the blood show

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Five Years
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Mark Harris
Untitled
1993
Collage (pigment and
acrylic medium on cut paper)
87 × 58 cm

blood

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Blood provides life itself, because without it we die. This complex blend of fluids, chemicals and cells, so recognisable when we cut ourselves flows otherwise unseen in our arteries, veins and capillaries. The only directly visible blood vessels and flow of blood are in the retina at the back of the eye seen with an ophthalmoscope. Ever since we evolved from a single cellular organism, blood has been necessary to provide oxygen and nutriments to our organs and to carry waste products to be excreted. Blood takes part in the functioning of every cell of every organ in the body. It is responsible for providing the 'internal milieu' or homeostasis and equilibrium within the body so that, inspite of chemicals such as oxygen, carbon dioxide, glucose, sodium, potassium and cellular elements continuously leaving and entering the blood, its composition remains amazingly constant and uniform. This constancy is by virtue of many regulatory processes, but also of the very rapid transit of blood around the body, by the pumping action of the heart and the elasticity of the arteries.

As the left ventricle contracts to force blood out into the arterial system the blood pressure rises to around 120mmHg (Systolic blood pressure) and at the end of ventricular contraction, the aortic valve closes and pressure remains within the large arteries of approximately 70mmHg (Diastolic blood pressure) The arteries are elastic and expand in systole to give the characteristic pulses which we can feel in the wrists, temples, neck etc. This elasticity evens out the blood flow/pressure somewhat, but for some unknown reason our organs rely on pulsatile flow for their well-being. The average velocity of the blood flow is 40cm per second, but reaches a maximum of 120cm per second at the height of systole. If a large artery is severed the blood will spurt to a height of at least one metre until the circulation empties and the person dies from haemorrhage. In states of acute haemorrhage the blood pressure has been quite well maintained until over one quarter of the circulating blood

volume is lost using compensatory mechanisms such as a rising heart rate and peripheral vasoconstriction mediated by the hormones adrenaline and noradrenaline within us. As we age and our arteries get less distensible (harden) and in certain disease states the blood pressure rises (hypertension) which eventually, if left untreated, has a deleterious effect on the brain, kidneys and the heart itself.

An adult has approximately 5 litres of blood. When we are resting the output from the heart is about 5 litres per minute, but when we exercise this increases at least 7-fold. All our mammalian organ systems such as the muscles, brain, liver and kidneys and the complex enzyme reactions which allow them to work, can only function within a very, very narrow limit of temperature and pH. All metabolic processes occurring in cellular activity produce heat and waste products and in an exercising muscle, for example, blood not only brings oxygen and glucose for metabolism, it carries away heat, carbon dioxide and lactic acid. The rapid passage of blood tends to minimize even small, local changes in temperature and carries the heat away to be lost in radiation and evaporation from the skin.

Blood *is* thicker than water, but in fact blood is 80% water and proteins constitute only 18% of blood with the rest being inorganic salts such as sodium and potassium chloride and smaller organic molecules than proteins such as amino acids. The water passes freely in and out of all cells of all organs as well as the fluids which surround them. The vital blood gases, oxygen and carbon dioxide constitute no more than 0.1% of the total volume of blood even if oxygen is required for the continuation of life and carbon dioxide, though a by-product of metabolism is the regulator of breathing and maintains the acid-base status of the body.

The plasma proteins, albumins and globulins, mostly manufactured in the liver have various functions but together they provide a colloid osmotic pressure which is crucial for the regulation and distribution of water in the body. If the levels of these proteins fall, for example with advanced liver disease, then we swell up and develop oedema. Other constituents include antibody (gamma-globulin), fibrinogen and other clotting factors and the lipoproteins including cholesterol which have complex functions relating to transport of vital amino acids and other agents.

When blood is taken out of the body it clots to a solid mass unless treated with a chemical such as heparin. If anticoagulated blood is put in a test tube

and spun in a centrifuge, the cells, the formed elements, separate from the liquid plasma and the so called packed-cell volume (or haematocrit) at the bottom of the tube (around 45% in the normal healthy individual) is a good measure of whether or not we are anaemic. Most of the cells are the erythrocytes, the red blood cells and the rest are white cells (leukocytes) and the tiny platelets (thrombocytes).

Red cells of which there are normally $5.10^6.mm^3$ are red because they contain the wonder molecule, the iron containing haemoglobin which has a great affinity for oxygen, the carriage of which is the main function of the red cell. Each red cell shoots around the body in 45 seconds, travelling through narrow capillaries which cause a distortion of the shape and a great deal of wear and tear so that the life of each cell is no more than 100 days during which the cell will have travelled over 700 miles. 1% of the red cells are replaced every day, though this rate will increase enormously after haemorrhage for example. The cell contains no nucleus and is little more than a haemoglobin containing sac, but does have a metabolism to maintain the integrity of the cellular membrane and to maintain a high level of potassium in the cell and a low level of sodium – the opposite of the plasma. The cells are manufactured in the bone marrow of the long bones, ribs, sternum and vertebrae from precursor cells under the influence of the hormone erythropoietin produced in the kidney and also requiring vitamin B12, folic acid, iron, copper and many other trace elements such as cobalt. It is now possible to supply the hormone erythropoietin to patients who do not make it themselves, such as those with severe renal failure who in years gone by were anaemic to such an extent that their lives were ruined by fatigue.

The remarkable, iron containing haemoglobin molecule has the capacity to combine rapidly and reversibly with both oxygen and carbon dioxide so that, in the lungs where it meets oxygen in large quantities, greater than the concentration of carbon dioxide, the molecules will become saturated with oxygen and give up CO_2 which is then breathed out. In the tissues, where the concentration of CO_2 is higher and the tissues are somewhat more acid, the oxygen leaves the haemoglobin and is available for tissue metabolism. CO_2 is taken up and is also dissolved in the plasma to go to the lungs for the cycle to be repeated. 1 gram of haemoglobin combines with 1.36ml of oxygen. Blood saturated with oxygen is bright pink and when desaturated after leaving the tissues, then it is blue. These colour changes can be seen clinically in

disease states in the lips particularly and are nowadays used routinely for monitoring in hospitals with a machine known as a pulse oximeter. Patients are blue with severe lung disease or with certain types of congenital heart disease (blue babies) and are said to be cyanosed. The term blue-blooded for royalty and aristocrats probably came from the appearance of the blue, desaturated blood in the veins of delicate hands of fair-skinned people who have never undertaken manual work. The converse of this is red-blooded with haemoglobin in its state of being fully saturated with oxygen, the implication of which is vigour and potency – usually of the male.

Carbon monoxide also has a tremendous infinity for haemoglobin, colouring it a brilliant cherry red, but this combination is irreversible and leaves no room for the combination with oxygen, so that even though the person is very pink, they severely lack oxygen and may very well die.

Anaemia is the cause of pale lips and especially, the conjunctivae of the eyes and may well present with lack of energy or stamina. A shortage of iron from dietary insufficiency or lack of vitamins (lack of B12 causes pernicious anaemia seen in the elderly), chronic loss of blood, for example from excessive menstrual loss, failure of the bone marrow, abnormal cell formation with the leukaemias or excessive break down of the red cells in various disease processes are common causes.

Iron is present in food in very small amounts so the body stores it for when it requires it in the form of ferritin in the liver, having been transported in the blood as a substance called transferrin which is a beta-globulin. Iron is also recovered from haemoglobin after the end of a ced cell's life and is treated in the same way.

The white blood cells, known as leukocytes are present in far fewer numbers than the red cells, (7000 per cubic mm of blood) but have a very interesting and important role in the defences of the body against tumours,bacteria, viruses and parasites. The granulocytes (polymorphonuclear leukocytes) are present in the greatest quantity (62%) and are manufactured in the bone marrow. These polymorphs are found in three different types, neutrophils, eosinophils and basophils depending on their appearance when stained and examined under the microscope. The lymphocytes (30%) and the monocytes (5%) come from the lymphoid tissue, lymph glands, spleen, thymus etc. The neutrophils seek out, ingest and destroy bacteria, a process known as phagocytosis and they also have the capability of changing shape and

squeezing themselves out of the blood vessels between the cells of the capillary wall and can move around in the tissues heading off to areas of inflammation. Their average life is only 6 hours so that it is necessary to manufacture more than 100 billion of these cells per day. The monocytes can also leave the blood and undertake phagocytosis in the tissues when they are known as macrophages. A collection of dead neutrophils, macrophages, bacteria and necrotic tissue all collected in a cavity is pus. In the healthy individual the production of white cells is in a steady state, but in the presence of infection in the body, the production is stepped up dramatically, probably triggered by agents released from these cells themselves.

Lymphocytes are a crucial part of the immune system, only 2% of which are in the blood at any one time – the rest being in the lymphoid tissue. The B-lymphocytes are responsible for the production of specific antibodies when challenged by a foreign protein and this is the basis for vaccination against various diseases. The T-lymphocytes are of 4 types each with specific functions to defend the body against viruses, fungi and certain bacteria such as TB as well as tumours and transplanted organs – helper T-cells (also called T4 cells), suppressor T-cells, cytotoxic T-cells (also called effector or killer cells) and memory T-cells. The T4 cells are those primarily invaded by the human immunodeficiency virus causing a reduction in numbers and thus allowing unusual opportunist infections to overwhelm.

The third type of cellular component in blood are the tiny platelets formed in the bone marrow from giant cells known as megakaryocytes. They have a life of only a few days and are responsible for forming a cellular plug to a damaged vessel wall by firstly sticking to the damaged and exposed collagen and then aggregating in huge numbers under the influence of chemicals produced by the platelets themselves to form a clot. Aspirin, as a side effect of its analgesic activity, reduces platelet function and is of value in preventing heart attacks and strokes if taken in a small dose on a daily basis.

A remarkable feature of blood is its ability to flow freely in the blood vessels, but if a small vessel is breached then it clots in an attempt to seal the hole and prevent further haemorrhage. This balance between haemorrhage and intravascular coagulation is an enormously complex system involving a huge number of factors. A loose plug formed from platelets is strengthened by a protein known as fibrin derived from fibrinogen in blood when a complex cascade of clotting reactions occurs after exposure of the blood to a

negatively charged surface such as damaged vessel lining or the glass of a test tube. The lining of blood vessels, known as the endothelium is probably responsible for both the smooth running of blood within them, but also for triggering the coagulation cascade when damaged. There are at least 12 known clotting factors, genetically controlled, some of which may be absent such as factor VIII in haemophilia and which is inherited as a sex-linked condition – carried via the female and appearing only in the male. A genetic mutation, supposedly from Queen Victoria allowed the condition to be passed into the Russian and Spanish Royal Families. The young son of Tsar Nicholas II and heir to the Russian throne was possibly the most famous sufferer from this disease. The condition is extremely painful and crippling with spontaneous bleeding episodes, especially into the joints which become progressively destroyed, unless treated with factor VIII extracts from human blood. Factor VIII is now also available in a heat-treated form to destroy any viruses (the viro-inactivated form) and in addition can nowadays be safely produced by recombinent DNA techniques.

Formation of clots within the vessel is known as thrombosis and can occur when blood flow is sluggish as in the veins of the legs when we are at rest for long periods of time, for example, lying in bed after surgery or on a long-haul flight. It also very commonly occurs if the lining of the artery has been damaged by fatty, atheromatous deposits as in the coronary arteries or the vessels going to the brain. Pieces of thrombus can occlude small vessels or break off to travel to a more distant organ, causing damage. A venous thrombosis in a leg or pelvic vein will travel to the heart, if dislodged and then to the lungs and may well cause death from pulmonary embolism – a common cause of death in the postoperative period unless precautions are taken to anticoagulate the blood with low doses of heparin.

On the surface of the red blood cells are specific antigens which react with blood from other people or animals. The antigens are similar and are known as A and B with some people having both (AB) and some people having neither (Group O) During infancy we develop antibodies to these antigens so that type A blood reacts with type B blood and O blood reacts with both and AB with neither. In addition to this ABO system there are many other antigens in human blood, such as the rhesus factor and many, many others, perhaps as many as 500 billion so that each human individual may be as unique in blood grouping as with finger prints. It is not known why such a

complex system has evolved. People with AB blood can be universal recipients because they do not have the AB antigens and group O (rhesus negative) blood can be given to anyone and although strict cross matching is always undertaken, in a dire emergency, uncrossmatched O-negative blood can be given with a fair degree of safety.

Fortunately for those of us who require a blood transfusion, simple cross-matching for the ABO and rhesus factors is sufficient in the vast majority of cases. When a transfusion is mismatched or the wrong blood has been administered in error, then the red cells aggregate ie. clump together and then break up releasing free haemoglobin into the blood stream which blocks up the kidneys if in sufficient quantity and the person may die or lose renal function. If a rhesus positive baby develops in a rhesus negative mother, without treatment, the mother starts to produce anti-rhesus antibodies which cross the placenta into the baby and destroy the developing red blood cells. At best the baby is born oedematous, jaundiced and severely anaemic but at worst dies in utero.

Stored, donated blood and blood products, such as washed and concentrated red cells, plasma, platelet concentrate and all the clotting factors are used on a regular basis in hospitals all over the world, particularly during major surgery, trauma and the treatment of the leukaemias (cancer of the white blood cells) and are completely invaluable.

Blood transfusion has saved countless lives, but it can also kill and maim. One of the greatest fears, even with meticulous crossmatching and testing for agents in the donated blood, has been the transmission of blood bourne diseases. The transmission of malaria, for example has been reported. Before routine testing, hepatitis B and C have been transmitted, the latter being very unpleasant with repeated bouts of a destructive hepatitis eventually leading in some cases to death from liver cancer. The infection of a cohort of sufferers from haemophilia, already a grossly disadvantaged population, with the Human Immunodeficiency virus (HIV) and the subsequent development of AIDS has been one of the tragedies of modern medicine. In addition to these well known viruses, there are also lesser known agents such as Cytomegalovirus (CMV) which many of us have been exposed to during our lives and are carriers with no pathological consequences to ourselves. If this CMV containing blood is transfused to a vulnerable person, such as a baby, or someone with an inadequate

immune system for example, with AIDS or after a transplant, then the CMV will cause a severe and intractable disease, affecting many organs particularly the nervous system as an encephalopathy, a necrotizing retinitis leading to blindness, a polyradiculopathy and multifocal neuropathy.

It is known that the virus particles are harboured within the white cell component of the stored blood (the so-called buffy coat) and if the blood is leukocyte depleted by a process in the Blood Bank, then the risks of transmission are greatly reduced. In the very near future, all transfused blood will be leukocyte depleted not only that destined for the very high risk groups, because there is also the fear that the prion, a sub-viral particle thought to be responsible for Creutzfeldt-Jakob disease, the human version of Bovine Spongiform Encephalopathy (BSE) could also possibly be transmitted in the white cells.

It is comforting for those of us involved in using blood products for patients that we can be confident that these agents are as safe as is humanly possible. Even though the risk of transmission of disease through blood transfusion is now very, very small indeed, the Medical Profession is anxious, as indeed is the Lay Public, that blood and blood products are only used if absolutely necessary and our criteria and protocols for use are becoming ever tighter.

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