Blood cells

Part one – Bone marrow

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This article, the first in a five-part series on blood cells, describes bone marrow – the spongy tissue found within the intraosseous spaces of bones (Fig 1). Its function is production of blood cells, a process known as haemopoiesis.

In addition to haemopoietic stem cells, bone marrow also contains endothelial cell progenitors and marrow stromal cells (also known as mesenchymal stem cells or MSCs) – these give rise to fat cells, bone cells and cartilage.

There is evidence that MSCs may be capable of giving rise to cells of a wide range of tissue types (Herzog and Krause, 2003; Krause et al, 2001). Once committed to the haemopoietic process, stem cells express a surface marker designated CD34 and these cells are often referred to in the literature as CD34+ stem cells.

It should be stressed that, at any given time, most stem cells are in the resting phase of the cell cycle, which is known as G0. In response to a stimulus, the stem cell undergoes an asymmetric division producing a daughter stem cell, which normally returns to G0, and an active stem cell that undergoes repeated maturation/proliferation division cycles to produce mature blood cells.

Blood-forming marrow is red in colour and has a volume of 1.1–1.7l in adults and 1.2–1.6l in children. In children, this marrow fills the interior of virtually all bones. In adults, who have a larger volume within their bones much of the marrow space is filled with yellow (fatty) marrow – red marrow is found only in the ends of long bones and in the axial skeleton in adults. There is a marked, and unexplained, discrepancy between the volume of red marrow per unit body volume in adults and children.

Within the red marrow, the functioning haemopoietic tissue is organised into ‘haemopoietic cords’ – this is the parenchyma of the marrow.

The vascular spaces (sinuses) of the marrow are lined with specialised endothelial cells which regulate passage of cells from the marrow into the circulation – they retain immature cells while allowing mature blood cells to penetrate the incomplete basal lamina (Kern, 2002).
Stromal cells form the framework of the bone marrow and include:

- Fibroblasts;
- Adipocytes;
- Macrophages;
- Osteoblasts;
- Osteoclasts.

Growth factors secreted by stromal cells help to regulate the production of blood cells.

**Function**

As stated, the principal role of the bone marrow is to produce blood cells. It can also act as a functional reservoir, releasing mature and almost-mature blood cells in response to an urgent demand. It is believed that the bone marrow is the site of maturation of B lymphocytes, key components of the immune system (Parkin and Cohen, 2001).

Several distinct types of blood cells are produced by the marrow, functions of which will be described in later articles in this series. The main types are red blood cells, platelets and white blood cells. Red blood cells are haemoglobin-containing, anucleate cells which deliver oxygen to tissues, with secondary functions including transport of carbon dioxide from tissues and acid/base balance. Platelets are small anucleate cell fractions that play a key role in early stages of coagulation. And white blood cells are made up of a number of different cell types which carry out various functions within the immune system:

- Lymphocytes;
- B cells – produce antibodies;
- T cells – direct cell killing, organise immune response;
- T helper cells;
- T suppressor cells;
- Cytotoxic T cells – natural killer cells;
- Granulocytes;
- Neutrophils;
- Eosinophils;
- Basophils;
- Monocytes, which migrate to tissues and become macrophages;
- Dendritic cells. These are not produced directly within the marrow but are derived from marrow cells and are key components of the immune system.

**Haemopoiesis**

The most widely accepted model of haemopoiesis is the hierarchical model. In this, pluripotent stem cells give rise to progenitor cells – a more committed class of stem cell, each of which can only produce a limited range of blood cells (Fig 2). There is an alternative linear hypothesis in which progressively more mature progenitor cells give rise to different cell populations – though this is not widely adopted.

Diagrams of the hierarchy of blood cell productions usually show a single stem cell giving rise to a single example of each mature cell-type – this is purely an illustrative convenience. In reality, it has been estimated that between the HSC and the circulating blood cells there are between 17 and 19.5 effective cell divisions giving between 170,000 and 720,000-fold amplification (Mackey, 2001). A single multipotent stem cell can regenerate the entire haemopoietic system of a lethally irradiated mouse.

Adult bone marrow has a great functional reserve; in response to blood loss or red cell destruction, it can expand output eightfold. Although there are many more red cells than white in the bloodstream, normally only 25 per cent of marrow is devoted to erythropoiesis (red cell production) and 75 per cent to leucopoiesis (white cell production). This reflects the lifespans of the cells – around 120 days for red cells but only a few days for most white cells, although some lymphocytes can survive for many years (memory cells). An average person produces their weight in red cells, white cells and platelets every seven years (Mackey, 2001).

**Bone marrow sampling**

A nurse may be asked to assist at diagnostic sampling of bone marrow. In adults this is normally performed using a local anaesthetic, while in the case of very nervous adults or young children a general anaesthetic may be preferred.

The nurse’s role is emotional support and general care of the patient – the technical aspects of the sampling will be dealt with by the haematologist. A small quantity of marrow is taken by syringe, called an aspirate, and usually a core of bone and marrow tissue called a trephine biopsy.

The aspirate is the most useful sample for identifying individual cell types, while the trephine biopsy reveals the marrow architecture and allows a more accurate estimate of the marrow cellularity. The findings of a bone marrow sample are invariably accompanied by an interpretive report from a haematologist or histopathologist.

A distinction can be made between pathological conditions primarily affecting the marrow and those that are secondary to other disorders.

The prime examples of the former are the haematological malignancies (leukaemia, myeloma, myeloproliferative disorders) and the marrow failure syndromes such as aplastic anaemia (Campbell, 2000). Examples of the latter include pernicious anaemia (in which the primary defect is malabsorption of vitamin B₁₂) and iron deficiency anaemia (in which the primary defect is chronic blood loss or dietary insufficiency) (Campbell, 2004). Conditions primarily affecting the bone marrow are mainly, although not exclusively, the province of the haematology specialist nurse. Patients suffering from loss of marrow function, whether due to malignancy or marrow failure, will be anaemic and will be prone to repeated infections, bleeding and bruising.

**Keywords**

Bone marrow, Blood cells, Haemopoiesis

**REFERENCES**


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