

Basic Concepts and Indications for Transplantation

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I. Introduction

A. The immune system comprises various components that work in tandem to provide immunity and maintain homeostasis. The use of hematopoietic stem cell transplantation (HSCT) to treat various malignant and nonmalignant diseases in the last 30 years has become an increased standard treatment for many conditions. Knowledge of basic concepts of HSCT provides a foundation for understanding the intricacies of transplantation to provide quality care and better support to patients and their families.

1. Basic concepts of transplantation (Devine, 2013)

a) Hematopoiesis and immunology provide the scientific basis for HSCT. Two types of bone marrow exist: red bone marrow and yellow bone marrow. Red bone marrow produces hematopoietic stem cells that create red blood cells, white blood cells, and platelets and is found in the long and flat bones. Yellow bone marrow and fat cells produce stromal stem cells that produce fat, cartilage, and bone and are found in the long bones.

b) Components of hematopoiesis

(1) Hematopoietic stem cells develop prior to birth and are produced in the long bones during childhood and then the axial skeleton in adulthood.

(2) Bone marrow microenvironment: The bone marrow stroma is the housing unit and hub of cellular activity.

(3) Cellular adhesion molecules

(4) Chemokines, cytokines

c) The main objective of hematopoiesis is to maintain the peripheral blood with the proper level of blood components. The pluripotent stem cells mature and differentiate into the myeloid or lymphoid progenitor cells within the bone marrow (see Figure 1-1).

(1) Myeloid progenitor cells mature into the following:

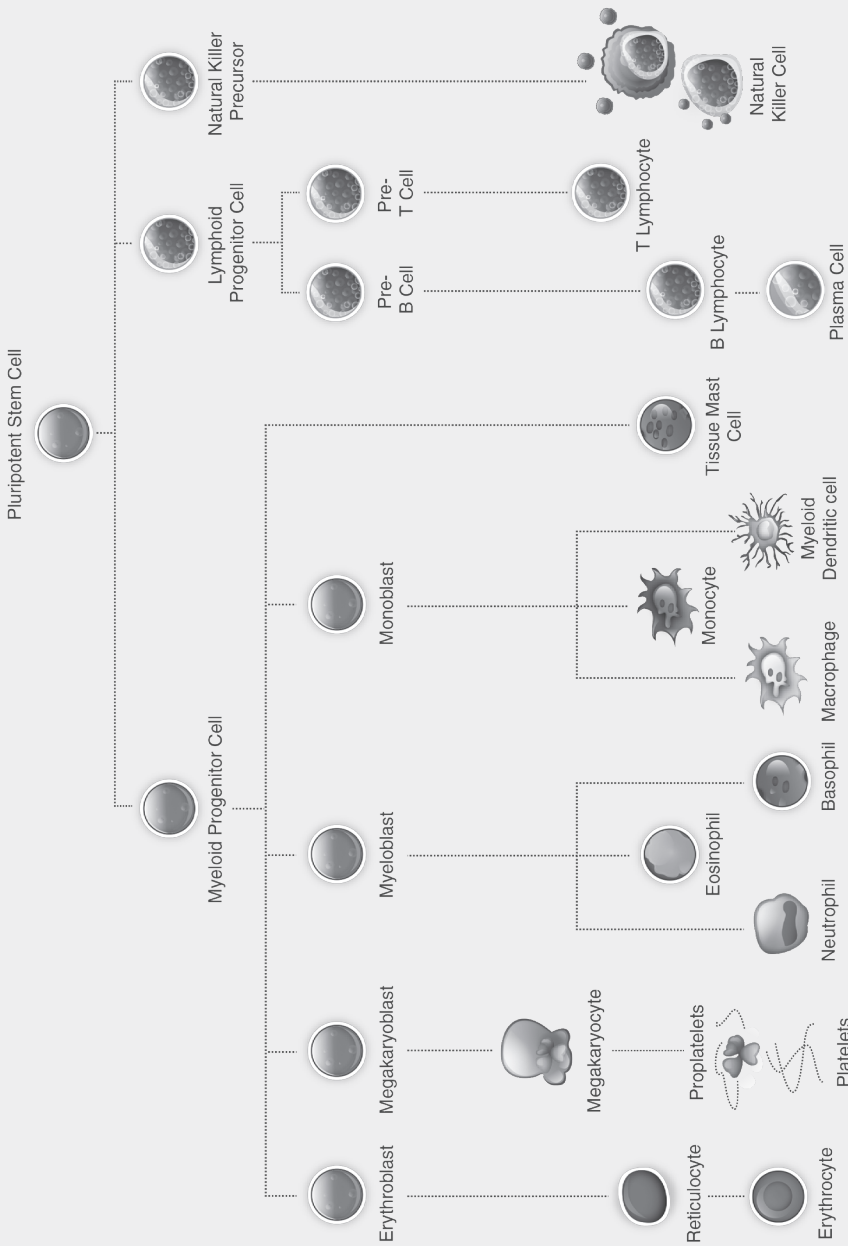
(a) Megakaryocytes (produce platelets)

(b) Erythrocytes

(c) Mast cells

(d) Myeloblasts

Figure 1-1. Hematopoiesis



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- (2) Lymphoid progenitor cells mature into the following:
 - (a) Small lymphocytes, which differentiate into bone marrow-derived cells (B cells) and thymus-derived cells (T cells)
 - (b) Natural killer (NK) cells
 - d) Immune function is dependent on hematopoiesis.
 - e) Primary organs of the immune system are involved in production, maturation, and immune activity.
 - (1) Bone marrow
 - (2) Thymus gland: Located in the anterior mediastinum and forms T cells
 - (3) Lymph nodes: Bean-shaped glands that cluster throughout the body in the neck, chest, axillae, abdomen, and inguinal region and function as an immunologic filter
 - (4) Spleen: Organ responsible for filtering white cells, platelets, and other substances
 - f) The immune system consists of innate immunity and acquired immunity.
 - (1) Innate immunity occurs naturally and uses phagocytes that release inflammatory mediators and NK cells.
 - (2) Acquired immunity is the response of either B cells or T cells to antigens.
 - (3) B-cell activation can be T-cell dependent or independent.
 - g) Hematopoiesis is affected by senescence (loss of the cell's power to divide and grow) (Allsopp & Weissman, 2002; Nuss, Barnes, Fisher, Olson, & Skeens, 2011; Shao et al., 2013).
 - (1) Hematopoietic stem cell senescence naturally occurs with age but also is affected by cancer treatment and transplantation.
 - (2) Reduction in size of thymus and function of immune cells (not necessarily a reduction in number) is called *immunosenescence*.
 - (3) Reduced size and function of thymus after puberty
 - (4) Decreased cell-producing marrow with age
 - h) Immune function
 - (1) Myeloid cells are the first responders to injury and are not pathogen specific.
 - (2) Lymphoid cells respond later and are pathogen specific.
2. Donor identification (allogeneic only) and types of transplantation (Bray et al., 2008). Types of transplant include autologous and allogeneic (see Table 1-1).
 - a) Human leukocyte antigen high-resolution typing provides the degree of genetic match between a matched unrelated donor and a recipient in preparation for allogeneic transplantation.
 - b) A better match is preferred because
 - (1) Potential for improved overall survival with a matched donor and recipient
 - (2) Reduced incidence of graft-versus-host disease (GVHD)
 - (3) Improved engraftment rates
3. Role of the caregiver
 - a) Provide physical and emotional support.
 - b) Assist with physical recovery following HSCT.
 - c) Assist with take-home medication administration.

Table 1-1. Types of Allogeneic Hematopoietic Stem Cell Transplantation

Type of Transplant	Cell Source	Advantages	Disadvantages
Syngeneic	Identical twin	No need for immunosuppression	No graft-versus-tumor effect
Matched sibling/related	Human leukocyte antigen (HLA)-identical relative	No potential stem cell contamination Access to cells because donor is related	Only 25% of population has a sibling match Risk of graft-versus-host disease (GVHD)
Mismatched related	HLA-nonidentical relative	No potential stem cell contamination Increased number of potential donors	Increased risk of GVHD Increased risk of graft failure related to HLA disparity
Matched unrelated	HLA-identical unrelated donor	No potential stem cell contamination	Increased risk of GVHD Limited numbers of non-Caucasian donors Waiting period to identify donor
Mismatched unrelated	HLA-nonidentical unrelated donor	No potential stem cell contamination	Increased risk of GVHD High treatment-related mortality
Umbilical cord blood	Umbilical cord unit	Easy access to cell source	Limited number of cells Delayed time to engraftment Increased infection rates

Note. From "Basic Concepts of Transplantation" (p. 15), by D. Niess in S.A. Ezzone (Ed.), *Hematopoietic Stem Cell Transplantation: A Manual for Nursing Practice* (2nd ed.), 2013, Pittsburgh, PA: Oncology Nursing Society. Copyright 2013 by Oncology Nursing Society. Reprinted with permission.

- d) Perform care of central venous catheter (e.g., flushing and dressing changes).
 - e) Assess for signs of infection (e.g., fevers).
 - f) Monitor temperature.
 - g) Perform food preparation.
 - h) Provide transportation to and from the hospital or office.
 - i) Aid in symptom identification.
 - j) Communicate with healthcare team.
4. Informal/family caregiver self-care
- a) Rest
 - b) Balanced diet
 - c) Exercise/stress reduction
 - d) Management of personal health needs (e.g., medications) and personal support
5. Goals of therapy
- a) Nonmalignant diseases: Cell line replacement (e.g., chronic granulomatous disease, sickle-cell disease, aplastic anemia)
 - b) Malignant diseases: Tumor ablation

6. Graft-versus-tumor effect
 - a) Promoted by withdrawal of immunosuppressant therapy
 - b) Promoted by donor lymphocyte infusions
 - c) Decreased in the absence of acute GVHD
 - d) Associated with higher rates of cancer relapse
 7. Immune reconstitution (Storek & Witherspoon, 2004)
 - a) Dependent on patient's hematologic response to preparative regimen
 - b) Dependent on rate of engraftment
 - c) Dependent on survival and longevity of mature lymphocytes present at the time of transplant
 - d) Delayed in patients with chronic GVHD
 - e) Quantitative recovery of immune function does not always correlate with qualitative recovery.
 - f) Immune reconstitution may take months to years.
 8. Phases of immune reconstitution
 - a) Numeric recovery of bone marrow elements
 - b) Functional recovery of cellular interactions
- B. Indications for transplantation (Pasquini & Zhu, 2016)
1. Common malignant and nonmalignant diseases treated with HSCT (see Table 1-2)
 2. Autoimmune diseases treated under a clinical trial (Sullivan, Parkman, & Walters, 2000)
 - a) Scleroderma
 - b) Multiple sclerosis
 - c) Systemic lupus erythematosus
 - d) Rheumatoid arthritis
 - e) Crohn disease

Table 1-2. Common Diseases Treated With Hematopoietic Stem Cell Transplant

Type of Disease	Autologous Transplant	Allogeneic Transplant
Malignant		
Hematologic malignancies	Hodgkin disease Non-Hodgkin lymphoma Multiple myeloma	Acute lymphocytic leukemia Acute myeloid leukemia Chronic myeloid leukemia Myelodysplastic syndromes Non-Hodgkin lymphoma Juvenile myelomonocytic leukemia
Solid tumors	Neuroblastoma Sarcoma Germ cell tumors Brain tumors Breast cancer Ovarian cancer Melanoma Lung cancer	—

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Table 1-2. Common Diseases Treated With Hematopoietic Stem Cell Transplant (Continued)

Type of Disease	Autologous Transplant	Allogeneic Transplant
Nonmalignant		
Hematologic	–	Severe aplastic anemia Fanconi anemia Thalassemia Sickle-cell disease Diamond-Blackfan anemia Chédiak-Higashi syndrome Chronic granulomatous disease Congenital neutropenia
Immunodeficiency	–	Severe combined immunodeficiency disease Wiskott-Aldrich syndrome Functional T-cell deficiency
Genetic	–	Adrenoleukodystrophy Metachromatic leukodystrophy Hurler syndrome Hunter disease Gaucher syndrome
Miscellaneous	–	Osteopetrosis Langerhans cell histiocytosis Glycogen storage diseases
<p><i>Note.</i> Based on information from Ezzone, 2009; Nuss et al., 2011; Pasquini & Wang, 2011.</p> <p>From "Basic Concepts of Transplantation" (p. 14), by D. Niess in S.A. Ezzone (Ed.), <i>Hematopoietic Stem Cell Transplantation: A Manual for Nursing Practice</i> (2nd ed.), 2013, Pittsburgh, PA: Oncology Nursing Society. Copyright 2013 by Oncology Nursing Society. Reprinted with permission.</p>		

Key Points

- Nursing care of patients undergoing hematopoietic stem cell transplantation (HSCT) requires an understanding of basic hematopoiesis and immunology principles.
- As knowledge of the immune system has expanded, the patient population that might benefit from HSCT also has expanded beyond hematologic malignancies.
- Whether patients have a diagnosis of cancer or other illness, informal/family caregivers require rigorous education and support to assist with the necessary care throughout the transplant process and beyond into recovery and survivorship.

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Study Questions

1. Which of the following is an example of a myeloid cell?
 - A. Thymus-derived cells (T cells)
 - B. Bone marrow-derived cells (B cells)
 - C. Monocytes
 - D. Natural killer cells
2. Several factors affect immune reconstitution following hematopoietic stem cell transplantation (HSCT). These include all of the following EXCEPT:
 - A. Recipient's response to conditioning regimen
 - B. Viral infections
 - C. Chronic graft-versus-host disease
 - D. Longevity of mature lymphocytes present at the time of transplant
3. Hematopoiesis occurs primarily in which area?
 - A. Bone marrow
 - B. Spleen
 - C. Thymus gland
 - D. Lymph nodes
4. Which of the following statements is true about innate immunity?
 - A. It occurs in response to T-cell activation.
 - B. It occurs in response to B-cell activation.
 - C. It is a natural process that uses phagocytes that release inflammatory mediators in response to infections or illness.
 - D. It is a natural process that occurs primarily in the spleen.
5. Which is NOT a common indication for allogeneic transplantation?
 - A. Acute myeloid leukemia
 - B. Myelodysplastic syndrome
 - C. Chronic myeloid leukemia
 - D. Breast cancer
6. Graft-versus-tumor effect is promoted by which of the following?
 - A. Withdrawal of immunosuppressive therapy
 - B. Administration of donor lymphocyte infusion
 - C. A and B
 - D. Increased dose of immunosuppressive therapy
7. Which of the following is NOT a role of a caregiver?
 - A. Provide physical and emotional support.
 - B. Assist with recovery following HSCT.
 - C. Assist with medication administration.
 - D. Recommend over-the-counter medications for management of post-HSCT symptoms.