CHAPTER 1

Donor and graft selection strategy

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Introduction

A key component of the decision-making process of an allogeneic hematopoietic cell transplant is selection of the appropriate donor and graft. The best donor is an HLA-matched sibling. However, this option is available only for one third of patients. While the choice of a graft type is often determined by the transplant center preference and experience, there are advantages and disadvantages with each option.

What are the donor options?

In the absence of an HLA-matched sibling, an alternative donor is pursued. The options of donors are:
1 HLA-matched sibling (including one antigen/allelic mismatch)
2 Unrelated volunteer adult donor (MUD donor) (including one antigen/allelic mismatch).
3 Umbilical cord blood (UCB).
4 Haploidentical donor.

What are the graft sources?

Initial allogeneic transplants were done using bone marrow grafts. However, more options are currently available. The sources of hematopoietic grafts are:
1 Peripheral blood (PB).
2 Bone marrow (BM).
3 UCB.

Donor options

HLA matching is the most relevant factor when choosing a donor. Details of HLA typing are explained in Chapter 2. Some pertinent details are outlined next.

HLA matching for donor selection

HLA antigens are either "high expression" such as HLA-A, B, C (class I), DRB1 (class II), or "low expression" such as DQB1, DPB1, and DRB3/4/5 (all class II). The "high expression" antigens play a pivotal role in the transplant setting because of *high antigen density* on the cells. (We will refer to DRB1, DQB1, and DPB1 as DR, DQ, and DP, respectively, throughout this chapter.) An HLA-matched sibling is usually the preferred donor. A haploidentical donor ($\geq$ 4/8 match) is defined as a first degree relative that shares at least one full haplotype with the recipient (i.e., it cannot be mismatched in both loci of any HLA alleles).

For unrelated donors, HLA matching at the allele level of HLA-A, B, C and DRB1 (8 alleles) is done according to National Marrow Donor Program (NMDP) recommendation. An ideal donor is 8/8 HLA-match. When there is more than one 8/8 HLA-matched donor, additional HLA matching at the DQ and DP may be helpful to identify a better candidate (see Chapter 2). For example, with DQ typing, 10/10 matched donors may be favored. On the other hand, DP matching is only seen in about 20% of 10/10 HLA-matched donors. Nevertheless, groups of "permissive" versus "non-permissive" mismatching have been identified based on cross-reactivity profiles. Permissive mismatching (found in ~70% of 10/10 HLA-matched donors) means two mismatched DP alleles will have a favorable outcome (less non-relapse mortality (NRM)) similar to

a HLA-matched DP. The use of DQ and DP matching has not been universally recommended.

Each single locus mismatching in classical HLA loci (A, B, C, and DRB1) is associated with ~10% reduction in overall survival particularly for "early stage" disease. Earlier data showed that the worst "bone marrow" mismatches were HLA-A or HLA-DRB1 alleles, and the worst PB mismatch was HLA-C antigen. However, more recent data showed that the type (allele/antigen) and locus (HLA-A, B, C, or DR) of mismatch have equal impact on survival outcome. The only exception is a favorable outcome with the permissive mismatch of C*03:03/C*03:04.

HLA matching of UCB

Due to the immaturity of UCB T-cells, HLA matching is less stringent when using this graft source. UCB should be at least a 4/6 (A/B and DRB1) match using HLA-A and B (DNA-based low resolution/antigen level) and DRB1 (DNA-based high resolution/allele level). Outcomes of 4/6 UCB transplants are comparable to that of HLA-matched unrelated donors, albeit with an increased risk of NRM. When using a "single" unit of UCB, HLA-C antigen mismatching was shown to increase transplant-related mortality (TRM), particularly, if combined with HLA-DRB1 mismatching. When using double UCB units (as in most adult patients), there are no guidelines for HLA matching *between* the two units as long as minimum requirement of 4/6 HLA matching is present of each unit with the patient's HLA. Nevertheless, some centers prefer to use at least a 4/6 matching *between* the two units.

When a HLA-matched unrelated donor or a mismatched unit is used, it is essential to test the recipient for pre-formed donor-specific anti-HLA as described next.

HLA antibodies

About one-third (33%) of recipients have antibodies directed against HLA class I or II. However, only 5–10% of those recipients have "donor-specific" HLA antibodies (DSA). High titer (>1,000–2,000 MFI; mean fluorescent intensity) of DSA is associated with risk of graft rejection. Risk of graft rejection with DSA is higher when using NMA, compared to myeloablative regimens. Testing recipients for DSA is crucial when using HLA-mismatched, unrelated, haploidentical donors or mismatched cord units. Higher CD34+ cell/kg in PB grafts compared to BM grafts may overcome negative impact of DSA, particularly when the titer is considered low, that is, <1,000 MFI.

How is DSA tested?

HLA antibody testing is done by initial screening of the recipient's serum using the "Panel Reactive Antigen" (PRA) assay. PRA determines the percentage of random people's sera against which the recipient could have antibodies. If PRA is positive, "Single Antigen Beads" (SAB) test is performed to identify whether the antibodies are against DSA or not (requires blood test from the donor). DSA may be mitigated by therapeutic plasma exchange (TPE), rituximab, bortezomib, and/or intravenous immunoglobulin.

The following is a description of the pros and cons with each of the donor options.

HLA-matched sibling

An HLA-matched sibling is favored in most cases, if available. Any full biological sibling (same biologic parents) of the patient would have a 25% chance of being fully HLA-matched, 25% of being HLA-non-matched and 50% of being HLA-haploidentical matched. DSA testing is not required in the setting of HLA-MSD. In addition, another advantage of a HLA-MSD is that he/she would be readily available for graft procurement for the potential need for future cell donations such as donor lymphocyte infusion (DLI) or a CD34+ cell boost-"graft boost".

Unrelated volunteer adult donor (MUD donor)

When a fully HLA-MSD is not available, a HLA-MUD donor is sought through registries. In the United States, the NMDP represents a major source for volunteer donors. In addition, The Bone Marrow Donors Worldwide (BMDW) organization has data for over 25 million volunteer donors. Once again, the ideal donor is 8/8 HLA-matched with the patient. HLA-MUD donors are typically available for donation after about 8 weeks but may not be available for another cell donation for DLI or graft boost. Thus, transplant centers may opt to store an extra portion of the HLA-MUD graft (if feasible) for future use.

UCB

When a fully HLA-matched donor (whether a MSD or MUD donor) is not available, an UCB donor can be considered. UCB would be promptly available, but is not available again for DLI or graft boost. More details on UCB use is outlined below under graft sources.

HLA-haploidentical donor (haplo donor)

Recent introduction of post-transplant cyclophosphamide (PTCy) made HLA-haploidentical transplant a feasible option even in a center not specialized on this type of transplant. When a fully HLA-matched donor (whether a MSD or MUD donor) is not available, a haplo donor can be considered. A haplo donor is typically a first degree relative like a parent, a child or a sibling. The majority of patients have a haplo donor (exceptions include adopted and old patients with no children). While the haplo donor would be readily

available for the donation transplant centers with no adequate expertise in performing HLA-haploidentical transplants may opt to use HLA-mismatched from unrelated donors. The choice between haplo- and UCB- transplant often depends on the center preference and experience. The choice between UCB and haploidentical transplant remains controversial until the CTN 1101 clinical trial comparing haplo BM *vs* UCB with reduced intensity regimen, is completed.

Clinical differences among different types of donors are summarized in Table 1.1.

Graft composition

There are biological differences among the three sources of grafts (PB, BM and UCB) due to their different composition. These grafts are primarily composed of:
- CD34$^+$ cells, which make ~1% of the entire graft composition.
- Lymphocytes (mainly T-cells, and also B-cells and natural killer (NK) cells).
- Myeloid precursors.
- Monocytes (with potential for cytokine release).
- Other cells (e.g., endothelial progenitor cells and mesenchymal cells).

The CD34$^+$ cell dose is the primary determinant of successful engraftment. However, other components (in particular, the T-cells = CD3$^+$ cells) play pivotal roles in transplant outcomes. Simply stated, CD3$^+$ cells (T-cells) mediate the following four immunological processes:
1 Engraftment.
2 Immune reconstitution to prevent infection.
3 Graft-versus-tumor (GvT) effect to prevent relapse.
4 Graft-versus-host-disease (GvHD).

While engraftment, immune reconstitution, and GvT are favorable processes, GvHD is not.

PB graft

Although the initial transplants were done with BM grafts, PB grafts are now more commonly used. Main advantages of using PB grafts are faster and more secure engraftment (thus preferred for NMA and RIC regimens) and immune reconstitution, and less relapses (via GvT effect). However, chronic GvHD (cGvHD) continues to be a major long-term complication of PB grafts.

A PB graft is collected by apheresis procedure. Typically, donors receive growth factor injection for 4 days and then undergo leukapheresis for 1–2 days. The recommended CD34$^+$ cell dose in a PB graft is at least 4×10^6 CD34$^+$ cells/kg of recipient weight, while a dose of $< 2 \times 10^6$ CD34$^+$ cells/kg is discouraged to avoid risk of engraftment failure (See chapters 5 and 6).

BM graft

BM was the initial graft source used for allogeneic transplantation. BM grafts, by virtue of having less T-cells, have higher risk of engraftment failure (particularly when using NMA conditioning regimens), delayed immune reconstitution, and potential risk of neoplastic disease relapse (less GvT effect). However, they are associated with less risk of cGvHD and clinical trials have shown equivalent survival outcomes when compared with PB in hematologic malignancies.

BM is harvested in the operating room under general anesthesia. It is typically a 1-day surgery with the risks of complications common to general anesthesia, as well as bleeding, pain, and, rarely, traumatic surgical injury. The recommended cell dose in a BM graft is 4×10^8 TNC

Table 1.1 Comparison of the different graft sources.

	HLA-MSD	HLA-MUD	Haplo Donor	UCB
Priority	First Priority	First alternative	Next alternative	Next alternative
Availability	Readily available	Procurement time of 4–8 weeks or longer	Readily available	Promptly available
Cost	Donor testing and collection	Registry search, donor testing and collection	Donor testing and collection	Expensive: A single UCB unit is ~ $30,000 −$50,000
DLI and graft boost	Available	May be available	Available	NOT available*
Graft manipulation trials	Donor available to consent	Requires Registry approval	Donor available to consent	NOT possible*

*Once thawed, the whole UCB unit is infused and generally not amenable for cellular manipulation in usual circumstances.

(total nucleated cells)/kg of recipient weight for hematologic malignancies. A dose of $<2 \times 10^8$ TNC/kg is discouraged. The TNC (rather than the $CD34^+$ cell count) is used to determinate the cell dose in the BM graft since the interim cell dose evaluation (during the harvest procedure) is routinely done using the quick hemocytometer cell counter of TNC.

Why is BM graft is preferred in children with hematologic malignancies?

In children, BM graft is used more than PB mainly to avoid the long-term complications of cGvHD. The risk of engraftment failure in children is less with BM graft as they always receive enough $CD34^+$ cells (due to their small body weight compared to the donor). Children may also tolerate infectious complications (if delayed immune reconstitution) better than adults, who often have medical comorbidities. The risk of relapse of neoplastic diseases (by virtue of less GvT) of the BM graft may be reduced by myeloablative regimens, which children can tolerate better than adults.

UCB graft

UCB units are cryopreserved (voluntarily donated) in several cord banks. UCB banking is recommended for public use. Storing UCB for personal use (i.e., reserved for the same baby if he/she develops disease in the future) is generally discouraged, because the probability of a newborn using his/her own UCB is too small, around 0.04–0.001%. While cord blood baking started in the 1980s in the United States, FDA regulations have only been imposed since 2011. Any UCB unit stored without conforming with the FDA regulations issued in late 2011 is considered "unlicensed", and its use is currently available only under FDA approval (considered investigational use). Units stored according to the FDA regulations are "licensed," and are available for routine use in the United States. One of the advantages of UCB units is that they are promptly available. They are typically of small volume with 1 log fewer TNCs and $CD34^+$ cells/recipient weight (compared to PB and BM grafts). However, for most adults, 2 units (double cord transplant) are used for a successful transplant. When double cord units are used, eventually only one UCB engrafts and the other one vanishes after providing cellular immune support during the early post-transplant time. UCB has more immature T-cells and, thus, is less immunologically reactive. Consequently, they are associated with higher risk of engraftment failure (particularly with NMA regimen), delayed immune reconstitution and potential for neoplastic disease relapse (limited GvT effect). The risk of GvHD with UCB depends on the degree of HLA disparity with the recipient. Due to the immaturity of the cord blood T-cells, HLA matching is less restrictive. An ideal UCB unit should have at least 3×10^7 TNC/kg of recipient weight. When performing a double UCB transplant in adults, each unit has to have at least 1.5×10^7 TNC/kg of recipient weight. Since the $CD34^+$ cell dose in the UCB is about a log less than that in PB or BM graft, at an average of 3×10^5/kg (~1% of TNC) for an adult, slow engraftment is expected. It is also to be noted that UCB is typically negative for antibodies to CMV. In routine clinical practice (outside clinical trials), UCB is not available for future use (e.g., DLI).

Differences among the three sources of graft sources are summarized in Table 1.2.

Which graft type should I use?

Although several transplant centers tend to use one type of graft more than another, it is often prudent to consider several factors when selecting the type of the graft for each individual patient. As a general rule, UCB or haploidentical graft are typically reserved for recipients with no available HLA-matched donors. The decision-making to choose between PB and BM is summarized in Table 1.3.

Non-HLA factors

What if more than one HLA-matched donor is available?

HLA matching is the most relevant factor when choosing a donor. However, the following factors are to be considered when there is more than one equivalent donor. The order of preference of these factors is often based on institutional preference.
1 CMV status of the donor and patient.
2 ABO blood matching with the patient.
3 Gender of the donor.
4 Age of the donor.
5 Weight discrepancy between the donor and the patient.
6 Availability (domestic or international) and timeframe of availability.
7 Killer cell Immunoglobulin-like Receptors (KIR) status of the donor using techniques such as KIR B content score.

CMV status

Most of the population acquire CMV infection when young and remain seropositive for life. CMV remains dormant in leukocytes and can be re-activated when the host becomes immunocompromised. For a CMV negative patient, ideally, a CMV negative donor should be used, whenever possible. However, for patients who are CMV positive, either CMV negative or positive donor can be used. Some centers prefer to use CMV positive donors for CMV positive patients (i.e., CMV matching) to allow the transfer of CMV immune lymphocytes (from the donor) to the patient to combat post-transplant CMV reactivation. The latter approach, although not systematically studied, may be beneficial with T-cell depleted transplants (in particular with anti-thymocyte

Table 1.2 Comparison of the three hematopoietic graft sources.

	PB	BM	UCB
Prevalence of use	Most common	Common in pediatric transplants	Common in pediatric transplants
Feasibility	- Donor evaluation - Apheresis	- Donor evaluation - Harvesting of BM	Cryopreserved units
Donor's risks	- Central venous access (if used) - Electrolyte imbalance - Hyperviscosity (MI and CVA in high-risk donors)	- General anesthesia - Hypovolemia with big volume harvest	None
Graft composition			
Cell dose target	CD34$^+$ cells: $\geq 4 \times 10^6$/kg	TNC: $\geq 4 \times 10^8$/kg	TNC: $\geq 2.5 \times 10^7$/kg (single UCB). TNC: $\geq 3 \times 10^7$/kg (double UCB)
Average CD34$^+$ cell dose	4–6×10^6/kg	2–4×10^6/kg	3×10^5/kg
Average T-cell (CD3$^+$) dose	$\sim 3 \times 10^8$/kg	$\sim 3 \times 10^7$/kg (one log less than PB)	$< 1 \times 10^7$/kg
G-CSF primed cells	YES (at all times)	NO*	NO
CMV status	Positive or negative	Positive or negative	Negative
Clinical outcome			
Engraftment	Fast	Slow	Slowest
Immune reconstitution	Fast	Slow	Slowest
Relapse risk	Low	High	Highest
cGvHD risk	High	Low	High (if mismatched)

* Unless donor is, uncommonly, primed by G-CSF before harvest.
MI: myocardial infarction, CVA: cerebrovascular accident, cGvHD: chronic graft-versus-host-disease, TNC: total nucleated cells.

Table 1.3 Factors to consider when selecting PB or BM graft.

Factor	PB	BM
• Disease type	Appropriate for all indications, in particular: - Neoplastic diseases (better GvT).	Appropriate for severe aplastic anemia, and BM failure diseases (no GvT needed). - Thalassemia and sickle cell disease.
• Disease status	Appropriate for all disease statuses, in particular, refractory or active neoplastic disease (better GvT).	Acceptable for neoplastic diseases when in remission.
• Conditioning regimen: MA, RIC, NMA	Appropriate for all regimens, and including RIC and NMA.	Risk of engraftment failure is high with RIC or NMA regimens (less T-cells).
• Active infection (or multiple comorbidities) at the time of transplant	Preferred (faster immune reconstitution).	Better avoided because of delayed immune reconstitution.
• ABO mismatching	No need for RBC depletion.	Requires RBC depletion which may compromise CD34$^+$ cell dose.
• Children	Acceptable	Usually preferred

MA: myeloablative, NMA: non-myeloablative, RIC: Reduced intensity conditioning

Table 1.4 ABO blood matching of donor and recipient.

		Recipient			
		A	**B**	**AB**	**O**
Donor	A	compatible	MAJOR/minor	minor	MAJOR
	B	MAJOR/minor	compatible	minor	MAJOR
	AB	MAJOR	MAJOR	compatible	MAJOR
	O	minor	minor	minor	compatible

Major/minor (bi-directional)=both mismatch complications can happen.

globulin). UCB are always CMV seronegative and, thus, may be a good option for a CMV seronegative patient who does not have other HLA-matched donor options.

ABO blood type

The commonest blood group types are A and O (each is 40–45%). ABO blood type matching is not required for a successful transplant. However, ABO mismatching can result in complications. Matching between recipient and donor depends upon the interaction between the ABO antigen (on RBCs) and isohemagglutinins (anti-A and anti-B) in the plasma. Donor/recipient matching are either compatible or mismatched (major, minor or bi-directional) as outlined in Table 1.4.

Major and bi-directional (major and minor) mismatches are best avoided, if possible.

- **ABO major mismatch** (e.g., A graft and O recipient). This mismatch carries risk of two complications:
  ○ *Acute hemolysis* upon infusion of the graft. Clinically significant hemolytic reaction is uncommon due to routine RBC depletion of BM grafts and minimal RBC content in the PB grafts. It is recommended that volume of RBCs in the graft be<0.3 ml/kg.
  ○ *Delayed erythroid engraftment and pure red cell aplasia:* This may occur when the residual recipient's plasma cells (making anti-A and anti-B) survive for several weeks and suppress the donor's erythroid engraftment. This may be treated with rituximab.

Anti-A is typically stronger than anti-B; thus, an A graft is less desirable than a B graft when there is a major ABO mismatch.

- **ABO minor mismatch** (e.g., O graft and A recipient). This does not carry risk of significant hemolysis upon infusion of the graft due to dilution of the infused isohemagglutinins in the recipient's plasma (unless small RBCs volume in a child with very high donor isohemagglutinin titer). The primary concerns of this mismatch are two complications:
  ○ *Passenger lymphocyte syndrome (PLS):* This rare but serious complication can happen between days +5 and +15 of transplant. In this case, the donor's plasma cells (passenger lymphocytes) may become activated shortly (within a few days) of the transplant making high titers

of isohemagglutinins that induce hemolysis of the recipient's RBCs. This is an urgent life-threatening medical condition that causes acute anemia and requires therapeutic plasma exchange (TPE) until the high isohemagglutinin titer subsides.
  ○ *Delayed hemolysis* (up to 4 months) of residual recipient RBCs by donor-derived isohemagglutinins. This is often self-limiting and resolves spontaneously.

What about Rh incompatibility?

Rh incompatibility is of little clinical significance in the transplant setting. If an Rh negative recipient receives an Rh positive graft, he/she will unlikely form anti-D because of immunosuppression. However, caution is needed if an Rh negative recipient is alloimmunized (i.e., with anti-D) and receives an Rh positive graft. In that case, acute hemolysis may occur upon infusion of the graft. For example, an Rh negative recipient who is alloimmunized via prior pregnancy (has anti-D) receives a CD34+ cell graft that has RBCs which are Rh positive then the graft RBCs will undergo acute hemolysis upon infusion.

Should we check isohemagglutinin titers in all patients?

Isohemagglutinins are the IgM Anti-A or anti-B antibody that are naturally occurring and can increase with repeated transfusion. Isohemagglutinin titers of the recipient are important in case of major ABO mismatch. Some centers use TPE to decrease the titer prior to infusion of the graft. There is no well-established definition of a high titer, but titers>1:32 may be clinically significant.

Table 1.5 summarizes the complications of ABO mismatching and measures to prevent them.

Donor gender

Female donors can impact transplant in two ways:
1 Female donor grafts may produce anti-HY antibody (HY gene of the Y chromosome) in male recipients, and this may be associated with higher risk of GvHD. Of note, anti-HY antibody is being investigated as a biomarker of cGvHD.
2 Multiparous female donors may have been alloimmunized during prior pregnancies against HLA, which also imposes a risk of cGvHD.

Table 1.5 Complications and preventive measures with ABO incompatibility.

Type of Mismatch	Risks	Prevention
Major mismatch (e.g., A graft and O recipient)	• Infusion hemolytic reaction. • Delayed erythroid engraftment. • Pure red cell aplasia (PRCA).	**RBCs depletion** of the graft can minimize infusion hemolysis. **TPE** (of recipient) can minimize infusion hemolysis and may also decrease risk of PRCA.
Minor mismatch (e.g., O graft and A recipient)	• Infusion hemolytic reaction (uncommon). • PLS (within few days of transplant), a medical emergency treated with TPE. • Delayed hemolysis (of residual recipient RBCs) of no clinical significance.	**Plasma depletion** of the graft. **Close monitoring for hemolysis** between day +5 and +15 (typical time for PLS).

TPE: therapeutic plasma exchange.

Thus, multiparous women are usually avoided as donors, and male donor is preferred for a male transplant recipient.

Donor age

The quality of the CD34+ cells may decline with age. Furthermore, older age can be associated with comorbidities that may influence the donor's safety for donation. Thus, the NMDP uses young volunteer donors whenever possible. However, there is no well-defined donor maximum age cutoff. Studies have shown that outcome of older HLA-matched sibling is not inferior to that of younger HLA-MUD donors in certain diseases.

Donor weight

The CD34+ cell yield from a donor is generally proportional to his/her body weight. Thus, a big weight discrepancy between the recipient and the donor may be clinically significant. This problem may be encountered when an adult (higher weight) recipient is receiving an haplo product from his young children (lower weight). In case of BM harvest, NMDP (and most centers) mandates that the maximum BM volume that can be harvested to be 20 ml/kg of the donor's weight. Thus, a PB product (with expected higher yield of CD34+ cells) may be preferred if the recipient's weight is significantly higher than the donor's.

Availability

The volunteer donor registries are worldwide. Extended search through international registries can be time-consuming and, thus, not appropriate for an urgent transplant (i.e., needed within 4–8 weeks). Other available donors (including haplo and UCB) may be preferred in this setting.

KIR status

KIR are expressed on NK-cells and are involved in the graft cytotoxic (GvT) effect. The KIR complex includes inhibitory (type A) and stimulatory (type B) motifs that are either centromeric (toward the chromosomal centromere) or telomeric (toward the chromosomal telomere). The higher the B content (particularly centromeric), the more stimulatory (cytotoxic), the NK-cells of the graft. Inhibitory KIR binds to KIR ligand (encoded by HLA-C) on the target cells. In case of HLA-C mismatching, this inhibitory signal does not occur, inducing NK cytotoxicity (GvT). A study has shown that patients with AML who received HLA-C mismatched graft with KIR 2DS1 had lower relapse rate. However, these findings have not been validated, and KIR status is not routinely sought when identifying an appropriate donor. This is a subject of ongoing research.

SUMMARY

The following is a summary of ideal graft and donor selection with an algorithm depicted in Figure 1.1.

- HLA typing of the patient and siblings (if available):
  - Matched sibling identified = best option.
  - If no matched sibling:
    - Adult (HLA-MUD) and UCB registry search
    - Identification of haplo donors.

The following are recommendations when using an alternative donor.
- MUD donor:
  - 8/8 HLA-matched MUD donor is next preferred if no HLA-MSD.
  - DP permissive mismatching and DQ matching may be considered if multiple 8/8 HLA-matched donors are available.
- Haplo donor:
  - Can be used if no 8/8 HLA- MUD donor is available.
  - DSA testing: if positive DSA → avoid use especially if titers are high.
- Cord blood:
  - Can be used if no 8/8 HLA-MUD donor is available.
  - At least ≥ 4/6 matched for HLA-A, B (low/intermediate resolution) and DRB1 (high resolution).
  - DSA testing: if positive DSA → → avoid use if titers are high.
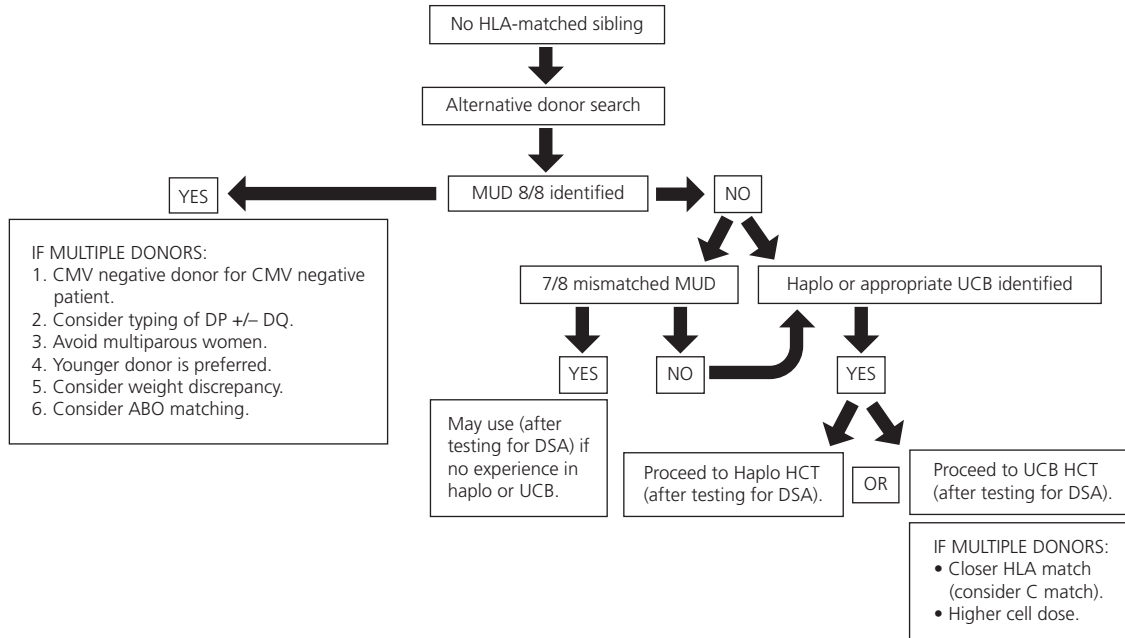
Figure 1.1 Algorithm for selection of a graft/donor for allogeneic transplant.

Abbreviations

BM:	bone marrow
FDA:	Food and Drug Administration
PBSC:	Peripheral Blood Stem Cell
UCB:	Umbilical Cord Blood
RIC:	Reduced Intensity Conditioning
TNC:	Total nucleated cells
MA:	Myeloablative
NMA:	Non-myeloablative
NMDP:	National Marrow Donor Program

Selected reading

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