

## Navigating in the Sea of Science and Technology

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Let me begin by saying how deeply honoured I feel to be invited to deliver the 16<sup>th</sup> Gordon Arthur Ransome Oration. I thank the Master and the Council of the Academy of Medicine, Singapore, for bestowing on me this cherished honour.

Like many colleagues of my generation, I have always held Prof Ransome in the highest respect and admiration. I had the extreme good fortune and privilege of working under him on my return to Singapore from London in the mid 60s. Not having had the experience of learning and practising medicine in Singapore myself, I was struck by the wealth of clinical materials, the florid clinical presentation of patients and the relative shortage of resources for laboratory diagnostic support and therapy. Operating in this demanding and challenging environment was physician extraordinaire Professor Ransome. His clinical prowess in diagnosis was legendary. His intuitive power combined with a sharp eye for details and inordinate patience characterised his approach to any diagnostic problem. His philosophy was to bring the maximum power of all his senses, including the sixth, to bear on the clinical challenge before him and to come to the correct diagnosis by the bedside with the minimum of laboratory or radiological aid. Perhaps it was the relative shortage of the latter that had helped to hone his diagnostic skill to that extraordinary level. In him we had an example of innate talent and capability blossoming under pressure of circumstances. A lesser person could never have risen to his level of attainment. As I fondly remember, it was an inspiring experience to learn from this master diagnostician. He was very kind, generous and patient in sharing his vast clinical experience and wisdom, but most of all, he taught by example, by what he actually did at the bedside. His clinical credo was to go to the laboratories only after an exhaustive bedside investigation and a clinical diagnosis. Ultimately, it called for judgement based on keen observation, rigorous analysis and intuitive insight.

It is interesting to speculate how Prof Ransome would view the practice of medicine 40 years later in the new millennium, and whether he would continue to enjoy pre-eminence in our present-day context if he was working in our midst. The exponential growth in medical knowledge and the consequent development of diverse specialties, the massive infusion of technology and the substantial increase in diagnostic and therapeutic capabilities have radically impacted the way medicine is practised. And the driving force behind these developments is the accelerating application from the growing body of scientific knowledge in the practice of medicine. This is likely to gain greater momentum in the foreseeable future.

The science of medicine is poised to grow. How the profession responds to the growth and its ramifications will determine the quality of care we deliver to our patients. The most obvious issue that confronts all of us today is that of information overload coupled with the rapid obsolescence of knowledge. New ideas and concepts about diseases are proffered, the latest and most sophisticated and powerful equipment promoted and breakthrough drugs with better efficacy announced. The constant bombardment has to be sorted and assessed, to separate the wheat from the chaff. This is a major task quite beyond the capability of individual doctors.

Clearly it has to be done collectively, preferably at the institutional level to ensure independence, fairness and objectivity as is attempted in the UK by NICE (National Institute for Clinical Excellence). In practice, problems relating to scope of coverage, speed of the process, quality control and ultimately provision of adequate resources have emerged. They need to be expeditiously resolved. Such a sieve is essential to assist doctors in keeping up with the rapid changes and benefit from the real advances that come along.

It is also important to know whether a given advance incurs additional cost and whether this can be justified by the benefit accruing to the patient and society, e.g. shorter hospital stay and earlier return to work. The benefit in human terms such as quality of life should clearly be considered although this is less amenable to quantification, and can be a contentious issue in the balance against cost. The rise of health economics in this context is therefore not unexpected. However, the availability of independent authoritative guidance, though highly valuable, is in itself not sufficient to ensure quality patient care. It can only supplement, not replace, clinical judgement and a holistic approach.

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As in all aspects of modern life, information technology (IT) plays an increasingly important role in the medical profession. The wide dissemination of and ready access to an inordinate amount of medical information through IT has profoundly influenced the practice of medicine. First and foremost, it enables members of the profession to keep up with developments and advances, new ideas and new products worldwide, from the convenience of the computer workstation. The sheer speed and ease of access to information has aggravated the problem of information overload which has just been alluded to. Paradoxically, IT itself can actually help lessen the load. With the increasingly powerful palm-tops and hand-held computers, the bulk of useful and important information can be stored in these handy, portable miniaturised devices and can therefore be readily retrieved when needed. This releases the mind from the heavy memory load to think, to analyse and to innovate.

With access to the large computer databases, comprehensive meta-analyses, clinical research and public-health policy formulation are also greatly facilitated. Besides promoting communication between doctors and facilitating continuing medical education, IT can be a powerful tool in making clinical decisions. By simulating the whole clinical decision process, IT can be a valuable tool for decision analysis in dealing with complex clinical problems. It can also help in predicting clinical outcome through multivariable statistical models, although it has been noted that compared to expert clinicians, currently available statistical models are not significantly more accurate though they are more consistent.

The use of IT for such functions is expected to increase as user-friendly software packages become more widely available and as experience accumulates including a better understanding of their benefits and limits. However, the best available quantitative IT tools today, no matter how well designed, can only support and not replace the experience and sound reasoning skills of a good physician. But with time, the capabilities of artificial intelligence are likely to advance.

As we increase our understanding and knowledge of how our clinical mind works this will become translated into ever more powerful simulator software. The combination of the best of human biology with the best of technology portends awesome possibilities. Can the computer replace the doctor? I think not, until it can master interpersonal chemistry and acquire the intuitive faculty which we call clinical sense. These two areas defy analysis and formulation and cannot conceivably find their way to the software package. But then, we should not underestimate what IT and science can do, including simulating human activities which we ourselves do not yet understand.

The completion of sequencing of the human genome and major advances in genetics have given a big boost to biomedical research. The projected economic value of such research especially to the pharmaceutical industry has attracted generous research funding in the relevant areas ranging from drug discovery and pharmacogenomics to gene therapy and cell replacement therapy. Related upstream research, such as genomics, proteomics, and work on stem cells (adult and embryonic), has also enjoyed strong support. The enormous amount of valuable data generated by the human genome project and the need to analyse and interpret these data is being managed by the emergence of the multidisciplinary science of bioinformatics that has its foundation in computer science, physics, mathematics and biology. Bioinformatics, by its vast capacity for storing, retrieving, sorting out, analysing and interpreting DNA and protein sequence data, will make significant contribution to functional genomics, deeper understanding of disease, discovery of drug targets and even individualising therapy.

The ultimate target of all these research is the patient and clearly as doctors we have a pivotal role to play. The assessment of efficacy and side effects of new treatment modalities require clinical trials in which doctors are called upon to exercise independent clinical judgement. For those of us who are more strongly grounded in the basic sciences, especially those who have had training in basic research, the opportunity to be involved in a wide range of exciting biomedical research is most welcome. Many clinicians working in hospitals are already involved in research that brings the power of basic science and technology to bear on clinical problems. This area of research labeled clinical research is an important component in the biomedical research web and has also enjoyed increased funding support. The question often asked is how much of the busy clinician's time should ideally be spent on research with the consequent impact on time for clinical work and how the remuneration is to be structured such that there is no disincentive to do research.

Apart from the contribution to the greater biomedical good, research actually confers benefit in the quality of clinical work itself. An inquiring mind that comes with involvement in research sharpens the intellect and fosters an innovative mind-set. These are highly desirable attributes in the clinician. In an academic setting these qualities are crucial and here research is rightly given the great emphasis it deserves.

As our understanding of the genetic basis of disease increases, not only curative but also preventive medicine will receive a big boost. Actually disease prevention will gain increasing prominence as the identification of responsible genes and knowing how they bring about diseases will allow us to try and modify the intrinsic disease processes and to minimise or

eliminate specific environmental factors that contribute to the clinical expression of these genes or aggravate the consequences of their expression.

More radically, screening for the culprit genes in the early IVF embryo at the pre-implantation stage is being attempted for certain inherited diseases. Embryos found to carry such genes are not implanted so as to prevent parental transmission of these diseases. Such pre-implantation genetic intervention has, as expected, attracted much ethical debate and controversy, one main concern being that it could eventually be extended to selecting desired characteristics and the creation of designer babies, a possibility that many find abhorrent. Most medical conditions are of course not due to single gene aberrations that lend themselves to direct genetic manipulation. The majority of diseases have a polygenic background, and the challenge of identifying the cohort of abnormal genes responsible for each of these diseases and the complex interactions within each cohort of genes has yet to be overcome in most cases.

Technology may well breach this barrier in time. We should be prepared for new opportunities and also be aware of the ethical and social constraints. Advances in DNA diagnostics have now made possible the diagnosis of certain diseases before their clinical manifestation. If there are ways to intervene and prevent these clinical diseases, early intervention is the logical course of action, as in the example of multiple endocrine neoplasia. The ethical problem arises when the latent diseases indicated by genetic screening are not preventable and clinically have no effective treatment, e.g. Huntington disease. Should genetic tests for such conditions be withheld on the ground that they cause devastating anxiety and hopelessness in the affected individuals and family members, without there being any chance of influencing the outcome? Should genetic test results and genetic information in general, be withheld from potential employers, insurance companies, or even potential marriage partners for fear of discrimination and rejection? Would such anxiety lead to rejection of all genetic tests including those that can indeed help prevent clinical disease? Should claims linking genetic variants to disease be more rigorously tested before they are accepted, since, besides high penetrance single gene diseases, genetic tests only indicate statistical risks?

These are some of the questions that have become the stuff of much heated debate with the rapid extension of the reach of DNA diagnosis. Indeed as advances in genetic medicine have captured wide media and public attention, it has become increasingly challenging for physicians to educate and counsel patients on the indications, benefits and limitations of genetic testing in the management of a wide range of diseases. The use of stem cells to create tissues for replacement therapy has also evinced strong societal response. The prospect of cure of debilitating diseases due to loss of normal functioning tissues has raised hope among patients. The use of adult stem cells or cord-blood stem cells has incurred no ethical problems, but not embryonic stem cells and foetal germ cells. Embryonic stem cells derived from 5-day old embryos have the greatest plasticity in differentiating into various tissues but sacrificing the early embryo to derive the stem cells is morally repugnant to those who believe that each early embryo is no less a human person than an adult or child from the moment of union of sperm and egg. On the other hand, there are those who believe personhood comes much later in foetal life (40 days to 4 months after fertilization of the egg) and others who point out that an egg fertilized in-vitro has only about 17% chance of developing into a live birth, in the best of hands.

The Bioethics Advisory Committee's position has recently been announced and accepted by the Government. The early embryo (less than 14 days old) is accorded a special status but this status is not equivalent to that of an adult or child. Derivation of stem cells from the early embryo for research will be closely regulated by a statutory authority and will be approved only if it can be shown to be essential for the purpose of the research. Those who have reservations on such research should not be coerced to participate as donors or as researchers. Therapeutic cloning as a source of stem cells will be even more rigorously regulated while reproductive cloning is categorically disallowed. It is a delicate balance between protecting individual rights and welfare, respecting individual beliefs and allowing biomedical research to develop to its full potential for the benefit of patients.

The development of medicine over the last three or four decades has been characterised by the growth of specialties. The specialties are largely a reflection of the rapid growth in the science of medicine. They provide high-quality in-depth care for patients with diseases that fall within their respective areas. In the 60s and 70s, internists used to indicate their special interests as appendages to their designations, e.g. physician with an interest in a specialty, be it nephrology or cardiology, or any other specialty. The commitment to general medicine remained substantial. The last two decades, however, has seen the specialties growing to the point where general medicine is reduced to what falls between the many expanding specialist stools. The virtue of first managing the patient as a whole and then if necessary to assign him to appropriate specialised care is increasingly recognised. It certainly makes for more efficient use of the specialist services, and areas not covered by the specialists would receive the appropriate attention. However, given the present advanced stage of development of specialisation, one practical alternative would be for a specialist, say a nephrologist, to also assume responsibility for

general medicine and declare this commitment by calling himself a nephrologist with an interest in general medicine!

Science and technology have given us the wide range of modern diagnostic tools and tests which have clearly helped us make speedy and accurate diagnoses. However, it would be a mistake if in harnessing laboratory technology we pay less attention to clinical observation and assessment. Certainly, a person like Prof Ransome would be loath to allow his clinical acumen to atrophy from over reliance on technology and taking clinical short-cuts.

As physicians we are taught first to exercise judgement based on careful clinical examination and study of the patient. Laboratory tests are to be an aid and not a replacement for clinical assessment. In any case laboratory tests are not infallible, despite their growing capabilities, apparent precision and aura of authority. They have to be interpreted in the context of secure clinical findings. Used in this way they would have served to enhance the outstanding diagnostic acumen of Prof Ransome if he had access to them.

Although technology has vastly enhanced our diagnostic and therapeutic capabilities, skilful application of technology alone is clearly not sufficient to make a good physician. The art of medicine remains a critical component in the process of healing the sick and should not be allowed to be crowded out by the sheer weight of technology. The art of healing is based on human understanding, interest in humanity and compassion, and expressed in intuition and judgement that inspires trust and instils confidence. It enables a close bond and rapport to be established with the patient through tact, warmth and openness in communication.

Indeed the process of meticulous history taking and thorough physical examination helps to build and enhance this bond which humanises healthcare and adds to the power of technology in healing. One could speculate to what extent the rising number of litigious patients is a reflection of a general weakening in the doctor-patient rapport, an unintentioned consequence of growing dependence on technology. The fact that patients are partially informed, or misinformed, thanks to the pervasive influence of the Internet, could have contributed to the problem. In any case, it behoves us to ensure that the art of medicine takes its rightful dominant place alongside the growing power of technology in order to provide the optimal level of care for our patients.

Science and technology will undoubtedly continue to bring many wonderful opportunities for medicine. They will enable us to do more and better for our patients. The prospect is indeed exciting. As doctors we will have to continually learn and unlearn to benefit from the exciting technological advances coming our way. Continuing education is no longer simply an exercise in “brushing up” to refresh memory. It will entail learning new concepts, adopting new paradigms and using new techniques and tools. The latter is well demonstrated in the introduction of robot-assisted and telerobotic surgery and the use of virtual reality for surgical planning and training.

Actually as doctors we ourselves play a key role in contributing to these advances through research, especially research that applies basic science to solve clinical problems and through clinical trials. We also have the responsibility to ensure that the new technologies are used appropriately and efficiently. Most importantly, however, we should never lose sight of the fact that these advances in the science of medicine are but aids and tools to assist us in the work of healing the sick.

This is what Prof Ransome would have strongly advocated. Our clinical sense and judgement, human understanding and patients’ trust and confidence, lie at the heart of the practice of medicine, even as we embrace the many blessings and challenges from the rising tide of opportunities in the sea of science and technology.