Professor Seah Cheng Siang (1922-1990)

- MBBS, Singapore
- Member, Royal College of Physicians of Edinburgh
- 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
- Founder, Gastroenterological Society of Singapore
Following his demise in June 1990, the Council of the Academy established the Seah Cheng Siang (SCS) Memorial Research Fund, to perpetuate the memory of the distinguished Physician, Academician and Past Master of the Academy of Medicine.

The primary objective of the Fund was to promote medical research in Singapore. In early 1991, the SCS Memorial Research Fund was renamed the SCS Memorial Fund and included

- An endowed annual lectureship: “The Seah Cheng Siang Memorial Lectureship”
- A Gold medal to be awarded annually to the top candidate in the Master of Medicine (Internal Medicine) exams.
- Research/Travelling Fellowships
My Personal Perspectives

- As I was a foreign medicate graduate, I was posted by MOH to MUIII, SGH as a house officer, specifically to be assessed by Prof Seah for fitness to practice in Singapore.

- My first GWR with him, he asked me how I would induce diabetes in rats. Thankfully I knew the answer: (Alloxan / Streptozotocin - having managed a diabetic rat during 2nd year medical school physiology). Indeed I must have passed the litmus test!
My Personal Perspectives

- **Master Clinician** – He did not need a CT scan to diagnose abdominal masses or neurological deficits. The CT scans that were so cleverly and expeditiously obtained by my registrar and consultant were merely to confirm Prof’s findings.

- The Combined Medical Rounds held in turn at SGH by the 3 Medical Units were a showcase of his abilities. Often in an auditorium with standing room only, Prof Seah could extract from patients the crucial and most elusive piece of history that everyone else had missed, or dissect the most complex of cases and come up with the final diagnosis. These were far better than any Case Records of the Mass General Hospital that are published in the NEJM.
Caring – Class status of patients was not a criterion for receiving Prof Seah’s undivided attention. He would spend as much time with a vegetable seller as a civil servant.

Meticulous – Then there is that legend that, before his GWRs, HOs and MOs would iron case notes so that they would not have dog ears and that the ward sister/NO would position bedside tables at ruler measured distances. Whether urban legend or otherwise, this was really about setting standards.

Teacher – Prof Seah taught by inspiring awe, respect and setting standards. One tried one’s best simply to please him.
## Seah Cheng Siang Lecturers

<table>
<thead>
<tr>
<th>Title</th>
<th>Lecturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inaugural The life and times of Seah Cheng Siang</td>
<td>Chew Chin Hin</td>
</tr>
<tr>
<td>2nd Clinical skills in an age of technology</td>
<td>James W Lance</td>
</tr>
<tr>
<td>3rd Research &amp; the practising physician – Gastroenterological perspective</td>
<td>Lawrie W Powell</td>
</tr>
<tr>
<td>4th Primary gastrointestinal lymphoma in Hong Kong</td>
<td>David Todd</td>
</tr>
<tr>
<td>5th Human immunodeficiency virus and the respiratory system--pulmonary manifestations of acquired immunodeficiency syndrome</td>
<td>Homer A Boushey</td>
</tr>
<tr>
<td>6th Autoimmunity and the Nervous System</td>
<td>John Newsome-Davis</td>
</tr>
<tr>
<td>7th The aetiology of gallstones</td>
<td>Ian A D Bouchier</td>
</tr>
<tr>
<td>8th New antithrombotic agents</td>
<td>Marc Verstraete</td>
</tr>
<tr>
<td>9th Gastric cancer--where are we now?</td>
<td>Lam Shiu Kum</td>
</tr>
<tr>
<td>10th Going places--a rheumatological odyssey</td>
<td>Feng Pao Hsii</td>
</tr>
<tr>
<td>11th Temporal lobe epilepsy – The past, present and future</td>
<td>Simon D Shorvon</td>
</tr>
</tbody>
</table>

*Lim SH, Ng KY, Chew CH, Annals Academy of Medicine 2007; 36 (7): 525-40*
<table>
<thead>
<tr>
<th>Title</th>
<th>Lecturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory bowel disease: Are we different from the West</td>
<td>Ng Han Seong</td>
</tr>
<tr>
<td>The rocky road from Dolly to human embryonic stem cells: Has it been a worthwhile and justifiable scientific pursuit?</td>
<td>Alan Colman</td>
</tr>
<tr>
<td>Systemic sclerosis: State of the Art</td>
<td>Carol M Black</td>
</tr>
<tr>
<td>Liver transplantation--lessons learnt and future horizons</td>
<td>Roger Williams</td>
</tr>
<tr>
<td>The changing face of cardiology practice, training and research in Singapore</td>
<td>Chia Boon Lock</td>
</tr>
<tr>
<td>Chronic disease management – Lessons learnt from the treatment of diabetic nephropathy</td>
<td>Napier Thomson</td>
</tr>
<tr>
<td>Advances in the management of viral hepatitis in the last decade</td>
<td>Liaw Yun-Fan</td>
</tr>
<tr>
<td>Post antibiotic era: Bad bugs, no drugs</td>
<td>Victor Yu</td>
</tr>
<tr>
<td>Obesity is a problem – what do we have to do to tackle it?</td>
<td>Ian Caterson</td>
</tr>
<tr>
<td>Improving survival outcomes for gastric cancer</td>
<td>Yeoh Khay Guan</td>
</tr>
</tbody>
</table>

Adapted from Lim SH, Ng KY, Chew CH, Annals Academy of Medicine 2007; 36 (7): 525-40
The 22nd Seah Cheng Siang Memorial Lecture

Renal Transplantation in Singapore:
A Historical Perspective, Controversies, Challenges and Future Directions

A Vathsala, National University Health System
### Timeline of Transplantation in Singapore

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1970</td>
<td>First Cadaveric Renal Transplant</td>
<td>July 8 1970</td>
</tr>
<tr>
<td></td>
<td>Medical Therapy, Education and Research Act</td>
<td>May 1973</td>
</tr>
<tr>
<td></td>
<td>First Living - Related Renal Transplant</td>
<td>July 31 1976</td>
</tr>
<tr>
<td>1980</td>
<td>First Bone Marrow Transplant</td>
<td>July 25 1985</td>
</tr>
<tr>
<td></td>
<td>Human Organ Transplant Act</td>
<td>June 1987</td>
</tr>
<tr>
<td></td>
<td>First Pediatric Renal Transplant</td>
<td>February 18 1989</td>
</tr>
<tr>
<td></td>
<td>First Bone Transplant</td>
<td>June 14 1989</td>
</tr>
<tr>
<td></td>
<td>First Cardiac Transplant</td>
<td>July 6 1990</td>
</tr>
<tr>
<td></td>
<td>First Liver Transplant</td>
<td>September 29 1990</td>
</tr>
<tr>
<td></td>
<td>First Spousal Renal Transplant</td>
<td>March 4 1991</td>
</tr>
<tr>
<td></td>
<td>First Skin Transplant</td>
<td>March 1998</td>
</tr>
<tr>
<td></td>
<td>Interpretation Act</td>
<td>June 1998</td>
</tr>
<tr>
<td>2000</td>
<td>First Lung Transplant</td>
<td>November 19 2000</td>
</tr>
<tr>
<td></td>
<td>Human Organ Transplant Act, Amendment</td>
<td>January 5 2004</td>
</tr>
<tr>
<td></td>
<td>Human Organ Transplant Act, Amendment</td>
<td>January 1 2008 (Muslims)</td>
</tr>
<tr>
<td></td>
<td>Human Organ Transplant Act, Amendment</td>
<td>November 2009 (Age &gt;60)</td>
</tr>
</tbody>
</table>
July 8 1970:

The first cadaveric kidney transplant in Singapore
1948: University Department of Medicine formed under the leadership of Prof Ernest Monteiro with the able assistance of Dr Khoo Oon Teik with subspecialties of Renal Medicine and Cardiology.

1961: The first use of haemodialysis in Singapore was on a patient with acute renal failure, an RAF serviceman who had been involved in a motor accident while preparing for the Grand Prix.
1968: Chronic hemodialysis for end stage renal failure was initiated. Led by Dr Lim Cheng Hong and the support of prominent citizens such as Tan Sri Rumme Shaw, an attic above Medical Unit II at SGH was converted into a chronic hemodialysis unit in 1970.

1968: However, the high costs of dialysis prompted consideration for a renal transplant programme
Deceased Donor Kidney Transplantation in Singapore, 1987

4.7 RTX/yr pre HOTA
Legislation Covering Deceased Donor Donation in Singapore

Expressed consent

The Medical Therapy, Education and Research Act, 1972

“Any person of sound mind and eighteen years of age or above may give all or any part of his body for education,… transplantation… The gift takes effect upon death.”
The Human Organ Transplant Act, 1987

Presumed consent

“... makes provision for the removal of kidneys from the bodies of persons who are citizens or permanent residents who have died from accidents, for transplantation purposes only. Muslims and persons over 60 years old are exempted from the provisions of the Act.”
Legislation Covering Deceased Donor Transplantation in Singapore

Presumed consent

**The Human Organ Transplant Act, Amendment 2004**
- Extension to non-accidental causes of death
- Extension to liver, heart and cornea donation

**The Human Organ Transplant Act, Amendment 2008**
- Extension to Muslims

**The Human Organ Transplant Act, Amendment 2009**
- Removal of 60-year upper age limit

Organ Specific Objection Cards
- Kidney
- Heart
- Liver
- Cornea

HOTA Objector’s Register
Deceased Donor Renal Transplantation in Singapore, 1976-2011

4.7/yr pre HOTA

41.6/yr post HOTA, 11 pmp
Live-Donor Renal Transplantation in Singapore, 1976-2011

31 Singaporeans/PR transplanted in 2011 = 8.2 pmp
Outcomes of Renal Transplantation in Singapore (1999-2009)

<table>
<thead>
<tr>
<th>SRTR USA, 2004</th>
<th>1 Yr (%)</th>
<th>5 Yr (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Living-donor Graft</td>
<td>95.4</td>
<td>82.9</td>
</tr>
<tr>
<td>Deceased-donor Graft</td>
<td>90.7</td>
<td>72.1</td>
</tr>
</tbody>
</table>

% Graft Survival

<table>
<thead>
<tr>
<th>Years Post Transplant</th>
<th>0%</th>
<th>25%</th>
<th>50%</th>
<th>75%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Living-donor Graft</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deceased-donor Graft</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

% Patient Survival

<table>
<thead>
<tr>
<th>1 Yr (%)</th>
<th>5 Yr (%)</th>
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</thead>
<tbody>
<tr>
<td>Living-donor Graft</td>
<td>97.6</td>
</tr>
<tr>
<td>Deceased-donor Graft</td>
<td>91.1</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>1 Yr (%)</th>
<th>5 Yr (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Living-donor Patient</td>
<td>98.8</td>
</tr>
<tr>
<td>Deceased-donor Patient</td>
<td>96.7</td>
</tr>
</tbody>
</table>

SRTR USA, 2004

SRTR 2010, Singapore Renal Registry 2009
Factors Contributing to Success of Renal Transplantation

- More potent immunosuppression
- Better stratification of immunological risk
- Better prophylaxis against infections
Outcomes of Renal Allografts

Adapted from Stewart F, *Organ Transplantation*, 1999; Vincenti et al 2011
Antigen Presentation: Direct Allorecognition

Recipient Lymphocyte from circulation

CD4+ T Cell

Allograft

Donor Antigen Presenting Cell

Donor Macrophage
Antigen Presentation: Indirect Allorecognition

Recipient Lymphocyte from circulation

Recipient Regional Lymph Node

Recipient Antigen Presenting Cell

CD4+ T Cell

TCR

Ag
Antigen Recognition

Antigen Signal Transduction / Cytokine Synthesis

Cytokine Signal Transduction
Clonal Expansion

- T LYMPHOCYTE
- DNA
- NUCLEUS
- CD3
- CD4/8
- TCR
- p70s6
- IL-2R

Clonal Expansion Process:
1. T LYMPHOCYTE with NUCLEUS containing DNA and TCR.
2. Activation by IL-2R.
The Efferent Response

EFFERENT

T Cell Activation and Clonal Expansion

Alloantibody production

Activated B cell

Cytotoxic T cell mediated graft death

Perforin / Granzyme B

Activated macrophage

Delayed type hypersensitivity

Denton MD, Lancet 1999
Acute Cellular Rejection

Acute Tubulo-Interstitial Rejection

Acute Vascular Rejection
1. ANTIGEN RECOGNITION

2. ANTIGEN SIGNAL TRANSDUCTION

3. CYTOKINE SIGNAL TRANSDUCTION

4. CLONAL EXPANSION
Factors Contributing to Success of Renal Transplantation

- More potent immunosuppression
- Better stratification of immunological risk
- Better prophylaxis against infections
Evolution of Anti-HLA Antibody Detection

Cytotoxicity

- Anti-HLA Antibody

- Membrane Attack Complex

- Dye

Enhanced Cytotoxicity

- Anti-Human Globulin

- Membrane Attack Complex

Flow Cytometry

- Fluorescent Anti-Human Globulin

- CD19 or CD3 (B cell or T cell)

- Flow Cytometer

*Bray et al. Immunol Res 2004; 29: 41*
Luminex Assay: Detects Anti HLA Antibodies

Alloantibody

PE anti-IgG

Purified HLA protein

Dual-colored bead
Immunosuppressive Protocol post Renal Transplantation

- **POD 1**: Mycophenolate
- **POD 2**: Mycophenolate, PREDNISOLONE 30 mg/day
- **POD 3**: Mycophenolate, PREDNISOLONE 30 mg/day, p.o. CYCLOSPORINE / TACROLIMUS
- **POD 4**: Mycophenolate, PREDNISOLONE 30 mg/day, p.o. CYCLOSPORINE / TACROLIMUS

- CYCLOSPORINE / TACROLIMUS LEVELS
- IL2rAb
- ALS
- Transplant
Acute Rejection in 1st year Post Transplant

Scientific Registry of Renal Transplants (SRTR), USA 2010
Outcomes of Kidney Transplantation at NUHS: 1987-Present

T1/2 = 20.6 years
6 mth AR (2008-2012) = 5%

Percent Survival

T1/2 = 14.6 years
6 mth AR (2008-2012) = 8.3%

68.9%
82.3%
86.4%
94.2%

Acute Rejection, SRTR 2005–2009

SRTR 2010
Factors Contributing to Success of Renal Transplantation

- More potent immunosuppression
- Better stratification of immunological risk
- Better prophylaxis against infections
- Cytomegalovirus
Efficacy of Valganciclovir in Preventing CMV Disease

Factors Contributing to Success of Renal Transplantation

- More potent immunosuppression
- Better stratification of immunological risk
- Better prophylaxis against infections
- Lifelong funding for immunosuppression and anti-infectives for Singaporeans/PRs
Financial Support for Renal Transplantation in Singapore

- **3 M’s**
  - Medisave - Hospital expenses, Monthly deductions for immunosuppressive drugs ($300/month)
  - Medishield - Monthly deductions for immunosuppressive drugs ($200/month, lifetime limit)
  - Medifund - for the needy
- **Government subsidy for immunosuppressive drugs**
  - 50% subsidy for Cyclosporine, FK506, Mycophenolate
  - Life of the kidney
  - Subsidy for Valganciclovir for CMV prophylaxis since 2007
Strategies to Increase Access to Renal Transplantation in Singapore - 1

Living Donor:

- Pre-emptive transplant
- Laparoscopic donor nephrectomy

Flank Approach  Laparoscopic Approach
Strategies to Increase Access to Renal Transplantation in Singapore - 2

**Living Donor:**
- Reimbursement of costs of donor evaluation, surgery and follow-up (removes disincentives)
- Cross match positive transplant
- ABO incompatible transplant

<table>
<thead>
<tr>
<th>Component</th>
<th>Average Cost</th>
<th>Payment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-surgery evaluation</td>
<td>$2500</td>
<td>- Paid directly to hospital</td>
</tr>
<tr>
<td>Donor Surgery &amp; Hospitalization</td>
<td>$2000-8000</td>
<td>- Paid directly to hospital</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- From KDF/PDC Donor Fund (for needy donor)</td>
</tr>
<tr>
<td>Loss of income</td>
<td>$2500-5000</td>
<td>- From NKF (for needy donor)</td>
</tr>
<tr>
<td></td>
<td>(Sg median monthly income of 2.5k X 4-8 weeks)</td>
<td></td>
</tr>
<tr>
<td>Medishield / Insurance</td>
<td>$200-300 per annum</td>
<td>- From NKF (for needy donor)</td>
</tr>
<tr>
<td>Post donation follow-up</td>
<td>$100-300 per consult</td>
<td>- From NKF (for needy donor)</td>
</tr>
</tbody>
</table>
Immunosuppressive Protocol for ABO Incompatible Living Donor Transplants

Mycophenolate

- iv HYDROCORTISONE 1 g/day
- PREDNISOLONE 30 mg/day

Tacrolimus

- iv Immunoglobulin 1 g/kg/dose
- iv Thymoglobulin 1.5 mg/kg/day

Rituximab

Immunoadsorption

D-8  D-6  D-4  D-2  POD 2  POD 6  POD 10  Transplant
Strategies to Increase Access to Renal Transplantation in Singapore

Deceased Donor:
- Use of older donors
- Explant biopsy of marginal kidney
- Dual kidney transplant for suboptimal biopsy scores

Remuzzi G, NEJM 2006; 354:343-352
Are there unmet goals in transplantation?
Challenge # 1: Chronic Allograft Failure

Graft Survival

Years Post Transplant

Cecka M, Clinical Transplants 2008: 2
Graft Survival for Deceased Donor (Non-ECD) Kidney Transplants

SRTR 2010
Patient Survival for Living Donor Kidney Transplants

SRTR 2010
Immunosuppression Use Post Transplant

SRTR 2010
Acute Rejection in 1\textsuperscript{st} year Post Transplant

Scientific Registry of Renal Transplants (SRTR), USA 2010
Non-Immunologic Mechanisms

- Immune responsiveness
- Tissue incompatibilities
- Pre-sensitisation
- Immunosuppression

Chronic Rejection

Acute Rejection

Immunologic Mechanisms

Non-Immunologic Mechanisms

Pre-existing Donor Injury: Hypertension, Reduced Renal Mass

Delayed Graft Function
- Cold Ischemia Time
- Ischaemia reperfusion

Calcineurin Inhibitor NTX
Hypertension
Recurrent Disease
Infections
Hyperlipidemia

Adapted from Vathsala A. Annals Academy of Medicine (Singapore) 2005
Impact of Donor Specific Anti HLA Antibodies on Graft Survival

Patients were tested once, post Tx in 2002, and followed for 4 years

Lachmann, Terasaki et al. Clinical Transplants 2006:189
Calcineurin Inhibitor Induced Nephrotoxicity

Co-Stimulatory Blockade: Belatacept
Challenge #2: Immunosuppressive Complications - Mortality due to Infections and Malignancy

Causes of Death in Renal Transplant Patients

- Acute Myocardial Infarct: 16%
- Other Cardiac: 8%
- Infections: 8%
- Malignancy: 12%
- Uremia: 12%
- Died at Home: 36%
- Bleeding from the Gastro-intestinal Tract: 8%
- Other: 8%

Singapore Renal Registry, 2008
### Incidence of Malignancies

#### TABLE 3. Treatment-emergent adverse events in the safety population

<table>
<thead>
<tr>
<th></th>
<th>Sirolimus conversion (n=551)</th>
<th>Calcineurin inhibitor continuation (n=273)</th>
<th>P&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>70 (12.7)</td>
<td>14 (5.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Herpes simplex</td>
<td>48 (8.7)</td>
<td>12 (4.4)</td>
<td>0.032</td>
</tr>
<tr>
<td>Fever</td>
<td>24 (4.4)</td>
<td>1 (0.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aphthous stomatitis</td>
<td>23 (4.2)</td>
<td>1 (0.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>21 (3.8)</td>
<td>1 (0.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>Acne</td>
<td>10 (1.8)</td>
<td>0</td>
<td>0.036</td>
</tr>
<tr>
<td>Malignancies, n (%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Total</td>
<td>21 (3.8)</td>
<td>30 (11.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Skin carcinoma</td>
<td>12 (2.2)</td>
<td>21 (7.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Challenge #3: Non Immunosuppressive Toxicities of Immunosuppressant Drugs

**Cyclosporine**
- Nephrotoxicity
- Neurotoxicity
- Hypertension
- Hyperlipidemia
- Ectodermal

**Azathioprine**
- Cytopenias
- Liver dysfunction
- Alopecia
- Pancreatitis

**Steroids**
- Osteoporosis
- Weight gain
- Hyperglycemia
- Body changes
- Cataract
- Easy bruising

**Tacrolimus**
- Nephrotoxicity
- Neurotoxicity
- Hypertension
- Hyperglycemia
- GI toxicity

**Mycophenolate**
- Cytopenias
- GI toxicity

**mTOR inhibitors**
- Hyperlipidemia
- Cytopenias
- GI toxicity
Campasia: A Pilot Randomised Controlled Trial of the Effectiveness and Safety of Campath-1H (MABCAMPATH®) as an Induction Agent for Prevention of Graft Rejection and Preservation of Renal Function in Patients Receiving Kidney Transplants

Vathsala A et al. Transplantation 2005, 90:765
Challenge # 4: Large Gap between Supply and Demand for Organs

USRDS 2011, SRR 2009
Number of Patients Waiting for a Deceased Donor Renal Transplant in Singapore
## Outcome of Potential Donors Referred in 2007

<table>
<thead>
<tr>
<th></th>
<th>HOTA Donors</th>
<th>MTERA Donors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of potential</td>
<td>60</td>
<td>26</td>
</tr>
<tr>
<td>donors referred</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-actualised donors</td>
<td>36</td>
<td>24</td>
</tr>
<tr>
<td>Actualised donors</td>
<td>24</td>
<td>2</td>
</tr>
</tbody>
</table>

### Reasons for Non-actualisation of Referred Donors

<table>
<thead>
<tr>
<th>Reason</th>
<th>HOTA Donors</th>
<th>MTERA Donors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain death criteria not met</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Life support withdrawn or died prior to brain death</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Medically unsuitable</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>No consent from coroner</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>No next of kin available</td>
<td>Not applicable</td>
<td>3</td>
</tr>
<tr>
<td>No consent from next of kin</td>
<td>Not applicable</td>
<td>6</td>
</tr>
</tbody>
</table>

Figure II-6. OPO Conversion Rates in 2008

(0% to 56.6%)
Median
8.8% in Singapore

Percent of Eligible Deaths Converted to Donors

Goal: 75%
Range: 48% to 84%

OPO

Patient with Irreversible Brain Injury

Donor

Brain death

Hospital - ICU

Organ

Organ Transplant

Recipients with Organ Failure
Challenge # 5: Ethical Practice of Medicine

Transplantation is superior to Dialysis with respect to survival &

There is a large gap between supply and demand

USRDS 2007

Singapore Renal Registry
Transplant Commercialism is now a regrettable and unfortunate consequence of the success of transplantation.
“In the late 1700s, before the invention of the porcelain denture, wealthy Europeans flocked to surgeons who would replace missing or damaged teeth with fresh ones bought from another person. The sellers were typically the poorest of the poor…. The 18th century caricaturist Thomas Rowlandson expressed his disdain in his famous drawing, “Transplanting of Teeth,” which depicts a soot-covered chimney sweep sitting amid a gaggle of bewigged surgeons and patients. One surgeon is removing the poor sweep’s tooth while, nearby, a ruddy-cheeked woman impatiently awaits its delivery into her vacant tooth socket. “

Focus online, News from Harvard Medical, Dental and Public Health Schools, March 7 2008
In United Kingdom

Who buys organs?

In Singapore
Who sells organs?

From Scott Carney

Rami sold her kidney to a broker named Dhanalakshmi who used to have a shop outside Devaki Hospital in Chennai.

From David Rothman New Yorker

Filipino men showing their scars from kidney operations, Manila, August 1999
Location Where Transplant Was Performed

- Restructured
- Private
- Overseas

Year of Transplant:
- 1999
- 2000
- 2001
- 2002
- 2003
- 2004
- 2005
- 2006
- 2007
- 2008
- 2009

SRR, 2009
The Real Price of Transplant Tourism

- Infections (Hepatitis, AIDS, Other)
- Other complications
- Imbalance of access to healthcare
  - Rich vs. poor
  - Men vs. women
  - Race
- Fewer altruistic donations
- Cost to professionals and society
- Loss of moral compass
Live Donors

Deceased Donors
You didn't tear up your tuition notes. Someone else also learnt from them.

You didn't discard your old clothes. Your siblings played in them.

You didn't bury your grandmother's ornaments. Your daughter wore them on her wedding day.

You donated your organs...

Somebody lived

Pledge your organs with

Society for Organ Retrieval & Transplantation

Call: 93886 32630
Email: info@sortcochin.org
www.sortcochin.org

What will you be remembered for?

Don't take your organs to heaven. Heaven knows we need them here.
The Creation of Neo Organs

- Injection of growth factor(s) into a wound or organ may induce regeneration of the organ by pluripotential stem cells.

- Donor (or self cells) are incorporated into three-dimensional scaffolds of biodegradable polymers, such as those used to make dissolvable sutures. The entire structure of cells and scaffolding is transplanted, where the cells could replicate, reorganise and form new tissue.
Cloning

- Donor ewe
- Egg provider
- Isolated mammary cell
- Isolated egg
- FUSION
- Surrogate mother
- Clones
The Future of Cloning

- Completely differentiated cells may be re-programmed to return to multi-potential embryonic cells

Prospects for Organ Transplantation:

- Cloning transgenic animals after appropriate genetic manipulations
- Cloning stem cells or incomplete or body parts
- Cloning of embryos and complete organisms is likely to remain banned

Dolly and Bonnie
Xenotransplantation

“A cat will look down to a man.
A dog will look up to a man.
But a pig will look you straight in the eye and see his equal.”

Sir Winston Churchill
Conclusions

- Kidney transplantation is the best treatment for end stage kidney failure. However, there are many challenges to achieving this best therapy for all those in need:

- Achieving best outcomes so as to minimize graft loss and patient death is a challenge.
- While T cell mediated rejection seems to have been overcome, there are currently no effective therapies for chronic / antibody mediated rejection.
- Calcineurin inhibitors, the mainstay of immunosuppression in transplant, are invariably associated with renal damage.
- Immunosuppressant mediated immunosuppressive and non-immunosuppressive complications contribute to morbidity and mortality.
- New immunosuppressants that minimize toxicities while achieving specific immunosuppression are still needed.
Conclusions

- The search for operational tolerance remains a holy grail in transplantation.
- Stem cell therapies, tissue engineering, cloning and xenotransplantation may hold the promise of an inexhaustible supply of replaceable body parts for the treatment of organ failure.
- Demand for organ parts to replace failing ones far exceeds the supply. Increasing the supply of donor organs is the biggest challenge and doing this ethically is a moral imperative.
- As we work towards the betterment of the lives of our patients, the most critical challenges we face are those to our own humanity and professionalism.
Another major illness (that ails the medical profession today) is the commercialisation of medical practice...

INTRODUCTION
Since the late 40s, Medicine in Singapore has undergone much change both in practice, as well as, in the patterns of diseases. As a house physician in 1951, the common conditions dealt with were infections, like malaria, pyogenic diseases, amoebiasis and pneumonia. One can still remember also the adolescents with acute nephritis and rheumatic fever. The degenerative diseases were not common.

THE PROFESSION’S MAJOR ILLNESSES TODAY
At this juncture, it will not be out of place to examine what is ailing the profession today. This having been done, Medicine tomorrow will be in a healthier state.

The profession has been divided into a private and public sector. This divisive effect has created the “holier than thou” attitude held by one or the other, heightened by righteous indignation. There is no place for this in Medicine. Each doctor in each area has his own pertinent role and therefore there is no necessity for comparison.

Another major illness is the “commercialisation” of medical practice, with economic objectives set as important goals at the expense of the doctor-patient relationship. For example, massive