Chapter 1
The Development and Structure of the Bone Marrow Hematopoietic System

ABSTRACT

The bone marrow is a complex, finely regulated system that widely extends in the body. It has unique development, microstructure, and functional characteristics that adapt to the flocculating body needs in steady-state and stress conditions. The bone marrow is an essential tissue for investigating most hematologic disorders. The study of the pathobiology of human bone marrow facilitates understanding many of its observed changes in benign and malignant conditions. This chapter explains the bone marrow development from the embryo to early infancy and throughout life, emphasizing the critical function-regulating features and the role of different cellular and humoral elements. The discussion of the concept and functions of the hemopoietic niches focuses on the maturation of different hemopoietic lineages within the bone marrow.

INTRODUCTION

The hematopoietic tissue is extended throughout the body and exhibits multiple functions, including its elements' proliferation, maturation, maintenance, senescence, and final destruction. It has a finite control regulated by lineage-specific factors and broadly-acting biological factors. In addition, the hemopoietic tissue is continuously communicated with other body systems through a finely adjusted homeostatic signaling network, allowing hemopoiesis to be sensitively responsive to fluctuating body needs.

The bone marrow is the final site of hemopoiesis from the late fetus through postnatal life and throughout life. It is structurally and functionally complex, exhibiting age and context-related adaptation.

This chapter will highlight the dynamics of the hemopoietic system focusing on the following main aspects:

A. The embryonic development of the hemopoietic tissue and its microenvironment.
B. An overview of bone marrow structure and Components
C. The main elements and functions of the bone marrow stroma
D. The development, differentiation, and regulations of different hemopoietic lineages
E. The concept of the hemopoietic niches and their differential functions

DOI: 10.4018/978-1-6684-5818-1.ch001

THE ONTOGENY AND DEVELOPMENT OF THE HEMOPOIETIC SYSTEM

The hemopoietic tissue appears as early as the first week of gestation from blood islands within the yolk sac. Then, it progresses through 4 main developmental and functional stages.

The Embryonic Development of Hemopoietic Tissue

The Stages and Timeline of Hematopoietic Development

Four distinct developmental stages of hematopoiesis are recognized; each has distinctive features, anatomic location, and regulatory control. At first, hemopoiesis develops from the embryo's inner cell mass through gastrulation, in which the two-layer embryonic disc develops a third cell layer (mesoderm) and a primitive gut.

Meanwhile, two subsequent waves of hematopoiesis develop within the embryo, a primary transient one that starts extra-embryonically from the inner cell mass of the yolk sac 30 days post-conception (DPC) is principally committed to rapid production of erythroid progenitors. The second definitive wave starts intra-embryonically within the aorta-gonad--mesonephros AGM from a hemogenic-endothelial progenitor called Hemangioblast. The hemopoietic stem cells (HSCs) then relocate to the fetal liver and eventually to the bone marrow, which is their final destination and is committed to lifelong maintenance and control of hematopoiesis.

The transition from primitive to definitive hematopoiesis induced by microenvironmental stromal cells within the AGM and fetal liver involves cellular and molecular signals, among which HoxB4 is a crucial factor.

Table 1 outlines the comparative features of primitive and definitive hematopoiesis.

Table 1. Comparison of primitive and definitive hematopoiesis

	Primitive hematopoiesis	Definitive hematopoiesis
Location and time post-conception	Yolk sac at 7 DPC	AGM at 2 Weeks P.C.
Cell of origin	A common endothelial/ hematopoietic progenitor (Hemangioblast) in the blood islands of the yolk sac	Primitive HSCs relocated to definitive hematopoiesis in AGM, fetal liver, and fetal marrow. Influenced by molecular signals from stromal cells, which play a crucial role in such “education.”
Products	Large erythroblasts with embryonic hemoglobins (Gower I & Gower II).	• HSCs, erythroid cells, and non-nucleated erythrocytes (larger than adult red blood cells) & contain adult hemoglobins • Megakaryocytes appear by the 12th week PC • Mature neutrophils appear after the 16th week PC • Long-term repopulating stem cell (LTR-HSC)

continued on following page