The Charitable Way
LONDON, Dec. 20 (AP) Mrs. Nolan, right, of Australia, campaigning with friends in Downing Street here today just before the arrival of Australian Prime Minister Gough Whitlam. She is trying to get British and Australian Government aid to help cure her son, Anthony, who is suffering from a rare bone disease. Mrs. Nolan has also started an Anthony Nolan Appeal Fund to assist Westminster Hospital to treat all children suffering of blood and bone marrow diseases. (AP CABLEPHOTO)
CORD BLOOD APPROACH

• Today global network of public cord blood banks - 500,000 cord blood units.

• Nearly 30,000 transplants reported to WMDA to date

• 2009 cord blood became second most common source of transplant stem cells.

• Clinical trials using UCB Stem Cells
  – wide variety of conditions including stroke, spinal injuries, cerebral palsy and a wide variety of other degenerative conditions.
The Anthony Nolan Cord Blood Programme

Register → Cell Pharmacy

Cord Blood Bank

Cord Blood Pharm
Why Cord Blood?
SOME PATIENTS DO NOT HAVE SUITABLE ADULT DONORS

- Estimated time delay: 2 months
- Access failure: 28%
- UK self-sufficiency: 38%
- Efficiency: UK 70% vs. Overseas 35%
- Total allo-therapies: 38%

Diagram:

- Allo-mandatory 73 pts
  - Sibling? 5w
    - Yes: Sib. 13 (19w, 7-40)
    - No: Unrelated search 60 pts
      - 38%: UK register 23
      - 33%: Overseas 20
      - Tx? 11w
        - Yes: VUD Tx 16 (26w, 11-49)
        - No: VUD Tx 7 (29w, 12-56)
      - No: Tx? 14w
        - Yes: VUD Tx 23 pts (29w, 12-56)
        - No: NO Tx 37 pts (28w, 2-68)
      - 23w

King’s Survey, 2005
CORD BLOOD PROS AND CONS

• Advantages:
  – Donor safety/attrition
  – ‘Off-the-shelf’= time
  – Reduced match stringency= equitable access
  – Long-term Sustainability

• Disadvantages:
  – (Speed) Engraftment
  – DLI
How many Cord blood Units we need to store?
SIZE FOR UK

Probability to find at least 1 HLA-A,B low and DRB1 high match


All patients

Non north western European patients

<table>
<thead>
<tr>
<th>Probability to find at least 1 HLA-A,B low and DRB1 high match</th>
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<tbody>
<tr>
<td><strong>Against 150,000 Anthony Nolan Donors</strong></td>
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<tr>
<td>80% chance for 5/6 (50% non-predominant)</td>
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<tr>
<td>≈ 50,000</td>
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<tr>
<td>Raise to 80% chance for 5/6 to non-predominant</td>
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<tr>
<td>≈ 150,000</td>
</tr>
</tbody>
</table>

2,000

722

0 20 40 60 80 100
0 50,000 100,000 150,000

% Probability

Donor Sample

0 50,000 100,000 150,000

% Probability

Donor Sample
Impact of cell dose and HLA Match on survival. Data presented by Dr. Pablo Rubinstein at the 5th International Umbilical Cord Blood Symposium held in Los Angeles in May 2007.

DECISION FLOW CHART

- **Unit received**
- **>48 hours**
  - <500 x 10^6 cells: Discarded
- **32-38 hours**
  - >500 x 10^6 cells: Research
- **<32 hours**
  - >1200 x 10^6 cells: Clinical

- We currently have a lower threshold for populations currently under represented in our register.
  - Cell numbers are total nucleated cells.
DOSE

- Preference of bigger units make obsolete many units stored in the cord blood banks (internal competition)

- Prospective thresholds could raise until a level that makes new units highly competitive:
  - NC12x10^8 and CD34 4x10^6

- Unfortunately, this makes necessary large collection programmes that are highly inefficient (up to 80% of units are discarded)
COLLECTION
COLLECTION

- Raised platform
- Adapted shelf
- Hole for specially adapted bowl
- Paperwork holder
- Wheels for manoeuvrability
COLLECTION

- Place the placenta in adapted bowl
- Pull cord through and hang
COLLECTION

• Clean the cord with sterile solution and sterile swabs
• Reduces risk of cross contamination
COLLECTION

- Insert cannula
- Close to birth clamp to maximise collection
- PATIENCE!!!
COLLECTION

• DRAINED!!
COLLECTION

- Life saving cord blood
i.e. Transport issues
Directive 2004/23/EC and its technical requirements

HTA

FACT-NETCORD

Grade C

Recep  Proces  Cryopres

CD34/CFU
IDM/ MICROBIOLOGY
BLOOD TESTS

INTELLIGENT” LABELING

QMP
SOP

ID (confidentiality)
RELEVANT DATA (critical steps)
ELECTRONIC RECORDS

QC CLINICAL DATA

TRANSPORT

ANCB FACTORY

ship log
Transport

CLINICAL ANALYSIS

freezer

REGISTER
PROCESSING FACILITY

Ground floor:

- Manufacture
- Cryogenics
- Distribution
- Reception

CRF CBIS
Cryoservice/ MVE/Chart

FMS
Reference samples

3k
3k
6k
6k
6k
RECEPTION

The sample is received in the cord blood bank. The paperwork and sample are checked. Check none of the packs are leaking. Monitor the data logger.
INITIAL SAMPLE

An initial 1ml sample to be taken for total nucleated cells counts
PROCESSING

The cord blood bag is attached to SEPAX® kit using a sterile connection.

All the procedure is performed in a close system.
PROCESSING

Our process utilises the SEPAX® cell separation device which is a fully automated and turn-key system that allows safe and efficient processing of blood and its components for various applications in stem cell banking.

The kit is placed on the SEPAX® machine and an automated programme to perform a volume reduction is carried out.

The SEPAX® process takes approx. 35 minutes.
A pre-cooling of the stem cell bag is carried out whilst mixing using the CoolMix to bring the cells to 4 C before the addition of the cryo-protectant.

The DMSO-dextran (5ml) is added over 10 minutes using a syringe pump whilst on the CoolMix.
SEALING

Remove air and fill the whole tube so as 3 segments can be made and utilised for post thaw analysis.
PROCESSING

Weigh the bag, in order to calculate final volume.
FREEZING

Overwrap bag as quarantine.
FREEZING

Use the canister for the cryotank adding the corresponding labels.
FREEZING

Put the final sample in the cryotank for its long term storage
DIAGNOSTIC SAMPLES

Mother’s blood and a cord fragment is processed and stored for virology tests, blood group and HLA typing.
DIAGNOSTIC SAMPLES
BACTERIOLOGY

From cord plasma and red blood cells (waste product) inoculate volume to perform bacteriology tests.
QUALITY CONTROL ASSAYS

We evaluate the results so as to obtain, the NC/ml, TNC, TNC yield, CD34+/ml, total CD34+ and CD34+ yield, to constantly monitor and evaluate the performance of our procedures.

We regularly partake in national NEQAS and international proficiency testing schemes to ensure the quality of our assays.

Virology:

• Hep B, Hep C, HIV, HTLV I-II, Syphilis, CMV, Toxo

HLA typing & blood group

Haemoglobinopathies
WHY NATIONAL PROGRAMMES?

- Meeting National Regulations
- Pre-defined Quality
- Easy Logistics
- Better Feedback
- R&D using CB surplus
- Economic control (auto-sufficiency)
PRIVATE vs PUBLIC CORD BLOOD BANKS

Same concept but different targets:

- Public CBB: A new allogeneic network, focused in the product and in the recipient safety

- Private CBB: First speculative application of the Regenerative Medicine principle, focused in the donor
BUT, WHAT IS A CORD BLOOD BANK?
BIOETHICS AND CORD BLOOD

- AUTONOMY: Each individual has the right to freely choose their own course of action and to choose what happens to them.
- NON-MALEFICENCE: Do not harm!
- BENEFICENCE: Actions taken should do good

Women’s Will and Midwife-Obstetrician’s Responsibility
## COMMERCIAL BANK PITFALLS

*(Fox et al, 2007)*

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<table>
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<tbody>
<tr>
<td>1</td>
<td>Commercial CBB should not represent the service they sell “doing everything possible”</td>
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<tr>
<td>2</td>
<td>More than 95% allogeneic searches find a potential donor</td>
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<tr>
<td>3</td>
<td>Few cases of really autologous transplantation has been reported (mainly there are related)</td>
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<tr>
<td>4</td>
<td>If stored publicly, 90% of units are available after a 10-years period</td>
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<tr>
<td>5</td>
<td>Collection in a non-trained environment could increase the risk of neonatal anemia (early clamping)</td>
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<tr>
<td>6</td>
<td>Collectors should disclose any benefit received from the company</td>
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<tr>
<td>7</td>
<td>Commercial bank for Regenerative Medicine relies on expansion technology still unsuccessful</td>
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CONCLUSION: THE CORD BLOOD MOVEMENT

• Cord blood represents an actual (real) product (not virtual lists)
• Ethical (naturally discarded product)
• Cost-benefit (lower inventories, less maintenance, highest efficiency and self-sufficiency)
• Potential to expand access, improve outcomes and open new doors in therapy (new paradigm)
• Potential to develop a biotechnological and biopharmaceutical platforms (biotechnology/biopharmacy)
• Reconcile public and private interests (same answer to different questions)
THANK YOU
Prof Alejandro Madrigal
Dr Sergio Querol
Susana Garcia Gomez
Robert Davy
Dr Roger Horton
Daniel Gibson
Pam Sami
Chris Leonforte
Laura Fry
Kieran Herrity
Guy Parkes
Terie Duffy & dedicated collectors at Kings
Linda Moss & dedicated collectors at Leicester
All Anthony Nolan Cord Blood Programme donors