Donor selection: ensuring patient and donor safety

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Types of Risk

• Risk to Recipient
  – Typically transmitted or derived from donor product (e.g. infection, malignancy, auto-immune disease)
  – TC responsibility to balance risk/benefit

• Risk to Donor
  – Registry- unrelated - responsibility (but what about RD?)
  – Hard evidence generally does not exist
  – At best retrospective donor registry data, case reports and expert opinion
  – “If in doubt, say NO”
How do we reduce/prevent recipient and donor risk?

• Medical eligibility at multiple time points for UD
  – At recruitment (strict criteria but broad)
  – At verification typing (current)
  – At work-up (extensive)

• This may be compressed for RD
  – Important to address some broad criteria BEFORE HLA typing
How do we reduce/prevent recipient and donor risk?

• Extensive medical history
  – Travel history
  – Vaccines etc
  – Drugs/medication
  – High risk behaviour
• Full examination
• Lab tests
  – U&E, FBC, LFT, Blood group, Virology
• Additional tests
  – Pregnancy test
  – CXR, ECG
  – ?bone marrow/ultrasound
Who Do We Exclude? The Top 20 at recruitment...

- Overweight 38.54%
- Back - No description 9.15%
- Underweight 6.57%
- Depression 2.92%
- Arrhythmia/heart block 2.10%
- Disc Prolapse 2.03%
- Sciatica 2.00%
- Asthma 1.89%
- Back pain 1.86%
- Back – fracture 1.38%
- Whiplash 1.17%
- Psoriasis on UVA 1.14%
- PCOS 1.14%
- ME/Post-viral syndrome 1.10%
- Eczema 0.89%
- Latex allergy 25 0.86%
- Blood Transfusion 0.79%
- Psoriasis not on UVA 0.76%
- Coeliac Disease 0.69%
- Ulcerative Colitis/Crohns 0.69%
Reasons for donor medical deferral at recruitment and CT-stage

- Overweight
- Back
- Cardiac
- Autoimmune
- Diabetes
- Cancer
- Infection
- Surgery
- Tattoo
- Pregnancy
- Other
Medical reasons for failing the medical

• Late donor deferrals for medical reasons are uncommon
• In general, they are related to occult medical conditions that could not have been picked up at an earlier stage:
  – blood pressure
  – abnormal laboratory indices
  – ECG
  – chest x-ray
These are very safe procedures, but…

• No procedure is 100% safe
• No direct physical benefit to the donor/voluntary

• Exclusions may be:
  – Absolute/Qualified
    • Cancer vs asthma (depends on severity)
  – Time dependent
    • Hypertension – can donate if it is controlled
  – Route specific
    • BM vs PBSC (e.g. back pain or gout)
Bone marrow harvesting

- Done under GA; donor prone
- Marrow aspirated from both iliac crests
- Maximum 20mL/kg
- Passed into bag with citrate @ 7:1
- Filtered to remove debris, larger particles
Donor weight

• Bone marrow:
  – Risks of anaesthesia
  – Local injury

• PBSC:
  – Potential for more central lines
PERIPHERAL BLOOD STEM CELL COLLECTION

- From mobilised donors: G-CSF, plerixafor
- Using cell separators – continuous or intermittent flow
- Low-density MNC drawn from a dynamic interface between RBC and plasma
Short term side effects of donation

- Bone marrow: **pain** (82% back or hip*), relating to **general anaesthetic** (throat pain, headache, nausea and vomiting) and **blood loss** (fatigue and weakness), immobility, pelvic fractures, cardiovascular events, sepsis, fat embolism

- Peripheral blood: **access-related** (bruising, thrombosis), **apheresis-related** (parasthesiae, palpitations, faintness), G-CSF-related (bone pain 97%*, fever)

- Pain commonest symptom followed by fatigue (BM 59% v PBSC 70%)*

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*Miller JP et al, Biol Blood Marrow Transplant, 2008*
Side Effects of G-CSF

• Common
  – bone pain (97%), headache (38%) & myalgia (20%)

• Less common
  – nausea, vomiting, diarrhoea, fatigue, redness etc at injection site, insomnia

• Rare
  – splenic rupture, 7 cases 1997-2006 (splenomegaly >90%)

• Causation/precipitation of MDS/AML
  – Considered but much data to disprove
Pain Post-Bone Marrow Donation

Percentage of Donors

Grade 3 - 4
Grade 2
Grade 1

N =

Back  1493  1355  1128
Hip   1492  1355  1128
Throat 1493  1354  1127
Muscle 1493  1354  1127
Headache 2505  1861  1128

2 Days 1 Week 1 Month 1 Year

Percentage of Donors

0% 20% 40% 60% 80% 100%

2 Days 1 Week 1 Month 1 Year

CIBMTR
Center for International Bone Marrow Transplant Research
Non-Pain Symptoms Post-Bone Marrow Donation

Fatigue    Site Reaction   Insomnia       Nausea       Dizziness      Anorexia

N =      2505     1486             2505      1486             2505      1486              2505      1486              1493
1354             2505     1486
1861     1129              1861      1129             1861       1129             1861      1129              1237
1127             1861     1128
Serious Adverse Events:
NMDP PBSC Donors 1999-2006

• 42 Total SAEs in 5962 donors (0.7%)
  – 34 Serious by virtue of hospitalization
    • 25 with symptoms: headache, N & V, chest pain, bone pain, low calcium
    • 4 central line complications
    • 4 low platelet counts
    • 2 pneumonia
    • 1 asthma
    • 1 DVT
  – Other serious
    • 1 low platelet count without hospitalization
  – No deaths
Severe events in allogeneic donors: EBMT study

- 338 BMT teams in 35 European countries
- 51,024 HSCT (54% BM and 46% PB)
- Between 1993-2005
- 5 donor deaths (within 30d)
  - 1 BM and 4 PB;
  - SAH, PE, MI – 3
  - All in related donors
- 37 SAEs – 4.32/10,000 BM donors
  - 10.76/10,000 PB donors (p<0.05)
- Study retrospective, underreporting likely

Halter J et al, Haematologica, 2009
Deaths resulting from donation

- Horowitz and Confer: 6 BM (2 pre-collection), 3 PB. Causes – VF, MI, PE, stroke, cardiac/respiratory arrest, sickle crisis
- Halter et al: 1 BM; 4 PBSC all related donor
- Siddiq et al: 3 related PB donors died after 23 – 28 months due to subarachnoid haemorrhage, MI, pulmonary embolism
- WMDA SEAR: One unrelated donor deaths reported 2003-2018
- Estimate 1/10,000 – 1/20,000 deaths after donation
- Deaths from cancer

Halter et al, Hematologica, 2009; Siddiq et al, Cochrane Database Syst Rev, 2009
Horowitz and Confer, Hematology, 2005
Unrelated adult stem cell donor medical suitability: recommendations from the World Marrow Donor Association Clinical Working Group Committee


*Bone Marrow Transplantation* 2014 Jul;49(7):880-6.
On-line tool

- Principles of assessing donor medical suitability
- [http://www.worldmarrow.org/donorsuitability](http://www.worldmarrow.org/donorsuitability)
- These guidelines exist as an aid to unrelated adult haematopoietic stem cell donor registries in assessing the medical suitability of their donors.
- However, donor registries are reminded that these guidelines are not intended to supersede local laws or requirements of national legislative bodies
Donor risk

Donation of hematopoietic stem cells (HSC) is an act of altruism, and may be to a recipient in a different country, with quite different moral, cultural and religious values.

Whilst it is recognised that the process of donation carries a small but unavoidable risk of harm to the donor, it is both the moral and legal responsibility of donor registries and donor centres to minimise any avoidable risk. This includes medical conditions that may increase the risk of harm to the donor before, during, and after the collection of HSC.

For this reason, medical criteria governing conditions that may increase donor risk are necessarily stringent, and certainly more so than would be the case if the individual were undergoing a procedure for therapeutic benefit.

In many cases it is difficult to establish a rigorous evidence base as justification for the criteria. In such cases, expert opinion of the underlying physiology of disease will be sought, and combined with knowledge of the known physiological changes associated with donation, as well as experience gained through several decades of HSC donor follow-up and adverse event reporting.

In general, if there is any doubt about the safety of the donor in the presence of a particular medical condition, it will be recommended that any donor with that condition be prevented from donating.
On-line tool: background

Recipient risk

By contrast, our recommendations regarding conditions that may put the recipient at risk are more lenient.

For many patients, an unrelated donor HSC transplant represents the only possibility of disease cure or long-term remission. Because of the diverse nature of HLA tissue-types, many patients will have a limited number of potentially matched donors. In such cases, donor medical conditions that may present a risk to the recipient alone should be reported to the transplant centre, who are best placed to make an informed risk-benefit judgement on whether to proceed with that particular donor.

There are obvious exceptions to this, however, in particular the carriage of transmissible agents which may have more deleterious effects in the recipient. These include infectious agents such as HIV, viral hepatitis and HTLV, prion-related diseases such as Creutzfeld-Jacob Disease, and carriage of autoreactive lymphocytes causing multi-system or severe single-organ autoimmune diseases, such as systemic lupus erythematosus, multiple sclerosis or inflammatory bowel disease.
On-line tool: data

A

Acupuncture, see Tattoo, body piercing and acupuncture
Alcohol intake
Alcoholism, see Alcohol intake
Allergy
Alopecia areata, see Single organ autoimmune disease
Anaemia
Anaphylaxis, see Allergy
Angina, see Coronary artery disease
Ankylosing spondylitis, see Back complaints
Antiphospholipid syndrome, see Thrombosis and Thrombophilia
Antithrombin III (ATIII) deficiency, see Thrombosis and Thrombophilia
Aortic regurgitation, see Valvular heart disease
Aortic stenosis, see Valvular heart disease
Arrhythmia
Arterial thrombosis, see Thrombosis and Thrombophilia
Asthma
Atrial fibrillation/flutter, see Arrhythmia
Atopy, see Allergy
On-line tool: risk to recipient

Tattoo, body piercing and acupuncture

Created by Paulien Kort (administrator), last modified on Mar 28, 2018

Contents

- Condition
- Individual at risk
- Guidance at RECRUITMENT for adult volunteer donor and maternal donor (cord blood donation)
- Guidance at CT/WORK-UP
- Justification for guidance
- References

Condition

Any acupuncture, body piercing, permanent or semi-permanent make-up or tattoo.

Individual at risk

Recipient
On-line tool: risk to recipient

Guidance at RECRUITMENT for adult volunteer donor and maternal donor (cord blood donation)

ACCEPTABLE

Guidance at CT/WORK-UP

ACCEPTABLE at the discretion of the requesting transplant centre, who should be informed where and when the procedure occurred.

Nucleic acid testing (NAT) for hepatitis B, C and HIV are recommended.

Justification for guidance

There is a risk of transmission of blood-borne viruses, particularly hepatitis B and C, through the use of inadequately sterilised equipment used for tattoo, acupuncture and body piercings. A 4 month deferral is recommended from the date of the procedure, but this may be reduced by the transplant centre if it is thought that the risk of acquiring an infectious disease is outweighed by the risk of delaying transplantation.

4 months allows for the ‘window period’ between disease exposure and the earliest the disease may be detected by modern nucleic acid testing (NAT) assays.

References

On-line tool: risk to donor

Arrhythmia
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This page was last modified on 18 May 2016, at 10:06.

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- Condition
- Guidance at RECRUITMENT for adult volunteer donor and maternal donor (cord blood donation)
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- Qualified Guidance
  - Acceptable
  - Unacceptable
- References
- Notes

Condition
An abnormality of cardiac electrical activity, most commonly diagnosed by electrocardiography.

Guidance at RECRUITMENT for adult volunteer donor and maternal donor (cord blood donation)
QUALIFIED, SEE BELOW

Guidance at CT/WORK-UP
QUALIFIED, SEE BELOW

Individual at Risk
Donor
On-line tool: risk to both

Anaemia

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Individual at risk

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Conclusion

- Donor assessment is important to ensure safety of both the recipient and the donor.
- Recipient risk should be discussed with TC (and patient) – risk/benefit.
- Donor risk should be ‘absolute’ for UD, but might be a balance for RD.
- Donation is well tolerated, but not without risk.
- Harmonization of assessment and eligibility internationally (for UD and RD) is important.