

## 16th Seah Cheng Siang Memorial Lecture – The Changing Face of Cardiology Practice, Training and Research in Singapore<sup>†</sup>

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### Introduction

Professor Seah Cheng Siang was one of the most illustrious physicians of his era. During his professional career, he held the following positions: Head, Department of Medicine, Thomson Road General Hospital (1960-71); Head, Department of Medicine III at the Singapore General Hospital (1971-87); Master of the Academy of Medicine (1970-73); Clinical Professor and Deputy Director, Postgraduate Medical School, National University of Singapore.

I was very fortunate to be his medical officer for 1 year at the Thomson Road General Hospital in 1966. Subsequently, we had an excellent working relationship, when I was Head of the University Department of Medicine II at the Singapore General Hospital from 1981 to 1983. Being an excellent clinician, a passionate teacher and an outstanding researcher, I am confident that he would have approved the title that I chose for my lecture – “The Changing Face of Cardiology Practice, Training and Research in Singapore”. “The Changing Face” refers to the 4 decades from 1966 to 2006.

### Cardiology in Singapore in the 1960s

Clinical cardiology in Singapore in the 1960s was extremely florid. It was not uncommon in a typical adult medical ward to see patients with end stage rheumatic valvular, hypertensive and ischaemic heart disease, intractable heart failure, malignant hypertension, and sometimes even syphilitic aortic aneurysm. One such patient was a 34-year-old woman who presented with severe heart failure, loud cardiac murmurs and an enormous heart (Fig. 1).<sup>1</sup> Later pericardiocentesis showed that she was suffering from tuberculous pericardial effusion and severe rheumatic valvular heart disease.

In the ensuing years, as our economy and standard of living improved, rheumatic fever became increasingly rare. It is now difficult to find a patient with mitral stenosis in the ward to teach our medical students. Today, our cardiovascular disease pattern is identical to that in the developed Western countries with coronary heart disease

(CHD), stroke, hypertension, and diabetes mellitus being the major problems.

### Ten Great Achievements of Cardiology in the 20<sup>th</sup> Century

According to Eugene Braunwald, a world renowned cardiologist from Harvard University, the 10 great achievements of cardiology in the 20th century were as follows: (1) Electrocardiography, (2) cardiac catheterisation, (3) coronary angiography, (4) cardiovascular surgery, (5) invasive cardiology, (6) the coronary care unit, (7) cardiovascular drugs, (8) preventive cardiology, (9) echocardiography and (10) pacemakers and internal defibrillators.<sup>2</sup>

Today in Singapore, we can proudly say that we are highly advanced in all these 10 areas, ranging from the humble 12-lead electrocardiogram (ECG) to coronary artery bypass graft surgery and coronary angioplasty, which were first performed in this country in 1980 and 1984 respectively.

### Electrocardiography

Despite recent advances in specialised technology such as echocardiography, nuclear cardiology, coronary angiography etc, the ECG still plays a pivotal role in cardiac management. In patients presenting with ST elevation myocardial infarction (STEMI), the ECG can indicate not only the site, size and age of the left ventricular infarction, but it can also diagnose whether there is concomitant infarction of the right ventricle. Further, it can reliably indicate the site of the coronary occlusion.<sup>3</sup> Figure 2 shows a patient with inferior STEMI and concomitant right ventricular infarction. Based on the ECG abnormalities, a diagnosis of occlusion of the proximal right coronary artery was made and this was later confirmed by coronary angiography. Currently, many such patients are successfully treated with immediate coronary angioplasty.

### Echocardiography

Figure 3 shows the classical M-mode echocardiographic findings of a patient with left atrial myxoma.<sup>4</sup> It was performed in February 1976 and, most likely, was the first

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echocardiographic procedure carried out in Singapore. In the past 30 years, echocardiography has made spectacular progress and has revolutionised the practice of cardiology.<sup>5</sup> At present, virtually all cardiac abnormalities (except for coronary artery disease) can be diagnosed easily and accurately at the patient's bedside using this non-invasive technique (Fig. 4).

### Coronary Heart Disease

The leading causes of death in Singapore have altered dramatically in the past 4 decades. In 1957, tuberculosis was a prominent cause of mortality. Today, cancer is the main cause, followed by ischaemic and other heart diseases, with pneumonia and stroke in the third and fourth places.

#### Pathology

Our knowledge of the pathology of coronary artery disease has advanced considerably in recent years. Not too long ago, it was widely believed that atherosclerosis is an inert lesion similar to a “graveyard of cholesterol debris encased by a connective tissue scar”. However, we now know that this is a completely wrong concept of the atherosclerotic plaque, which actually is an active inflammatory lesion.<sup>6</sup> Due to the excellent work by the late Michael Davies from London, we now know that coronary atherosclerosis is one disease presenting as 2 different pathologies and 2 different clinical manifestations, as reflected by the stable and unstable plaque.<sup>7</sup> And it is the unstable plaque that ruptures resulting in coronary thrombosis and acute myocardial infarction (AMI).

#### Clinical Management

In the early 1960s, management of CHD was primitive on hindsight. Patients who suffered an AMI were kept in bed for about 5 weeks, with very little active treatment. Since then, we have made tremendous progress in our understanding of, as well as our ability to diagnose and treat the disease. Today, we have highly effective treatments such as healthy lifestyle practices, excellent drugs like the statins, beta-blockers, angiotensin-converting enzyme inhibitors and antiplatelet agents, and well-proven revascularisation procedures such as coronary artery bypass graft surgery, and coronary angioplasty and stenting.

However, an important problem still remains unresolved. In about 50% of cases, the first clinical manifestation of CHD is either AMI or sudden death – a situation many regard as “too little, too late”. Therefore, the greatest challenge today is how to prevent an AMI or sudden death before it occurs. The usual strategy is to risk stratify an individual based on the clinical history, the risk factors profile and complemented by a non-invasive stress test and, in selected patients, coronary angiography.

Currently, there is an intense debate in Singapore and

globally regarding whether coronary artery calcium score and non-invasive multi-slice CT coronary angiography (Fig. 5) should be used more widely to improve our diagnostic accuracy. Hopefully, this important issue will be settled in the next few years.<sup>8</sup>

### Lipids

I vividly remember speaking at a grand-round on the role of cholesterol in CHD at the Thomson Road General Hospital in 1966, chaired by Seah Cheng Siang. It ended with the unanswered question – “cholesterol – guilty or not guilty?”.

#### The Framingham Heart Study

The first proof that high cholesterol, hypertension, cigarette smoking and diabetes mellitus were all major risk factors for cardiovascular disease came from the landmark Framingham Heart Study, which started in 1948.<sup>9</sup> Indeed, the concept of “risk factor” was first introduced by the Framingham investigators. They later confirmed that the more risk factors an individual has, the greater will be his risk of developing cardiovascular disease. These remarkable findings paved the way for preventive cardiology, which has saved millions of lives all over the world. Today, the primary prevention of cardiovascular diseases, mainly by healthy lifestyle practices, as well as optimal treatment of diabetes mellitus, hypertension and dyslipidaemia, has become extremely important in Singapore.

#### Statin Therapy

The management of patients with high LDL-cholesterol levels has taken a major leap in the past 10 years with the introduction of statin therapy. Today, statins play a critical role in the secondary prevention of CHD as well as in primary prevention in high-risk individuals.<sup>10</sup>

It is likely that in the next few years, elevation of HDL-cholesterol will become increasingly important. The results of a few ongoing HDL-cholesterol elevation trials are awaited with great interest.

### Developmental Milestones in Singapore Cardiology

#### Cardiology at the Singapore General Hospital

The first coronary care unit (CCU) in Singapore was started by Charles Toh in 1967, with a major contribution to its success by Low Lip Ping (Fig. 6). It was situated in Medical Unit II (subsequently University Department of Medicine II) at the Outram Road General Hospital, now the Singapore General Hospital (SGH).<sup>11</sup> In 1973, this CCU was replaced by a new CCU with 6 beds in the same Department (Fig. 7). It was also equipped with a coronary care ambulance (Fig. 8). When the present SGH started in 1981, a new Cardiology Department headed by A Johan was formed and this Department's CCU (which remains till

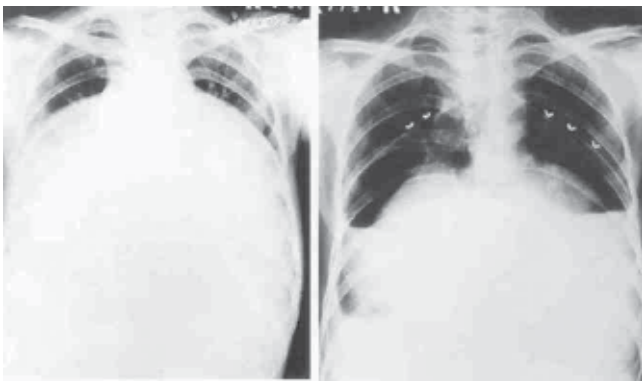


Fig. 1. Left panel. Chest X-ray showing an enormously enlarged heart. Right panel. Chest X-ray after pericardiocentesis. Arrowheads indicate a very thin pericardium. The translucent areas below the pericardium reflect air which has been injected into the pericardial sac after pericardiocentesis.

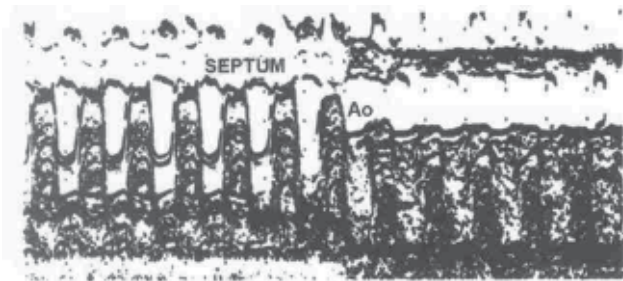


Fig. 3. M-mode echocardiography showing left atrial myxoma. (Ao = aorta). This figure has been previously published in the *Singapore Medical Journal* 1977;18 (1):68-75, and is reproduced with the kind permission of the Editor.



Fig. 5. 64-slice EBCT scan of the heart showing normal coronary arteries. (The photograph is reproduced by courtesy of Dr James Yip, Consultant Cardiologist, National University Hospital).



Fig. 2. Electrocardiogram showing inferior ST elevation myocardial infarction together with right ventricular infarction. Coronary angiogram showing total occlusion of the proximal right coronary artery.

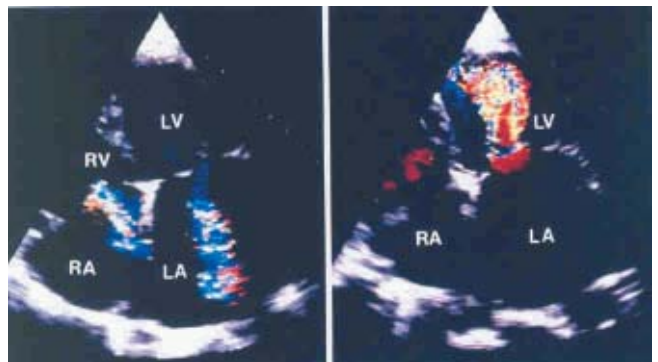


Fig. 4. Two-dimensional and Doppler echocardiography showing mitral stenosis and regurgitation and tricuspid regurgitation. The left panel was recorded in systole and the right panel in diastole. (RA = right atrium, LA = left atrium, RV = right ventricle, LV = left ventricle).



Fig. 6. The first coronary care unit in Singapore, which started in 1967 at the Outram Road General Hospital.

today) is shown in Figure 9.

The SGH Department of Cardiology and Department of Cardiothoracic Surgery subsequently evolved to become the Singapore Heart Centre in 1994 and the National Heart Centre in 1998. In the successive leadership of SGH Cardiology, A Johan was followed by Arthur Tan and Lim Yean Leng, with Koh Tian Hai and Terrance Chua being



Fig. 7. The coronary care unit, which started in 1973 at the Singapore General Hospital. The photograph was taken around 1976.



Fig. 9. The coronary care unit of the Department of Cardiology at the Singapore General Hospital in 1981.

the current Medical Director and Deputy Medical Director, respectively, of the National Heart Centre.

On the University side, the University of Singapore [now the National University of Singapore (NUS)] did not have a Department of Cardiology. Cardiology practice, teaching and research were all carried out within the 2 University medical units at SGH, which were the University Departments of Medicine I and II. Nevertheless, University cardiologists at SGH made many important contributions to the progress of cardiology in Singapore. They were the first to pioneer: (1) Cardiac catheterisation and angiography in 1964 (together with SB Roy, who was a visiting expert), (2) the CCU in 1967, (3) M-mode echocardiography in 1976 and two-dimensional echocardiography in 1980, and (4) electrophysiology in 1981. Cardiology at the University Department of Medicine II was under the charge of Charles Toh from 1961 to 1975 and Chia Boon Lock from 1975 to 1985.



Fig. 8. The coronary care ambulance, which was introduced soon after the coronary care unit was started in 1973 at the Singapore General Hospital. The photograph was taken around 1976.

### *Cardiology at the National University Hospital*

The NUS clinical departments started moving over to the National University Hospital (NUH) in 1985. Cardiology at NUH began as the Division of Cardiology, Department of Medicine, from 1986 to 1989 with Chia Boon Lock as its Head. During this time, cardiac surgery and coronary angioplasty were started. Ambulatory blood pressure monitoring was also introduced for the first time in Singapore.

In 1989, the Cardiac Department was formed with Maurice Choo as its first Chief of Department, followed subsequently by Christopher Chew, Chia Boon Lock, Lim Yean Teng, and currently Tan Huay Cheem.

In 2001, the National Healthcare Group (NHG) formed The Heart Institute comprising cardiology and cardiac surgery at NUH, Tan Tock Seng Hospital, Alexandra Hospital and NHG polyclinics, with Lee Chuen Neng as its director.

Today, the major players of cardiology in Singapore are the cardiologists in the restructured hospitals of the 2 health care clusters, as well as cardiologists in the private sector.

### **The Future**

#### *Rising Healthcare Costs*

One of the biggest issues in Singapore and all around the world is the rapid escalation of healthcare cost. There is no simple solution to this enormous problem, except to say that almost all healthcare systems strive to deliver the highest standard of medical care at the lowest possible cost and expenditure.

#### *Genomic Medicine and Stem Cell Therapy*

Today, the greatest excitement is the promise of genomic medicine and stem cell therapy to dramatically change the

way we treat our patients.<sup>12</sup> Currently, Singapore is internationally renowned in embryonic stem cell research. Following the announcement of the working draft of the human genome sequence by President Bill Clinton on 26 June 2000, Dr Francis Collins, Director of the Human Research Genome Institute, United States of America said – “I would be willing to make a predication that within 10 years, we will have the potential of offering any of you the opportunity to find out what particular genetic conditions you may be at increased risk for, based upon the discovery of genes involved in common illnesses like diabetes, hypertension, heart disease and so on”.<sup>13</sup>

More recently, Dr Collins said – “By 2015, we will see the beginnings of a real transformation in the therapeutics of medicine, which by 2020 will have touched virtually every disorder... and the drugs that we give in 2020 will for the most part be those that were based on the understanding of the genome, and the things that we use today will be relegated to the dustbin”.<sup>14</sup>

However, since 2020 is quite some time away, it is important to emphasise that, in the meantime, we should actively pursue the current therapies that have been proven to be beneficial. In the landmark INTERHEART study, which involved about 30,000 AMI patients in 52 countries (including Singapore), Salim Yusuf and co-workers found that 9 traditional risk factors accounted for about 90% of the risk in these patients, with abnormal lipids and cigarette smoking accounting for about 66%.<sup>15</sup> Yusuf strongly believes that the risk of cardiovascular disease can be greatly reduced if all these traditional risk factors are aggressively treated and that currently, we are just not doing enough.

### Cardiology Training in Singapore

In 1966, there were only 4 adult cardiologists in Singapore. Today, there are 98 cardiologists in the Singapore Medical Council’s registry of specialists, or 23 cardiologists per 1 million population. This proportion is higher than that in England (15 cardiologists per 1 million population), but lower than that in the United States of America.

The number of cardiologists in Singapore will increase steadily, because every year there are about 6 cardiology trainees who will complete their training locally and pass the exit examination of the Advanced Specialist Training programme. An adequate number of cardiologists is necessary because Singapore is striving to be the medical hub for the region and globally, and also because some specialists, including cardiologists, will be required to pursue research in life science by being clinician scientists.

In the early days, many of our cardiologists had their training totally or partially overseas, because a structured training programme did not exist in Singapore. Currently,

our trainees spend 3 years in the Advanced Specialist Training programme in cardiology of the Academy of Medicine and the NUS Division of Graduate Medical Studies. There has been 59 graduates of this programme, and the majority have then gone to renowned cardiac centres overseas for further training in a sub-specialty.

### Cardiology Research in Singapore

The birth of cardiology research in Singapore could not have been more illustrious, as recounted by ES Monteiro at the Fifth Asian-Pacific Congress of Cardiology, which was held in Singapore in 1972. The *British Heart Journal* reported his speech, which said that it was in Singapore that cardiac beri-beri was first successfully treated, when he injected a crude extract of the discarded rice polish, leading to the recovery of the patient.<sup>16</sup>

Subsequently in 1959, T J Danaraj was the first to report (a) the high prevalence of CHD in Indians in Singapore<sup>17</sup> and (b) renal artery stenosis and hypertension due to primary aortoarteritis or Takayasu’s disease.<sup>18</sup> The first epidemiological survey of blood pressure in Singapore was carried out by Seah Cheng Siang and his team in 1977.<sup>19</sup>

In the past 20 years, many papers have been published by our cardiologists in prestigious journals, such as the *American Heart Journal*, *Journal of the American College of Cardiology*, *Circulation*, *European Heart Journal* and even the *New England Journal of Medicine*.<sup>20-23</sup> These papers involved research in many areas of cardiology, such as acute myocardial infarction, cardiovascular epidemiology, echocardiography, coronary angioplasty, molecular cardiology, and cardiac arrhythmias and electrophysiology. Singapore has also been involved in a few landmark international mega-studies such as the RENAAL, CHARM, INTERHEART and the ongoing ONTARGET study.

The future appears to be even more promising with: (1) the launch of The Singapore Consortium of Cohorts study, which is the Singapore equivalent of the Framingham Heart Study and (2) the recent appointment of Judith Swain, a world renowned researcher, as the Executive Director of the Singapore Institute for Clinical Science, which will spearhead translational and clinical research in Singapore.

### Epilogue

I would like to end on a philosophical note by reviewing the current status of cardiovascular disease in Singapore.

The age-standardised death rates (between 35 and 64 years) for ischaemic and other heart diseases and also for stroke have decreased markedly in 2003 compared to 1997.<sup>24</sup> In addition, in 2004, the life expectancy at birth was 77 years for males and 81 years for females, which was

significantly greater than that for both genders in the 1960s. Furthermore, the prevalence of diabetes mellitus, hypertension, high blood cholesterol and cigarette smoking have all decreased in the 2004 compared to the 1998 National Health Survey. However, unlike the marked decrease in age-standardised death rates, the reduction in mortality rates as a percentage of total deaths in the whole population for ischaemic and other heart diseases, as well as for stroke, has been much smaller. One of the possible reasons for this difference is because cardiovascular mortality increases exponentially with age and Singapore has one of the fastest ageing populations in the world.

Perhaps, as recommended by some experts, the best strategy for all of us is to strive “to die young at the latest possible age – not just for ourselves, but for the entire population”. The best example of this achievement is the world renowned researcher on cigarette smoking, Sir Richard Doll, who died in 2005 following a short illness, at the age of 92 years.<sup>25</sup> But alas for many of us, this is something that may be difficult to attain.

## Conclusion

For the past one hour, I have taken you on a journey, a very personal journal, on the progress of cardiology in Singapore in the past 4 decades. This journey in many ways parallels the spectacular success story of Singapore as a nation state – from the past to the present, and from the present to the future.

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