As for the alleviation of the degenerative diseases of old age, we still have much to achieve. In global terms, infectious disease, poverty and conflict pose far greater challenges to youth and to the sum of human happiness than do the ravages of cancer in an ageing population. Nevertheless, we still face many professional challenges if we are to consolidate our gains and to sustain the momentum of beneficial change in medical knowledge and medical practice through the next millennium. We will need to continue to challenge orthodoxies and established practices, to nurture research and creativity, and to nurture the ideals and benefits of international cooperation. The final article in this series will address the challenges and opportunities in cancer research and treatment in the 21st century.

Further reading

1. Watson JD, Crick FHC. Molecular structure of nucleic acids. *Nature* 1953; **171**: 737.
2. Kohler G, Milstein C. Continuous cultures of fused cells secreting antibody of pre-defined specificity. *Nature* 1975; **256**: 495–7.
3. Howard A, Pelc SR. Nuclear incorporation of P-32 as demonstrated by autoradiographs. *Exp Cell Res* 1951; **2**: 178–87.
4. Goodman D, Russell CA. *The Rise of Scientific Europe 1500–1800.* London: Hodder and Stoughton/The Open University, 1991.
5. Rutkow IM. *Surgery: An Illustrated History.* St Louis, MO: Mosby, 1993.
6. Cantor D. Cancer. In Bynum WF, Porter R (eds). *Companion Encyclopaedia of the History of Medicine, Vol. 1.* Oxford: Oxford University Press, 1993: 537–61.

World Wide Web references (http://)

W1. www.vh.org/Providers/Textbooks/SnydersMedHx
Professor Snyder's online medical history
W2. www.mic.ki.se/history.htm

The Karolinska Institute's medical history archive
W3. www.nature.com/Nature2
Historical articles
The original paper describing the structure of DNA
The obituary of Charles Babbage

Visits to Departments of Surgical Oncology in Europe

As part of the educational role of the *European Journal of Surgical Oncology*, the Editors have decided to introduce a regular section in EJSO designed for departments of surgical oncology throughout Europe to indicate to our readers their encouragement for visits from trainees (both clinical and research). It is generally understood that persons who are willing to visit the centres have arranged their own funding unless otherwise stated. Any of our readers who would wish to visit the centres should contact the institution to plan the visit in more detail.

The Department of General Surgery, Institut Gustave-Roussy, Villejuif, France
The Institut Gustave-Roussy is located just outside Paris. The Department of General Surgery is a 102-bed unit with 10 full-time and two part-time surgeons, 12 attendants and residents. One psychotherapist works full-time with the team. Three thousand and four hundred operations a year are carried out in six operating theatres. The range of tumours treated are: gynaecological, gastro-intestinal, hepatic, breast, skin, thyroid, urological, bone and soft tissue. There are several outpatient clinics per week. Surgical staff participate at least once a week in multidisciplinary clinical committees. Surgical staff meet once a week to discuss cases and new protocols. Two foreign residents are part of the staff every six months.

The Department is an integral part of the most important cancer institute in France with 507 beds and 700 doctors and research workers.

The Department of Surgery, University of Heidelberg, Heidelberg, Germany
The Department of Surgery at the University of Heidelberg is a 200 bed unit with special clinical section of Surgical Oncology, Vascular Surgery and Trauma Surgery. The Section of Surgical Oncology was instituted in 1982 to provide facilities for rapid translation of new treatment concepts into clinical practice. The section includes a special, well-staffed 20-bed unit, an outpatient clinic and a unit for oncological documentation. Special treatment facilities include intraoperative radiation therapy in a dedicated operating suite and isolated extremity perfusion. Major clinical activities concern treatment of oesophageal cancer, liver tumours, retroperitoneal malignancies and treatment of tumour recurrence. Clinical protocols currently under evaluation address IORT for soft tissue sarcoma and rectal cancer, adjuvant treatment of colon cancer, adjuvant immunotherapy following curative resection of colorectal liver metastases and chronomodulated neoadjuvant treatment of advanced liver metastases.

Visitors are welcome. If they stay for prolonged time periods and have good command of the German or English language, active participation in the section's scientific activities is encouraged.

Contact: T. Lehnert, MD, Section of Surgical Oncology, Department of Surgery, Im Neuenheimer Feld 110, D-69120 Heidelberg, Germany. Fax: +49-6221-565506; E-Mail: thomas_lehnert@krzmail.krz.uni-heidelberg.de

The Department of Surgery and Surgical Oncology, Robert-Rössle-Hospital, Charité, Humboldt University, Berlin, Germany
The Robert-Rössle-Hospital is a 200-bed specialized oncology center and is part of the Charité Clinic in Berlin. It is located on the campus of the Max-Delbrück-Center for Molecular Medicine, one of the large central biomedical research facilities in Germany. The Department of Surgery and Surgical Oncology is a 68-bed unit including a highly equipped eight-bed intensive care ward. The most frequently treated tumour entities are GI-tract cancers and hepatic malignancies, breast cancer, thyroid cancer, malignant melanoma and bone and soft tissue sarcoma. Active clinical research protocols are based on hyperthermia, isolated limb perfusion with TNF, and photodynamic therapy, as well as innovative staging procedures in cancer. A special research unit (OP 2000) is engaged in all aspects of telemedicine and computer-aided surgery. There is a close cooperation with basic research groups on the campus with projects in tumour invasion and metastasis, multi-drug resistance, hereditary cancer syndromes and gene therapy.

Visitors are welcome. Depending upon knowledge, active participation in the clinical and scientific activities is encouraged.

Contact: Prof. Dr P. M. Schlag, Robert-Rössle-Klinik.Lindenberger Weg 80, 13122 Berlin, Germany. Tel: 0049-30-9417 1400; Fax: 0049-30-9417 1404; E-mail: schlag@rrk-berlin.de