Table 3-12. Components of Laboratory and Procedural Evaluation of HPC Donors

CBC with differential
Comprehensive metabolic panel
Hemoglobin S screening (hemoglobin solubility or electrophoresis)
Serum pregnancy test
ABO and Rh
Urinalysis*
SPEP*
INR/PT/PTT*
Chest x-ray*
EKG*

*Optional, ordered at clinician discretion, not required by NMDP.
CBC = complete blood count; EKG = electrocardiogram; HPC = hematopoietic progenitor cell; INR = international normalized ratio; PT = prothrombin time; PTT = partial thromboplastin time; SPEP = serum protein electrophoresis.

Suitability to Donate One Product Type Only

Occasionally, a donor may be deemed medically suitable to donate only one type of HPC product. For example, a potential donor may be deferred from HPC(M) donation because of increased risk of anesthesia complications related to diagnosis of malignant hyperthermia or obstructive sleep apnea. A potential donor may be deferred from HPC(A) donation because of poor venous access, current treatment with lithium, sensitivity to *Escherichia-coli*-derived recombinant protein products, or presence of other exclusion criteria or health concerns. Additionally, some donors prefer to donate a particular HPC product type, and those with the strongest preferences may decline to donate the alternate product. In NMDP experience, the number of donors who decline to donate one type of HPCs is small.

Unique Suitability Considerations

Several unique considerations for suitability are considered below, while Table 3-13 offers some examples of more common suitability concerns and reasons for medical deferral.

Height and Weight. Obtaining an accurate donor height and weight is an important part of donor safety evaluation and can influence the HPC product quality and recipient outcomes as well. Ideally, donor and recipient should be closely matched in weight such that it is reasonable to expect an adequate recipient-weight-based cell dose might be collected from the donor. Height and weight guidelines, or body mass index (BMI), which is often used in addition to or as an alternative to height and weight, are just one piece of a more holistic donor health profile that helps to standardize evaluation across networks and guide further evaluation for risks that may be associated with peripheral or central venous catheter placement, anesthesia, or ability to perform a marrow harvest. Obesity is associated with a higher incidence of symptoms and AEs in HPC donors.

Autoimmune Disorders. A careful history and examination of donor autoimmune disorders is important for both donor and recipient safety. G-CSF has the potential to cause a flare or exacerbation of an existing autoimmune disorder, such as psoriasis or rheumatoid arthritis, in the donor. Additionally, adoptive transfer of autoimmune disorder from donor to recipient has been reported. Depending on the diagnosis and severity of the autoimmune disorder, as well as anticipated outcome if donation were to temporarily exacerbate the condition, a donor may still be suitable for donation if both donor and transplant center are

Table 3-13. Common Reasons for Medical Deferral

HPC(M) Deferral	HPC(A) Deferral	Deferral for Both
Age >60*	Age >60 (unrelated)*	BMI >45*
BMI >35 with comorbidities*	BMI >40 with comorbidities*	Sickle cell anemia (homozygous)
Obstructive sleep apnea	Sickle cell trait	Significant or recurrent concussion or traumatic brain injury
Chronic obstructive pulmonary disease	Autoimmune disorders (eg, moderate to severe psoriasis; rheumatoid arthritis; fibromyalgia)	Current or history of malignancy treated with chemotherapy, immunotherapy, or external radiation
Asthma with recent exacerbation or bronchospasm	History of splenic injury	Connective tissue disorders
History of myocardial infarction or other significant cardiac disease	History of deep vein thrombosis	History of stroke or transient ischemic attack
Personal or first-degree relative history of malignant hyperthermia, pseudocholinesterase deficiency, or other severe reaction to anesthesia	Celiac disease, ulcerative colitis, Crohn disease	Serious mental illness or substance use that prevents or poses risk to ability to safely complete workup and donation
Iron deficiency or other anemia with unacceptable hemoglobin level	History of iritis, uveitis, episcleritis, or retinal injury	Type I diabetes mellitus
Chronic pain, osteoporosis, fracture, hip surgery, or other significant musculoskeletal disorder	Frequent, severe, or uncontrolled migraines or migraines with stroke-like symptoms	

*NMDP-specific age and BMI guidelines.
BMI = body mass index; HPC(A) = HPCs from apheresis; HPC(M) = hematopoietic progenitor cells from marrow.

informed of and accept the potential risks. In some cases, a donor with an autoimmune disorder may be suitable for HPC(M) donation only.

Concussion/Traumatic Brain Injury. Embolic stroke and intracranial hemorrhage (ICH) have both been reported as AEs in a small number of HPC(A) donors worldwide. NMDP is aware of six HPC(A) donors with documented donation-related ICH or possibly donation-related ICH from 2008 to May 2022; of these six donors, two had a documented history of concussion or mild traumatic brain injury (TBI) and one sustained a very mild head injury (unclear if contributory) within a day after donation. In most of the case reports of ICH in non-NMDP donors, it is not known whether those donors had any history of concussion/TBI and is not suggested as a potential cause of the event. Furthermore, the pathophysiology of these events is not well understood. It is known that concussion/TBI can cause acute friction, shear, and edema to the delicate intracranial

tissues and, in some cases, a lasting impact on brain chemistry, microvasculature, and even structure. Additionally, it has been documented that G-CSF has a transient, reversible impact on the coagulation system and hemostasis, and both G-CSF and the apheresis procedure itself can cause mild to moderate thrombocytopenia. These effects, coupled with other unknown but likely contributing factors, may theoretically predispose some donors to donation-related ICH.

Interestingly, most other HPC donor registries worldwide have not documented many, if any, donation-related ICH in their donors. Thus, it remains unclear what role, if any, prior concussion/TBI plays in donation-related ICH. For this reason, the approach to donor suitability regarding this topic varies widely across HPC donor registries, but most do recommend some consideration of donor prior head trauma and further evaluation of any related long-term sequelae or permanent deficits. Since 2008, NMDP has developed and modified a thorough donor concussion/TBI history evaluation and corresponding suitability guidance as one effort to prevent future donation-related ICH. This evaluation includes assessment of number and severity of injuries, duration of symptoms, prolonged side effects or recovery, and any injury resulting in chronic neurologic symptoms or other deficits. Evaluation might also include review of prior brain imaging and medical records if available.

SARS-CoV-2. The COVID-19 pandemic has had widespread, global impact on HPC donation and transplantation and continues to present unique practical and logistical challenges at nearly every point in the process, from registering, identifying, and evaluating HPC donors to donor and collection center availability and collecting and transporting HPC products to recipient locations. To date, there have been no reported cases of known transmission of COVID-19 from donor to recipient via HCT/Ps. Additionally, there is no substantial evidence to suggest adverse effect of donor COVID-19 vaccination on recipient transplant outcomes. Still, there may be some risk to the donor, clinicians, and allied health staff involved in donor care if the donor is exposed to or tests positive for COVID-19. Thus, screening donors for COVID-19 history, risk factors, vaccination status, and/or acute symptoms, in addition to testing donors before the start of recipient conditioning, start of donor G-CSF, donor travel for donation, or stem cell collection have all been proposed and implemented by some registries as risk mitigating strategies. At this time, NMDP does not require predonation COVID-19 testing of donors, although this may be requested if specifically required by the collection center or if the donor reports an exposure or symptoms before collection. Additionally, cryopreservation of the HPC product, such that the donor may successfully complete donation before recipient myeloablative conditioning, increased during the height of the pandemic and continues to be used as a strategy in a greater proportion of cases than before the pandemic. However, cryopreservation is not without its own logistical and ethical challenges, and important questions have been raised about the continued practice of cryopreservation in a post-pandemic era (see Chapter 7).

Clonal Hematopoiesis. Clonal hematopoiesis (CH) refers to a distinct population of hematopoietic cells that share an acquired somatic mutation. CH of indeterminate potential (CHIP) is further characterized by the size of the clonal population and presence or absence of dysplasia, marrow blasts, and cytopenias. Prevalence of CH increases with age and is estimated to occur in approximately 10% to even 20% to 30% of persons age 50 and older. CH is believed to be present in 15% to 20% of HPC donors over the age of 40. CH can be transferred from donor to recipient via HSCT. Donor CH impact on the HPC recipient is complex and not completely understood. Certain mutations may confer competitive advantage or more favorable outcomes, while others are associated with increased risk of complications such as

donor-derived leukemia. It is believed most mutations are likely benign, having no impact on recipient outcomes either way. Presently, there are no consensus guidelines on donor screening for CH. There are limited data from robust clinical studies to support screening all donors, or even donors of a certain age, for CH before allogeneic HPC donation. Additionally, there is a knowledge deficit of the role and outcome of individual mutations. Currently, the known benefits of predonation sequencing do not outweigh the known costs and perceived risks. The practice of selecting younger, well-matched donors over older donors may avoid potential instances of CH transplantation.

Mental Health. Mental health assessment is an essential element of the donor health evaluation. Donors with anxiety disorder, depression, posttraumatic stress disorder, bipolar disorder, schizophrenia, and other diagnosed mental illness may be suitable if their symptoms are generally well controlled with or without medication or other therapies; if their mental disorder and associated symptoms do not significantly interfere with activities of daily life or ability to follow through with donation-related activities; and if the collection will not cause undue burden or exacerbate the donor's mental condition. Cryopreservation of HPCs in advance of recipient ablative conditioning may be considered if there is concern about the donor's commitment or potential for donor to become unavailable for collection after clearance.

Special Considerations for Related and Pediatric Donors

Related Donors

A related donor is a blood relative of the HSCT recipient. A potential related donor is identified by their relative—the recipient in need of a transplant—and tissue typed to determine if they are an HLA match. Most countries do not have a central organization responsible for related donor management, so this work has historically been done by the same transplant center caring for the recipient. More recently, some unrelated-donor registries such as NMDP have undertaken this work as well, offering a service to transplant centers who wish to outsource the related-donor workup and management for a variety of center- and donor-related reasons.

The risk-benefit profile of related donors is different than that of unrelated donors, so they may feel more obligation or external pressure to donate. In the related setting, the donor and recipient may be in the same geographic location. If evaluated at the same center, the transplant team should take care to avoid any conflict of interest in the donor evaluation. Ideally, the recipient and related donor are each managed by separate clinicians or care teams.

Eligibility and suitability evaluation of related donors is much the same as for unrelated donors. However, related donors more often may be older than unrelated donors. Sibling donors, for example, are likely to be close in age to their sibling recipients and older, as the incidence of hematologic disease treated by HSCT increases with age. Thus, related donors may require additional evaluation of complex medical histories or existing medical conditions to assess their risks for donation-related AEs. Additionally, given the nature of the relationship between related donor and recipient, there is often a greater willingness on the part of the donor to assume donation-related risk to benefit their relative. For this reason, there may be slightly less restrictive suitability evaluation for related donors in some situations. Determination is made by the donor center evaluating clinician in collaboration with the transplant center, collection center, and/or related donor themselves after education on the additional potential risks and benefits. Medical deferral of related donors may pose additional challenges due to the sensitive nature and inherently complex moral calculus of related-donor donation.