

Chapter-1

Medicine in 21st Century— Where Are We Heading?

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“The new millennium is a remarkable time for medicine, when the potential for bettering human health is unequalled in history. Despite the potential obstacles and unforeseen challenges, the possibilities for progress in medical science and the opportunities for medical research have never been greater. The ongoing revolution in biomedical science is of an unprecedented magnitude, is accelerating dramatically, and promises almost unlimited opportunity for the betterment of humankind.” (David Nathan, pediatric hematologist writing in a special issue of JAMA 2001).¹

SEQUENCING OF THE HUMAN GENOME

In 1944 Avery, McCloud, and McCarty showed that DNA is the stuff that genes are made of and in 1953 the double helical, anti-parallel, complementary nature of DNA was published by James Watson and Francis Crick and finally, in 2003, we marked the completion of the “finished sequence” of the human genome.²⁻⁵ The chemical consequences of the complementary structure of DNA underlie much that we do today in molecular biology and genomics. This knowledge of basic science has been accompanied by a phenomenal burst of technology with the ability to amplify DNA using the polymerase chain reaction [PCR], rapid identification of sequence variation, high throughput sequencing of genes, quantification of messenger RNA by real time PCR and precise evaluation of proteins by MALDI-TOF and crystallography. In fact the race is on to provide the complete human genome sequence for an individual (3 billion bases) at a cost of US\$1000.⁶

Genetic Diseases

This knowledge of molecular genetics has led to a remarkable improvement in the diagnosis of genetic diseases and currently, OMIM lists 1,500 identified disease genes, and for just over 1,000 of these there are molecular tests and therefore in the clinic, rather than making diagnosis by goodness fit of phenotypic features we increasingly rely on precise molecular assays.^{7,8} We now use this information for antenatal diagnosis where at 10 weeks of pregnancy we can confirm the presence of the genetic defect by a chorionic villous biopsy. This understanding of the molecular defect we hope will ultimately result in gene therapy or repair. Hacıen Bey and colleagues have successfully treated severe combined immunodeficiency [SCID] by introducing the gene for the interferon receptor packaged in a lenti-virus.⁹ Many hurdles remain to ensure sustained function of the gene at physiological levels and prevent untoward effects like insertional mutagenesis [two patients in the SCID gene therapy trial developed acute leukemia], but science will find solutions.¹⁰

Laboratory Diagnosis

DNA based tests are currently available for precise diagnosis and quantification of disease: we now diagnose and monitor therapy of many viral diseases by real time PCR the notable examples

being hepatitis B and C, cytomegalovirus and HIV. We can track the source of a hospital outbreak of bacterial infection like staphylococcus by DNA fingerprinting.¹¹ Automation has made it possible for us to process large numbers of patient samples rapidly and precisely and information technology allows us to make results available almost instantaneously for clinical decisions to be made. In the virtual laboratory of the 21st century bar coded blood samples will be transported through a pneumatic system, sorted, centrifuged, moved into automated equipment depending on the test required and robotically transferred for storage at the correct temperature for retest if required. Anatomical pathology is moving from descriptive to a much higher accuracy based on a battery of antibodies against specific tissue antigens, cytochemistry and in-situ hybridization with DNA probes.¹²

Therapeutics

The understanding of the pathophysiology of disease at the molecular level will see a whole host of new molecules of “targeted therapy” and imatinib (Glivec) for chronic myeloid leukemia is an excellent example of how this has changed the whole algorithm of management where we will now do a bone marrow transplant only for a patient who relapses or is refractory to this drug or to new molecules that are being developed.¹³ The evolving science of nanotechnology will see new innovations in drug formulations and delivery systems and recombinant and transgenic technologies are making it possible to produce therapeutic proteins free of infectious agents, in large amounts at low cost. However there is concern on the antimicrobial front where resistance is becoming a major problem and the numbers of new molecules on the shelf are few and we may soon have infections for which we do not have an active agent.¹⁴ Colistin is being resurrected since pseudomonas infections resistant to the carbapenems are being seen. We know that one size does not fit all and no patient responds exactly in the same way to a given drug but the science of pharmacogenetics is progressing and we may soon have a chip which will characterize all the drug metabolizing enzymes in a given patient and help to predict response and toxicity.¹⁵ The whole process of new drug discovery will be driven by the new systems biology which is based on targeting genes and their protein products.¹⁶

BIOTECHNOLOGY AND ENGINEERING

A revolution in disease diagnosis began in the 1970s with the introduction of computed tomography, magnetic resonance imaging, and ultrasonic imaging.¹⁷ The development of these imaging modalities has been accompanied by exciting advances in 3-dimensional image reconstruction, quantitative image analysis, and image enhancement - advances that were made possible by improved computational power and algorithms. PET scans linked to CT scans now make it possible not only to get a 3 dimensional image but also provide information on functional status of the tissue and presence of residual tumor. The use of computers and robotics promises to facilitate complex endoscopic procedures by virtue of voice control over the networked operating room, enhancement of dexterity to facilitate microscale operations, and development of virtual simulator trainers to enhance the ability to learn new complex operations.¹⁸ Linear accelerators can focus radiation precisely to the tumor with minimal damage to surrounding normal tissues: the so called gamma knife.

The Promise of Stem Cells

The whole new science of stem cell biology and the belief that even adult stems cells have ‘plasticity’ with the ability to trans-differentiate into other cell types suggests that the next decade will witness a revolution in regenerative medicine.¹⁹ Hematopoietic and mesenchymal stem cells are being expanded ex vivo and used to revascularize ischemic myocardium and treat many neurological disorders from Stroke to Parkinson’s disease. However biologists are skeptical as to

whether adult stem cells are truly plastic and only rigorously controlled clinical trials with careful follow up will prove whether this is real. Embryonal stem cells have innate capacities to differentiate into almost all cell types and can potentially be used to regenerate any tissue but there are ethical problems in the creation of cell lines from human embryos.²⁰ *The race is on, but physicians and scientists must not in their enthusiasm to prove that these new therapies are effective, stray from the truth or we will witness further debacles like the one from South Korea.*²¹ Patients also must not be given false hope that stem cell therapies are effective before the results of clinical trials are out.

MEDICINE IN INDIA IN THE 21st CENTURY

“We reap what we sow, we are the makers of our own fate. The wind is blowing; those vessels whose sails are unfurled catch it, and go forward on their way, but those which have their sails furled do not catch the wind. Is that the fault of the wind? We make our own destiny.” Swami Vivekananda quoted by finance minister P Chidambaram presenting the Union Budget 2006 in parliament at Delhi.²²

The last decade has witnessed a dramatic change in India with an increase in GNP per capita of Rs.1700 in 1999 to Rs.155000 in 2006 and there is a rapidly expanding middle class who are better informed and can afford good quality medical care.²³ *However India is not shining for the vast majority of our population in the villages who still do not have the basic necessities of clean safe drinking water, sanitation, adequate nutrition and access to basic hospital services. This problem is compounded by the population growth which remains unchecked* in certain states and the projected population for the country in 2050 is 1.628 billion, and we will move up over China as being the country with the world’s highest population.²³ The present government’s rural health mission if successfully implemented can significantly improve the health of the majority of our people who live in the villages of India and we as a medical community have to be a part of this program.

COMMERCIALIZATION OF MEDICINE IN THE 21st CENTURY IN INDIA

We are witnessing a significant change in the attitudes and values of the medical profession in an environment where health is reduced to an industry and we no longer talk of ‘the patient’ but of a consumer. Capital and its acquisition is the driving force for health care providers and many unhealthy practices are becoming accepted as the norm. *Numerous state of the art hospitals are coming up to meet the demands of medical tourism: however, the ethics of diverting scarce manpower resources to service foreign clientele, when we have only 0.6 physicians/1000 population compared to 2.6/1000 in the US, needs to be examined carefully.*²⁴ The public will no longer perceive the physician as healer but just another provider out to make his money. We as a profession need to check this change in direction and revive a value based system of medical ethics. We need role models where service and commitment along with a high degree of professional excellence are the defining points of a good doctor.

Medical Education

We are witnessing a proliferation of medical colleges in India with the directory of medical schools listing 202 as of April 2006, many based on capitation.²⁵ This is not necessarily a bad thing if most of the income generated is used to develop the infrastructure for a good quality medical schools and a well equipped teaching hospital. Insistence on quality and maintenance of standards are vital and the Medical Council of India must honestly implement this in all medical schools. Our present system of education needs to be drastically changed keeping in mind the advances in medicine and so also must the examination system which remains archaic.

Medical Research

The number of medical schools in India where some level of research is being carried out are few. Most graduates would choose to specialize and enter private practice or a corporate hospital where the income is high and few remain in academic institutions to teach and carry out research either basic or clinical. This must change if our medical schools are to maintain standards in an era of great advances in molecular biology and medicine.

The 21st century is witnessing great progress and India can be proud of the fact that in the areas of information technology and pharmaceuticals we can compete globally. The economy is improving with a major increase in the GNP per capita and this means that people are able to spend more on health. However, we must not leave behind the majority of our people in villages and urban slums. The medical profession, with the benefit of education, must not forget its social responsibility.

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