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THE FUTURE OF PAEDIATRICS

When predicting the future, it is always pertinent to salvage clues from the past. As evident throughout this book, for at least a century and a half the Royal Children's Hospital (RCH) has had an illustrious history, which is manifest in the enormous respect garnered not just in the local community but also nationally and internationally. The hospital has been part of great discoveries, its corridors resonating with the footsteps of many pioneering clinicians.

The discipline of child health itself has seen a period of enormous growth and specialisation, with the RCH at the forefront ever since its foundation. RCH's early adoption of research as a mechanism to improve patient care has meant that for several decades the hospital has been leading the way. Examples of this include establishing the country's first paediatric research unit, which became operational in 1948. In 1951, the University of Melbourne passed regulations allowing students to carry out research for postgraduate degrees at the hospital. Currently, the university's Department of Paediatrics hosts 116 PhD candidates, who through their investigations are attempting to advance science pertaining to children. Other significant developments, including several of the great discoveries associated with the hospital, are highlighted elsewhere in this book. As child health research matures and increases in complexity, newer strategies, technologies and ways of working in multidisciplinary teams will be needed, and indeed are already emerging, to continue to improve health care for children and young people. In this spirit of collegiality, the partner organisations of the Melbourne Children's Campus—the Royal Children's Hospital, the University of Melbourne, the Murdoch Children's Research Institute, and the Royal Children's Hospital Foundation—strive to pursue the hospital's mission.

What do the discoveries of the past mean for paediatrics at the Melbourne Children's Campus? Improvements to care mean that many children who would have died during the hospital's first hundred years are now likely to survive. In addition, higher numbers of vulnerable neonates, whether born prematurely or with serious congenital conditions, are surviving—albeit often with significant neuro-disability. There are many more survivors of children's cancers, who also have special residual health considerations. As acute infectious diseases have diminished in importance (other than during pandemics, of course), non-communicable chronic diseases become increasingly prevalent and proportionally significant to children and young people's health and wellbeing. Even severe chronic

The new Centre for Health Analytics, Melbourne Children's Campus, 2021.

diseases of childhood may be best managed outside a hospital. Additionally, in several jurisdictions now, the importance of adolescent health problems is being increasingly recognised in relation to this age-group's significant and increasing morbidity and mortality. Young people's mental health is definitely a concern, with presentations to emergency departments already rising worryingly around the world.

So, how will the RCH respond? Can a preventative rather than reactive approach be offered to such children and young people with chronic health conditions? Several recent developments are preparing us for the changes that future health care will demand. Examples include the Complex Care service, which allows better interdisciplinary care and care coordination for the increasingly complex needs of children admitted to hospital, and improved capacity and functionality of its world-leading Hospital-in-the-Home service. Since the Melbourne Children's Campus introduced an electronic medical record system in 2016, extensive clinical data and information that previously did not exist are now available to guide clinical care, improve our operations, and inform research. Following this lead, other hospitals in the Parkville medical precinct have recently introduced the same system. In August 2020, a big-thinking, \$22 million, five-year grant from the RCH Foundation was the catalyst for the creation of the Centre for Health Analytics at the Melbourne Children's Campus. The first centre of its kind in Australia, it will help realise the shared vision of the campus partners by unleashing the power of data to improve health, making us international leaders in the use of data to improve all aspects of patient care, operations, education and research.

Another example of a partnership improving care and fostering excellence is the Melbourne Children's Campus Mental Health Strategy, released before, but adapting with agility to, the February 2021 report of the Royal Commission into Victoria's Mental Health System. Again, the strategy was funded via the RCH Foundation. Improving clinical services, research and education to transform society's response to this growing problem is essential; the strategy will enable the RCH to deal with the burgeoning mental health crisis afflicting young people.

Efforts to reduce chronic ill-health and promote wellbeing are informed by research undertaken at the Murdoch Children's Research Institute. The Melbourne Children's LifeCourse Initiative began in 2013 and hosts more than 20 separate population-based longitudinal studies (including two trans-generational studies), involving more than 40,000 participants aged from 0 to 35 years and generating 1 million data points and 80,000 biospecimens. There are at least 10 further clinical and specialist exposure studies, with a total of more than 10,000 participants. Few centres worldwide have such extensive population and clinical studies designed to answer questions central to early-life health and development. These studies have already shaped policy and clinical care nationally and internationally. They will provide a unique basis for new approaches to prevention

and treatment across childhood and adolescence that will be needed in the next few decades.

Also run on campus through the Murdoch Children's Research Institute is Generation Victoria (GenV). Its main aim is to create large, parallel, whole-of-state birth and parent cohorts that will enable researchers to explore the problems affecting Victoria's children and their families with greater speed and precision than is currently possible, leading to better understanding of the critical links between the environment, genes, physical characteristics and later outcomes across the life course. GenV will identify novel approaches to reducing the disease burden of all children, and the adults they become, focusing initially on child development and learning, mental health and wellbeing, pre-term birth, obesity and diabetes, infection, immunity and allergy.

When the Human Genome Project was completed in April 2003, it reported, after 13 years of study, a fully sequenced composite human genome (composite because the genome was amalgamated from 13 anonymous participants, rather than from one individual). Since then, DNA sequencing techniques have advanced so rapidly that it is now possible to sequence an entire human genome in just 24 hours! Mapping the sequence to a reference genome and analysing variants from the reference using bioinformatics take longer, but timeframes have shortened such that child health is already benefiting greatly from the revolution occurring in genomics. Whole-exome sequencing (an exome is the protein-coding portion of the genome—approximately 1 per cent of the entire genome) has been available to children at the RCH since June 2016, thanks to the Victorian Clinical Genetics Services, a partnership that links the hospital to world-leading expertise in genomics. As well as enabling screening for disease and improving disease diagnostics, genomics leads us towards personalised medicine such as pharmacogenomics (treating conditions like cystic fibrosis by using new small-protein modulators according to the particular gene mutations carried by the individual patient) and cancer therapeutics.

Corrective replacement of faulty genes in monogenic disorders has already been demonstrated as feasible in treating ADA (severe combined immunodeficiency), chronic granulomatous disease, blindness due to Leber's congenital amaurosis, and cystic fibrosis, using viral vectors, liposomes and stem cells. The ability to identify disease-causing variants through genomics means that the future will see an increase in such gene therapies. New strategies to correct genetic causes of disease include RNA therapeutics using anti-sense oligonucleotides to alter the processing of endogenous RNA, messenger RNA to elicit expression of proteins in the cytoplasm of target cells (as already employed in several COVID-19 vaccines) and other RNA treatment constructs. New routes of delivery are being explored for protection against Sars-Cov-2, as well as for treatment of cystic fibrosis, including specific targeting of the lungs via inhalation using nanoparticles



as a vector for the mRNA. How rapidly this will become part of clinical care remains to be seen, but such techniques will almost certainly help shape health care in the future.

The first study to describe gene editing using CRISPR-Cas-9 was published in 2012. Though not controversial for treating recognised clinical conditions resulting from genetic mutations, gene-editing technologies bring us to a stress point in human ethics, due to their potential for applications beyond this remit, to change gene variations not traditionally associated with disease, or even those that confer risk without certainty that the individual will develop disease or disease manifestations. It will be crucial to develop leadership and competencies in both clinical and research ethics specifically pertaining to childhood and adolescence. This has been recognised through the development of the Children's Bioethics Centre at the RCH, but there can be no doubt that the ethical considerations of new developments in genomics, personalised medicine, gene therapies and the use of health data will increase in complexity.

In the future, chronic diseases that affect children will need a response that is different from the predominantly hospital-based care offered today. It will become essential to connect patients, their families and community-based services with the hospital in order to provide great, network-based health care everywhere, consistent with the RCH's vision statement. Nascent in the development of the required technologies are telehealth platforms and virtual care models. The RCH has begun programs that will position it as a leader in both of these areas. Family-centred care will be adapted to shift care into the homes of our patients. When managing chronic disease, we will move towards a pre-emptive rather than reactionary response to any change in a patient's health status, with earlier, home-based interventions using digital communication and feedback systems. These models of health care will benefit from technologies such as wearables and other in-home monitoring tools.

With all these rapidly developing medical, genetic and technological advances, it will be extremely important to translate discoveries into improved health care. Currently, research translation is inefficient, with most research findings never reaching the patient. One way to improve this is to involve more clinicians in research, and to strengthen their research skills. The RCH will develop its clinician-researchers through the Melbourne Children's Clinical Research Incubator. Additionally, the Melbourne Children's Clinical Trials Centre will ensure that the RCH is at the front in the race for high-quality evidence on the safety and efficacy of new treatments.

The Department of Paediatrics at the University of Melbourne will continue to collaborate with the RCH in training the next generation of the workforce, who will graduate with the skills required in a changing health landscape. This partnership fosters research

Entrance to Department of Paediatrics, University of Melbourne, on the Melbourne Children's Campus, 2021.

and lifelong learning, connects RCH clinicians with expertise across the entire university (for example in the digital transformation of health, bioengineering, law and ethics), helps develop RCH leaders, and advocates for policy changes to improve the health, safety and wellbeing of children and adolescents.

The RCH is a world-leading hospital and contributes to the great care of the community it serves. Nevertheless, while we discuss new genetic technologies and therapies, the shameful truth is that around the world nearly one million children aged under five years still die each year from pneumonia (one child every 39 seconds). As we brace for the damage to child health caused by climate change, it is well recognised that it is children in the developing world who will bear the brunt. The future provides an opportunity to offer greater collaboration, leadership, advice, training and support to other countries in our region. To this end, Melbourne Children's Global Health was launched in December 2018. It aims to help our region reach the United Nations sustainable development goals, especially by reducing inequity and improving child and adolescent health and wellbeing in disadvantaged populations.

The future of paediatrics cannot be predicted in its entirety. But we can envisage a role for the RCH as a leading, world-class hospital that will adapt with agility to the changes coming, by appreciating its history and understanding the more recent developments described here. As we navigate the second year of the COVID-19 pandemic, it becomes increasingly clear that serving the best interests of children and young people requires great leadership. How do we maximise the potential of everyone who works on our campus, and contribute to the health and wellbeing of society as a whole, when we know that unfair discrimination and bias lead to poorer health, especially for our First Nations people but also among other groups in our diverse nation? We must nurture our entire workforce, and celebrate, value and promote them equitably on the basis of their talents—irrespective of gender, ethnicity, disability or sexuality. This was not always done during the first 150 years of the hospital's existence, but it will be for the next 150.

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