50

THIS IS WHAT *Hope* LOOKS LIKE

Volume II

*Celebrating **50 Years** of Renal Transplantation & Medicine*

Singapore General Hospital

50

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Volume II

Singapore General Hospital
SingHealth

National Library Board Singapore Cataloguing in Publication Data
ISBN: 978-981-18-0443-4
Title: This is What Hope Looks Like
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Designed and printed by Oxford Graphic Printers Pte Ltd

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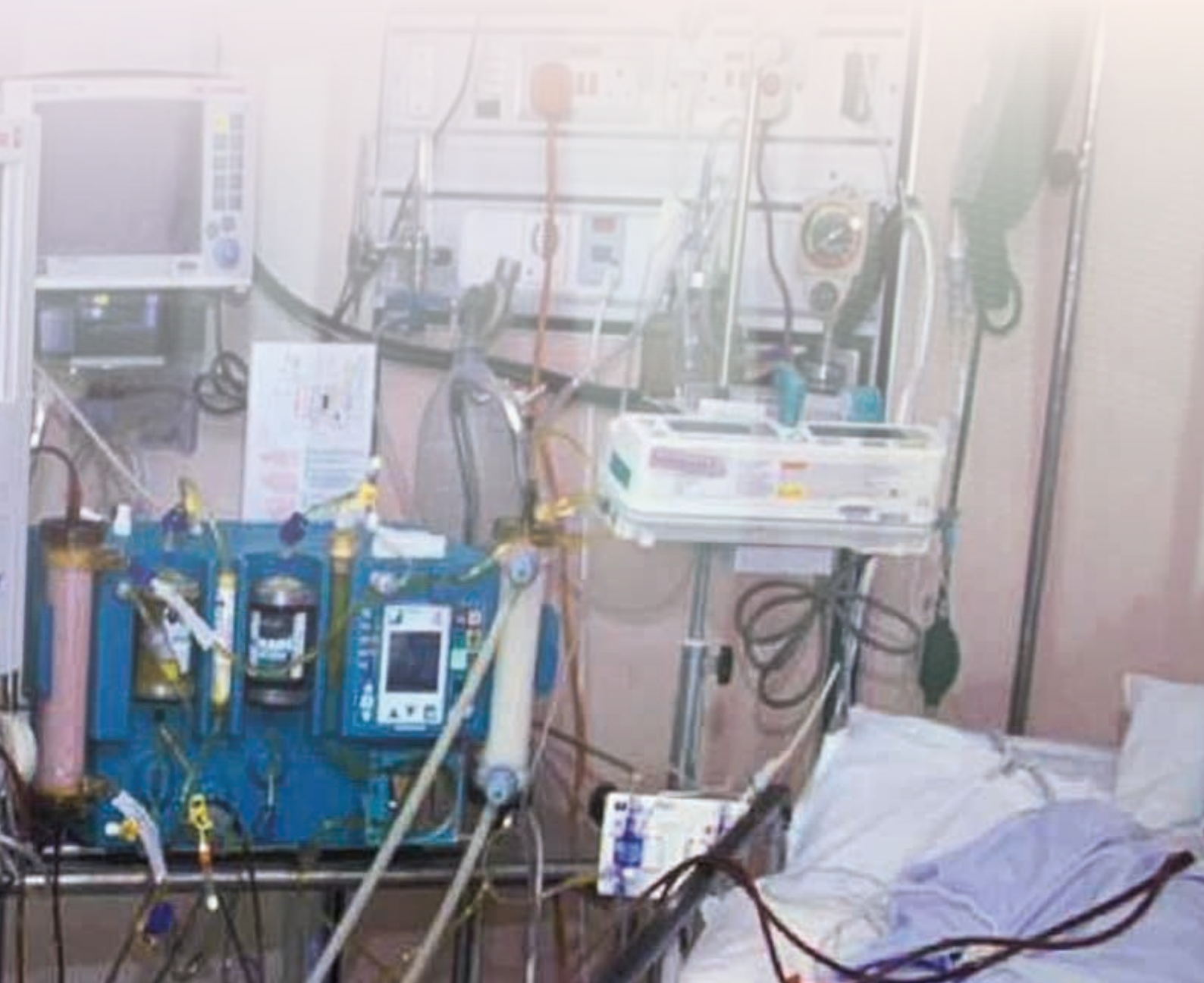
Advancing Renal Medicine through New Specialties

> *Nephrologists have always been on the lookout for novel therapies and novel therapeutic interventions through new medication and devices to improve patient's quality of life and survival outcomes.*

- Associate Professor Marjorie Foo



Interventional Nephrology

Associate Professor Tan Chieh Suai, Senior Consultant
Head of Department of Renal Medicine, Director of Interventional Nephrology

Since the inception of the department, the performance of invasive and diagnostic procedures in patients with chronic kidney disease has always been an integral part of nephrology care. Some of the procedures performed by the pioneering nephrologists in the department include renal biopsies in both native and transplanted kidneys, as well as the placement of acute shunts for haemodialysis, non-tunnelled haemodialysis (HD) catheters and acute peritoneal dialysis (PD) catheters.

As technology evolved over the years, the practice of these procedures has continued to improve. Renal biopsies used to be performed blind with the aid of X-rays and bony landmarks. The first percutaneous needle aspiration renal biopsy was performed by Nils Alwall from Sweden in 1944. However, more well-known is the technique described by Kark and Muehrcke in 1954, involving the approximation of the kidney site by the transfer of bony landmarks to the patient's back from a preliminary intravenous pyelogram film, and the insertion of the Franklin modification of the Vim-Silverman biopsy needle into the flank of the patient to obtain renal tissue. In 1962, radiological images were introduced for kidney localisation, and subsequently replaced by ultrasound real-time imaging for renal biopsy, which has remained the gold standard for renal biopsy in this day and age and is still being practiced by nephrologists in our own department. Real-time ultrasound imaging was also introduced in the early 1990s in SGH for the insertion of temporary dialysis catheters and renal biopsies. It quickly became the standard of care (whereas previous techniques relied on body landmarks as guides) till today.

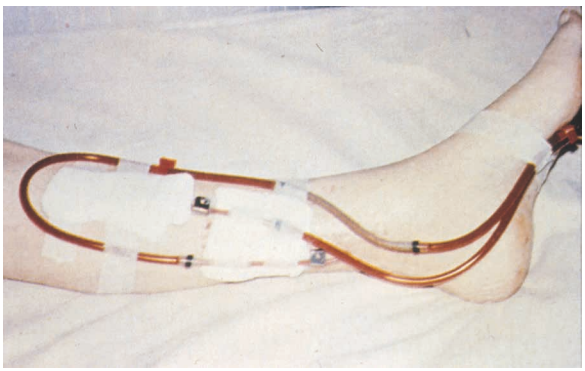


Figure 1
An example of an arteriovenous shunt that was created by the surgical team for a patient who required chronic haemodialysis in the mid-1970 to 80s.

Similarly, the first HD access was performed by Georg Haas in 1924 using glass cannula to obtain blood from the radial artery and cubital vein. However, the true landmark maintenance HD access was born in USA in 1960 by Scribner, who inserted two thin-walled Teflon cannula with tapered ends into the radial artery and cephalic veins, with the external ends connected by a curved Teflon bypass tube. In our department, between the mid-1970s and 1980s, temporary shunts for acute HD were placed by nephrologists in the radial artery and nearby vein while shunts for chronic HD were placed by the surgical teams (Figure 1). Although the Scribner shunt eventually fell out of favour due to its high rates of thrombosis, infection and dislodgement, it served as the stepping-stone towards the development of our current day HD arteriovenous fistulas and grafts. Currently all arteriovenous fistula and grafts performed in SGH are created by dedicated vascular surgeons with excellent success rates and outcomes. The nephrologists continue to be the ones to place both acute and chronic HD catheters for patients when HD is indicated.

Figure 2
The treatment room within ward 42 where catheter insertions and renal biopsies were performed. It has been converted to a storeroom. The original electrical, oxygen and code blue panels (black arrow) were not dismantled.

Figure 3
The first interventional suite (INS 1) was setup in 2007 for the performance of non-tunneled haemodialysis catheter procedures and renal biopsies.

Many of the renal procedures were initially performed at the bedside. Needless to say, there were many difficulties, including the lack of proper equipment in different wards, unfamiliarity of different staff nurses, and the lack of a controlled sterile environment. The procedures were eventually migrated to the treatment area (Figure 2) within Ward 42 (Block 4 Level 2), and eventually with the growth of nephrology in SGH, they found a new home in a dedicated area called the Interventional Nephrology Suite 1 (Figure 3) which was set up in 2007 to perform catheter insertions and renal biopsies.

As the dialysis population continued to grow, it was recognised that a functioning access was critical to the delivery of life-saving renal replacement therapy, and that a functioning access in both HD and PD continued to be the Achilles heel of renal replacement therapy. In the year 2000, the American Society of Diagnostic and Interventional Nephrology was formed to promote excellence in dialysis access care to improve outcomes for patients with kidney disease. It rapidly became the rallying point for nephrologists to re-focus their attention on dialysis access care. Inspired by the ability of nephrologists in overseas academic centres to perform endovascular procedures to salvage failing or thrombosed vascular access under X-ray guidance and insert long-term peritoneal dialysis catheters, the Department of Renal Medicine embarked on this journey with the aim of improving the lives of dialysis patients in Singapore.

In 2009, our first interventional nephrologist, Dr Yang Wen Shin, was trained under the Human Manpower Development Programme (HMDP). Upon his return, he started performing endovascular procedures together with the interventional radiologists in the interventional radiology centre, carrying on till 2012. In 2011, Dr Tan Chieh Suai started the acute start PD programme by teaming up with the vascular surgeons to insert PD catheters at the Ambulatory Surgical Centre (ASC). This helped to decrease the waiting time for PD catheters in the hospital as they were able to tap on unused sessions in the ASC to fast track insertions. In 2012, Dr Tan was awarded the SingHealth HMDP to pursue training in diagnostic and interventional procedures in the United States of America. Upon his return from training in 2013, plans were made to set up a multidisciplinary interventional nephrology suite and programme that

Figure 4
Interventional Nephrology Suite 2 (INS 2) was set up in 2015. It is equipped with fluoroscopy equipment for the performance of endovascular interventions.

Figure 5
2017 INS 2 entrance door to recovery area for patient who had undergone intervention procedures.

was dedicated to vascular access care in Singapore. A key strength of this collaboration was that the various disciplines could closely share viewpoints and experiences in different aspects of both the surgical and medical aspects of management of our complex renal patients. This plan was finally realised in 2015 (Figure 4 to 6) when the angiography suite was completed and started performing interventional procedures to salvage malfunctioned HD accesses. The interventional nephrology programme was also one of the first to integrate the skills of Advance Nurse Practitioners (APN) in SGH. Ms. Ng Li Choo was our first vascular access APN. Together with the rest of the APNs in the department, they attended to patients who presented themselves at the emergency department with dysfunctional access, including assessment and listing of patients for procedure.

To date, the multidisciplinary service comprising interventional radiologists, vascular surgeons and nephrologists perform approximately 1,000 endovascular procedures in the interventional

Figure 6
Recovery area for patient who had undergone interventional procedures in INS 2.

nephrology suite each year. Building on the strength of cross-disciplinary collaboration, the interventional nephrology service has embarked on several initiatives to improve the outcomes of endovascular procedures in dialysis patients. These include quality improvement initiatives to decrease both waiting time for procedures and length of hospitalisation for patients admitted with blocked access, such as via protected procedural slots for vascular access cases, and standardised protocols to ensure that patients for procedures are correctly prepared the night before. Other ongoing initiatives include hotlines for dysfunctional vascular accesses and tele-health services for patients in the National Kidney Foundation dialysis centres, where patients with vascular access issues, such as dropping access flows, can easily consult a nephrologist and make plans for monitoring or early elective angioplasty, all while avoiding the hassle of a visit to the emergency department which adds stress to both patient and the healthcare system.

Improving outcome through research has also been one of the pillars of the interventional nephrology service. We have conducted pilot studies on the role of drug-coated balloons in dialysis access angioplasties, imaging protocols for angioplasties, novel devices to aid dialysis access cannulation, and obtained grants from the National Kidney Foundation and Singapore-Massachusetts Alliance for Research and Technology to build stents for dialysis access interventions.

The training and education of the next generation of interventional nephrologists (Figure 7) is also another pillar of the interventional nephrology

Figure 7
The pioneering batch of interventional nephrologists and radiographer. (From left to right) Dr Pang Suh Chien, Dr Tan Ru Yu, Dr Tan Chieh Suai, Mr. Tsai Fu Chieh.

service. Dr Darren Lee, Dr Tan Ru Yu, Dr Pang Suh Chien and Dr Alvin Tng are our homegrown talents trained in interventional procedures. Dr Tan Ru Yu was awarded the SingHealth HMDP to pursue training in diagnostic and interventional procedures in Australia in 2017. Upon her return, she started the ultrasound surveillance clinic to further enhance the outcome of endovascular interventions in our centre. Today, the IN (Interventional Nephrology) programme has hosted observership programmes and hands-on fellowships for nephrologists in the region. Additionally, the biennial interventional nephrology workshop started by the department in 2016, focusing on vascular access issues and providing hands-on opportunities, has grown in strength and attendance over the years, attracting participants both locally and from the region (Figure 8 and 9). Our IN service has also been invited as speakers for regional conferences, including the Congress of Asian Pacific Society of Dialysis Access (APSDA) and Dialysis Access Synergy (DASY), to name a few.

Today, the Interventional Nephrology programme and service is one of the flagship programmes of the Department of Renal Medicine at SGH. Our commitment to excellence in clinical service, research and education (Figure 10) will continue to push the programme to greater heights.

Figure 8
Associate Professor Tan Chieh Suai providing a procedural demonstration to participants at the Interventional Nephrology Workshop.

Figure 9
The Interventional Nephrology Workshop at SGH has attracted participants from countries around the region to learn the highest standards of interventional nephrology procedures.

Figure 10
Associate Professor Tan Chieh Suai demonstrating the insertion of a central venous catheter under ultrasound guidance to junior residents from the SingHealth Internal Medicine Residency Programme in 2017.

Critical Care Nephrology

Dr Manish Kaushik, Senior Consultant
Director of Critical Care Nephrology

Acute Kidney Injury (AKI), previously referred to as Acute Renal Failure (ARF), is a well-established nephrological occurrence in patients admitted to hospital and may require dialysis support. In fact, the first instance of dialysis in Singapore, performed on 5 July 1961, was on a patient with ARF.[1] Management of AKI has been an integral service provided by the Department of Renal Medicine since its inception in 1973. Over the years, the burden of AKI at SGH has increased. In a recent epidemiological study at SGH, 422 episodes of AKI were observed in 404 patients over 100 days. Furthermore, 32.6% of referrals were from acute care units and overall, 27% of patients with AKI required dialysis support.[2] Having anticipated this challenge, and to ensure provision of state-of-the-art, efficient and safe service to patients, the department had planned for and supported training of personnel in different aspects of Critical Care Nephrology (CCN) over the years. In addition, the department also equipped itself with the latest advances in CCN technology to care for these increasingly complex patients. A culmination of these efforts has helped the department in establishing a CCN service arm that encompasses AKI and Extracorporeal Blood Treatment (ECBT) and Extracorporeal Organ Support (ECOS) service (Figure 1), while also providing a platform for education and research catering to local and regional healthcare professionals.

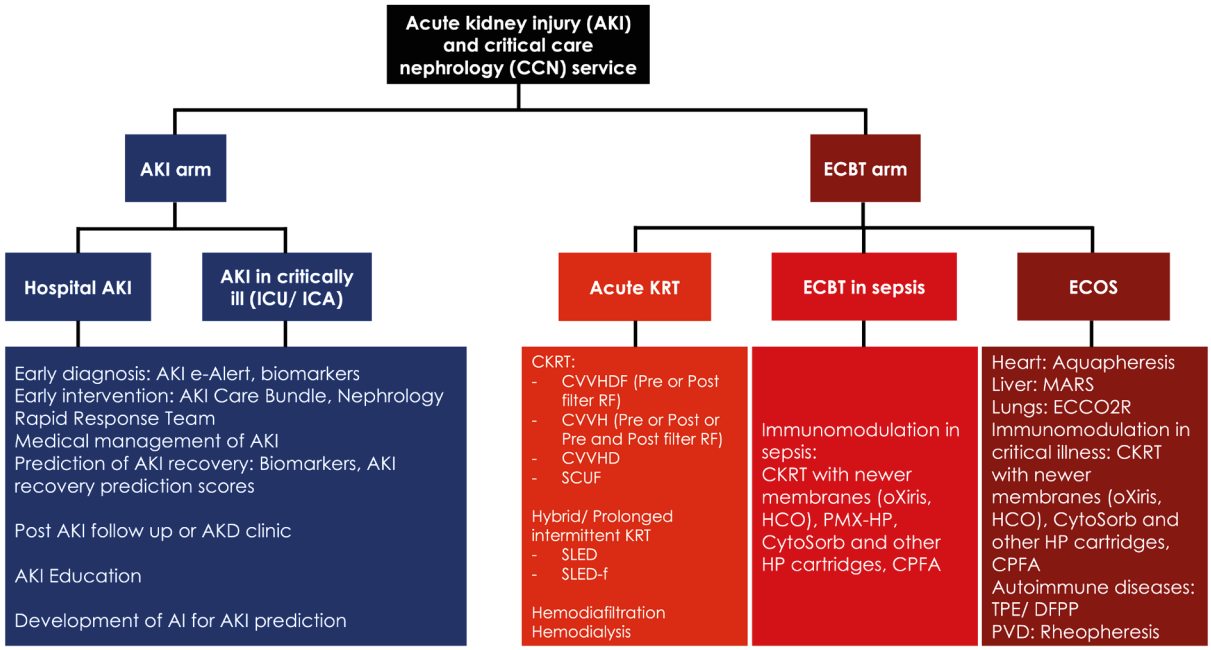
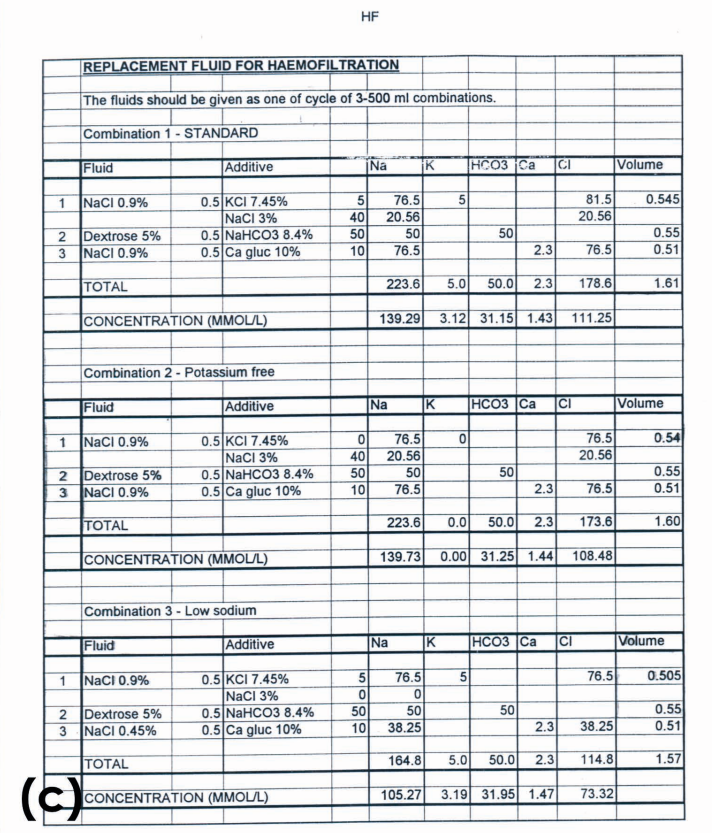


Figure 1
Overview of Acute Kidney Injury (AKI) and Critical Care Nephrology (CCN) service at the Department of Renal Medicine of SGH. AKD: Acute Kidney disease.

CPFA: Coupled plasma filtration adsorption
CKRT: Continuous kidney replacement therapy
CVVHD: Continuous venovenous haemodialysis
CVVHDF: Continuous venovenous haemodiafiltration
CVVH: Continuous venovenous haemofiltration
DFPP: Double filtration plasmapheresis
ECBT: Extracorporeal blood treatment
ECOS: Extracorporeal organ support
ECCO2R: Extracorporeal carbon dioxide removal
HCO: High cut-off membranes
HP: Haemoperfusion
MARS: Molecular adsorbent recirculating system
PMX-HP: Polymyxin haemoperfusion
SCUF: Slow continuous ultrafiltration
SLED: Slow low efficiency dialysis
SLED-f: Slow low efficiency diafiltration
TPE: Therapeutic plasma exchange



HF

REPLACEMENT FLUID FOR HAEMOFILTRATION

The fluids should be given as one of cycle of 3-500 ml combinations.

Combination 1 - STANDARD

	Fluid		Additive		Na	K	HCO3	Ca	Cl	Volume
1	NaCl 0.9%	0.5	KCl 7.45%	5	76.5	5			81.5	0.545
			NaCl 3%	40	20.56				20.56	
2	Dextrose 5%	0.5	NaHCO3 8.4%	50	50		50			0.55
3	NaCl 0.9%	0.5	Ca gluc 10%	10	76.5			2.3	76.5	0.51
	TOTAL				223.6	5.0	50.0	2.3	178.6	1.61
	CONCENTRATION (MMOL/L)				139.29	3.12	31.15	1.43	111.25	

Combination 2 - Potassium free

	Fluid		Additive		Na	K	HCO3	Ca	Cl	Volume
1	NaCl 0.9%	0.5	KCl 7.45%	0	76.5	0			76.5	0.54
			NaCl 3%	40	20.56				20.56	
2	Dextrose 5%	0.5	NaHCO3 8.4%	50	50		50			0.55
3	NaCl 0.9%	0.5	Ca gluc 10%	10	76.5			2.3	76.5	0.51
	TOTAL				223.6	0.0	50.0	2.3	173.6	1.60
	CONCENTRATION (MMOL/L)				139.73	0.00	31.25	1.44	108.48	

Combination 3 - Low sodium

	Fluid		Additive		Na	K	HCO3	Ca	Cl	Volume
1	NaCl 0.9%	0.5	KCl 7.45%	5	76.5	5			76.5	0.505
			NaCl 3%	0	0					
2	Dextrose 5%	0.5	NaHCO3 8.4%	50	50		50			0.55
3	NaCl 0.45%	0.5	Ca gluc 10%	10	38.25			2.3	38.25	0.51
	TOTAL				164.8	5.0	50.0	2.3	114.8	1.57
	CONCENTRATION (MMOL/L)				105.27	3.19	31.95	1.47	73.32	

(c)

Figure 2
Hospital compounded replacement fluid for continuous kidney therapy.

Evolution of Critical Care Nephrology at SGH

A breakthrough in the management of patients with AKI was the introduction of Continuous Renal or Kidney Replacement Therapy (CRRT or CKRT) in 1977 by Dr Peter Kramer.[3] The evolution from "adaptive technology" to "integrated technology" over the years eventually led to the launch of the first-generation PRISMA by Gambro in 1994, a CRRT platform designed specifically to deliver acute dialysis in ICU environments.[4] Development in technology, membranes, techniques and modalities allowed improved safety and performance, and expanded the areas of application of extracorporeal therapies to cardiac, liver and pulmonary support. CCN, a multidisciplinary branch of medicine to deal with medical issues at the crossroads of intensive care and nephrology, was thus born in 1998.[5]

The Department of Renal Medicine at SGH has kept abreast with developments in other parts of the world and was quick to adopt these recent advances into its clinical practice. The evolution of CCN in SGH can be looked at in four major periods spanning four decades: 1981 to 1990, 1991 to 2000, 2001to 2010, and 2011 to 2020.

1981-1990:

In the early years AKI service was provided as part of routine nephrology work and dialysis for acutely unwell patients was performed using conventional chronic dialysis equipment available at that time. From the records, we can trace back the history of CRRT at SGH to 1985, when continuous arteriovenous haemofiltration (CAVH) was first implemented. The first ever manuscript describing CRRT in Singapore, authored by Professor Woo Keng Thye and Associate

Professor Lina Choong, who was a Registrar then, was published in the Singapore Medical Journal in 1987.[6] In this article they described how continuous arterio venous haemofiltration (CAVH) was employed for patients with ARF who had unstable circulation or severe hypotension, the commonest category of such patients being post cardiac surgery patients. In those early years, there were no commercially available fluids for CRRT. Fluids needed to be compounded by the pharmacy or physicians themselves in the ICUs. Associate Professor Lina Choong was one of those responsible for the development of a variety of CRRT fluid compounding formulas. The compounded fluids could be mixed with an aim to achieve the desired solute and fluid control, and thereby allowed "personalised" CRRT prescription for each patient (Figure 2).

1991-2000:

Under the headship of Professor Woo Keng Thye, CRRT continued to develop at SGH in the 1990s. Like in other parts of the world, SGH had to adapt machines to deliver CRRT. The first of such machines was the Gambro AK-10, the first computerised controlled dialysis machine (Figure 3a). The peristaltic pump-driven blood flow allowed angioaccess via double lumen vascular catheters, thereby minimising complications associated with cannulation of larger arteries. With time, the department acquired the first-generation Baxter BSM-22 machine to deliver CRRT (Figure 3b). Ultrafiltration with the machines mentioned was regulated by adjusting the height of the haemofilter with respect to the patient and by using a closed-system urine measurement bag with urine meter. Another development was the use of commercially available peritoneal dialysis fluid to serve as CRRT fluid. These advances made CRRT more accessible to the critically ill ICU patients. As the technology evolved, SGH acquired the second-generation PRISMA machines in 1999 for CRRT and they served as the work horse for almost two decades till 2015, over which time they were gradually replaced by the third generation CRRT machines (Figure 4). Concomitant to the birth of CCN in 1998, SingHealth awarded the Health Manpower Development Programme (HMDP) scholarship to Associate Professor Tan Han Khim, to train in "Critical Care Nephrology" under Professor Rinaldo Bellomo at Austin Hospital, Hiedelberg in Victoria of Australia from 1998-1999. Associate Professor Tan Han Khim

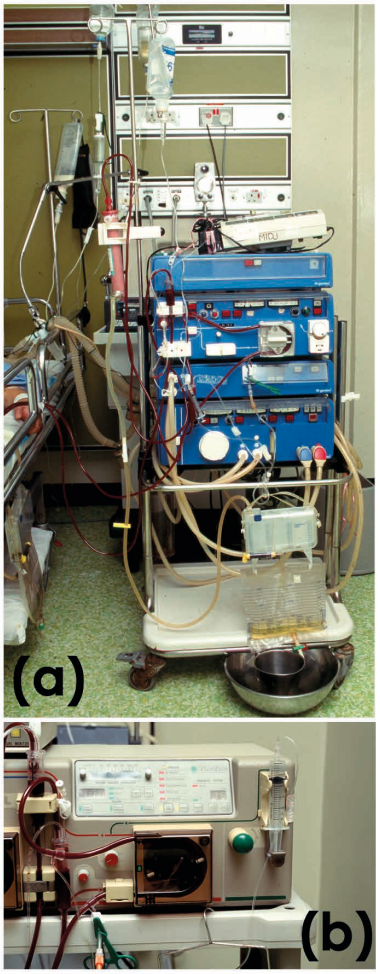


Figure 3
a) Gambro AK-10 dialysis machine
b) Hospal BSM-22 continuous kidney replacement therapy machine

was the first nephrologist in Singapore to be trained in CCN. In those early years and the years to follow, the CCN service owed much of its evolution to Associate Professor Lina Choong, who was the Director of the Haemodialysis Services and oversaw technological support provided to the CCN arm.

2001-2010:

The first decade of the 21st century saw the department make significant advancements and introduce new therapies under the headship of Associate Professor Wong Kok Seng. Upon his return from HMDP, Associate Professor Tan Han Khim successfully applied for a National Medical Research Council (NMRC) grant for CRRT research in 2001 and SingHealth Research grant to establish Molecular Adsorbent Recirculation System (MARS) liver dialysis service in 2002. During this period, he pursued

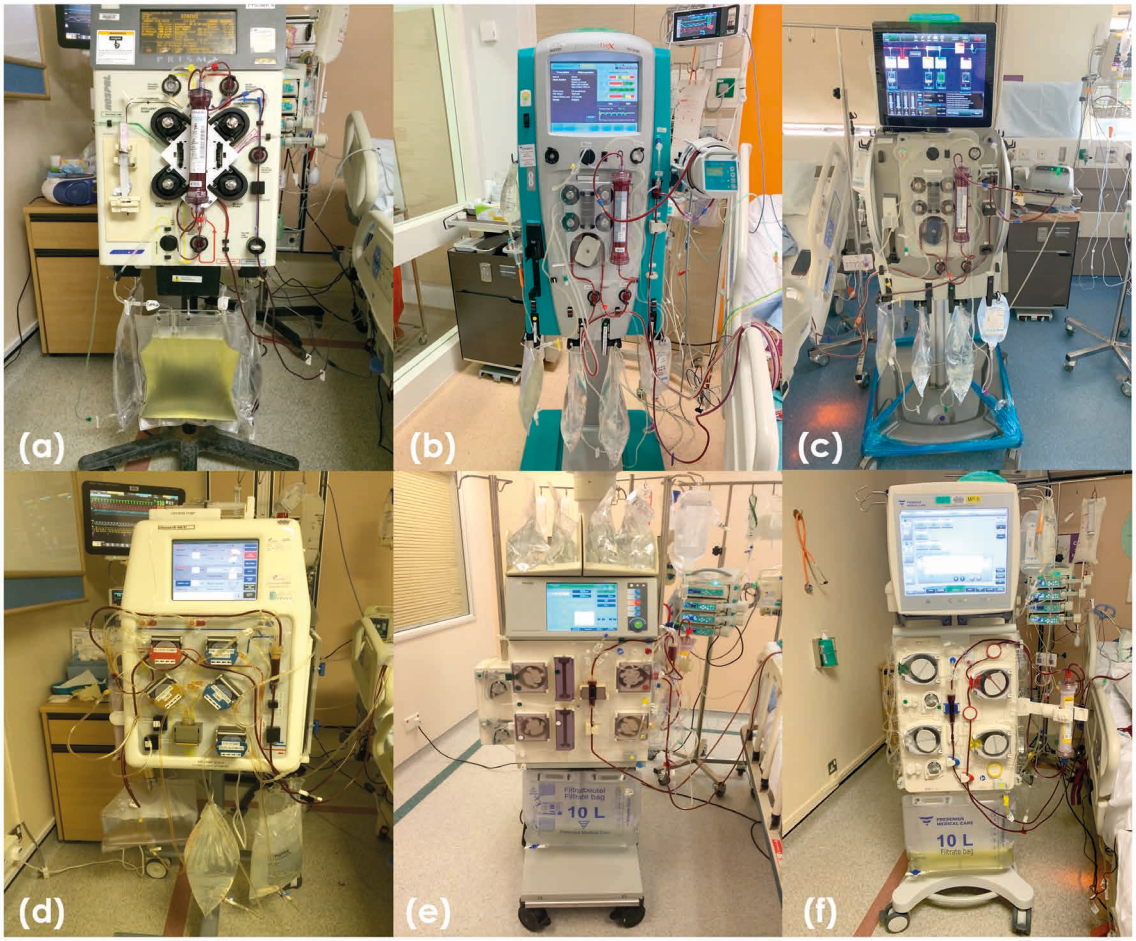


Figure 4
Different generations of continuous kidney replacement machines used at SGH:

a) Hospal PRISMA (second generation)
b) Baxter Prismaflex (third generation)
c) Baxter Prismax (fourth generation)
d) Infomed HF440 (third generation)
e) Fresenius Medical Care multiFiltrate (third generation)
f) Fresenius Medical Care multiFiltrate Pro (fourth generation)

active research in CRRT and MARS and published numerous articles on the same.[7,8] In recognition of his contributions to the field he was conferred Doctor of Medicine (MD) by the National University of Singapore in 2005. He was also the primary investigator in Singapore for the I.M.P.A.C.T. (Intermittent Modular Plasma Adsorption of Cytokines and Toxins) trial in 2009, which looked at the role of immunomodulation in patients with sepsis by Coupled Plasma Filtration Adsorption (CPFA), a modified extracorporeal blood purification technique. Additionally, SGH Department of Renal Medicine introduced membrane separation based therapeutic plasma exchange service in 2003, to treat patients with autoimmune disorders affecting kidney and kidney transplant recipients. Also, during this period, SGH upgraded the PRISMA CRRT platform to the third-generation Prismaflex machines (Gambro/Baxter) in 2006. During the above periods, given the fact there was only one trained CCN personnel, CCN was still a part of routine service provided by the department. The model of service delivery involved Nephrology providing dialysis support and expert advice on management of AKI in the ICUs. The ongoing advances and education in CCN at SGH stoked existing dreams of training nephrologists to pursue a career in CCN.

2011-2020:

The current decade has been particularly exciting for CCN in SGH as it comes of age and as the Department of Renal Medicine cements its credentials in CCN. The department, under the headship of Professor Chan Choong Meng and the SingHealth HMDP scholarship together gave support to Dr Manish Kaushik to pursue a Fellowship in "Critical Care Nephrology and Cardiorenal Syndromes" under

Figure 5
Renal Intermediate Care Area (RICA).
Eight-bedded RICA, including 2 beds for isolation and capability for haemodynamic monitoring, non-invasive ventilation and various extracorporeal blood treatment therapies including continuous kidney replacement therapy.

the mentorship of Professor Claudio Ronco at the International Renal Research Institute Vicenza (San Bortolo Hospital) from 2011-2012. Upon his return, and in keeping with the department's vision under the headship of Associate Professor Marjorie Foo, he placed his focus on elevating CRRT at SGH to become a "centre of excellence" in the specialty and to establish SGH as a centre for CCN and education and training. The goals were systematically pursued by firstly, intensifying the existing training programme for nurses and doctors in CRRT. Secondly, prescription, monitoring and delivery of CRRT were standardised and a protocol for regional citrate anticoagulation for CRRT was introduced in 2014. Additionally, CCN service established a collaborative working partnership with the intensive care services and especially the SGH Burns Centre. Also, the upgraded Renal Intermediate Care Area (Renal ICA), which became operational in 2012, allowed extension of CRRT beyond the realm of ICUs (Figure 5). In 2017, CRRT prescription and monitoring was transferred from manual to online on the electronic medical records (EMR) of patients (Figure 6). This proved to be a major step as it allowed real-time audit of the therapy and facilitated planning for future quality improvement and research endeavours. In addition, many new milestones in extracorporeal therapies and organ support were established during this decade and some of the major ones are as recorded in the next section. The highlighted achievements translated into the sharing of experience by SGH with many countries in the region.

Despite the rapid progress in the field of extracorporeal therapies, an area that needed further development was hospital AKI outside of the ICUs. This became even more apparent as a prospective observational study performed by the department in 2015-2016 highlighted the burden of AKI at SGH.[2] Based on this study, 75% of AKI were found to have developed in patients admitted to non-renal specialties and 67.4% of referrals for the condition

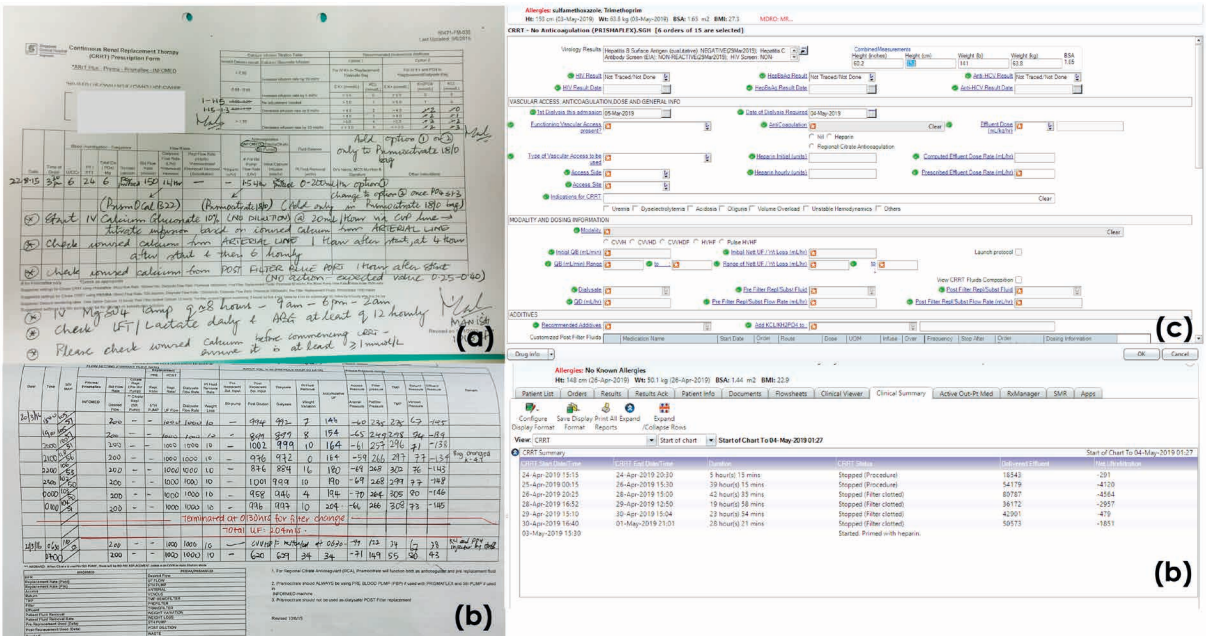


Figure 6
Evolution of continuous kidney replacement therapy prescription and monitoring chart.
a) manual continuous kidney replacement therapy prescription (pre-2017)
b) manual continuous kidney replacement therapy monitoring chart (pre-2017)
c) online continuous kidney replacement therapy prescription (since 2017)
d) online continuous kidney replacement performance record of individual patient (since 2017)

were from general wards or non-acute care areas. To optimise the care of hospitalised patients with AKI, the department supported Dr Teo Su Hooi for the SingHealth HMDP grant to gather experience in "Improving Care and Outcomes of Hospital and Community-Acquired AKI using Information Technology and Bundle Care Delivery System". Dr Teo pursued her HMDP in 2017-2018 under the guidance of Professor Zoltan Endre at University of New South Wales in Sydney, Australia. Upon her return, Dr Teo has worked to set up an AKI electronic-alert system to allow early diagnosis and recognition of AKI and an AKI Care Bundle to be triggered by an AKI e-Alert, both for the general management of patients with AKI. This important project intends to decrease the onset of new end stage renal failure (ESRF) post-AKI. In addition, there are plans to open up post-AKI clinics to follow through and optimise post-AKI care and identify early patients progressing to chronic kidney disease or ESRF.

The Current Status of CCN at SGH

The CCN service in its current model was started in 2015. It has four dedicated physicians and three nurses that help deliver this service and educate and train residents, physicians and nurses. The CCN team works very closely with the haemodialysis team as the two teams share common resources in terms of machines, portable reverse osmosis units, manpower and so on.

Clinical Services

The current clinical services provided by the CCN are as outlined in Figure 1. Essentially the CCN service has an AKI arm and an extracorporeal blood treatment (ECBT) and extracorporeal organ support (ECOS) arm. Between them, the two arms provide comprehensive care for patients with AKI including early diagnosis, non-dialysis management of AKI, diverse spectrum of blood treatment therapies and post-AKI follow up. In addition, the CCN supports plasma therapies including membrane separation therapeutic plasma exchange (TPE), double filtration plasmapheresis (DFPP), immunoadsorption (IA) and coupled plasma filtration and adsorption (CPFA) (Figure 7, Figure 8 and Figure 9). In 2019, Medical Board SGH approved further manpower support to CCN service to facilitate efficient and safe delivery of various therapies and to decrease the impact of increasing workload on non-acute dialysis care.

Date	Significant milestones in extracorporeal therapies in Critical Care Nephrology at SGH
1985	Establishment of Continuous Renal Replacement Therapy (CRRT) service at SGH
2002	Molecular Adsorbent Recirculating System (MARS) for acute liver failure
2003	Membrane Separation Therapeutic Plasma Exchange
2009	Coupled Plasma Filtration Adsorption (CPFA) for sepsis
16 January 2013	High Volume Hemofiltration (HVHF) for sepsis
6 September 2014	CRRT with regional citrate anticoagulation (RCA) in patients with burns and acute kidney injury
7 February 2017	CRRT prescription and monitoring migrated online for SGH
15 March 2017	CRRT prescription and monitoring migrated online for NHCS
16 February 2018	CRRT with arterio-venous fistula (AVF) as vascular access
25 March 2018	CRRT with RCA in a patient on extracorporeal membrane oxygenation (ECMO)
4 April 2018	Hemoperfusion using Polymyxin coated hemoadsorptive column for rapidly progressive interstitial lung disease
11 April 2018	Concurrent CRRT with centrifugal plasma exchange (in parallel configuration)
11 May 2018	Hemoperfusion using Polymyxin coated hemoadsorptive column for gram negative sepsis
28 September 2018	oXiris hemofilter for sepsis associated AKI
26 October 2018	RCA for Double Filtration Plasmapheresis (DFPP) in ABO-incompatible kidney transplant
28 January 2019	DFPP for immune mediated neurological diseases
23 February 2019	Extracorporeal Carbon-dioxide Removal (ECCO2R) with Novalung / Prismaflex
9 July 2019	Use vasopressor norepinephrine for hemodynamic support in Renal ICA
20 September 2019	Concurrent CRRT and membrane separation therapeutic plasma exchange (in series parallel configuration)
30 April 2020	RCA for membrane separation therapeutic plasma exchange

Selected Milestones in Critical Care Nephrology at SGH.

Currently, all referrals for AKI are done on EMR and responded to by the CCN team or the on-call senior resident. All patients with AKI who are admitted to ICU (Medical, Surgical, Burns, Cardiac, Cardiothoracic, Neurology and Neurosurgery), Intermediate Care Area (ICA) / High Dependency Units (HDU) are reviewed daily by the CCN service. SGH CCN team also works in collaboration with the intensivists in Medical and Surgical and other ICUs to deliver the best care to patients. At the time of this update, SGH has a fleet of 27 machines (17 Prismaflex, 8 multiFiltrate Pro and 2 Prismax), for CRRT and two machines (Infomed HF440) for plasma therapies and haemoadsorptive therapies. CRRT and ECBT/ ECOS conducted within the ICUs are prescribed by the nephrologists. CRRT in ICUs is performed by the ICU nurses, whereas CRRT in the Renal ICA and all other specialised haemoadsorptive and plasma therapies are performed by dialysis nurses.

SGH is very uniquely placed as it shares the campus with the National Heart Centre Singapore (NHCS), National Cancer Centre Singapore (NCCS) and SGH Burns Centre. The shared campus has allowed successful working relationships with these institutes and has helped unique applications of the extracorporeal therapies to be developed. For example, the NHCS is a high-volume centre for extracorporeal membrane oxygenation (ECMO). Additionally, NHCS has a well-established heart failure service and is the national centre for ventricular assist device (VAD) support. This has allowed us to acquire immense experience in managing AKI and performing CRRT in patients on ECMO and VAD (Figure 10). Also, the Department of Renal Medicine at SGH was a participating department for the national grant to study the role of peripheral ultrafiltration in the management of diuretic resistant heart failure.

Our collaboration with the SGH Burns Centre has been very productive in terms of patient care and we have recently published and shared our experience of dialysis support in critically ill severe burn injury patients. SGH also has a very strong bone marrow, liver and heart-lung transplant services. These patients provide us unique opportunities and enrich the experience of the CCN service. This also provides the senior residents with an interest in CCN with a variety of learning experiences.

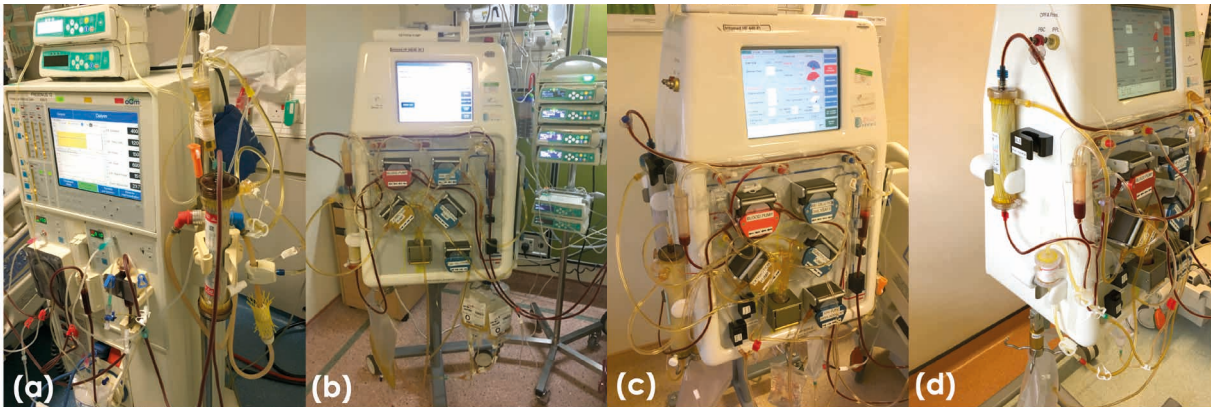


Figure 7
Various plasma therapies performed by Department of Renal Medicine at SGH.
a) Membrane separation therapeutic plasma exchange using Fresenius Medical Care 4008 S dialysis machine
b) Membrane separation therapeutic plasma exchange using Informed HF440 machine
c) Double filtration plasmapheresis using Infomed HF440 machine
d) Immunoadsorption with Glycosorb immunoadsorption column using Infomed HF440 machine

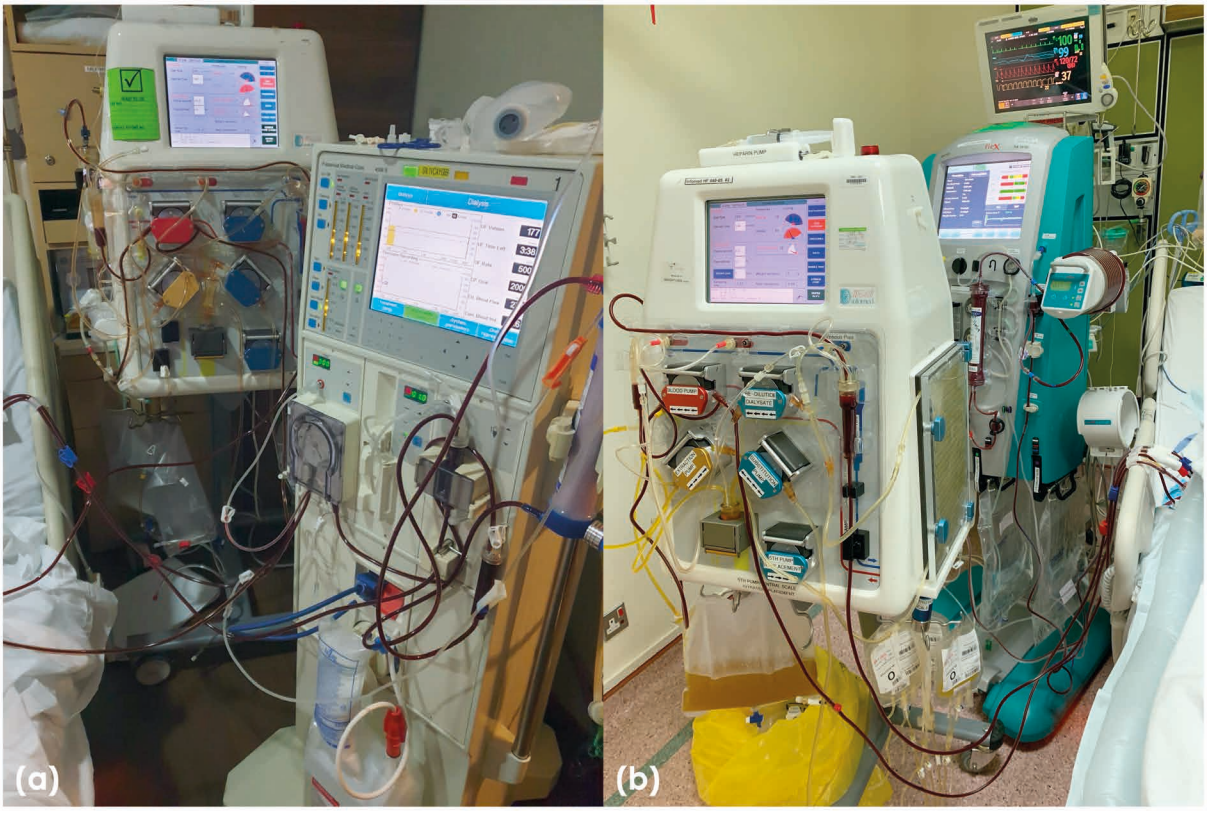


Figure 8
Concurrent therapies performed by Department of Renal Medicine at SGH.
a) Concurrent membrane separation therapeutic plasma exchange using Infomed HF440 machine and haemodialysis using Fresenius Medical Care 4008 S dialysis machine.
b) Concurrent membrane separation therapeutic plasma exchange using Infomed HF400 machine and continuous kidney replacement therapy using Baxter Prismaflex machine.

Figure 9
Extracorporeal organ support at SGH.
a) Molecular adsorbent recirculating system (MARS) for acute liver failure performed by Associate Professor Tan Han Khim and SSN Muhammad Bin Sulaiman.
b) Coupled plasma filtration and adsorption for immunoadsorption for immunomodulation in sepsis.
c) Polymyxin haemoperfusion for immunomodulation in sepsis with gram negative bacteria.
d) Extracorporeal carbon dioxide removal.

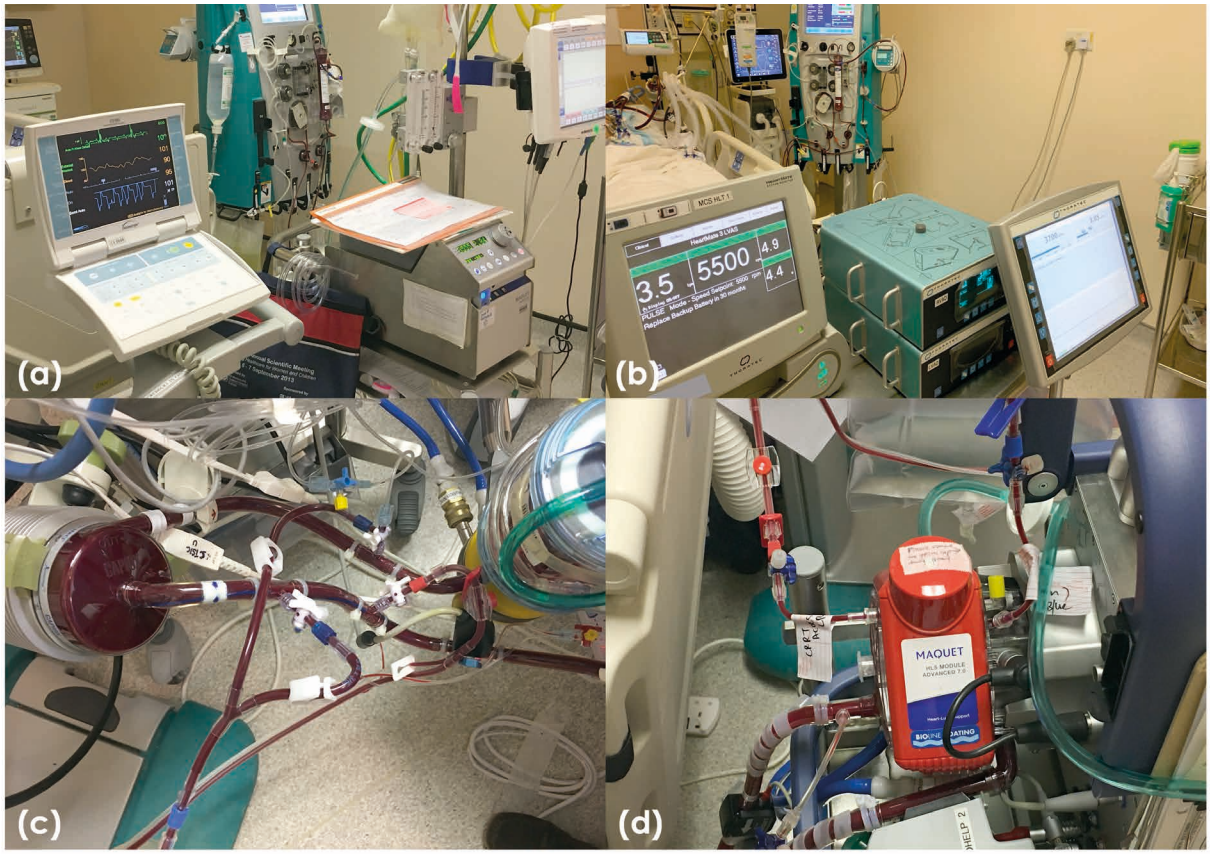


Figure 10
Continuous kidney replacement therapy in cardiac and cardiothoracic intensive care units.
a) Continuous kidney replacement therapy in a patient on intra-aortic balloon pump and extracorporeal membrane oxygenation.
b) Continuous kidney replacement therapy in a patient with left and right ventricular assist devices.
c,d) Continuous kidney replacement therapy integrated into extracorporeal membrane oxygenation circuit.

Education

Education is one of the core beliefs of the CCN team. The education efforts are aimed at all levels including residents, nurses, nephrologists and intensivists in Singapore and the region (Figure 11). The faculty is invited to speak at various regional and international meetings and participate in training programmes and workshops. The faculty of CCN has a strong pedigree in education. Associate Professor Tan Han Khim is the Programme Director for the SingHealth Senior Residency Programme in Nephrology. Dr Manish is the immediate past Chair of the Programme Evaluation Committee and Core Faculty of the Residency Programme. Dr Teo Su Hooi is a Core Faculty member of the Nephrology Residency Programme in addition to her duties in the Internal Medicine Junior Residency Training Programme. Senior Nurse Clinician and Advanced Practice Nurse Ng Li Choo Michelle runs the SGH CRRT Nurses Education and Training Programme, which has since been passed over to the Nursing Education Division (Figure 12).

The faculty conducts regular teaching sessions for both the junior and senior residents in Renal Medicine and Critical Care as part of the Residency Teaching in Pulmonary and Critical Care Medicine and SingHealth Anaesthesia Residency Programme. To further facilitate education efforts there are various courses held at the national and regional level in collaboration with Singapore Society of Nephrology (SSN), for example, courses in CRRT & ECBP. The faculty has also been invited to deliver lectures in regional and international meetings like the annual Asia Pacific AKI and CRRT meeting, Vicenza course

Figure 11
Education activities of critical care nephrology team.
a) Nurse Clinician Amy Lim teaching basics of continuous kidney replacement therapy to nurses in Bangladesh.
b) Senior Nurse Clinician (APN) Michelle Ng teaching basics of continuous kidney replacement therapy to physicians and nurses during a State of the Art Nursing Course.
c) Associate Professor Tan Han Khim and Nurse Clinician (APN) Maslinna Binte Abdul Rahman teaching basics of plasma therapies to physicians and nurses at the Singapore Society of Nephrology Continuous Kidney Replacement Therapy and Extracorporeal Blood Purification Course.
d) Dr Teo Su Hooi teaching basics of prolonged intermittent kidney replacement therapy to physicians and nurses at the State of the Art Nursing Course.
e) Dr Manish Kaushik showing the various machines and treatments to an overseas physician observer at SGH.

in AKI and CRRT and International Symposium of Intensive Care and Emergency Medicine in Brussels, and to share with and/or train physicians and nurses in Bangladesh, Brunei, China, Fiji, India, Malaysia, Philippines and Vietnam.

The CCN faculty regularly conducts teaching sessions for nurses as part of the SGH CRRT Nursing Course (conducted every six months), Nanyang Polytechnic Advanced Diploma in Nursing, and National University of Singapore Advanced Critical Care Nursing. These sessions are in addition to the regular in-service teaching sessions conducted in SGH.

The aforementioned coordinated and sustained efforts have also helped SGH to set up a Singapore Medical Council (SMC) approved Fellowship in Critical Care Nephrology, that allows applicants to experience the whole spectrum of AKI and CCN over a three to 12-month period. In addition, the SGH CRRT Observership Programme has allowed industry to partner SGH to facilitate education and training in CCN within the region.

Figure 12
Dr Manish Kaushik with Nurse Clinicians Amy Lim and Michelle Ng who have helped drive many of the dialysis related initiatives of the department including critical care nephrology.

Research

Over the years, research has been a passion for the faculty and despite the challenges posed by their clinical workload, they have consistently contributed to the science and literature. The areas of research have focused on understanding the epidemiology of AKI, delivery and anticoagulation of ECBP therapies, and the use of adsorptive therapies in sepsis.[2,8,9] We have published in the field of CRRT timing and complications, extracorporeal carbon dioxide removal and AKI outcome and concurrent therapies.[10-13] Examples of the collaborative efforts were the publication of our experience with management of patients with severe burns injury with RRT, role of peripheral ultrafiltration in diuretic resistant heart failure, and case reports published on ECOS with CRRT and TPE in patients with thyroid storm and multi-organ failure.[14-19] In addition, CCN faculty and residents have made many oral and poster presentations at numerous meetings.

Awards and Merits

The ongoing work of CCN service has received recognition through various awards and merits. Amongst the notable awards, the faculty have won multiple Best Faculty awards for their contributions in education. CCN was an integral part of the SGH Burns Centre team that won the Best Team Award (Clinical Improvement) at Singapore Health Quality Service Awards (SHQSA) in 2018 for multidisciplinary management of severe burn injury patients (Figure 13). Similarly, Team "Analysis Dialysis" won the Best Team Merit (Clinical Improvement) Award at SHQSA 2020 for its improvisation in blood return protocol for CRRT. The research effort and contribution of Nephrology Senior Resident Dr Liew Zhong Hong was recognised with the Best Mini Oral Presentation Award at the 2nd Asia Pacific AKI & CRRT Meeting held in 2018 in Taipei, Taiwan (Figure 13).

Future Directions

The CCN service will continue in its endeavours to constantly improve the quality of the clinical work, education and research that it delivers. On the clinical side the immediate next step is to establish the AKI e-Alert system hospital-wide to enable early diagnosis and recognition of AKI and thus early initiation of AKI management, with an aim to decrease new onset

ESRF after AKI. This will be aided by the post-AKI follow-up clinic.

Another field SGH CCN aims to embark on is onco-nephrology, especially with regards to acute renal complications in cancer patients. Cancer patients contribute up to 20% of the referrals for AKI, and with ongoing advances in cancer management and increasing survival rates we believe we are rightly positioned to advance ourselves in this field.

We intend to build on the groundwork already done with regards to AKI in heart failure patients on VAD and other mechanical circulatory support devices including ECMO and AKI post cardiac surgery.

The transfer of clinical and RRT data to EMR has opened up further avenues for research that concentrate on quality and precision therapy. There are plans to do further research in the field of anticoagulation for CRRT, quality improvement in CRRT, AKI e-Alert and artificial intelligence in AKI, and CRRT adsorptive technology for sepsis and AKI.

Another field of ECBT that the CCN faculty plans to further their expertise in is membrane separation-based plasma therapies. Given the variety of patients treated at SGH, these therapies are likely to find increasing applications. We plan to enhance our armamentarium with innovative ECBT and extend their use as described in literature. For example, we are planning to extend our DFPP service to neurological patients and rheopheresis for patients with peripheral vascular disease. In addition, work is being done to explore novel ways for immunomodulation in sepsis with adsorption-based ECBT.

Through the Fellowship Programme, we aim to train physicians to become ambassadors of CCN in their respective countries and to build relationships with their centres for future partnerships in AKI and ECBT research.

Figure 13
Awards and merits of the critical care nephrology team.

a) Dr Manish Kaushik with the Singapore General Hospital Burns Centre Team that won Best Team Award (Clinical Improvement) at the 2018 Singapore Health Quality Service Awards (SHQSA).

b) Nurse Clinician Amy Lim and Dr Manish Kaushik with the Intensive Care Nursing Team that won the Best Team Merit Award (Clinical Improvement) at the 2020 SHQSA.

c) Dr Liew Zhong Hong won the Best Mini Oral presentation award at the 2nd Asia Pacific AKI and CRRT Meeting 2018 (Taiwan).

Conclusions

CCN has evolved by leaps and bounds from its formative years and today stands as an integral pillar of the Department of Renal Medicine. CCN has been able to thrive due to the vision and unwavering support of the senior leadership, and the unrelenting hard work of faculty and nurses. The desire to do our best for the patients has been our core thought and the faculty has embraced the latest advancements in the science in order to achieve this. CCN is a classic example of teamwork in practice and the collaborative work we undertake with other disciplines is the best demonstration of this. With many new areas to develop, and young physicians demonstrating keen interest in CCN, the future certainly holds great promise for the specialty of CCN at SGH and beyond.

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Renal Bone Disease

Dr Wong Jiunn, Consultant

SGH was the pioneer hospital in Singapore in providing nephrology services to the whole of the nation. Chronic kidney disease-metabolic bone disorder (CKD-MBD) together with anaemia are two of the most well-known complications of chronic kidney disease (CKD). All nephrologists have the knowledge and ability to manage CKD-MBD as it forms part of nephrology training and in SGH, a large number of patients happen to have issues related to CKD-MBD.

Parathyroidectomy for Advanced Renal Hyperparathyroidism

Caring for this groups of patients often involves practitioners from multiple specialties. Our surgical colleagues are the ones we rely on to perform parathyroidectomy for our patients who have failed medical therapy. Over the years, we have worked with many surgical colleagues with an interest in head and neck surgery, some of whom were Dr Abu Raff, Professor Soo Kee Chee, Dr Dennis Lim, Dr Gerald Tay and the late Dr Jeremy Ng.

Associate Professor Lina Choong was the first person who took up the responsibility of coordinating the care of these patients by establishing a parathyroidectomy clinical care pathway. One of the most feared complication after surgery is the hungry bone syndrome. Post-operative hypocalcemia before starting intravenous calcium through a central line puts the patient at risk of seizures. Anticipating hypocalcemia and using an alkaline phosphatase-based titration protocol for calcium infusion, we have almost eliminated incidents of severe hypocalcemia following parathyroidectomy. The protocol that we developed only required patients in high dependency units for 1 day and have their calcium monitored once per day rather than several times a day. A parathyroidectomy work group comprising surgeons, pharmacists, nephrologists and administrators was formed under her leadership to ensure that care coordination was as seamless as possible. Regular meetings were held to discuss issues related to patients who were undergoing parathyroidectomy. For patients who could not undergo major surgery, alcohol ablation of the parathyroids by interventional radiologists were an alternative therapy to treat renal hyperparathyroidism. Even though multiple sessions were needed, this was a useful alternative for patients with advanced hyperparathyroidism.

I joined this work group soon after I decided to specialise in CKD-MBD. After returning from training in Sydney, I had helped to refine the relevant guidelines further in an effort to prevent occurrences of hypercalcemia. Furthermore, multiple publications have since emerged from our collaboration as a tight-knit multidisciplinary workgroup.

Bone Disease in Transplanted Patients

The success of kidney transplants has dramatically changed the life of many patients suffering from end stage renal failure (ESRF). The first successful kidney transplant in Singapore was performed in 1970 at SGH. By the year 2019, more than 1000 kidney transplants have been performed at the hospital. 50 years on, the kidney transplant programme at SGH is yet growing from strength to strength. With increasing knowledge and experience accumulated over the years, we are now performing more complex transplants, many of which were deemed impossible in the past. Our transplant allograft survival rate has also improved dramatically. However, we are also increasingly seeing long-term side effects related to renal transplantation, bone disease being a major one among them.

Bone disease, being one of the commonest complications of CKD often antedates transplantation, and bone disease post-transplantation is in large part due to pre-existing bone damage acquired during the years of renal insufficiency and dialysis. Renal transplantation is the treatment of choice for ESRF. The restoration of vitamin D synthesis, clearance of phosphate and reduction of parathyroid hormone levels are all beneficial to the bone after transplantation. However, restoration of glomerular function does not always reverse bone disease. New bone disorders may emerge due to post-transplantation factors such as immunosuppressant use and persistent hyperparathyroidism. It has been

Figure 1
Dr Manju Chandran is a senior consultant endocrinologist at SGH and a global key opinion leader in the field of Endocrinology and Bone Metabolism. She set up the Osteoporosis and Bone Metabolism Unit in 2007 and subsequently the multidisciplinary transplant bone osteoporosis clinic in 2008.

reported that 22.5% of kidney transplant recipients experience a fracture during the first five years after kidney transplantation — an incidence that is four times that of the general population.

The focus of the transplant team in SGH has always been to ensure good renal allograft performance as well as patient survival. Though bone disease has long been recognised as a distinct entity post-transplantation, it was not until 2007 that the Director of the Renal Transplant Programme at SGH, Associate Professor Terence Kee, upon realising that management of renal transplant patients should be more holistic decided to include bone health as an integral component of care for these patients. The first clinic dedicated to look after renal transplant patients with regard to their bone health was established by Associate Professor Manju Chandran, one of the few specialists in Singapore at that time with experience in managing metabolic bone disorders (Figure 1). Having moved to Singapore after completing her Fellowship in Endocrinology and Metabolism at University of California San Diego School of Medicine, USA and having worked for three years at Alexandra Hospital, she moved to SGH and had set up the Osteoporosis and Bone Metabolism Unit in the Department of Endocrinology in 2007 with the support of Dr Goh Su Yen, the Head of the Endocrinology Department then. It was in early 2008 that she was invited by Associate Professor Terence Kee to set up a collaborative clinic for post renal transplant bone health care with the support of senior management. A Transplant Bone Health Care Protocol was drawn up and the Renal Transplant Bone Osteoporosis Clinic opened its doors to the first kidney transplant recipient in May of 2008. The clinic started operating once a month out of the LIFE Centre (Lifestyle Improvement and Fitness Enhancement Centre) the goal of the LIFE Centre being to offer one-stop care i.e. Physician, Nurse Clinician, Physiotherapist and Dietitian services to patients with metabolic bone disorders. The clinical observations she drew from her years of treating our Singaporean kidney transplant recipients piqued her curiosity about the differences she was noticing in their bone health as compared to Western populations and this led her to embark on clinical research projects exploring these unique characteristics in our patients. She has since published extensively on the topic of bone health in our transplant population as well as presented and spoken at numerous international congresses on the subject. The Lee Foundation SingHealth Transplant Grant that she was awarded in 2016 enabled the Osteoporosis and Bone Metabolism Unit to purchase the novel Trabecular Bone Score Software that can be applied retrospectively to Dual Energy X-Ray Images to provide a non-invasive index of bone microarchitecture. Her recent publication in Clinical Transplantation, co-authored with colleagues

from the Department of Renal Medicine as well the Department of Nuclear Medicine and PET, highlighted the finding that major osteoporotic fracture rates post renal transplantation in our Singaporean population were lower than that being reported in the West. Why this is so remains to be now explored. Important studies such as these have influenced how bone health in kidney transplant patients are managed in Singapore, as well as have resulted in Western researchers relooking at their own data on fractures post renal transplant.

Despite the interest and work already done by Associate Professor Lina Choong and Associate Professor Manju Chandran, there were still significant gaps in our knowledge of renal transplant bone disease and CKD-MBD. The lack of a dedicated nephrologist with a primary interest in bone disease made timely decision making a challenge. It was with this in mind that I decided to start my own training in the management of bone disease in patients with CKD at Westmead Hospital, Sydney under the mentorship of Professor Grahame Elder in 2013 (Figure 2). Upon my return in 2014 following an enriching fellowship experience in Sydney and under the guidance of both Associate Professor Lina Choong and Associate Professor Manju Chandran, I started a bone clinic at the Transplant Centre, aimed exclusively at looking after kidney transplant recipients, as well as a bone clinic dedicated to looking after patients who had underwent parathyroidectomy for severe renal-related hyperparathyroidism, along with any patient who had difficulties managing CKD-MBD.

As we move forward, the renal bone service aims to continue to improve the lives of our patients. We seek to achieve this by undertaking further research into the area of transplant bone disease and CKD-MBD, with specific focus on the unique characteristics of our local population and their needs. Another goal that we have is to expand the outreach of our educational programmes by training our clinical and allied healthcare professionals in bone health in patients with CKD and post-renal transplant bone diseases. We thus hope to provide the best available, cutting edge holistic health care to every one of our deserving renal patients.

Figure 2
Dr Wong Jiunn is Singapore's first nephrologist to have received dedicated training in managing mineral and bone disorders in chronic kidney disease under Professor Grahame Elder who is a key opinion leader having contributed to the Kidney Disease Improving Global Outcomes (KDIGO) CKD-MBD guidelines among many others.

Chapter 5
Coming Together in Crisis

"I have found that anything that does not work well can be the basis of improvement. Every incident, every patient complaint provides learning of some sort."

- Associate Professor Lina Choong

The Hepatitis C Outbreak

Dr Sobhana DO Thangaraju, Consultant
Deputy Medical Director of the Renal Transplant Programme

The mood was a sombre one. Though it was only four days to Christmas, red, teary eyes filled the room. Heads bowed to observe a minute's silence in respect for the patients who had passed away. Just prior to that, Professor Chow Wan Cheng, Division Chairman of Medicine at that time, had led a dialogue session regarding the Hepatitis C (HCV) outbreak that had paralysed the long running Renal Transplant Programme of SGH. In the midst of the profound sadness, there was a quiet but palpable determination to improve care and make amends to affected patients and their families.

The year in question was 2015, which started out no differently from any of the previous years. Patients who had completed living kidney donor assessments were being scheduled for their elective transplant surgeries. As was often the case, there was increased deceased donor kidney transplant activity towards the end of the year, in this case 2014, and these patients were at times being admitted to the wards for various early post-transplant care. The renal transplant ward, housed at Ward 64A, therefore found itself being busy.

Adding to the bustle, these patients were transferred to Ward 67A temporarily to allow for planned renovation works in Ward 64A to commence on 6th April. Whilst the additional single rooms in Ward 67A were a welcome in the care of immunocompromised patients, there was a significant difference in layout, requiring the nurses from Ward 64A to adapt quickly.

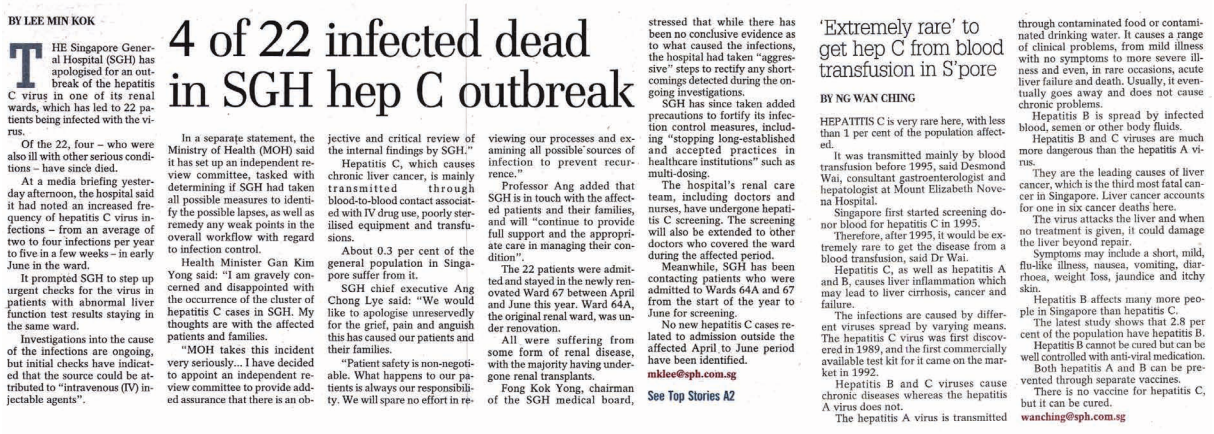
Confirmation of Outbreak and Immediate Measures

The first two cases appeared at the end of April, one involving a recent deceased donor transplant recipient from November 2014 and another a patient who had received an overseas transplant several years before. Derangement in their liver tests had prompted HCV screening. As other organ recipients of the same deceased donor were not diagnosed to have post-transplant HCV, it was thought that dormant HCV had been unmasked after intense immunosuppression following a recent treatment for rejection. As for the second patient, it was hypothesised that he had acquired HCV following his overseas transplant, which was not an uncommon occurrence as well. It had not yet become apparent that a calamity was awaiting us all.

A further two patients were diagnosed by mid-May. With an annual HCV incidence not exceeding four cases a year, it was unusual to see this cluster of cases within a month. Greatly concerned, Associate Professor Terence Kee, Medical Director of the renal transplant programme in SGH, alerted the dialysis centre to initiate investigations as three of these patients had previously received dialysis treatment in SGH. However, investigations in May did not reveal the dialysis centre as the source of infection.

By the end of May, a total of eight patients were diagnosed with HCV, and the transplant team was reeling from the death of the first infected patient. The National Organ Transplant Unit (NOTU) was also informed and donor transmitted infection was again ruled out. In the ensuing days, the Renal Medicine Head of Department (Associate Professor Marjorie Foo Wai Yin), Professor Chow Wan Cheng and Director for Infection Prevention and Epidemiology (Dr Ling Moi Lin) were all alerted to possibility of an outbreak having taken place.

The Infection Prevention (IP) team worked expeditiously to review all patient charts, mapping their movement in the hospital. Rosters were examined to identify common staff involved in the care of the affected patients. Visits were made to Ward 67A and other areas of care such as the Urology Ward, Urology Centre and Diagnostic Radiology Department to review practices. Staff from these various work areas were also interviewed and available literature on similar outbreaks was reviewed.



BY LEE MIN KOK

4 of 22 infected dead in SGH hep C outbreak

THE Singapore General Hospital (SGH) has apologised for an outbreak of the hepatitis C virus in one of its renal wards, which has led to 22 patients being infected with the virus.

Of the 22, four – who were also ill with other serious conditions – have since died.

At a media briefing yesterday afternoon, the hospital said it had noted an increased frequency of hepatitis C virus infections – from an average of two to four infections per year to five in a few weeks – in early June in the ward.

It prompted SGH to step up urgent checks for the virus in patients with abnormal liver function test results staying in the same ward.

Investigations into the cause of the infections are ongoing, but initial checks have indicated that the source could be attributed to "intravenous (IV) injectable agents".

In a separate statement, the Ministry of Health (MOH) said it has set up an independent review committee, tasked with determining if SGH had taken all possible measures to identify the possible lapses, as well as remedy any weak points in the overall workflow with regard to infection control.

Health Minister Gan Kim Yong said: "I am gravely concerned and disappointed with the occurrence of the cluster of hepatitis C cases in SGH. My thoughts are with the affected patients and families.

"MOH takes this incident very seriously... I have decided to appoint an independent review committee to provide added assurance that there is an objective and critical review of the internal findings by SGH."

Hepatitis C, which causes chronic liver cancer, is mainly transmitted through blood-to-blood contact associated with IV drug use, poorly sterilised equipment and transfusions.

About 0.3 per cent of the general population in Singapore suffer from it.

SGH chief executive Ang Cheng Lye said: "We would like to apologise unreservedly for the grief, pain and anguish this has caused our patients and their families.

"Patient safety is non-negotiable. What happens to our patients is always our responsibility. We will spare no effort in reviewing our processes and examining all possible sources of infection to prevent recurrence."

Professor Ang added that SGH is in touch with the affected patients and their families, and will "continue to provide full support and the appropriate care in managing their condition".

The 22 patients were admitted and stayed in the newly renovated Ward 67 between April and June this year. Ward 64A, the original renal ward, was under renovation.

All were suffering from some form of renal disease, with the majority having undergone renal transplants.

Fong Kok Yong, chairman of the SGH medical board, stressed that while there has been no conclusive evidence as to what caused the infections, the hospital had taken "aggressive" steps to rectify any shortcomings detected during the ongoing investigations.

SGH has since taken added precautions to fortify its infection control measures, including "stopping long-established and accepted practices in healthcare institutions" such as multi-dosing.

The hospital's renal care team, including doctors and nurses, have undergone hepatitis C screening. The screening will also be extended to other doctors who covered the ward during the affected period.

Meanwhile, SGH has been contacting patients who were admitted to Wards 64A and 67 from the start of the year to June for screening.

No new hepatitis C cases related to admission outside the affected April to June period have been identified.

mklee@sph.com.sg

See Top Stories A2

'Extremely rare' to get hep C from blood transfusion in S'pore

BY NG WAN CHING

HEPATITIS C is very rare here, with less than 1 per cent of the population affected.

It was transmitted mainly by blood transfusion before 1995, said Desmond Wai, consultant gastroenterologist and hepatologist at Mount Elizabeth Novena Hospital.

Singapore first started screening donor blood for hepatitis C in 1995.

Therefore, after 1995, it would be extremely rare to get the disease from a blood transfusion, said Dr Wai.

Hepatitis C, as well as hepatitis A and B, causes liver inflammation which may lead to liver cirrhosis, cancer and failure.

The infections are caused by different viruses spread by varying means. The hepatitis C virus was first discovered in 1989, and the first commercially available test kit for it came on the market in 1992.

Hepatitis B and C viruses cause chronic diseases whereas the hepatitis A virus does not.

The hepatitis A virus is transmitted through contaminated food or contaminated drinking water. It causes a range of clinical problems, from mild illness with no symptoms to more severe illness and even, in rare occasions, acute liver failure and death. Usually, it eventually goes away and does not cause chronic problems.

Hepatitis B is spread by infected blood, semen or other body fluids.

Hepatitis B and C viruses are much more dangerous than the hepatitis A virus.

They are the leading causes of liver cancer, which is the third most fatal cancer in Singapore. Liver cancer accounts for one in six cancer deaths here.

The virus attacks the liver and when no treatment is given, it could damage the liver beyond repair.

Symptoms may include a short, mild, flu-like illness, nausea, vomiting, diarrhoea, weight loss, jaundice and itchy skin.

Hepatitis B affects many more people in Singapore than hepatitis C.

The latest study shows that 2.8 per cent of the population have hepatitis B.

Hepatitis B cannot be cured but can be well controlled with anti-viral medication.

Both hepatitis A and B can be prevented through separate vaccines.

There is no vaccine for hepatitis C, but it can be cured.

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On 9 June, Chairmen of Medical Board (CMB), Professor Fong Kok Yong, was appraised of the findings. The Ministry of Health (MOH) was also informed of the potential outbreak and ongoing investigations surrounding it. Immediate cessation of multi-dose insulin vial use in Ward 67A was enforced. Optimisation of infection prevention practices such as standardisation of nursing workflow to ensure one-way flow of items between soiled and clean work areas, cleaning of medical equipment after each use and disinfection practice of dialysis machines were reviewed and best practice guidelines were instituted accordingly. Hand hygiene was reinforced. Disposable kidney dishes replaced traditional reusable ones. By 24 June, the hospital had implemented global cessation of multi-dose vials across all wards, including other common intravenous medications such as lignocaine, saline flush and sodium bicarbonate. The IP team conducted regular audits on hand hygiene and drug administration. Environmental cleaning in the wards was also enhanced.

The transplant ward relocated back to Ward 64A on 28th August. Unfortunately, the scale of the outbreak had proved to be much graver by this time, with a total of 21 infected patients of the same HCV 1b genotype and seven mortalities. Further phylogenetic studies were conducted for the first time by the Department of Molecular Pathology under the leadership of Dr Lynette Oon. Gene sequencing performed on repeat samples of affected patients confirmed that the HCV strains were indeed identical.

Two external agencies, the Centre for Disease Control and Prevention from the United States of America and A*STAR in Singapore, later validated these findings to be accurate in the course of their investigations. Director of Medical Services (DMS), MOH, Associate Professor Benjamin Ong, who was informed of the outbreak on 1st September, instructed that further inquiries be conducted.

As instructed by DMS, a Quality Assurance Review Committee was formed by SGH along with representatives from MOH in September to complete further investigations and ensure that adequate measures had been taken to curb the outbreak. All nurses from Ward 64A, doctors from the Department of Renal Medicine, interventional radiologists from Department of Diagnostic Radiology and transplant surgeons from Department of Urology underwent HCV screening due to their close contact with renal

Hepatitis C generally does not kill quickly

Linette Lai

A liver specialist is surprised that at least four people are suspected to have died within months of being infected with hepatitis C.

This is not a virus that kills quickly, Dr Desmond Wai told The Straits Times about the deaths linked to the virus at the Singapore General Hospital.

In his experience, even those with a weakened immune system – such as kidney failure patients – would take at least five to 10 years to develop severe liver damage.

The only exception, he said, is a rare and aggressive strain of the virus known as fibrosing cholestatic hepatitis C.

If someone who has a severely weakened immune system is infected with this particular strain, he could become critically ill in a matter of weeks.

"But this is very rare," he stressed. "In more than 20 years of practice, I've seen only two cases."

He added: "For someone healthy like you or me, hepatitis C... would take approximately 20 years to cause severe liver damage."

Even for someone who is ill and whose immune system has been compromised, said Dr Wai, the serious problems take as long as five to 10 years to emerge.

Such problems include liver cirrhosis – or scarring of the liver – liver cancer or liver failure.

Hepatitis C affects an estimated 0.3 per cent of the Singapore population. It is usually transmitted through infected blood and other body fluids.

The virus takes between two weeks and six months to incubate before people begin showing symptoms, such as fatigue, fever and weight loss.

The majority of people do not show symptoms and may not even know that they are infected.

Around 20 per cent of people infected with the virus will be able to get rid of it on their own without the need for medical intervention, said Dr Wai. Of the remaining group, nine in 10 people can be cured using antiviral medication.

He highlighted the example of one of his patients who contracted acute hepatitis C after a kidney transplant in China.

"I've seen her for more than a year and she's very stable, there's minimum damage to her liver," he said.

On average, Dr Wai sees one hepatitis C case every two months.

"Frankly speaking, this disease does not kill," he said. "We need to wait for more information from the Ministry of Health before we know what is going on."

patients, but all were subsequently confirmed to be negative. A Medical Review Committee chaired by an external party appointed by MOH (CMB of Changi General Hospital, and also a hepatologist, Professor Teo Eng Keong), was convened to review the mortalities in the HCV cluster.

In the meantime, a dedicated team of hepatologists, Professor Chow Wan Cheng, Drs. George Goh Boon Bee, Thinesh Lee Krishnamoorthy and Tan Hiang Keat, were assigned to manage the affected patients.

It was a fortuitous coincidence that novel direct antiviral agents (DAA) with high cure rates were changing the paradigm of HCV treatment that very year. Though they had been used in liver transplant patients, there was no published literature nor approval for use in patients with renal impairment or renal transplants. Nonetheless, their timely discovery gave hope for interferon-free therapy, which unfortunately carried the risk of kidney allograft failure as a sequele. Treatment guidelines were carefully drafted by the workgroup. As DAAs were also impermissibly expensive, Dr Crystal Lim, Master Medical Social Worker and her team of medical social workers (MSWs) and pharmacists assisted with access to these medications.

"Success is not final, failure is not fatal, it is the courage to continue that counts."

Winston Churchill

Figure 1
Press Conference chaired by senior management, Professor Ang Chong Lye (CEO), Professor Fong Kok Yong (CMB) and Associate Professor Tracy Carol Ayre (Chief Nurse) on 6th October 2015.

Rallying as a Family after Public Disclosure

Following the confirmation of the outbreak upon phylogenetic studies, completion of internal investigations and briefing of Minister for Health, Mr. Gan Kim Yong on 25 September, a press conference chaired by SGH leaders, Professor Ang Chong Lye (Chief Executive Officer), Professor Fong Kok Yong (CMB) and Associate Professor Tracy Carol Ayre (Chief Nurse), was held on 6th October 2015 (Figure 1). SGH unreservedly apologised for the outbreak and the impact it had on the affected patients.

"We would like to apologise unreservedly for the grief, pain and anguish

this has caused our patients and their families."

Ang Chong Lye

Concurrently, the renal medicine team proceeded with open disclosure to affected patients and their families, which had by now increased to 22 of whom eight had perished. SGH also filed a police report on 20 October to ascertain if there had been any foul play.

Over the subsequent months, CMB, CEO, Associate Professor Terence Kee and MSWs (Mr. Andy Sim, Ms. Crystal Lim, Ms. Faith Wong, Ms. Goh Soo Cheng, Ms. Jackie Erh and Ms. Janelle Chan), visited the families of the bereaved at their homes. Family conferences were held with hospital leadership, renal doctors and MSWs to listen to and address the questions raised by the families. Infected patients were given timely and appropriate treatment, costs of which was fully borne by SGH. Further financial and psychoemotional assistance was rendered to all. Families were reassured that SGH was ready to provide them with a just process and support through the difficult time.

In a mission to identify the earliest infected patient and other unknown infected cases and to ascertain if the various measures instituted had broken the chain of transmission, nearly 1,000 patients who were admitted to the affected wards from January to September 2015 were identified for screening. Three patients who were asymptomatic for HCV infection were detected through screening and treated accordingly, bringing the total affected patient numbers to 25 of whom 20 were renal transplant patients.

After the news broke, social media was rife with speculation and accusations. Staff morale was inevitably affected. To temper the spread of false information, regular townhall sessions were held to appraise staff of ongoing efforts to manage the outbreak. Group Chief Executive Officer, SingHealth, Professor Ivy Ng and SGH senior management motivated staff through regular staff memos to stay focused and continue to provide the best care to patients while keeping patient safety their supreme priority. Associate Professor Tracy and Associate Professor Terence Kee rallied nurses to remain united and strong as one nursing team even as they worked

tirelessly to strengthen and tighten the processes and standards over several months. Medical social workers provided emotional support for the doctors and nurses of the renal medicine unit as they soldiered on in the face of the public outcry. Mrs. Tan-Huang Shuo Mei, Director of Communications and Service Quality and her team guided frontline staff in answering queries that came through dedicated outbreak hotlines and other channels. Colleagues from all walks of life at SGH send text messages of encouragement and cards to remind those affected that they are not alone in the turmoil. Heartwarmingly, SGH was able to become united as one family to journey through the crisis.

Communications also provided regular updates through the media as well as our corporate website and social media platforms to keep the public informed. It was important to provide accurate and timely information of key developments to avoid unnecessary speculation and to restore public confidence.

Outcomes of Independent Investigations

Appointed by MOH, an Independent Review Committee (IRC), chaired by Professor Leo Yee Sin, (Director of the Institute of Infectious Diseases and Epidemiology) was convened on 28th September to review the HCV cluster and measures instituted for infection prevention in SGH, and to identify further areas for improvement. In addition to a local team of resource persons with the appropriate expertise, the IRC also appointed two teams of American experts from the CDC and the John Hopkins Health System to strengthen its capabilities. SGH fully cooperated with the review, which was facilitated by SGH senior management and the Infection Prevention and Nursing Division represented by Associate Professor Tracy and Deputy Director of Nursing, Ms. Chiang Juat Lan.

The final report was released on 8 December 2015 and made available to the public on the internet. Investigations conducted over two months revealed multiple overlapping factors including gaps in infection prevention and protocols at SGH renal medicine wards. The gaps cited included deviations from standard protocol in administering intravenous procedures, inefficient workflow in affected wards, and contamination of medical equipment and contact surfaces as a result of inadequate cleaning and disinfection practices. Deliberate harm, drug diversion and product contamination were ruled out as possible causes for the outbreak. Fortunately, the enhanced infection prevention measures instituted earlier by SGH had slowed the spread of the infection, with no further cases detected after moving back to Ward 64A.

The IRC recognised that though there were delays in reporting the HCV outbreak, they were not deliberate. It highlighted shortfalls within MOH and SGH in recognising and managing the outbreak of an unusual healthcare-associated infection such as HCV. Improvement of the national notification system and assigning of a designated team within MOH (which was then lacking) to investigate potential outbreaks were among several of their recommendations. Of

Figure 2
The Independent Review Committee released their report of the HCV outbreak at SGH on 8th December 2015.

the eight deaths, the IRC assessed that HCV was likely a contributory factor in seven. Concurrent to the release of the IRC report, the police also ruled out foul play upon conclusion of their investigations.

The IRC also made recommendations to address the identified gaps to SGH, which was further extended to all healthcare institutions. Both SGH and Minister for Health, Mr. Gan Kim Yong, accepted the findings of the IRC and extended their apologies to the public with a promise to close these gaps.

Independent panels convened by MOH and SingHealth found four senior officials from MOH and 12 in leadership positions in SGH to be responsible for the gaps that existed in their management of the outbreak and infection control. In March 2016, they received disciplinary action that included stern warnings and financial penalties for failing to intervene early and to ensure that the disease notification system was effective.

"An error does not become a mistake until you refuse to correct it."

John F Kennedy

SGH Interventions following IRC Recommendations

Based on IRC recommendations, SGH proceeded to institute several measures encompassing key elements of its processes, technology, people and culture.

Through the collaborative effort of Nursing Division, Operation Performance Management Department and Infection Prevention, processes that would allow staff to carry out tasks safely and effectively such as administration of IV medications, obtaining of blood specimens and performing of blood glucose monitoring were standardised. These were video recorded and made available in the e-learning system. A hospital-wide Infection Prevention Refresher Course covering these procedures was initiated on 31 October 2015 for doctors and nurses. This had been incorporated into the orientation curriculum and existing competency assessments, with such assessments being repeated every year.

Enhanced environmental hygiene and audits for infection prevention were instituted hospital-wide, with increased frequency of cleaning as per best practices. Nurse clinicians and senior nurse managers were expected to make clinical rounds and be on the ground to provide supervision and identify issues during peak periods and mornings. SingHealth Infection Prevention Audit group was formed for cross institutions audits. A second committee, SingHealth Report Implementation Committee, was formed to develop and oversee implementation of a sustainable cluster-wide action plan to effect recommendations for improvement in infection prevention measures. Both committees were led by Professor Tan Kok Hian, SingHealth Group Director, Academic Medicine and Head and Senior Consultant, Perinatal Audit and Epidemiology, Maternal-Fetal Medicine, KK Women and Children's Hospital.

Tools and techniques that would allow more efficient work processes and effective communication were adopted. Medication carts and computer-on-wheels for blood taking were modified to prevent contamination. Needleless connectors were implemented hospital-wide from December 2016. Through IT surveillance, virology tests that were due to be performed and results if positive could be readily detected in kidney transplant recipients.

Strategies to address awareness, knowledge gaps, delineation of key responsibilities and compliance to standard operating procedures were reviewed. The roles and responsibilities of nurses, facilities management and environmental services staff were clearly defined, and appropriate training was rendered. Senior Nurse Manager then Elena Bte Mohamed Ayob systematically guided Ward 64 through the various stages of changes from 2015.

A heightened surveillance and detection framework beyond standard indicators were established to allow for robust escalation of outbreak notification and reporting. Central to this, the "Nerve Centre" was formed for comprehensive investigation of potential nosocomial outbreaks and follow up.

Starting from November 2015, a strong education programme was started to promote high standards of infection control practices and share best practices across the entire SingHealth cluster

including Bright Vision Hospital and SingHealth Polyclinics. SingHealth resolved to renew and enhance emphasis on patient safety with the birth of the "Target Zero Harm" Campaign turning zero tolerance to any patient harm into a key motto for years to come.

SGH implemented the necessary changes within one month as required by the IRC report, to the satisfaction of MOH.

Ministry of Health Interventions following IRC Recommendations

A national task force led by Minister of State for Health, Mr. Chee Hong Tat, was formed to study best practices in outbreak control. Mr. Chee came to visit the healthcare team and the task force identified four ways to better deal with unusual infections. First, National Outbreak Response Team, comprising a "SWAT team" of infectious diseases experts who could be mobilised at short notice was set up on 1 March 2016 to respond to outbreaks. Second was the use of data analytics and information technology systems to improve the detection of potential outbreaks and strengthen capabilities to respond to them in Singapore. Within MOH, the Communicable Diseases Division was made responsible for overseeing all infectious diseases and outbreak reporting.

The list of notifiable diseases under the Infectious Diseases Act was re-examined, along with the modes of notification, time frames and escalation process. As a result of these measures, a circular on the guidelines for acute HCV notification was released on 15 June 2016 with a clearer definition of what constituted acute HCV infection. Reporting time frame for notifiable diseases was standardised to 72 hours with the exception of pre-specified diseases such as Zika virus infection.

Additionally, MOH instituted reporting processes for mortality, serious reportable event and blood-borne infection incidences of transplant patients within pre-stipulated time frames of the event.

"It does not matter how slowly you go, as long as you do not stop."

Confucius

Rebuilding the Renal Transplant Programme from its Knees to the Heavens

At the peak of the outbreak in August 2015, the programme ceased further transplant activities on its own accord. An official interim moratorium was declared on 4 September. Patients were offered the option of transfer to National University Hospital (NUH) for the purpose of transplants either from deceased or living donors during this period. Thirteen patients of whom 11 were eventual recipients of deceased donors proceeded for transplant at NUH. However, the vast majority of patients requested to wait until the suspension was lifted to have their transplant performed in SGH.

In addition to inter-cluster audits, practices and processes in the Department of Renal Medicine were further scrutinised by an extension survey of the Joint Commission International (JCI) Accreditation on 13 April 2016 as part of an SGH-directed initiative (Figure 3). It was imperative that SGH was able to hold itself to the highest standards before it recommended for its programme to be resumed. Having satisfied the rigours of the various audits, the suspension of the Renal Transplant Programme was eventually lifted on 13 May 2016. Keeping the emphasis on "Target Zero Harm" close to its heart, the programme successfully performed its 1000th deceased donor kidney transplant in 2018.

Figure 3
Associate Professor Terence Kee answering questions during a special and rigourous JCI audit organised after the HCV outbreak.

Ward 64 further received accolades for its exemplary teamwork and outstanding performance in patient care when it was awarded Teams UP! Award in 2018. Maintaining a consistently high standard of care under the stewardship of Senior Nurse Manager then Ms. Leong Siew Teing, Ward 64 was again handed the Unit Excellence Award in 2019.

Driven to champion patient safety from this gruelling experience, Associate Professor Terence Kee along with Professor Kenneth Kwek and seven other cyclists, rode 195km to raise more than $20,000 for Target Zero Harm Awards.

What had initially begun solely as a problem for the Renal Transplant Programme eventually led to a widespread system change not just in the renal wards and SGH but across all SingHealth institutions and other healthcare providers under MOH and in Singapore in general. The recovery from a sentinel event such as this could only be possible due to the involved and focused leadership of SGH and SingHealth at the time. Although impossible to fully assuage the suffering of the infected patients and make up for the lives lost, the gigantic impact they made on healthcare in Singapore shall be forever remembered and honoured.

"Those who cannot remember the past are condemned to repeat it."

George Santayana

Coronavirus Outbreaks and Renal Medicine

Dr Jasmine Chung, Consultant
Professor Tan Ban Hock, Senior Consultant
Department of Infectious Diseases, SGH

Throughout the course of history, disease outbreaks have emerged to significantly devastate civilisations and continually change the way we live. One of the most notorious pandemics of the 20th century was the 1918 Spanish Influenza, which affected as many as 500 million people' leaving at least 50 millions of them dead.[1] Since then, there were three further influenza pandemics – Asian Flu (H2N2, 1957 – 1958), Hong Kong Flu (H3N2, 1968 – 1970) and Swine Flu (H1N1, 2009 – 2010). Apart from influenza, the transmission of other respiratory viruses or zoonoses of pandemic potential was accelerated by anthropogenic, behavioural and societal changes in the last century - the various coronavirus epidemics/pandemics are a case in point.

Coronavirus Outbreaks in the last Two Decades

Coronaviruses (CoVs) are a group of enveloped viruses typically harboured in mammals and birds. Bats, in particular, are important reservoirs of such viruses (Figure 1). To date, there are seven serotypes known to infect humans. Four serotypes, HCoV-229E, HCoV-NL63, HCoV-OC43, and HCoV-HKU1, typically cause mild, self-limiting respiratory tract infections, while SARS-CoV, MERS-CoV and SARS-CoV-2 had caused global outbreaks with significant case fatality rates in the last two decades.[2-5]

Severe acute respiratory syndrome coronavirus (SARS-CoV) emerged through recombination of bat SARS-related coronaviruses (SARS-CoVs). The recombined virus infected civets and humans and adapted to these hosts before causing the SARS epidemic. Middle East Respiratory Syndrome coronavirus (MERS-CoV) likely spilled over from bats to dromedary camels at least 30 years ago and has since then been prevalent in dromedary camels. HCoV-229E and HCoV-NL63 usually cause mild infections in immunocompetent humans. Swine acute diarrhoea syndrome (SADS) emerged in piglets. This disease is caused by a novel strain of Rhinolophus bat coronavirus HKU2, named SADS coronavirus (SADS-CoV).

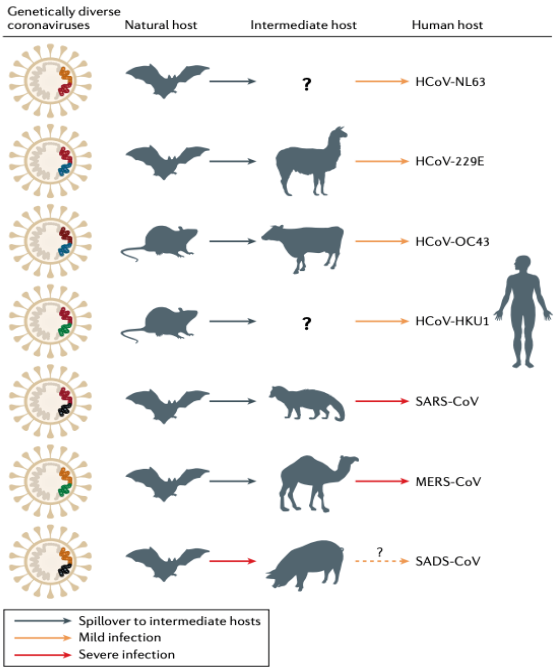
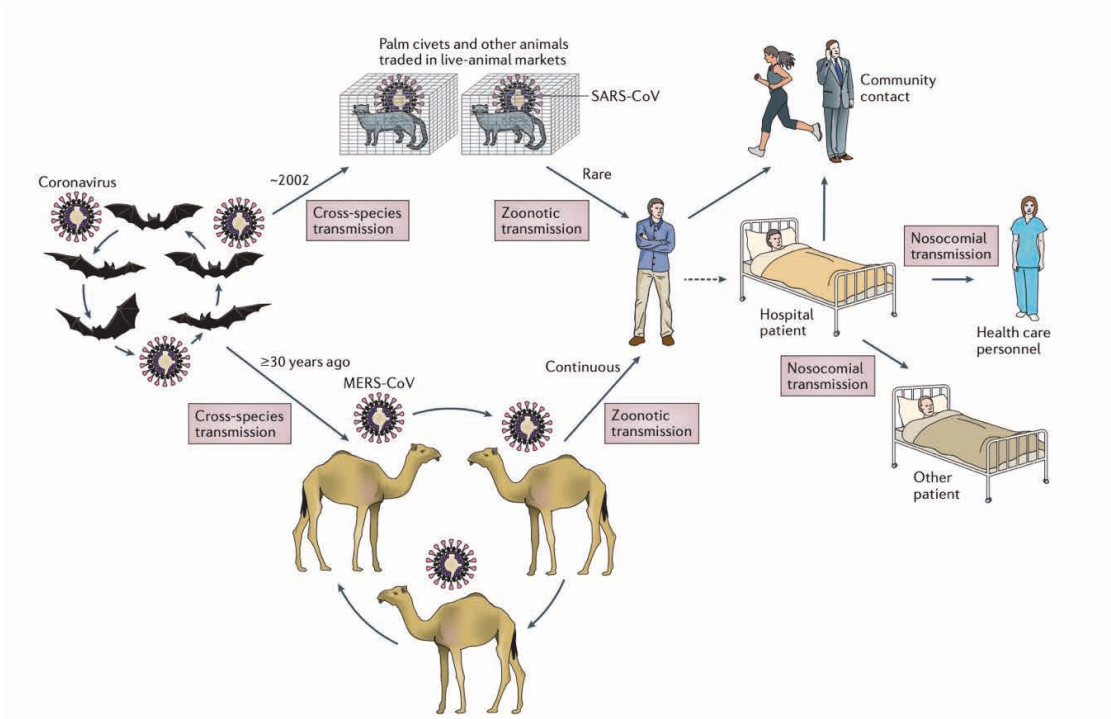


Figure 1.[5] Source: Cui et al. Nat Rev Microbiol. 2019; 17(3): 181 – 91

For the outbreak strains of CoVs, bats were the animal reservoirs, passing it to humans through intermediary hosts, namely civet cats for SARS-CoV and dromedary camels for MERS-CoV. Pangolins are thought to be the intermediary hosts for SARS-CoV-2. Person-to-person transmission of coronaviruses is mainly through droplets (emitted when coughing or sneezing) or direct contact through contaminated fomites. Transmission can occur both in the community or within healthcare facilities. In addition, asymptomatic transmission of CoVs can occur and cause widespread community transmission, as illustrated by SARS-CoV-2. In the 21st century, we live in a highly interconnected world. International travel has facilitated the spread of Coronavirus Disease 2019 (COVID-19) globally, and within three months of the discovery of SARS-CoV-2, COVID-19 was declared a global pandemic by the World Health Organisation (WHO) on 11 March 2020 (Figure 2).[2,6,7]



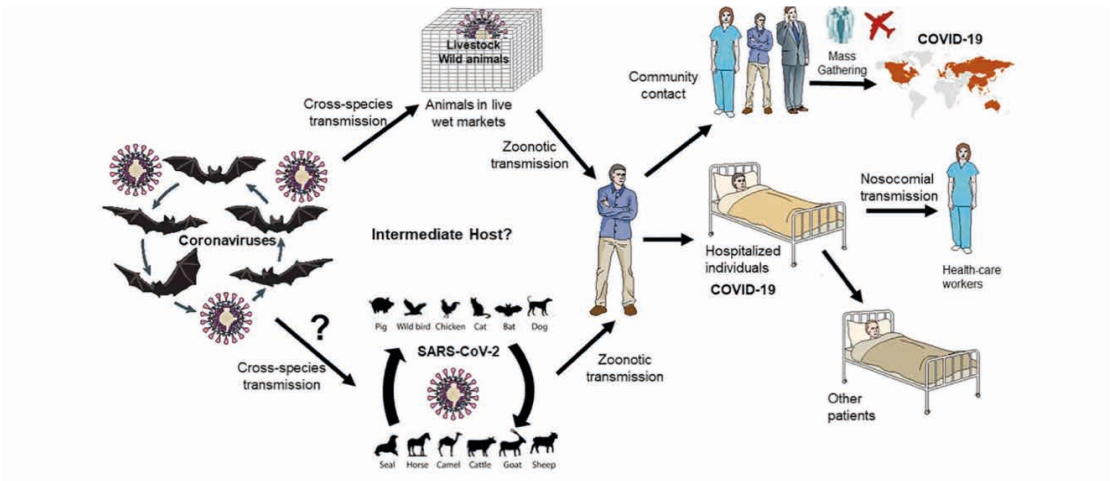


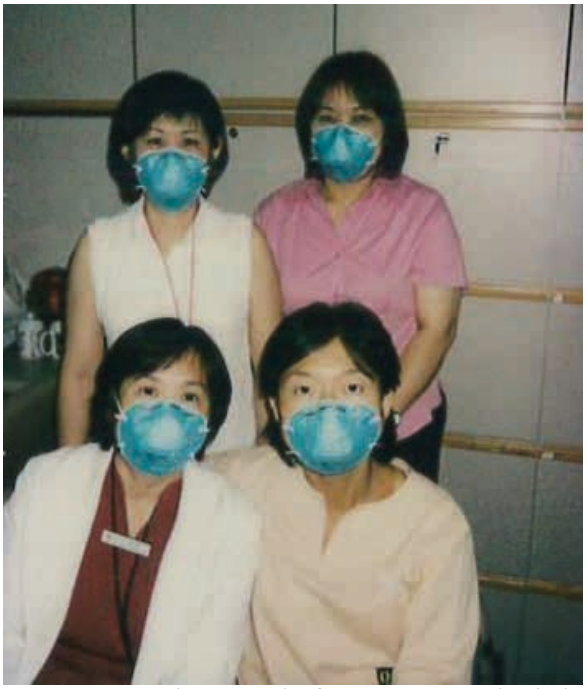
Figure 2. Adapted from de Wit E et al, and El Zowalaty et al.[2,6] Transmission of SARS-CoV, MERS-CoV and SARS-CoV-2 from bats to humans. Person-to-person transmission is facilitated by droplet and contact transmission both in the community and in healthcare settings.

Table 1: Table comparing SARS, MERS, and COVID-19[2,4,7,11-16]

	SARS	MERS	COVID-19
Median incubation period, days	6.4 (95% CI 5.2-7.7)	5.2 (95% CI 1.9-14.7)	6.4 (95% CI 2.1-11.1)
Comorbidities which may be associated with more severe infections	Diabetes mellitus Chronic hepatitis B Presence of medical co-morbidities Elderly	Cardiovascular disease Diabetes mellitus Hypertension Chronic lung disease Cancer Presence of medical comorbidities Obesity Elderly	Cardiovascular disease Diabetes mellitus Hypertension Chronic lung disease Cancer **Chronic kidney disease** Elderly
Clinical presentation	Initial phase - Fever, myalgia, malaise, chills or rigours, headache Respiratory phase[a] – Cough, dyspnoea, respiratory failure Other symptoms – Sore throat, rhinorrhoea, chest pain, pleurisy, diarrhoea	Initial phase – Fever, cough, sore throat, chills, myalgia, arthralgia Respiratory phase[a] – Dyspnoea, respiratory failure, multiorgan failure Other symptoms – Nausea, vomiting, diarrhoea, abdominal pain and dizziness	Initial phase - Fever, cough, sore throat, nasal congestion, anosmia, dysgeusia, headache, myalgia, malaise Respiratory phase[a] – Dyspnoea, respiratory failure, arrhythmias, acute cardiac injury, and shock Other symptoms – Sore throat, rhinorrhoea, headache, nausea, vomiting, diarrhoea
Severity of illness	Mild, asymptomatic infections reported. **Dyspnoea and pneumonia more common.** **25% require ICU admission**	Mild, asymptomatic infections reported **Severe infections with respiratory failure, and organ failure more common** **More severe than SARS – in one series, 89 % required ICU care and 72% mechanical ventilation**	Mild (80%) [b] Severe (15%) [c] Critical (5%) [d]
Secondary transmission	Usually occurs in healthcare facility	Usually occurs in healthcare facility	Occurs in close contacts; largely community transmission
Reproductive number, R_o	2-5	<1	**1.4 – 5.5**
Number of individuals affected	8, 096	2, 494	99,363,697[e]
Number of deaths	774	858	2,135,9599[e]
CFR, %	11	35	<1 – 12.3

Abbreviations:
SARS: Severe Acute Respiratory Syndrome, MERS: Middle East Respiratory Syndrome, COVID-19: Coronavirus disease 2019, CFR: Case Fatality Rate

[a] Respiratory phase usually develops after 5-7 days past the onset of symptoms
[b] Mild cases of COVID-19 are defined as those with symptomatic infections, upper respiratory tract infections/mild pneumonia
[c] Severe cases of COVID-19 are those with dyspnoea or hypoxia
[d] Critical cases are those with respiratory failure, shock and/or multiorgan failure requiring intensive care management
[e] Cases listed on WHO COVID-19 Dashboard as of 26th January 2021.



In 2003, SARS epidemic was the first coronavirus outbreak the department faced but responded to the challenges with unity and resilience. Here, transplant coordinators wear N95 masks for the first time.

Clinical Features of Outbreak Coronaviruses

The clinical features of these outbreak CoVs are summarised in Table 1. Although the damage from COVID-19 is less severe compared to SARS or MERS, it is highly transmissible. It has infected more people and resulted in a pandemic of a much larger magnitude than SARS or MERS. In addition, asymptomatic or pre-symptomatic transmission has been reported and this is likely to have contributed to its widespread transmission.[8-10]

Recognizing Emerging Coronarvirus Infections in Patients with Renal Conditions

Although most patients with emerging CoV infections present with respiratory illness, the astute clinician must be aware that end stage renal failure (ESRF) patients may have atypical presentations, and respiratory symptoms may not necessarily be reported.[17-20] Isolated gastrointestinal symptoms are not uncommon. One end stage renal failure patient infected with SARS had presented with fever and gastrointestinal bleeding[17] while another haemodialysis (HD) patient with COVID-19 had presented with diarrhoea.[18]

In addition, asymptomatic CoV infections can also occur in the ESRF patient. Asymptomatic MERS has been described in a HD patient in Riyadh.[21] Based on the unit's experience at SGH, an asymptomatic HD patient who was prepped for renal transplant surgery was tested positive for SARS-CoV-2 hours prior to planned surgery.

To improve the clinical care and outcomes of outbreak CoV infections in patients with renal disease, we can address these three key areas.

1. The impact of CoVs on the kidneys and clinical outcomes of SARS, MERS and COVID-19 in patients with underlying renal disease.

2. The impact of CoV outbreaks on dialysis units and the infection control strategies to mitigate risks.

3. The impact of CoV outbreaks on the renal transplant programme

The Impact of Coronaviruses on the Kidneys and Clinical Outcomes of SARS, MERS and COVID-19 in Patients with Underlying Renal Diseases

SARS, MERS and COVID-19 may cause acute kidney injury (AKI) in 5% to 15% of cases, and their mortality rates are higher in patients with renal diseases.[22] The exact mechanism of kidney injury is unclear, but it is possible that the cytokines released during severe infection or direct viral cytopathic effects may cause kidney damage. The angiotensin converting enzyme (ACE) expressed on renal tubular cells serve as targets for SARS-CoV and SARS-CoV-2; while the dipeptidyl peptidase-4 (DPP-4) targets are for MERS-CoV.[22-24] When acutely affected with these CoVs, patients may feel unwell; their intake may be poor, or they may have significant gastrointestinal losses. Patients with severe infections may also go on to develop secondary bacterial infection with septic shock. These factors contribute to the development of pre-renal failure. In other instances, patients with chronic kidney disease (CKD) may be inadvertently placed on non-steroidal anti-inflammatory agents with resultant interstitial kidney injury. The risk of progression of CKD is increased, and some patients may require dialysis support. Invariably, outcomes in this group of patients are poorer.[24-27] It is therefore very important that fluid balances are closely

monitored, particularly in this group of patients. Medication orders also need to be scrutinised.[24]

The outcomes of SARS and MERS in dialysis patients appear even more severe, with majority of the patients requiring supplementary oxygen therapy or ventilatory support, and mortality rates were above 70%.[21,28-31] Based on preliminary data, the clinical course of COVID-19 in dialysis patients appears milder compared to SARS and MERS.[18,32-34] As the COVID-19 pandemic is still evolving, we have to await more data before we can comment on outcomes in dialysis patients.

Little is known about SARS or MERS in renal transplant patients, but based on case reports and case series, the disease appears severe. AlGhamdi et al, reported on MERS in two renal transplant recipients; the infection was severe in one patient and he passed away, while the other patient survived.[35] In the current COVID-19 pandemic, the disease also appears more severe in the renal transplant population compared to the general population. In a single centre observational study of 20 renal transplant recipients with COVID-19, a significantly higher proportion of patients had severe infection (73% required oxygen therapy) and case fatality rates were higher at 25%, compared to 2.3% reported in the general population.[7,36]

The Impact of Coronavirus Outbreaks on Dialysis Units and the Infection Control Strategies to Mitigate Risks

From the 2012/2013 MERS outbreak in Saudi Arabia, it is evident that MERS can cause transmission clusters and high mortality in HD facilities.[21,37,38] In Jeddah, the heavy workload in the dialysis unit, overcrowding (space between patients < than 1.2m), and potential lapses in use of personal protective equipment could potentially have contributed to the outbreak.[38] When the cases were isolated and changes to infection control practices were made, the outbreak was contained.

Learning from the experience in Saudi Arabia in 2013, infection control measures were instituted in dialysis units soon after MERS was reported in Korea. As a result, very few transmissions occurred at these units. At Kyung Hee School of Medicine, all visitors had their temperature monitored, hand hygiene practices were reinforced, and surgical masks were applied to all patients attending the dialysis unit. When any index case was identified at their dialysis unit, patients who were contacts were quickly isolated, and affected healthcare workers (HCWs) were placed on quarantine. No further transmission occurred.[39]

Video consultation started becoming part of routine renal practice during the COVID-19 Pandemic.

With COVID-19, it was not surprising then that another outbreak occurred in a dialysis unit in Wuhan; five HD patients were affected. The index patient in the unit had been exposed to an infected family member.[33] As the COVID-19 pandemic continues to evolve and spread rapidly across the world, various international professional bodies have issued guidelines to mitigate the risk in dialysis facilities. Healthcare workers are trained to use protective personal equipment, recommended to be evaluated if they are unwell, and urged to inform their superiors if they have come into contact with positive cases. For the dialysis patients, they are instructed on the importance of good hand and respiratory hygiene, advised to inform staff of clinical symptoms in advance of arrival at their dialysis unit, and have their temperatures assessed at the start and end of each dialysis session.[40,41] In addition, universal use of face masks and scheduled dialysis sessions are recommended.[41]

The renal transplant programme has been a strong advocate of hand washing and monitors its hand washing rates in the transplant wards. It discovered the most important factor to improve hand washing rates is developing a hand washing culture through role modelling by senior staff and supporting peer reminders even to senior staff when hand washing is missed. Patients are also encouraged to remind staff in the renal transplant ward.

Learning from our experiences with SARS, as soon as the COVID-19 epidemic was reported in China, SGH's pandemic response systems were activated, and infection prevention measures were enhanced in all areas including the inpatient dialysis unit. All HCWs had to don surgical masks in all clinical areas (at a minimum), and in high-risk areas, the use of N95 masks, goggles, face shields and personal protective equipment (PPE) were mandated. A strategy of having dedicated teams assigned to dedicated areas with dedicated machines was also implemented. In addition to the isolation ward, a renal acute respiratory infection (ARI) ward was set up to cohort ESRF patients presenting with respiratory symptoms (but do not fulfill definition of a suspected case) with the view to exclude COVID-19 prior to transfer to an open ward. In the last hospital infrastructure upgrade after SARS, plumbing infrastructure had already been upgraded to allow for the provision of outstation dialysis (e.g. isolation wards, ARI wards), and these rooms could easily be converted into makeshift outstation dialysis units in the hospital.

The Impact of Coronavirus Outbreaks on the Renal Transplant Programme

For SARS, the disease was severe in transplant recipients and cities experiencing community transmission, such as Toronto and Singapore, had to temporarily close their transplant programmes.[42] While SARS eventually came under control, the COVID-19 pandemic is expected to be long-drawn, and transplant programmes cannot be suspended indefinitely.

SingHealth-Duke NUS Transplant Centre had at the start of the COVID-19 outbreak envisioned and planned a tiered approach to transplantation (See Figure 1). Resources permitting, transplantation can proceed as per usual if there are no or limited local transmission. In the event of wide-spread community transmission, the deceased and living donor programmes may have to be suspended. The COVID-19 situation is fluid and decision for transplantation may have to be evaluated on a case-by-case basis, guided by emerging data.

Figure 1: Decision making grid on patient selection for transplant during pandemics

		Urgency of transplant[b]		
		Low	Intermediate	High
Complexity of transplant[a]	Low	Defer	✓✓	✓✓✓
	Inter-mediate	Defer	✓[c]	✓✓[b]
	High	Defer	Consider deferring	✓[c,c]

[a]The complexity of the transplant is determined by (a) surgical complexity, (b) extent of medical co-morbidities, and (c) immunological risk.

[b]In general, medically urgent transplants are performed for patients with (a) liver failure with a high 28-day mortality, (b) heart failure patients who are on mechanical circulatory support (MCS) with evidence of device-related complications or those who require continuous high dose inotropic support, or (c) patients with end stage lung disease who cannot sustain long on the wait list. Semi-urgent transplants are indicated for patients with hepatocellular carcinomas. There is a low indication for transplant for stable heart failure patients who are well supported on MCS, and dialysis patients with no access issues.

[c]Decision to proceed with transplantation is contingent on the availability of manpower, operating theatre facilities, medical equipment, surgical and intensive care beds, blood products, and adequacy of PPE.

To mitigate the risk of peri-transplant COVID-19, recipients and donors are actively screened for COVID-19 through a multimodal screening process (clinical history, SARS-CoV-2 PCR, and chest radiology) just prior to transplantation. The coordination of these tests may be logistically challenging and cost of transplantation has increased, but this is necessary for transplant to proceed safely. To mitigate the risk of acquiring COVID-19 post-transplant, SingHealth Duke-NUS Transplant Centre has also in conjunction with Novartis developed an educational resource to teach patients about the importance of practicing good personal, hand and respiratory hygiene, as well as to use appropriate face masks when they travel out of their home.

Conclusions

In the last two decades, we have witnessed three novel CoV outbreaks and they will not be the last. Outcomes in renal patients with novel CoVs infections are likely poorer compared to the general population, and effective therapeutics are not yet available. Pandemic preparedness and good infection control practices are therefore still key to breaking the chain of transmission and ensure that our patients are adequately protected.

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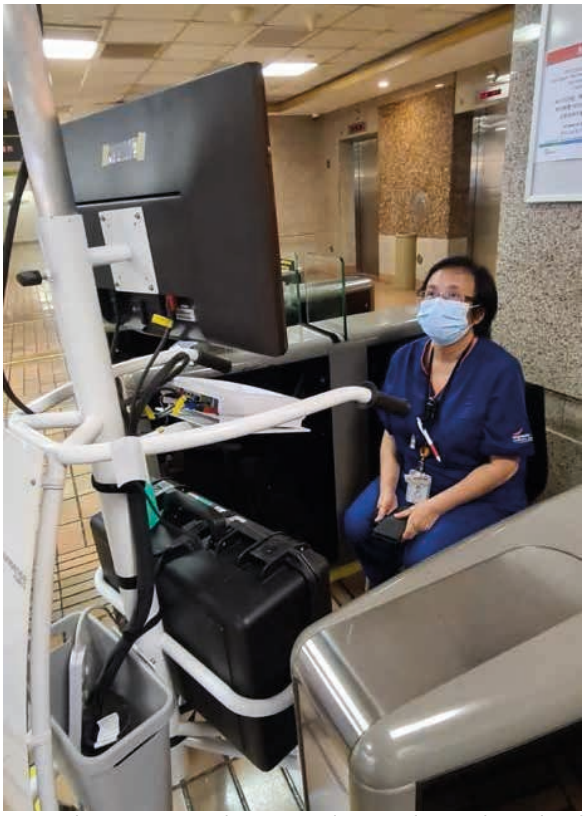
Senior residents, residents and pharmacist awaiting their turn to receive influenza vaccination in the ward.

COVID-19 introduced a new term called social distancing where we had to keep safe distances from other people so as to avoid COVID-19 transmission. As a result, meetings such as the weekly department meeting were done virtually over the zoom video conferencing platform.

The proper donning of personal protective equipment and pre-emptive screening of suspected patients for COVID-19 proved effective against nosocomial outbreaks of COVID-19 at SGH. As a result, physicians from the renal transplant programme took turns to be rostered to the acute respiratory wards, of which two were under the management of the Department of Renal Medicine.

Associate Executive Jenny Leong from the renal transplant programme helps visitors fill up disclosure forms before they enter the hospital.



During the COVID-19 Pandemic, transplant coordinators have played their part in the fight against COVID-19 by being deployed to the perimeter stations, monitoring for visitors to the hospital with fever. Even senior staff like manager Lu York Moi here watches the entrance of Block 4 like a hawk for febrile visitors using the thermal scanner.

Dr Ho Quan Yao (Consultant Transplant Nephrologist) and Dr Jasmine Chung (Consultant Transplant Infectious Disease Physician) were instrumental in driving many of the protocols, research projects and publications that arose during the COVID-19 Pandemic. They became the think tank for COVID-19 measures required by the renal transplant programme.

Chapter 6
Training to be a Nephrologist

> *Last but not least, every medical education programme should remember that the betterment of patient care is the primary objective and with that lies the human side of medicine.*
>
> *- Associate Professor Jason Choo*

Evolution of Nephrology Training in SGH

Associate Professor Jason Choo, Senior Consultant
Director of the Glomerulonephritis and Chronic Kidney Disease Programme
Director of Academic Nephrology
Immediate past Programme Director of SingHealth Renal Medicine Residency Programme

Professor Woo Keng Thye
Emeritus Consultant and Advisor

SGH was the birthplace of nephrology training in Singapore. In its early phase, nephrology training was modelled after the United Kingdom (UK) model of training, which was based upon an apprenticeship structure and required a summative assessment towards the end of training to determine suitability for a specialist designation.

The department saw its humble beginnings in 1973 when it was founded by the late Dr Lim Cheng Hong, who was at the time a Chest Physician. Under the Commonwealth Fellowship in Nephrology, Dr Lim was in St Mary's Hospital in London for 12 months from 1968 to 1969 with Professor William Stanley Peart. Dr Lim had later also visited various nephrology units in North America, UK and Australia. His close contacts with the likes of Dr George Schreiner, Dr Barry Hulme, Professor Priscilla Kincaid-Smith and Professor Jim Lawrence ultimately shaped the foundation of what was then the renal unit in SGH.

Helmed by Dr Lim Cheng Hong, the department was joined by two senior registrars, namely Dr Pwee Hock Swee who eventually spent six months at the Peter Bent Brigham Hospital in the United States of America, and Dr Chan Yat Wah who came under the tutelage of Dr Jim Lawrence at the Royal Adelaide Hospital in Australia. These stints were made possible under the Colombo Plan Fellowship but only as observers.

In 1975, Professor Woo Keng Thye joined the department as a registrar. Dr Pwee and Dr Chan were both away on fellowships at the time. Dr Lim Cheng Hong was assisted by Dr Gordon Ku who was the only trained nephrologist from the University (trained under the guidance of Professor John Moorhead from the Royal Free Hospital in UK) under Medical Unit II. Renal consult calls were possible with further help rendered by Professor Lim Pin and Professor Khoo Oon Teik. At the time, consult calls were a mixture of both medical and renal calls at a frequency of once every three weeks. Renal calls, which lasted one week, included travel to the neurology intensive care unit in Tan Tock Seng Hospital for assessment of brain-dead patients for deceased donor renal transplantation. Professor Woo Keng Thye thereafter led the way in nephrology training, being in 1976 the first in Singapore to be recognised as a properly accredited nephrologist under the auspices of an Australian training programme. This was his journey in his own words, which as well those who was trained thereafter.

"The Australian programme for Nephrology training commenced in 1976. The chief censor was Jim Lawrence and the President of the FRACP College was Kincaid-Smith. I wrote to the college and arrangements were made for censors to visit the Renal Unit in SGH (with Dr Lim's agreement) and after formal accreditation, I was the 12th candidate enrolled for the Nephrology Accredited Programme leading to FRACP in Nephrology. The other 11 were based in Australia. I spent two years in local training with Dr Lim and Professor Seah Cheng Siang as my supervisors. Professor Seah was Director of Post-Graduate Education in Singapore and had started the MMed course with the Australian nephrologists and was well known to them. Every six months the Australian College would have their guys meet and assess me through viva voce and watch my presentation of papers in Singapore and elsewhere at various nephrology meetings which I had to attend as part of my training where I would have to present papers. At the end of each year I had to sit for an exam and be ranked with the other eleven.

The training programme consisted of three years including one year core training which was compulsory in Australia, though core would usually have been two

Orientation day for new renal medicine senior residents with their faculty in 2015.

years. Of the other two years, six months had to be spent in the lab doing research techniques. I spent six months on Immunology with Professor Chan Soh Har at the WHO Lab in MacAlister Road and learned how to do research and write papers. The other six months involved rotation through Dialysis, Transplant and Clinical Nephrology. My final year was spent with Professor Priscilla Kincaid-Smith under the Colombo Plan Scholarship. In those days, fellowships offered by the Singapore government only lasted for six months. Three months later, Professor Kincaid-Smith, upon a visit to Singapore where she was invited by the Academy, met with the Director of Medical Services Dr Andrew Chew and Dr Lim thereafter extended my stay in Melbourne to one year. In fact, Professor Kincaid-Smith had preferred that I stayed for two years and did a thesis, but I refused. That was in 1978. Upon my return Dr Lim wanted me to help train the younger guys. At the Royal Melbourne Hospital, I was immersed in running clinics, ward work, research training, and had various research projects going with Professor Judith Whitworth and Professor Kincaid-Smith.

Some years later, Dr Vathsala applied nephrology training and was accepted as a registrar. A year after that, Dr Grace Lee and Dr Lina Choong also joined us. All of them spent six months in research training at the WHO lab with Professor Chan Soh Har and learned on the job about dialysis and transplant plus clinical nephrology. But even with them being registrars we wanted them to enter a specialty area as we needed to train them in preparation for further training overseas. Each of them went to separate centres for a one-year HMDP fellowship, during when they received clinical training but we wanted them to also train in an area of research, as well as bring whatever techniques they learned back home. Dr Vathsala sought out Barry Kahan, while Grace went to Richard Glassock and Lina to Robert Schrier.

In 1980, Professor Evan Lee was chosen by the University for nephrology training as it intended to set up a Department of Nephrology at the new Kent Ridge Hospital. He joined us for certain days of the week and at other times also went to Professor Kincaid-Smith's renal unit at the Royal Melbourne Hospital for training.

In 1989, Professor Tan Chorh Chuan also spent six months on full time with us and afterwards went to Oxford University to train with Professor Radcliff, who had recently then won the Nobel Prize.

From 1987 to 1999 we enrolled two of our new registrars, Dr Wong Kok Seng and Dr Wei Serh Sherng, in nephrology training through a three-year accredited programme ran by the Specialist Training Committee set up by MOH. As it happened, I was the Chairman of the Renal Specialist Training Committee. At the time, I drew up the syllabus which included a six-month research stint and six-monthly rotation through dialysis and transplant and clinical nephrology, and one year of overseas training. As for Dr Wong and Dr Wei, I gave both of them a written exit, which they proceeded to pass with flying colours. This exam was optional, but the exit interview or oral exam was compulsory. After this, the other committee members were not keen to continue with the written exam. I had wanted to fashion it like the one in the Australian College but had received no support for that. The next one we had was Dr Tan Han Khim. I sent him to Professor Rinaldo Bellomo at the Austin and Repatriation Medical Centre, Victoria, Australia in 1998 as I wanted someone trained in haemodialysis and continuous renal replacement therapy as well as research into haemodialysis. He did well on all counts."

By the early 2000s, post medical school graduation, house officers would have to spend one year in various specialty combinations consisting of general medicine, orthopaedics, general surgery, obstetrics and gynaecology or emergency medicine in order to obtain their license to practice. After which, one could continue as a medical officer on a six-monthly rotational basis arranged by MOH. In order to become a nephrologist, the requirements included three years of basic specialist training in internal medicine followed by a high bar exam, either the Masters of Medicine from the National University of Singapore or Membership of the Royal College of Physicians from the United Kingdom. This was followed by three years of advanced specialist training in Renal Medicine with a compulsory six-monthly rotation through General Nephrology, Haemodialysis, Peritoneal Dialysis and Kidney Transplantation. The balance of 12 months of training was dependent upon the trainee's progress as well as the department's manpower requirements. Teaching

Before there were senior residents, there were registrars...Dr Cynthia Lim, Dr Htay Htay, Dr Tan Ru Yu, Dr Sheryl Gan, Dr Teo Su Hooi and Dr Irene Mok were among the last group of registrars to complete the 3 year advance specialty training programme in renal medicine before it was replaced by the SingHealth Renal Medicine Residency Programme.

Renal registrars in 2012 before a team building event.

was opportunistic in nature with lunchtime sessions a mixture of didactics with other more case-based discussions. Each trainee was tagged onto a mentor throughout the three years, who served as a resource person and a supervisor for clinics and patient discussions. At the end of the three years, suitability and recommendation for exit viva examination by the Joint Committee of Specialist Training was determined by the Head of the Renal Medicine Department. This was the mainstay of training for many years with many Nephrology Consultants in Singapore and the region trained in this manner.

However, based on surveys and interviews with specialists and graduate medical trainees in 2006 and 2007, feedback with regards to a lack of training structure as well as insufficient supervision and protected training time, Ministry of Health, with the recommendation of Specialist Accreditation Board, embarked upon a reformed training programme across all specialties in Singapore. The structure of which to closely mirror that of the US residency model.

Faculty, senior residents and potential candidates for the training programme during the SingHealth Residency Open House. The Open House was very much an annual family affair with faculty bringing their children along to join in the fun.

2010 dawned a new era in post graduate training in Singapore with the formation of graduate medical education offices across each of three sponsoring institution: SingHealth, National University Health System and National Healthcare Group. The SingHealth Renal Medicine Senior Residency Programme started in 2013 under the umbrella of MOH Specialists Accreditation Board with the Residency Advisory Committee and Accreditation Council for Graduate Medical Education International (ACGME-I) Institutional and Residency Review Committee providing oversight and guidance. Exit examinations were administered by examiners chosen by the Residency Advisory Committee. Within each sponsoring institution, the programme is helmed by a programme director who reports to their institutional Graduate Medical Education office which helps provide resources and logistical support to the programme. Associate Professor Marjorie Foo was the first programme director to set up the Renal Residency programme and the programme accepted its first 5 senior residents in July 2013. Associate Professor Marjorie Foo subsequently stepped down in April 2014 to take up headship of the Renal Medicine Department at SGH. Associate Professor Jason Choo then took over as programme director from April 2014 to December 2019 while Associate Professor Tan Han Khim succeeded Associate Professor Jason Choo in 2020.

The training structure mimics the United States residency programme with strict rules encompassing duty hours, protected training time, procedural credentialing and graduated supervised training. The first 2 years of training are under ACGME-I auspices and the final 1 year under the Joint Committee of Specialist Training guidance. Under MOH requirements, residents are mandated 16 hours of protected training time every 4 weeks with rotations in General Nephrology, Haemodialysis, Peritoneal Dialysis, Kidney Transplantation and Geriatric/General Medicine. Senior Residents are also rotated to Changi General Hospital as a participating site under the programme to increase their breadth and experience of nephrology. Senior residents are trained under the 6 ACGME core competencies of Patient Care, Interpersonal and Communications Skills, Practice Based Learning and Improvement, Systems-based Learning, Professionalism and Medical Knowledge. In comparison to the older apprenticeship system, feedback to residents are done through formative and summative assessments based on all 6 competencies with 6 monthly formal reviews done by the Core Competency Committee whose first chairperson was Associate Professor Tan Chieh Suai. Senior Residents are given formal feedback and points of improvement are to be discussed with their mentors. After 3 years of training, eligible senior residents are assessed in a summative manner through a viva examination

administered by an examination committee appointed by the Residency Advisory Committee. Since the start of the residency-based programme, there have been 13 graduates from the year 2016 (n=5), 2017 (n=1), 2018 (n=4) and 2019 (n=3) who are now working as nephrologists in various institutions in Singapore as well as Malaysia.

In addition to the Clinical Competency Committee, the residency programme also maintains a Programme Evaluation Committee that seeks input from all stakeholders to provide feedback to the Programme Director with the aims of encouraging and monitoring programme improvement practices. The first chairperson was Dr Manish Kaushik. The programme also went on to win Best Medical Subspecialty programme within the SingHealth Residency fraternity two years in a row in 2018 and 2019.

From July 2020 onwards, under advice from the Residency Advisory Committee and the programme directors, the programme duration has been lengthened to 42 months with 6 months rotations each of Haemodialysis, General Nephrology, Glomerulonephritis, Peritoneal Dialysis, Kidney Transplantation, Acute and Interventional Nephrology and Geriatric/General Medicine.

As I write these last few paragraph in April 2020, with the COVID-19 pandemic escalating, education has taken a major sidestep into cyberspace especially with the mandatory social distancing rule. Tutorials and didactics are all done via teleconferencing with opportunistic bedside teaching during rounds taking centre stage. The wide usage of teleconferencing has created opportunities for senior residents rotated to other institutions to participate in teachings as a group online despite the need to segregate according to clinical practice areas.

The future of nephrology education? It is interesting to note that nephrology like any other subspecialty has become infinitely more complex. The challenge would be to continue to attract likeminded residents to join the nephrology family. The key word here is family as education should entail interprofessional education across the spectrum of healthcare professionals who look after patients with kidney diseases. Despite the Renal Medicine

The last clinical competency committee meeting in Renal Medicine in November of 2019 before Associate Professor Jason Choo (right, behind Associate Professor Tan Han Khim) stepped down as Programme Director of the SingHealth Renal Medicine Senior Residency Programme. Associate Professor Tan Han Khim (right, front) subsequently took over as Programme Director.

Senior residents anxiously awaiting the announcement from the Chief Examiner in 2017 on whether they had successfully cleared their oral exit examinations for specialist accreditation as nephrologists in Singapore.

Residency programme being resident centric, and some amount of adult self-directed learning being necessary, education should be integrated into the seamless care of patients we are entrusted. This could be in the form of simulations or reflective case-based discussions involving patients, nurses, allied health, social workers, junior doctors and senior physicians. With the advent of high-fidelity simulations, harnessing technology to allow experiential patient care immersion can probably improve resident learner retention of information as well as fine tune the art of medical judgement.

Last but not least, every medical education programme should remember that the betterment of patient care is the primary objective and with that lies the human side of medicine. The inculcation of empathy, the upholding of medical ethics, the reflection of personal biases, the harnessing of interdisciplinary viewpoints and the interplay between arts and medical practice should remain steadfast as the foundation of any training programme well into the future.

Associate Professor Jason Choo explaining the pros and cons of joining the SingHealth Renal Medicine Senior Residency Programme to interested residents in 2019.

Associate Professor Jason Choo leading an educational session at the renal registrar review and retreat (4R) course, which is an annual 1 to 2 day course where all senior residents in renal medicine attend and network.

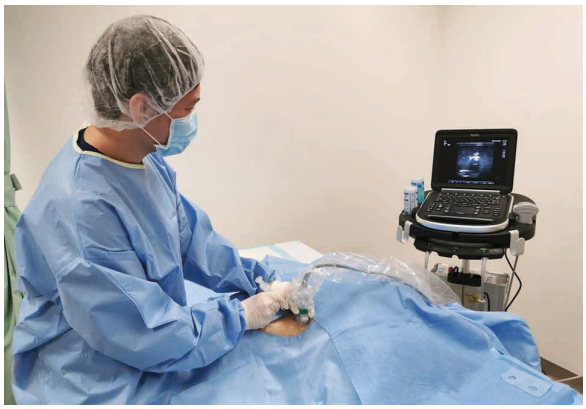
Faculty and residents from the SingHealth Renal Medicine Residency Programme supporting its booth at the SingHealth Residency Open House in 2018.

The 4R event has become an excellent opportunity for faculty and senior residents to network and learn best practices from each other.

Dr Teo Su Hooi celebrates her successful completion of her Advanced Specialist Training Programme with faculty and examiners in 2015 at the NKF Building.

Welcome party for new senior residents at Dr Manish Kaushik's home in 2017.

Dr Teh Swee Ping learning to insert a dialysis catheter under the watchful eyes of Dr Tan Chieh Suai and Dr Roy Debajyoti Malakar during the annual nephrology procedure simulation course for incoming renal medicine senior residents.



Dr Charles Ng, a 1st year renal medicine senior resident learning how to perform ultrasound guided dialysis catheter insertion.

Dr Riece Koniman and her trainee, Dr Carolyn Tien taking a break during the simulation course held in the Academia Building.

Dr Saradha Anantharaman learning how to do a renal biopsy with faculty Associate Professor Chionh Chang Yin from Changi General Hospital during the simulation course.

Graduation day for Dr Sherry Phang and Dr Riece Koniman at the SingHealth graduation ceremony in 2018.

Renal transplant didactic lectures on Thursday evenings with transplant coordinators as well as senior residents from SingHealth and Tan Tock Seng Hospital.

Senior Residency learning how to perform microscopic examination of urinary samples in the laboratory in 2018.

Renal Medicine senior residents at a research meeting where they review and critique on posters of research work done in the department.

Faculty would often take their teaching sessions outside of the tutorial room. Here, Dr Tan Ru Yu introduces senior residents to the different type of dialysates for haemodialysis at the haemodialysis centre.

Renal Medicine Senior Residents are encouraged to complete a research project and present / publish their findings. Here is Dr Teh Swee Ping at the AKI CRRT 2019 Conference in Malaysia.

Senior residents after successfully sitting for their specialist exit oral examinations conducted at the NKF Centre in 2016.

Examiners and Renal Medicine Senior Residents who successfully cleared their exit oral examinations in 2018.

Senior Residency Oral Exit Examinations in National University Hospital in 2019.

Training to be a Renal Physician

Associate Professor Terence Kee
Senior Consultant, Singapore General Hospital

In 1996, fresh from houseman ship at Alexandria Hospital and National University Hospital, I step into the hallowed grounds of SGH. Being a foreign graduate from Australia, I had no idea what SGH was about except the stories I heard from my father when he was a medical officer and registrar in the Medical Unit where he worked under Professor Seah Cheng Siang. It must have been destiny to have spent my first year as a medical officer in the three busiest units of SGH which was Cardiology, Renal Medicine and Respiratory Medicine. All 3 postings were an eye opener but, in the end, I fell in love with Renal Medicine. After 6 months in Renal Medicine, I had no hesitation to repeat Renal Medicine as one of my posting after I was accepted into the SGH training programme for Internal Medicine which was probably the embryonic form of the current residency programme. The SGH training programme for Internal Medicine Trainees was for 3 years with all postings done in SGH. I think I was the only Medical Officer during my times to have been crazy enough to spend 1 year in Renal Medicine. After successfully completing the 3-year SGH training programme for Internal Medicine and fortunately passing my MRCP at the first go in Edinburgh, I was torn between Emergency Medicine and Renal Medicine This was because I had also spend a year in the Accident and Emergency Department and experienced a fulfilling time doing resuscitations and managing trauma! But I remember that early morning in the critical care area of the Accident and Emergency Medicine when Professor Vathsala suddenly walked in and said "Terence! Do you want to join us? ". The rest is history.

In those days, life as a registrar was very tough. We covered by blocks and there would only be 1 registrar covering a block of SGH. Worst still, we only had pagers and they kept beeping the moment it was 8:30 in the morning. Furthermore, SGH did not have a lot of phones and we always had to compete with the nursing staff for first use of the phone. I do recall one day where there were simply too many pages and I went to the stairway at Block 4 to cry

because it was just too overwhelming. Fortunately, I had very good colleagues like Christopher Lim (who is now a Professor and Head of the Nephrology Unit at Universiti Putra Malaysia) where we helped each other to clear the rounds and blue letters (which was usually 20 to 30 per day) even if it wasn't our area of coverage or day to be on call. There were also plenty of dialysis catheters to insert in those days and I recall how we used to do the lines together and compete on who could insert the catheters the fastest. I think we were really good, considering we didn't have ultrasound to guide insertions and didn't have complications. We also shared an office together and joked about our mutual hardship, calling our salary "blood money". And there were the grand ward rounds on Monday mornings where Professor Woo would drill us with questions. Registrars and Medical Officers always took the grand ward rounds seriously and we would come back on Sunday evenings to summarise the cases and prepare answers for possible questions that Professor Woo would ask the next morning. Christopher and I would always be near each other during the grand ward rounds so that if one of us got into trouble, the other would rescue with the answer to Professor Woo's question. I really appreciated the grand ward rounds a lot as it forces you to study in depth so that you could shine in front of everybody when Professor Woo look in your direction.

Unlike today, we didn't have many registrars to share the call workload. There came a time when Christopher and I had to do alternate day calls for

a while. Furthermore, we had to answer blue letters in Tan Tock Seng, Changi General and KK Women and Children Hospital. So, you can imagine, we were travelling all around Singapore for 24 hours and we got to know the layout of these hospitals pretty well. We also didn't stay in hospital then and it was frustrating to return home, only to be asked to go back to answer another blue letter. Eventually, Associate Professor Wong Kok Seng who was Head of Department then agreed to allow registrars to stay in hospital for their calls. Despite the frantic taxi rides from one hospital to another while everyone was fast asleep, we still had time to treat our junior doctors with food from nearby hawker centres.

Despite the long rounds, numerous blue letters and sleepless calls, I felt all this was worth it. I was in a Department where I was learning exponentially each day thanks to the diverse case mix in the patient population and that the Department had Singapore's finest nephrologists such as Professor Woo Keng Thye, Associate Professor Wong Kok Seng, Professor Vathsala and Associate Professor Lina Choong. Though they were strict and often scolded me, they never failed to lend a listening ear or provide a gentle voice of caution when the situation called for it. We hardly any didactic lectures and what we learnt was what we were told by the bedside by our revered teachers or what we read before answering a blue letter. If you have a good mentor, you will always remember him/her for the rest of your life. My mentor was Professor Vathsala who essentially started early to groom me for a lifelong career in transplantation and academic medicine. Professor Vathsala always ensured that I would have one oral abstract to present at a scientific meeting every year. Naturally, this resulted in many weekends spent alone at the transplant office collecting and analyzing data, which would sometimes last till late in the eerie night. When the data was ready to be presented, my powerpoint slides would have to be vetted under great scrutiny by Professor Vathsala. Such reviews would happen after office hours and I recall that we stayed till 2 am in the morning, eating pizza and revising my slide presentation together. I respected her a lot for her efforts as she would often get calls from home about when she was coming home. Fortunately, such hard work paid off when I became the first renal registrar to be awarded the best oral presentation by a registrar at the SGH Annual Scientific Meeting in 2003. I also remembered my many tea sessions with Professor Vathsala in the ward 42 tea room where she would counsel me and even once, offered me a loan when I was short of cash! (she discovered I was doing locum in the Accident and Emergency Medicine Department on the weekends when I was not on call to help pay off my wife's student loan).

The last day as a registrar was spend in Professor Woo's huge office in Block 6 Level 6 where I sat for the viva examination in the presence of Associate Professor Wong Kok Seng, Dr Grace Lee, Dr Pary Sivaraman and Professor Evan Lee. It was daunting to be quizzed in front of so many distinguished faculty but thankfully, all the questions asked were cases that I had seen time and time again as a registrar. I also remembered Professor Vathsala calling me after the examination and how I lamented that I forgot what a haplotype was. When I reflect on my training days, we didn't have a lot of structured teaching, but it was all compensated by the immense hands-on clinical experience – learning by osmosis can work!

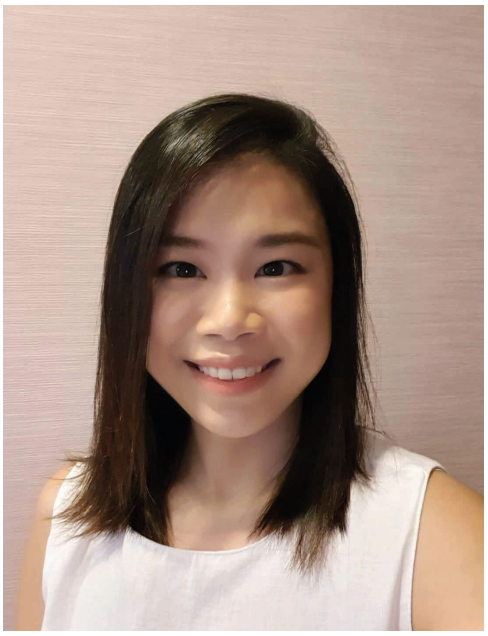
Dr Ng Chee Yong
Consultant, Changi General Hospital

Renal Medicine... I am sure whoever that has lived through a posting in this specialty, be it House Officer, Medical Officer, Junior Resident or Senior Resident will not be inclined to describe it as the kind that's a walk in the park. It was tough... especially so when it came to the night calls. When I was running between Block 4, 5, 6, and 7, Emergency Department, Dialysis Centre, Renal ICA (and hopefully my bed) at around three in the morning while trying to attend to countless calls, it was during such moments that I would start to wonder, "Why me, why keep calling me, why am I here instead of being with my family?" However, all these questions were promptly answered whenever I saw my patient smiling at me during the next morning round. Hey, he was the one who woke me up at 3am, struggling in his non-rebreather mask and almost kicked me when I was trying to set a dialysis catheter. So ultimately, it was the job satisfaction that kept me going.

My three years were tough, especially when I needed to juggle family and work - my daughter was born a few months after my training started and my boy arrived right before my exit exam! I would have to describe my three years of training as character building! The next time I face a challenge in life, instead of asking "Why me?", I will do so with a smile and instead say, "Try me!"

Dr Tay Hui Boon
Associate Consultant, Seng Kang General Hospital

Renal training has for me been one of the things that I had always wanted to do. Even back when I was a House Officer in general medicine in Tan Tock Seng Hospital, I knew that I wanted to become a renal physician one day. So, I went to SGH Renal for my first and last MO posting before joining them as a senior resident. But in addition to that, being the one thing, I wanted to do most in my career, it had been one of the hardest things in my life for me to do. I loved the work initially, but after having my first child while still in training, things got so busy that I burned out and became unable to cope. At the lowest point, I no longer enjoyed the work, wondered why I had embarked on training in the first place and had thoughts about giving it up. Yet it is often the difficult things in life that really make us discover what it is that drives us. I received a lot of counselling from my bosses in the department during that time and will never forget the advice my mentor gave me then, that even if we choose to escape from our problems, those things that we cannot face and overcome will just come back in a different form in the future. Without the guidance and practical support of many people in the department and the grace of God, I would not have been able to complete my training. Looking back, I had learned so much over my years in the Renal Department at SGH and they had shaped the way I think as a clinician forever.

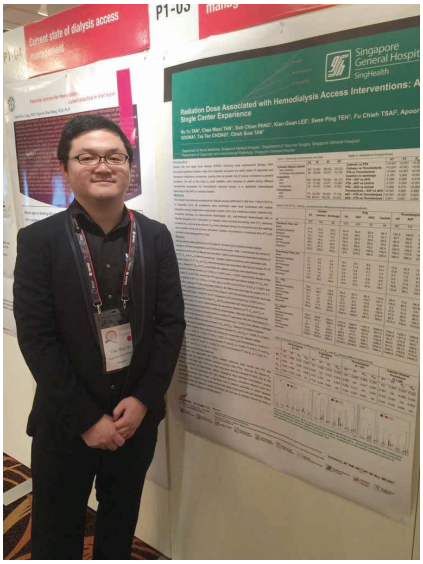


Dr Lee Pei Shan
Associate Consultant, Sengkang General Hospital

I had wanted to be a nephrologist ever since I became a House Officer. Thus, I was elated when I was accepted to the Renal Medicine Senior Residency Programme. I liken my experience in the family of renal medicine to being part of the Avengers. Multiple colorful and inspiring personalities who bring out the best in each other, and motivated by our common desire to provide the best for our patients - be it through extending our hours to review patients and allay concerns of their loved ones, or taking on research projects to try answering difficult clinical questions. The Senior Residents of Renal Medicine generally have a reputation in the hospital for being particularly stern, but like the Hulk, we've got a Bruce Banner inside of us! Residency has been particularly humbling – colleagues become family, tears are shed, and laughter is shared. I am grateful for this journey, and while I may not survive if I am put through it a second time, I would not have chosen any other path!

Dr Tan Chee Wooi
Senior Resident Year 3

Do I have regrets about joining the family of Renal Medicine? Yes, sometimes – when the work gets overwhelming with calls coming non-stop. However, most of the time I would say no as I have learned so much from my patients, mentors and colleagues! Most importantly, I had found my long-lost buddies (my batch mates whom I affectionately called "bears") who have been so supportive throughout this journey. If you ask me, it is truly a love-hate relationship between Renal and me!



Dr Ng Rui Zhi
Senior Resident Year 2

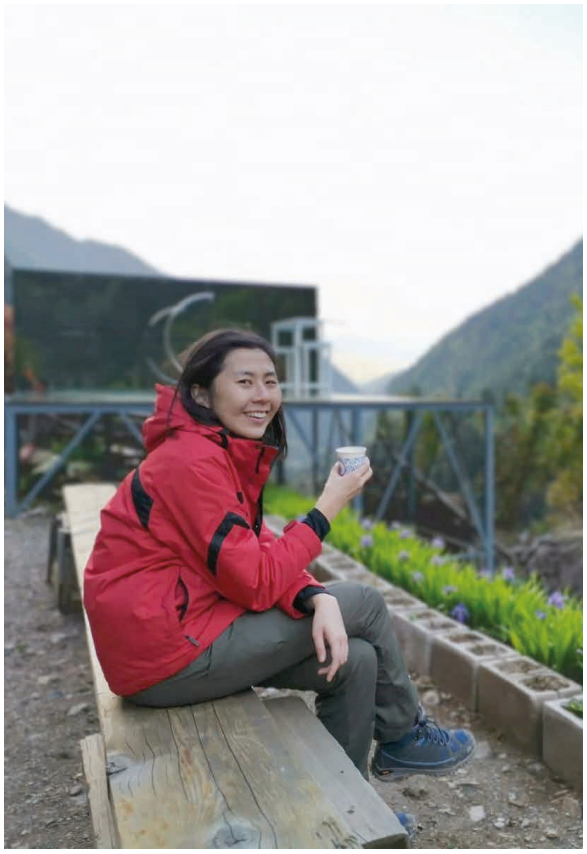
The journey so far in Renal Senior Residency has been exciting as well as stressful and I am still amazed at how my colleagues and seniors manage to remain calm under stress. It stretches our limits and surprises us with what we can accomplish. Renal also has very good teachers who inspire us. One example being at the beginning of my training, I was uncertain on how to do a renal biopsy properly and was always apprehensive whenever I have to do one. I was fortunate to have a few consultants who were very clear in explaining how to do it correctly. Subsequently my technique improved, and I became more confident in doing renal biopsies, for which I am grateful as it is an essential skill for all nephrologists.

Dr Teh Swee Ping
Senior Resident Year 2

I am always thankful to have guidance from some of the most dedicated personnel in renal medicine.

Dr Liew Zhong Hong
Senior Resident Year 2

The department has groomed me to become a better Resident and a doctor. I owe that to my patients, nurses, seniors and teachers from within this particular department, as well as from many others. They have helped me find strength that I never thought I could muster and taught me the meaning of resilience. Someone once said "Resilience means you experience, you feel, you fail, you hurt, you fall. But you just keep going!". It has been an uphill, but definitely fulfilling journey. It gives me great satisfaction at the end of the day to see the smiles on my patients' faces and to know that somehow, no matter how little it was, we have helped to make a difference towards a better quality of life for them all.



Mabel Tan
Senior Resident Year 1

Renal... I love the subject but hate the calls! I do care for the patients yet, feel frustrated and trapped witnessing how their lives are being broken. I am constantly learning, unlearning, relearning and struggling to keep up with this rapidly changing field of medicine. I love clinical medicine but feel overwhelmed by the pace and also the extent of multitasking that is expected of me. These conflicting emotions probably take a toll on every senior resident without he or she even realising it. Yet I have never regretted joining Renal Senior Residency or ever entertained one single thought of leaving this specialty. Six months in, and Renal Medicine has already become the narrative of my life. Almost every waking hour I have is spent doing something related to renal. The painful daily grind of a working day, or the sporadic little kind acts that make me smile... these have become the most integral parts of my life. My peers have become my family and closest confidants. Our seniors are just one text away even in the most unearthly hours. I don't think there is any other way... the only way to go onwards, upwards and 2.5 more training years right ahead!

Training Overseas

Dr Terence Kee at Westmead Hospital in New South Wales of Australia where he did his HMDP in 2004 in Advanced Renal, Pancreas and Islet Cell Transplantation.

Dr Manish Kaushik during his HMDP in 2011 where he trained in critical care nephrology. He was under the mentorship of Professor Claudio Ronco at the International Renal Research Institute Vicenza (San Bortolo Hospital) from 2011-2012.

Dr Sheryl Gan with other renal fellows during her HMDP in 2014 at the University Health Network, Toronto, Canada where she focused on Nocturnal and Home Haemodialysis as well as Geriatric Nephrology.

Dr Tan Ru Yu at Blacktown Hospital in Sydney, Australia during her HDMP in interventional nephrology in 2017.

Chapter 7

Future of Renal Medicine

Wearable Artificial Kidney (WAK)

Associate Professor Marjorie Foo
Senior Consultant and Director of Peritoneal Dialysis Programme
Principal Investigator, Automated Wearable Artificial Kidney (AWAK) First-In-Human trial

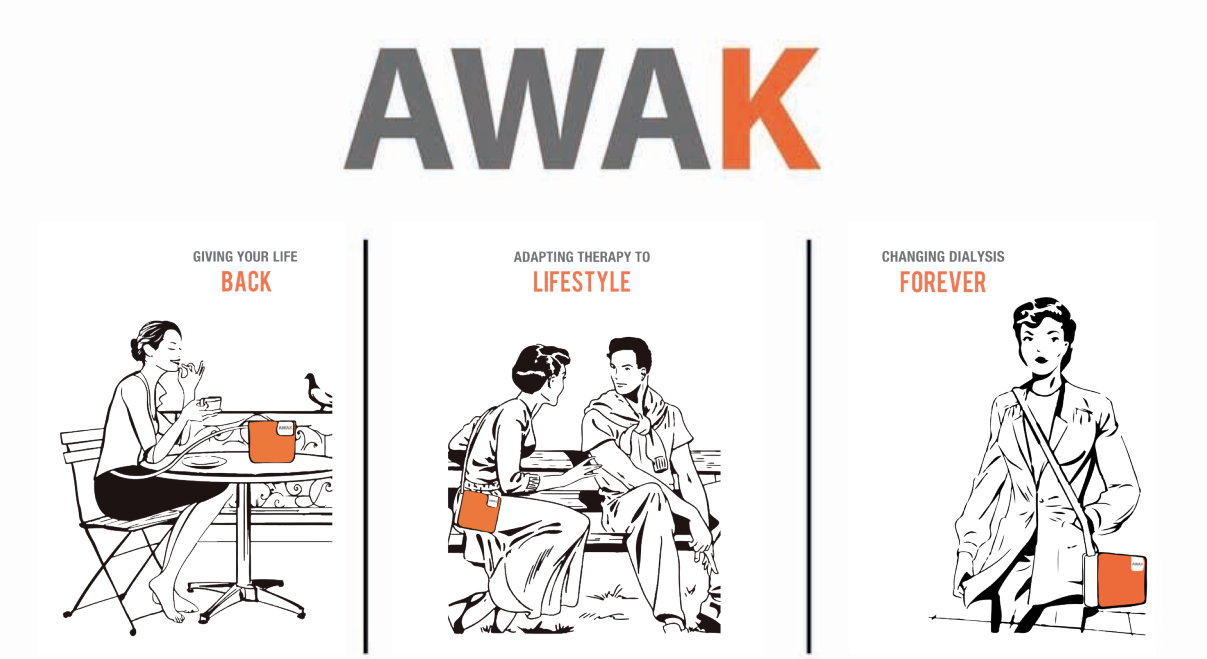
The AWAK PD is a compact device that weighs less than 2kg and enables dialysis to be performed "on-the-go".
Source: AWAK Technologies Pte Ltd

Kidney failure is one of the most dreaded diseases that can befall an individual and his or her family. Though treatment is available, the cost that comes with it poses a catastrophic economic burden to most patients and their families. The global burden of chronic kidney disease (CKD) has increased despite a worldwide reduction in non-communicable diseases. This is due to a worldwide increase in the incidence of hypertension, diabetes mellitus (DM), obesity, and ageing populations. DM and hypertension-related CKD account for a substantial portion of mortalities whereas DM-related CKD is what accounts for the increase in disability-adjusted life years (DALY).[1]

The role of the nephrologist has always been the preservation of renal function and the improvement of patient survival through transplantation and renal replacement therapy in the event of end-stage kidney disease. Organs are scarce which makes dialysis renal replacement therapy the next best option for survival. Nephrologists have always been on the lookout for novel therapies and novel therapeutic interventions through new medication and devices to improve patients' quality of life and survival outcomes.

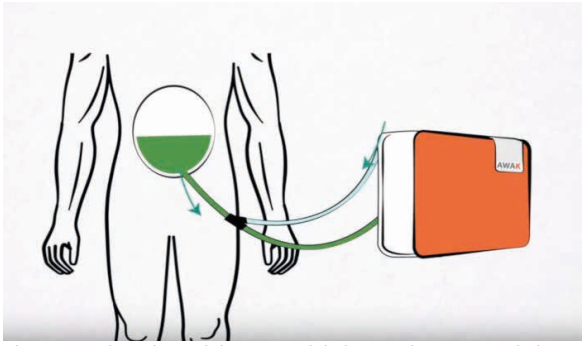
Dialysis treatments are costly both economically and environmentally. It uses a vast amount of water and electricity and generates a considerable amount of carbon footprint. The development of wearable artificial kidney (WAK) is one of the ways in which treatment can be made more environmentally friendly and also provides more freedom of movement for the duration of the treatment.[2]

WAK research has always focused on haemodialysis due to the vast number of patients on the modality but it has been met with multiple challenges of vascular access, anticoagulation, discard of ultrafiltrate, and wearability.[3,4] WAK for peritoneal dialysis originated in the United States 15 years ago but did not develop further due to lack of funds. The idea has resurfaced with the revival of sorbent technology



The AWAK PD device allows dialysis to be performed "on-the-go", overcoming the challenge of long hours of therapy and connection to dialysis machines, currently faced by patients with end-stage renal failure.
Source: AWAK Technologies Pte Ltd

based on Redy© Sorbent.[5] The Redy© sorbent was designed for use in portable haemodialysis and in the case of peritoneal dialysis (PD), it has been modified to regenerate dialysate during PD therapy. Other WAK in development include the Vincenza wearable (ViWAK), which is designed to be wearable for 12 hours with Icodextrin last dwell.[6] ViWAK also allows for remote monitoring, but there has not been any clinical trial performed for this device so far. Carry-life device is another system that uses an adsorbent cartridge, ion exchange and active charcoal to deliver dialysis.[7] Clinical trial was done on five patients over an eight-hour period and clearance results were encouraging, but larger and more conclusive clinical studies are still pending. WEAKID, a device sponsored by European Union lead by Netherlands is also in the early phase of safety trials.



The AWAK is based on tidal peritoneal dialysis and runs spent dialysate through a sorbent that can reconstitute fresh dialysate to be reinfused into the peritoneum.
Source: AWAK Technologies Pte Ltd

Associate Professor Marjorie Foo with members from the Investigational Medicine Unit during the trial for AWAK.

Dr Marjorie Foo at the American Society of Nephrology meeting sharing the experience of AWAK with the international nephrology community. The US Food and Drug Administration (FDA) granted Breakthrough Device designation to the AWAK PD device in January 2019.

The idea of dialysate regeneration in PD has allowed for the development of one of the earliest PD WAK in Singapore, developed in collaboration with AWAK Technologies. This is a system that makes use of tidal PD. The spent dialysate is run through a sorbent at a fixed rate and the enrichment module will reconstitute fresh dialysate that will be reinfused into the peritoneum. The continuous tidal and regeneration of fluids reduces the need for a vast amount of fluids to achieve adequacy. The regeneration of fluids also reduces transportation costs, indirectly offering a positive impact on the carbon footprint of PD. The AWAK device has completed its first-in-human trial with good safety data recorded. This clinical trial version will need enhancement in the sorbent to improve efficiency and in its design to improve acceptability and wearability.

Many WAKs are currently being designed, developed, and trialed in both Europe and Asia. The ultimate aims of these devices are to enable patients to enjoy a better quality of life and flexibility of treatment, as well as experience improvements to their lifestyle. When it comes to PD, infection is the Achilles heel of the therapy; be it for exit site or peritonitis, reducing the frequency of connections is one of the ways to prolong technique survival. In a closed WAK system, the incorporation of UV light sterilisation can potentially prevent and reduce infections in PD.

WAK is one of the ways PD can be performed and is another device in the armamentarium for patients to choose depending on their daily lifestyle needs. A wearable can be put at the bedside to be used as a miniaturised automated PD machine. The development of nanotechnology will have the potential to further reduce the size of the WAK and improve portability.[8] However, for WAK to revolutionise the way dialysis is done, it must be made accessible and affordable, easy to use, efficient in toxin removal, environmentally friendly, and with a secure network for data monitoring and storage.

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Extracorporeal Blood Purification

Dr Riece Koniman, Consultant
Associate Professor Tan Han Khim, Senior Consultant

Introduction

In SGH, the Acute Kidney Injury and Critical Care Nephrology services provide not only the standard acute renal replacement therapies such as continuous renal replacement therapy, but also extracorporeal blood purification. Extracorporeal blood purification refers to the removal of selected target humoral disease mediators from the blood compartment in order to ameliorate a disease. The concept, in its original form, was meant for application to severe sepsis and septic shock. Removing systemic cytokines from circulation was shown in early studies to be possible using Continuous Venovenous Haemofiltration (CVVH).[1,2] Studies showed that the effluent generated during CVVH contained substances that could reproduce systemic signs of septic shock in recipient study animals.[3] We now know that these substances are cytokines. Over the years, newer blood purification techniques have been developed, and their uses have also been extended to other diseases whose pathophysiology was also driven by blood borne humoral disease mediators. Autoimmune diseases such as systemic lupus erythematosus is one such example.

This review examines blood purification as adjuvant therapy in not only sepsis, but also other non-septic diseases and organ support. Rigourous data in the form of randomised controlled trials (RCT) are often lacking. Most data are derived from case series and anecdotal data. Thus, there is an element of empiricism when using blood purification that is not based on unequivocal organ recovery, disease remission and ultimately patient survival data. Therein, lies both the science and the art of using different blood purification tools to treat different conditions of different severities.

Sepsis Immunomodulation

Coupled Plasma Filtration Adsorption (CPFA)

In CPFA (Figure 1), plasma filtration is coupled to sorbent technology. First, plasma is filtered and passes through the sorbent column, whereby cytokines, inflammatory mediators and/or toxins are adsorbed. The purified plasma is then returned to the blood within the extracorporeal circuit and passes through a haemodialyser, whereby small water-soluble toxins and fluid are further removed, before returning to the patient. This technique was originally developed for the treatment of severe sepsis in critically ill patients in the mid-1990s but was later applied in other clinical settings such as poisoning, drug overdose and even autoimmune diseases. In SGH, a total of five patients had CPFA as adjunct treatment of sepsis between 2008-2012, as part of a clinical trial by HaemoLife Medical, Inc. The advantages of CPFA included the regeneration of plasma which avoided the use of plasma replacement fluids, and the high selectivity of humoral mediator removal by the sorbent columns. However, a multi-centre RCT in Italy in 2014 failed to show any survival benefit.[4] Moreover, many companies also have their own proprietary sorbent mix with different affinities for different mediators, with the latest sorbent cartridges being developed by Jafron in China, thus making it hard to judge the clinical efficacy and safety profile of individual sorbent devices. As a result, the use of CPFA has dwindled over the years.

Polymyxin B Haemoperfusion (PMX-HP)

PMX-HP (Toray Industries Ltd, Tokyo, Japan) (Figure 2) has been commercially available for use in Japan since the 1990s. It is mainly used to treat patients with endotoxic or gram-negative septic shock who are otherwise unresponsive to conventional treatment. This adsorption column involves immobilising Polymyxin B to polystyrene fibers and offers high affinity binding to circulating endotoxin and direct adsorption of inflammatory cells and mediators. Results on the efficacy of PMX-HP have been conflicting. The EUPHAS trial (Early Use of Polymyxin B Haemoperfusion in Abdominal Sepsis), a multi-centre RCT of 64 patients with severe sepsis or septic shock from intraabdominal infections, found

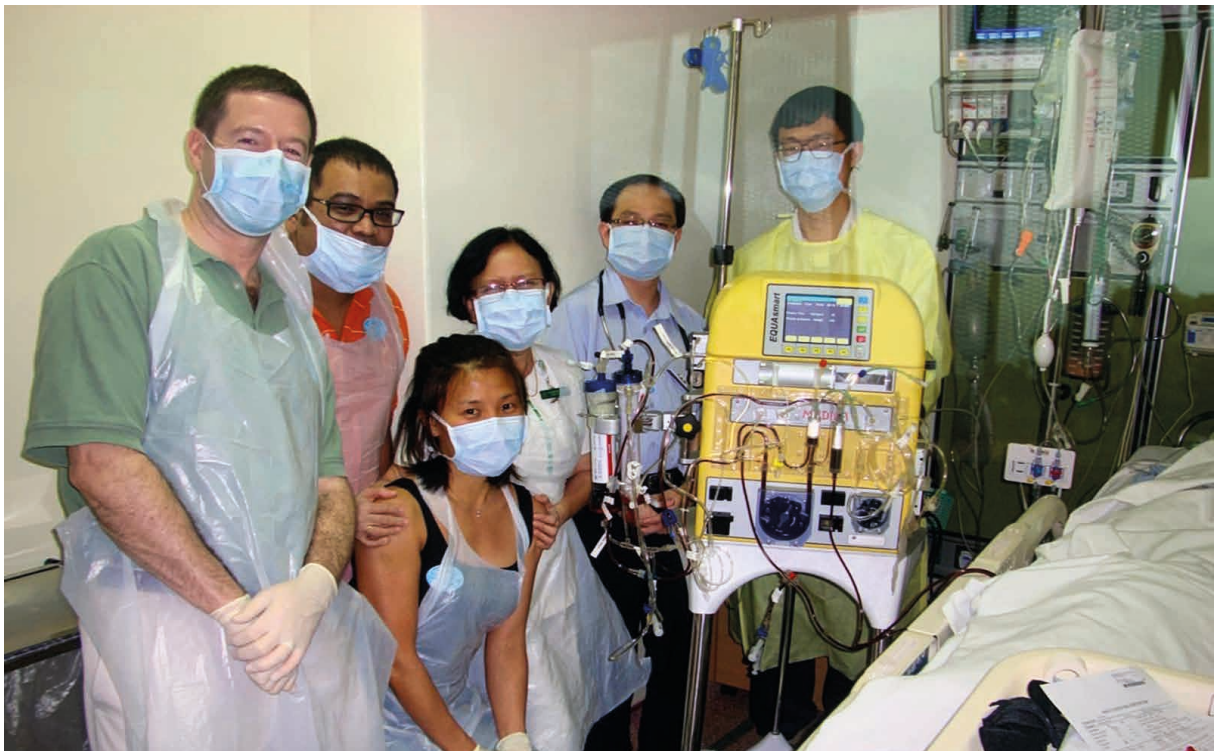

Figure 1
Coupled Plasma Filtration Adsorption (CPFA).

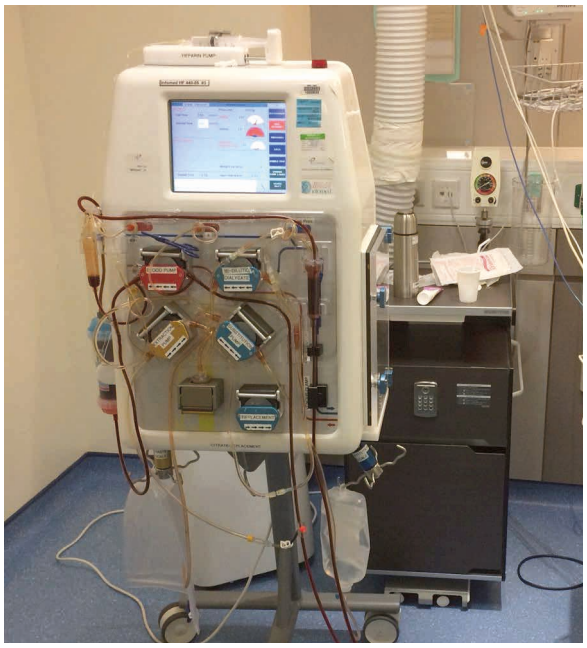

Figure 2
Polymyxin B Haemoperfusion (PMX-HP)

improvement in the haemodynamic status and 28-day mortality.[5] However, a recent meta-analysis of RCTs in 2018 found no benefit in the 28-day mortality.[6] There has also been emerging evidence on the use of PMX-HP for rapidly progressive interstitial lung disease.[7,8] In fact, the first PMX-HP performed in SGH, on 4 April 2018, was on a patient with dermatomyositis-related fulminant interstitial lung disease. The patient had a total of three PMX-HP therapies with improvement in the ratio of arterial oxygen partial pressure to fractional inspired oxygen, but subsequently died. The second PMX-HP, on 11 May 2018, was performed on a patient with gram-negative sepsis. To date, a total of five patients had undergone PMX-HP therapy in SGH. Despite its conflicting results thus far and the fact that more rigourous studies are needed, PMX-HP has been well tolerated and is a safe treatment for a targeted subgroup of patients who will otherwise have an unacceptably high mortality, and its use may affect our future practices in the management of patients with severe sepsis and septic shock.

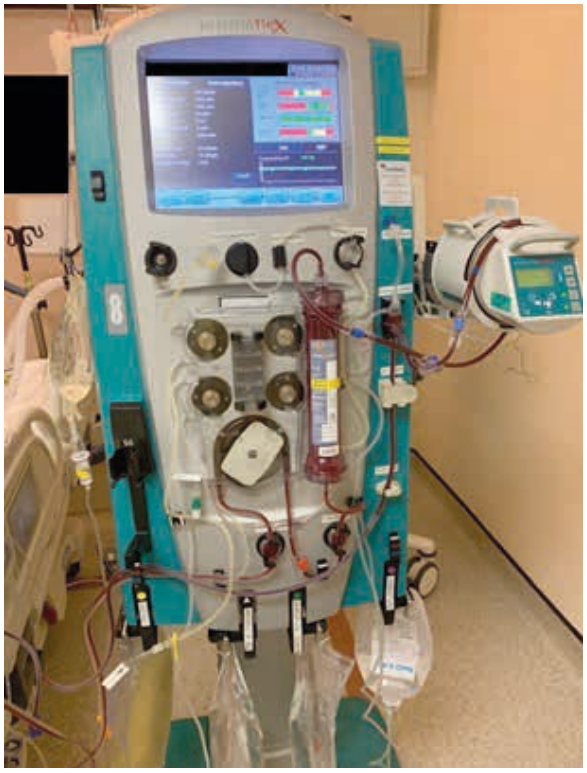

Figure 3
Continuous renal replacement therapy with oXiris® filter

Continuous Renal Replacement Therapy (CRRT) with Adsorbing Filter oXiris®

oXiris® (Baxter, Meyzieu, France) (Figure 3) is an AN69-based heparin-grafted membrane, which is modified with a positively charged polyethyleneimine layer and has the capacity for adsorption of endotoxin and cytokines. There has been emerging data to support its use in acute kidney injury with severe sepsis. Some studies demonstrated that the use of oXiris® filter leads to a decrease in the levels of cytokines (such as IL-6) and endotoxins, and improvement in haemodynamic status.[9,10] However, given its inherent adsorptive limitation for sepsis mediators, we decided it would be prudent to electively change the oXiris® filter every 12 hours for three consecutive days, even if there was no clotting or adverse circuit pressures, for a critically ill patient with severe sepsis and acute kidney injury. The first CRRT with oXiris® filter was performed on 28 November 2018. By day 4, there was a reduction in the vasopressin requirement of the patient. This case report was published in 2019.[11] Currently, we are continuing with this frequent oXiris® filter change approach for critically ill patients with Covid-19 and we will be publishing this data soon. We will also be increasingly incorporating the use of CRRT with oXiris® filter in critically ill septic patients with acute kidney injury, and if results are promising, it may become a standard therapy in the future.

Cytokine Immunoadsorption (IA)

In recent times, cytokine IA technique has gained much interest based on the hope that it can improve survival in severely ill septic patients. There are many other commercially available cytokine-adsorbing haemofilters, and CytoSorb® technology (CytoSorbents, Monmouth Junction, NJ, USA) is one among them. CytoSorb® is a haemoperfusion cartridge filled with polymer beads which allows for the adsorption of cytokines and a host of other inflammatory mediators as blood passes through it in the extracorporeal circuit. It has been used around the world for various inflammatory conditions including sepsis, burn injury, acute respiratory distress syndrome, liver failure and trauma. We have procured the supply for these cytokine-adsorbing haemofilters and will be commencing their use on selected groups of patients as indicated once the haemofilters are available.

Liver Support

Molecular Adsorbent Recirculating System (MARS) Albumin Dialysis

MARS (Figure 4) was first developed in the 1990s, and it was first used in SGH in 2002 following funding by a SingHealth research grant. MARS is composed of a blood circuit, an albumin circuit and a classic dialysis circuit. It not only allows for the selective removal of albumin-bound toxins which accumulate in case of liver failure, but also allows for simultaneous kidney detoxification. It can be used to treat fulminant liver failure and acute-on-chronic liver failure, either as a bridge to recovery or liver transplant. In SGH, the first patient to be treated with MARS therapy was a critically ill patient with hepatocellular carcinoma who underwent extensive liver resection and developed post-operative sepsis with hyperbilirubinemia. Since then, approximately 50 sessions of MARS albumin dialysis had been performed on 12 patients. Subsequent RCT and meta-analysis on MARS therapy did not find a beneficial effect on patient survival.[12,13] This apparent lack of survival benefit, together with the availability of better antiviral drugs to suppress hepatitis B flares and the establishment of the SGH Liver Transplant Programme in 2005, led to a

reduction in the use of MARS. The last MARS albumin dialysis performed in SGH was in May 2018.

Plasma Therapies in Humoral-mediated Disease

Therapeutic Plasma Exchange (TPE)

TPE is clinically proven for the management of various renal, haematological, neurological, and metabolic conditions. During TPE, plasma is separated from the whole blood and during this process, plasma-borne humoral disease mediators such as antibodies, antibody complexes, immune complexes or antigens are removed from the body. Red blood cells are then returned along with replacement fluid such as plasma or albumin back into the patient. In SGH, haematologists had been performing centrifugation TPE, which involved plasma separation using Haemonetics apheresis machine. On the other hand, nephrologists were using membrane plasma filtration with Fresenius 4008S machines as an alternative TPE technique up until 2016. Since 2016, there had been a transition to Informed HF40 machines for membrane plasma filtration TPE. Over the years, the list of indications for TPE has been expanding because of accumulating evidence of its treatment success and safety. Similarly, we have seen an increasing load of TPE in SGH. There was a total of 65 TPE performed in 2015, which grew to 148 in 2019, and this number is expected to continue to grow in the future.

Double Filtration Plasmaphresis (DFPP)

The removal of anti-ABO antibodies from the recipient's serum prior to ABO incompatible living donor kidney transplantation is necessary to avoid hyperacute rejection. Although TPE and IA have been widely used for the removal of anti-ABO antibodies, DFPP (Figure 5) has become an attractive alternative to selectively remove the immunoglobulin fraction from the plasma because of its higher selectivity, the minimal need for replacement fluids, and the lower cost. DFPP was first developed in Japan in the early 1980s by Agishi et al. and incorporates two filters with different pore sizes in the system.[14] The first filter (plasma separator) separates plasma from the whole blood, and the filtered plasma then passes through the second filter (plasma fractionator) whereby small molecular components are extracted and returned to the patient while larger molecules are selectively removed and discarded. In SGH, the first DFPP was performed in 2016 for an ABO incompatible living kidney transplantation recipient, and from then till 2019 a total of 182 DFPP had been performed. Due to the scarcity of deceased kidney donors, the cumulative experience in ABO incompatible living donor kidney transplantation, and the relatively good

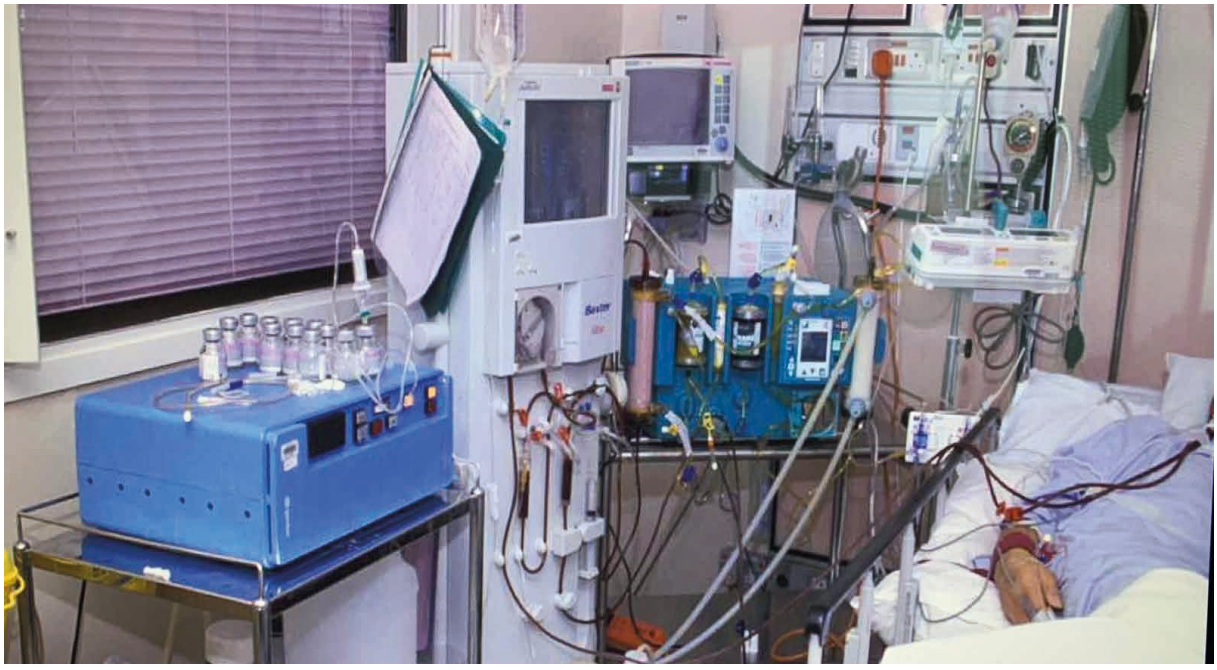

Figure 4
Molecular Adsorbent Recirculating System (MARS) albumin dialysis

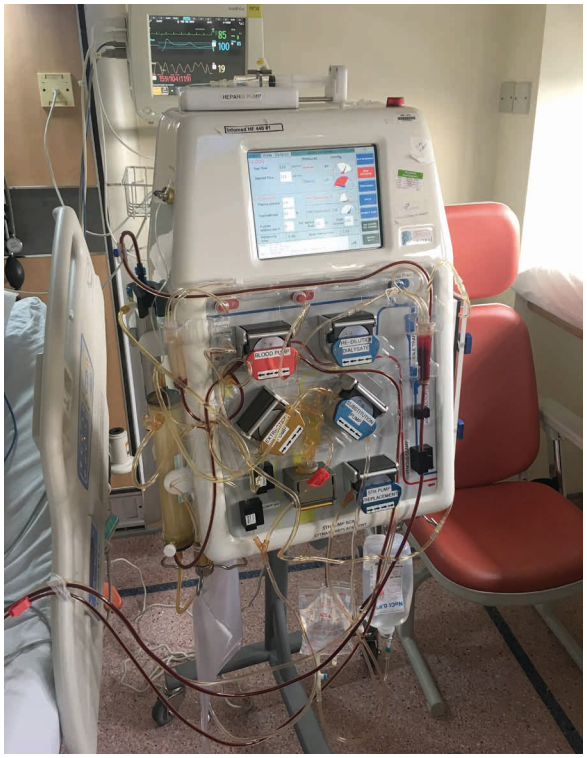

Figure 5
Double filtration plasmapheresis

Figure 6
Glycosorb® immunoadsorption

patient and renal outcomes, it is anticipated that in the future the number of ABO incompatible living donor kidney transplantation will continue to grow in order to expand the donors' pool, and there will therefore be an increasing use of DFPP.

Heparin is generally used as anticoagulation in DFPP. To mitigate the risk of bleeding from systemic heparin and with the cumulative experience on the use of regional citrate anticoagulation (RCA) in CRRT, we started performing DFPP with RCA on 26 October 2018, and has since protocolised the RCA prescription for use in DFPP.

Glycosorb® Immunoadsorption

Glycosorb® IA (Figure 6) was first used in SGH as part of the desensitisation therapy for Singapore's first ABO incompatible living donor liver transplant, which was successfully performed on 14 July 2017. Since then, the use of Glycosorb® IA has mainly been extended to ABO incompatible living donor kidney transplantation recipients. Glycosorb® is a bio-specific affinity column containing immobilised blood group A or B antigen linked to a sepharose matrix, and it specifically removes anti-A or anti-B antibodies. This procedure has been gaining popularity because of its high specificity for ABO antibodies while not removing other essential plasma components including clotting factors, and the fact that no plasma replacement fluid is needed. This technique is also particularly desirable for recipients with high baseline ABO antibody titer pre-transplantation as it enables large plasma volume apheresis per session, thus reducing the number of sessions required. The main drawback of Glycosorb® is its high cost. To date, Glycosorb® IA had been performed successfully on three patients in SGH. There has been no RCT comparing DFPP and antigen-specific IA so far, but with emerging data and increasing experience with the use of Glycosorb® IA, it may be incorporated into the standard desensitisation regimen in a selected group of patients in the future.

Conclusions

Extracorporeal blood purification is often an adjuvant therapy to the mainstay of treatment, for example intensive care unit supportive care or the use of immunosuppressant agents in transplantation or autoimmune diseases. However, there are still many unanswered questions with regards to the use of extracorporeal blood purification, such as the timing

of initiation of therapy, the optimum dose and intensity of therapy, and the efficacy of the treatment. The timing, dose or intensity of therapy is often analogous to renal replacement therapy in acute kidney injury, although these are less well studied with other device modalities including extracorporeal blood purification. There is also a lack of RCT comparing the various extracorporeal blood purification techniques. Even the relative efficacy of different plasma separation methods for TPE (centrifugation versus membrane plasma filtration) in various conditions such as thyroid storm or liver failure remains uncertain, and practical logistical consideration is the usual way of deciding which modality to use. The types of dialysis machines used for the different blood purification modalities are also different, as some companies will advise on the use of all consumables from the same manufacturer whereas others may allow the use of third-party devices such as PMX-HP.

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Towards Integrated Renal Care from Beginning to End

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Background

The prevalence of chronic kidney disease (CKD) in Singapore was 15.6% in 2007 and projected to increase to 24.3% by 2035.[1,2] CKD patients are at risk of progression to end stage kidney disease (ESKD), cardiovascular events and mortality.[3] Patients reaching ESKD require renal replacement therapy (RRT) or kidney transplantation to prolong their lives. The costs of dialysis and transplantation has taken up disproportionate amounts in healthcare budgets in all jurisdictions.[4] Therefore, it was suggested that the detection of CKD at earlier time points in the trajectory, along with appropriate management and earlier referral would lead to both clinical and economic benefits.[4]

An increasing number of patients was initiated on definitive dialysis in Singapore from 729 (age-standardised rate (ASR) 170.8 per 1,000,000 residential population) in 2006 to 1,166 (ASR 185.3 per 1,000,000 residential population) in 2016.[5,6] The most common causes of ESKD among incident dialysis patients in Singapore in 2017 were diabetes mellitus (67.1%) and chronic glomerulonephritis (14.6%).[6] Unplanned emergent initiation of RRT exposed patients to the risks of poorer survival, longer hospitalisation and more frequent hospital admission.[7-9] Unfortunately, the proportion of ESKD patients initiating on RRT with haemodialysis catheter access in Singapore has been high (ranging from 64.9% to 98.8%).[7-9]

Early CKD detection, early intervention, and timely referral to renal physician have been shown to improve patient outcomes (including for ESKD rate, mortality rate and hospital stay at initiation of RRT) and reduce healthcare costs.[4,10,11] Early identification of asymptomatic early CKD patients through screening of at-risk population in primary healthcare allows for early implementation of CKD management and apt referral to renal physician. For advanced CKD patients, CKD education and appropriate planning for RRT have also been shown to improve patient outcomes and expenses.[12] Multidisciplinary care of advanced CKD patients have been shown to improve mortality and hospitalisation rates, slow renal function decline and increase the number of patients who were initiated on dialysis with permanent access.[12-19]

In the recent years, patient-centric care has come into prominence. Nowadays, patients want to have a say in their kidney care plan. In one study, up to 61% of dialysis patients surveyed expressed regret at having started dialysis and half reported that they selected dialysis care because it was their physician's preference.[20] A timely multidisciplinary care approach may allow advanced CKD patients and their families time to assimilate the information and weigh treatment options available to make informed choice on their kidney care plan.

The main goals of CKD management are retardation of CKD progression, treatment of CKD complications, and adequate preparation when RRT is required. With a big at-risk and CKD population in Singapore, CKD management has to be done on a large-scale and with a coordinated, multipronged and multidisciplinary approach from early to advanced CKD.

Coordinating CKD Care with Primary Healthcare

Holistic Approach in Lowering and Tracking CKD (HALT-CKD) national programme is an ongoing coordinated effort from Ministry of Health (MOH) and local institutions to prevent the development and slow down the deterioration of CKD in Singapore. The programme involves collaboration among MOH officials, renal physicians, primary healthcare physicians and coordinators from all three healthcare clusters in Singapore (which encompass all the local public hospitals and polyclinic systems). Since 1st July 2017, the programme identifies and monitors the progress of all polyclinic patients with CKD stage 1 to 4 and optimises CKD interventions of these patients.

Low clearance clinic multidisciplinary team meeting with Associate Professor Jason Choo leading in discussions.

One of the strategies involves shared care of stage CKD 3B and 4 patients (eGFR 15 to <45ml/min/1.73m^2) between renal physicians in hospitals and primary healthcare physicians. These patients are referred to renal physicians in hospitals with the aims of confirming cause of CKD, optimising treatment of CKD and underlying causes, monitoring and treatment of CKD complications, and appropriate planning of RRT if required. In order to prepare for the increase in referrals to hospitals, SGH Renal Medicine had to optimise workflow relating to referral criteria, workload and discharge criteria. Together with the renal departments in other SingHealth institution, common referral criteria were established for ease of referral by primary healthcare counterparts. SGH renal physician workload was reviewed and a target number of new referrals to be reviewed by the renal physicians was set to ensure a rational waiting time for these new referrals. There remains an urgent need to balance the workload in SGH renal medicine, which is being reviewed and optimised with related ongoing qualitative projects.

Setting Up of Multidisciplinary Clinic for Advanced CKD

SGH is one of the largest tertiary hospitals in Singapore. By 2018, the Department of Renal Medicine had managed more than 20,000 unique patients, including 3,196 newly referred patients and 406 ESKD patients who were initiated on RRT in the same year. A multidisciplinary kidney care clinic (called Low Clearance Clinic (LCC)) was set up in SGH in August 2015 with the aim of improving patient outcomes by promoting the consistency and streamlining the processes in advanced CKD-related care through integration of care among physicians and allied healthcare groups. The clinic used a patient-centric model with reference to similar clinics at overseas centres in the United Kingdom and Canada. The current LCC team at SGH comprises

renal physicians, palliative physicians, advanced nurse practitioners, medical social workers, , renal coordinators, advanced care planning coordinators, pharmacists and dieticians. The patients are reviewed by the different healthcare professionals on an 'as-needed' basis and patients' issues are discussed in multidisciplinary meetings. The team works in close collaboration with the renal transplant team, vascular surgeons, community patient advocates and hospices to facilitate and enhance patient care. In addition to providing CKD and ESKD counselling, the renal coordinator is also the primary coordinator of the various kidney care services for these patients. The timeline for the change of LCC team composition is shown in Figure 1.

Table 1 Timeline on SGH Low Clearance Clinic Team Composition

Timeline	Low Clearance Clinic (LCC) Team Composition
08/2015 • Start of LCC • Start of multidisciplinary meeting • Inclusion of option of NKF Befriender Programme	1. Renal physician 2. Advanced practising nurse 3. Renal coordinator 4. Renal medical social worker 5. Pharmacist 6. Dietitian
04/2016 • Start of transplant counselling	1. Renal physician 2. Advanced practising nurse 3. Renal coordinator 4. Renal medical social worker 5. Pharmacist 6. Dietitian 7. Transplant coordinator
08/2016 • Start of palliative care (renal supportive care team) • Inclusion of Assisi hospice care team	1. Renal physician 2. Advanced practising nurse 3. Renal coordinator 4. Renal medical social worker 5. Pharmacist 6. Dietitian 7. Transplant coordinator 8. Palliative physician 9. Renal-palliative nurse 10. Advanced care coordinator
01/2017 • Change of transplant counselling from onsite review back to referral basis **11/2017** • Inclusion of option of Renalhealth Dialysis Centre tour **01/2019** • Start of individual renal physician LCC	1. Renal physician 2. Advanced practising nurse 3. Renal coordinator 4. Renal medical social worker 5. Pharmacist 6. Dietitian 7. Palliative physician 8. Renal-palliative nurse 9. Advanced care coordinator

Table 2 Baseline Characteristics of Patients seen at the Low Clearance Clinic versus Usual Nephrology Clinic

Characteristics	Low Clearance Clinic (n=167)	Usual Nephrology Clinic (n=527)	P-value
Age, mean (SD)	68.1 (12.1)	66.0 (12.6)	0.059
Gender, n (%) – Male – Female	 111(66.5) 56 (33.5)	 283 (53.7) 244 (46.3)	0.004
Ethnicity, n (%) – Chinese – Malay – Indian – Others*	 132 (79.0) 24 (14.4) 11 (6.6) 0 (0)	 375 (71.2) 97 (18.4) 43 (8.2) 12 (2.3)	0.091
Comorbidities, n (%) – Diabetes mellitus – Ischaemic heart disease – Cerebrovascular accident	 126 (75.4) 65 (38.9) 22 (13.2)	 358 (67.9) 141 (26.8) 31 (5.9)	 0.065 0.003 0.002
Aetiology of CKD, n (%) – Diabetes – Chronic glomerulonephritis – Hypertensive nephrosclerosis and vascular disease – Others**/Unknown	 119 (71.3) 24 (14.4) 20 (12.0) 4 (2.4)	 340 (64.5) 76 (14.4) 84 (15.9) 27 (5.2)	0.230

Statistical significance p<0.05

**Other ethnicities in usual nephrology clinic include 6 Eurasian*

***Other aetiologies in low clearance clinic versus usual nephrology clinic (n; %) include obstructive uropathy (1; 0.6% vs. 9; 1.7%) and polycystic kidney disease (3; 1.8% vs. 14; 2.7%).*

Multidisciplinary Clinic Patient Outcomes

We explored the patient outcomes between patients who exited LCC (through initiation of dialysis, transplantation or deceased) from August 2015 to December 2018 compared to patients who exited usual nephrology clinic from January 2017 to December 2018. In total, 167 patients from LCC and 527 patients from the usual nephrology clinic were reviewed. The mean age in the LCC cohort was 68.1±12.1 years compared to the usual nephrology clinic cohort of 66.0±12.6 years (p = 0.059). The LCC cohort has higher proportions of males (111 (66.5%) vs 283 (53.7%); p = 0.004) and patients with baseline ischaemic heart disease (65 (38.9%) vs 141 (26.8%); p = 0.003) and cerebrovascular accident (22 (13.2%) vs 31 (5.9%); p = 0.002). The baseline characteristics of the two cohorts are shown in Table 2.

Comparing long-term kidney care plans, there are higher proportions of the LCC cohort who chose peritoneal dialysis and renal supportive care compared to the usual nephrology clinic (Table 3, Figure 1) Comparing the types of access at the start of dialysis, there is a higher proportion of the LCC cohort who had peritoneal dialysis catheter inserted and lower proportion who had temporary dialysis catheter compared to the usual nephrology clinic (Table 3, Figure 2) Despite these improvements, there is room to do even better, especially in increasing the number of patients initiating on haemodialysis with arteriovenous access and increasing the number of patients for pre-emptive transplantation.

Table 3 Outcomes: Long Term Kidney Care Plan and Access at Initiation of Dialysis

Outcome	Low Clearance Clinic (n=167)	Usual nephrology clinic (n=527)	p-value
Long term kidney care plan, n (%)			
– Haemodialysis	71 (42.5)	326 (61.9)	<0.001
– Peritoneal dialysis	56 (33.5)	159 (30.2)	
– Renal supportive care	37 (22.2)	40 (7.6)	
– Transplantation	3 (1.8)	2 (0.4)	
Access at initiation of dialysis*, n (%)			
– Arterio-venous fistula/graft	18 (14.2)	67 (13.7)	0.001
– Peritoneal dialysis catheter	45 (35.4)	99 (20.2)	
– Temporary dialysis catheter	64 (50.4)	324 (66.1)	

Statistical significance p<0.05
**127 from Low Clearance Clinic and 490 from usual nephrology clinic had initiation of dialysis. Of the 490 from the usual nephrology clinic, 1 who was started with temporary dialysis catheter chose transplantation as long term plan, while 3 others who were started on temporary dialysis catheter and 1 who was started with arterio-venous fistula eventually chose renal supportive care.*

Moving Forward

Population-based studies provide one of the ways forward for CKD research. There is a need to have baseline data on local disease and complication burden, disease trajectory and patient outcomes. There is a collaborative effort among renal physicians in all healthcare clusters to create a nationwide CKD database to continuously collect such data. This data will allow hypothesis generation for future CKD therapies.

We are also focusing on understanding the pathogenesis of CKD aetiologies and progression with the hope of finding suitable new therapies to slow down CKD progression. There is an ongoing collaboration with NUHS clinicians and basic science researchers from Duke-NUS and A*STAR in the research of transcriptomic, proteomics and metabolomics in diabetic kidney disease.

From the qualitative and operational perspectives of CKD care, ongoing qualitative projects are being conducted to explore front loading investigation for new referrals, establishment of discharge criteria based on CKD prognostic modelling, and possibility of a CKD shared care model with primary healthcare physicians.

The LCC team aims to streamline and modify the team and workflow to maximise efficiency. Preliminary work is being done to review the payment package for LCC patients. Active studies are being carried out to review the role and value of multidisciplinary care in advanced chronic kidney disease patients in Singapore. These studies will be looking at patient outcomes, patient-reported outcomes, healthcare provider-reported outcomes and cost-effectiveness analysis of multidisciplinary kidney care clinic. Future

studies are being conceptualised to review the role of telemedicine, explore patient-reported outcomes in renal supportive care clinics and cost structuring of multidisciplinary kidney care clinics.

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The Low clearance clinic is operated by a multidisciplinary team that meets weekly to follow-up on complex patient care plans.

Biologics in Nephrology

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Introduction

The use of biologics in nephrology is not new, and in fact, biologics have been in use in renal transplantation for the past three decades. The first licenced monoclonal antibody was Orthoclone OKT3 (muromonab-CD3) which was approved in 1986 for use in preventing kidney transplant rejection. It worked by binding to and blocking the effects of CD3 expressed on T-lymphocytes, but its use was limited due to reported side effects and reduced effectiveness from the human anti-mouse antibody response, and it was soon withdrawn.[1] Currently, biologics are used widely in renal transplantation for various indications, before and early or late after renal transplantation in both high- and low-risk recipients. Several monoclonal and polyclonal antibodies are being used in desensitisation for ABO-incompatible renal transplantation, induction, rescue therapy of steroid-resistant acute rejection, treatment of post-transplant recurrence of primary disease such as nephrotic syndrome or atypical haemolytic–uremic syndrome (aHUS), and in late humoral rejection.

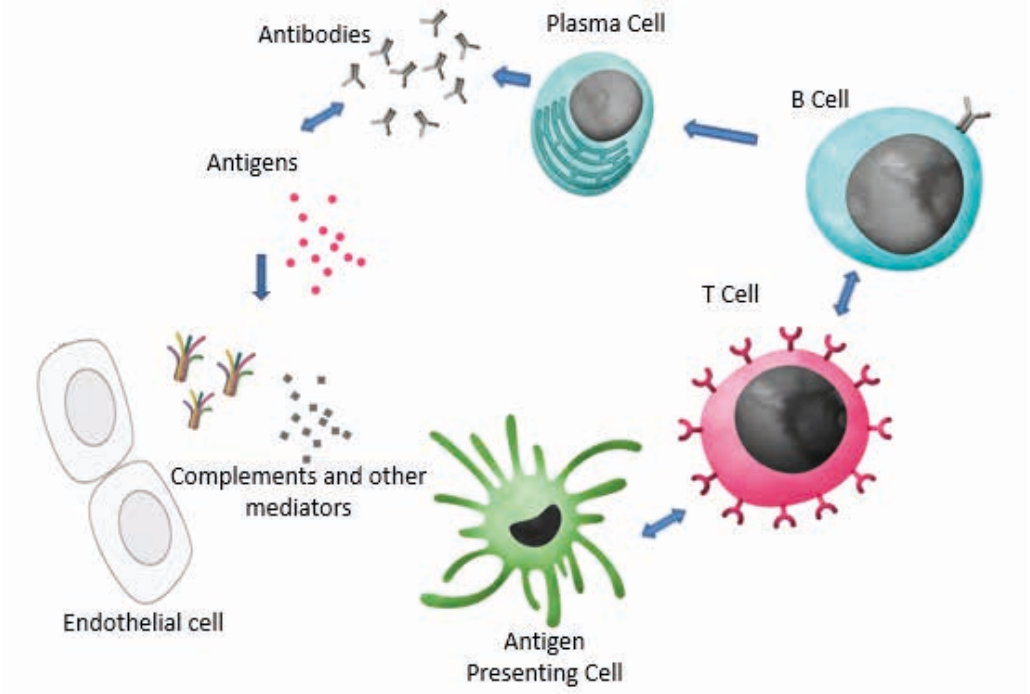
In immune mediated glomerulonephritis, the underlying pathological abnormality lies in the immune mediated injury and inflammation within the glomeruli.[2] Current treatment strategies consist of general supportive measures, given concurrently with conventional immunosuppression, usually involving high dose glucocorticoids with or without cytotoxics, thus resulting in exposure to potentially serious side effects. The number of biologics used successfully in the treatment of glomerular diseases have increased significantly in the past two decades, especially in inducing remission (often the most hazardous part of the journey), and in refractory and relapsing disease.

Biologics can be broadly defined as any therapeutic agent derived from microbials, proteins, antibodies, cells, or tissues. They were initially designed for neoplastic diseases in oncology, but expanded into the realms of transplantation and autoimmunity in the fields of rheumatology, dermatology and nephrology. More specifically, biologics are biotherapies that specifically target different mediators and pathways involved in the physiopathology of diseases. Biologics can target a single molecule such as a specific cytokine, cell receptor or an enzyme. Biologics can be in the form of monoclonal antibodies, usually partly humanised (X-mab) or receptor constructs, which are fusion proteins based on a natural receptor fragment linked to an immunoglobulin frame (X-cept). The first mouse monoclonal antibody was developed in the 1970s and in the last few decades we have witnessed a flurry of antibodies being developed, with 600 entering clinical studies and since the 1990s, at least one biologic approved per year for clinical use.[3]

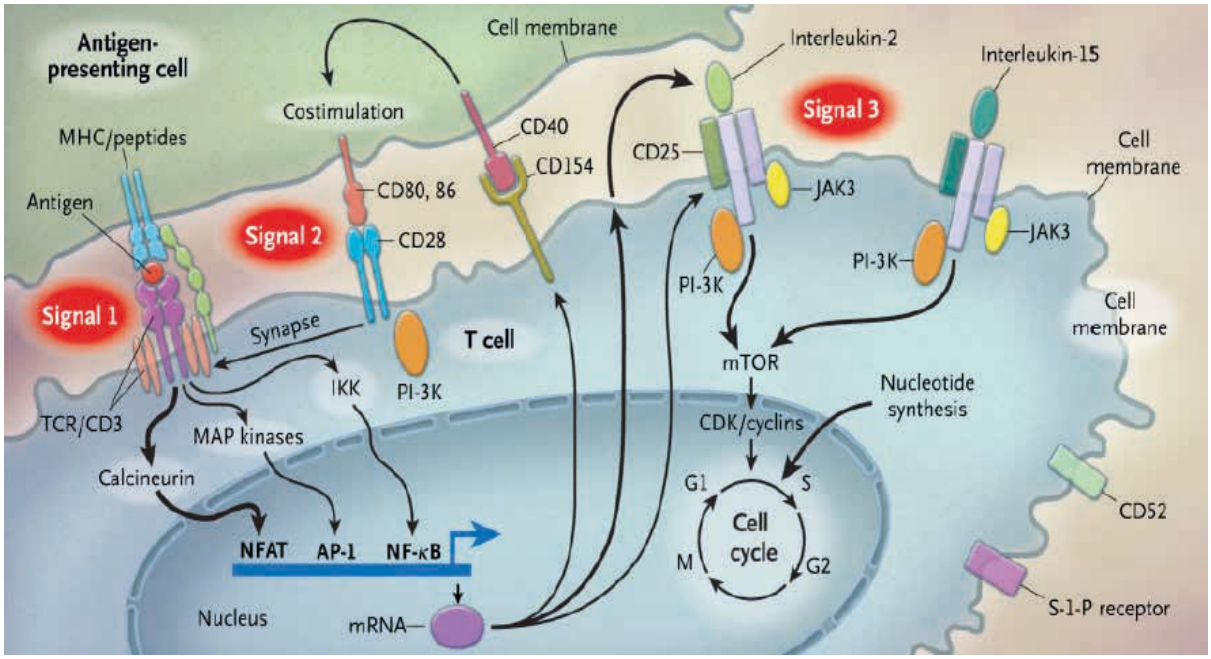
So, what's so hot about biologics? Why are they touted as the next big thing in almost all fields? This is because as much as we have progressed, standard therapy still fails us in a substantial proportion of patients. Even when successful, standard therapy often produces serious side effects and long-term sequelae. Biologics with their targeted therapeutic strategy can have several theoretical advantages: reduce the spectrum of side effects associated with standard drugs, provide consistent long-term efficacy, result in fewer long-term complications and increase the ease of administration. In this review, we will summarise the use, efficacy and safety of some of the more commonly used biologics in use in renal transplantation and glomerular disease.

Immune Targets of Biologics

To understand how biologics work, we need to first understand how the immune system works (Picture 1). Productive immune response is the result of a complex interplay of various cell types with either direct or indirect effector functions. The antigen presenting cell (APC) stimulates T cells and B cells via a 3-signal pathway (Picture 2). B cells, with the help of T cells, mature into antibody producing plasma cells. The antibodies produced bind to antigens, triggering activation of complement and other mediators. The targeting of specific cell types or components of the pathway can result in depletion or suppressed activity,



Picture 1
Overview of the immune system



Picture 2
3-signal pathway.[4]
An antigen on the surface of APC binding with T-cell receptors constitutes "signal 1," transduced through the CD3 complex. Costimulation, or "signal 2," delivered when CD80 and CD86 on the surface of dendritic cells engage CD28 on T cells. Signals 1 and 2 activate three signal transduction pathways: the calcium–calcineurin pathway, the RAS–mitogen-activated protein (MAP) kinase pathway, and the nuclear factorkB pathway. These pathways activate transcription factors that trigger the expression of many new molecules, cytokines (e.g., interleukin-15) which activate the "target of rapamycin" pathway to provide "signal 3," the trigger for cell proliferation.

and in this way we can essentially mitigate the body's dysregulated immune response in the pathogenesis of disease.

Blocking T Cells

T cell depleting agents/polyclonal antithymocyte globulins were first used in the 1960s and have been widely used in renal transplantation for the past three decades. [5] Rabbit ATG (rATG) (Thymoglobulin; Genzyme, Cambridge, MA, USA) and equine ATG (Atgam; Pfizer, New York, NY, USA) are polyclonal antithymocyte antibodies prepared from the sera of rabbits and horses immunised with human thymocytes respectively. Their diverse mechanisms of action include lymphocyte depletion by T cell apoptosis and complement-dependent lysis, interference of surface, adhesion, and trafficking molecules, and induction of T-regulatory and natural killer cells.

Today, rATG continues to be widely used as an induction agent despite the development of newer biologics. While historically used for high-risk patients (retransplants, extended criteria donation, or donation after cardiac death), its use has recently been extended to living donor transplantation. Its benefits include reduction in delayed graft function and it has been incorporated into nephrology guidelines as one of the recommended induction agents.[6] It is generally well tolerated, but symptoms related to cytokine release, myelosuppression, and in rare cases serum sickness may occur. Other problems can include increased cytomegalovirus (CMV) and other viral infections, and the data for increased risk of posttransplant lymphoproliferative disorder (PTLD) with rATG are at present mixed. [7,8]

Blocking Co-stimulation

Interleukin-2-receptor antagonists (IL2RA) block "signal 3" in the T cell stimulation pathway by blocking the binding of IL2 to its receptor, thereby preventing lymphocyte activation and proliferation.[9] We are familiar with two such agents, namely Basiliximab (Simulect, Novartis) which is a recombinant chimeric mouse/human IgG1 monoclonal antibody, and Daclizumab (Zenapax, Hoffmann-La Roche), a humanised monoclonal antibody (discontinued in 2009).[10] In 2009, the Kidney Disease: Improving Global Outcomes (KDIGO) group and European Renal Best Practice Advisory Board recommended in their set of clinical guidelines for kidney transplant recipients to receive IL2RA as first line induction therapy, except in patients with high immunologic risk, who are suggested to undergo lymphocyte depletion.[11] In our centre, we still routinely use IL2RA for low immunological risk renal transplants and reserve the use of rATG for higher immunological risk renal transplants performed for ABO incompatible or sensitised recipients.

Abatacept is a recombinant fusion protein made up of cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) linked to the Fc fragment of IgG1. CTLA-4 is a T cell membrane protein with high affinity for CD80 or CD86 (also known as B7-1 and B7-2) which are the co-stimulatory molecules expressed on APCs, part of "signal 2" in T cell activation. Abatacept results in the inhibition of the costimulatory signaling of T cells, selectively blocking T cell activation and has been used in rheumatoid arthritis and evaluated in patients with lupus nephritis on top of a mycophenolate or cyclophosphamide-based immunosuppression protocol.[12-14] We can conclude from these studies that abatacept permits reduction of proteinuria but offers no difference in end point for remission rate compared to placebo. Abatacept was investigated for use in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) but failed to show promise and there is also limited information on its use in steroid dependent nephrotic syndrome (MCD/FSGS).[15-17]

Belatacept (minimal change disease and focal segmental glomerulosclerosis) is a fusion protein composed of the Fc fragment of a human IgG1 immunoglobulin linked to the extracellular domain of CTLA- 4. It differs from abatacept by only two amino acids and has a higher binding affinity to CD80/CD86 (four times more than abatacept), resulting in a 10-fold higher in-vitro potency compared with abatacept. The Belatacept Evaluation of Nephroprotection and Efficacy as First-line Immunosuppression Trial (BENEFIT) was an international phase III trial designed to evaluate belatacept-versus cyclosporine-based regimens in approximately 650 adult patients receiving kidney transplants from living or standard criteria deceased donors[18]. Belatacept was well tolerated by patients and resulted in equivalent patient and graft survival, superior renal function, and a trend toward less chronic allograft nephropathy. Belatacept-based therapy also generated a trend towards improved cardiovascular and metabolic profiles. The downside was that rates and grades of

acute allograft rejection were higher in the belatacept-based regimens versus the cyclosporine group but investigators reported that the majority of the acute rejection episodes occurred early (within the first three months), showed no sign of recurrence, and were resolved with treatment. The subsequent three-year BENEFIT follow-up study confirmed equivalent rates of patient and graft survival and reported that belatacept-based regimens demonstrated advantages for long-term renal function which remained stable throughout follow-up, unlike the cyclosporine group, which declined over time.[19] There were also no cases of acute rejection from year 2 to year 3 in the belatacept groups, confirming that those episodes tended to occur in the immediate time period after transplantation and were subsequently unlikely to recur.

As promising as it sounds, there are several barriers to belatacept use which include:

i. Risk of PTLD which although rare, was more common in the belatacept groups, particularly amongst patients who were Epstein–Barr virus negative recipients

ii. Formulation (intravenous dosing requiring regular infusion visits): After the initial induction phase of belatacept, patients are required to maintain a 28-day infusion schedule over the lifespan of their allograft in combination with daily immunosuppression. Patients with very poor peripheral access may require more invasive line placement to ensure administration. This may lead to additional infectious risk that outweighs the benefit of the agent.

iii. Cost of belatacept is triple that of equivalent calcineurin inhibitors (CNI), not including nursing resources and disposables associated with its intravenous dosing. [20]

Blocking B Cells

B cells have a unique and central role in normal immunity. They interact with APCs, act as APCs themselves and provide co-stimulatory support to T cells (interaction between the CD 40 on the B cell and CD 40L on the activated T cell, amplified by BAFF (B cell activating factor) also known as BLyS (B lymphocyte stimulator)), and are responsible ultimately for the development of B cells into plasma cells and immunoglobulin production.

Rituximab

Rituximab is a chimeric murine/human monoclonal antibody against the CD20 antigen on B cells, resulting in the almost immediate depletion of B cells after the first dose, with aim of preventing plasma cells activation and hence production of auto-antibodies. It has no effect on matured plasma cells and existing circulating auto-antibodies. [21] Rituximab was first licensed for use for the treatment of non-hodgkin's lymphoma in the 1990s and has been approved for use in rheumatoid arthritis since 2006. Thereafter it has been used increasingly in autoimmune diseases. Dosing schedules range from IV rituximab 375mg/m2 BSA weekly x 2-4 doses (lymphoma protocol) to IV rituximab 1g two weeks apart (RA protocol). It is generally accepted that after a dose of rituximab, the B cell depletion will last for a period of six months to one year. With growing evidence of its efficacy, many adaptations have been made, including modified shorter courses or prolongation of treatment at fixed dose intervals and usage for maintenance therapy. It is generally considered a safe drug and most adverse events include minor infusion reactions have only rarely put limits on its use. True estimates about the incidence of infections directly related to rituximab are difficult to obtain because most patients receive concomitant immunosuppression, but rituximab is usually not associated with an increased risk for common or opportunistic infections.[22-26]

Rituximab in renal transplant is always administered in conjunction with IV immunoglobulin and/or plasmapheresis and was first used in ABO-incompatible renal transplant where it replaced the more invasive splenectomy as part of the recipient-preconditioning protocol, and is now also used in many desensitation protocols for highly sensitised patients. It is also used in selected acute and chronic humoral rejection. [27]

Rituximab is a therapeutic option to induce and maintain remission in patients with AAV. Conventional immunosuppression has changed AAV from a highly fatal one to a chronic disease with remission and relapses, albeit with persisting issues of therapy related toxicities, primary treatment failures and high relapse rates. Rituximab has been found to be not inferior to cyclophosphamide for remission induction

and was superior to cyclophosphamide in patients with relapsing disease and superior for remission maintenance in comparison with azathioprine. [28-31]

Rituximab has been used as induction therapy for lupus nephritis, particularly in refractory cases or in conjunction with low dose conventional immunosuppression in selected cases. The disappointing results of the EXPLORER trial (Exploratory Phase II/III SLE Evaluation of Rituximab trial included 257 patients randomised to the addition of rituximab or placebo to the standard therapy of immunosuppressive agents and corticosteroid) and the LUNAR trial, a multicentre phase II trial which failed to show superiority of rituximab versus placebo (given in addition to mycophenolate mofetil and steroid based therapy) have been explained by several factors: too few patients, strong placebo effects, use of background therapies including liberal steroid use, heterogeneous outcome measures and patient population.[32-33] Uncontrolled studies and meta-analyses data suggest rituximab use could be most beneficial in refractory patients, patients who experience a new flare-up after intensive immunosuppressive treatment or patients intolerant to standard therapy.[34-37]

The use of rituximab in idiopathic membranous nephropathy (IMN) has grown exponentially in the past decade. Ruggenenti was the first to use rituximab as first-line therapy in IMN and to publish on the largest retrospective cohort of 100 patients, with excellent results reported.[38] In July 2019, the MENTOR trial of rituximab versus cyclosporine A (CsA) for IMN in adults was published.[39] MENTOR randomised 130 IMN patients with proteinuria ≥5 g/day despite at least three months of RAS blockade, and an eGFR ≥40 mL/min/1.73 m^2 to receive CsA for 12 months or two rituximab infusions, 1g each, administered 14 days apart and repeated at six months in case of partial response. The primary outcome was a composite of complete (CR) or partial remission (PR) of proteinuria at 24 months, which 60% in the rituximab group achieved versus 20% in the CsA group ($P < 0.001$). In addition, of these patients, 35% of rituximab patients had CR versus none in the CsA group. Rituximab was also associated with less common adverse events and better-preserved kidney function. The RI-CYCLO trial which was completed by December 2019 is assessing the efficacy (primary endpoint CR at one year) and safety of rituximab versus cyclophosphamide/steroids in 76 patients with membranous nephropathy.[40] Another major trial, Sequential therapy with TAcrolimus and Rituximab in primary MEmbranous Nephropathy (STARMEN), completed on 30 June 2019, randomised 86 patients to sequential therapy with tacrolimus for six-nine months plus single dose of rituximab (1g) or cyclophosphamide/steroids.[41] The primary endpoint was the proportion of patients reaching either CR or PR at 24 months. At the time of writing this review, the results of these trials were yet to be made public.

For rituximab use in refractory nephrotic syndrome, most of the literature comes from paediatric experience. Randomized controlled trials (RCT) in children with steroid and CNI dependent minimal change disease showed greater decrease in proteinuria, and higher percentage weaned off drug compared to standard therapy and its use is mainly supported by case reports and small case series.[42,43] It has also been used as rescue therapy in those who are refractory to conventional treatment, and patients with drug dependent disease or drug related toxicities.[44-46]

Other novel fully humanised anti-CD20 monoclonal antibodies include Ocrelizumab (examined in the BEGIN and BELONG studies, terminated prematurely due to lack of response and adverse effects), Ofatumumab (use limited to off-label treatment of refractory SLE) and Obinutuzumab (ongoing phase II trial in lupus nephritis with CR as primary endpoint (ClinicalTrials.govIdentifier NCT02550652)).[47-48] Epratuzumab is a recombinant humanised IgG1 monoclonal antibody directed selectively against the CD22 antigen on the surface of mature B cells, and acts as an immunomodulatory non-depleting agent as opposed to an acutely cytotoxic one. Three phase II randomised, double blind trials with Epratuzumab unfortunately showed no statistically significant difference in SLE disease activity when compared with placebo.[49,50]

Blocking B Cell Activating Factors (Belimumab and Blisibimod)

B-cell-activating factor (BAFF), also commonly known as B-lymphocyte stimulator (BLyS), plays a key role in cell survival and serves as a maturation factor for B-cells through its interaction with BAFF receptor (BAFF-R), stimulating B-cell proliferation and

counteracting apoptosis. In addition, BAFF has also been found to be necessary for plasma cell survival, and targeting this molecule would reduce the production of autoantibodies by immortalised plasma cells in many autoimmune diseases. Belimumab (BLM) is a human IgG1-λ mAb that binds and neutralises soluble BAFF while Blisibimod is a "peptibody" – a fusion between the Fc portion of IgG and a peptide sequence selected for its ability to bind with high affinity to BLyS.

The efficacy and safety of this new drug had been tested in two pioneering multicentre, double blind randomised controlled trials, BLISS-52 and BLISS-76 which included 1,684 lupus patients with mild to moderate disease activity (of note: without lupus nephritis).[51,52] These studies demonstrated a significant improvement in disease outcome with 10mg/kg of belimumab as compared to placebo. The beneficial effects of belimumab were measured using the SLE responder index (SRI), which combines the SLE disease activity index (SLEDAI), the British Island lupus assessment group (BILAG) and the physicians' global assessment (PGA).

The BLISS-52 group showed SRI rates one-year post treatment as 58% (p=0.0006), 51% (p=0.00129), and 44% in the belimumab 10mg/Kg, 2mg/Kg and placebo groups respectively. This demonstrates a significant clinical benefit with increased doses of belimumab. In addition, belimumab treatment also reduced SLE-related flares, normalised C3 levels and reduced steroid usage. The BLISS-76 trial further supported the significant clinical benefits of belimumab shown by the BLISS-52 trial, with the results demonstrating reduced active disease, relapse rates, time to onset of relapse and steroid requirement compared to placebo, in a dose-dependent manner. Furthermore, they showed that belimumab significantly reduced the risk of severe relapses over the trial period compared to placebo, with 26.5% of the placebo arm reporting a severe flare compared to only 18.5% in the low-dose treatment arm (p=0.023). Overall, the results from these studies provide robust evidence for the use of belimumab in the treatment of SLE, and it was based on the results of the BLISS trials that in 2011 belimumab was approved by the FDA and EMA, becoming the first drug approved for SLE for over 50 years.[53] Since the approval there has been an ongoing seven-year follow up of lupus patients assessing the tolerability and efficacy of belimumab SLE disease activity index in addition to standard of care therapies. The results remain positive with a sustained reduction in corticosteroid use and low rates of adverse effects.[54] The authors also described a 70% decline from baseline in auto antibodies and dsDNA at seven years after treatment.

The Efficacy and Safety of Belimumab in Patients with Active Lupus Nephritis (BLISS-LN) study (ClinicalTrials.gov Identifier NCT01639339) , involving 448 patients, met its primary endpoint demonstrating that a statistically significant greater number of patients achieved Primary Efficacy Renal Response (PERR) over two years when treated with belimumab plus standard therapy compared to placebo plus standard therapy in adults with active LN (43% vs 32%, odds ratio (95% CI) 1.55 (1.04, 2.32), p=0.0311). Belimumab also demonstrated statistical significance compared to placebo across all four major secondary endpoints: Complete Renal Response (CRR) after two years (the most stringent measure of renal response), Ordinal Renal Response (ORR) after two years, PERR after one year, and the time to death or renal-related event. In BLISS-LN, safety results for patients treated with belimumab were generally comparable to patients treated with placebo plus standard therapy. The safety results are consistent with the known profile of belimumab. The full study is expected to be published by end 2020.

The SynBioSe-1 study was a 2A, open-label, single arm proof-of-concept study that treated 16 SLE patients on mycophenolate who had severe, refractory SLE with LN. Patients underwent CD20-mediated B cell depletion with Rituximab (1g on days 0 and 14) followed by belimumab 10 mg/kg (on days 28, 42, 56, and every four weeks thereafter). The protocol called for all to have their glucocorticoids (60 to 7.5 mg/day) and mycophenolate tapered (to zero). The study endpoints at 24 weeks examined SLEDAI scores, immunologic effects (Autoantibodies, Neutrophil Extracellular Traps or NETs) and safety outcomes. As expected, they demonstrated a significant rise in BlyS levels following rituximab therapy, which was subsequently diminished with belimumab treatment. Rituximab and belimumab led to specific reductions in ANAs, autoantibodies and diminution of NET formation. Significant clinical improvement was also seen with a low lupus disease

activity state achieved in 10 patients, renal responses in 11 patients and concomitant immunosuppressive medication (mycophenolate mofetil)) tapered in 14 of the 16 patients.[55] SynBioSe-2 study (ClinicalTrials.gov Identifier: NCT03747159) is the randomised controlled follow-up to SynBioSe-1, which is estimated to complete by end 2020.

Blisibimod was tested in a phase II study (PEARL-SC) where patients with SLE showed improvement in their SRI when given Blisibimod 200mg SC weekly compared with placebo, on a baseline therapy of steroids plus mycophenolate mofetil. Results demonstrated a significantly greater reduction in proteinuria from week 8-week 24.[56] Results from a multicentre phase III RCT (CHASBLIS-SC1) however showed no significant difference in SLE disease activity compared with placebo and the follow-up trial in patients with LN (CHABLIS-SC2) was terminated prematurely. [57, 58]

Other Agents

a. Complement Targeted Therapy

Eculizumab is a recombinant, fully humanised hybrid IgG2/IgG4 mAb directed against human complement C5 to prevent the formation of membrane attack complex (MAC). It blocks the cleavage of C5 to C5a and C5b, where usually C5a functions as a potent pro-inflammatory peptide and C5b forms the first component of the MAC (C5b-9). It is approved for use in Paroxysmal Nocturnal Haemoglobinuria and Atypical Haemolytic Uremic Syndrome (aHUS). [59] The approval by FDA was based on the two studies by Legendre et al. Eculizumab treatment resulted in cessation of dialysis, large and sustained improvement in renal function, TMA event-free status and sustained improvement in haematologic parameters that correlated with aHUS disease activity. Due to its unique property in blocking the complement system, Eculizumab has been a therapeutic option for relative rare glomerular diseases that arise from dysregulation of the complement system. Case reports support use of eculizumab in patients affected by glomerulopathies secondary to complement alterations such as MPGN (C3N and DDD: abnormal activation of the complement alternative pathway, secondary to genetic mutations in complement regulators or the presence of autoantibodies inhibiting complement regulator activity)[60, 61] and demonstrate improvement in proteinuria and renal function. However, eculizumab use is limited by its extremely high price at almost $7000 USD per vial.

b. Cytokine and Interferon Targeted Therapy

Tumour Necrosis Factor-Alpha (TNF-α) Inhibitors such as Infliximab, Etanercept, and Adalimumab have been used in small pilot studies in patients with AAV, with no striking benefit compared with standard therapy.

Similarly, Interluekin-6 inhibitors such as Tocilizumab and Sirukumab used in SLE failed to show promise in safety and efficacy with reports of infective adverse events. However, tocilizumab is currently being investigated as a potential efficacious agent for antibody mediated rejection in kidney transplantation. Interferon (IFN)-targeted therapy were developed as IFN-regulated genes correlated to serologic disease activity markers of SLE such as anti-dsDNA antibody levels and complement levels. Of these, many molecules were aborted after phase I trials but some such as Anifrolumab, have gone on to the planning phase of phase II and III trials for patients with SLE and LN. (ClinicalTrials.gov Identifier NCT02547922)

Discussions and Conclusions

Biologics use in nephrology probably represents the most important advance in our field since the introduction of ACE inhibitors more than 30 years ago. The use of biologics in renal transplantation has been accepted as standard of care but in immune-mediated glomerulonephritis, clinical studies may not be as successful despite promising preliminary laboratory data due to the heterogeneity and complex nature of disease, study design and patient numbers. Some of the studied drawbacks of biologic use are that the neutralisation of a single cytokine or mediator may not always lead to the expected immunomodulatory effects in patients, due to redundant physiological pathways and that antidrug antibodies produced by the body will result in neutralisation or reduction in efficacy of drugs. In addition, clinicians have concerns over biologic-induced allergic/hypersensitivity reactions, lymphopenia which can increase infectious complication rates, limited long term safety data of repeated biologic use and baulk at the cost of

biologics. But for our patients, many of them long-suffering from a chronic relapsing-remitting course with toxicities from established standard therapies, biologics have offered them a much more palatable treatment option with less toxicity and significant improvement.

As we stand at the dawning of yet another decade, we find ourselves having to rewrite many of our previous treatment guidelines, for example, rituximab use in membranous nephropathy and AAVs. Many important clinical trials involving biologics challenging our usual clinical practice are expected to be published within the next few years, some of which SGH Renal has been part of. We are certain that biologic use in nephrology will grow exponentially and the future ahead looks promising.

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Surfing the Renal Silver Tsunami

Dr Sheryl Gan, Consultant
Director of Haemodialysis

Background and Epidemiology

As early as in the 1980s, the world has recognised that the population in many countries were and are ageing. Singapore is no different, then or now. The number of Singapore citizens aged 65 years old and above is increasing at a faster rate than our overall population growth. This group doubled from 220,000 in 2000 to 440,000 in 2015. The number of those aged above 65 years is expected to hit 900,000 by 2030. Hence, our Prime Minister Lee Hsien Loong raised this issue of our ageing population in the 7th Annual Ho Rih Kwa Lecture in 2015.[1] During this speech he mentioned, "Based on trends, if we project into 2050, even with immigration, the population pyramid (of Singapore) will be inverted." and, "We are going to be growing old faster than any society in the world."

We see similar trends in our local population with kidney disease. The Singapore Renal Registry showed that in 2018, more than seven in ten patients with the new diagnosis of chronic kidney disease (CKD) stage 5 were over the age of 60 years.[2] The age of our prevalent dialysis population has increased from a median age of 60.3 years in 2009 to 64.4 years in 2018. Patients aged above 60 years account for 64.6% of our prevalent dialysis population in 2018 compared to only 51.2% in 2009.[2]

With this, nephrology as a specialty has been increasing its focus in the realm of geriatric nephrology. This is with the aim to better prepare our healthcare teams and processes to cater to this special group of patients. This development has led to the first International Symposium on Geriatric Nephrology in 1985 and the Formation of the International Society of Geriatric Nephrology, which publishes its own journal. The training of nephrologists has also come of age with the recognition of geriatric nephrology being a requirement for nephrology training by the Accreditation Council for Graduation Medical Education (ACGME), and the publication of the online curriculum by the American Society of Nephrology.[3,4]

Dr Sheryl Gan with our medical social workers who are so vital to the holistic planning for renal replacement therapy and advance care planning.

Definition

The definition of geriatric patient varies in medical literature. It can refer to any patient who is between 50 to 80 years old.[5] The American Society of Nephrology defines this as a patient who is aged 65 years and above.[6] This varied definition illustrates that even within the area of geriatric nephrology, the types of patients we encounter are vast ranging and variable. They can range from the younger patients in their sixties to the centurions, from the active to the vary frail. Thus, the management of a geriatric patient in our renal clinics would require tailoring the management plans in accordance to the patient's overall health condition and personal choices.

Our Progress

Education and Increasing Awareness

For our patients to be able to make an informed choice, it is vital to educate them and their loved ones. With regards to the topic of treatment options in end stage renal failure (ESRF), we know that the median survival of those aged above 60 on dialysis is significantly lower than the younger patients, regardless of dialysis modality.[2] In addition, this survival disadvantage is augmented in the presence of significant comorbid health conditions such as diabetes.[7] Therefore, Renal Supportive Care (RSC), or non-dialysis treatment, is a reasonable choice for some patients with ESRF.

In our centre, 81% of participants of a study involving 103 dialysis patients above the age of 70 years old, had no decision regret about starting dialysis on the Decision Regret Scale.[8] However, there was 8% among them who had voiced regrets over their decision to start dialysis and 16% would not have made the same decision if they had to do it over again. In addition, this study found that a lower information satisfaction (with regards to dialysis and non-dialysis options) and decisional conflict were significantly associated with decision regret. Comparing this to the international community, decision regret in the elderly on dialysis ranged from 7.2% in a Dutch study to 60.7% in a Canadian study.[9,10] Another local study surveyed 151 elderly CKD patients and their caregivers who attended outpatient clinics in the renal unit.[11] 40% of patients and 46% of caregivers were not aware of RSC as a treatment option in ESRF. Some of these patients and caregivers may not have yet undergone counselling on treatment options. However, this may itself be a reflection of the level of knowledge about RSC in the general population. Of those who were aware of RSC, 54% of patients and 42% of caregivers would choose this option. Meaning, in other words, that RSC is deemed as an acceptable treatment option for patients and caregivers. In both these studies, a large proportion of patients (41%, 49%) and caregivers (68%) would base their decisions heavily on what their physician recommends.

Recognising this, the team in Duke-NUS, led by Dr Eric A Finkelstein and in partnership with the Department of Renal Medicine, Palliative Medicine and Social Work Department have created information materials catering specifically to older individuals with advanced kidney disease and their caregivers. A qualitative study was initially done.[12] This highlighted how this group of individuals would be keen to know more about caregiver burden, symptom control and financial costs with regards to treatment options in ESRF. The team has therefore created videos and information booklets in both English and Mandarin to address the need for such information. Moving ahead, they hope to conduct a local multi-centre study to assess the acceptability and efficiency of such materials to patients and caregivers when it comes to making decisions on their treatment options. We look forward to the continued work on this front from the team.

Finally, it is pertinent that our healthcare teams be educated and updated on the topic. It is our great honour that our colleagues from the various organisations have and continue to allow us to

participate in their events to raise awareness on key topics in geriatric nephrology. These events include General Practitioners Update (2010), Singapore Annual Peritoneal Dialysis Meeting (2017), Asian Colloquium in Nephrology (2019) organised by the Singapore Society of Nephrology, National Kidney Foundation (NKF) Annual Symposium (2017, 2019) by NKF Singapore, and Palliative Care Symposium (2017) by the Academy of Medicine, Singapore, Renal Chapter. We also had the honour to help with the education of our allied health colleagues in the Renal Social Work Community of Practice (2018). The topics in geriatric nephrology has also been incorporated into our Senior Residency training curriculum to better prepare our young future nephrologists to meet the rising needs of the silver generation.

Advance Care Planning

The SGH Renal Department, in partnership with other departments from SGH and the Agency of Integrated Care (AIC), has been involved in the Advance Care Planning (ACP) project since its introduction locally in 2012. We started out small but the number of referrals and ACP sessions conducted has increased gradually over the years. Since then, our team has conducted over a thousand advance care planning discussions. Of these, over 200 participants had formally completed their discussions. Although our numbers remain small, they represent a momentous step towards implementing ACP in our local population for healthcare workers, patients and their loved ones.

The challenges we faced were gradually resolved over time. Firstly, we needed increased awareness and support from the healthcare teams. In an earlier study, only a proportion of renal healthcare workers acknowledged that ACP discussions were one of their responsibilities.[13] In addition, many did not feel prepared to be conducting such discussions. To address this issue, we have started to hold activities such as SGH Grapevine meetings and the "Living Well" photo competition. ACP has also been incorporated into the core teaching sessions for healthcare personnel such as nurses and junior doctors. This allows us to increase the number of ACP advocators and facilitators across the SGH campus and among our community partners such as the National Kidney Foundation and Kidney Dialysis Foundation.

Secondly, patient, family and community awareness are important factors. We found that close to 30% of our patients and families approached for ACP discussions felt that there was no need for them or that the topic is taboo. In addition, we also discovered there were some patients who faced challenges when it came to understanding the concept of ACP. As such, patient education videos are now played in the waiting rooms whilst they are waiting to see their doctor. We have partners in AIC to help tailor patient information materials and ACP discussions along with their record sheets to suit our local context and in our various local languages. Our recent Quality Improvement Project with the Internal Medicine Residents saw the development of materials to assist healthcare personnel to introduce the concept of ACP in the four major languages and improve the availability of information materials.

Next, the timing of the discussions was another challenge we faced. 35% of our patients or families felt that there was no urgency for the ACP discussion or they were not ready due to the patients' existing health condition. However, we also found that around 15% of our patients passed away before the ACP discussion could be conducted or completed. Thus, we have incorporated ACP discussions as part of our care for patients in the Renal Supportive Care Clinic and the Haemodialysis Disease Management Clinic. In addition, we have included prompts on medical admission notes and daily inpatient ward round notes to remind the healthcare team involved to review the ACP when the need arises. This is an area for which we are still doing fine tuning and looking into the continued feedback from patients, their caregivers and the healthcare team.

Finally, we felt it was important that the completed ACP discussion should be readily available to the managing healthcare team whenever the need arises. With the help of AIC, we have moved from the initial pen and paper records and leveraged on information technology to allow these discussions to be available on a confidential electronic health record system which is accessible to healthcare teams in restructured hospitals and polyclinics.

Moving ahead, our department will continue to play an active role in the development of the

ACP programme by being a part of the SGH ACP Workgroup, continued quality improvement projects in ACP and continued engagement of our patients and caregivers.

Renal Supportive Care

The area of RSC has grown from strength to strength in our department. We have been fortunate to enjoy the support of the Human Manpower Development Programme (HMDP) in sending a team to the United Kingdom for training in RSC. We recognise that the role of palliative medicine and symptom control is not limited to end of life care. Dialysis patients have a high symptom burden which will persist despite dialysis treatment.[14] It is not surprising that a high symptom burden is associated with poorer quality of life and mood in our patients.[15] Symptom control is ranked highly by patients as an outcome they wish to achieve in their treatment.[16] Hence, this area has been incorporated into our Senior Residency training curriculum and Peer Review Learning.

Secondly, HMDP in 2019 offered support for Visiting Experts from the Edinburgh Royal Infirmary – Dr Caroline Whitworth and Ms. Johanna Mackenzie, to share with us on the creation and development of their centre's "Choosing Wisely" programme and RSC care pathway. During the visit, we had the opportunity to meet with our colleagues and partners in other restructured hospitals, community care providers and Ministry of Health (MOH) to have a fruitful discussion on the topic of RSC. It was an insightful experience for the team, which benefited greatly from their visit.

A Glimpse of the Future

Rehabilitation

CKD is associated with functional impairment and frailty which is in turn is associated with lower quality of life and survival.[17] In addition, many patients see a decline in their function around the time of dialysis initiation, regardless of their pre-morbid function.[18,19] Rehabilitation can be defined as a process by which both form and function are restored after injury or illness, such that life can be lived to the fullest capacity correspondent to the degree of abilities and disabilities.[20] Rehabilitation has shown benefits in a select section of dialysis population after admission for acute medical illness or amputation, with between 20% to 100% of them able to return home.[21] Rehabilitation in the dialysis population also reduces mortality and improves psychosocial well-being and health related outcomes.[22] Nephrologists can play a role in helping rehabilitation with adjustment of health targets such as dialysis ultrafiltration and target weight, phosphate, and nutritional support. With the opening of the Outram Community Hospital, we have new and exciting opportunities for our team to partner our colleagues to achieve improved outcomes for our CKD and ESRD patients.

Integration of Care

Multidisciplinary clinics have been shown to lower mortality, reduce the risk of emergent dialysis initiation and reduce hospitalisation.[23,24] The older patients with CKD and their caregivers would benefit from a "one-stop" clinic where they can meet the managing team. This may hopefully also reduce the burden and stress placed on the caregivers. Another advantage is that the resultant multidisciplinary meetings allow for tapping of the various types of expertise available so that common goals can be set and challenges identified early. New projects that have started includes partnering our community nurses to allow for our patients to be supported without the need for their frequent travel to the hospital. Telemedicine, which was piloted in the management of vascular access issues in NKF Haemodialysis centres also achieves a similar goal. We hope these will serve as platforms from which we can leap forward to offer more areas of service for all of our patients, and not just the elderly ones.

Conclusions

In conclusion, geriatric nephrology in our centre has matured and grown through the last decade. This was only made possible with the tireless work of our healthcare teams of nurses, medical social workers and therapists. Our colleagues in the MOH, AIC, Duke-NUS and community also play a pivotal role. Thus, I am confident that our department and healthcare teams and partners will, together with our patients and caregivers, be able to surf the Renal Silver Tsunami with joy!

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Growing Up In SGH Renal

A Personal Journey

Associate Professor Lina Choong, Senior Consultant

Sometime in 1986 after completing my post-graduate examinations, allowing me to further specialise in internal medicine, I made the fateful decision to do Nephrology. It was not a well-trodden path but one where few had taken. There was also not much competition as many were drawn to cardiology or endocrinology and the like. However, it promised much hard work and perseverance under the eagle eye of the then current Head, Dr Lim Cheng Hong.

As a Medical Student

During medical school days, anything to do with nephrology was difficult to tackle. It started with physiology which seemed a lot harder to understand than the other disciplines. Then in year 4, came the histopathology of the different glomerulopathies in "Robbins" which was a nightmare to remember. After the entire struggle, I do not remember much of it being tested. Maybe the examiners found it just as difficult and decided that it was a topic for specialist physicians and to give it a miss altogether! As a student doing my year 3 Medicine posting, I clerked a young lady who had just admitted in uremia and had started dialysis in the Bowyer Block attic, the forerunner of today's SGH Dialysis Centre. Along the years as a training physician, registrar and consultant, I met up with this same patient, much more perky and kept alive by the advances of the time and pioneers of that era.

As a House Officer

During the year of housemanship when I did Medicine in SGH, I had the (mis)fortune of referring a case of Gentamicin toxicity as a "Blue" letter to "Renal". In those days, all the consultation letters were written on specially printed pads of blue paper - hence referred to as "blue letters". In strolled the then Dr Woo Keng Thye asking to see the case. This was the time where juniors always followed senior doctors whenever they came to see a case of yours, to hear their opinions and to take instruction from them. He asked for the I/O chart and you could literally imagine me a house officer cringing because I had to tell him we did not put up one. He asked, "This patient has

Associate Professor Lina Choong as a faculty at a State of the Art Nephrology Nursing Symposium in 2017.

renal failure and you are not interested in the intake and output?". That was a lesson I never forgot. But he of course, would not remember this. I have often repeated this story to students to emphasise how important pointing out mistakes is to the learner. Having a mistake highlighted, you are unlikely to forget it ever. In those days, chronic peritoneal dialysis was quite unknown and I still remember reading an old case which I clerked as a house officer of PD related peritonitis which I misdiagnosed as gastroenteritis.

As a Medical Officer

Fast forward to the next year after a 6-month posting in Government Outpatient Clinic as a rookie medical officer completed, I was sent to the "unpopular" Renal posting. Dr Howe Hwee Siew now consultant in Rheumatology in TTSH and Dr Leow Khee Fong who went into primary healthcare formed a threesome caring the patients in the general ward, high dependency area and the dialysis centre. At that time, we only had Ward 42 to look after. The layout of the ward has not quite changed from 1982 when I started there. However, management of the renal patients has evolved quite a bit since then. As Medical Officers, we shared night calls with Cardiology. So a single medical officer looked after 2 entire floors

Associate Professor Lina Choong at the Chapter of Renal Physician Lecture and Dinner in 2016.

during the night. The activity was mostly in the CCU which is the same central area of Ward 44 today. During the day, our time was spent mostly on patients on renal replacement therapy.

Many patients presented late in their renal failure course and would be uremic. This is in stark contrast to present day when such presentation is relatively rare. They were also much younger and had less comorbidity. Most of them were good kidney transplant candidates, if only there were facilities to keep them alive and sufficient living or cadaveric donors. Acute peritoneal dialysis using the stiff Braun peritoneal dialysis catheter was the initiating dialysis modality. As Medical Officers we did countless such insertions in green theatre gown, cap and mask. There was the time during the procedure where we had to wait for the 2 litres of PD fluid to drain into the peritoneal cavity before we could test if the flow was satisfactory. It seemed interminably long especially around lunch time where we would get someone to apply some pressure to the bag of dialysate. These patients would get hourly to 2 hourly exchanges. We also had a variable potassium replacement protocol using 7.45% potassium chloride injected in the dialysate bags to replace potassium deficits measured on the daily serum potassium level. Because patients started off so uremic, we often had cases of dialysis disequilibrium. Each course usually lasted about 3 days. If there was no space to transit to haemodialysis, they would be discharged with the catheter in situ to return the following week for the next treatment. The current renal intensive care area actually housed 7 single rooms (rooms 8, 10, 12, 14, 16, 18 and 20) for this purpose. In addition, the first three rooms had double doors for added infection control to accommodate newly transplanted patients. There was an heater in each of the rooms to warm up the PD fluid.

Haemodialysis was through external arteriovenous shunts, a practice long abandoned once dialysis catheters came onto the market. These shunts were put in by the surgeons. During my MO years (1982-86), Professor Foong Weng Cheong and Abu Rauff did most of them. They were a nightmare to manage as clotting was very common. Once the peripheral limb vessels were used, they could not be used again as they had to be ligated.

In 1982, the dialysis centre in ward 42 was a large single room with the stations along the sides. The space was needed because the equipment took up a lot of space. While a single dialysis machine is able to dilute the concentrate, pumps dialysate and blood through relatively small hollow fibre dialysers allowing for diffusion of solute and ultrafiltration now, each component of dialysis then had to be assembled. Dialysate was mixed centrally and piped into each station. Tap water and not treated water for dialysate that we know of today was not used until the centre in Ward 42 was sent up. At that time, deionisers were used and not a reverse osmosis system. Many patients died of dialysis dementia from aluminium toxicity. Treated water eliminated cases of dialysis dementia. The next time dialysis dementia would be mentioned except as history of dialysis was when we used Aluminium hydroxide (Alternagel) as a phosphate binder. While there was a fear that this will also lead to dialysis dementia as written in the journals, this was not our experience. Blood pumps and monitors were much larger and large Multitec Kiil plate dialysers which had to be built up with cellophane sheets were still in use.

In those years, calls were continuous from the daytime duty hours and we would not go off until the next day's lunchtime if we were lucky.

As a Registrar

I returned to Renal Medicine in 1986 after stints in various Medical Units in SGH and TTSH units as a Medicine trainee as we were known in those days. Dr Vathsala Anantharaman started earlier than Dr Grace Lee and myself as we took our MMEd exams later. We learnt to perform renal biopsies in the treatment room between the current rooms 4 and 6 in Ward 42. Our trainers then were Dr Pwee, Dr Woo KT and Dr Akira Wu who had just come to Singapore from Australia. We used the Vim-Silverman needle where good timing and precision was required because of the 3 steps needed to cut the core of renal tissue. The kidney's location was surface-marked by measurement from a good x-ray of the kidney, ureter

Associate Professor Lina Choong celebrate Chinese New Year with the renal coordinators and administrative staff of the department.

Associate Professor Lina Choong is a regular participant of the regular Renal Medical Officers' farewell dinner organised by the department.

and bladder (KUB). No ultrasound was available when we started training. One or 2 years later, the Department managed to get a slot every Thursday for a technician to surface mark the kidney for us and we would aim for that spot marked with permanent marker. When we cleaned the patient, we hoped that all our markings whether from KUB or ultrasound scanning would not get wiped away. Later we would do biopsies at the radiology department until we got our own ultrasound machine when we did our own marking. We also moved to using the "gun" biopsy. Throughout this time, Mdm. Chin Yook Mooi has been with us on this journey. She is our trusty technician who till today processes our slides so that we trainees could read the them before our renal histopathologist, Dr Gilbert Chiang got his hands on them.

We learnt the art of inserting haemodialysis catheters for dialysis under the tutelage of Dr Pwee Hock Swee. The subclavian vein was used until reports of central venous stenosis arose after which we switched to the internal jugular vein. There was no ultrasound assistance in those days nor was there much of an interventional radiology service. Whenever we had difficulties, we called the anaesthetists because they put in more internal jugular catheters lines than anyone at that time.

Slowly but surely haemodialysis took over from acute PD as the emergency dialysis modality. SGH Renal Unit took in referrals from all corners of Singapore. While we were training and even after accreditation we travelled to every hospital to see patients. Some hospitals who had physicians trained in peritoneal dialysis such as Toa Payoh Hospital started their patients on acute PD before calling us. All patients requiring dialysis had to be transferred to SGH. We were, until the Renal Division in NUH under Professor Evan Lee started up in mid 1980's, was the sole provider of specialist renal services.

The only private Haemodialysis centres in the early years were run by Asia Renal Care under Dr Gordon Ku and Dr Beatrice Chen as well as Grace Polyclinic under Dr Chia Yam Pong. However, most patients could not afford private dialysis fees. Before I joined the department, a self-dialysis unit had been set up in 1975 in an unused kitchen in Alexandra Hospital (AH) with donated funds from NKF. We had 2 side rooms in SGH for training such patients to perform their own dialysis. This little training centre also trained patients for Home Haemodialysis. A second self-dialysis unit in Tan Tock Seng Hospital (TTSH) was set up in 1983.

Directly under our care were the patients in haemodialysis centre (at SGH), SDDU (self-dependency dialysis units in AH and TTSH) and Home Haemodialysis programme. While Home Haemodialysis was privately funded by the patient or their own medical benefits (a rarity in those days), patients for the SDDU programme had to undergo a selection process much like that of the Seattle committee of the 1960's. There was virtually nothing by way of medical insurance to help these patients except the government hospitals. Those dialysing in SGH and then self-dialysis centres were charged $10 every session in the early days, the equivalent of an outpatient visit at that time.

The nursing officers in charge of these centres was integral in the management of the patients in these programmes. I still remember the days when they would bring all the patient's files for our regular SDDU meeting to report to Dr Lim Cheng Hong on their progress. We scribed while our consultants suggested changes to dialysis prescriptions and medications.

The National Kidney Foundation of Singapore (NKF) had opened its first centre in 1982 at Kwong Wai Shiu Hospital but it was not until 1987 when its next dialysis centre was built. This provided an added avenue for needy patients to continue with haemodialysis. By 1996 they had about 10 centres.

Associate Professor Lina Choong with nephrologists from Singapore and Malaysia at the Asia Pacific Congress of Nephrology held in Beijing in 2018.

Chronic haemodialysis during those years made use of an acetate bath and hypotension was common. Symptoms were probably minimised because dialysis was not so efficient and we only had low flux filters. Reused dialysers was also routine and the wash area was fitted out to do manual cleaning of dialysers. In those years. Hepatitis B and C were common. While hepatitis B vaccination took on in the late 1980's we only had kits for Hepatitis C antibody testing in 1989. At an initial run, up to 30% of our chronic haemodialysis patients were positive for anti-HCV antibodies. This prompted a rethink of how the dialysis patients were nursed and cohorting of positive patients was started.

Bicarbonate dialysate also came in towards the end of the 1980's. Being new, it was priced higher than acetate dialysate. One of the early administrative tasks I was assigned was to determine if it was cost effective to move the entire dialysis centre to bicarbonate dialysate. Medical School did not prepare me for this but it was a matter of "dollars and sense" so how difficult could it be doing addition, multiplication and division after gathering the data? As it turned out, it was getting the data that was harder. Anyway, job completed, it was sent to Finance department and was accepted. Next was more traumatic having to deal with patient complaints when the price of dialysis was increased for those who were still on acetate bath. This stood me in good stead as in the years to come, more such decisions had to be made and management to be persuaded. All physician leaders will empathise with me on the learning of these skills.

I also worked with the Facilities department on the renovation of our Dialysis Centre to accommodate 20 stations from 10 stations. There were changes by Dr Lim Cheng Hong before final implementation but the experience in working with non-medical colleagues was useful for future projects. This was also when the water treatment system was changed from a deioniser to a reverse osmosis system by Waterman Pte Ltd.

Critical care nephrology was just taking shape. Instead of performing peritoneal dialysis we were able to treat the patients in the intensive care units who were haemodynamically unstable using continuous arteriovenous haemofiltration (CAVH) using Vygon single lumen catheters inserted in then femoral artery and vein. The patient's own arterial pressure powered the flow and standard hollow fibre dialysers allowed plasma fluid to be drained from the patient. Unfortunately, just like the external shunts of the past clotting was the problem and the patient's blood pressure was too unreliable. We soon switched to using the blood pumps from one of our dialysis machines (the familiar blue Gambro AK10) to deliver the positive pressure to the filter.

Associate Professor Lina Choong at the 2018 Association of Vascular Access and Interventional Renal Physicians Meeting in New Delhi.

We then used the double lumen catheters that are now available as venovenous access. CAVH became Continuous Venovenous Haemofiltration (CVVH). No one quite taught us how to do haemofiltration and we were grappling with the variables. Too much ultrafiltration, blood pressure fell very fast. What do we do during the first hour when ultrafiltration was started up? So, we fixed the amount of ultrafiltration per hour using roller clamps and infused an amount of replacement fluid having subtracted the negative per hour that we wanted. Not only did the nurses have to watch how fast the ultrafiltrate was coming out (it was an entirely manual process!) they also had to chart everything every hour and total it as we went along. What about the replacement fluid? We started with just normal saline and of course our patients became hypernatremic. We used sterile peritoneal dialysis fluid and patients could not tolerate the hyperglycemia. So we turned to making our own fluid. Luckily Microsoft Excel had come onto the market and I drew up a programme to calculate the concentrations of various elements and salts by mixing various fluids together. Bottles of normal saline, half strength and dextrose 5% formed the base in which we would add small quantities of 30% NaCl, 7.45% KCl, calcium and magnesium. I am quite sure the ICU nurses became quite disheartened whenever a patient needed CVVH. The Prisma machine came to us around 1990. One can just imagine the joy and delight of the ICU nurses not needing to mix solutions or measure the amount of ultrafiltration as there was sterile dialysate, 4 integrated pumps to do our bidding, weighing scales and automatic totalling.

Before I left for HMDP, I managed to complete a journal paper on Haemodialysis in Singapore. Happily, that is used to showcase what dialysis was like in those times. My HMDP attachment was on a topic unrelated to dialysis. I had chosen to improve on fluid and electrolyte management and perhaps learn some laboratory techniques. I had to wait my turn as only one registrar / senior registrar could go on HMDP at a time. Whilst in Colorado, I experienced how nephrology services were structured outside of Singapore. In the wards, the patients were much older than what we were used to at home. A case in point was a newly transplanted patient who was diabetic and an amputee. The consultant rounding turned to me and remarked that such a patient would not have received a kidney back where I came from. The profile of our patient now in age and comorbidity would be similar to what I saw back then 30 years ago in the US. In the laboratory, I studied calcium signal transduction in cultured vascular smooth muscle cell. I fed them with various cocktails and measured their contractility when pulsed with a vasoconstrictor agent. When I came back after my year overseas, I tried my hand at doing the same to mesangial cells having learnt the harvesting and culture technique from Dr Grace Lee and endothelial cells from Dr Yap Hui Kim's lab. Coincidentally, the Prisma was also showcased in the US when I was there. They did not appear to be doing any much better than we were in CVVH before this.

As a Senior Registrar / Consultant / Senior Consultant

It was also back to managing the HD services while trying to squeeze labwork in when I could. Dr Pwee Hock Swee had left for private practice and so did Dr Akira Wu. I had to see a lot of Dr Pwee's patients in addition to taking back my own. That is, whoever wanted to come back to me for follow up. A large bulk of these were kidney transplant recipients as he was the key person in the transplant programme. That was how I ended up with the large number I still have today.

The following are some of the key events that occurred under my watch:

Transfer of the Self Dialysis Programme Centres

In 1996 Dr Gordon Ku founded the Kidney Dialysis Foundation, a charity to provide haemodialysis to the needy patient. He had felt that the National Kidney Foundation was not providing adequately for all segments of the needy haemodialysis population.

The haemodialysis and critical nephrology team celebrated Associate Professor Lina Choong's birthday during one of their bimonthly meetings.

In the early 1990's, the demand for place in the SDDU programme was declining as there were no partners to help patients with haemodialysis. Economy was booming and jobs were easier to find. New patients were transiting to NKF's fully assisted dialysis instead. MOH decided to close the SDDU and transfer the existing patients to fully assisted dialysis so that the patient's helpers could be freed from this demanding task of turning up three times a week with the patient. I was asked to be the Medical Director as I had already been in charge of the operations of both of the dialysis centres at AH and TTSH. Dr Ku's Asia Renal Care management took over the manning of the AH centre first in April 1996 and subsequently TTSH in 1997. While at SGH various departments help out with different facets of management, many aspects of dialysis care had to be dealt with from scratch and procedures fleshed out. We had to look for doctors to round on patients. Specifications of equipment had to be detailed. Protocols for nurses to follow had to be written. For many years, renal physicians from SGH have quietly supported KDF patients in their capacity as rounding dialysis physicians.

SARS (Severe Acute Respiratory Syndrome)

The disease hit Singapore in 2003. It struck fear in all and the dialysis population was not spared. Within days, many infection control practices had to be instituted. At that time, we had both inpatients as well as outpatients coming to the dialysis centre. We knew that proximity and contact enhanced infectivity. Alternate dialysis stations were therefore used. We also decided to separate inpatients and outpatients to reduce contact between vulnerable groups. It was fortunate that at that time, KDF had been preparing to open their centre at Kreta Ayer to transfer cases from AH and return the premises to the hospital. Very quick discussions were held to use the new premises at Kreta Ayer for our outpatients. This arrangement went on for about 3 months until the situation died down and the SGH patients returned to the Dialysis Centre. However, this drove home the point that inpatients and outpatients have different care needs. Search was intensified to find a partner for setting up of an outpatient dialysis facility in SGH.

Setting Up the Renal Coordinator Unit

As the number of patients increased, it was inevitable that a lot of time had to be spent counselling patients on the concepts of renal failure and its treatment. I remember one day after having spent an entire half hour talking a patient through this that I could address his fears rather than the facts. Professor Woo had foreseen this and had our industrial partners such as Baxter and Janssen give us coordinators to counsel patients. A renal coordinator within the department was formalised and this was the beginnings of the renal coordinator unit. Its role was to educate patients, follow through on the key moments of their disease trajectory and to collect data to help the Head of Department with planning. They later include in their portfolio issues regarding renal bone disease and vascular access.

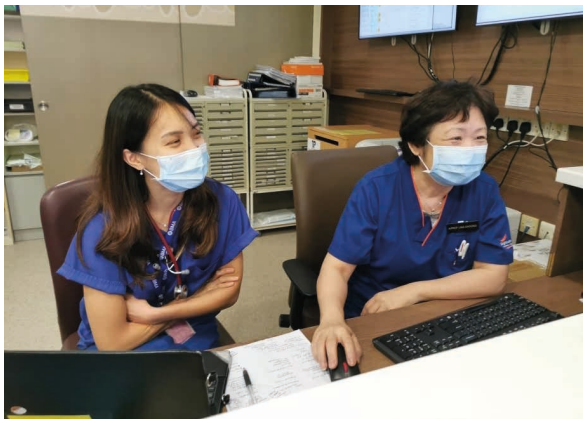
Setting Up RenalHealth Pte Ltd

For many years prior to the successful opening of Renal Health Pte Ltd, a search for a suitable partner had been initiated by Professor Woo. Finally Asia Renal Care was selected and held a 30% share in the partnership. I was appointed Medical Director and the centre opened in October 2007. I feel the most difficult aspect of this was persuading the outpatients from the current Dialysis Centre at Ward 42 to be a patient at RHPL. Many were worried about charges and we had to detail almost to the cent how they were to pay. We were fortunate to have Barbara Cheing who was temporarily seconded from SGH to help facilitate this.

Hepatitis C Outbreak in 2015

When this occurred, it was natural that the dialysis centre was considered as a possible cause. This was easily dispelled when it was realised that there was no connection in the way patients were

Associate Professor Lina Choong stayed back after the exit examinations to congratulate Dr Teo Su Hooi on her passing the exit vivas.



Associate Professor Lina Choong is known to spend a good time during her ward rounds teaching her junior doctors (here with medical officer Dr Natalie Liew).

seated. Most telling was that some were not even exposed to haemodialysis. The most stressful part of this, however, was the numerous audits we had to go through as infection control came under intense scrutiny. "There is no education like adversity." said Benjamin Disraeli. Because of this incident, the dialysis centre covered more ground than ever before in engaging staff and tidying up processes.

Other Experiences

You grow professionally and mature with experiences. I have found that anything that does not work well can be the basis of improvement. Every incident, every patient complaint provides learning of some sort. Because of this, quite a few quality improvement projects have originated in the Haemodialysis section.

Improvement in Haemodialysis Techniques and New Hemodialysis-related Therapies

Technological advances come quickly as industry is also fast to grasp all possibilities. We branched out to as many blood purification techniques as possible. From standard haemodialysis with bicarbonate, we instituted slow haemodiafiltration through the Fresenius ArtPlus dialysis machine purchased in 2003. This allowed bridging for patients from CRRT to intermittent haemodialysis so that patients could be downgraded from ICU's to Intermediate Care Areas when they did not need respiratory support. We started plasma exchange using this same machine when the haematology service could not cope with our cases especially at weekends. When the MARS machine came onto the market, we were the first to avail ourselves of the ability to perform liver dialysis. When the opportunity to purchase a cheaper CRRT machine with possibilities to do double filtration plasmapheresis, we grasped it. Some things did not work out immediately as predicted and may not make economic sense. They were and some are still terribly expensive treatments. But when we deal with patients, money is not as important. Support from the Nursing leaders were crucial in implementing new initiatives and making sure things ran smoothly. Much credit has to go to the Leaders in the Dialysis Centre of yesteryear – Monica Wong, Tan Ah Moey, Mona Lee, Susan Quek, Cheok Khee San, Neo Hock Bin, Wong Yew Hong and more recently Kan Foong Min, Michelle Ng and Ivy Liang. There were also trusty stalwarts like Johara, Hamidah, Lee Kum Ying, Wahida, Mary Tay.

Managing an Outpatient Haemodialysis Programme

I went for a Refresher HMDP in 1997 to observe how outpatient HD programmes were run in the US and how they were supported. Something I found very useful there was a checklist and multidisciplinary meetings which was attended by physicians, social workers, dieticians and on occasion, therapists. Any

Associate Professor Lina Choong is a champion of quality improvement, seen here having dinner with the team that worked on a quality improvement project in preventing intradialytic hypotension. This project received the Team Award for Target Zero Harm in 2020.

The gentleman standing on the right is Dr Quek Mong Seng, Professor Choong's devoted husband, who is considered an honourary nephrologist in the department because he frequently attend events organised by the department with his wife.

problems were flagged up for these various healthcare providers to manage. Due to manpower constraints, I could not implement multidisciplinary team meetings, I did manage to start a checklist where each aspect of patient care was detailed and if any changes were made. There was a lot of resistance when I trialed this because it entailed a considerable amount of work on the nurses part to collate biochemistry and therapy onto a single report. However, having such information is the basis of decision making and they caught on after a while.

The Age of IT

Seeing so many of routine tasks go online, we knew we had provide for printed dialysis report of a dialysis session and to order haemodialysis through the electronic Clinical Manager rather than the old traditional paper form. We quickly put in a request and fortunately, we didn't have to wait too long.

Post-op Parathyroidectomy Care

The clinical problem was that of lack of awareness of the hungry bone syndrome in the surgical units as well as our junior doctors who see these patients as "reviews" and may not be alerted to the rounding renal physician. So hypocalcemia was common in the earlier days and a mild state of "panic" will ensue. Another problem was the problem of intravenous calcium being started in a peripheral site rather than through a central line causing skin necrosis. Then there was no outpatient appointments given for calcium review or given for rather long durations. It was a chance for me to work with a multidisciplinary team including surgeons, pharmacists, nurses and the Quality department starting in 2002. A workflow had to be detailed and memos prepared for the patients to bring to unsuspecting house officers who clerk these patients. These memos had a long list of instructions and we hoped that these were

clear enough for the house officer to follow. From Clinical Coordinated Pathway, it was later promoted to a Care Process Model and this later went on-line. In addition, IT was able to create creative tiles in the Clinical Summary Tab, pulling trend information on serum calcium as well as orders for intravenous or oral calcium supplementation.

Voluntary Rounds at NKF

In late 2001, NKF was losing 2 of its fulltime medical staff to clinical practice in hospital. As a result NKF asked for SGH assistance in rounding in their centres. I took over Bukit Batok Centre. Unfortunately, the travelling was quite tough and I asked to be changed to a nearer centre and got Henderson. However, this gave me an opportunity to introduce my "rounding sheet" which they later converted to an electronic version.

During this time, other journeys relating to Nephrology were running parallel.

Nephrology Courses

The department ran several courses to interact with Family Physicians. We were all roped in the deliver lectures and perform demonstrations to them.

Involvement with the Society of Nephrology

Many of us were also involved with the Singapore Society of Nephrology. I started when I was a training registrar and Professor Woo Keng Thye was HOD. Working for the Society in different capacities allowed us to experience a different dimension of Nephrology and interact with many overseas practitioners as well as industry partners.

Research

Recombinant Erythropoietin reached our shores in 1989 as part of a clinical trial and I assisted Dr Pwee in running it in dialysis patients. That was my first experience in having to fill endless CRF's and how to do corrections. We did not have a trial coordinator shadow us like we do now. Our nurses helped with the paperwork. The trial monitor was truly patient.

Starting Up the Singapore Renal Registry

The Singapore Renal Registry started in 1993 in a little side room near the Ward 42 Dialysis Centre sponsored by the National Kidney Foundation. Data collection prior to this was sparse. Other new government hospitals were starting up and had renal departments. Professor Woo envisaged that a system to collect data nationally was needed. The Registry was later transferred under the purview of MOH. For many years, Professor Evan Lee and I gave guidance to the Registry on the statistics and training of the coordinators. In SGH, I acted as coordinator and later as Secretary of the advisory committee for the Registry.

Education

One cannot end without mentioning education of our future leaders and practitioners. We practise our art and we teach those following behind us. Year after year, we meet up with countless numbers of medical students, junior doctors and trainees, and give guidance to our peers who are specialists but not in our domains. Our juniors develop and become our colleagues eventually. It gives us much satisfaction when they surpass us in capabilities.

Just like many during our time who took up medicine when Singapore was entering the First World, our experiences have been rich and varied. We hope we have improved our patients' lives and those who come after us will continue to do so in the years to come.

Lai Yean Ling
Assistant Nurse Clinician
Ward 64E

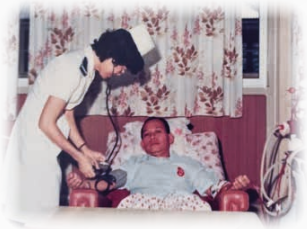
Seet Sor Kuan
Senior Nurse Manager
Ward 55

Christina Oh
Senior Transplant Coordinator

Tan Li Kheng
Nurse Manager
Clinic J

Dr Lee Puay Hoon
Senior Principal Clinician Pharmacist
Petrina Fan
Pharmacy Practice Manager II

Lu York Moi (Manager, Left) and Ms. Janice Ho
(Transplant Coordinator, Right)



Kwong Yock Poi
Nurse Manager
Renal Unit, Singapore General Hospital
Self-Dependent Dialysis Unit, Tan Tock Seng Hospital

Pusparani D/O V.Kalimuthu
Senior Patient Service Associate
Ward 42

Mohamad Rizal Bin Mohd Razali
Transplant Coordinator

Tee Ping Sing
Transplant Programme Manager
(Operations)

Life in Renal Medicine

Memories, sharing and reflections from our family

Nadrah Binte Hamzah
Nurse Clinician
Ward 55

Elena Bte Mohamed Ayob
Deputy Director (Nursing)

Wu Sin Yan
Nurse Clinician
PD Centre

Theresa Soh
Nurse Manager

Maureen Ng
Renal Registry Coordinator

Maslinna Binte Abdul Rahman
Nurse Clinician (Advanced Practice Nurse)

Krishnasamy Thanaletchumi
Assistant Nurse Clinician
PD Centre

Norashikin Ahmad
Patient Service Associate Executive
Transplant Centre

Becky Teo
Senior Associate Executive
Diabetes and Metabolism Centre

Foo Shook Mun
Senior Associate Nurse
Clinic J

Koh Keng Yong
Manager
Renal Transplant Programme

My Journey as a Nurse – A Life Much Loved

Ms. Theresa Soh, Nurse Manager
Department of Renal Medicine (SGH)
Self-Dependent Dialysis Unit (TTSH)
(1983-1997)

After graduating as a qualified nurse, I was posted to work in a general medical ward in SGH. My eagerness to learn and hands-on approach to my work saw me made quick progress in nursing, to the point where I felt ready to take the next step in my career. Pursuing the Intensive Care Nursing Course helped me gain the skills and knowledge I needed to transit to my desired role.

Dealing with change is never easy. Figuring out how to be part of a new work culture can be frustrating at times. You need to sacrifice your time and may sometimes have to work for long hours. I was not confined to just working in the general ward but was shuttling between the Coronary Care Unit and the Renal Unit that were located in two separate side rooms of the ward.

During my postings there, another senior nurse and I were fortunate to be able to assist Dr Lim Cheng Hong perform haemodialysis for a patient with acute renal failure using the twin coil artificial kidney. It was a tedious process using the twin coil dialyser as it needed to be primed with blood. The dialysate had to be manually prepared but it was a worthwhile experience. We had to monitor the various parameters at frequent intervals throughout the process of dialysis. For the bath fluid, we had to monitor the conductivity every hour and replace it when it was indicated. It was a labourious task but a rewarding one as we got to learn new procedures along the way.

The Renal Unit later engaged two trained renal nurses from overseas and started off with two patients for the nurse-assisted programme, which was conducted in a side room in the ward. The device used was a Kiil dialyser which consisted of three grooved boards with two sheets of Cuprophane membrane sandwiched between each pair of boards. The blood flows through the shunts in between the membranes while the dialysate flow outside the membrane envelope in an opposite direction. Excess fluid was removed by the use of negative pressure on the effluent line. Dialysate was prepared in a large tank manually and then pumped out to the Drake Willock machine. Patients would come in after work, have their dinner and bath, and thereafter dialysis would then commence. They would sleep during dialysis till next morning when they go off to work after dialysis is completed. It was a process they had to go through three times a week.

After each session, the Kiil dialyser needed to be dismantled and scrubbed, then reassembled and sterilised for the next use. In addition, the dialysate tank also needed to be cleaned and scrubbed to be ready for use again. The blood lines were also washed, flushed and filled with sterilant. All these tasks had to be performed manually by the nurses.

The unit was later shifted to a converted attic where there were more beds. The team of nurses expanded and were given bigger roles in their work. The unit also expanded its scope of services such as assisted-dialysis, interim dialysis for living related kidney donor transplant candidates, dialysis for acute renal failure, home dialysis and continuous ambulatory peritoneal dialysis.

The nurses all had different roles which they had to take on. The weekends came to be known as washing days. While some nurses would be nursing the peritoneal and acute dialysis patients, the rest would have to dismantle, wash and scrub the Kiil dialysers, then reassemble and disinfect them to be ready for the next use. The blood lines needed to be washed and flushed and then filled with sterilant. On Sundays, two nurses had to scrub, wash and disinfect the huge tank that held the dialysate. It was so huge that they had to climb into the tank in order to do the cleaning. One of the nurses also had to clean and sharpen the needles used for dialysis and send them for autoclaving before they could be used again. Another chore involved the packing of pre- and post-dialysis dressing pack which were also sent for autoclaving. Most of the work had to be done manually, unlike the present time when everything has become so convenient due to advances in technology.

The unit was shifted to the new SGH in the year 1981. The Kiil dialyser was still in use but was later replaced by plate dialysers and then subsequently by

hollow fiber dialysers. The duration of each dialysis session was gradually reduced to an average of four to six hours. The new unit was upgraded with reverse osmosis technology and the buffer solution was also changed from acetate to bicarbonate.

I left the unit for the Medical Intensive Unit SGH in 1983 and later when the hospital was restructured, I was transferred to Tan Tock Seng Hospital (TTSH) and worked in the Neurology ICU there.

Later on, in 1990 I was transferred to the Self-Dependent Dialysis Unit (SDDU) in TTSH to stand in temporarily for another Nursing Officer who was due for retirement. The SDDU only had two Nursing Officers to manage the centre, which could hold a maximum of 80 patients. The centre operated two shifts daily from Mondays to Saturdays. I was a bit apprehensive as I had at that time not been in touch with dialysis for many years. However, I decided to accept the role and persevere in my new assignment. Our duties extended to the ICU in the main hospital too when it came to acute cases. Our work often went beyond working hours, and we were sometimes being activated on our off days.

It was in 1997 when we were informed that our patients would be transferred to the Bishan haemodialysis centre operated by the Kidney Dialysis Foundation (KDF). This is a charitable organisation that provides subsidised dialysis treatment to needy patients. We were supposed to be seconded there for three months to help the patients settle in. In KDF, nurse-assisted dialysis was offered with three shifts daily and all items used for patients were disposable. I am glad to mention that a number of patients who were from SDDU have remained in the programme, meaning they have been in dialysis for more than 30 years.

Basically, nurses are the ones mainly providing care for these patients, and their key responsibility is to identify their essential needs. Haemodialysis patients need support to adapt to their predicament, and nurses can help them overcome their problems and fears of the disease by reducing anxiety, enhancing adaptability, supporting decision making, providing emotional support and education. Therefore, nurses' awareness of the need for high quality care can improve patients' outcomes.

The days in the life of a dialysis nurse can vary greatly. Their responsibilities can change based on the situation they find themselves in. They are more than just technical experts in delivering dialysis treatments as they have to deal with a diversity of other issues such as maintaining highly complex haemodialysis machines and adhering to strict infection control policies and procedures.

In an outpatient dialysis unit, the nurse is responsible for providing the dialysis therapy as ordered by the physician as well as educating patients to comply with their fluid, dietary and medication regimens. For nurses, it is difficult to maintain a healthy work-life balance, as working with any patient with a chronic illness can be very demanding. The patients may become verbally and/or physically abusive. They can feel frustrated and their expectations of nurses can take a toll on the latter's emotional health and ability to cope. This may lead to caregiver fatigue.

It is rewarding to help patients stay healthy while they are on dialysis. When patients share stories about their own milestones and even celebrations on their journey in dialysis, we as nurses are able to be counted in. It is rewarding to know they have managed to stay alive to mark those moments because of the dedication of the nurses who has touched and changed their lives in many ways.

Challenges Faced in Setting Up the Self-Dependent Dialysis Unit in Tan Tock Seng Hospital

Ms. Kwong Yock Poi, Nurse Manager
Self-Dependent Dialysis Unit (TTSH)
(1971-1993)

The Self-Dependent Dialysis Unit (SDDU) in Tan Tock Seng Hospital (TTSH) ran two patient-shifts a day, with patients going there three times a week (Mon/Wed/Fri or Tues/Thurs/Sat) for a four-hour dialysis session. The centre started initially with only three patients, two of whom were males and one a female.

The concept of self-dialysis was introduced mainly to help lower costs. Patients were taught to handle the whole haemodialysis process by themselves with minimal help from the nursing staff. At that time, they only had to pay S$10 per dialysis

session. However, to be admitted to the programme, they had to meet certain criteria. They had to be 45 years old or younger and be employed. Housewives who had to look after children were also accepted. The initial dialysis sessions were conducted in SGH so that the patients will become familiar with the whole process. On their transfer to SDDU, they were usually accompanied by their spouse or helper. They were then introduced to the basic concept of sterility and supervised in the priming of blood lines and dialysers. After these few steps, they would attempt self-needling. Through literally blood, sweat and tears, they gradually became more confident and successful. The staff were still on hand to help with the more difficult cases.

The staff will monitor patients during dialysis through taking blood pressures and seeing to problems that arise. The patients and helpers would also conclude dialysis by themselves, with staff at times helping to remove their needles when necessary. They would also wash the bloodlines and dialysers as well as refill the sterilant for the next use. Both lines and dialysers were used for up to six times if possible.

Going for dialysis three times a week and meeting others with the same condition created a camaraderie amongst them and gave rise to a support network for themselves. Blood profile tests were done every two months, while skeletal and chest X-Rays were taken annually. Patients were required to go to SGH for their regular check-ups with their renal physicians while staff would go to SGH every month with the patients' files to meet with the renal physicians to review all the tests results.

There were only two staff stationed in the centre; one took the morning shift and the other the afternoon shift. The main hospital would deploy a staff to go over when any of the SDDU staff needed to take leave.

On rare occasions, SDDU was asked to dialyse acutely ill patients in the intensive care unit (ICU) at TTSH. The staff would then have to transport the dialysis machines to the ICU, set up the equipment and initiate dialysis there.

The centre functioned until the end of 1997 when all the patients were transferred to the care of the Kidney Dialysis Foundation.

Reflections of My Association with SGH Renal Unit

Ms. Krishnasamy Thanaletchumi
Assistant Nurse Clinician, PD Centre
(1989-2015)

Through all my working life, which started at the impressionable age of 19, I have known of no other occupation apart from nursing. It is therefore little wonder that what started as only a job soon became my preoccupation, my profession and eventually my lifelong calling. Then, an untoward development that occurred in my personal life some 30 years ago drew my attention to the agonising plight of kidney patients and their families. My aunt suffered kidney failure and, in due course, was put on peritoneal dialysis (PD). I witnessed first-hand the pain and suffering of my aunt as a patient, and also the anguish and distress felt by her family, both emotionally and financially.

This experience obviously had a profound impact on me such that when I joined the Renal Unit at SGH in the early nineties, the patients meant much more to me than mere routines and records that made up my daily work. Something in me made me go well beyond the clinical procedures and duties to develop bonds at a personal level with the patients, their caregivers and family members.

Upon reflection, I realise that I had then unconsciously created in myself a set of personal goals and a mission towards alleviating the difficulties of renal patients and their families. I have attempted to recall what these were, which are as follows:

1. To become a teacher, counsellor and friend to patients and caregivers alike with the aim of raising their awareness about the ailment, its prognosis and any ongoing treatment.

2. To maximise patients' capability and confidence in performing self-dialysis.

3. To maintain a photo journal of the various phases

of patients' treatment at the Renal Unit, from initial registration and training to ongoing PD sessions. This is to show patients the progressive improvements they are making in assisted dialysis.

4. To help patient to resume as near normal a lifestyle as possible.

5. To brighten the lives of patients, especially the elderly, the lonely and the needy by organising birthday parties and also functions to celebrate festivals like Lunar New Year, Hari Raya, Deepavali and Christmas.

6. To encourage the families of more affluent patients to donate unused surplus dialysis fluids to needy patients to help alleviate their financial burden. Here, we got our own family members involved in supporting this initiative by assisting with transportation.

I was certainly fortunate that the above wishes came to fruition in time through the unflinching support of colleagues and the encouragement of the management of the Renal Unit. Another heartening development in the above-mentioned drive to support the patients and their families was the contributions of pharmaceutical companies like Baxter and FMC in coming forward to subsidise patients for their overseas trips to China and Australia. They also contributed generously towards educational programmes and social events organised by the PD Centre.

Casting my mind back to a decade or earlier, it fills me with immense joy and satisfaction that we were collectively able to contribute in a small way to lighten the burden and raise the spirits of the less privileged amongst us.

My Nursing Experience in Peritoneal Dialysis

Ms. Wu Sin Yan, Nurse Clinician
PD Centre (2006 to Present)

It is hard to believe that I have been in nursing for over 30 years. My first exposure to dialysis was when I was assigned to a patient on acute peritoneal dialysis (PD) during my senior student nurse training in Hong Kong. We used two-litre single bags for patients on continuous ambulatory peritoneal dialysis (CAPD) and performed a connection procedure to a Y-set spike system with iodine sponged connection shield to cover every part of the connection of each exchange.

Throughout the years, the advancement in technology has allowed for innovations in PD which have improved the way we provide treatment. The progression of PD systems has included the introduction of O-set and Y-set systems to allow for "flush before fill" which reduces the risk of peritonitis. The different connection assist devices reduce the risk of touch contamination for patients with visual impairment or poor dexterity and thence allow them more autonomy to perform PD at home. The innovation in the double-bag system used in CAPD exchanges have been associated with a reduction in peritonitis rate, which allows for PD to be a more sustainable treatment option for patients with end-stage renal failure. The different models of smaller, more portable cyclers with memory cards and cloud-based remote patient management (PRM) systems have also created a streamlined method for us to track our patients' progress.

Dialysis solutions were modified specifically for long dwell and to more biocompatible solutions to improve the duration of PD and the patient's quality of life. Peritoneal catheters were reconfigured, and surgical techniques were refined in order to reduce the number of catheter-related complications.

The first PD nursing course for PD nurses was conducted in 2004 with the participation of multidisciplinary healthcare professionals and included PD-related topics in anatomy and physiology, infectious and non- infectious complications, psycho-social issues, diet and pharmacology. The course equipped PD nurses with knowledge and skills and enabled nurses to adopt a more holistic approach when managing PD patients together with a multidisciplinary healthcare team. With collaboration and support from renal specialty nursing and renal ward nurses in 2017 and 2018, a more structured PD education forum for patients with sharing sessions was successfully organised. This was subsequently expanded to include other hospitals' PD programmes and resulted in the first Singapore PD Forum in 2019.

The variety of educational talks, social and recreational events gave PD patients and their families adequate support and essential knowledge needed to improve their quality of life.

Without the contributions from our PD nurses, a successful PD programme would not be possible. They should therefore take great pride in the development and success of PD in Singapore. PD nurses have enthusiastically embraced the concept of self-care and home dialysis and have been educating and empowering the patients and their families to do so. They do not only help patients obtain the skills and knowledge necessary to perform PD, but also coordinate, support and guide patients and their caregivers throughout their course of PD therapy.

The Highlight of My Career in the Renal Department

Ms. Foo Shook Mun, Senior Assistant Nurse
Clinic J (1981-2012)

In July 1981, I was transferred from the Emergency Medicine Department to a Specialist Outpatient Clinic – 'J' Clinic. At that time, 'J' Clinic was the first functioning specialist clinic and was officially opened by our late Prime Minister, Mr Lee Kuan Yew. I was part of the clinic's pioneering team that had the honour to welcome him.

I was privileged to serve in the Renal Unit as requested by Dr Lim Cheng Hong and assisted him in 'M' Clinic on Tuesday and Friday mornings. Dr Lim founded the Department of Renal Medicine in SGH and is considered to be the Father of Nephrology in Singapore. I remembered the Department honouring him with a Festschrift on 26 September 1996. Life was tough back then due to the shortage of staff but I still enjoyed working in the Department. I had to work fulltime in 'J' Clinic which served the Plastics and Burns Unit but covered 'M' Clinic every Tuesday and Friday morning. Both clinics were very busy with patients referred from polyclinics all over the country as well as those discharged from Medical Unit 2, which was situated at the Bowyer Block.

Looking back at the old days, one memory that stands out is when I was requested to perform for one of the renal transplant section's events in the year 1997. Together with a staff nurse who was my colleague then, we belted out the song "Never Say Goodbye" which was actually the English version of a Cantonese opera tune "Dai Noi Fa (The Empress Flower)"! This is for me the most memorable moment in my life and is still fresh in my mind as if it happened just a week ago. In just the wink of an eye, years had passed since that day. Joining forces to perform this opera number brought our relationship so much closer, which actually helped in our work as it made us more efficient. During this period, I interacted often with renal transplant patients and all of us gradually became good friends. Even today, when I happen to meet them at bus stops or on the MRT, my patients still remember me and we will exchange warm greetings with each other. I can feel that they think I am very important to them because of the years of care I had provided for them. This brings joy and happiness to me, especially when I can see that these renal transplant patients are still healthy both mentally and physically. It makes me feel proud to be part of the transplant team that had been nursing them.

I take this opportunity to congratulate the Department of Renal Medicine for reaching the 50th Jubilee of Renal Transplantation. May we all stay safe and stay healthy in the midst of the COVID-19 pandemic!

My Journey at a Specialist Outpatient Clinic

Ms. Tan Li Kheng, Manager
Clinic J (1997-2005)

In 1997, I was appointed as Clinic Supervisor at Specialist Outpatient Clinic (SOC) J and became involved in managing both the renal outpatient clinic and plastic & reconstructive surgery outpatient clinic, which came under this SOC. Both disciplines shared the eight consultation rooms available. Over time, the renal outpatient attendance and workload increased. The morning clinics started to overrun and spilled into the afternoon sessions. Professor Woo Keng Thye, then Head of the Department of Renal Medicine approached us on this matter and enlisted the help of the SOC Manager and team to relocate renal outpatient clinic from SOC J to SOC M.

SOC M was located at the furthest end from the entrance of level one of the Specialist Outpatient Clinic building but is more brightly lighted with a pleasing window view. On Tuesdays and Fridays, the outpatient renal clinic would usually be rowdy and noisy with many transplant patients coming for their appointments. The transplant team would make preparations, pushing trolleys carrying additional pink-colored patient files down to the clinic from the office located next to Ward 42. Transplant coordinators would call for patients in a friendly tone, check on their compliance to treatment schedule, review their blood test reports and assess their general health.

Performing blood taking for patient before consultation was one of the clinic nurses' daily task when phlebotomist service was not yet available at the SOC clinical laboratory. Transplant patients would arrive very early with some queuing before 8am, have their blood test done and then leave the clinic with friends or family to the nearby cafeteria for breakfast. They would return to the clinic later to check on the availability of their test results. Some patients would hang around anxiously in the clinic's waiting area for their blood test report to be ready. There were those who would repeatedly request the treatment room nurses to call the laboratory technicians and check if their blood test report was ready.

I recalled that one of the most common laboratory renal tests ordered by renal physicians was a 24-hour urine collection for assessing patients' kidney function to facilitate diagnosis and treatment. The nurse involved would issue patients with a five-litre plastic container and give them detailed instructions on the steps for complete urine sample collection over a 24-hour period. To achieve accuracy for the test, nurses had to remind patients to urinate completely into the container, then mark the container with an arrow, sticker or line to indicate the total amount of urine collected. They were then instructed to pour out a small amount as a sample, empty the container and bring it back to the clinic for the nurse to record their total urine volume for the laboratory analysis. The instructions for the 24-hour urine collection had to be repeated and demonstrated to many elderly patients who had difficulty remembering the steps, even though a pamphlet was provided to serve as a visual prompt. Back then, we often wished that a recorder with play back function was available to lighten this burden. Sometimes, there would still be patients who would bring a full container of urine back to the clinic!

It was a daily routine for the clinic healthcare attendants to wash the returned empty urine containers or discard any urine left over after measurement in the disposal room. The fishy and acidic smell of the urine was unbearable at times. During washing, the sound of water gushing in and out of the plastic containers could be heard from the disposal room behind the clinic. After washing, the containers would be lined neatly in rows on racks and stood tilted at an angle for easier drying. Eventually, this process of washing and reusing the five-liter containers discontinued after a quality improvement project was done.

In March 2003, the sudden outbreaks of SARS found me and my colleagues gripped with panic and anxiety. It was a challenging and tough time for healthcare workers as we had to follow strictly hospital guidelines and stringent infection control measures, such as to don and doff PPE and N95 masks to protect ourselves and patients in clinical areas.

Many of us were besieged with fear and faced uncertainties in the light of news of healthcare workers becoming infected. Family members were worried about the safety of our working environment and we had to reassure them on this issue. I choose to stay vigilant, checking on the guidelines diligently for updates and changes on infection control measures and communicating these to team members for compliance. The constant wearing of N95 mask caused marks and line sores over every user's face. Frequent and constant hand washing with anti-microbial agents and hand rubs also caused dryness around the fingertips. Protective consumables such as masks, gowns and gloves were used up very fast and needed constant topping up. Luckily, colleagues in the Material Management Department were very helpful, accommodating and processing any urgent ad hoc request raised by us.

Facilities engineers were also busy doing minor renovations, such as adding shower heads to the toilet cubicles so that staff could take a bath and change out of their scrubs before heading home in their casual wear. This helped prevent any cross infection.

There was also a need to scale down the volume of non-urgent clinic appointments. Many of the clinical team members willingly volunteered to work past office hours, calling up patients in stable condition to defer any scheduled appointment to a later date. Call centre staff also experienced a surge in call volume with anxious patients calling in with various enquiries and requests for medication top up.

In my nursing career at SOC, I had witnessed the financial and emotional burden faced by patients suffering from end stage renal disease and their caregivers, along with the agony of a long wait for kidney transplant, which was the only alternative to dialysis treatment. Many patients became financially depleted, requiring subsidies and waivers to pay for their rising medical bills and cost.

Doing volunteer work makes me happy. During my off days, I enjoy volunteering for hospital and community charity events such as Project Groom Over, President's Challenge and most of all the Singapore Transplant Games which encouraged transplant patients to participate actively in sports after transplantation.

I am proud of the fighting team spirit of our patients, supportive caregivers and multidisciplinary healthcare providers – including physicians, nurses, ancillary staff, coordinators, dieticians, pharmacists, medical social workers and therapists – working together to improve patient health and achieve the best outcomes.

Renal in my Heart!

Ms. Eleana Mohamed Ayob
Deputy Director (Nursing)
(1998 to Present)

I joined Ward 42 in 1998 as a Staff Nurse after graduating from Nanyang Polytechnic. While working in Ward 42, I nursed patients with renal diseases and also those who had undergone renal transplantation or were scheduled to undergo one. The experience and knowledge that I gathered during my years in Renal Medicine is priceless! Over the years, the process of learning has indeed strengthened my clinical and leadership skills even as I continue to navigate the organisational complexities of the healthcare industry throughout my career.

The nurses working in Renal Medicine now have an expanded role and enjoy improved work processes, which are not just for themselves but also to help them achieve better patient care and outcomes. All of these is owed to the fantastic leadership found in Renal Medicine - from Professor Woo Keng Thye (I remember always looking forward to and enjoying his Monday Grand Rounds), to Professor Chan Choong Meng, Associate Professor Marjorie Foo and now the young and ever enthusiastic Associate Professor Tan Chieh Suai ! As for myself, I of course am grateful for the guidance offered by my mentor, Sister Susan Quek, who has groomed me and bestowed me with so much precious knowledge all these years!

What is dearest to me is not only the clinical experience I had gained but friends whom I made in the Department of Renal Medicine. Not just my nursing friends but everyone in the renal healthcare team – doctors, renal and transplant coordinators, social workers, dietitians, psychologists, and physiotherapists – friendships and networks that I gained and have treasured till this day.

Renal Medicine will always have a special place in my heart and I pray that the department will continue to excel in patient care!

My Experience in Kidney Transplantation

Ms. Seet Sor Kuan
Nurse Manager
Ward 55 (1996 to Present)

My first encounter with kidney transplant patients was back in 1996 in the General Surgery Unit where such patients were nursed post-operatively. In 1998, Urology was separated from the General Surgery Unit, and so the management of kidney transplant patients was taken over by urologists in partnership with renal physicians.

In the 1990s, the majority of kidney donors were deceased, while living donors were harder to come by. There are two different types of living transplant donors: living-related or non-related. Living kidney donor transplantation was first successfully carried out in 1976 between related donor-recipient pairs and subsequently between a living non-related pair in 1991. During those days, there were a lot of myths going around that donors will become physically

weaker, or their remaining kidney would fail if they donated their kidney.

Over the past 20 years, I have seen significant changes in professional care for kidney transplant. Living kidney donor transplantation has become more common in response to events and activities organised to help raise public awareness of living kidney donation. After much effort, the public is more forthcoming in donating their kidneys to their loved ones.

In 2009, the first ABO incompatible living related kidney donor transplant – from mother to son was completed successfully. It is heartening to see the relationship between living donors and their recipients become closer. They encourage each other during the journey towards transplantation and rejoice together when the transplanted kidney is functioning well.

The current healthcare system has improved significantly compared to the past. In SGH, kidney transplant patients are now fortunate to have a multidisciplinary team of healthcare professionals looking into their physical, psychosocial and financial needs. This multi-disciplinary team consists of the medical/surgical team, nurses (inpatient and outpatient), specialty nurse for post-transplant bone disease follow-up, physiotherapist, pharmacist, transplant coordinator, dietitian and transplant medical social worker. With support from the multidisciplinary team, transplant recipients are more assured of success and can look forward to their new life.

Nursing Education

With advances in technology and because of the complexity of kidney transplantation, nursing of transplant patients requires increasingly specialised set of knowledge and skills. Our organisation ensures that nurses are equipped with the latest knowledge and skills for caring this vulnerable group of patients. In 2018, the training department in the SingHealth Alice Lee Institute of Advanced Nursing revised the training curriculum to include the management of other types of organ transplant, such as the liver, pancreas and lungs.

Sponsorships are available for those wishing to pursue the Advanced Diploma in Nephrology – Urology Nursing, various transplant related courses/ in-service talks and seminars, as well as the overseas Health Manpower Development Plan (HMDP) Fellowship Programme to gain new knowledge and skills. For example, Clinical Care Pathway (CCP) for deceased donor recipients and Model of Care for living donors were adopted from overseas clinical practice and implemented after nurses returned from HMDP. A CCP is a multi-disciplinary management tool that adopts an evidence-based practice catering to a specific group of patients. It provides clinical guidelines and promotes organised and efficient patient care in acute settings.

Nursing Care

Nursing a kidney transplant patient is similar to nursing any patient who has undergone major surgery. The emphasis is on drug therapies, laboratory monitoring and ensuring fluid and electrolyte balance. Nurses need to be vigilant in keeping track of specific timings for taking blood, administration of medication and transfusion of blood products, as well as coordinating with allied healthcare workers. Healthcare technology has clearly improved the quality of life for patients. Simple things such as wound suturing first started with the use of non-absorbable sutures, then staples, and now, absorbable sutures. Most surgeons are making use of absorbable suture nowadays, though a minority are still using staples. Hence, there are no longer stitches to be removed for nurses. Patients do not need to return to the hospital or outpatient clinic to have their sutures removed, making it less painful as compared to non-absorbable sutures and with less scarring.

In 2001, hand assisted laparoscopic surgery was first introduced and performed on a living donor. This minimally invasive surgery (keyhole surgery) has reduced the risk of complications and shortened the length of stay in the hospital, thus allowing for faster recovery. Today, kidney transplant donors can be discharged as early as on the third day post operation. As for living donor transplant recipients, the length of stay ranges from six to fourteen days unless they are ABO incompatible where the length of stay can be up to a month.

Patient Family Education

Patient education is another important element in getting potential transplant recipients mentally, physically and emotionally ready while waiting for

donated kidneys. Education helps in gaining patient cooperation and compliance with medical treatment after transplantation is performed. Nurses play an important role in patient education as we are with the patients round the clock. The same group of nurses is usually assigned to take care of the same patients so that the patients will feel more assured and comfortable seeing familiar faces. Patient education continues throughout their stay in the hospital so that they will be ready for self-care before they are discharged from the hospital. This is because it will be a new, challenging and lifelong journey that requires the patients' commitment and compliance with all advice given by the multidisciplinary team.

Emotional support from patients' next of kin is also important after transplant surgery. With effective infection control measures in place, the policy of restricting visitors has been revised from none to two visitors.

Kidney transplantation is still the best treatment for end stage renal failure. Healthcare providers will do everything possible to provide the best care in order to optimise patients' quality of life. However, the responsibility still lies on the transplant recipients themselves to carry on with their new life in the best way forward. After all, how long a transplanted kidney can be kept alive depends very much on how well patients take care of it!

My Nursing Journey

Ms. Nadrah Binte Hamzah
Nurse Clinician, Ward 55
(2004 to present)

I graduated back in 2004 as a registered nurse and was attached to the Renal Ward in SGH for five years. In between I took my Bachelor of Health Science, Nursing as well as my Advanced Diploma in nursing, specialising in Nephro-Urology. I am proud to be a Nephro-Urological trained nurse since 2010, and I had since then been posted to the Urology Ward where I began my journey in nursing of new renal transplant patients. It is a beautiful journey that has produced great memories, and I must say it is one on which I have always been committed to giving my best to all my transplant patients.

I lead and train a team of transplant nurses which consists of a nurse clinician, senior staff nurses and staff nurses. I am responsible for disseminating updated information and coordinating the latest workflow for various stakeholders with regards to renal transplant. The team of nurses that I work with are dedicated, caring individuals who are ready to give the best of care for the patients. I believe having such a strong team will ensure a smooth and seamless care for every patient.

I represented the nursing team during the phase where hardcopy CCP (Clinical Care Pathway) were being converted to e-CCP (electronic-Clinical Care Pathway) for deceased donor renal transplant, ABO incompatible living transplant and living donor renal transplant. My part involved reviewing of the nursing care agenda to be included in the e-CCP.

We completed the conversion of hardcopy CCP to e-CCP in January 2018. The first e-CCP was activated in February 2018 for living donor renal transplant. CCP is a multidisciplinary healthcare management tool in which the different tasks or interventions by the professionals (physicians, nurses, pharmacists, physiotherapists, medical social workers, dieticians and transplant coordinators) involved in patient care are carried out according to plan. All healthcare professionals involved in this clinical pathway put in great time and effort to ensure seamless care for every patient from admission till discharge. With all the documents going electronic, it is now much easier for all who are participating in the care to view the documents when necessary.

I am also a patient advocator and would not hesitate to speak up for my patients. I always seek to maintain an excellent standard of care for my patients. I constantly provide education to patients and their next of kin in clear and simple terms so they can easily understand what was being taught. It is a great achievement and joy to see that my renal transplant patients are discharged well and able to lead a new life without having to go through dialysis again.

I am glad to have received compliments from patients such as, "She is such a cheerful person who brightens up the room whenever she enters.", "Answers our queries well.", "Patient and friendly", " Showed great care and concern for me when my pain

was unbearable.", "Very responsive when I in need of her service.", " Provides good and clear explanations on the next step, for example scanning, X-ray." and "Kept checking on me now and then, making sure I was well.". Other general comments complimenting me for being very courteous and caring, very attentive, patient and helpful, providing very good customer service to patients and urging me to keep it up were words that have kept me going till now – this year, would be my 16th serving as a nurse in SGH!

I am also very pleased to have received the Most Outstanding Transplant Nurse Award back in 2018. That has motivated me to be a good role model and I take every opportunity to apply my advanced knowledge and skills to clinical practice. I will continue to impart my knowledge to junior nurses in nursing renal transplant recipients and will continue to supervise them in their clinical practice to ensure proper care is being delivered. With passion, dedication, professionalism and expertise in caring for my transplant patients, I can reassure patients that they are in good hands!

My Memories of Working in the Renal Department

Ms. Maslinna Binte Abdul Rahman
Nurse Clinician (Advanced Practice Nurse)
(2005-Present)

I have been working in the Renal Department for 15 years, mainly caring for patients who have been through kidney transplantation. As a newly graduated nurse working in the Renal Ward, I had witnessed the pain and agony patients on dialysis go through. I was assigned to nurse patients on dialysis for a year before being transferred to work in the kidney transplant section of the ward. Reminiscing on my early days working in the kidney transplant section, I remember being in awe seeing how a patient transit from being dialysis dependent to an almost normal looking healthy individual. I personally find greater pleasure seeing young patients receiving this new lease of life. As I spent more time caring for patients with kidney transplant, my hunger for knowledge grew. This became the impetus for me to advance my knowledge in nephrology nursing. I did my specialisation in Nephro-Urology in 2008, my Bachelor degree in 2010, Master of Nursing in 2013 and eventually became a full-fledged Advanced Practice Nurse (APN) in 2016.

There has been great advancement in nursing education over the past decade and advanced practice nursing in renal medicine has emerged as a dynamic and exciting aspect of nephrology nursing. SGH minted its first Renal APN in 2011 and since then, nephrology nursing has diversified into more specialised branches. Advanced practice nursing in nephrology has achieved enormous progress since its introduction. In 2013, the training ladder was crafted for the role of the Renal APN in the Kidney Transplant Programme. Since becoming a full-fledged Renal APN in 2016, I have been performing my role in both inpatient and outpatient settings. As a Renal APN, I am able to extend my care beyond bedside inpatient nursing as I am now qualified to provide other value-added services to this group of patients. Moving forward, there are plans to expand our services in the Kidney Transplant Programme. The Renal APNs will provide rapid access to care for renal transplant recipients who require ad-hoc medical attention. This will help offload emergency attendance and protect renal transplant recipients who are immunocompromised from potential sick contacts in the emergency department. For stable kidney donors who opt for remote monitoring, Renal APNs will provide them with teleconsultation services so they can enjoy greater convenience and better accessibility to medical care.

Currently, the Renal Department has two Renal APNs, two Renal APN interns, two Renal Resident Nurses and a Renal Specialty Nurse. This is a vast expansion in renal nursing and will grow as nephrology nursing continues to progress. There has also been a shift in the practicing paradigm for care provision to patients. Patients are now treated more often in the community and their cases can be followed up via teleconsultation. This has actually been the standard of care for patients with blocked renal vascular access since 2018. With advances in technology, the proliferation of smart phones and patients becoming better informed, telemedicine is expected to develop further. Remote monitoring will make healthcare more convenient and accessible to those who are suitable for such a model of care. There are plans to extend this model of care delivery to other groups of renal patients. I wish the Department

of Renal Medicine all the best in its endeavour to shift the paradigm of healthcare delivery to remote monitoring and telemedicine for the benefit of our patients.

My Experiences with the Renal Transplant Team

Ms. Lai Yean Ling
Assistant Nurse Clinician, Ward 64E
(2009 to present)

My years of experiences in the renal transplant team has allowed me to build a strong background in nursing and kept my motivations alive. It has been very interesting and I find myself loving not just what I do, but also my patients. However, just like everyone else, I am not exempted from obstacles and challenges. It is these obstacles and challenges that gave me the chance to develop my learning skills, to learn to become a team player within the renal transplant team, and to enhance my critical thinking skills. I feel very proud to be able to share my nursing experience with my colleagues, friends and family.

My Journey in the Department of Renal Medicine

Ms. Becky Teo
Senior Associate Executive
Diabetes and Metabolism Centre (1988-Present)

I joined Singapore General Hospital Renal Outpatient Specialist Clinic J in November 1988, which was later relocated and renamed Clinic M. Clinic M was thereafter segregated into three different sections - Renal Clinic (General Nephology Clinic), Renal Transplant Clinic (relocated to Transplant Centre in 2013) and Peritoneal Dialysis Clinic (relocated to Diabetes & Metabolic Centre in 2015).

When I was assigned to J Clinic, I was given many tasks to perform, such as working at the front counter and taking my turn to assist doctors in the clinic. Even though life was tough during that period due to the shortage of staff, the staff nurses, assistant nurses and healthcare assistants were all able to work happily together as a team. There was great fun and laughter with all the staff working hand in hand, looking out for each other and bonding like one big, happy family. I do miss those good old days! As I recall, back in the 1990s, we used to trace case notes from MRO (Medical Records Office), with huge trolleys carrying many case notes parked at the back of the clinic. Every day before the clinic started, all case notes would need to be sorted and distributed to the rooms of the various doctors according to the list of patients scheduled for them each day. After each consultation, the case notes had to be returned to the same trolley from where they had been retrieved. At the end of the day, the staff who was assigned to receive the trolley from MRO had to check through the list to ensure the case notes were placed neatly back to the trolley before returning it to them.

During those years, our Renal Clinics were equipped with computers. All laboratory test results had to be faxed to the clinic at the back room. Staff that were assigned to assist the doctors had to collect the printed results and make sure each individual patient's results were charted and filed in his/her transplant file. After each consult, all laboratory test requests for the next appointment had to be explained to patients and included special instructions for specific tests and specific days on which blood had to be drawn. In those old days, each clinic handled approximately 30 to 50 patients. Sometimes, thinking back, I was practically zooming up and down the clinic like I was on roller skates due to the high volume of patients in each and every one!

But nowadays, everything is computerised. Life is much easier but the number of patients being seen in the clinics has also tripled. Even though we are not required to manually trace the results anymore, we still need to ensure investigation results are available for doctors to review during their clinic sessions. I remember that in the good old days, there was a special day assigned for renal transplant patients to take their blood in order to determine the dosage for the administration of cyclosporine. This resulted in an estimated 70 to 100 patients turning up for the blood test every Friday. Every patient had to bring their own liquid cyclosporine, along with a measuring syringe to facilitate consumption after blood taking. There is so much less hassle now with the capsule formulation of cyclosporine made available.

I enjoy working in the Renal Department. I have spent my youth in this department, seeing it gradually grow to what it is today. Time flies and by now, I have worked in the department for some 32 years.

I would like to take this opportunity to congratulate the Department of Renal Medicine on their 50th Anniversary of Renal Transplantation.

My Journey in the Renal Department

Ms. Norashikin Ahmad
Patient Service Associate Executive
Transplant Centre (1991-Present)

I would like to take this opportunity to say thank you to the Renal Department for providing all the guidance and nurture me into what I am today. It has been 29 years filled with experiences of all kinds in SGH; most of them have made for wonderful memories. I found it an enjoyment to be working with the Renal Team.

I took the first step in my journey in the year 1991, when I was posted to Clinic L serving the Department of Ophthalmology. In 1992, I was transferred to Clinic J. Clinic J was used by both the Plastic Surgery and Burns Unit as well as the Department of Renal Medicine. This was where I started to become acquainted with physicians such as Professor Woo Keng Thye, Dr Grace Lee, both from Renal Medicine as well as Professor Tan Kok Chai and the late Dr Julian Wee from Plastic Surgery.

From the Department of Renal Medicine, I learned a lot on how to take better care of my kidneys. Being present during patient-doctor consultations, I was able to pick up knowledge about the functions of the kidneys and how the outcomes can be bad if they are not properly taken care of, such as having to undergo dialysis. Seeing the fistulas created and bulging veins on the renal patients, I thought to myself that dialysis must have been very painful for them.

In the Department, I also got to learn more about dialysis and transplant, especially on the causes of end stage renal disease e.g. System Lupus Erythematous, Glomerulonephritis and Diabetes Mellitus. Diabetes Mellitus, I was told, is the main cause of renal failure. From this department, I learned how to manage my diet and maintain a healthy lifestyle to keep away from this medical problem. In Plastic Surgery, I learned about topics such as liposuction and burn injuries.

I was then working in Clinic J as a Permanent Assistant. The doctors and nurses taught the staff and I learned a lot along with the patients, especially when they also shared their own stories and problems with me. During that time, I assisted the doctors. For each clinic, the number of patients could be as high as 30 to 40, and my main task was, after the doctors had done their review, to provide laboratory forms to patients and label them manually. Looking back, it was very tedious and tiring. During the old days there was a serious shortage of staff with the number of patients increasing in each clinic. However, there was still great teamwork and caring colleagues. The staff worked very closely together and because of the great teamwork, every day was tiring yet enjoyable.

In 1999, the Department of Renal Medicine was moved to Clinic M. This was a very busy clinic, with the number of patients on some days as high as 100 per shift. Sometimes I felt like I was wearing roller skates because I was moving so fast from one consultation room to another, especially because the Renal Clinics did not yet have computers in those days. All test results would be faxed to the back room of the clinic. Staff that were assigned to assist the doctors needed to collect the printed results and make sure those of each individual patient are charted and filed in the patient's transplant file. After each consultation, the contents of all investigations forms for the next appointment had to be explained to patients, including special instructions for specific tests and the specific days for drawing blood.

I also work closely with transplant coordinators and the group of doctors posted from NKF to SGH. My network in my job had therefore grown and I found that meeting more people and learning about what they do had inspired me to work like them. As I remember it, in 1992, every Friday morning was set aside as transplant clinic day. Every patient was chasing after their blood test results (which were in hard copies brought down by the laboratory porter) from the assistants before the doctors arrived – just try to imagine over 100 over patients chasing after you!

But now, everything is computerised and life is much easier. Even though we are not required to trace the results anymore, we still need to ensure that investigation results for each appointment are available for the doctors to review during their clinic session. I have been in the Transplant Centre since

2013. I am grateful to be where I am now and excited for what I have done in my 29 years of service with SGH, not forgetting with the Department of Renal Medicine. SGH has indeed become my second home! I would like to take this opportunity to congratulate the Department of Renal Medicine on their 50th Anniversary.

My Journey in Renal Medicine from Clerk to Senior Patient Service Associate

Ms. Pusparani D/O V.Kalimuthu
Senior Patient Service Associate
Ward 42 (2001 to present)

I began my career as a Ward Clerk and rose through the ranks to eventually become a Senior Patient Service Associate. My current job entails the general management of the patients who are admitted to the Renal Ward. I have been using my experience and initiative to innovate, assisting my team of nurses to embark on multiple projects related to bed management and admissions for renal biopsies. Other responsibilities in my job include the handling of bed assignments and census updates, ward reception, patients' medical records, administrative duties, and the provision of limited patient care.

I enjoy working in this ward and every day find myself looking forward to going back to my duties in the ward, where I can do my best for my staff and patients. For years, I have not taken even a day of medical leave. However, my hard work and dedication over the years have not gone to waste for it was recognised by my ward sisters who nominated me for the Gold Service Quality award.

I find satisfaction in my job because it lets me bring joy to my patients. Seeing them happy even though they are suffering pain from needle pricks during dialysis and the smiles they still have on really makes my day. When a patient has been informed by the doctor that he has end stage renal failure and the whole family is feeling sad and down, I will go forward to hold their hands, comfort them and listen to them so that their fears will be alleviated.

After many years, some patients might return to the ward when they are visiting one of their friends who have been admitted for renal problems. These patients still remember the old staff working in this ward and will ask for them, taking the opportunity to share memories of what they went through during dialysis or CAPD. They would usually praise the nurses for the services they provide not just to them, but also their friends who are needing such treatment. Their gesture of gratitude gives me greater energy and strength to do my job for patients more effectively.

My ward sisters have always advised me to continuously strive to enrich and upgrade myself. With such peer support from them and others, I have completed a course in tour guiding and I intend to enrol in other management courses in the near future to upgrade my skills so I can perform my role better.

During this COVID-19 Pandemic in 2020, having learned from the SARS outbreak I was able to provide ideas to help add several new key measures to the framework for Disease Outbreak Response System Condition (DORSON), which had reached Orange by then.

I like to take this opportunity to congratulate the Renal Department on their 50th Anniversary. Kudos to all the doctors and staff for their continuous effort and the support they have given me – I would not have been able to achieve all that I did just by myself.

Our 25-Year Journey: Privileged to give Care, New Life and New Hope to Kidney Disease Patients

Dr Lee Puay Hoon
Senior Principal Clinician Pharmacist (1998-Present)

Ms. Petrina Fan
Pharmacy Practice Manager II (2000-Present)

Since 1996, pharmacists participate in the nephrology ward rounds to provide treatment recommendations and respond to enquiries related to drugs. The Grand Ward Round occurred every Monday morning at Ward 42 where Professor Woo Keng Thye led the rounds, with doctors, nurses and allied health professionals such as pharmacists. Pharmacists will always remember his teachings, especially on the "five causes of acute kidney injury", "list of nephrotoxic drugs" and "first kidney transplantation performed in SGH".

During the early days in SGH Ward 42, pharmacists provided direct patient care to ensure safe and effective use of medications. They would review the inpatient medication charts, optimise drug therapies, and provide drug counselling to patients and caregivers. In addition, pharmacists promoted life-long learning by providing continuing education for doctors, nurses and other allied health professionals.

Over the years, the pharmacists' scope of clinical work in managing kidney patients has expanded. We have the privilege to provide direct care for chronic and end stage kidney disease patients in both inpatient and outpatient settings. With strong support of doctors from the Department of Renal Medicine, pharmacists have joined the dedicated multidisciplinary transplant team to improve kidney transplant recipients' health-related outcomes. We continue to partner with doctors and various healthcare professionals from this department to provide direct patient care to other patients with Glomerulonephritis and those on supportive care for end stage kidney disease.

Upon reflecting on our 25-year journey with patients suffering from kidney diseases and with the multidisciplinary healthcare team in SGH, we feel privileged to be given the opportunity to make a positive impact on patients' health and wellness, as well as be part of the passionate renal care teams. Whilst we endeavour to live up to our motto of "Patients. At the Heart of All We Do", we are thankful that our care teams, patients and caregivers can open their hearts and place their trust in us to deliver quality care. Our patients and colleagues have been very supportive in our clinical research efforts. They often encourage us to continue to advance our practice and refine our skills and believe that their contributions to our research would benefit others.

This year marks the 50th year for the Renal Transplant Programme in SGH; we celebrate our milestones and achievements, as well as poignant memories shared between our patients, ourselves, and Renal Medicine!

Memories of the Singapore Renal Registry

Ms. Maureen Ng
Renal Registry Coordinator (1993-2002)

In 1993, I was privileged to be working at the Singapore Renal Registry during its start-up phase and this has been the most memorable experience in my working life. The registry collected data from various renal units and dialysis centres on renal disease incidence rates, patient demographics, comorbidities and outcomes.

When the renal registry first started, there was not much data available for end stage renal disease (ESRD). Over time, the number of patients with ESRD increased and the establishment of the renal registry was timely for handling the collection of data for these patients. Data for ESRD was collected mainly from the Singapore General Hospital and the National University Hospital.

A notification process was designed and implemented to enable the renal registry to monitor the treatment type and status of individual patients. The process was set up to allow dialysis centres to send monthly statistics to the renal registry. New data and any change of existing modality were also submitted to the registry for updating.

My key responsibility was to collect data for new and existing patients receiving renal replacement therapy in healthcare institutions and transplant centres. The most fulfilling and satisfying experience was to see the first Renal Registry Report published in 1997. It was my proudest moment to see all the hard work put together and finally translated into the first such report in Singapore. This first report contained tabulations on incidence and prevalence for dialysis patients. In 2001, the management of the renal registry was taken over by the Ministry of Health under the care of the Clinical Trials and Epidemiology Research Unit. Currently, the National Registry of Diseases Office under the Health Promotion Board is responsible for managing the Singapore Renal Registry.

Memories of Renal Transplantation at SGH – The Transplant Games

Ms. Koh Keng Yong
Manager
Renal Transplant Programme (1999-2007)

The best memories that I have of my days at the renal transplant programme in SGH were all the activities that we organised for patients; the highlight of which were the Singapore Transplant Games (STG). Every two years, our department will take turn with the National University Hospital to co-organise the STG with the Society of Transplantation and invite transplant recipients from various programmes from SGH, National Heart Centre, Singapore National Eye Centre and the National University Hospital. At STG, patients competed in table tennis, badminton, and track and field events such as three kilometre walk and 100-metre dash. Those who did well at the STG would be selected to represent Singapore at the bi-annual World Transplant Games (WTG). Singapore has been sending participants to the WTG since 1987.

The STG showed the athletic prowess of our patients who have received a lifesaving organ transplant such as a kidney, heart or liver. From the late 1990s to early 2000s, I participated at the WTG as Team Manager for the Singapore team. As part of my responsibilities, I attended practices with the athletes to prepare them for the World Games. It was during such times that I witnessed the hardiness of our patients, their commitment to winning and their competitiveness, all of which should make Singapore proud!

At the WTG, while our contingent was small, we never failed to come together to support and cheer for every team member during their competition. It is also during such times and in between competitions where we got to know each other better, not forgetting the family members who accompanied them. During the early 2000s, the Singapore contingent built a reputation as strong contenders in the table tennis and badminton events. These two events had yielded many medals for Singapore.

Memories and Reflections of My Role as a Transplant Coordinator

Ms. Lu York Moi
Manager
Renal Transplant Programme (1995-2021)

I joined SGH as a clinical transplant coordinator in the year 1995. Initially, I was not very confident that I could do the job as I had no experience in this field. However, my mentor Professor Vathsala Anantharaman guided and coached me, helping me to eventually gain enough confidence.

For a patient who needs to go through an organ transplant, it will be a long process that he/she has to undergo, be the organ from a living donor or a deceased donor. To a patient it can be a scary, stressful and confusing process. Therefore, it is extremely helpful when someone is available, who would be able to help guide, answer questions and coordinate the transplant process from start to finish. A transplant coordinator, I feel, is therefore a very important job and the nature of the work can be very meaningful.

In my role as a transplant coordinator, I build relationships with patients and their families through providing education which empower them to actively care for their own health. In this way I can help patients manage their own life after a transplant. As a transplant coordinator, I focus on guiding the patients through each phase of the transition to the "new normal", monitoring their progress during the initial months post-transplant and ultimately helping to oversee their health on their own. In kidney transplant, the survival of the transplant depends very much on patients adhering to their medication regimen, so we have to ensure they adhere with medication instructions for the rest of their lives.

For patients whose transplant is failing, they can often help themselves to slow down the progression of the disease through dietary and lifestyle changes. This is where I play an important role by holding patients' hands and lending them a listening ear. In this manner, I believe I will help lessen their load and reduce their tension, burden, fear and uncertainties. I am passionate about giving patients the information they need so they have the knowledge they need to take ownership over their health.

Years ago, I ran a one-woman show as a clinical transplant coordinator in our Renal Transplant Unit. Now, there is a coordinator to cover each aspect of the transplant process, which I think is much better. We are much more effective when we can work as a team to obtain the best results. Throughout my career, I had been learning and trying to understand chronic kidney disease so that I am better able to empathise with renal disease patients.

My most memorable moment in my career is knowing how organ transplant saves lives. The procedure is however only the beginning of a new life journey for the patient - a journey that I am proud to be part of. For me, the best part of my career is being able to see someone who is really sick return to good health. I had seen adolescents grow up and go to college, get married and have children of their own.

My main motivation comes from providing excellent service to every patient with whom I come into contact. I look for opportunities to improve my patient counselling skills so that each patient I interact with will have a positive experience. I reflect on how organ transplant saves lives from time to time.

I feel motivated by leading a team and helping each member grow. This is the reason why I am inspired to impart all the knowledge I gained as a transplant coordinator to my younger colleagues. Having nurtured and developed the skills of my younger colleagues is the most fulfilling of my job and that keeps me going.

Transplant coordinator takes on a multifaceted role as nurse, dietician, counsellor, teacher and a friend to the transplant patients. Being a transplant coordinator in SGH involves working with individuals from various racial, cultural, religious and socio-economic backgrounds. We are part of a multidisciplinary team assessing patients in the pre-transplant phase right through to transplant offering support physically, emotionally and financially. Transplant coordinator continuously reviews, monitors and educates as well as organised social functions and assist the patient support group. Transplant coordinators play a central and crucial role to the success of the Transplant programme and we hope to see the programme grow to benefit more patients.

Memories of My Days in the Renal Transplant Program at SGH

Ms. Janice Ho
Transplant Coordinator (2006-2011)

One of the treasured memories that I have of my time with the renal transplant programme was to coordinate transplantation from the oldest living kidney donor in Singapore up till to that time in 2009. The 75-year old granny who donated one of her kidneys to her beloved daughter showed me just how amazing it was for this living donor to so selflessly give to the one she loved. The other great memory I have was to coordinate an ABO incompatible kidney transplant in 2011. With these precious memories, I can claim to have witnessed and understood the entire transplant process. Most importantly, they are also about achievements that gave me a sense of pride in my work and made my role as a transplant coordinator more meaningful.

During the five years of working as a transplant coordinator at SGH, I gained valuable exposure and experience. I am indeed grateful for all the invaluable guidance from my Programme Directors, Transplant Managers and my very professional and ever helpful colleagues. I would like to thank the Department for allowing me to be a part of the team and would like to offer them my best wishes for their continued success. Happy 50th Anniversary!

My Memories of Working in the Renal Transplant Unit

Ms. Christina Oh
Senior Transplant Coordinator
(2004-2009)

My years of service with the renal transplant unit stretched from 2004 to 2009. It was a meaningful time to be in the field of transplantation due to the following reasons:

1. The Human Organ Transplant Act or HOTA was undergoing several amendments to improve the access of Singaporeans to kidney transplantation.

2. ABO incompatible kidney transplantation services was established at SGH to increase opportunities for patients to undergo kidney transplantation.

3. There was funding for transplant counsellors to help improve awareness and education about kidney transplantation.

4. The transplant registry was undergoing digitalisation to improve the recording and analysis of transplant related data. .

While it has been more than 10 years since I left, the memories of my days there are all filled with fun, laughter and "positive challenges". The experience I gained there has also helped me journey on to other areas in healthcare with the necessary work ethics and discipline in place to ensure that we provide patients with the best care possible.

Lessons in Life

Mr. Mohamad Rizal Bin Mohd Razali
Transplant Coordinator
(2006-2007)

Early Years

It would be an understatement to say that the best years and most memorable chapter of my nursing career was when I had the opportunity to be seconded to the renal transplant programme in 2006. I was able to witness a diversity of medical expertise and a remarkable degree of proficiency even as the very best was brought out in everyone involved.

Humility

One of many life lessons which I had learned very well was about humility as expressed in these words: *Don't think less of yourself but think of yourself less.* Every Monday, Professor Vathsala would conduct a morning round where every participant would have the opportunity to present on a topic. It did not really matter what your title or designation was; everyone would listen without prejudice or an ounce of judgment but simply respected each other's professionalism. That made learning extremely delightful and appealing for all of us. What resulted was a greater sense of empowerment when we were running clinics as we were able to make use of any we gained more meaningfully.

Work and Play

All work and no play makes Jack a dull boy, as the saying goes. That's why we worked hard, but played even harder! It made what was stressful work more manageable. In terms of welfare and taking care of my colleagues, I would take my hats off to the department for they really cared for every individual staff. The camaraderie among us was apparent and even before the now prevalent mindfulness culture had hit our shores, the sense of bonding and togetherness was clearly present in our midst.

COVID-19

These are fast changing times. The new normal will cause some disruption and I personally feel there is no way to run from it. In fact, the sooner we embrace it, the sooner we will get use to the new habits which we must acquire. This is also a time for us all to remember and appreciate the relationships we have built as a medical fraternity; regardless of rank or job description, let together work mindfully towards better patient care outcomes.

Thank You

I would also like to take this opportunity to extend my heartfelt appreciation and gratitude to SGH Renal Department for having been a part of my career most importantly, for dishing out life lessons that I would remember for the rest of my days.

Thank you, SGH Renal Department and Transplant Unit!

Ms. Tee Ping Sing
Transplant Programme Manager (Operations)
(2007 to present)

My favourite memories with the SGH Renal Transplant Family revolve around the opportunities that were opened up for me to handle the coordination of organ procurement and living kidney transplant cases. The coordination of organ procurement cases was a very intense and emotional, yet meaningful experience. In the intensive care unit (ICU), we see different families when they are at their most fragile moments. We went through many cases with the ICU staff, other transplant teams and the families. Seeing the family members' at both their weakest and calmest times, I learned so much about life in this job. I was extremely fortunate to be able to influence the mindsets of some of the families, making a meaningful event out of what might otherwise have been nothing more than a tragedy. I remembered

saying this to the daughter of a donor: 'Your daddy is a hero, thank you!' I remembered the very first time I saw a pumping heart in the operating theatre and was truly amazed and touched by the true meaning of organ transplantation.

I also really enjoy coordinating living kidney donor transplant cases. Our patients with different backgrounds and family dynamics had come under our care for the same reason – they are all here for a new lease of life. I have learnt and grown the most by learning from my patients and colleagues. Thank you to the transplant family for all the memories and opportunities over the years. Best wishes to you for continued success. Happy Birthday!


西安交通大学

From Our Friends Around the World

Congratulatory Notes

Best Wishes for the Department!

It has been a great honour to be granted an opportunity to join the Renal Transplant Programme at SGH in the first place, and again to be invited to write an article about my experience at SGH for the 50th Anniversary of the programme.

The opportunity to join the programme came as part of my Societe Internationale d'Urologie (SIU) scholarship programme lasting from March until October 2009, which involved a fellowship in the Departments of Urology and Renal Medicine. The training I received covered urology subjects, living donor transplantation, deceased donor transplantation, transplant immunological risk stratification and ABO-blood group incompatible kidney transplantation.

Returning back to Indonesia after completing the training, on top of having been updated on the latest urology procedures, we were able to let our transplant programme apply Doppler ultrasonography to immediately evaluate graft perfusion and better understand transplant immunology. Nowadays, laparoscopic donor nephrectomy is already practiced in the living donor programme here.

A flu outbreak broke out during my training period at SGH, and although not as malicious as the current COVID-19 pandemic, it still forced us to introduce some level of precaution and adaptation in our medical practice. This supposed obstacle, however, did not hinder the eagerness and effort of Associate Professor Terence Kee as the head the renal transplant team and all its members to keep giving their best performance, which I deeply respect and regard as an example for my current practice during the ongoing pandemic.

Finally, this being the 50th Anniversary of the Renal Transplant Programme at SGH, I would like to take the opportunity to express my gratitude and also wish for the programme to be more successful, save more lives, and achieve more collaborations in the future.

Dr Egi Edward Manuputty
Consultant Urologist
Cikini Communion of Churches Hospital, Indonesia
SIU Trainingship Scholar

On the Occasion of Fifty Years of Kidney Medicine at Singapore General Hospital

The practice of kidney medicine has evolved dramatically in the last half century. Breathtaking innovations such as dialysis and kidney transplantation are now essentially taken for granted. Interestingly, in the early years of maintenance dialysis therapy, the dialysis was usually managed in the patients' own homes. Over the ensuing decades, however, in-centre haemodialysis became the principal modality of dialysis in most countries around the world, despite the benefit of home dialysis on quality of life. Writing this in the middle of a pandemic also underscores the benefit to home-based dialysis.

Singapore General Hospital has been a leader in the promotion of home dialysis, particularly home peritoneal dialysis. They now have one of the largest cohorts of peritoneal dialysis patients in the world. The nephrologists dedicated to peritoneal dialysis bring passion and expertise to the programme, which benefits the lives of those living with end-stage kidney disease.

I send sincere congratulations to you on this happy anniversary.

Professor Joanne M. Bargman
Director of Peritoneal Dialysis
University Health Network
Toronto, Canada

Things Might be Bad, but We Still Have Each Other!

Dear SGH Friends,

How time flies! In 2018, the most unforgettable thing that happened to me was that I went to study in SGH, Singapore's flagship hospital and well-known worldwide. Singapore is a beautiful developed country in Southeast Asia, is named as one of the four Asian Tigers, and of which I am thus glad that my daughter was offered a four-year scholarship to study there.

I arrived in Singapore on 1st Sept 2018. Even though I visited SGH for only one month, I was very glad to have been there. During the first week of my arrival, Dr Marjorie Foo, then head of the Nephrology Department (we met at a conference held in Guangzhou in 2017), invited me to introduce my hospital and hometown Xi'an, a historic city known as the Capital City of 13 Dynasties. When I did the introduction in both the Chinese and English languages, the doctors present were excited and impressed. Xi'an Jiaotong University is very famous in China, having been founded 82 years ago. The tourist hotspots like the Terra-Cotta Warriors which is one of the Eight Wonders of the World, and delicious snacks like the Chinese hamburger and cold noodles, are all full of attraction!

During the first two weeks, I followed Dr Marjorie Foo on ward rounds and outpatient clinics. I also participated in meetings, clinical discussions and student tutorials. In just 10 working days, I saw nearly 120 patients on either peritoneal dialysis or having received a renal transplant. I also visited the clinical pharmacology department and for the last two weeks, followed Dr Tan Chieh Suai who was excellent at interventional nephrology. He also took me to have a look at his animal model which was used to trial interventional procedures.

Even though my stay lasted for only one month, I did learn a lot. I truly appreciated how innovative, professional and dedicated Dr Foo and Dr Tan were, and the same could be said of their team. Our common interest in relation to our work made me excited, so I invited Dr Foo, Dr Tan and their colleagues to China in 2018 and 2019. While there, they participated in our Xi'an hospital's 80th anniversary celebrations and also our Fourth Forum on Prevention and Treatment of Chronic Renal Disease. We discussed all aspects of kidney diseases and together visited our dialysis centre and clinical laboratory. We shared our respective experiences in the management of severely ill patients, And concluded our exchange, full of confidence with regard to our cooperation in the future.

In view of the COVID-19 situation, you might not be able to freely celebrate the 50th anniversary of your department, but nonetheless I would like to send my blessings to all of you. We are proud that COVID-19 is under much better control now in both Singapore and China now. I am confident that with eyes open and hearts full of compassion, you will use SGH's achievement in fighting COVID-19 to benefit neighbours both near and far.

On behalf of the faculty, students and staff of Xi'an Jiaotong University, we salute your accomplishments and sincerely wish that the SGH Department of Renal Medicine will continue to thrive and succeed.

Stay safe,
Your good friends forever,
Dr Rongguo Fu
Head, Department of Nephrology
The Second Hospital of Xi'an Jiaotong University Xi'an,
Shaanxi Province, China

Happy 50th Anniversary to The Department of Renal Medicine, SGH!

I had a very pleasant experience during the SGH Renal Biopsy Clinicopathological Workshop 2018 where I could learn directly with individual slides and lots of cases, finally the most important thing was a lot of opportunity to ask the experts in or outside classes. Incredibly good clinicopathological atmosphere! Another conference that should be attended was 18th Asian Colloquium in Nephrology in 2019 where I could learn at the same time network with nephrologists in Asia. The coverage of topics was current and vast. Nice nephrology ambience. Congratulations once again!

Dr Reny Duarsa
Nephrologist
Kasih Ibu General Hospital, Bali Indonesia
GlomCon Podocin Fellow 2020/2021

Thank You for the Foundations!

Coming all the way from Malaysia to acquire my training in nephrology/renal medicine, I was a Registrar in the Department of Renal Medicine, SGH from the years 1999 to 2002. It was a valuable and enriching experience working in Singapore General Hospital (SGH), where I was exposed to great learning opportunities.

There were only a handful of Renal Registrars at that time. We had to cover for renal referrals not only from SGH itself, but also referrals from Tan Tock Seng Hospital, Changi General Hospital, Kandang Kerbau Hospital (KKH) and Alexandra Hospital (AH). It was this vast clinical exposure in various renal cases that made my nephrology training meaningful and fruitful. The then Head of Department, Professor Woo Keng Thye, who came from the same hometown as me, Ipoh, Malaysia, was my great teacher during my registrar training ship. In particular, his bedside teaching during grand ward round twice weekly was invaluable.

Both living and deceased donor kidney transplantation were already carried out widely in SGH then. In a retrospective study that I carried out in 2002 to study the long-term outcome of renal allografts in patients with IgA nephropathy, we found that SGH had the largest series of patients with IgA nephropathy undergoing renal transplantation hitherto reported. Deserving a special mention, I am indebted to Professor Dr Vathsala who was my mentor and from whom I learned the latest management in renal transplantation.

Having left SGH for 17 years, I still feel what I have learned during my traineeship in SGH benefited me a lot in my subsequent careers in Malaysia as it had helped me to build a strong foundation in general nephrology, dialysis and renal transplantation.

In conjunction with the 50th anniversary for renal transplantation, I would like to congratulate the Department for its great achievement and for being the centre of excellence for renal medicine, in particular renal transplantation, in this part of the world. I am confident it will continue to be the pioneer in renal medicine in this region in the many more years to come.

Dr Ng Yew Sang
Consultant Nephrologist
Fatimah Hospital
Ipoh, Malaysia

SGH Renal Will Always be the Best!

Dear Renal Family,

Let me begin by saying I really miss the family! I am where I am, and who I am because of the well-rounded training and nurturing by SGH Renal Department, the birthplace of Nephrology in Singapore. I realised that if I were to write about my nearly 7-year experience in SGH, it would become a chapter itself already! I shall keep it short and sweet. I can vividly remember everything started with an interview in O'Briens café with Professor Chan Choong Meng on 11 Jan 2011 for my application as a service Registrar, and he asked me if I was ready for a training with "heavy workload". I said yes on the spot (without really knowing what I would go through!), and embarked on my journey from July 2011.

Dr Darren Lim with fellow registrars doing a song performance for the 4R event organised by the Singapore Society of Nephrology in 2012.

It turned out to be the best decision in my life, and I am forever grateful for the given opportunity to join the family. It was the most demanding intellectual experience for me with a steep learning curve, but I was fortunate to have met the most dedicated faculty that comprises some of the best clinicians and the most passionate educators, who truly put their heart and soul into the training programme. Receiving training in the largest healthcare cluster provided me an unparalleled exposure of both breadth and depth, there was no paucity for complicated and challenging cases even in the daily ward rounds. I'll always remember Emeritus Professor Woo Keng Thye's Grand Ward Rounds which were full of ethical, historical and philosophical lessons in addition to his wisdom and clinical acumen. The great academic culture has pushed me to be a better nephrologist, and being able to confidently take care of renal patients holistically. I am indebted to Dr Terence Kee and Dr Tan Chieh Suai for being my direct supervisors throughout my training and given me continuous and selfless guidance. Thank you to Dr Marjorie Foo and Dr Jason Choo, the Programme Directors of Renal Senior Residency for giving me the precious opportunity to represent the Residents. And to the entire department, I have learnt from each and everyone of you, including dialysis / transplant coordinators and Renal social workers.

There are so much more than that. The true friendship and camaraderie we grew among us along the journey after being through thick and thin, the unique memories of department gatherings at Dr Manish's place, various residency outings, Renal Got Talent Night, the nerve-wracking 4R, the fun we had for the yearly "Nephrology Idol" contest (and our memorable videos), and many more!

"A teacher affects eternity; he can never tell where his influence stops." In short, my experience at SGH Renal was immeasurably enriching – intellectually, personally, and professionally. Those years were an incredible gift, and no amount of "thank you" can adequately express how much I appreciate it. SGH Renal will ALWAYS BE THE BEST! Happy 50th Anniversary to the Renal Transplant Programme, best wishes for the department, and I truly look forward to seeing you in our next gathering!

Dr Darren Lee Kian Guan
Consultant Nephrologist
Pantai Hospital
Penang, Malaysia

A Treasure-like Experience

It was another typical autumn day in United Kingdom but imagine my surprised when my house mate told me that Professor Woo Keng Thye has called and left me a message that he would like to speak to me regarding my application to become a registrar in Singapore General Hospital (SGH). The next day, I waited and Professor Woo did manage to carry out an informal interview with me, which was followed by an actual meeting up in his office in April 2001.

Knowing renal medicine will be my destiny, I started my first day of my infant life in SGH in October 2001, having made the nursing quarter as my home in the first month. My first on call arrived pretty soon and it was surely a memorable one as Associate Professor Tan Han Khim brought me to see renal consultations across the island in his BMW. The renal consults included assessing a potential heart beating donor at Tan Tock Seng Hospital and prescribing Continuous Renal Replacement Therapy (CRRT) at Changi Hospital. CRRT then equate to manually replacing different concoction of fluids. Those were also the days that we were called through a pager, doing on calls from home or flagging town a taxi to go to Changi General Hospital etc. with clear navigation instruction, else risked stuck in a jam.

Although life was tough with few of us around, it was never a dull moment. At one point, the registrar pool has decreased to 2 members – me and Associate Professor Terrence Kee. We were basically doing call back to back with no complaint what so ever. Our office at the 6th floor was our second home. As year passed by, the department grows bigger via more registrars and fellows (Dr Suhail, Dr Arvind, Dr Niranjan, Dr Roger Tan, Dr Yang Wen Shen, Dr Loh Ping Tyug and Dr Angeline Goh). Having regular lunch time fellowship in houseman canteen was a norm. We were close to our medical officers and enjoyed a reasonably active social life. We were so glad that some of them actually decided to join renal medicine and become the senior consultants of today – Associate Professor Jason Choo, Associate Professor Tan Chieh Suai and Dr Manish Kaushik.

Overall I have spent nearly 5 years in SGH and although I have left in 2005, it was just like yesterday that I was still in SGH. It was a huge responsibility wearing the black name tag as we were held accountable for our action made when we attended referrals, managing in and outpatients plus handling various referrals from within and outside SGH. With the primary physician system, I could truly follow up the progress of patients. If we were to make a wrong decision, we will have to make right the decision and action, no matter how painful it will be. "Two wrongs don't make a right", that would be motto as being constantly reminded by my next door neighbour, Professor Chan Choong Meng. A big shout out to my immediate supervisors, Dr Stephen Chew and Professor Vathsala for their mentorships. Whenever I have any problems, I can also count on my senior consultants and consultants - Professor Woo Keng Thye, Associate Professor Wong Kok Seng, Associate Professor Lina Choong, Associate Professor Tan Han Khim, Professor Chan Choong Meng and Associate Professor Marjorie Foo for their words of wisdom and encouragement. I always felt supported with whatever decision that I have made.

Severe Acute Respiratory Syndrome (SARS) came in 2003 and caught us by surprised. One of the case was landed in surgical ward with acute kidney injury. Both Professor Vathsala and I attended the case as a peripheral consult case without knowing the patient has already contracted SARS. After a physical examination without any form of Personal Protective Equipment (PPE), she commented that the patient has tachycardia for no apparent reason. 12 days later, I received a call from Professor Woo, who sat in the SARS hospital task force, to inform me that I have been exposed and asked me to undergo home leave for one day. That was really a close call! Soon we are made to realise the seriousness of SARS and we were all separate into different teams with no inter team member contact is allowed. That was probably the first time that I have tasted what 'virtual medicine' meant. Sadly, we have lost great colleagues during the invasion.

My not so short stint in SGH taught me about efficient planning and effective management with whatever resource that is granted to us. As healthcare cost is largely unsubsidised in the republic, we had to be careful as to not burden our patient financially. Even though the clinics were busy, we were always

treated well by our dear nursing colleagues. A hot and fresh coffee always made our busy clinic day a sheer bliss. Dr Lou Huei-Xin, our renal pharmacist was always patient and work hand in hand with us in delivering the best clinical research practice and prescribing habit. Similarly, wards nurses, Continuous Ambulatory Peritoneal Dialysis (CAPD) and Haemodialysis (HD) nurses were all fantastic and accommodating.

During the transplant clinic day, Professor Vathsala would walk from room to room to discuss cases with us, a trait that I have picked up and practice until today. I learned that good communication and being respectful toward each other is one of the vital ingredients if we were to be successful in life. Similarly we had post clinic Peritoneal Dialysis (PD) and HD discussion sessions with Associate Professor Marjorie Foo and Associate Professor Lina Choong whom I cherished. Not to forget the once per week guidance session from Professor Woo.

The transplantation programme was pretty much alive and buzzing with life. It was always well organised. Ms. Lu York Moi and her power girls were amazing, which make my transplant training exhilarating. The transplant coordinator room also doubled as a chit chat and distressing place. I had seen a fair share of transplantation done and was always happy to see a new lease of life that followed.

Somehow despite the hectic lifestyle, I still managed to find time to write. It was quite a struggle in the beginning, one piece of good advice was from Associate Professor Tan Han Khim where he shared with me that to make an article acceptable, it should have simple sentences that illustrate the important points. The first breakthrough came with the publication on the usage of mupirocin and its impact on rates of exit site infections and peritonitis, which was accepted by the Nephrology, Dialysis and Transplantation Journal.

To me, renal medicine is unique as it is the only field of medicine that can sustain a failed organ and provide a new lease of life through transplantation. It is challenging as we have to deal with complex medical cases which comes with it the breadth of ethical issues. Since SGH is the birth place of nephrology, it has the most collective treasure-like experience of the senior nephrologists. Having going

Happy Reunion with Professor Christopher Lim at the Singapore Malaysia Nephrology Forum held in Singapore.

through the robust programme, it has enabled me to be professional, competent, compassionate and in lifelong learning through constant deliberation, collaboration and networking. I always thought that I would be joining the private sector after my return to Malaysia but to my own surprise I have remained in public institution to continue my professional learning and teaching journey.

I wish to end by wishing SGH renal transplantation centre a very happy Golden Jubilee and long live the vibrant transplant culture. May SGH continue its long tradition of regional and international academic and clinical excellence.

Professor Christopher Lim
Head of Medical Department and Nephrology Unit
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia

A Beacon of Light

The Department of Renal Medicine at SGH has been a beacon of light for those with renal disease in Asia for so many years. The dialysis programme in Singapore showed the world what could be done to extend dialysis across a nation and into the communities in every corner of the island. The transplant programme has shown us all that determination and training can provide the confidence to establish a successful programme. My first visit to SGH was actually in 1971, about a year after your first transplant, but it was to be many years before I was able to engage with your transplant teams. It was my great pleasure to get to know my very good friend, Professor Vathsala Anantharaman, as she returned from working with Barry Kahan in Houston to establish Transplant Nephrology at SGH. I also recall many discussions with the then medical director of NKFS, Dr Feidlhem Wood and others, about the needs for deceased organ donation in Singapore and the strategies for success. Terence Kee joined us for a period of training in renal transplantation at Westmead in Sydney and returned to SGH leaving us sorry to see him go, but delighted to see the strengthening of the renal transplant programme in Singapore. We have all watched how, over the past ten years or so, you have extended care employing many innovative strategies to provide for Singaporeans in need of transplantation.

It is a great pleasure to many of us who have witnessed the growth of both Singapore and the Singapore General Hospital Renal programme over the past 50 years, to see such a strong and principled team delivering excellence of care to all in need. While none of us can know what the future holds in our fast moving field, we can all be assured that the Singapore community will remain at the forefront for delivery of treatment for Chronic Kidney Disease. The SGH team, with their dedication and expertise, will undoubtedly retain a strong place in the global approach to the problems of kidney disease over the next 50 years.

Professor Jeremy Chapman
AC FRACP FRCP FAHMS
Past President The Transplantation Society
Editor in Chief Transplantation Journals

NSW GOVERNMENT Health
Western Sydney
Local Health District

An Absolute Honour

It is with great pleasure I congratulate you on the 50th Anniversary of Kidney Transplantation and Medicine at the Singapore General Hospital. It is an absolute honour for me to commend and praise your team of transplant health professionals for providing the amazing care and support to all your patients with kidney transplants since 1970. Your continuing commitment to those with kidney failure and chronic kidney disease is outstanding and is a wonderful example of leadership, goodwill and dedication. Despite the many challenges and barriers, you have strived to achieve the best in all aspects of care and have saved many lives with kidney failure. It has been both exciting and inspirational for me to watch how you and your team have advanced transplantation research in Singapore and is a true exemplar for the world. On behalf of the Westmead Kidney and Kidney Pancreas Transplant Unit, I wish you and your team all the very best in the many decades to come.

Kind regards

Professor Germaine Wong
Director of Renal and Transplant Medicine
Westmead Hospital
Sydney, New South Wales, Australia

Duke Surgery
Duke University School of Medicine

Congratulations on Work Well Done!

Congratulations on your achieving 50 years of renal transplantation at Singapore General Hospital. This is an important milestone in patient care and programme building, and you have provided consistent, strong leadership to your growing programme. Kidney transplantation offers improved quality of life and length of life for patients with end stage renal failure, and having the alternative therapy of kidney transplantation offers hope and life to many people in Singapore.

You have also built a collaboration with basic scientists to study how to improve kidney transplantation at your centre and elsewhere, and it has been my privilege to collaborate with you on a project aiming to understand risk factors for kidney transplant rejection that may be determined by our genetic background. We will continue to work on this project together. It was a delight for me to visit Duke-NUS in Singapore several years ago and to see first-hand all that you and your colleagues are doing, including growing the liver and composite tissue transplant programmes.

I am confident that the kidney transplant programme will continue to grow and serve the needs of the Singapore community with outstanding outcomes based on your commitment to quality clinical care, research, and teaching. Again, please accept my congratulations on work well done. Thank you for your continued collaboration and friendship.

Sincerely,

Stuart J. Knechtle, M.D.
William R. Kenan, Jr. Professor of Surgery
Executive Director, Duke Transplant Centre

Wishing Continued Success in the Future!

Astellas would like to extend our heartfelt congratulations to Singapore General Hospital's Department of Renal Medicine for 50 years of excellence in renal transplantation. Working with the Renal Transplant team has always been a pleasure throughout the years and we at Astellas hope to continue this tradition. One of the memorable experiences with the team was the celebration of Christmas at the SGH Transplant Patient Update 2019. During the event, the patients not only attended a short informative lecture, but also participated in exercises and games.

The Renal Transplant Programme has grown immensely, providing an array of services that benefit the community, putting patients at the heart of what the team does. With such an established programme, we cannot wait to see what the Renal Transplant team will do the next 50 years. Congratulations once again and Astellas wishes the Renal Transplant Programme a continued success in the future.

Ms. Rachael Yap
Senior Marketing Manager
Astellas Pharma Singapore Pte Ltd

Proud to be part of your journey!

Novartis Singapore would like to wholeheartedly congratulate SGH Renal Transplant Programme on the occasion of this significant milestone of national importance in renal transplantation. Novartis is proud to have been partner in this journey with SGH and contributing to bend the curve of transplant patient outcomes. We are proud that our medicines have helped to extend lives and brought smiles to hundreds of families. We are also honoured by your participation in several landmark kidney transplant clinical trials that Novartis conducted in Singapore. We thank you also for continuing to consider us for supporting your efforts to continuing medical and patient education.

Mr. Thomas Antony Choolackal
Business Manager, Immunology
Novartis (Singapore) Pte Ltd

Acknowledgements

We would like to express our deepest appreciation to our supporters who provided funding for this scholarly book project:

Dr Goh Tiow Seng

Astellas Pharma Singapore Pte Ltd

Novartis (Singapore) Pte Ltd

DKSH Singapore Ptd Ltd

Teleflex Medical Asia

Department of Renal Medicine Education, Training and Research Grant

We would like to acknowledge to our supporters who provided photos and other materials for this anniversary book:

Dr Chan Kong Thoe

Ms. June Tien, Education Resource Centre, Singapore General Hospital

Ms. Michelle Felicia Scully, Department of Communications, Singapore General Hospital

Mr. Jerry Wong, Department of Communications, Singapore General Hospital

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