

The 4th Tan Tock Seng Hospital Oration: Challenge for the Medical Profession in the 21st Century⁺

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Mr Chairman, Distinguished Guests, Friends and Colleagues:

I am greatly honoured to speak at the 4th TTSH Oration following such distinguished luminaries like Dr Chew Chin Hin, Dr Chen Ai Ju and Professor N Balachandran. I also wish to thank all of you who are present this evening. We are indeed fortunate to be alive at this moment in history. We are not only entering a new millennium—we are witnessing a new dawn in medicine—a future that is both exhilarating and yet frightening but one that holds great promise and which will change the practice of medicine forever.

In the next hour, I will try to show you some glimpses of this new dawn and persuade you that the future is now. I will concentrate on 5 areas—this is more from personal bias rather than any academic reason. They are (1) age and ageing, (2) alternative medicine, (3) AIDS, (4) the human genome and (5) the information revolution.

1. Age and Ageing

Throughout the world, populations are ageing. The chief cause of population ageing is a change in the balance between fertility and mortality rates. Basically, ageing comes about from interaction between intrinsic (genetic) and extrinsic (environmental and life-style) factors. Although immortality is not yet achievable, there are now real possibilities of improving the course of human ageing through modulation of both intrinsic and extrinsic processes. Better housing, better environment and improvements in medical treatment have pushed back the average life span. In the past century, life span in the U.S. has gone up thirty years from 46 to 76 years. However, in this new century new biological and genetic research will further increase our life span.

It is estimated that out of 80 to 100,000 genes in the human genome, as many as 7000 might modulate ageing. Even if only 1% were truly important, a total of 70 would merit detailed study.

(a) The Telomere Story

One of the most exciting research in ageing has resulted from the genetic study of a rare medical condition called “Progeria”. Fewer than 30 children in the world suffer from this condition. All these children start off as normal babies, but all of a sudden they begin to age and suffer prematurely from heart disease, crippling arthritis, blindness or stroke and most will die of old age in their mid-teens. Scientists have now found that the telomeres in certain cells of these children are extraordinarily short. Telomeres are “biological clocks” and are specialised DNA-protein complexes found at both ends of linear chromosomes. Every time a cell divides, the telomeres get shorter. Once the telomere shrinks to a certain level, the cell can no longer divide, its metabolism slows down, it ages and dies.

An enzyme called telomerase is able to rebuild telomerase after they have shortened. Unfortunately, adult cells do not produce telomerase. It only exist in the sperm and egg and the developing foetus. Scientists have now genetically engineered copies of the gene that is involved in making telomerase in the test-tube and inserted these genes into skin cells taken from an old man. After 2 years, these cells are still dividing and their telomeres never get shorter—they have become immortal cells. The medical implications of such work is truly profound. It promises treatment for macular degeneration, for ageing skin and skin damaged by burns, for atherosclerosis and a host of degenerative diseases. Scientists believe that in the next 10 to 20 years it will be possible to slow ageing in humans. Professor Lee Silver, a prominent geneticist from Princeton University, feels that within the next 100 years it will be possible to build the first immortal man or woman. The question then will be “why die?”—such a concept is both fascinating and frightening!

(b) Embryonic Stem Cell Technology

Another way to increase life span is to find replacement parts for diseased organs. In our medical student days, we

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have heard of stem cells. Stem cells are the undeveloped ordinary cells of a very early-stage embryo (no more than 64 cells). Many of these embryos have been grown in a laboratory from fertilized eggs; they were produced for in-vitro fertilisation but were later discarded or donated for research purposes.

Embryonic stem cells are pluripotent and have the ability to develop into any cell in the body. These stem cells do not actually develop into organs but they do begin to resemble the organ cells e.g. stem cells introduced into a disease kidney become much like ordinary kidney cells. The other kidney cells “educate” and integrate the new cells until the organ is effectively regenerated. Other sources of stem cells are from the bone marrow, peripheral blood and the blood in the umbilical cord of new born infants. Hence, with stem cell technology, one can actually regenerate new organs and tissues that are damaged e.g. in strokes, spinal cord injury, damaged cartilage in osteoarthritis, people with heart failure and pancreatic stem cells in diabetes. At the moment Christopher Reeves a.k.a Superman may not “fly” again. That may take another 10 to 20 years. Most scientists believe that by 2050 man will be able to replace many body parts with this technology. Indeed embryonic stem cell technology has been touted by the journal *Nature* as the top scientific discovery in the year 1999.

2. Alternative Medicine

Alternative medicine, loosely defined as treatments and practices not commonly taught in medical schools and used in hospitals, is “big business”. A survey in the U.S. in 1997 revealed that 42% of Americans have tried at least one form of alternative therapy and that 80% are satisfied with the result. These people spent US\$27 billion dollars yearly on alternative therapy. As more and more people use alternative therapy and the two systems i.e. alternative and main stream medicine began to be used side-by-side, the name complementary therapy was born. Infact, in some well-known academic centres, these two forms have merged to be known as integrative medicine. Among the common complementary therapies are acupuncture, aromatherapy, Ayurvedic medicine, chiropractice, herbal medicine, homeopathy, massage, meditation, reflexology, yoga and tai-chi.

In an attempt to inject more science and research into alternative therapy, a National Institute of Health virologist, Dr Stephen E Strauss, in October 1999 became the first permanent director of the National Center for Complementary and Alternative Medicine (NCCAM) with a budget of US\$70 million dollars to do research on the subject. Because of market pressures and patient demand, prestigious medical centres in the U.S., such as Beth Israel

Medical Center in New York, Cedars-Sinai Medical Center in Los Angeles, Stanford Medical Center in Palo Alto and University of Pittsburgh Medical Center, are using alternative therapy in treating some of their patients. However, there are detractors of alternative therapy—among them is the respected emeritus editor of the *New England Journal of Medicine* Dr Arnold Relman and the Church of England. Many of such detractors have referred alternative therapy as a politically correct term for what used to be called quackery and “homeopathy” as people paying big bucks for a highly diluted mixture that is essentially pure water.

3. AIDS—A Global Challenge

A recent study suggests that AIDS evolved from a benign Simian infection into a human killer in the early 1930s—long before it was recognised as a disease. It started in remote Africa until jet travel, big cities and the sexual revolution spread it worldwide.

On June 4th 1981, the Center for Diseases Control Newsletter Morbidity and Mortality Weekly (MMWR) published a report of 5 cases of an unusual pneumonia in Los Angeles. On July 3rd, the same publication reported an outbreak of 41 cases of Kaposi’s sarcoma, a rare skin cancer in 41 homosexual men in New York. In a short span of 20 years, the disease had infected more than 34 million people worldwide and killed 19 million people.

In the worst affected community in Africa-Botswana, more than 1 in 3 adults are infected. This is equivalent to 90 million people out of the U.S. population of 270 million or more than 1 million out of 3.5 million Singaporeans. More than 50% of these people will die in the next 5 to 7 years. Within the next decade in Africa, there will be more people in their 60s and 70s than there are in their 40s and 30s.

The future Africa will be a land of the elderly and the orphaned. The situation is so serious that the U.S. Government now regards the world AIDS epidemic to be a threat to the U.S. national security. Soon it will surpass both the bubonic plaque of the 1300s and the influenza epidemic of 1918 and 1991 in deadliness. The global AIDs epidemic will be mankind’s greatest health challenge ever.

4. The Human Genome

The history of the human genome probably started in 1866 when Gregor Mendel, an Austrian monk, suggested that discrete, hereditary units are passed along family lines to produce recognisable traits. These units are later termed genes. In 1910 in studies of the fruit fly, Dr Thomas Hurst Morgan, a researcher at Columbia University, showed that genes are carried on chromosomes and in 1944, researchers at Rockefeller Institute showed that genes are made of DNA. In 1953, Drs James Watson and Francis Crick

working in Cambridge, U.K. described the structure of DNA molecule as a double helix structure i.e. a double ladder twisted upon itself. In 1977, a technique was developed to read the chemical bases of DNA namely adenine (A), thymidine (T), guanine (G) and cytosine (C). This technique increases by a thousand times the rate at which DNA information can be sequenced. In 1986, the NIH and U.S. Department of Energy decided to sponsor the Human Genome Project—an attempt to map out all the 23 pairs of the human chromosome and work started in 1988.

The NIH part of the project is under the direction of Dr Francis Collins at the National Genome Research Institute at Bethesda, Maryland. He heads a consortium of 1100 scientists and the work is carried out in 16 centres in the U.S., U.K., France, Germany, Japan and China. The whole project costs about US\$3 billion. In the private sector, his “challenger” is Dr Craig Venter, a former researcher from NIH and now the President and CEO of Celera Genomics in Rockville, Maryland.

On Monday, 26th June 2000, President Clinton and Prime Minister Tony Blair announced simultaneously both in Washington and London that scientists have completed a rough map of the genetic make-up of a human being and are only a few years away from a complete map.

The application of the Human Genome Project is fundamental in two underlying universal principles. First of all, all diseases have a genetic component and second—no one is perfect. Each human being has 5 to 50 genetic flaws. Through the mapping of the human genome, such “bad” genes can be identified and this discovery may be used for purposes of preventive medicine, gene therapy and drug therapy. The gene responsible for cystic fibrosis has been identified and individuals can now determine their carrier status and risk of passing their genes to their offspring. It has also been cloned and has been used in scientific trials for the purpose of gene therapy. Other “bad” genes that have been identified are genes for Marfan’s disease, achondroplasia, sickle-cell anaemia, haemochromatosis—and also common diseases like hypertension, diabetes mellitus, cancer, schizophrenia and heart disease. An example of gene therapy is the recent report of two children in France with severe combined immunodeficiency who were successfully treated. However, gene therapy is not without danger. Eighteen-year-old Jesse Gelsinger died after receiving an experimental gene therapy for an inherited liver disease [ornithine transcarbamoylase (OTC) deficiency] in the University of Pittsburgh. He reacted to the viral vector that led to an immune response which caused multiple organ failure.

According to the WHO, globally today, 5% of children are born with a congenital or hereditary disorder and about

40% of adults are genetically predisposed to common diseases during their life-time. Gene therapy by replacing a defective gene or altering it will have the advantage of actually treating the cause of disease and not just the symptoms. For targeted drug therapy, the picture is still more complicated. Researchers must first identify the genes responsible for the disease, then identify the proteins made by these genes, determine the function of that protein in the body and then devise the therapeutic agent. Hence, a lot of work needs to be done.

On the other hand, such knowledge is not without risks and dangers. It can be exploited for commercial purpose or lead to a new world of “designer” babies and genetic discrimination. When we are able to change the future through the alteration of our very genes, the challenge is to think not only for ourselves but also about how our decisions will affect those who come after us.

5. The Information Revolution

The information revolution is changing everything in our world. Health care in this century will be changed drastically by the introduction of the computer and the Internet technology. In 1996 alone, investment in medical information technologies in the U.S. reached US\$15 billion and presently there are 35,000 medical websites. In 1998, 22 million Americans reported surfing the net for medical information and this number will increase to over 30 million this year. Electronic medical information systems can be divided into systems used to manage medical transactions, physician-support technologies to improve medical practice and patient focussed technologies to change how people manage their own care. All these have profound effects on the delivery of health care but each has its own problems and challenges.

One of the most significant results of this information revolution is in the field of patient education. We all know that communication is a vital part of all aspects of “doctoring” and effective communication can help our patients to understand their illness, including its cause, prognosis and natural course. Yet because we do this poorly, millions of patients are turning to the Internet for medical information and are exposed to the dangers of misinformation and fraudulent claims. Our knee-jerk response is to blame such poor doctor-patient communication on the decreased time we spend with patients because of the heavy patient load. Often we rush to blame managed care (as in the U.S.) and bureaucracy for interfering with the doctor-patient relationship. Are we as doctors blameless. Perhaps we misunderstand people’s needs to be told complex information several times. Perhaps we use overly complex language or we provide too much information all at once, which simply overwhelms and

confuses patients. Very often doctors fail to tailor our information to a person's educational status and we do not assess and explore how much information our patients have actually taken in.

What are the fundamental objectives of patient education. Greater understanding about one's disease is inherently worthy but only to a limited degree. Knowledge for knowledge's sake is a dubious goal. If patient education is to matter, it needs to improve patient's lives by accomplishing valuable objectives i.e. improve disease-specific knowledge and self-management skills, improve self-esteem and reduce illness-related anxiety or mortality.

Although "empowering" the patient and enhancing doctor-patient partnership are in vogue, there is the danger of the doctor losing leadership in such a partnership. Many doctors still expect to lead and to use one's training and experience to filter the available guidelines and evidence in order to advise the patient. Once the health professional becomes an information provider and is non-directive and goes along with what the patient chooses, the patient will eventually be the loser. Internet medical sources should

therefore augment not replace doctors's advice and, it is helpful to remember the Internet provides many sources of data, not guarantees of useful, truthful information. To quote George Lundberg, former editor of *JAMA* "The day you can regulate the Internet is the day we have one world government. It's not going to happen".

In the final analysis, the aim of medical information technology must be to increase productivity, reduce cost and result in a more knowledgeable consumer. Important issues like liability, privacy, economics and ethics have yet to be solved.

6. Conclusion

The coming of a new millennium as with so many other anniversaries is an event of enormous social, emotional and spiritual power. There is so much progress in medicine that each step brings along a host of other issues and problems. I have but touched the tip of the iceberg and like to conclude with a Chinese proverb which states "May you live in interesting times".