The Australian Corneal Graft Registry: 35 Years in Sight

Presented by Miriam Keane, PhD, Executive Director, ACGR
As part of the College of Medicine and Public Health Medicine and Bioscience Seminar Series
28th August 2019
The Cornea

- Clear window at front of eye
- Function can be affected by:
  - Disease
  - Trauma
  - Infection
- These may cause:
  - Poor vision
  - Pain/discomfort
  - Structural issues
Corneal Transplantation

- AKA corneal graft
- AKA keratoplasty
- Replaces diseased or damaged cornea with tissue from a donor
- Performed for over 100 years
- Evolution of multiple techniques
Corneal Transplantation

- Multiple layers
- Different layers affected by different diseases
- Full-thickness replacement (Penetrating Keratoplasty)
- Partial replacement (Lamellar Keratoplasty):
  - Epithelium
  - Endothelium
Corneal Transplantation

- B) Penetrating Keratoplasty (PK)
- C) Lamellar keratoplasty (LK)
- D) Deep Anterior Lamellar Keratoplasty (DALK)
- E) Descemet’s Stripping Endothelial Keratoplasty (DSEK) + variations (DSAEK, UT-DSEK)
- F) Descemet’s Membrane Endothelial Keratoplasty (DMEK)

The Australian Corneal Graft Registry

- Corneal transplant outcomes register
- Research tool
- Established in May 1985 (2020 will be our 35th birthday)
  - Emeritus Professors Keryn Williams and Doug Coster
- Used to inform data collection internationally
The Australian Corneal Graft Registry

The goals of the ACGR:

- To measure graft survival and visual outcomes after corneal transplantation
- To investigate risk factors for graft failure
- To examine changing patterns of practice
- To return amalgamated, de-identified results to all contributing surgeons, eye banks and other interested parties
Data Collection - Registration

► At time of corneal graft
  ► Eye Banks around Australia:
    ► Provide demographic data on donor
    ► Forward Registration form to surgeon
  ► Surgeon
    ► Obtains patient consent for inclusion
    ► Provide demographic data on recipient
    ► Outline eye health history of recipient
    ► Detail the surgery performed
Data Collection - Registration

- Surgeons all around Australia provide data
- Number of operating surgeons varies per year
  - Steady increase in last 10 years
  - Approximately 120 current operating surgeons
Data Collection - Follow-up

- Requested by ACGR
  - March and September
  - 1 to 3 yearly intervals between follow-ups
- Over 900 contributors to date
- Exact date patient last seen by practitioner
- Report on outcomes
  - Graft survival
  - Complications
  - Visual outcomes
  - Further surgery
Reasons for Corneal Transplantation

- Pain relief: 2%
- Improved vision: 13%
- Pain+Vision: 5%
- Pain and/or vision + structural: 5%
- Structural reasons: 11%
- Not specified: 65%
Reasons for Corneal Transplantation

- **PK**
  - Pain relief: 3%
  - Improved vision: 62%
  - Pain+Vision: 16%
  - Pain and/or vision + structural: 4%
  - Structural reasons: 5%
  - Not specified: 5%

- **DALK**
  - Pain relief: <1%
  - Improved vision: 5%
  - Pain+Vision: 2%
  - Pain and/or vision + structural: 5%
  - Structural reasons: <1%
  - Not specified: <1%

- **DS(A)EK**
  - Pain relief: 17%
  - Improved vision: 75%
  - Pain+Vision: 1%
  - Pain and/or vision + structural: 1%
  - Structural reasons: 5%
  - Not specified: <1%

- **DMEK**
  - Pain relief: 86%
  - Improved vision: 8%
  - Pain+Vision: <1%
  - Pain and/or vision + structural: <1%
  - Structural reasons: <1%
  - Not specified: <1%
Data Analyses

- Survival
  - Kaplan Meier Survival Curves
  - Cox Proportional Hazards Regression
- Rejection
  - Presence of any/repeat episodes
  - Time to first episode
- Best Corrected Visual Acuity
  - Level of BCVA
  - Time to 6/12 attainment
  - Improvement
- Improvement in pain
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<tr>
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<tr>
<td>PK</td>
<td>25801</td>
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<tr>
<td>TK</td>
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<tr>
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<tr>
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The ACGR Database 1985 to 2018

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<tr>
<td>DS(A)EK</td>
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<td>70%</td>
</tr>
<tr>
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The ACGR Database 1985 to 2018

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<th>Primary non-function</th>
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<td>82%</td>
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<td>&lt;1%</td>
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<td>78%</td>
<td>22%</td>
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<tr>
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<td>51%</td>
<td>19%</td>
<td>11%</td>
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<tr>
<td>Total</td>
<td>37099</td>
<td>77%</td>
<td>22%</td>
<td>2%</td>
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Primary non-function: graft didn’t clear and begin healing as expected.
Graft Survival - Graft Type

- Kaplan Meier survival curve
  - Likelihood of survival (0 to 1)
  - From time since event
  - 1 = every case surviving
  - 0 = every case followed for that length of time has failed
  - A curve reaching 0 doesn’t mean that all cases have failed, just those with the longest follow-up

- Great variation in numbers per group
- Different lengths of follow-up

<table>
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<tr>
<th></th>
<th>1 Year</th>
<th>5 Years</th>
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<tr>
<td>PK</td>
<td>17649</td>
<td>6754</td>
<td>2707</td>
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<tr>
<td>LK</td>
<td>670</td>
<td>209</td>
<td>57</td>
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<tr>
<td>DALK</td>
<td>898</td>
<td>150</td>
<td>7</td>
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<tr>
<td>DS(A)EK</td>
<td>2970</td>
<td>584</td>
<td>10</td>
</tr>
<tr>
<td>DMEK</td>
<td>560</td>
<td>24</td>
<td>NA</td>
</tr>
</tbody>
</table>
Factors Affecting Graft Survival - Evolving Techniques

- Surgeon learning curve
  - Time and experience that a surgeon requires to achieve an optimal level of competence with a technique
    - Reduction in frequency of adverse events
    - Decrease in time taken to complete procedure

- Later grafts
  - Significantly better survival
  - Significantly lower PNFG
  - For high-volume, experienced surgeons
    - Better outcome vs. low volume
    - Not significant between 1-56 & 57+
Factors Affecting Graft Survival - Follow-up

- Dependant on graft era - lag time
- Most pronounced for most recent grafts
  - If eye regrafted, prior graft failed
  - First follow-up request at 1 year
  - Prior to this most followed grafts are failures
- Primary non-functioning grafts
  - Higher proportions in EK (<1% vs. 5% vs. 11%)
May affect differences seen in other variables

- Poorer outcomes in new techniques due to lag time?
- Certain groups for other variables more common in later eras due to changes in practices?
Factors Affecting Graft Survival - Indication for Graft

- **Keratoconus (25%)**
  - Treatment with PK or DALK

- **Fuchs’ Endothelial Corneal Dystrophy (16%)**
  - Treatment with PK or EK

- **Pseudophakic Bullous Keratopathy (15%)**
  - Treatment with PK or EK
## Factors Affecting Graft Survival - Indication

<table>
<thead>
<tr>
<th>Condition</th>
<th>1 Year</th>
<th>5 Years</th>
<th>10 Years</th>
<th>15 Years</th>
<th>20 Years</th>
<th>25 Years</th>
<th>30 Years</th>
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<tbody>
<tr>
<td>Keratoconus (n=9300)</td>
<td>6554</td>
<td>2729</td>
<td>1322</td>
<td>741</td>
<td>372</td>
<td>136</td>
<td>15</td>
</tr>
<tr>
<td>Pseudophakic Bullous Keratopathy (n=5531)</td>
<td>3234</td>
<td>766</td>
<td>162</td>
<td>35</td>
<td>6</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Fuchs’ Endothelial Dystrophy (n=6032)</td>
<td>3472</td>
<td>1228</td>
<td>336</td>
<td>80</td>
<td>15</td>
<td>5</td>
<td>1</td>
</tr>
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</table>

*p<0.001*
Graft Type by Graft Year by Indication

- Pseudophakic
- Bullous Keratopathy
- Fuchs' Endothelial Dystrophy
- Keratoconus
Factors Affecting Graft Survival

- Graft type
- Graft era
- Indication for graft
- Combination?
Fuchs’ Endothelial Dystrophy

- PK vs. DS(A)EK vs. DMEK - quite separate
- PK cohorts have similar survival
- DS(A)EK cohorts similar since 2009
- DMEK recent cohort better survival
Pseudophakic Bullous Keratopathy

- PK vs. DS(A)EK vs. DMEK - some overlap
- Most recent cohorts have poorest survival
- DS(A)EK 2009-2013 better than 2004-2008
Factors Affecting Graft survival - Disease Severity

- **Percentage of grafts for pain - Fuchs’**

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>PK</td>
<td>22%</td>
<td>19%</td>
<td>25%</td>
<td>32%</td>
</tr>
<tr>
<td>DS(A)EK</td>
<td>NA</td>
<td>20%</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>DMEK</td>
<td>NA</td>
<td>NA</td>
<td>10%</td>
<td>3%</td>
</tr>
<tr>
<td>Total</td>
<td>22%</td>
<td>19%</td>
<td>12%</td>
<td>8%</td>
</tr>
</tbody>
</table>

- **Median pre-graft vision - Fuchs’**

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<tr>
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<tbody>
<tr>
<td>PK</td>
<td>6/36</td>
<td>6/36</td>
<td>6/36</td>
<td>6/60</td>
</tr>
<tr>
<td>DS(A)EK</td>
<td>NA</td>
<td>6/36</td>
<td>6/24</td>
<td>6/18</td>
</tr>
<tr>
<td>DMEK</td>
<td>NA</td>
<td>NA</td>
<td>6/24</td>
<td>6/18</td>
</tr>
<tr>
<td>Total</td>
<td>6/36</td>
<td>6/36</td>
<td>6/24</td>
<td>6/18</td>
</tr>
</tbody>
</table>

- Highlights the difficulty of comparing like with like
Comparing Like with Like?

- Individual analyses split by graft type
- Outcomes for individual indications for graft
- Comparing pre and post visual outcomes
- Multivariate analyses
- What we aim to do in our major reports
  - Latest report in 2018
  - Analysed data collected to 31st July 2017
Results from The Australian Corneal Graft Registry 2018 Report
Results from The ACGR 2018 Report

- PK multivariate analysis results
  - Indication for graft
  - Donor age group
  - Donor/recipient sex match/mismatch
  - Interstate transportation of donor corneas
  - Pre-graft raised intraocular pressure
  - Pre-graft inflammation and/or steroid use
  - Pre-graft corneal neovascularisation
  - Graft size
  - Number of previous grafts in other eye
  - Lens status pre/post graft
  - Graft era
  - Volume of PK registered by surgeon and level of follow-up
  - Post-graft corneal neovascularisation
  - Post-graft herpetic infection
  - Post-graft microbial keratitis
  - Post-graft rise in intraocular pressure
  - Post-graft rejection episode/s
Results from The ACGR 2018 Report

- PK multivariate analysis results
  - Indication for graft
  - Donor age group
  - Donor/recipient sex match/mismatch
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- Lens status pre/post graft
- Graft era
- Volume of PK registered by surgeon and level of follow-up
- Post-graft corneal neovascularisation
- Post-graft herpetic infection
- Post-graft microbial keratitis
- Post-graft rise in intraocular pressure
- Post-graft rejection episode/s
PK - Interstate Transportation of Cornea

Multivariate confirmed

- Grafts performed with corneas transported interstate had significantly poorer survival (p<0.001)

Previously reported by us

The influence of Australian eye banking practices on corneal graft survival

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>20</th>
<th>24</th>
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<td>Different State</td>
<td>876</td>
<td>404</td>
<td>183</td>
<td>93</td>
<td>48</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td>Same State</td>
<td>14607</td>
<td>6574</td>
<td>2778</td>
<td>1329</td>
<td>649</td>
<td>305</td>
<td>91</td>
</tr>
</tbody>
</table>
Negative Results Also a Positive

- Older donors provide viable corneas
- Cause of donor death does not affect graft survival
- Time from donor death to enucleation of eye extended
  - Up to 24 hours

→ Wider donor pool
Results from The ACGR 2018 Report

- DS(A)EK multivariate analysis results
  - Indication for graft
  - Donor age group
  - Central endothelial cell count
  - Australian State where performed
  - Pre-graft raised intraocular pressure
  - Recipient sex
  - Graft size
  - Incision size

- Graft Year
- Lens status pre/post graft
- Volume of PK registered by surgeon and level of follow-up
- Post-graft corneal neovascularisation
- Post-graft rise in intraocular pressure
- Post-graft rejection episode/s
Results from The ACGR 2018 Report

- DS(A)EK multivariate analysis results
  - Indication for graft
  - Donor age group
  - Central endothelial cell count
  - Australian State where performed
  - Pre-graft raised intraocular pressure
  - Recipient sex
  - Graft size
  - Incision size
- Graft Year
- Lens status pre/post graft
- Volume of PK registered by surgeon and level of follow-up
- Post-graft corneal neovascularisation
- Post-graft rise in intraocular pressure
- Post-graft rejection episode/s
DS(A)EK - Graft and Incision Sizes

- Hazard ratio for smaller grafts 1.63
- Largest incision group has poorest survival
- Steady reduction in % in this group
  - 100% pre 2011, 20% since 2014
- May be uncontrollable factors involved

<table>
<thead>
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<th>Incision Size</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>8</th>
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<tr>
<td>Less than 8.25 mm</td>
<td>566</td>
<td>338</td>
<td>90</td>
<td>32</td>
<td>5</td>
<td></td>
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<tr>
<td>8.25 mm or more</td>
<td>1530</td>
<td>1052</td>
<td>350</td>
<td>100</td>
<td>11</td>
<td></td>
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</table>
Results from The ACGR 2018 Report

- DMEK multivariate analysis results
  - Donor age group
  - Cornea pre-cut by eye bank
  - Recipient age group
  - Graft year
  - Australian State where performed
Results from The ACGR 2018 Report

- DMEK multivariate analysis results
  - Donor age group
  - Cornea pre-cut by eye bank
  - Recipient age group
  - Graft year
  - Australian State where performed
Results from The ACGR 2018 Report

- <50 significantly poorer
- 60 - 69 and 70 - 79
- More recent analyses also found a difference for <50 vs. 50 - 59
- No significant differences between other groups
- Adds evidence to reports of surgeon experience
- Only 1% of DMEK donors in 2018 were under 50
  - Down from 15-17%

### Table: graft survival probabilities

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<th>Age Group</th>
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<th>3</th>
<th>4</th>
<th>5</th>
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<td>Under 50 years</td>
<td>23</td>
<td>11</td>
<td>6</td>
<td>1</td>
<td>1</td>
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<tr>
<td>50 to 59 years</td>
<td>51</td>
<td>16</td>
<td>4</td>
<td>1</td>
<td>NA</td>
</tr>
<tr>
<td>60 to 69 years</td>
<td>102</td>
<td>37</td>
<td>13</td>
<td>1</td>
<td>NA</td>
</tr>
<tr>
<td>70 to 79 years</td>
<td>81</td>
<td>41</td>
<td>7</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>80 years and older</td>
<td>19</td>
<td>9</td>
<td>2</td>
<td>1</td>
<td>NA</td>
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</tbody>
</table>

Probabilities are markedly higher for <50 when compared to 50-59, 60-69, and 70-79. Probability is lowest in 80 years and older.
The Future

- Current publications being written on
  - Infections
  - Corneal dystrophies
- Annual feedback with stakeholders
- Community engagement
- New techniques continue to be developed
- Continued increase in grafts?
  - Increase in data
  - Increase in analyses
  - Increase in impact
Acknowledgments

- DonateLife - The Australian Government Organ and Tissue Authority
- Contributing surgeons, eye banks and follow-up practitioners

- Our team
  - Miriam Keane - Executive Director
  - Nora Coffey - Project Officer
  - Vicky Jones - Administrative Officer
  - Keryn Williams - Scientific Director
  - Richard Mills - Medical Director

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2018 report: http://hdl.handle.net/2328/37917