Structure and function of red and white blood cells

Barbara J Bain

Abstract
Red cells have a major function in transport of oxygen and minor functions in regulation of local blood flow and transport of carbon dioxide. Neutrophils and monocytes are phagocytic cells that are part of the innate and also the adaptive immune response. Eosinophils have their major function in protecting against multicellular parasites, and basophils participate in this process. B cells are part of the adaptive immune response, specifically differentiating to plasma cells, which are responsible for humoral immunity. Some T cell subsets and natural killer (NK) cells mediate cellular immunity, both innate and adaptive, while other T cell subsets suppress the activity of B cells, helper T cells and cytotoxic T cells. NK cells and cytotoxic T cells are important in defence against tumours.

Keywords B cell; basophil; cytotoxic T cell; eosinophil; eryptosis; erythrocyte; haemoglobin; helper T cell; leucocyte; lymphocyte; monocyte; natural killer cell; neutrophil; oxygen transport; red cell; red cell senescence; reticulocyte; suppressor T cell; T cell; white cell

Key points

- Erythrocytes have a major function in oxygen transport, with more minor roles in transport of carbon dioxide and regulation of vasodilation
- Neutrophils and monocytes are phagocytic cells that contribute to both innate and adaptive immune responses
- Monocytes differentiate into macrophages, which function as phagocytes, antigen-presenting cells and immune modulators, and in iron storage
- Eosinophils and basophils have a role in protecting against parasitic infections
- Lymphocytes interact with neutrophils, monocytes, macrophages and dendritic cells, and have a major role in innate and adaptive immune responses

Introduction

The red cells (erythrocytes) and white cells (leucocytes) are normally produced in the bone marrow, being ultimately derived from a pluripotent haemopoietic stem cell. White cells comprise granulocytes (neutrophils, eosinophils, basophils), monocytes and lymphocytes. Note that the term ‘granulocyte’ should not be used as a synonym for neutrophil; it has a broader meaning.

Red cells

The human red cell can be regarded as a miracle of evolution. Once past the reticulocyte stage, it has lost not only its nucleus, but also organelles such as mitochondria, Golgi apparatus and endoplasmic reticulum with its ribosomes, and has assumed the form of a hollowed-out disc. This disciform shape provides a large surface for the exchange of oxygen. The lack of organelles means that the red cell is flexible and can easily deform to pass though capillaries and splenic sinusoids.

Haemoglobin is a metalloprotein composed of four α- or α-like and two β- or β-like globin chains, each globin chain enclosing a haem moiety. The major function of red cells is the uptake of oxygen from the lungs and its delivery to the tissues, by oxygenation of the ferrous (Fe^{++}) ions of haem. Around 98% of oxygen transport is by red cells, only 2% being transported in the plasma. The red cell has a diameter greater than that of a capillary; the need to deform and squeeze through the capillary is likely to improve transfer of oxygen from the erythrocyte to the tissues.

The red cell is also capable of transporting carbon dioxide from the periphery to the lungs, by binding carbon dioxide, as carbamate, to the N-terminal end of the α-globin chain, with its subsequent release as carbon dioxide in the lungs. However, the red cell is only responsible for transporting about 15% of the carbon dioxide, the rest being transported in the plasma. Deoxyhaemoglobin also functions to generate nitric oxide from nitrite, and can thus contribute to vasodilation in the peripheral tissues. The confining of haemoglobin within the red cell means that there is protection against the ability of oxyhaemoglobin to inactivate nitric oxide, which occurs when there is intravascular haemolysis, leading to vasoconstriction and a thrombotic tendency.

The constituent parts of the haemoglobin molecule are synthesized and assembled in erythroblasts in the bone marrow. This requires the presence of ribosomes, on which globin chains are assembled, and mitochondria, which are required for some stages of haem synthesis. The reticulocyte retains mitochondria and ribosomes. This means that haemoglobin synthesis can continue for the 1–2 days the reticulocyte spends in the circulation, and up to 10% of such synthesis occurs in these cells. The pairing of two dissimilar globin chains and the cooperativity between them are essential for the sigmoid oxygen dissociation curve, which ensures efficient uptake of oxygen in the lungs and efficient delivery in the tissues (Figure 1). The oxygen affinity of normally structured haemoglobin means that such uptake and delivery of oxygen is achieved at a red cell count/haemoglobin concentration/haematocrit that does not lead to hyperviscosity.

Other requirements must be met for the red cell to fulfil its major function — transporting oxygen. The following are

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Please cite this article in press as: Bain BJ, Structure and function of red and white blood cells, Medicine (2017), http://dx.doi.org/10.1016/j.mpmed.2017.01.011

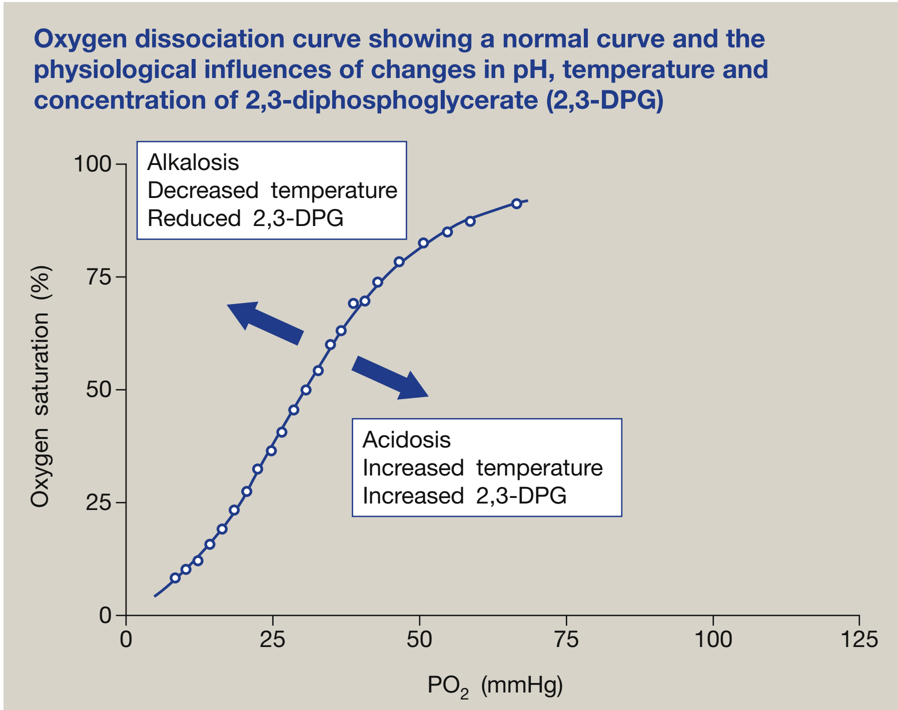

Figure 1

essential for normal function: a permeable membrane; maintenance of the disciform shape and cell flexibility; the ability to convert methaemoglobin (which is spontaneously produced and cannot transport oxygen) to haemoglobin; production of energy in the form of adenosine triphosphate and generation of a reduction potential in the form of nicotinamide adenine dinucleotide (NADH) by means of the Embden–Meyerhof pathway; generation of further reduction potential in the form of NADH phosphate (NADPH) by means of the pentose shunt; and the ability to produce 2,3-diphosphoglycerate (2,3-DPG), which interacts with the haemoglobin tetramer to reduce oxygen affinity and improve oxygen delivery to the tissues. An increased concentration of 2,3-DPG can compensate for anaemia. NADH and NADPH protect the erythrocyte from endogenous and exogenous oxidants. Relevant metabolic pathways are summarized in Figure 2.

The structure of the red cell reflects its function: a cell membrane encloses cytoplasm that has haemoglobin as the major component, with carbonic anhydrase the second most abundant protein. The membrane is composed of a lipid bilayer through which pass various proteins with diverse functions including the transport of anions, water and glucose and the binding of the lipid bilayer at various points to the underlying cytoskeleton, thus maintaining the cell shape (Figure 3). The cell membrane has other functions at the end of the erythrocyte's lifespan of about 120 days. Red cell senescence is the result of a conformational change in a membrane protein, band 3, leading to the appearance of a senescence-specific antigen recognized by autologous immunoglobulin (Ig) G, marking the cells for removal by macrophages.[1] In addition, aged red cells are also more susceptible to oxidant stress and therefore to eryptosis. In this process, there is externalization of membrane phosphatidylserine leading to binding to CD36, the phosphatidylserine receptor on macrophages, with resultant phagocytosis.[1]

Neutrophils

Polymorphonuclear neutrophils are produced in the bone marrow and circulate in the blood before migrating to the tissues, where their main functions are fulfilled. Their lifespan in the circulation is about 7–10 hours and in tissues is 1–2 days. Most neutrophils have a nucleus divided into two to five lobes separated from each other by a thin filament. A minority, referred to as band forms, have a non-lobulated nucleus in the shape of a curved band; with maturation, the nucleus of the band forms develops lobes.

The neutrophil cytoplasm contains some ribosomes, small numbers of mitochondria, glycogen and granules of various types.[2] Only the primary or azurophilic granules are visible by light microscopy. On May–Grünwald–Giemsa (MGG)-stained blood films, they are lilac. They contain myeloperoxidase, defensins, lysozyme, neutrophil elastase and cathepsin G. The secondary, specific or neutrophilic granules are visible by electron microscopy, and on MGG-stained films are responsible for the pink tinge of the cytoplasm. They contain lactoferrin, transcobalamin, collagenase, gelatinase, lysozyme and cathelicidin. Tertiary granules, also below the level of resolution of the light microscope, contain gelatinase and lysozyme. Neutrophil alkaline phosphatase is contained within secretory vesicles.

Neutrophils are part of the innate immune system. Their functions include: margination; adhesion to the endothelium; transcellular and paracellular migration through the endothelium

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