Review Article

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Paradigm Shifts In The Future Delivery of Healthcare

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Significant shifts are being observed in the current paradigms that would impact on the future delivery of healthcare in the coming decades. This review highlights the essential principles of these shifts in paradigm and discusses the implications to healthcare professionals and society at large.

Most of the significant medical advances that have taken place over the past 50 years have evolved in small incremental steps and the magnitude of these changes are only evident when one looks back over a long period of time. But the current signals are revolutionary in nature and will therefore have a greater and more rapid impact on health, disease and life span of the human species.

Humanity has seen many such revolutions in the past. The Agricultural Revolution occurred thousands of years before Christ, the Industrial Revolution in the 18th century and more recently, touching our own lives, the IT/Digital revolution occurring in the latter part of the 20th century. The 21st Century revolution is the Revolution in Healthcare which will have similar profound impact in the way we live as a civilisation. The reason for this, is that for the first time in human history, we see the merger of the advances in biomedical sciences with that of the advances in physical sciences, namely IT & Digital technologies. We are beginning to use, in healthcare, the digital technologies as vehicles for global dissemination and incorporation of the biomedical advances into medical practice

Advances in IT follow Moore's Law, doubling the number of transistors in an integrated circuit every 2 years thereby reducing the cost of technology and/or doubling productivity. (1) In contrast, the medical and biotechnological advances in the past have been slow to be adopted into medical practice or to demonstrate productivity benefits. For example, the initial adoption of thrombolytics in post MI patients was extremely slow, even with significant mortality benefits shown in landmark trials. (2) However, the Healthcare revolution of the future will be touched by aspects of Moore's Law and the productivity benefits should follow rapidly.

Let us review some examples of biomedical advances that will have major impact in the future delivery of healthcare.

Mapping of the human genome

Disappointment has been expressed in some quarters that the mapping of the human genome around the turn of the century has not borne the expected rewards even a decade later. I tend to disagree. Perhaps we have not seen the many solutions that were expected but the direct and indirect benefits have been enormous. Just to name a few:

- The number of targets for new drugs have increased manyfolds. (3)
- The project has given birth to new fields of science: the study of proteins (Proteomics), the study of metabolites (Metabolomics) and many examples of the impact of pharmacogenetics improving the benefit to risk through personalised medicines.

Yes, the numbers are still not there but the story is still not complete and only time will tell.

Redefinition of diseases

We will continue to "redefine diseases" learning from the field of Oncology. Oncologists have perhaps been fortunate in dealing with diseases with a cell- based pathophysiology. Most other diseases have traditionally been system specific disorders. The days of developing global therapies for many cancers are over. The cancer therapies will continue to be designed towards specific molecular targets in sub sets of patients such as HER2 + breast cancer or BRAF + melanomas.

This need for redefinition is also illustrated in Alzheimer's disease. Many potential new

medicines have failed to show benefit when tested in a broad group of Alzheimer's patients but do so when tested in sub groups with specific APOE4 genotypes, confirming that Alzheimer's is not a single disease but perhaps a syndrome with different ages of onset and prognosis.(4) With a dementia epidemic confronting society, it is hoped that progress will be made in offering some real relief to this debilitating disease. A similar approach is necessary in the Cardiovascular and other Therapeutic areas by sub setting common diseases such as Hypertension and Heart Failure using genetic and biomarkers to develop more specific and targeted therapies

Emergence of new diseases

The future will continue to see the emergence of "New Diseases". Some of these will be "real new diseases" due to genetic mutations, environmental toxins and even new pathogens. There will also be existing diseases such as Non -alcoholic Steatohepatitis (NASH) coming into prominence due to the growing global epidemic of obesity and Type 2 DM, as well as to the availability of newer diagnostic criteria and tools. NASH will soon become the commonest cause of Hepatic carcinoma and Liver transplantation. There are currently no approved therapies, although metformin or pioglitazone may help by improving insulin sensitivity. Fortunately, promising molecules targeting the liver pathways in bile acid & lipid metabolism are currently in advanced trials and should reach clinical practice in the coming years. (5)

One of the issues with technological advances is that by using new diagnostic tools and criteria, we are redefining existing diseases. Is the Coronary Artery Disease of the past, diagnosed using exercise ECG and perhaps coronary angiogram, the same disease when diagnosed with sophisticated imaging and biomarker technologies? Could we extrapolate the same outcomes data and prognosis generated from older studies to today's patients? These are questions that need to be asked constantly as the medical advances influence the way diseases are diagnosed and managed with the consequent impact our decisions will have on healthcare systems.

The rise of biopharmaceuticals

Most of the medicines in clinical practice have traditionally been small molecules. A significant growth in large protein molecules through humanised biopharmaceuticals has occurred only in the last decade, especially as cancer and immune therapeutics. (6) This will accelerate further in the next decade, including exciting options in other disease areas such as asthma and vascular disorders. The disadvantages of Biopharmaceuticals include the cost (because they are difficult to develop & manufacture) and the need for parenteral administration. Ongoing research, including nanoparticles as transporters or the synthesis and administration of the active sites, may perhaps see non-parenteral (possibly even oral) modes of delivery in the future.

Innovative combinations therapies

Exciting "Innovative Combinations" with significant patient benefits will emerge. The development of devices to deliver inhaled steroids with either Long Acting Beta Agonists or Long Acting Muscarinic Antagonists and the recent approval of triple therapy for Chronic Obstructive Pulmonary Disease are indeed complex technological innovations. These technologies will accelerate in the future, as the molecular pathways of diseases, such as HIV, Diabetes, NASH, as well as in cancer and immunological disorders, offer the opportunity to develop a "cocktail" of targeted medicines in the form of combination therapies.

The use of Companion Diagnostics, with drug and diagnostic packaged together, will emerge as we subset diseases based on biomarkers and offer targeted therapies.

Curative therapies for chronic diseases

Most of the medicines for chronic diseases are not curative of the disease, with some notable exceptions in infectious diseases and perhaps in Oncology. Many medicines could alter the course of the disease, in changing the curve of progression with significant impact on morbidity and mortality, but they are still not curative. The prime reason is that the intervention takes place too late in the pathophysiological process. A good example is Parkinson's disease. The symptoms

develop only when the patient has lost around 70% of the nigrostriatal neurones. Although available therapies offer significant improvements in the symptoms and may delay progression, future developments will focus on early pre-symptomatic diagnosis, not only in Parkinson's disease and other neurodegenerative diseases but also in other therapy areas. The availability of advanced imaging technologies and ongoing research on biomarkers will allow potential patients to be screened noninvasively earlier in the disease process. The key issues will be the identification of "high risk" patients for screening and the cost implications of such an approach.

Electroceuticals

However, the technology that will transform the treatment of neurological disorders will be the emerging development of Electroceuticals or Bioelectronic medicine development. (7) The search for therapies for common degenerative neurological disorders have been disappointing. The question arises whether we have been barking up the wrong tree! Here is an organ which is primarily driven by neuro-electrical impulses AND the Blood Brain Barrier has evolved to prevent the transfer of toxins and therefore, medicines into the brain. One could argue that trying pharmaceuticals to treat CNS disorders is not a great strategy!! This exciting new development is the introduction of biochips into the brain to enhance neural transmission, perhaps even as a drug device combination. It would mimic the use of drug eluting stents in the coronary arteries. We already have a first, an alliance between the R&D organisations of two global companies from different industries, Pharma (GlaxoSmithKline) and IT (Google). This alliance has been set up as a new subsidiary solely focused on neuroscience development.

3D bioprinting

The 3D Bio Printer is a mind-boggling technology that is already making inroads in many industries and beginning to do so in healthcare. (8) Printing exact plastic replicas of a patient's organ, surgeons are already using training and for pre-operative familiarisation of complex surgical procedures. This technology even allows the synthesis of partially humanised organs using stem cell culture as in the case of the replacement ear offered recently to a 3-year-old girl. 3D printing could expand not only to supply medical devices, prostheses and laboratory equipment, but further down the line, even medicines, bespoke and in close proximity to the individual patient, in hospitals & pharmacies and perhaps eventually in the patient's own home!!

Digital revolution: the advent of artificial intelligence

The technology that will probably have the biggest impact in transforming the healthcare systems and will also have enormous ethical and social implications is that of AI or ARTIFICIAL INTELLIGENGE. (9) Although Robotic intelligence is a very visible part of AI and does create the illusion of a world run by robots, AI goes beyond the use of Robots. It is indeed a scientific endeavour which allows Machines to find solutions to complex problems in a human like fashion. It is about accumulation and analysis of big data through algorithms, which are initially designed by humans. The key is to allow the machines to learn and then design secondary algorithms for themselves. AI is NOT intended to replace humans but to act as adjuncts to human tasks. It is analogous to how we used MACHINES to replace human tasks in agriculture and industry.

Our homes as tomorrow's hospital

The move to eventually make our homes as tomorrow's hospital is already underway. What makes remote home care possible is not only the use of AI, Robotic assistance and Telemedicine but also the development of biosensors in our homes. Bodily fluids of patients could be continuously monitored virtually and in real time and appropriate actions taken. Smart toilets with embedded biosensors are a reality even today as research projects. The only question is as to how soon and how widely will "home biosensors" be applied in real practise?

Technological advances: the dangers & challenges

i) ***Technology Creep:*** Although technological advances bring enormous benefits, we need to manage its dangers and challenges as we are used to managing fire, nuclear energy and

indeed medicines. Technological advances can develop insidiously and in no time can take over our lives, as we have seen with the social media fiasco on Facebook. "*By plucking a chicken one feather at a time, no one notices"* so said Mussolini when he was trying to introduce fascism into Europe!!

ii) ***Changing roles of doctors:*** Some roles and tasks undertaken by doctors will disappear and be handed over to Robots & AI applications. Indeed, Doctors will need to develop a culture of acceptance and partnership with AI with consequent **enhancement** of their roles. Doctors will be relieved of low level tasks, will retain and enhance specialised tasks and most importantly, this will allow the opportunity for careers to be extended into later life. It will need considerable changes in attitudes, education & training of not only doctors and Healthcare Professionals but also the wider society. Many new professions currently not designated as Healthcare Professionals will be core players in the delivery of healthcare. There will develop considerable shifts in Doctor-Patient relationships, far more than what we see today. Some aspects of this shift, including patient empowerment, will continue to be welcomed but others will result in confusing responsibilities between patients, healthcare professionals and other stakeholders.

iii) ***Ethics of AI:*** We need to handle the enormous ethical and social aspects of AI. The initial algorithms are built by humans. Any biases and prejudices introduced by the humans would be magnified by machine learning robots. Robots are machines not humans; they do not differentiate between right and wrong, at least at the outset. The ongoing issues of confidentiality, data privacy and consent will be further exaggerated with the expansion of AI based technologies. Indeed, a world with robots and AI could dehumanise emotions. Susan Greenfield the neuro-pharmacologist, has already expressed serious concerns of a generation of youngsters, even today, growing up on social media with dehumanised emotions. What would the world be if, as some experts are suggesting, the Robots eventually develop emotion and even conscious self-awareness. Would this be the doomsday scenario for Homo sapiens?

iv) ***Funding of technological advances:*** Where will all the funding come from? Can the resource poor countries afford the technology, even if it is made available and accessible. Would it create a two-tier system and a two-tier world? There are no clear solutions on offer but society, the medical profession and politicians need to discuss all the politically sensitive options. Funding of healthcare is a global issue affecting the developed world as well as resource poor countries. How can we talk about funding these technological advances when we currently have over a billion adults and children who can't afford glasses to correct their vision and when half the population of the world do not have basic sanitation and clean water supply? Novel approaches and funding models need to be entertained to address this issue. Breaking down barriers and blurring of boundaries could result in benefits to all. The key in tomorrow's world is NOT to build WALLS but to build BRIDGES. For example, the collaboration and sharing of developmental risks between GlaxoSmithKline and the Bill & Melinda Gates Foundation has enabled significant progress in the development of a vaccine for Malaria. Initiatives by the European Governments, termed Advanced Market Purchase schemes, to acquire and distribute the entire supply of vaccines through their overseas aid program are also welcome. Such Public-Private Partnerships to support the development of vaccines and medicines for the neglected diseases are innovative approaches in funding that will lead to positive outcomes for patients. Similar models should be considered to deliver relevant technologies to resource poor countries.

v) ***End of Life decisions:*** Medical advances have without doubt prolonged life and will continue to do so at an accelerated pace in the future. Living to reach 100 years and beyond

will become the norm. Human beings have always searched for immortality or created narratives to ensure life doesn't end for them in the current form. We now have venture capital funds investing into research in search of the Elixir or "Amirtham" of immortality! But prolonging life is not the end of the story. It takes us to the beginning of life and the search for the meaning and purpose of life. We have through medical advances taken some control of our lives, but the question now being asked is whether we should have control of our death. Difficult and sensitive questions on end of life decisions and even euthanasia will become increasingly discussed. I do not know whether there is a right or wrong answer, and these are complex questions on ethics, religion and society. But as a medical community, we need to engage, contribute and participate in these discussions.

In conclusion, enormous advances in Healthcare with the combined force of biotechnology, digitalisation and artificial intelligence will be transformative and bring considerable benefits to society. However, we should be willing to address the complex financial, ethical and social implications of these advances and modify the training of doctors & Healthcare Practitioners to adapt and respond to these challenges. Above all. we need to pause and reflect on the optimal balance of life, its meaning and purpose, end of life decisions and death itself.

References:

1. Mack CA. Fifty years of Moore's Law. IEEE Transactions on Semiconductor Manufacturing 2011; 24(2):201-207
2. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Lancet 1994; 343:311–322
3. Santos R, Ursu O, Gaulton A, Bento P et al. A comprehensive map of molecular drug targets. Nature Reviews Drug Discovery 2017; 16:19-34
4. Cia-Chen Liu, Takahisa Kanekiyo, Huaxi Hu & Guojun Bu. Apolipoprotein E and Alzheimer disease: risk, mechanisms and therapy. Nat Rev Neurol 2013; 9(2):106-118.
5. Oseini AM & Sanyal AJ. Therapies in non-alcoholic steatohepatitis. Liver International 2017;37(1):97-103
6. Moorkens E, Meumissen N, Huys I, Declerck P, Vulto AG & Simoens S. The Market of Biopharmaceutical Medicines: A Snapshot of a Diverse Industrial Landscape. Front Pharmacol. 2017; 8:314.
7. Famm K, Litt B, Tracey KJ, Boyden ES & Slaoui M. Drug Discovery: A jump start for Electroceuticals. Nature 2013;496:159-161.
8. Bishop ES, Mostafa S, Pakvasa M, Luu HH et al. 3D bioprinting technologies in tissue engineering and regenerative medicine: Current and future trends. Genes & Diseases 2017; 4(4):185-195
9. Acompora G, Cook DJ, Rashidi P & Vasilakos AV. A survey of ambient intelligence in healthcare. Proc IEEE Inst Electr Electron Eng 2013; 101(12):2470-2494