Cord Blood

Should we save the baby’s cord blood?

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Objectives

• To provide a framework for answering a family’s questions about cord blood storage.

• To provide resources for families who choose to donate to a public bank.

Case 1

• A 5 month old male infant of mixed ethnic background seen for consideration of allogeneic SCT for B-precursor ALL
• He initially presented for medical attention with URI symptoms and fever and was found to have organomegaly with a white blood cell count of 96,000 with preponderance of blasts on peripheral smear, hemoglobin of 8 and platelets 25,000.

Case 1

• He was treated initially with 5-drug induction chemotherapy following a protocol for infants and referred for SCT due to poor prognostic significance of his cytogenetic abnormality
• The best result from initial HLA typing of 2 siblings was 4/6 match. His parents were haploidentical.

Case 1

• Search of NMDP and international registries were similarly disappointing with the preliminary search revealing at best a 4/6 match. His likelihood for an appropriate match was low due to ethnic background (Father - Northern European and Mother-Vietnamese)
• Search of cord blood registries demonstrated a potential 4/6 match product with a “good” cell dose

Case 1

• He underwent unrelated-donor cord blood transplant in CR1
• He had prompt leukocyte engraftment on GCSF with ANC >200 on day +12 and >500 by day +15;
• Post-Transplant course was complicated by moderate GVH (grade II skin, grade I GI) successfully treated with a brief pulse of steroid
What is a Transplant?

• Frequently referred to as a bone marrow transplant
  – High dose chemotherapy and/or radiation followed by infusion of cells capable of repopulating the bone marrow and making blood cells.

  But….
  Transplants are changing

The source of bone marrow stem cells

• Family members – siblings or parents
• Unrelated donors
• The patient themselves – ie an autologous transplant

The source continued-

• Bone marrow (obtained in the operating room)
• Peripheral Blood Stem Cells (often mobilized with G-CSF)
• Cord Blood

  So
  For this reason, many now call the process a Stem Cell Transplant
  (this is not quite correct and so will likely evolve as well)

One more thing…

• Different preparatory therapies are used as well to eliminate the cancer, “make room” in the marrow and decrease immune function that could cause rejection of the new cells.

  • They now can be of two major types:
    – Myeloablative
    – Non-myeloablative

Haplo-identical – one chromosome matches

  Biological parents must be at least this
  6/6 includes match at A, B, DR
  8/8 includes match at A, B, C, and DR
  10/10 includes match at A, B, C, DR, and DQ

  Mismatches cannot be all in the same class
  or
  How would the immune system talk?
To Summarize So Far

- Auto vs Allo
- If Allo
  - Related or Unrelated
  - Ablative vs non-myeloablative
  - Bone marrow vs PBSC vs Cord Blood
    - And how mismatched will we tolerate

Cord Blood: A Primer

- Currently there are over 100,000 cord units stored – in private and public domain
  - Nearly 70,000 at the NMDP
  - The C. W. Bill Young Cell Transplantation Program established the National Cord Blood Inventory (NCBI). The goal of the NCBI is to collect and store 150,000 cord blood units with the NMDP as the Cord Blood Coordinating Center

Cord Blood
A primer continued.

- Well over 6000 cord transplants have occurred
- First used as a transplant source for a patient with Fanconi’s anemia in 1988 (related)
- First used for an unrelated transplant in 1993

Some Advantages

- Typically typed at time of collection
- Median time from identification to availability – 13.5 days
  - In contrast to 3-4 months for a bone marrow donor
- Re-scheduling the transplant is not problematic

Characteristics

- Greater proportion of highly proliferative cells
- Fewer cells per ideal body weight are needed
  - The cells have a greater expansion potential so a log/kg fewer cells are adequate
  - New data suggests that the more different a cord is the higher the number of cells needed in the cord
Hematopoetic Stem-cell Source

• Bone Marrow (6/6 match)
  – (now recommendation is 8/8)
  Advantage
  Large cell dose
  Faster engraftment
  Donor recall
  Disadvantage
  Can cause severe GVHD
  Lack of matched donors
  worsened with more
detailed matching
  Delays in finding donor and
availability

• UCB (4-6/6 match)
  Advantage
  readily available decreased GVHD
  can be more mismatched
  can schedule transplant easier
  no herpesvirus in the cord
  Disadvantage
  limited cell dose
can’t call donor back
  genetic disease


Disease Treated by Cord Blood

• Malignancies
  – Acute Lymphocytic Leukemia (ALL)
  – Acute Myelogenous Leukemia (AML)
  – CML
  – Myelodysplastic Syndrome (MDS)
  – Solid Tumors – Non-Hodgkins Lymphoma and a few
  case reports of others

• Immunodeficiencies
  – Severe combined immunodeficiencies (SCID)
  – Wiscott-Aldrich
  – X-linked lymphoproliferative Disease

Disease Treated by Cord Blood cont.

• Inborn Errors of Metabolism
  – Adrenoleukodystrophy
  – Osteopetrosis
  – Some Storage Diseases
  – Abnormalities of neutrophils or leukocytes

• Blood Disorders
  – Aplastic anemia
  – Fanconi’s anemia
  – Thalassemia
  – Sickle Cell Disease
  – Kostmann’s syndrome
  – Evan’s syndrome

Issues

• Newer typing techniques termed High
  Resolution Typing have retrospectively
demoted the level of match of many
previous transplants
• HLA disparity appears to impact rate of
engraftment as well
• Severe acute GVHD increases with
mismatch across all groups

Table 1 | Comparison of umbilical-cord blood transplantation with bone-marrow transplantation

<table>
<thead>
<tr>
<th>Typical stem cell</th>
<th>Days to neutrophil recovery</th>
<th>Neutrophil recovery % by day 60</th>
<th>Platelet recovery % by day 180</th>
<th>% of patients developing grade 1-4 acute GVHD by day 100</th>
<th>% of patients surviving patients after 3 years</th>
</tr>
</thead>
</table>
| BM cells
  (n = 113)         | 10 days                     | 18%                             | 18%                            | 16%                                                   | 61%                             |
| UCB cells
  (n = 2283)       | 20 days                     | 89%                             | 88%                            | 14%                                                   | 0%                              |

Adapted from NEJM 342, 1846-1854 (2000)

So the question from parents is –
Should I store my child’s cord blood?

The answer is YES

The follow-up question should be
- for private or public use?
AMA

- The utility of umbilical cord blood stem cells is greater when the donation is to a public rather than a private bank. Therefore, physicians should encourage women who wish to donate cord blood to donate to a public bank if one is available.
- Private banking should be considered in the unusual circumstance when there exists a family predisposition to a condition in which umbilical cord stem cells are therapeutically indicated.

ACOG

- Although ACOG takes no position for or against cord blood banking, it recommends that physicians disclose that there is no reliable estimate of a child’s likelihood of actually using his or her own saved cord blood later.
- Physicians should also disclose to their patients that it is unknown how long cord blood can successfully be stored.
- Financial interests or other potential conflicts of interests should be disclosed.

American Academy of Pediatrics

There is no strong evidence to recommend that cord blood be banked for an infant’s future use. The academy states that given the low odds that the blood will be used - somewhere between 1 in 1,000 and 1 in 200,000 - the cost of storing the blood is too high.

AAP Policy Statement January 2007

- Cord blood donation should be discouraged when cord blood stored in a bank is to be directed for personal or family use
  - Premalignant or genetic problems may already exist in the cord cells
- Directed cord blood banking should be encouraged when there is knowledge of a full sibling in the family with a disorder that may benefit from a transplant (although not raised to level of SOC)

What should we do as Pediatricains and as an organization according to these guidelines?

- Recruitment practices should be developed with an awareness of the vulnerability of the women and families.
- Accurate information of benefits and limitations of using the product should be provided.
- Banks should develop plan for any abnormal findings in the harvested blood

- Cord blood donation should be encouraged when cord blood is stored in a bank for the public good.
- Storing privately for “Biologic Insurance” should be discouraged
- Cord Blood collection and storage should comply with the FACT standards.
• Policies regarding medical information and problems with confidentiality should be developed
• Written permission should be obtained before onset of active labor
• IRB should review any research performed by banks
• Cord blood collection should not be performed with complicated deliveries – routine practice for delivery should be performed.

• Regulatory agencies should have active role.
• Professionals who recruit for for-profit placental cord banks should disclose financial or other conflicts of interests.
• Targeted efforts should be made to recruit underserved minorities.

Options:
Private and Public
Private in Public banks

An example of costs
Private Banking
• $1920 Pay in full Pricing for collection and processing
• $150 Private Medical Courier
• $125 yearly storage fees
• So first year cost is $2195
• You can prepay for 20-25 years with no increase in fees.
Sibling Cord Blood Program

- CHORI – Children’s Hospital Oakland Research Institute

Who is Eligible?
If you give birth in the United States:
- Your physician agrees that cord blood collection would be of value to you
- You currently have a child with a transplant-treatable condition
- The child you are expecting will be a full sibling (same parents) of the affected child

Who can refer patients to the Sibling Cord Blood Program?
The affected child’s hematologist or oncologist; or the mother’s obstetrician, or midwife

CHORI and ViaCord

- Initially an NIH funded program to demonstrate feasibility of donation
- More than 100 cords have been released
- Any expectant family with a child who has an established diagnosis of a disease that is currently treatable with cord blood may receive ViaCord’s premier cord blood banking and five years of storage services at no cost. Your child’s doctor will need to complete a medical referral form. If you would like more information please call toll-free 1-866 861-8435.

Cord Blood Registry (CBR) another private bank

- “Designated Transplant Program”
- Immediate and close relatives with a diagnosis (leukemia need to be in remission less than 4 years)
- Will waive $1875 processing fees and storage fees and charge only Medical courier fee of $150

LifeBankUSA

- Also has a program for families with affected sibs

There are many other smaller banks and families in these situations - All require that a referring physician explain the family medical situation.

Why do Private banks offer this service?
Donating to the Public

- Public cord blood donations can be made through the NMDP and associated hospitals or through Non-NMDP banks
  - There is no risk to the mother or the baby
  - Cord blood will not be collected if the OB does not feel it is safe for the mother or the child.
  - NMDP agrees with the position of the AAP

Requirements of Donation

The unit must be large enough
- This is usually between 3-5 ounces
The family and maternal health history must meet guidelines (similar to those needed to donate blood)
Tests of the cord blood and a sample of the mother’s blood must be free of infection and potential “other” problems

About 50% of the cords meet all the requirements for storage for public use – usual problem is one of number of cells in product.

When and where does one start the process?

- By the 34th week of pregnancy
  - Call the NMDP 1 (800) MARROW-2 (1-800-627-7692) or go to their web site
  - There are no NMDP participating hospitals in the Buffalo Area – so the NMDP will refer the expectant mother to Cryobanks International

Who Can Donate?

- Age: Donors must usually be 18 or older and in good health (some will allow >/16).
- AIDS: If you have, or are at risk for HIV/AIDS, you cannot become a cord blood donor.
- Cancer: If you have had cured local skin cancer (only simple basal cell or squamous cell) or cervical cancer, you still may be eligible. All other forms of cancer make you ineligible to donate cord blood.
- Diabetes: If you have medication-dependent diabetes, you may not be eligible to donate. Women with gestational diabetes will usually be eligible to donate. If you have diabetes, talk to your cord blood bank about your eligibility.
- Hepatitis: If you have positive Hepatitis B surface antigen or Hepatitis C, you are not eligible to donate. If you have any other history of hepatitis, a cord blood bank will evaluate your eligibility. You may still be eligible if you have received the hepatitis vaccine.
- Malaria: If you had malaria more than three years ago, you are still eligible. You are also eligible if you have finished a full course of antimalarial drugs more than six months ago.
- Organ or tissue transplant: If you have received a heart, lung, kidney, bone marrow or other organ or tissue transplant, you are not eligible to be a cord blood donor.
- Sexually transmitted diseases: Any history of sexually transmitted diseases within the last 12 months must be evaluated by the cord blood bank.
- Tattoos and skin or body piercing: If you have received any tattoos within the last twelve months, you are not eligible to be a cord blood donor. Circumstances and timing of ear, skin and body piercings are evaluated by the cord blood bank.

Cryobanks International

www.cryo-intl.com/enroll/donating
or 1-800-869-8608

- Has both a private and public bank
  - Will require the expectant mother to fill out consent form which includes history. Once it is reviewed a kit will be shipped to the family
Communities that are under represented in the NMDP

- Black and African American
- American Indian and Alaska Native
- Asian
- Native Hawaiian and other Pacific Islander
- Hispanic and Latino
- Multiple race

Case 2

- A four-year old diagnosed with T-cell leukemia (greater than 200,000/mcl peripheral blasts) with a large mediastinal mass
- Started on chemotherapy including steroids
- White count fell dramatically and he was discharged to home

But now for the social history….

Case 2 cont.

- Mom and Dad have 2 children together and mom is pregnant with the third
- Astute fellow talks to mom about banking
- Mom goes into labor on the night of diagnosis
- Fellow on call manages to have cord saved and sent to Oakland Bank

Clinical course cont.

- Child fails induction chemotherapy
- Given new agent with more targeted effect on T-lymphoblasts
- Typing of family shows no family matches including new infant who shares only half of the antigens
- Unrelated search poor as family background is African-American, Panamanian, and one grandparent from Korea.

Decision and Course

- Sibling’s cord used
- Child does develop Graft-vs-Host disease – controlled with meds
- Now off meds and doing well x 8 years
- Long term side effect – hearing loss

What should we do?

- Stay informed and encourage families to donate to the public bank
- Increase access of minorities to this information.
- Make information for public donation more readily available in OB offices.
Take Home

• Save the cord blood
  If a family member has a disease that their physician
  thinks might be cured with transplant – there are free
  resources for the family

IF NOT:
Then follow the AAP recommendations and store for
public use – it is a great and valuable resource and there
may be someone out there who needs this gift of life.