RCH Alumni

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The Royal Children's Hospital Melbourne

Aluminations

FROM THE RCH ALUMNI

January 2022 | In this issue:

Turning points in paediatric medicine

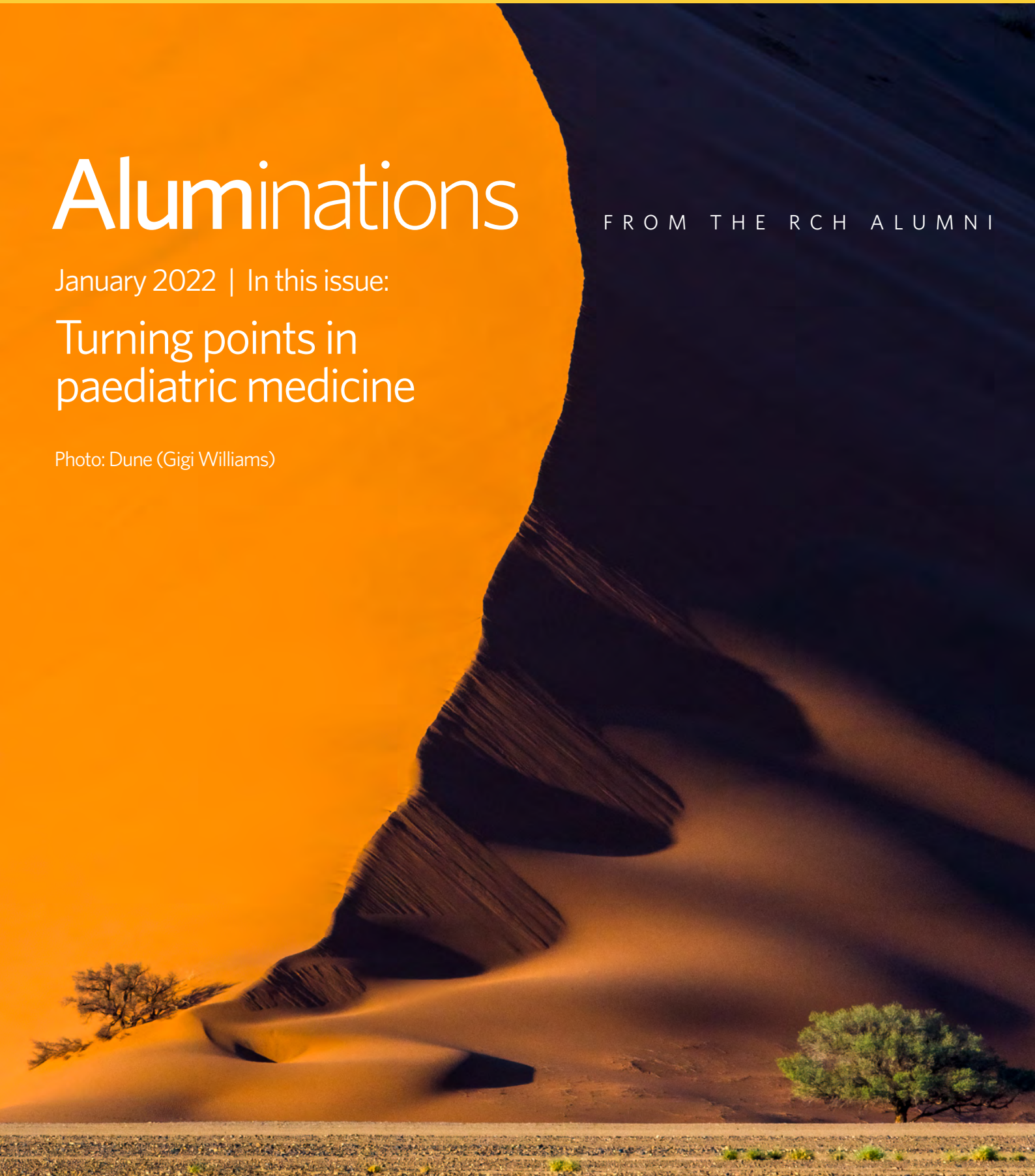
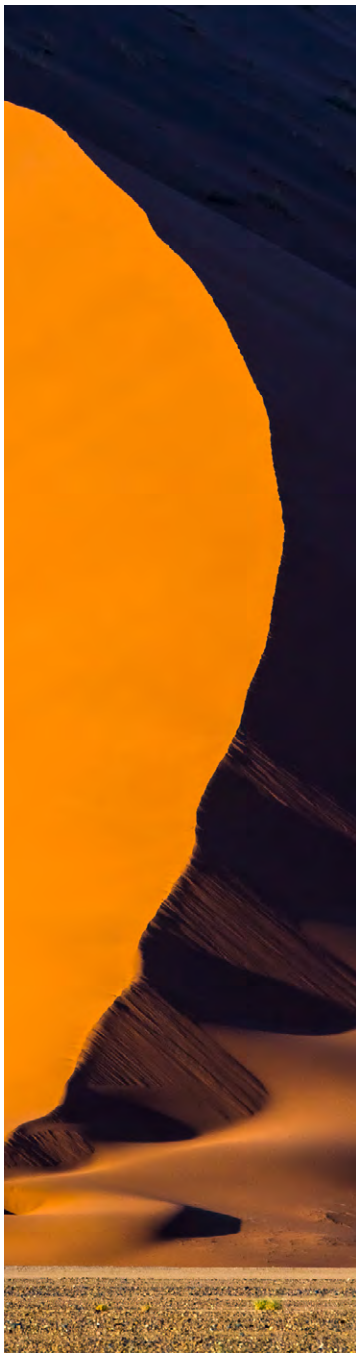


Photo: Dune (Gigi Williams)



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Cover picture – Dune | "This picture was taken in Namibia in Sossusvlei in the Namib Desert which is home to the world's oldest and biggest sand dunes. This is a small one! "Big Daddy' as it is known by is about 400m tall! With this one I was drawn to the strong lines of the majestic dune overpowering what look like tiny trees," says Gigi Williams

Credits

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The 2022 RCH Alumni Executive

Greetings from the President

Jim Wilkinson AM

As we near the end of this rather depressing year, with the continuing pandemic still impacting many around the world, I send greetings to all our Alumni members. Melbourne has had the dubious distinction, so we are advised by the former prime minister Tony Abbott and the national Treasurer Josh Frydenberg, of having been the most locked down city in the world, starting in March 2020 and having been "locked down for a total of around 280 days. Like many assertions from our political masters this claim may well be exaggerated and there were apparently some residents in Manila who were apparently locked down for 450 days.

We can certainly take some joy out of the renewed freedoms which have just opened for us as Christmas approaches. Life is showing faint signs of returning towards something that slightly resembles "normal" – though we still have some way to go and many of us are reserving judgement on what "the new normal" may mean in terms of our ability to resume normal life with travel within Australia and particularly overseas. However, we can certainly take some comfort in not needing to wear masks and being able to have visitors in our homes. My wife and I enjoyed the opportunity to host a small lunch party with neighbours and some friends after having been unable to enjoy such "wild" entertainment for the past two years. We are hopeful that we can look forward to no more lockdowns and continuing relaxation of all restrictions in the weeks ahead.

Having had our AGM earlier this month we now welcome a new Alumni executive team, although most of them have been valued members of the previous executive. I am looking forward to working with our new treasurer George Werther AO, who is a fresh face on the team and becomes the fourth/fifth to fulfil the role since the millennium following on from Wick (Sumitra Wickramasinghe) who served for 14 years, Peter Loughnan who filled the position for the next two years and then me (for six years). Garry Warne also took the role briefly in 2014, before becoming the secretary for seven years and he now becomes the Vice President thus relieving me of the need to fill both positions as I have done for the past two years. I am also grateful to Gigi Williams who ran the Educational resource Centre (ERC) for many years (now renamed "The Creative Studio") who has nobly agreed to look after the Alumni website, another job that I have had and which I am pleased to hand over to her very capable hands.

The other members of the executive team are of course Caroline Clarke, our secretary, Christine Unsworth AM, who for many years ran the Good Friday Appeal, Bronwyn Hewitt, former hospital archivist, and two former presidents – Ruth Wraith OAM and Kevin Collins. I thank them all for their continuing willingness to support the Alumni and to contribute so actively to our efforts.

Plans for next year's program are currently being developed and will be announced in the New Year. We certainly hope and expect that we will be able to return to the traditional "face to face" lunch meetings, though we are considering also having a Zoom option in order to allow those members who might enjoy the opportunity to join the meeting to do so from afar without the need to come to the hospital in order to participate.

Sadly, we have lost two members since the last Aluminations went to press. Jim Keipert died in October at the age of 98 soon after having made a remarkable contribution to our October Aluminations (The architects, engineers and builders of the Roman empire) and Don Cameron also in October, after a brave battle with pancreatic cancer.

The AGM was held in early November via Zoom and had 29 members present and apologies from 10 members. The President's report for the year was presented by Ruth Wraith and the financial report was presented by the Treasurer, Jim Wilkinson. Both reports were accepted, having been moved and seconded.

Election of office bearers followed with a single candidate having been proposed and seconded for each of the four positions. I was elected as the President for 2022 with

Garry Warne AM as Vice President, Caroline Clarke to continue as Honorary Secretary and George Werther AO as Treasurer.

In the absence of our anticipated Gala Dinner (which has been postponed until November 2022) the meeting was followed by a talk given by Prof Sharon Goldfeld, Director of the Centre for Community Child Health at RCH and Theme Director Population Health and Co-group leader of Policy and Equity at the Murdoch Children's Research Institute with the title "Radical Pragmatism – can we address the inequities in child health and development in a generation?". Her talk focussed on the widespread inequity and the gap in education, healthcare and prospects between the children of families who survive in a cycle of poverty and deprivation, often linked to multiple generations with unemployment, and those who belong to families at the other end of the social scale with better education and opportunities. After discussion that followed, the talk was greeted with applause from the audience. A recording of her talk is available at the RCH Alumni Website (rch.org.au/alumni) or by clicking here.

We look forward to resuming our regular Alumni schedule during 2022 with face-to-face lunches and a Gala Dinner after the AGM in November. We are currently pursuing discussions with the hospital administration and the Medical Staff Association to try to forge better links between the Alumni and those other vital hospital "teams". I wish all alumni members a happy festive season and New Year for 2022. Let us hope that it will be a better year!

Jim Wilkinson is current President of the Alumni and was former Head of Cardiology at RCH.

A huge thank you to our outgoing President Ruth Wraith OAM

Gigi Williams

It is my pleasure to write a short piece about Ruth's time as our President, especially as she was the first non-medical President and only the second woman to take on this role.

It was only in 2015 that senior allied health professionals were asked to join the RCH Alumni and many of us were humbled by the invitation and have enjoyed immensely the opportunity of continuing to interact with the medical colleagues we once worked so closely with.

Shortly after Ruth took the reins from Hugo Gold as our President in 2020, Covid struck and she has had to guide and navigate us through these incredibly difficult times. 'Zoom' has been an important way that we have been able to engage with our alumni colleagues and thank goodness for this technology.

Ruth has led us admirably during this time and there have been many opportunities for Alumni to connect and listen to various interesting speakers via our Aluminars or to read and contribute to our newsletter – Aluminations. The major down-side of this, of course, has been the inability of fellow alumni to join in face-to-face meetings and get-togethers and this may also have meant that not

as many of you have really got to know Ruth as otherwise would have.

As a refresher, Ruth retired in 2005 after being the Head of Child Psychotherapy for many years. She specialised in the treatment of children and families who had been damaged from a range of experiences such as child abuse, refugee experiences and natural and man-made disasters, including Ash Wednesday, Port Arthur, Coode Island, the Manresa Kindergarten Siege. through to

Black Saturday, as well as working with the impacted communities.

She first came to RCH Carlton in 1960 as an Occupational Therapy student before joining the Department of Psychiatry as a child therapist in 1963. As a result of her interest in community health she became one of the early international pioneers and leaders in disaster recovery.

Working with the local stakeholders Ruth also pioneered the establishment of the RCH Regional Mental Health Service centred in Mildura and Bendigo in the late 1980's and1990's and was chairperson of the steering committee that established the Australasian Society for Traumatic Stress Studies in 1990.

In 1991, she was awarded a Royal Children's Hospital Pied Piper scholarship to study the then emerging field of child trauma at UCLA and other US centres. She continued to upgrade her qualifications and obtained her Master of Child Psychoanalytic Psychotherapy Degree in 1995 (Monash University).

She has held many roles in her professional peak bodies, been recognised with a number of awards and has consulted to numerous bodies including the Foundation for Survivors of Torture, Victorian Government Departments of Education and Health (State Emergency Recovery Unit and Medical Displan) and the ANU Advisory Committee to the Australian Government on disaster recovery.

She was awarded the Medal of The Order of Australia (OAM), in the general division, in 2012 for service to community health.

In her term as the RCH Alumni President, Ruth has been incredibly supportive, thoughtful and thankful to her Executive team and it has been a pleasure to have served with her during this time.

We look forward to Ruth continuing on the Executive as a member and past President and hope that when we can meet again face-to-face that you will know a little more about her and feel free to come up and say 'hello.'

Gigi Williams was former head of the Educational Resource Centre (now Creative Studio) and is a current member of the Alumni executive.

Alumni member, Dr Elisabeth Northam, is honoured

Caroline Clarke

Congratulations to Alumni member Dr Lis Northam who was recently the guest Robert Vines Lecturer at the Australasian Paediatric Endocrine Group Annual Scientific Meeting. This lecture is a prestigious event which has been held since 1983 and has been delivered over the years by highly credentialed international speakers. The lecture is in memory of Bob Vines who was one of the fathers of paediatric endocrinology in Australia and practiced in Sydney until 1986.

The summary of Lis's excellent presentation is as follows:

"In 1992, the Chair of an NHMRC interviewing panel queried the rationale for doing cognitive assessments of children with type 1 diabetes, commenting that "diabetes does not affect the brain". Since then, there has been growing awareness that the central nervous system is indeed one of the organ systems impacted in T1D. This presentation will describe a thirty-year programme of research at The Royal Children's Hospital, Melbourne aimed at documenting the impact of T1D on the developing brain. Studies that explore the mechanisms underlying T1D-related neurotoxic effects on the brain and interventions designed to reduce these negative impacts will be described. Key players who have influenced empirical brain research in T1D across the globe and recent influential work of the DirecNet group in the United States will be discussed. The presentation will argue that brain effects and cognitive deficits in T1D populations, while relatively subtle, do affect educational and vocational outcomes and influence diabetes self-management. The presentation will finish by noting some persisting unknowns and future challenges in this important field of research".

Caroline Clarke, the Honorary Secretary of the Alumni, is a retired paediatric endocrinologist and hospital administrator.

Our invitation

Accounts of your involvement in turning points will be of particular interest. The idea of these is to capture the atmosphere and excitement that you experienced when you realised you were an eye witness to a significant turning point in paediatrics. We are not asking for the history of how a specialty developed; rather we are looking for a snapshot of the major events and how things changed at that time. Email your recollections to rch.alumni@rch.org.au

Best wishes,
Garry Warne AM
Editor, Aluminations

Light bulb moments in paediatric rheumatology

Roger Allen

Having completed General Paediatric training at RCH in 1980 I started my Rheumatology training at the British Columbia Children's Hospital in Vancouver in 1982 under the mentorship of Dr Ross Petty. On the wall of his office was a photo taken at the annual Juvenile Arthritis camp from the previous year. Of the 30-odd kids in the photo about a quarter were either in a wheelchair or using some form of walking support. Jump forward 40 years and if a child turns up to clinic in a wheelchair these days it is probably from a badly sprained ankle from playing netball the previous weekend. In 1984 I then moved on to the UK to train with Dr Barbara Ansell, the grand dame of our field. The evening routine involved getting the kids ready for bed each night applying their various splints to overcome joint contractures. Again jump 40 years and any splint today is probably for a greenstick forearm fracture from accidentally bouncing off a trampoline.

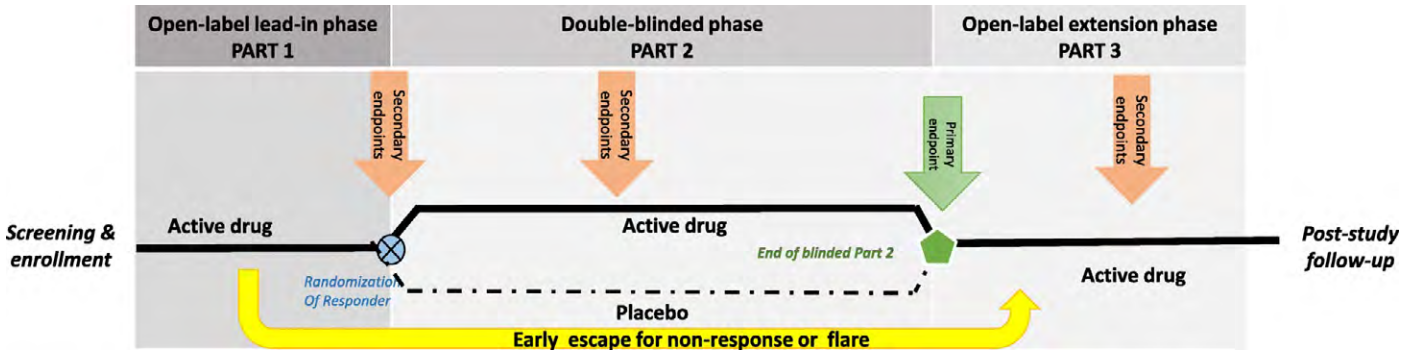
This is not to say that, in 2021, giving a parent and their child a diagnosis of juvenile arthritis is potentially any less concerning than it was back in the early 80's and before. The possible complications of inadequately controlled disease being no different now to what those pioneers in the field had to deal with every day. Clearly the advances in the therapeutic agents available over the past 20 years, particularly now with the biologic disease modifying antirheumatic drugs (bDMARDs) or just called "biologics", has completely changed the playing field – and certainly has led to some light-bulb moments for my career.

If I just go back to the early 1980's - what did we do back then? Ross Petty had been seen as somewhat of a renegade because around the time I arrived in Vancouver he'd started injecting long-acting corticosteroids into involved joints. Nonsteroidal anti-inflammatory (NSAID) medications, graduating up from good old aspirin, were routine and if one didn't work then combinations of different classes of NSAIDs were given at the same time. Not surprisingly side effects were not uncommon. Then there were the long-acting or disease modifying anti-rheumatic drugs (DMARDs) which in those days were hydroxychloroquine, penicillamine and gold injections. Interestingly gold had been used since the 1920's given a presumed similarity between adult rheumatoid arthritis and tuberculosis. It is fair to say some children did respond to these agents, including gold, but how they worked wasn't well understood. I must admit to being somewhat bemused by the fact I'd be a bit dismissive of parents putting copper bracelets around their child's wrists while at the same time I was busily writing a script for a different metal ie gold, albeit given by injection. Of course, almost every child at some stage was given prednisolone, at times for long periods, with the full list of subsequent long-term sequelae being a result. I remember Barbara Ansell, who to her credit hated excessive steroid use, saying to me you could always pick out her patients if the whole family came to clinic – "short with round faces".

I'll jump forward a few decades here and mention two organizations which have steered paediatric rheumatology in important clinical research directions. These are the Pediatric Rheumatology Collaborative Study Group (PRCSG) based in the US and the Paediatric Rheumatology International Trials Organization (PRINTO) based in Europe. These two organizations have combined to carefully study all the newer therapeutic agents used in juvenile arthritis and importantly have included our RCH Rheumatology unit in quite a number of the studies. Being included in these studies also benefited our patients as it gave us much earlier access to a number of the newer

therapies. Drugs such as methotrexate and leflunomide, as DMARDs, came in to the therapeutic armamentarium in the early 1990's with immediate impact, and was one of the early PRINTO/PRCSG studies to include RCH as a study site.

One important aspect of these trials was in the study design. Given natural concerns regarding the ethics of including a placebo arm for a paediatric population in any controlled trial, as seen in the figure, all children were started on the active drug, Part 1, and only stayed in a trial if demonstrating response. Then in Part 2, being double-blinded, half would continue with the active drug while the others went on to placebo. As soon as a child showed any evidence of breakthrough, they would be unblinded and if on placebo were returned to the active agent. All patients then entered Part 3 on active drug which continued to allow for longer follow-up periods of analysis.



Now for a definite "light-bulb" moment which coincidentally has a Melbourne connection!

Dr Mark Feldmann is a medical graduate from the University of Melbourne who became interested in autoimmunity, particularly relating to Graves' disease of the thyroid, having commenced a research career at the WEHI. In the 1980's much research was being done on intracellular pathways of immune mediated inflammation with isolation of a number of specific proteins ie cytokines. Given the obvious inability to obtain thyroid tissue to study, rheumatoid synovial tissue was a conveniently accessible alternative. By now working in London, he teamed up with Professor Ravinder Maini, a clinician/scientist adult rheumatologist, at the Kennedy Institute, Imperial College in London. Having developed an anti-cytokine agent, and seen its response in a mouse model of arthritis, they moved on to a human trial of what they called cA2, an anti-tumour necrosis factor (TNF) anti-cytokine later to become the first of the bDMARDs called infliximab. A controlled trial in adult rheumatoid arthritis patients, all of whom failing every therapy available at the time, then followed which was subsequently published in the Lancet in 1994.

By now I was back in Melbourne at RCH and remember attending the annual conference of the Australian Rheumatology Association (ARA), probably back in about 1993, where Mark Feldmann was a guest speaker. To a somewhat dumbstruck audience he showed some before/after video clips of the trial patients. He described how within a few hours of an IV infusion, the patients reported dramatic symptomatic relief; they felt more energetic and their joints had loosened up. Within several weeks, previously incapacitated people were playing golf and climbing stairs. Feldmann and Maini were awarded the Albert Lasker Award for Clinical Medical Research in 2003 and both have been knighted by the Queen for their work. Every time I hear that an Australian has been awarded the Nobel Prize my ears prick up anticipating to hear Feldmann's name, but not yet. Nevertheless, I anticipate – watch this space.

Mark Feldmann and Ravinder Maini

The variety of anti-cytokine therapies has continued to expand, although not all are available for paediatric use as yet. A useful "carrot and stick" aspect to the development and subsequent release of these agents was the passing of the "Pediatric Rule" by the FDA in the US in 1999. This gave pharmaceutical companies an additional period of protected patent for new drugs so long as specific paediatric studies were contemporaneously undertaken. In the table I have listed some of the current biologic agents available, indicating their specific cytokine/ inflammatory cell target and, in bold type, the agents for which the RCH Rheumatology team has participated in these international studies.

Target:	Agent:	TGA approved for Juvenile Arthritis
TNF	etanercept	on PBS
	adalimumab	on PBS
	infliximab	special access only
IL-1	anakinra	special access only
IL-6	tocilizumab	on PBS
JAK protein	baricitinib	special access only

The therapeutic trials and the responses seen also brought home that variations existed between some of the juvenile arthritis subtypes. Anakinra (anti IL-1) was trialled in polyarticular disease (ie 5 joints or more) with somewhat disappointing results. One of our RCH patients however did extremely well and, in fact, was the first child in the world to complete the trial in early 2002. What became apparent was that, although all the children were following a polyarticular course, the ones who had systemic onset disease (originally called Still's disease), ie fever, rash, serositis plus arthritis, did much better. Not previously appreciated, but now clinically apparent, was that it showed the cytokine profiles differed between arthritis subtypes so that not surprisingly responses followed using the appropriate anti-cytokine therapeutic target (another light-bulb switches on!).

Etanercept, an anti-TNF agent, was the first biologic commercially available on the PBS in Australia in about 1998. The chair of the Therapeutics Committee of the ARA said to me "look Roger, we know we'll get it for adult RA patients at some stage soon. We think it would be good if the kids got access first" so unlike, everywhere else in the world, Australian children had this biologic therapy made available six months before their adult counterparts. I thought that was a particularly magnanimous gesture from our adult colleagues.

The patent duration has now passed for many of the earlier biologics such that there are a number of "biosimilars" being developed which appear to impact to the same extent and are often considerably cheaper. Hospital pharmacies, including RCH, are being encouraged to move to these biosimilar agents. It should be mentioned that it is not only in arthritis therapy that these agents have been shown to have a major role. Management of inflammatory bowel disease, severe uveitis, various forms of psoriasis and importantly for the rheumatology team some forms of vasculitis, including Kawasaki disease, and what are called the "autoinflammatory diseases". This latter group of diseases express specific cytokine derangements, many of which have genetic relevance, such as familial Mediterranean fever and Muckle-Wells syndrome.

I retired from RCH in December 2019 so thankfully dodged the Covid bullet that has dominated so much of the hospital's activities these past 2 years. One important finding has been the important role of anti IL-6 therapy (tocilizumab) for adults with severe Covid infection requiring intensive care. This has led to a threatening scarcity of this agent for the juvenile arthritis population which, for some, there may not be an alternative agent of similar efficacy. It raises the potentially awkward (dare I say ethical) scenario of a 45-year-old obese, smoker who didn't bother with, or let alone refused, a Covid vaccination receiving tocilizumab in an adult ICU whilst our paediatric rheumatologists are having to tell parents their child might not be able to receive the drug on which they have been dependent. Thankfully Greg Hunt, the federal health minister, has become aware of this issue and is specifically working to guarantee supply for the juvenile arthritis population. Nevertheless, a recent memo from the ARA secretary mentions the company has suggested using up "sample packs" whilst eking out their current stock. Not an ideal situation to be in.

I guess one danger with any new wonder drug is thinking it has to be much better than what is currently being used. A recent study from paediatric rheumatology centres spread across North America reported that at 12 months around 70% of the patients are now on a biologic agent, the cost of which must be in the many multiple millions of dollars. A more measured process is through what is termed a "Treat to Target" approach (T2T) by which medication is only escalated if particular therapy targets aren't reached. These T2T targets are based on a scoring system covering such things as active joint count, physician (and importantly parent) global assessment,

inflammatory measurements etc. The T2T approach is much more the process followed at RCH such that Jonathan Akikusa, the head of Paediatric Rheumatology, tells me an article currently in preparation, will report about 30% of the RCH juvenile arthritis patients are on a biologic 5-years after diagnosis, usually in combination with methotrexate, but importantly with similar measures of disease outcomes to those reported in the international literature.

Some unexpected experiences have followed the success of these agents. Some years ago a mother of a boy I'd treated with anakinra (anti-IL-1) contacted me asking if I could write a letter. I'd sent him on to the adult world by then but she wanted a letter explaining that getting his daily subcutaneous anakinra injection might become an issue as he was about to be incarcerated having been convicted for aggravated assault. For my sake I rationalized that I had obviously done a fairly good job if he'd been physically capable of becoming a thug! Perhaps not my best example of successful transition to adult care!

So, what is the standard therapy approach currently being used at RCH, which clearly will vary across the various subtypes of juvenile arthritis:

For limited disease intra-articular steroid injections remains the treatment of choice.

For more extensive (polyarticular) disease invariably a DMARD, usually methotrexate is required. If after a few months control hasn't been adequately achieved a biologic agent, usually an anti-TNF, will then be introduced.

For systemic onset juvenile arthritis typically, corticosteroids will be required for a time but an IL-1 or IL-6 agent will be considered early in the disease course +/- a DMARD if significant joint involvement is persisting.

What of anti-inflammatory drugs – yes, they are still used but basically more for symptom control eg pain, morning stiffness, without underestimating their ability to impact on inflammation itself. And yes, prednisolone is still used but typically for as short a time as possible such as for bridging therapy particularly because we know any methotrexate impact can take around 6 to 8 weeks to be seen.

To finish I'll go back to another "light bulb" moment but not one lighting up brightly but rather, by contrast, lights that were slowly dimming down - while an overture was being played. In early 2009 I was sitting in the audience at Her Majesty's Theatre to watch the professional production of "Billy Elliot – The Musical". For those who saw it I'm sure you'll agree it was an extraordinary production particularly given the dancing skills of the children. I doubt if anyone watching in that audience was aware that one of the children on stage was an RCH rheumatology patient, on therapy, for her polyarticular juvenile arthritis.

Roger Allen is the former Head of Paediatric Rheumatology at the RCH.

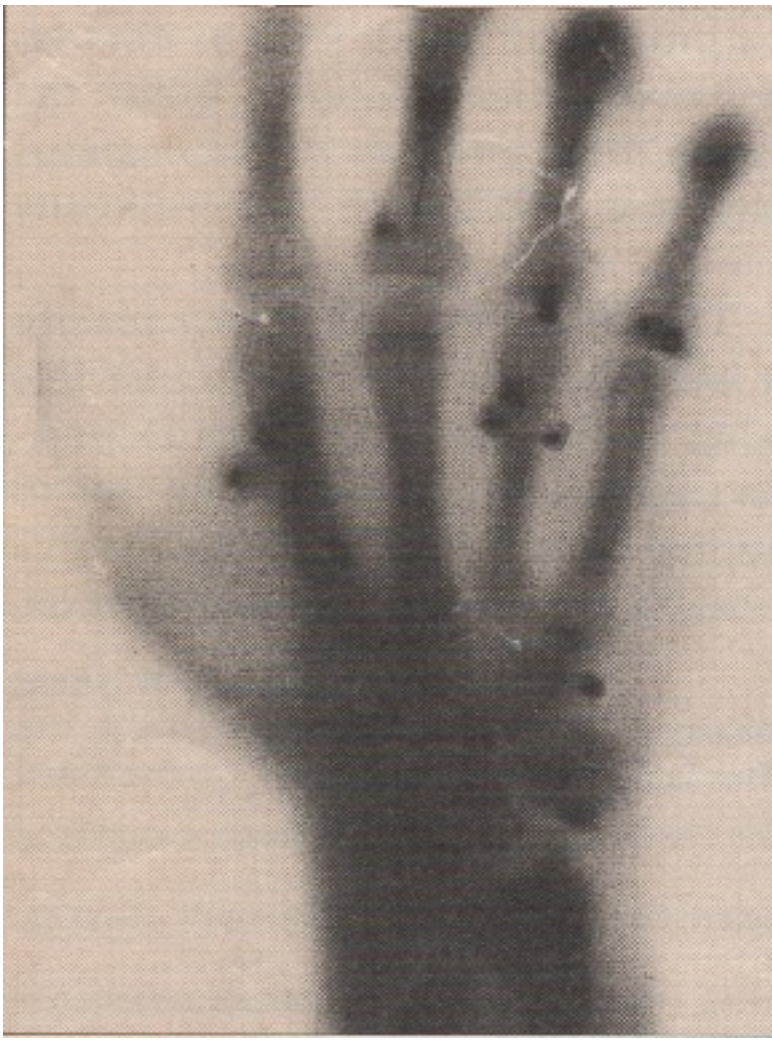
Turning points in radiology

David Boldt

Two physicists have received Nobel awards for significant developments or turning points in medical imaging diagnosis. It was said that Wilhelm Roentgen, the first ever Laureate in Physics (2001), had doubts about his own sanity when, on a November evening in 1895, he first observed luminescence resulting from x-rays. His continued investigations demonstrated their penetrative ability, including display of the bones in his wife's hand. The value in diagnosis of fractures and other skeletal pathology, and detection of metallic foreign bodies, such as bullets (pictured right), was recognised worldwide within weeks, as news of the discovery circulated by published paper, presentation and telegraph. X-radiation was rapidly taken up within medicine - and also by nonmedical entrepreneurs, such as sideshow displays at fair grounds and measurement of feet for shoe size, until the adverse effects of excessive radiation were recognised.

Subsequent advances in diagnostic radiology were essentially innovations by comparison with the revelation of computed tomography (CT) over 75 years later. Ultrasound (US), radionucleotides (RN), and nuclear magnetic resonance (magnetic resonance or MR), were by then in early use or under development, and remain today essential technologies in a comprehensive diagnostic medical imaging service. But their acceptance into clinical practice pales against the impact of CT, following initial clinical trials in the United Kingdom (1971-72) and first use in North America (1973). Tomography was a long established x-ray technique, using a moving beam of radiation and conventional film. Computer reconstruction of tomographic data was found to produce vastly more anatomical information. Suddenly, here was a new technology capable of displaying directly some of the differing soft tissues and fluids within solid organs, previously only seen by x-ray as a featureless lump, or "mass," in a comprehensive detailed display of anatomy.

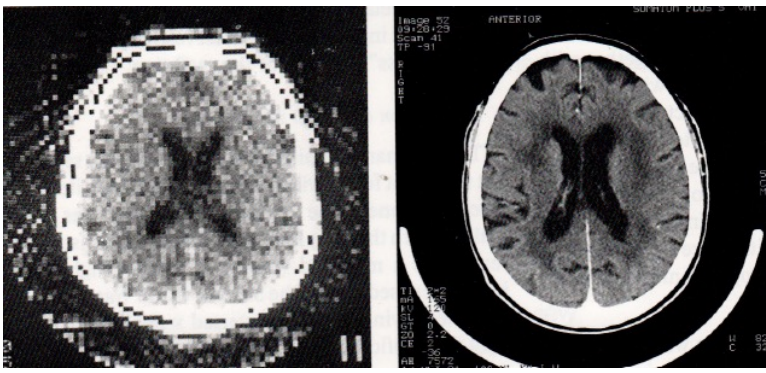
The only initial practical application of CT was to display the brain and its coverings, both soft tissue and bony skull, since each scan or slice took minutes to obtain, with some 10 to 15 scans required for a comprehensive examination. Further interminable minutes were then required for computer reconstruction of the data obtained. Scans spoiled with patient movement, including breathing, and it was necessary for x-rays to be beamed through a bag of water fitted closely around the cranium. These features of first generation



Gunshot in the hand, 1896. The first known Australian medical x-ray.

From G. Klempfner "The centenary of X-rays..." The Medical Journal of Australia, Vol. 163: p. 456. 6 November 1995

machines excluded use in other anatomical regions. The patient reclined or slept (uncooperative children with anaesthesia) on a relatively comfortable couch. The pictures from the first machines appeared composed of crude blocks (pixels), akin to a Lego creation or crossword (pictured below).



Comparable CT skull scans: left 1974, right 1994.

From G. Schwierz, M. Kirchgeorg, Siemens AG, Erlangen. In Electromedica 63 (1995) no. 1, p.4

However, the internal structure of the brain and major abnormalities could now be directly photographed, initially on polaroid film. Gone was the straining by observers trying to see if plain x-ray films of the head hinted at pathology through abnormal calcification inside the cranium. US could not adequately penetrate the bony skull to be of any value. (It is of major value in babies, before the skull bones ossify.) Radioisotopes detected some brain and dural pathology, but only as "fuzzy" abnormal radioactivity, lacking definition. Riskier, more invasive and less comfortable procedures, using x-rays obtained after injection of chemicals (contrast or "dye") into arteries and veins, or gases and oils into the spine or directly into the brain cavities (ventricles), provided essentially an indirect display, inferring the presence of leaked blood (haematomas) and tumours from distortion of ventricles, or from abnormalities of blood or cerebrospinal fluid circulations. CT directly displayed the extent and internal structure of haematomas, tumours and infarcts, and the enlargement or distortion of ventricles associated with abnormal brain development: all with much reduced patient risk and discomfort. I recall hearing, in 1973, that a presentation on CT to a large radiology meeting resulted in a standing ovation, such was the immediate recognition of this new technology.

The term "Emmy" scan was widely used initially to describe the examination, a major advertising coup for the British EMI company which sponsored research of the concept and built the first machines in clinical use. The generic acronym "CAT", for computerized axial tomography, followed and is now largely replaced by "CT". Rapid development of the technology in the USA, Europe and Israel eclipsed that of EMI. That company's initial involvement was perhaps something of an accident in any event. It was rumoured, and never refuted to my knowledge, Godfrey Hounsfield was given £20,000 by the company to research his concept, and told "Don't come back for more." His development of CT resulted in the second Nobel Laureate - and a lot of business for EMI.

While a radiology fellow in 1975-76 at the Hospital for Sick Children in Toronto, I attended the weekly paediatric session on the first generation CT unit in the nearby Toronto General Hospital. Early technical improvements resulted in the water bag being dispensed with, scan times becoming shorter, and pictorial resolution improving markedly (picture). With faster data acquisition patient movement could be overcome so that CT could be used in all areas of the body. Solid soft tissue structures in the abdomen, such as the liver, kidneys, adrenals, pancreas, spleen, and abnormal lumps or masses, could be defined, separate from overlying muscles and bowel; and their internal structure displayed. HSC installed the first whole body scanner in a North American (and possibly the world) paediatric hospital (1976) and the excitement of working with this machine was palpable: the potential seemed endless. No longer must patients suffer severe headache or worse following air encephalography and myelography. The need for angiography progressively reduced. At that time we did not worry too much about patient radiation dose, understanding the potential benefit outweighed that drawback. Patient referrals were from specialist physicians and surgeons, a necessary screening since in early years only limited numbers of machines were available. This ensured that scans for what might be thought trivial or inappropriate indications were largely avoided. There was, however, a recognition that radiation exposure would become a concern if, for example, every person with severe persistent or recurrent headache, or abdominal pain, had a CT examination to exclude cancer or other significant pathology. To some extent this potential for overuse did occur in later years with proliferation of machines.

Continuing development has led to more radiation efficient and faster machines, permitting display of the detailed anatomy in the chest and abdomen during a single breath-hold. Using injected contrast, displays of arterial and venous circulations have reduced the need for angiography, which requires catheters to be inserted into the femoral artery at the groin and manipulated to the injection position. For some 30-35 years past MR has eliminated the need for any x-ray exposure in many patients, but despite displays of brain and spinal anatomy far superior to CT, MR never had the same "WOW" reaction. CT remains an essential imaging tool, especially for abdomen and chest, and acute neurological emergencies.

From the late 1970s to mid 1990s the RCH had an unfortunate and frustrating history of being relatively slow to introduce multiple new imaging technologies appropriate in paediatrics. The only benefit of this was the hospital ultimately acquired machines of greater capability, often better suited for children, following early rapid technical development. From the mid 1970s children had been examined using early generation CT units at the Royal Melbourne and Alfred Hospitals, with obvious logistic, including anaesthetic, difficulties. Sicker children were denied CT because of the risks associated with safe transport. (This history was repeated with RN and MR.) The commissioning of a CT whole body unit, the most capable then available and costing some $1.3 million, occurred in 1982. Major renovation of half the radiology department, at extra expense, was necessary for this and simultaneous installation of an updated angiography suite, mainly but not wholly for cardiac work. Children suspected by a neurologist or neurosurgeon of having a life-threatening blood clot inside the skull no longer needed time-consuming and much riskier angiography. The first child examined after the CT was commissioned indeed had such a haematoma pressing

on the brain, and proceeded to timely surgical treatment. The machine was quickly busy with examinations of the brain and spine and other structures in the head, such as the inner ear; the chest and abdomen, particularly in oncology patients to assess the results of cancer therapy; and to provide high resolution of bone structure when required. There were some research projects. Anaesthesia or sedation was still necessary for uncooperative children and, on at least one occasion, lemurs examined on special request of Melbourne Zoo.

I was a member of a Health Commission committee, in the late 1970s, tasked with determining the number of CT units that South Australia would need. The conclusion (with which I too quietly disagreed) was four – one in each of the 3 tertiary level general Adelaide public hospitals and one in a private practice. The latter offered CT services to the (then) Adelaide Children's Hospital, across the road. Today CT is standard equipment in essentially all but the smallest or most remote radiology hospital or office practice.

David Boldt was Director of Radiology at RCH from 1981 to 1995.

A turning point in paediatric neurology – CT and MR imaging of the central nervous system

Kevin Collins

These notes reflect the viewpoint of a clinical paediatric neurologist, and they supplement David Boldt's more detailed historical account. David and I both trained and began working as consultants during the 1970s and have witnessed the early impact and growth of these new imaging modalities from the different perspectives of our chosen specialties.

There is little doubt that magnetic resonance (MR) imaging has provided a greater wealth of information about central nervous system (CNS) structure, chemical composition and function than has X-ray computed tomography (CT) imaging. However, if we define turning points by their "WOW! factor," many clinicians and radiologists would agree that the immediate impact of CT imaging was much greater – a game-changing truly novel development, and the culmination of research in mathematics, physics, engineering and medicine.

Before CT scans were introduced, we simply could not see images of actual brain or spine tissue. Apart from the limited information available from plain skull x-rays, we could only infer the presence of abnormal enlargement or displacement of tissue, or absence of tissue, from the size and shape of the CSF spaces within and around the brain (on an air encephalogram or ventriculogram) and spinal cord (on myelogram) or from the displacement of blood vessels (via cerebral angiogram).

These earlier procedures were complex, technically difficult and sometimes risky, involving as they did the injection of air or contrast material into the ventricles, subarachnoid spaces or major arteries respectively. In some situations, they could aggravate underlying brainstem or spinal cord compression.

In practice, these factors made it difficult for the clinician to weigh up the risks and benefits of such investigations in individual patients. Often we would inform our neurosurgical colleagues beforehand, in cases where the procedure might cause sudden worsening of the underlying problem.

So it is no exaggeration to say that most of us were "blown away" when we saw the early images of cross-sections of the brain and skull - for the first time in a living human being - revealing such features as normal brain tissue, haemorrhage, cerebral oedema, calcification, tumours or the dilated ventricles of hydrocephalus. And our excitement was not diminished by the coarsely pixelated appearance and what now seems the pitifully low resolution of these pictures, preserved as small Polaroid photographs attached to pages of the patient's hospital record.

The addition of intravenous contrast material provided more information about both brain tissue and blood vessels, but also an added risk of allergic reactions in the radiology suite. Over time, there has been increasing awareness of the tumour-inducing risk of high dose CT scan radiation on the immature brain.

Clinical MRI scanners came into general use in the 1980s, about a decade after CT. The first MRI scanner at RCH began working in 1994, after several years of referring children to MRI units at the Royal Melbourne and St Vincent's hospitals.

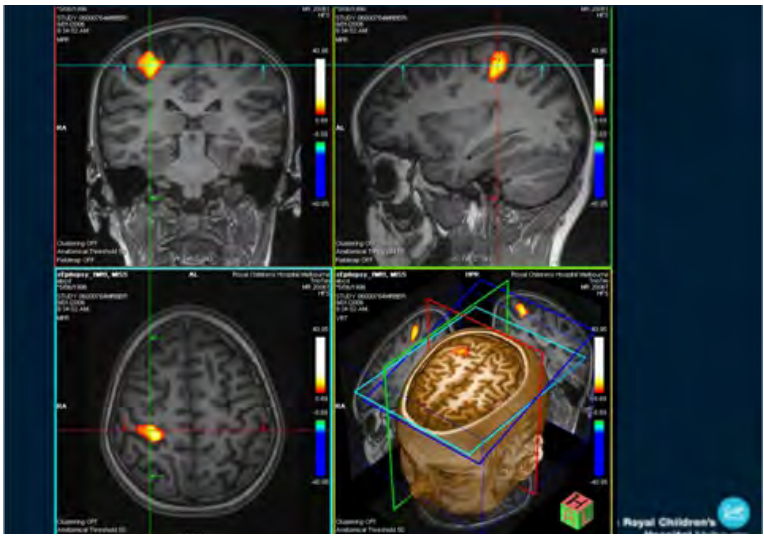
How does MRI differ from CT? While both modalities produce images representing "slices" of body tissues, the underlying physics of MRI is entirely different from that of X-ray CT – and to the simple clinician, much more complicated!

MRI provides more information about brain and spine tissue in several ways. These include greater sensitivity to inflammation and changes in water content, better ability to create images in multiple planes and better quality images where nervous tissue is close to bony structures (optic nerves, cerebellum, brainstem and spinal cord). We can now better identify inflammatory and demyelinating CNS diseases in childhood, and likewise the important range of pathologies (tumours, malformations and metabolic disorders) affecting the cerebellum and brainstem in early life. Further, because of the properties of flowing blood, useful MR images of cerebral blood vessels can be obtained without the need to inject contrast material.

In specialised centres, including RCH, a combination of multidisciplinary teamwork and advanced equipment has made it possible to identify previously unrecognised tiny areas of cortical malformation as the basis for intractable epilepsy with subsequent excellent outcomes from carefully planned surgery. Similar resources are required for functional MRI, in which changes in the oxygen content of haemoglobin are the basis for identifying brain areas activated during specific activities, such as language production or limb movement (picture). These findings are proving valuable particularly in research but also in neurosurgical management where "eloquent cortex" may be near a tumour, for example.

In paediatrics, a particular advantage of MRI as compared with CT is the absence of ionising radiation. Conversely, the noisy and potentially claustrophobic scanner environment increases the need for anaesthesia or sedation in infants, toddlers and younger children. In the past at least, this requirement often led to frustrating delays, partly alleviated at RCH by the creative use of a purpose-built mock MRI scanner with a child life therapist (play therapist) helping children to relax before their actual scan.

In summary, the arrival of CT scanning was indeed a memorable and exciting turning point in paediatric neurology, followed by an ongoing expansion of knowledge arising from MRI. This brief summary is neither complete nor up to date, but Alumni members may be interested to know that our former workplace now has no less than four MRI scanners on site, including an intra-operative MRI used in neurosurgery and a combined MRI-PET scanner to facilitate the care of children with cancer.



Functional MRI study (performed over 10 years ago) of left finger tapping showing activation of hand area in right central sulcus. Image kindly provided by Dr Tim Cain, RCH.

Kevin Collins is a past President of the Alumni and a retired paediatric neurologist.

Turning points in neonatology

Neil Roy

I think my generation of health professionals has been blessed to see huge advances in our various fields of endeavour, but perhaps no more so than in the field of neonatology, into which I entered almost by accident. The turning point came for me when I was a neonatal fellow in Toronto, brushing up on my neonatal skills before planning to return to Melbourne into private practice. Clare McKinnon resigned her position as head of Neonatology at the RCH and the Medical Director, LEG Sloan, rang me to see if I would like to come back to the RCH to be 2 IC to Geoff Gillam – how could I refuse?

What follows are some of the great turning points in neonatology which I have either witnessed or been fortunate to have had an involvement.

1961-62:
a turning point in neonatal care: ventilation

In the first decade after introduction of positive pressure ventilation for adults in the early 1950s, it was considered unethical to be offering it to newborn babies – it was "interfering with Nature". However in the early 1960s, Dr. Paul Swyer in Toronto and Dr. Mildred Stahlman in Nashville 'pushed the boundaries' and were allowed to try ventilation on babies who were 'certain to die'. The first survivor was in Nashville* in late 1961 ; the first survivor in Toronto was in early 1962, illustrated below.

Having worked as a fellow with Dr. Swyer in 1973-4 I was fortunate to be at his retirement dinner in 1986, when the first Toronto survivor (and 2nd in the world) was a guest of honour.

Pictured right are:

Top. Dr. Paul Swyer

Middle: The baby on the ventilator in 1962

Bottom: The 'baby' as a tall, handsome 24 year-old at Dr. Swyer's retirement dinner in 1986; he is being hugged by the fellow who cared for him, Dr. Maria Delivoria-Papadopoulos, who went on to become a prominent neonatologist in Albuquerque, New Mexico. Dr. Swyer was a visiting Professor to Melbourne and the Australian Perinatal Society in 1990.

Neonatal ventilation first came to Melbourne in 1965, when anaesthetist Dr. John Stocks at the Royal Children's used a modified Bennet ventilator on babies post-surgery, as described in Peter Yule's history of the RCH (1999); but only sporadic unsuccessful attempts at ventilating premature babies were made until in 1972 Dr. Jeff Tompkins at The Women's achieved success. Jeff had learnt to ventilate babies in Perth with Dr. Fred Grauag.

1963: A turning point in neonatal – and world – history

With thanks to Lex Doyle for bringing this to my attention and for the photo of JFK

On August 7th 1963 Jackie Kennedy, President John Kennedy's wife, gave birth to their fourth child, Patrick Bouvier Kennedy, at 34 weeks gestation (the first, Arabella, had been stillborn). As was common in that era, Patrick developed hyaline membrane disease (HMD), and despite the best current therapy at the Boston Children's Hospital (no ventilation there yet), including hyperbaric oxygen therapy, he succumbed on the 9th August at just 39 hours of age.

This triggered a huge surge in neonatal research, especially into the aetiology and treatment of HMD; this led firstly to the identification of surfactant deficiency as the cause - rather than accumulated respiratory tract secretions, the theory that had caused so much harm by the insistence on clearing the airway with thorough suctioning; this discovery led to the development of the various surfactants, starting with artificial surfactants (e.g. Exosurf and its variants) followed by the increasingly refined natural surfactants.

A second consequence of the death of Patrick Bouvier Kennedy is a theoretical one – its likely effect on world history. If Jackie had gone to full term with Patrick or even if he had survived as a prem it is highly likely that Jackie Kennedy would not have been available to join the President in Dallas on November 22nd, in which case he may well not have used an open-topped car, and ..... History may have turned out differently!

1991 - Introduction of surfactant to Melbourne

In 1991 the magic new therapy for RDS, surfactant replacement, was first used at The Women's; I can hear Peter McDougall protesting – "No! It was first used at the Children's." Let's just say it was used at about the same time at both hospitals. In those days it was the artificial surfactant Exosurf, which was later replaced by the more effective bovine and then porcine extracts. Even so the initial results were dramatic, with a decrease in mortality rate of 50% in babies <1500g with RDS.

1993 - Introduction of High Frequency Oscillatory Ventilation (HFOV) to Melbourne.

This was first used at the Women's in 1993 – "No!" cries McDougall again, "It was first used at the Children's." Again it was introduced about the same time, led by Dr. Brian Timms, recently returned from post-graduate training in Cleveland. The machine used then was the Sensormedix. There is no doubt that the further development of this technique has to be credited to the team at the Children's – Peter McDougall, Peter Loughnan and ICU technician Mark Hochman – who refined its use and ran national training programs for its use. The Women's did make a further significant contribution with the development of a humidification system to prevent 'rainout' in the circuit; this development was by Ed Hingeley, biomedical engineer at the RWH.

1980 – the 'birth' of IVF and its consequences

In 1980 Australia's first – and the world's 3rd – 'test-tube' baby was born at The Women's. Then in 1984 the world's first IVF quads were born, also at The Women's. They made world headlines; Ken Mountain

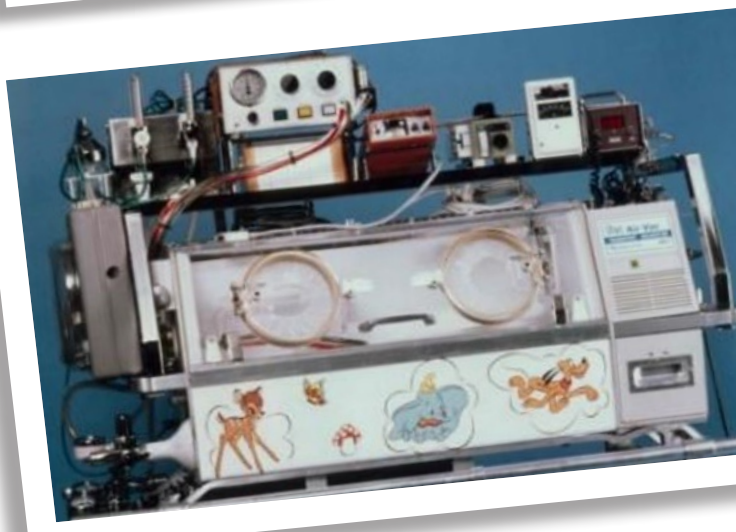
was the paediatrician, but because he was a private practitioner he was not allowed to speak to the press – it was considered 'advertising'. So they needed a hospital spokesperson; because Bill Kitchen was away I was the next available person and was able to tell the world how well the babies were doing. Within hours I was receiving excited phone calls from my cousins in the UK saying "Neil. We've just seen you on TV"!

The quads were of course the result of the process at the time of transferring multiple embryos in the hope that at least one might 'take'. I looked after several sets of quads and triplets, and there were numerous sets of twins. These in turn led to a rapid increase in prematurity rates and immense pressure on NICU facilities. Because of this and the family difficulties with large multiples the number of embryos transferred was reduced firstly to two and then only single. Over the years the improved success rate of single embryo transfer has obviated the need for multiple transfers.

1976 - The introduction of N.E.T.S.

Undoubtedly the greatest turning point in my career was to be in the right place at the right time to set up Victoria's neonatal transport system. While I was in Canada doing my fellowship training in Toronto and Hamilton, Bill Kitchen and a group of supportive paediatricians and senior nurse Maureen Gleeson from the Mercy had been developing plans for the introduction of such a service. With great political skill and the support of Prof. Lance Townsend at The Women's they succeeded in obtaining approval – and funding – for the new service. I was back in Melbourne for only 6 months, and the only person in Melbourne with neonatal transport experience – having done transports in Hamilton – so the Director's job seemed to have been made just for me!

I started on July 1st 1976 and my secretary Lyn Cox and the first 6 nurses started a month later. The first 3 months were a flurry of activity, selecting and organising equipment and protocols, designing forms, educating the nurses in special requirements for transport and a huge amount of liaison and negotiation with the 4 hospitals with NICUs, the ambulance service, potential referring paediatricians, GPs and their hospitals. We thought we did pretty well to have the service up and running only 2 months after the nurses started – on October 4th. The Minister for Health officially opened the service that morning, just as the first patients arrived at The Women's – an 'overflow' transfer of twins from the Queen Vic.! Serendipitously the twins' family name was Love! The Love family remained friends of NETS for many years – we even celebrated our 21st anniversary at their family winery in 1997.



Top: The first 6 NETS nurses
Middle: The first NETS equipment set-up
Bottom: Arrival of Love twins

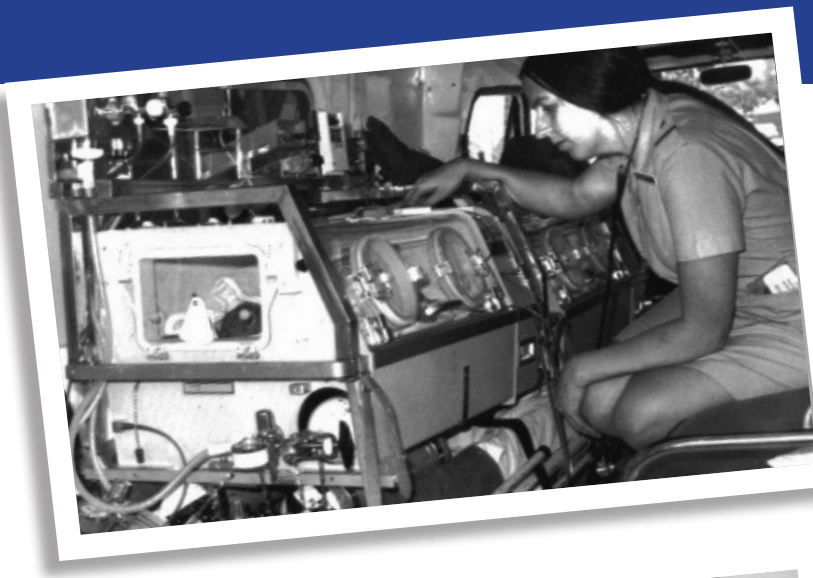
Perhaps our most famous trip in the first 3 months was the retrieval of the quads from Horsham. The mother had been diagnosed with quads at 29 weeks only the day before (no ultrasound in those days) and had been planning to transfer to Melbourne the next day but came into labour overnight. We flew to Horsham via Air Ambulance in what the pilot later confessed was the roughest flight he'd ever had – they closed Essendon Airport shortly after we left. We set up in an adjoining delivery room as the local obstetrician Eric Miller performed textbook vaginal deliveries at 2-3 minute intervals, which gave us just enough time to dry each baby, get them breathing with 'frog' breathing (yes – it works!) and put them 'top-and-tail', one pair per incubator. Only the boy developed mild respiratory distress and we only needed minimal oxygen. We had to return by road, through driving rain, thunder and lightning, taking 4½ hours, with a stop at Ballarat to replenish oxygen supplies. On arrival at the Mercy we were met by the press, who next day dubbed us the "Quad Squad" on the front page of the Herald-Sun! The babies all did well, and are shown with the 'squad' 30 years on – a lawyer, a specialist physician, a town planner and a company PA.

The next exciting phase for NETS was when we officially started using the Air Ambulance, the first trip being in June 1977 – to Ouyen in the Mallee for a badly asphyxiated baby; having taken great care to warm the incubator in the plane on the way up so that we could have a nice warm cot to warm the baby, imagine my dismay when (after landing at 2 a.m. on a grass airstrip lit by kerosene flares) we were met by an open utility to take us into the hospital! Unfortunately even a warm incubator would not have saved that poor baby.

Three days later the second, more successful, air ambulance trip, also at night, was to Robinvale for a prem; the excitement on landing this time was having to make a preliminary approach to clear the cattle off the grass strip!

Conclusion

So there you have some turning points that have been highlights of my career – a fortunate one indeed. And there's just one more – not paediatric; as a JRMO at the Alfred Hospital in December 1966 as the Orthopaedic Resident I held the retractor at the first hip replacement in Melbourne (and 3rd in Australia). The surgeon was John Cloke, aided by Clarke McNeur, using the McKee Farrar metal-on-metal device. The procedure was a success and took 4½ hours – a long time to hold a retractor! Maybe that was the most important turning point for me, for I have been the grateful recipient of more recent devices – on both sides!



Top: Quads in the ambulance
Middle: The "Quad Squad"
Bottom: 30 years on

Neil Roy was formerly Director of the Neonatal Emergency Transport Service

A "Wow moment" turning point in cardiology

How investigation and treatment of congenital heart disease came good in the 1970s

Jim Wilkinson

The paediatric sub-specialty of "Paediatric Cardiology" emerged gradually in the late 1950s and 1960s. A few adult cardiologists began to recognise that with the early successes of cardiac surgeons in palliating or correcting heart defects this was a rapidly advancing area of cardiology practice. Management of most acquired heart diseases (hypertension / coronary artery disease, rheumatic heart disease) had changed very little over the preceding decades, but the beginnings of cardiac surgery and the arrival of heart lung bypass machines was bringing dramatic changes, especially for congenital heart defects. Some paediatricians and radiologists were beginning to seek training in cardiac investigation that were documenting the anatomy of cardiac defects and the associated pathophysiology, using the new techniques of cardiac catheterisation. A young paediatrician at the Royal Children's Hospital in Melbourne – Dr Alexander Venables spent two years in England training in cardiology, some of it with Dr Paul Wood (a Melbourne University graduate) at The National Heart Hospital in London. He returned to Melbourne in 1955, becoming a consultant to the "Cardiac Investigatory Clinic" alongside Dr Mostyn (Mick) Powell, who had started the service. He later took over the clinic when Mick Powell retired in 1963 and became the first Director of Cardiology when the Department was finally established formally in 1968, though his appointment then and later remained that of a "Paediatrician" rather than a "Paediatric Cardiologist".

However, many affected children became symptomatic and died in the early weeks of life and open-heart surgery, necessitating cardio-pulmonary bypass, could not be performed on young infants. Epidemiological studies showed that the mortality during infancy or early childhood for patients born with cardiac abnormalities was around 35%. Submitting affected infants to cardiac catheterisation to diagnose the nature of the heart defect from which they suffered was difficult and dangerous and a substantial proportion of infants who had such procedures deteriorated or died in the hours after the investigation.

My own introduction to cardiology training started in 1968, as a paediatric RMO at Birmingham Children's Hospital in UK. The initial investigation of infants who were thought to have a significant cardiac defect was "venous angiography" in which radio-opaque contrast was injected via a cannula in an axillary vein, introduced via the medial cubital vein using a surgical "cutdown" (a technique with which I rapidly became experienced). A substantial dose of contrast was injected while the infant, who was often not anaesthetised, was comforted by a nurse. A series of film plates were taken in rapid succession using a mechanical "film changer", or roll film.

Once processed the films were carefully reviewed by cardiologist and radiologist with the expectation that sufficient information would be there to allow a diagnosis of the cardiac defect (e.g., Transposition / Pulmonary Atresia / Coarctation of the Aorta / Hypoplastic Left Heart syndrome). Unfortunately, the non-selective nature of the contrast injection could lead to errors in diagnosis, and it was obvious to all involved that selective angiography should provide better anatomic detail. However, the large size and relative stiffness of cardiac catheters that were available at that time discouraged the use of selective cardiac catheterisation and angiography in most small infants.

Many of the infants were significantly hypoxic and often acidotic because of their cardiac defect which was, in many cases, "ductus dependent". The use of ionic contrast agents gave a volume load and toxic effects which compounded their metabolic disturbance with frequent adverse effects. All too often they required urgent surgery or a balloon septostomy to palliate their problems, but the likelihood of survival was often reduced by their very poor condition.

Obviously, what we needed was an option for immediate treatment that would improve hypoxia and reduce acidosis and a diagnostic modality that did not require the passage of stiff catheters or injection of toxic contrast material.

I started working as a consultant in Liverpool (at The Royal Liverpool Children's Hospital) in June 1974. Over the following two years we became aware of promising research involving the possible use of Prostaglandin E, given intravenously, to stop the ductus arteriosus from closing and in some cases to encourage it to reopen if already closed or closing. The work was being led by Dr Peter Olley in Toronto and led to the first clinical use of Prostaglandin E1 or E2 in Toronto and by Dr John Neutze at Green Lane Hospital in Auckland, New Zealand in 1975/76.

At much the same time research using new modalities of Echocardiography was beginning to produce "cross sectional" (2 dimensional) images of cardiac anatomy. Previously single crystal transducers had been employed to gain information about cardiac structure and function using A(amplitude) or B(Brightness) mode scanning, and later M(Motion) Mode, but these were of limited practical use for many cardiac defects, especially more complex abnormalities. These had been developed over the preceding twenty years. Their main practical use was to record "M Mode traces" which showed the lines of movement of cardiac structures detected by a single narrow beam of reflected ultrasound (see picture).

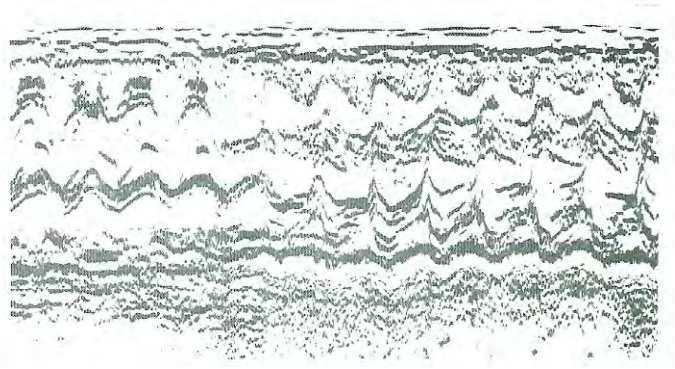


Fig 1: M Mode Scan showing aortic root and left ventricle / septum / mitral valve

The use of oscillating transducers and multi-crystal transducers showed promise of being able to visualise intracardiac anatomy with cross sectional images in "real time" and in considerable detail, in a "non-invasive" manner. This technology was developed by a number of researchers and in several centres, though the early images lacked fine detail and were somewhat "crude".

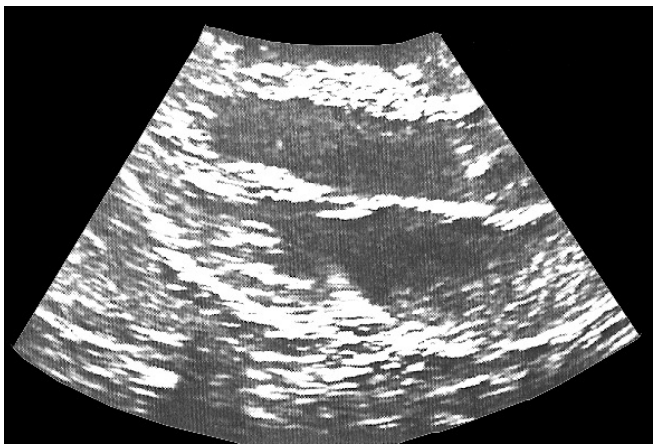


Fig 2: 2 D Echo from the 1970s era with "long axis scan" showing cross sectional image of aortic root and left ventricle/ septum / mitral valve

Dr David Sahn in California (San Diego) was one of the leading workers in the field in the mid-seventies.

These two developments changed the practice of paediatric cardiology dramatically. In Liverpool where I was working, we obtained our first cross sectional echocardiography machine in 1977 and started to employ Prostaglandin infusion in the same year. The effect of Prostaglandin was almost "magical" in many infants with immediate improvement in oxygen saturations and / or relief of the intense dyspnoea / grunting respirations which were in evidence prior to the infusion being started.

2D echo, which became available at much the same time was a dramatic addition to our diagnostic capabilities as we could, in many cases make an accurate diagnosis of such defects as transposition or hypoplastic left heart syndrome even without the need for angiography. Amazing improvements in image quality over the next few years and the arrival of colour Doppler in the eighties led to increasing accuracy of "non-invasive diagnosis". Our willingness to abandon angiography in sick infants followed gradually but made a huge difference, though I personally had adopted selective angiography with cardiac catheterisation and discontinued the use of venous angiography in 1975. Now we seldom need to submit sick infants to invasive cardiac catheter procedures for purely diagnostic purposes.

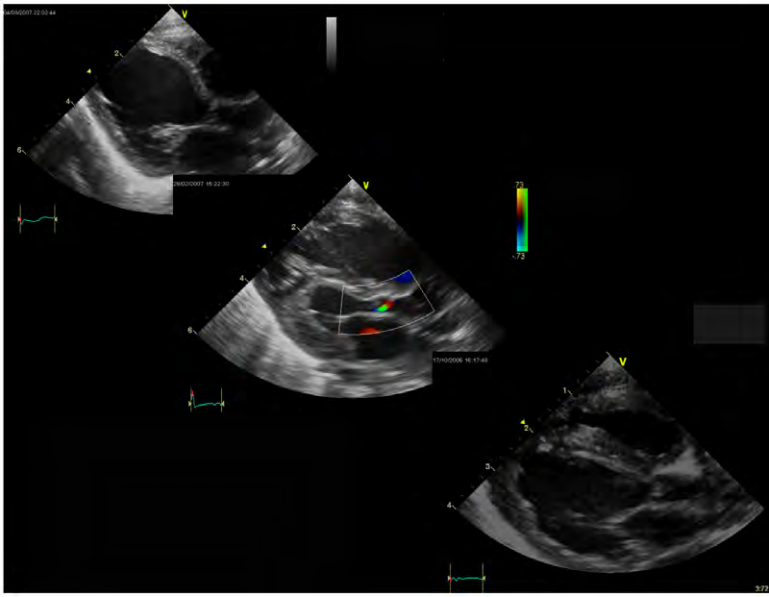


Fig 3: More sophisticated 2D Echo images with colour Doppler from 1980s

Alongside all that the arrival of prostaglandin therapy for sick neonates with ductus dependent defects in the late seventies was an enormous and dramatic step forward and made a huge change to the prognosis for many sick infants. Where the baby has been extremely hypoxic such as in transposition, pulmonary atresia or severe Fallot's Tetralogy, it became possible for the infants to have an atrial septostomy or go to the operating theatre in good or excellent condition, thereby improving markedly the likelihood of survival.

During the 1980s the option of prenatal (foetal) echocardiography became a realistic option and resulted in the diagnosis of congenital heart disease prior to delivery. That in turn facilitated the delivery of such patients within a tertiary centre and early institution of Prostaglandin E1 where required.

The introduction of Prostaglandin therapy at The Royal Children's Hospital in Melbourne took place in the late 1970s and availability of 2D Echo followed by around 1980 so that these options were readily available and in regular use by Dr Venables and his team, especially by Dr TH Goh, who pioneered the use of Cross-Sectional echocardiography in Melbourne, before my appointment to succeed Dr Venables when he retired in early 1988.

Jim Wilkinson is current President of the Alumni and was former Head of Cardiology at RCH.

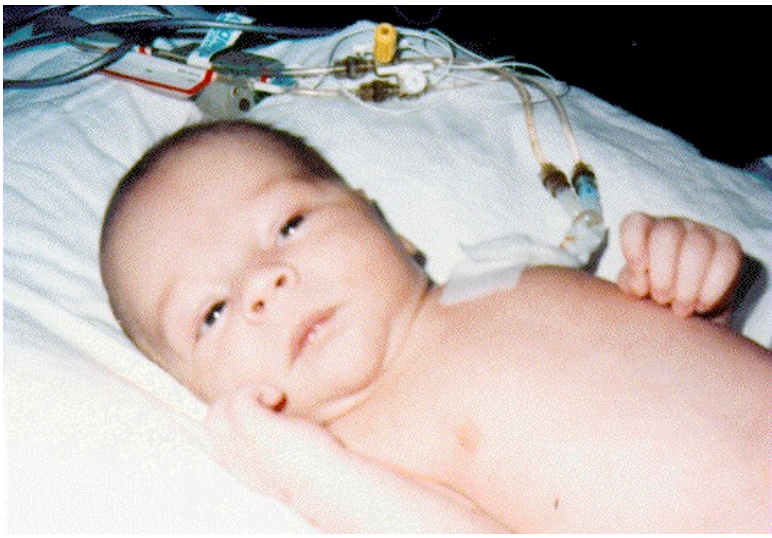


Fig. 4 An infant with a critical cardiac defect on PGE infusion (looking well)

Off the sheep's back

Tony Weldon

I commenced Medicine in 1961 and commenced my paediatric journey at RCH in 1968. Like all alumni, regardless of discipline, the period during which we forged our various career paths has seen a multitude of turning points – more so than in any other previous similar period. For some alumni, they were directly responsible for those changes and developments; for others, like myself, we have borne witness to these.

I was a Registrar at RCH from 1969 to 1971 and during that time worked in the Respiratory/Gastro. Unit in 9 East (on reflection of the orientation of that version of the hospital it in fact should have been 9 South!!).

In retrospect the notion of having infants and children admitted in the same ward area with varying degrees of severity, bronchiolitis at one end and gastroenteritis at the other, is a complete anachronism. I wonder whether anyone did a survey to determine the rate of cross infection – how many children with bronchiolitis went home with gastro. and vice versa! But no doubt we were meticulous in our handwashing and other techniques!

As I recall, part of that job was acting as Registrar to the Genetic-Metabolic Unit consisting solely of David Danks. It was not an onerous job. However, part of it was to accompany David on his rounds to see patients who had been referred to him because of their dysmorphic features. After all, at that time, the name of the game was simply to recognise that one odd looking child may have a similar condition to another one. Genetics in the late 60's and early 70's consisted of being able to perform a crude karyotype – that was it!

I remember the disappointment that flooded Dr. Danks's face when, after his first day back from a vacation, he successfully recognised a syndrome in such a patient. His success rate was so low that he reckoned he was lucky to be able to make such recognition about once a year – thus, he had little to look forward to for the remainder of that particular year!

One patient stands out in my fast-dimming memory – a young child with Menkes Disease (Kinky Hair disease). I recall feeling the brittle unusual coiffure of that child. But at the same time, I remember David talking of the similarity to the wool of sheep he had seen and that farmers had recognised that this defect in the wool related to a deficiency of copper in the pasture on which those sheep fed. This observation led to the publication in The Lancet on May 20 1972 of a Preliminary Communication titled "Menkes' Kinky Hair Syndrome" by D. Danks et al. (Lancet 299:7760:1100-1103) with a subsequent 246 citations.

A subsequent article was published in Pediatrics by the same authors (Menkes' Kinky Hair Syndrome: An Inherited Defect in Copper Metabolism with Widespread Effects - Pediatrics August 1972: 56(2):188-201) and between July 1999 and October 2021 (the period over which these figures are available) the abstract for this article has been downloaded from the internet on 13,998 occasions.

This extract from 'Copper comes of age in Melbourne' by Julian F B Mercer & James Camakaris (Metallomics, Volume 8, Issue 9, September 2016, Pages 816–823) explains the background to that association David Danks was able to make back in 1971:

"David Danks was a clinical geneticist who was a mentor to both Jim and Julian. David was a remarkable man who essentially established clinical genetics in Australia.

After qualifying in Medicine in Melbourne in 1954, he developed a lifelong interest in genetic disorders, at a time when these disorders were seen to be rare and medically unimportant. He saw, however, that genetic diseases were "experiments of nature", in the memorable phrase of the famous English physician Archibald Garrod, and could be very useful in identifying unknown biochemical processes.

David became Professor of Paediatrics in the Royal Children's Hospital, Melbourne, and his passion for clinical genetics was encouraged by Dame Elizabeth Murdoch, then president of the hospital.

He went for overseas training with the top Medical Geneticists of the time, including Victor McKusick. On his return to Melbourne he established the Genetics Research Unit in 1967. Jim's first interaction with David Danks was spending a University student summer break period at the Genetics Research Unit doing a mini-research project (but not on copper!).

David encountered cases of the inherited copper disorder, Wilson disease, in the hospital, and his desire to understand and better treat this potentially fatal disorder stimulated his interest in copper disorders.

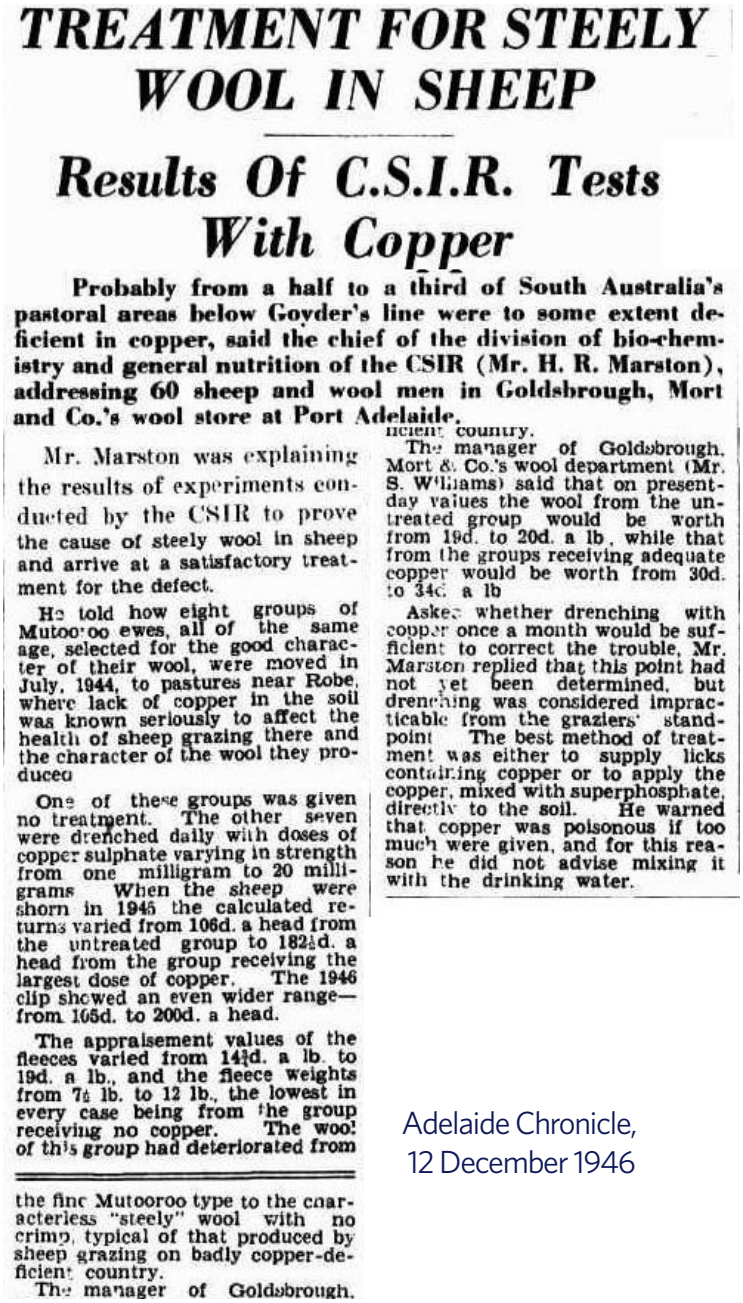
Showing his flexibility of mind, he found out about the copper research being carried out on animals in CSIRO, and in this way he learnt about the many clinical features exhibited by copper deficient animals, mainly sheep (steely wool, swayback, osteoporosis) and pigs (arterial tortuosity).

He was thus mentally primed to recognize these symptoms and solve the mystery of Menkes disease as an inherited systemic copper deficiency disease." Today, Google has allowed me not only to readily find multiple images of individuals with Menkes' Disease but also a reference from the Adelaide Chronicle of 12th. December 1946 detailing the possible treatment of options for sheep grazing in an area known for copper deficiency in its soil. So the connection between the importance of this trace mineral in sheep and other animals to homo sapiens took around 30 years!

This prescient observation by David Danks was indeed a turning point in the understanding of copper metabolism in man. Personally, I had nothing to do with it but can claim to have been there on the day that the "penny dropped". Subsequently, further work was done at RCH to understand the underlying mechanism for this deficiency and attempts at treatment were initiated.

A turning point indeed!

Tony Weldon is a retired General Paediatrician whose career was mainly in Frankston.



TREATMENT FOR STEELY WOOL IN SHEEP

Results Of C.S.I.R. Tests With Copper

Probably from a half to a third of South Australia's pastoral areas below Goyder's line were to some extent deficient in copper, said the chief of the division of bio-chemistry and general nutrition of the CSIR (Mr. H. R. Marston), addressing 60 sheep and wool men in Goldsbrough, Mort and Co.'s wool store at Port Adelaide.

Mr. Marston was explaining the results of experiments conducted by the CSIR to prove the cause of steely wool in sheep and arrive at a satisfactory treatment for the defect.

He told how eight groups of Mutooroo ewes, all of the same age, selected for the good character of their wool, were moved in July, 1944, to pastures near Robe, where lack of copper in the soil was known seriously to affect the health of sheep grazing there and the character of the wool they produced.

One of these groups was given no treatment. The other seven were drenched daily with doses of copper sulphate varying in strength from one milligram to 20 milligrams. When the sheep were shorn in 1945 the calculated returns varied from 106d. a head from the untreated group to 182½d. a head from the group receiving the largest dose of copper. The 1946 clip showed an even wider range—from 105d. to 200d. a head.

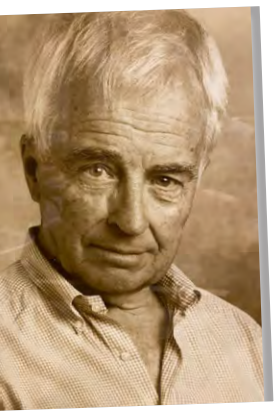
The appraisement values of the fleeces varied from 14½d. a lb. to 19d. a lb., and the fleece weights from 7¼ lb. to 12 lb., the lowest in every case being from the group receiving no copper. The wool of this group had deteriorated from the fine Mutooroo type to the characterless "steely" wool with no crimp, typical of that produced by sheep grazing on badly copper-deficient country.

The manager of Goldsbrough, Mort & Co.'s wool department (Mr. S. Williams) said that on present-day values the wool from the untreated group would be worth from 19d. to 20d. a lb., while that from the groups receiving adequate copper would be worth from 30d. to 34d. a lb.

Asked whether drenching with copper once a month would be sufficient to correct the trouble, Mr. Marston replied that this point had not yet been determined, but drenching was considered impracticable from the graziers' standpoint. The best method of treatment was either to supply licks containing copper or to apply the copper, mixed with superphosphate, directly to the soil. He warned that copper was poisonous if too much were given, and for this reason he did not advise mixing it with the drinking water.

Adelaide Chronicle, 12 December 1946

Memories of Alan Wakefield ("The Vicar")



Murray Stapleton

Having said goodbye to a 50 year stint as a plastic surgeon, I might well be accused of having a clouded memory and that things were really not better in my day, as I think they were. But things were better then. Nurses and doctors were trained on-the-job. We, all of us, lived in the place where we worked. We were exposed to various clinical teachers. It was 24 hours a day involvement. We were able to discuss cases with each other and enjoy the camaraderie of the friendship groups that we mustered. The destruction of the nurses' homes, in my view, was the end of nursing as I can remember it. The movement away from on-site teaching of nurses was a tragedy. Nursing, whatever else it is, is a craft and a craft cannot be learnt by Zoom or sitting in a university lecture room.

In those days the medical superintendent worked in a reasonably small office, his secretary was also in a small office, as were the pair who were part of the management. Nowadays the administration part of many hospitals extends for a whole floor. On reflection I don't see the difference from what was my experience to what is the case now. The dead hand of administration, as I see it, affects what one does. No more are eccentrics tolerated. One of the great eccentrics is the man about whom I write. There were many times when a hospital administrator would have arranged to sack Alan Wakefield.

The first plastic surgeon in Melbourne was Mr Benjamin Rank (later Sir Benjamin). His protégé was Alan Wakefield, "the Vicar". Both had very gruff exteriors. They were aggressive, they were persistent. They took no prisoners. It was up to Benjamin Rank to convince the Royal Children's Hospital and the Royal Melbourne Hospital that plastic surgery had arrived as a specialty. It wasn't an easy job because the surgeons in both institutions by and large saw plastic surgery as frivolous and unnecessary. With sheer persistence, eventually the Vicar was made head of the Plastic Surgery Unit at the Royal Children's and Mr Rank the head at the Royal Melbourne Hospital.

Reflecting on my own training, the person who taught me most, who inspired me most and who eventually was my partner, was the late Donald Marshall. But of all of my colleagues including my teachers, the one whom I miss most is the Vicar. I imagine many who were around in the Vicar's days would find my recollection rather curious. As I commenced my training as a plastic surgeon I heard so many stories of the Vicar and all of them were related to moments of aggression and none, as I recall, saw Alan Wakefield as anything but aggressive and a pioneer of plastic surgery particularly at the Royal Children's Hospital. When I began training as a plastic surgeon, one of my posts was to be the plastic surgical registrar at the Royal Children's Hospital. The head of the unit then was Mr George Gunther. The Vicar, having retired from surgery some years prior to that, went off to be a farmer to breed Murray Grey cattle and to foster his love of growing prize roses. Perhaps it was the economics of the time of farming that saw the need for the Vicar to come back to surgery and, in that sense, he was a sessional surgeon at the Royal Children's Hospital which is where we met. Even as a junior plastic surgeon trainee, it was clear around the bedside that it wasn't Mr Gunther who was the boss, it was the Vicar. Nobody dared make a comment that would upset the Vicar. All of the surgeons who were part of the unit then have now died. I guess therefore I can say it as I remembered it to be. There was no encouragement at all from on high to consider new ways of doing things and eventually, when I came back from finishing my training in England and was appointed a consultant at the Royal Children's Hospital, I found that to be immensely frustrating. The phrase around the bedside

so often I heard was "this is the way we have always done it". If there is no stimulation from on high to the younger surgeons, then the unit goes nowhere. I have the view that things are now different in that particular unit.

The Vicar did not tolerate fools. He told me that when he was working as a consultant at the Royal Melbourne Hospital there was an edict that the surgical packs henceforth would have a metal ring sutured onto the corner. No doubt that if there was a problem with the count, then an x-ray would show the pack buried within someone's abdomen. The Vicar objected to that and made it clear to the medical administration that he was not going to abide by such an edict. He was told that was bad luck and that was the way it was going to be. "Very well" said the Vicar and what happened thereafter was that when a pack was used by him, he cut the ring off! Nowadays that would be a sacking offence, but in those days, with personalities of the plastic surgical pioneers, nobody dared to take them on.

Well I recall later one day in my residency as the plastic surgical registrar, one morning I received a telephone call from a surgeon in the country. The surgeon asked for my permission, would you believe, for that person in question to come and see Mr Wakefield perform a hypospadias operation. I left school at the age of 15 and went off to work so, in my early days, I worked with various people with varying personalities and perhaps that stood me in good stead to relate to Mr Wakefield. Of course there was no way that I was going to give permission to the surgeon to turn up. I asked Mr Wakefield whether or not it would be appropriate for the man in question to visit. Mr Wakefield immediately responded and said "tell him the invitation is refused". So I conveyed that very message to the surgeon, but clearly the person, being devoid of common sense, actually turned up at the theatre door. He introduced himself to me so I invited him to sit in the tea room for awhile. I told the Vicar that the man in question was in the tea room, to which he responded "leave the bugger to me". So, with a voice louder than one was accustomed to hear when the Vicar was annoyed, he said to the surgeon "this morning I refused you permission. This afternoon that refusal remains, now leave." The operation proceeded with perhaps greater silence and in the tea room after it was done I took the risk of asking Alan why his approach was as it was.

He responded in this way, "Why did that person want to come and see an operation that I have spent my whole life trying to do the best? He would come and see one operation and go back to the country and destroy the lives of so many young children. That's why I told him to leave." On reflection, full marks to the Vicar.

In the operating room when the Vicar was operating, the only important individual in the room was the child on the operating table and if anyone in the theatre, be it nurses, be it doctors, be it anaesthetists, or anyone else including me, if the very best from those people was not for the child then they copped it. There was one exception and that was Sister Kate. The Vicar loved her. At the end of a difficult cleft palate procedure, the Vicar had trouble putting in the sentinel suture. As the Vicar was about to tie the suture in place, Sister Kate put the sucker into the child's mouth and sucked the suture and the needle into the bottle. Normally that would be cause for significant criticism, but not for Sister Kate. He looked at Kate and, with a half smile, said "Oh well, let's do it again".

As time passed and now as a consultant plastic surgeon in various places, I enjoyed conversations with the Vicar. I enjoyed his anecdotes. He remembered telling me one day that a trainee surgeon, who incidentally finished up being a plastic surgeon, was helping the Vicar perform a very difficult cleft palate repair. At the end of the two hour procedure, the surgical trainee in question asked the Vicar "Do you think that was really the right operation?" Imagine the rage, but don't imagine why the surgeon in question took a long time to eventually finish up as a plastic surgeon himself!

As our relationship grew and matured, the Vicar and I got on very well. Very little did our relationship have anything to do with plastic surgery. Both he and I shared an interest in farming; he went off to breed Murray Grey cattle and to grow roses and I had a similar interest. Indeed, one Friday the Vicar said to me that he wanted to come and stay at our house for the weekend to see the roses that I was growing. I was terrified. Gosh, the Vicar is coming home. He came and, when he left, it was clear that I had a lot to learn about growing roses. During that weekend I asked the Vicar what encouraged him to study medicine. He told me that he really wanted to be a barrister. He also said that he hated every day of being a doctor. The Vicar's mother wanted him to be a doctor, but he said "I would have studied anything rather than please her, so it was the next door neighbour, who was a surgeon, who told me, when I was thinking about going to university, that "Alan, you should do medicine", so I did".

He invited us to dinner at his home in Happy Valley one Saturday night. I remember it was raining and in the wee small hours after a very lovely dinner, there I remember the Vicar marching up and down his verandah with the rain pouring on the roof whilst he sang "Onward Christian Soldiers". This is this gruff man who was regarded as being humourless; not at all.

In my early days as a surgeon I also had a commercial pilot's licence and from time to time I would fly visitors and others to various parts of Australia. I was then

on the board of the Royal Flying Doctor Service. The annual meeting in this particular year was in Derby and I gathered a group who would want to come to Derby for a break. At that time the Vicar was increasingly troubled and became extremely disabled because of the pain and discomfort of a malignancy in his lower spine. I asked the Vicar would he like to come to Derby. Instantly he said "no"; he told us he "would be only a bother". I explained to the Vicar that I wanted him to think about it and that I would take an aeroplane that had a fold-back seat such that the two seats could flatten and that he could lie down for the whole of the journey. Perhaps it was because his wife told him he had to agree, so he came. 100 miles on the way to Ayre's Rock, that great edifice appeared on the horizon and I asked the Vicar to sit up and look at what was coming. He sat with some difficulty and made no observation other than "It looks like a bloody big stone to me". We stayed at Ayre's Rock (Uluru) and I took him, with some difficulty, to a couple of my favourite places around the base of this wonderful edifice. One was once called Maggie Springs. It had a pool next to the rock. The sky was deepest blue, there was very little wind, the trees were still and the only sound was the occasional birdsong.

After a degree of silence the Vicar said to me "Murray, this must be the most mystical spot on earth". Now whilst that might be a comment from many, coming from the Vicar it was a window into how this great man could think. On we went to Broome where the beach sands were pearly white, the sea deepest green and the day was still and beautiful. With difficulty he and I walked to the edge of the sand and he looked up and down the beach for a time and then said to me, "Murray, there surely can be no more beautiful place than this". My answer was "Alan, where have you been?" and his answer was "I've been to bloody plastic surgical meetings around the world and I don't want you to fall for that because life is worth more than your job". I promised him I would take that advice.

And now that the Vicar is long since dead, I miss him. I miss him for various reasons. I'd love him to share with what I have done which has nothing to do with plastic surgery. He was, in every sense, my champion man.

Murray Stapleton is a retired plastic surgeon.

An alternate reality

Agnes Bankier

Hopefully by the time you read this, Victoria will be open and on the way to full recovery.

Watching the hardship of the prolonged lockdown in Australia, I am inspired to share my own reality in Jerusalem, in a world where Covid has been handled very differently. Australians who managed to come here recently are clearly traumatised by the Victorian experience. It takes them some time to get accustomed to new freedoms and feel comfortable among people.

We arrived here from lockdown to lockdown in August 2020 but in the world of Zoom we barely noticed the change. We had frequent Zoom contact with family and friends. I even continued to chair RCH HREC from Jerusalem for 5 months after relocating!

At the peak of the pandemic there were 10,000 new cases per day. The hospitals reached their limits with Covid patients. Further lockdowns were not tolerated well, yet streets were deserted; shops, schools, public places, hotels and restaurants stayed closed. Even the skies were silent with no planes overhead. In a country

that welcomes millions of tourists per year, there were none.

The roll out of the Pfizer vaccine began in December 2020 with much publicity on all channels. Sport stadiums were open as vaccination centres, some other centres with multiple stations were open 24/7 all over the country, vaccinating up to 200,000 per day. The second shot, three weeks later, was scheduled with the first appointment. Corona testing stations were readily available free of charge.

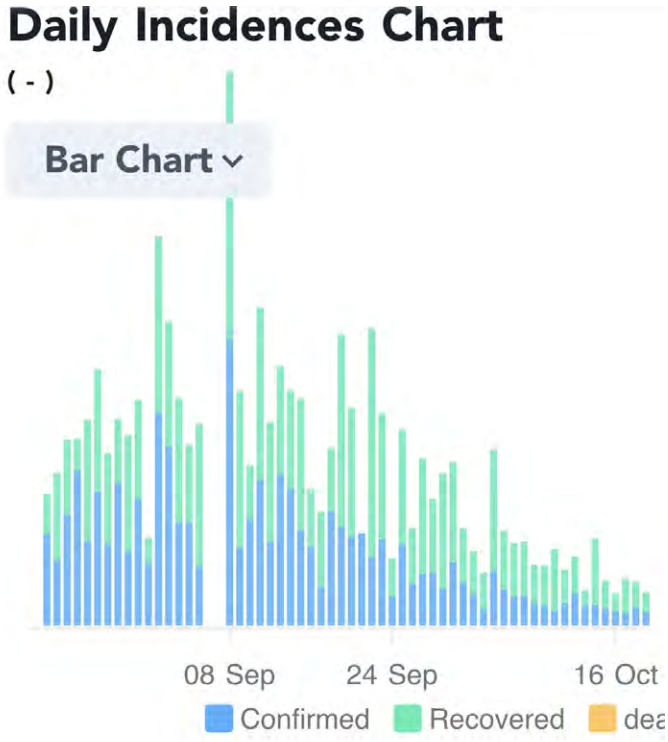
People bounced in and out of isolation until booster shots were offered from August 2021 and vaccination for children over 12, before the start of the academic year. All children were screened before school entry.

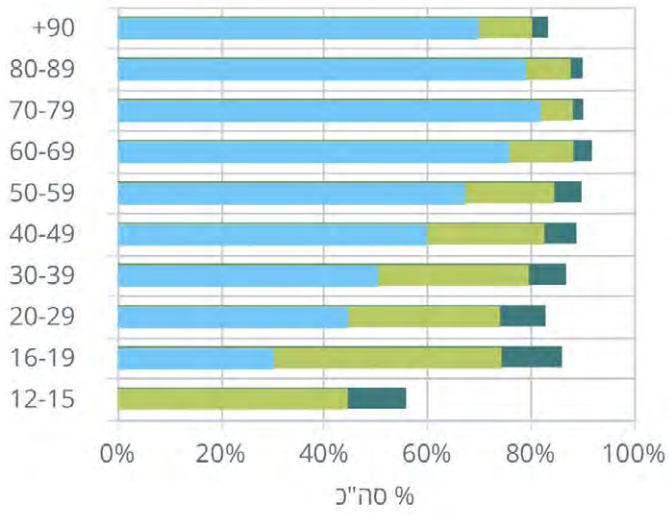
The 'green passport' reopened public places. Now that most of the population is triple vaccinated, the daily number of new cases has dropped to below that of Victoria. (see charts) From November, vaccinated tourists will be welcomed back. The pandemic is not over but life is closer to being back to normal.

We are still required to wear masks in enclosed public spaces but holders of a green pass can enjoy all manner of entertainment including concerts, restaurants, theatres, movies and gyms. More people prefer to work from home part time because they have a better work/life balance. We still live with repeated episodes of individual isolation particularly for the unvaccinated and young children. There is always a plan B for social arrangements in case someone needs to isolate but it is no drama any more,since vaccinated people are not as sick.

A new variant might appear and we might need booster shots, but life is good. Here the weather is predictable with four distinct seasons and no summer rain. People are out and about enjoying the rich cultural life and a multitude of possibilities for hiking, bike riding and touring, enjoying this ancient land. Come and see for yourselves. We are here to welcome you.

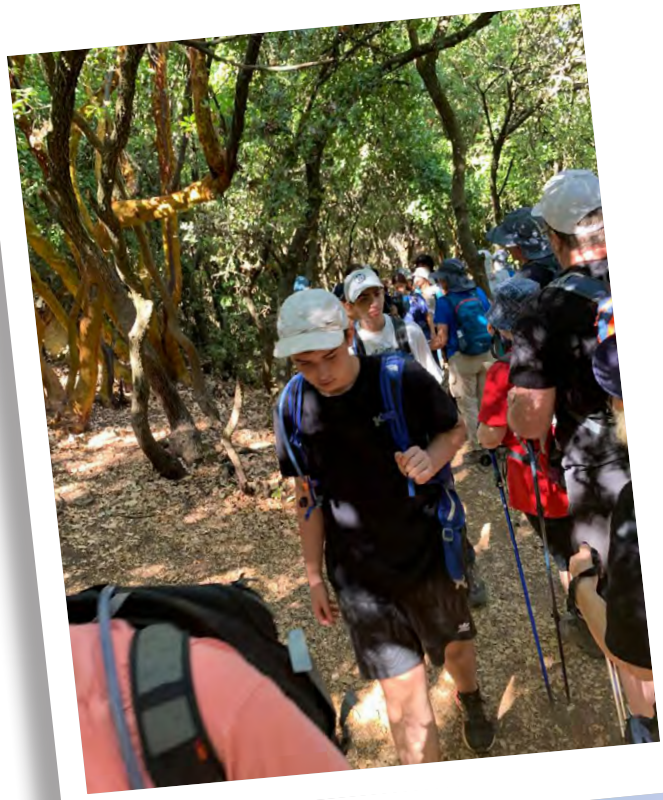
Prof Agnes Bankier OAM was a clinical geneticist in Melbourne for some 40 years and Director of the Victorian Clinical Genetic Services and Chair of the Royal Childrens Hospital Human Research Ethics Committee for the past 10 years She was President of the Human Genetic Society of Australasia and served on many of its committees, receiving Emeritus Life Membership. For her contribution to genetics and to genetic education, she was awarded an OAM in 2018. Agnes now lives in Israel with her children and grandchildren.





Life in Jerusalem

Photos contributed by Agnes Bankier OAM

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