# The
# Clinical
# Use
# of
# Blood

*in*
# Medicine
# Obstetrics
# Paediatrics
# Surgery & Anaesthesia
# Trauma & Burns

**World Health Organization**
**Blood Transfusion Safety**
GENEVA

# Contents

# Preface

Blood transfusion is an essential part of modern health care. Used correctly, it can save life and improve health. However, the transmission of infectious agents by blood and blood products has focused particular attention on the potential risks of transfusion.

The World Health Organization (WHO) has developed the following integrated strategy to promote global blood safety and minimize the risks associated with transfusion.

1   The establishment of nationally coordinated blood transfusion services with quality systems in all areas.

2   The collection of blood only from voluntary non-remunerated donors from low-risk populations.

3   The screening of all donated blood for transfusion-transmissible infections, including the human immunodeficiency virus (HIV), hepatitis viruses, syphilis and other infectious agents, and good laboratory practice in all aspects of blood grouping, compatibility testing, component preparation and the storage and transportation of blood and blood products.

4   A reduction in unnecessary transfusions through the appropriate clinical use of blood and blood products, and the use of simple alternatives to transfusion, wherever possible.

Many countries have established national blood transfusion services in accordance with WHO recommendations and guidelines. However, few countries have yet developed national policies and guidelines on the clinical use of blood or provide systematic education and training on the clinical use of blood and blood products.

In 1998, WHO published Recommendations on *Developing a National Policy and Guidelines on the Clinical Use of Blood*. This document was designed to assist Member States in developing and implementing national policies and guidelines and ensuring active collaboration between the blood transfusion service and clinicians throughout the management of patients who may require transfusion.

The Recommendations emphasize the importance of education and training in the clinical use of blood for all clinical and blood bank staff involved in

the transfusion process. The WHO team responsible for Blood Transfusion Safety (WHO/BTS) has therefore developed *The Clinical Use of Blood* to provide a set of comprehensive learning materials that can be used in undergraduate and postgraduate programmes, in-service training and continuing medical education programmes or for independent study by individual clinicians. The pocket handbook that accompanies the module is designed for quick reference by clinicians who need to make urgent decisions on transfusion.

*The Clinical Use of Blood* is not designed to replace conventional textbooks or to provide a definitive text on the clinical use of blood. Rather, its purpose is to provide an accessible learning tool that will assist prescribers of blood to make appropriate clinical decisions on transfusion and contribute to wider efforts to minimize the unnecessary use of blood and blood products.

The materials have been written by an international team of clinical and blood transfusion medicine specialists and have been reviewed by a wide range of specialists throughout the world. They have also been reviewed by the WHO Department of Reproductive Health and Research, the Department of Adolescent and Child Development, the Roll Back Malaria Initiative and the Human Genetics Programme. Nevertheless, clinical transfusion practice should always be based on national guidelines, where available. Users are therefore encouraged to adapt the information and guidance contained in the module and pocket handbook to conform with national guidelines and established procedures in their own countries.

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# Acknowledgements

# Introduction

*The Clinical Use of Blood* forms part of a series of learning materials developed by WHO/BTS in support of its global strategy for blood safety, outlined in the Preface.

In 1994, WHO published *Safe Blood and Blood Products*, a set of interactive learning materials designed for staff in blood transfusion services, public health laboratories and hospital blood banks who are responsible for the recruitment and selection of blood donors, and the collection, processing and issue of blood for transfusion. The materials contain four modules:

> Introductory Module: *Guidelines and Principles for Safe Blood Transfusion Practice*
>
> Module 1: *Safe Blood Donation*
>
> Module 2: *Screening for HIV and Other Infectious Agents*
>
> Module 3: *Blood Group Serology*

The modules are being used in many countries throughout the world, both as resource materials in pre-service and in-service training programmes and in distance learning programmes.

*Establishing a Distance Learning Programme in Blood Safety: A guide for programme coordinators* was published by WHO/BTS in 1998 to provide guidance for national blood programmes wishing to start a distance learning programme in blood safety using these materials.

## The Clinical Use of Blood

*The Clinical Use of Blood* complements the earlier learning materials produced by WHO/BTS by focusing on the clinical aspects of blood transfusion. It aims to show how blood and blood products can be used appropriately at all levels of the health care system in any country, without compromising standards of quality and safety.

It contains two components:

- A module of learning material designed for use in education and training programmes or for independent study by individual clinicians and blood transfusion specialists
- A pocket handbook for use in clinical practice.

### The module
The module provides a comprehensive guide to the use of blood and blood products and, in particular, ways of minimizing unnecessary transfusion. It is divided into three parts.

#### Part 1: Principles, products and procedures
Part 1 provides a foundation for clinical decisions on transfusion by introducing the principles of the appropriate use of blood. It provides a brief guide to normal physiology and the pathophysiology of acute and chronic blood loss and describes the characteristics of simple alternatives to transfusion (intravenous replacement fluids) as well as blood and blood products. It then gives a detailed guide to clinical transfusion procedures which can be used as the basis for the development of local standard operating procedures. Finally, it outlines the recognition and management of acute and delayed transfusion reactions.

#### Part 2: Transfusion in clinical practice
Part 2 begins with a brief summary of factors to consider when assessing and confirming the need for transfusion. It then focuses on six clinical areas in which transfusion may be necessary:

- General Medicine
- Obstetrics
- Paediatrics & Neonatology
- Surgery & Anaesthesia
- Trauma & Acute Surgery
- Burns

#### Part 3: The appropriate use of blood — putting it into practice
Part 3 explores how individual clinical and blood transfusion specialists can make a practical contribution to achieving the appropriate use of blood, both within their own hospitals and more widely.

### The pocket handbook
The pocket handbook summarizes key information from the module to provide a quick reference when an urgent decision on transfusion is required. It is important to follow national guidelines on the clinical use of blood if they differ in any way from the guidance contained in the module and handbook. You may therefore find it useful to add your own notes on national guidelines or your own experience in prescribing transfusion.

## Using the module
The module is designed for prescribers of blood at all levels of the health system, particularly clinicians and senior paramedical staff at first referral level (district hospitals) in developing countries, including:

- Clinical specialists
- Blood transfusion specialists
- District medical officers

- General practitioners working in isolation
- Postgraduate medical officers (registrars)
- Junior doctors
- Medical students
- Senior paramedical staff, such as nurse anaesthetists.

It will also be a useful resource for trainers in medical schools, university teaching hospitals, schools of nursing and continuing medical education programmes.

### Aims

The aim of the module is to assist you to:

1   Update your knowledge and understanding about blood, blood products and alternatives to blood transfusion.

2   Evaluate your own clinical practice in relation to the use of blood and blood products.

3   Minimize unnecessary transfusion through the appropriate clinical use of blood and blood products.

4   Evaluate the current availability and usage of blood, blood products and alternatives to blood transfusion in the hospital in which you work.

5   Identify ways of improving systems and procedures for the use of blood and blood products in your own hospital.

6   Plan ways of implementing any improvements you have identified as being necessary, both in your own practice and more widely.

7   Contribute to the promotion of strategies for the prevention and treatment of conditions leading to anaemia in order to reduce the need for blood transfusion.

### Key points

Each section begins with a list of important points to remember when making a clinical decision about the use of blood and blood products.

### Learning outcomes

At the beginning of each section, there is a list of learning outcomes. These outline what you should be able to do when you have completed that section. They provide a guide for your learning and will help you to review your own progress.

### Activities

As you work through each section, you will be asked to complete a number of activities that are designed to assist you to apply the principles of the appropriate use of blood in your own clinical environment. Some activities use a case study approach to strengthen your own clinical decision-making. Use these activities as a basis for discussion with members of your clinical team, perhaps as a starting point for developing local guidelines on clinical transfusion practice, and as an opportunity for teaching.

Other activities suggest that you evaluate different aspects of the clinical use of blood in your hospital and consider how approaches and procedures might be modified or improved in order to minimize unnecessary transfusion. Since the activities focus directly on your own clinical setting, your responses will largely be determined by local needs and conditions. Use them as a basis for discussion with colleagues about any measures that are needed in your hospital to improve the appropriate clinical use of blood, including the use of simple alternatives to transfusion, wherever possible.

The final section, Section 15: *Making It Happen: What can I do?* draws together your work on the activities. It provides guidance on conducting a review of records relating to transfusion and proposes working towards the establishment of a hospital transfusion committee and the development of guidelines on clinical transfusion practice, if they do not yet exist. As you work through the module, you should find it helpful to keep notes on your work on the activities and to use them to begin to prepare a plan of action for the appropriate clinical use of blood in your hospital.

## The evidence base for clinical practice

*The Clinical Use of Blood* has been prepared by an international team of clinical and blood transfusion specialists and has been extensively reviewed by relevant WHO departments and by Critical Readers from a range of clinical disciplines from all six of the WHO regions. It was also evaluated in two inter-regional workshops held in Zimbabwe in April 1997 and Cyprus in September 1997.

The content reflects the knowledge and experience of the contributors and reviewers. Since the evidence for effective clinical practice is constantly evolving, however, you are encouraged to consult up-to-date sources of information such as the Cochrane Library, the National Library of Medicine database and the WHO Reproductive Health Library.

WHO would be pleased to receive comments and suggestions regarding the materials and experience with their use. This will be of considerable value in the preparation of any future editions.

**The Cochrane Library.** Systematic reviews of the effects of health care interventions, available on diskette, CD-ROM and via the Internet. There are Cochrane Centres in Africa, Asia, Australasia, Europe, North America and South America. For information, contact: UK Cochrane Centre, NHS Research and Development Programme, Summertown Pavilion, Middle Way, Oxford OX2 7LG, UK. Tel: +44 1865 516300. Fax: +44 1865 516311. www.cochrane.org

**National Library of Medicine**. An online biomedical library, including Medline which contains references and abstracts from 4300 biomedical journals and Clinical Trials which provides information on clinical research studies. National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894, USA. www.nlm.nih.gov

**WHO Reproductive Health Library**. An electronic review journal focusing on evidence-based solutions to reproductive health problems in developing countries. Available on CD-ROM from Reproductive Health and Research, World Health Organization, 1211 Geneva 27, Switzerland. www.who.int

# Part 1

# Principles, products and procedures

# 1

# The appropriate use of blood and blood products

## Key points

1   The appropriate use of blood means the transfusion of safe blood products only to treat a condition leading to significant morbidity or mortality that cannot be prevented or managed effectively by other means.

2   Transfusion carries the risk of adverse reactions and transfusion-transmitted infection. Plasma can transmit most of the infections present in whole blood and there are very few indications for its transfusion.

3   Blood donated by family/replacement donors carries a higher risk of transfusion-transmissible infection than blood donated by voluntary non-remunerated donors. Paid blood donors generally have the highest incidence and prevalence of transfusion-transmissible infections.

4   Blood should not be transfused unless it has been obtained from appropriately selected donors, has been screened for transfusion-transmissible infections and tested for compatibility between the donor's red cells and the antibodies in the patient's plasma, in accordance with national requirements.

5   The need for transfusion can often be avoided by:
   ■   The prevention or early diagnosis and treatment of anaemia and conditions that cause anaemia
   ■   The correction of anaemia and the replacement of depleted iron stores before planned surgery
   ■   The use of simple alternatives to transfusion, such as intravenous replacement fluids, which are safer, less expensive and may be equally effective
   ■   Good anaesthetic and surgical management.

## Introduction

Blood transfusion can be a life-saving intervention. However, like all treatments, it may result in acute or delayed complications and carries the risk of transfusion-transmitted infections, including HIV, hepatitis viruses, syphilis and Chagas disease.

The transmission of infectious agents by blood and blood products has focused particular attention on the risks of transfusion. The safety and effectiveness of transfusion depend on two key factors:

■ A supply of blood and blood products that are safe, accessible at reasonable cost and adequate to meet national needs

■ The appropriate clinical use of blood and blood products.

This can only be achieved through a coordinated approach in which the blood transfusion service and clinicians work in close collaboration to manage the components of the transfusion process for which they are each responsible.

Section 1 explores why blood is often used unnecessarily, the potential risks associated with transfusion and the factors that determine whether the appropriate use of blood is possible.

## Learning outcomes

When you have completed this section, you should be able to:

1  Explain the potential risks associated with transfusion.

2  Assess the safety of the blood supplies available in your hospital.

3  Identify the prerequisites for the appropriate clinical use of blood.

4  Identify ways of minimizing the need for transfusion.

## 1.1 Appropriate and inappropriate transfusion

In this module, the appropriate use of blood products is defined as:

> 'The transfusion of safe blood products to treat a condition leading to significant morbidity or mortality that cannot be prevented or managed effectively by other means.'

Used appropriately, blood transfusion can save life and improve health. However, evidence from every region of the world indicates considerable variations in patterns of clinical blood use between different hospitals, different clinical specialties and even between different clinicians within the same team. This suggests that blood and blood products are often used inappropriately.

Like all treatments, transfusion carries potential risks for the recipient and is often unnecessary for the following reasons.

1 The need for transfusion can often be avoided or minimized by the prevention or early diagnosis and treatment of anaemia and conditions that cause anaemia.

2 Blood is often unnecessarily given to raise a patient's haemoglobin level before surgery or to allow earlier discharge from hospital. These are rarely valid reasons for transfusion.

3 Transfusions of whole blood, red cells or plasma are often given when other treatments, such as the infusion of normal saline or other intravenous replacement fluids would be safer, less expensive and equally effective for the treatment of acute blood loss.

4 Patients' transfusion requirements can often be minimized by good anaesthetic and surgical management.

5 If blood is given when it is not needed, the patient receives no benefit and is exposed to unnecessary risk.

6 Blood is an expensive, scarce resource. Unnecessary transfusions may cause a shortage of blood products for patients in real need.

### The risks of transfusion

In some clinical situations, transfusion may be the only way to save life or rapidly improve a serious condition. However, before prescribing blood or blood products for a patient, it is always essential to weigh up the risks of transfusion against the risks of not transfusing.

#### Red cell transfusion

1 The transfusion of red cell products carries a risk of serious haemolytic transfusion reactions.

2 Blood products can transmit infectious agents, including HIV, hepatitis B, hepatitis C, syphilis, malaria and Chagas disease to the recipient.

3 Any blood product can become contaminated with bacteria and very dangerous if it is manufactured or stored incorrectly.

**Plasma transfusion**

1 Plasma can transmit most of the infections present in whole blood.

2 Plasma can also cause transfusion reactions.

3 There are few clear clinical indications for plasma transfusion. The risks very often outweigh any possible benefit to the patient.

## 1.2  Blood safety

The risks associated with blood transfusion depend on the following factors.

1 The incidence and prevalence of transfusion-transmissible infections in the blood donor population.

2 The effectiveness of the blood donor education and recruitment programme and procedures for donor selection and screening, including the deferral or exclusion of unsuitable donors.

3 The quality of screening of all donated blood for transfusion-transmissible infections.

4 The quality of blood grouping, compatibility testing, component preparation and the storage and transportation of blood products.

5 The extent to which blood and blood products are prescribed only when there is no alternative to transfusion for the particular patient.

6 The reliability of the system for ensuring that patients receive blood that is compatible with their blood group, red cell antibodies and other special requirements.

The quality and safety of all blood and blood products must be assured throughout the process from the selection of blood donors through to the administration of the product to the patient. This requires a planned programme of regular blood donations by voluntary non-remunerated donors, the screening and processing of donated blood by trained staff working to national standards and the appropriate use of blood. It also requires:

1 National standards and specifications for blood products and a system of good manufacturing practice to ensure these standards are maintained at all times.

2 The development and correct use of standard operating procedures.

3 The training of all blood transfusion service staff and clinicians to develop and maintain their knowledge and skills.

4 Monitoring and evaluation (audit) to check that the correct procedures are being used correctly by all staff at all times.

5 An effective system of independent inspection and accreditation of the facilities that collect, process and distribute blood products.

Whatever the local system for the collection, screening and processing of blood, clinicians must be familiar with it and understand any limitations that it may impose on the safety or availability of blood.

## Blood donors

Resolution 28.72 of the World Health Assembly established the principle that blood donation should be voluntary and non-remunerated (unpaid). This policy has been adopted by many countries for the collection of whole blood. In some countries, however, the supply of plasma for the manufacture of plasma derivatives is still based on commercial programmes in which individuals receive payment for regular collections of plasma by plasmapheresis.

A system of voluntary non-remunerated blood and plasma donation is safer because the incidence and prevalence of transfusion-transmissible infections is invariably lower than among family or 'replacement' donors and paid donors. It also permits the use of donor education and selection procedures that encourage unsuitable donors to self-defer or self-exclude. It therefore enables more cost-effective use to be made of limited resources because fewer units of blood have to be discarded after screening because of evidence of infectious disease markers.

### Voluntary non-remunerated blood donors

**voluntary non-remunerated donor**: A donor who gives blood freely and voluntarily without receiving money or any other form of payment.

Voluntary non-remunerated blood donors give blood of their own free will and receive no money or other payment that could be considered a substitute for money. Their primary motivation is to help unknown recipients and *not* to obtain any personal benefit.

The principal reasons for promoting regular voluntary non-remunerated blood donation are as follows.

1 Voluntary non-remunerated donors have a lower incidence and prevalence of transfusion-transmissible infections than family/ replacement donors or paid donors. They have no financial incentive to conceal information (such as high-risk sexual behaviour or a history of injecting drug use) that may have exposed them to an infection that can be transmitted by transfusion.

2 Voluntary non-remunerated donors are more likely to be willing to donate blood regularly, which is important in maintaining safe and adequate supplies of blood.

3 The lowest incidence and prevalence of transfusion-transmissible infections is generally found among regular voluntary non-remunerated donors rather than first-time or occasional donors.

4 Regular donors are not financially motivated to donate too frequently and so are not placed at risk of anaemia through the depletion of their iron stores.

5 Regular donors are also more likely to respond to an appeal for blood donors during an emergency because they have already expressed a commitment to voluntary blood donation.

Module 1: *Safe Blood Donation* in the series of WHO learning materials, *Safe Blood and Blood Products*, describes how to develop a system of voluntary non-remunerated blood donation.

## Family or 'replacement' blood donors

In the absence of a strong national voluntary blood donation programme, many countries rely heavily on the family or friends of patients to act as replacement donors: that is, to give blood to replace the blood stocks used for those patients. However, research findings from a number of countries indicate that blood from family or replacement donors is found to be unsuitable more often than blood from voluntary non-remunerated donors and that it therefore presents a potentially greater risk to the safety of the blood supply.

**family or replacement donor**: A donor who gives blood when it is required by a member of the patient's family or community. This may involve a hidden paid donation system in which the donor is paid by the patient's family.

A reliance on family or replacement blood donors has the following disadvantages.

1 Members of the patient's family are under pressure to donate blood and may conceal potentially important information about their health status, particularly the risk of transmitting an infectious disease.

2 Relatives who cannot find suitable or willing donors within the family may seek replacement donors who are prepared to give their blood for payment. Donors who are paid by the patient's family are less likely to reveal any reasons why they may be unsuitable as donors.

3 There may be pressure to transfuse the blood that has been provided by replacement donors, even if the transfusion is eventually clinically unnecessary, because the family may feel that their blood should be used only for their relative.

4 In a replacement system of blood donation, the blood given to patients will not necessarily be replaced in type or quantity. As a result, the blood needs of the community may not be met adequately.

Where family/replacement donors are used, it is essential that the following donor selection and screening procedures are maintained.

1 All donors should be screened prior to donation to ensure that they meet national criteria for low-risk donors.

2 Donors should be informed that their blood will be used to replace the stock in the blood bank and will not necessarily be given to their relative or any other named patient.

3 The selection and screening of donors should be under the control of blood transfusion service staff who are familiar with the correct procedures.

## Commercial or paid blood donors

Commercial or professional donors receive money or other rewards (which can be exchanged for money) for the blood that they donate. They are usually motivated by what they will receive for their blood rather than by a wish to help others. They often give blood regularly and may even have a contract with a blood bank to supply blood for an agreed fee. Alternatively, they may sell their blood to more than one blood bank or approach patients' families and try to sell their services as replacement donors.

**commercial or professional donor**: A donor who gives blood for money or other form of payment.

Paid donors present a major risk to the safety of the blood supply for the following reasons.

1   Paying donors to give blood undermines the voluntary non-remunerated system of blood donation which is the foundation of a safe blood supply.

2   The highest incidence and prevalence of transfusion-transmissible infections are generally found among commercial or paid donors.

3   They are often undernourished, in poor health and may donate their blood more frequently than is recommended. This may have harmful effects on their own health as well as presenting a risk to the recipients of their blood or providing little or no benefit.

4   If donors are paid, it is usually necessary to charge patients for the blood they receive. Poor families may not be able to afford to pay for blood when they need it.

5   The ethical basis of paying individuals to provide blood (or any tissue or organ) is a cause of concern in many countries. The commercial procurement of blood, plasma and organs often leads to serious abuses and may result in adverse consequences. These include the transmission of serious infections both to patients and to the donors themselves through improper collection methods.

### Managing with limited supplies of blood

When blood is in short supply, or if it is not economic to maintain a blood bank, there can be serious pressure to take short cuts in providing blood for individual patients: for example, the correct selection criteria for donors may be ignored or virological testing may be rushed or omitted. If this occurs, you must be particularly aware that the risks of transfusion are increased and must take responsibility for deciding whether the transfusion is clinically justified.

One way of minimizing these problems is for the hospital blood bank to maintain a list of donors who can be contacted in an emergency and who agree to be tested regularly so that their blood is more likely to be safe when collected and used in an emergency. Rapid screening tests are suitable for testing blood donated in this kind of situation. In the case of unavoidable delay in the delivery of blood, the infusion of intravenous replacement fluids or some form of autologous transfusion or blood salvage (see Section 12: *Surgery & Anaesthesia*) may be used.

## Screening for transfusion-transmissible infections

The following infectious agents are transmissible by blood transfusion:

- Human immunodeficiency virus (HIV)
- Hepatitis B
- Hepatitis C
- Syphilis
- Chagas disease
- Malaria.

**transfusion-transmissible infection**: An infection that is potentially capable of being transmitted by blood transfusion.

**transfusion-transmitted infection**: An infection that has been transmitted by blood transfusion.

**incidence**: The proportion of a defined population becoming newly infected by an infectious agent within a specific period of time.

**prevalence**: The proportion of a defined population that are infected with an infectious agent at any particular time.

**window period**: The period of time between the moment of infection by a virus (e.g. HIV) and the development of detectable antibodies.

Every prescriber of blood should be aware of the occurrence, distribution and spread of transfusion-transmissible infections in order to be able to make informed judgements about the risks and benefits of transfusion.

New infections are called 'incident' infections. The term **incidence** describes the frequency of new infections in a defined population within a defined period of time. The term **prevalence** describes the proportion of a population who, at a given time, have evidence of the infection. The prevalence of an infectious agent, such as HIV antibody, can tell us what has already happened. The incidence tells us what is happening now.

The **window period** is the period during the development of a new infection in a previously non-infected person in which the person's blood may be very infectious, but the detectable antibody has not yet appeared. The probability of window period infection is very high in high-prevalence populations at risk of infection. However, the prevalence in the population may be low, at least for a time, because many or most of those at risk will not yet have been exposed to infection.

Individuals exposed to infection often become immune and resistant to reinfection with the same organism. However, some infections such as HIV, hepatitis B and hepatitis C remain present in the blood; this is often called a 'chronic carrier state'. The blood of individuals who are chronic carriers will transmit the infection to others.

Quality assurance and good laboratory practice are therefore essential in all areas of blood screening.

1   Every unit of donated blood should be screened for transfusion-transmissible infections using the most appropriate and effective tests, in accordance with national policies and the prevalence of the infection in the potential blood donor population.

2   All donated blood should be screened for:
   ■   HIV-1 and HIV-2 (anti-HIV-1, anti-HIV-2) antibody
   ■   Hepatitis B (HBsAg) surface antigen
   ■   *Treponema pallidum* antibody (syphilis).

3   Where possible, all donated blood should also be screened for:
   ■   Hepatitis C
   ■   Chagas disease: in countries where it is common
   ■   Malaria: in low-prevalence countries when donors have travelled to malarial areas.

4   No blood or blood product should be released for transfusion until all nationally required tests are shown to be negative.

**Other than in the most exceptional life-threatening situations, blood should not be issued for transfusion unless it has been obtained from appropriately selected donors and has been screened for transfusion-transmissible infections, in accordance with national requirements.**

Module 2: *Screening for HIV and Other Infectious Agents* in the series of WHO learning materials, *Safe Blood and Blood Products*, describes how to develop an effective programme of screening for transfusion-transmissible infections.

## Blood grouping and compatibility testing

Every hospital should have standard operating procedures to ensure that blood components to be transfused are compatible with the patient's red cells and the antibodies in the patient's plasma. Blood grouping and compatibility testing are described in detail in Module 3: *Blood Group Serology* in the series of WHO learning materials, *Safe Blood and Blood Products*.

### ACTIVITY 1

*The aim of the first activity is to help you to assess the safety of the blood products available for transfusion in your hospital and to weigh up the benefits and risks of transfusion for individual patients.*

*Talk to blood bank staff to find out as much information as you can about the following questions.*

**1  Prevalence of infectious agents**
*What is the prevalence of HIV, hepatitis B, hepatitis C, syphilis and any other transfusion-transmissible infections that are significant in your country among:*

- *The blood donor population*
- *The general population of the same age distribution?*

**2  Types of blood donor**
*How much of the blood supplied to your hospital is provided by:*

- *Voluntary non-remunerated donors*
- *Family/replacement donors*
- *Paid donors?*

**3  Screening for transfusion-transmissible infections**
*How effective are the procedures for screening the blood that is supplied to your hospital?*

- *What tests for infectious disease markers are performed on donated blood supplied to your hospital or collected by the hospital blood bank?*
- *Are these tests always performed?*
- *Are there any factors that might affect the effectiveness of screening for infectious agents, such as irregular or inadequate supplies of test kits or poor storage conditions?*

**4  Compatibility testing**
- *Is blood routinely tested for compatibility before its issue for transfusion?*

**5 Other factors influencing the safety of the blood supply**

■ *Is there an adequate, reliable supply of sterile disposable equipment, including needles, syringes and intravenous infusion equipment?*

■ *Are there facilities for its safe disposal by incineration to prevent theft and re-use?*

Section 6: *Clinical Transfusion Procedures* covers various aspects of blood safety in more detail. Section 7: *Adverse Effects of Transfusion* focuses on acute and delayed complications of transfusion, including transfusion-transmitted infections.

## Whole blood and blood components

**The majority of life-saving transfusion requirements can be met safely and effectively with whole blood.**

The provision of a safe and adequate supply of blood and blood products for transfusion is expensive. Even the production of whole blood involves significant capital expenditure on laboratory facilities, equipment for screening for infectious agents and refrigeration units. In addition, there are substantial recurrent costs, particularly for trained staff and essential supplies, such as blood collection packs and testing reagents. *Costing Blood Transfusion Services* (WHO 1998) provides a step-by-step guide to carrying out a detailed costing analysis of blood transfusion services.

Blood component separation and the collection of plasma and platelets by apheresis are more expensive than the processing of whole blood, and plasma derivative production involves very large capital investment and recurrent costs.

Blood component production and the availability of plasma derivatives enable a wider range of treatments to be provided for more patients and are usually more cost-effective. However, it is important to remember that the use of whole blood may be more cost-effective where resources are limited.

## 1.3 Prerequisites for the appropriate clinical use of blood

Transfusion always carries potential risks for the recipient, but these can be minimized by the appropriate use of blood.

The decision to transfuse blood or blood products should always be based on a careful assessment of clinical and laboratory indications that a transfusion is necessary. However, while responsibility for this decision must ultimately rest with individual prescribers of blood, the appropriate use of blood and blood products cannot be achieved in isolation from other elements of the health system. It is only possible as part of an integrated strategy in which the following elements are in place.

1   A national policy on the clinical use of blood, with appropriate supportive regulations.

2   A commitment by health authorities, health care providers and clinicians to the prevention, early diagnosis and effective treatment of conditions that could lead to the need for transfusion by strengthening public health and primary health care programmes.

3   A nationally-coordinated blood transfusion service that is able to provide safe, adequate and timely supplies of blood and blood products.

4   The promotion and availability of:
   ■ Simple alternatives to transfusion: intravenous replacement fluids (crystalloids and colloids) for the correction of hypovolaemia
   ■ Pharmaceuticals and medical devices to minimize the need for transfusion
   ■ Sterile disposable equipment for blood samples, injection and infusion.

5   National guidelines on the clinical use of blood to aid prescribers of blood in their clinical decisions about transfusion. These should include:
   ■ Standardized blood request form
   ■ Model blood ordering schedule
   ■ Standard operating procedures for all stages of the clinical transfusion process
   ■ Information on the specific characteristics of blood products, plasma derivatives, intravenous replacement fluids and pharmaceuticals
   ■ Clinical and laboratory indications for transfusion.

6   A National Committee on the Clinical Use of Blood.

7   A hospital transfusion committee in every hospital where blood and blood products are used.

8   Education and training in the effective clinical use of blood and blood products for all clinical and blood bank staff involved in the transfusion process.

9   Effective clinical transfusion practice in accordance with national guidelines on the clinical use of blood.

10  Monitoring and evaluation of the clinical use of blood.

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### ACTIVITY 2

*How far is the appropriate clinical use of blood and blood products possible in your hospital? Look back at the list of elements required to achieve it.*

*Are they all in place in your health district? If not, identify any of these elements that are lacking.*

## 1.4 Principles of clinical transfusion practice

Transfusion is only one part of the patient's management. It is essential to remember that the need for transfusion can often be minimized by the following means.

1 The prevention or early diagnosis and treatment of anaemia and the conditions that cause anaemia. The patient's haemoglobin level can often be raised by iron and vitamin supplementation without the need for transfusion. Red cell transfusion is needed only if the effects of chronic anaemia are severe enough to require rapid raising of the haemoglobin level.

2 The correction of anaemia and replacement of depleted iron stores before planned surgery.

3 The use of intravenous fluid replacement with crystalloids or colloids in cases of acute blood loss.

4 Good anaesthetic and surgical management, including:
- Using the best anaesthetic and surgical techniques to minimize blood loss during surgery
- Stopping anticoagulants and anti-platelet drugs before planned surgery, where it is safe to do so
- Minimizing the blood taken for laboratory use, particularly in children
- Salvaging and reinfusing surgical blood losses
- Using alternative approaches such as desmopressin, aprotinin or erythropoetin.

Transfusion, when required, cannot be isolated from other aspects of patient management. Figure 1.1 summarizes the key principles of clinical transfusion practice.

### ACTIVITY 3

*Are any national or local guidelines on the clinical use of blood available in your hospital? If so, do you use them to guide your own decisions about prescribing blood?*

*If no guidelines exist, try to find out whether any have been developed elsewhere in your country that could be used or adapted in your hospital.*

As a prescriber of blood and blood products, you can influence the way in which they are used. The improvements you can make in your own practice and the practice of those with whom you work can have a significant effect on minimizing the risks of transfusion for your patients.

*Figure 1.1: Principles of clinical transfusion practice*

**KEY PRINCIPLES**

1  Transfusion is only one part of the patient's management.

2  Prescribing should be based on national guidelines on the clinical use of blood, taking individual patient needs into account.

3  Blood loss should be minimized to reduce the patient's need for transfusion.

4  The patient with acute blood loss should receive effective resuscitation (intravenous replacement fluids, oxygen, etc.) while the need for transfusion is being assessed.

5  The patient's haemoglobin value, although important, should not be the sole deciding factor in starting transfusion. This decision should be supported by the need to relieve clinical signs and symptoms and prevent significant morbidity and mortality.

6  The clinician should be aware of the risks of transfusion-transmissible infection in the blood products that are available for the individual patient.

7  Transfusion should be prescribed only when the benefits to the patient are likely to outweigh the risks.

8  The clinician should record the reason for transfusion clearly.

9  A trained person should monitor the transfused patient and respond immediately if any adverse effects occur.

Some factors in ensuring the appropriate clinical use of blood, such as the effectiveness of antenatal care programmes or the availability of intravenous replacement fluids, will be beyond your immediate control. However, this module is designed to help you identify ways in which you can make an impact on clinical transfusion practice beyond the care of your own patients. However small your contribution, *you* can play a part in creating the conditions in which the appropriate clinical use of blood is possible.

# 2

# Blood, oxygen and the circulation

## Key points

1 Blood is composed of:
- Red cells containing haemoglobin whose primary function is to store and transport oxygen to the tissues
- White blood cells whose principal role is to identify, destroy and remove any foreign material that has entered the body
- Platelets which play a major role in the blood clotting mechanism.

2 In order to ensure a constant supply of oxygen to the tissues and organs of the body, four important steps must take place:
- Oxygen transfer from the lungs into the blood plasma
- Oxygen storage on the haemoglobin molecule in the red blood cells
- Oxygen transport to the tissues of the body via the circulation
- Oxygen release from the blood to the tissues, where it can be utilized.

3 The overall supply of oxygen to the tissues is dependent on:
- Haemoglobin concentration
- Degree of saturation of haemoglobin with oxygen
- Cardiac output.

## Introduction

This section highlights certain aspects of circulatory and respiratory physiology that have a direct bearing on the clinical use of blood products. It is only through having a sound knowledge of the physiological principles and mechanisms that operate in health that accurate and informed clinical decisions can be made when treating disease.

Section 2 is not intended to be a comprehensive review of physiology and you are advised to supplement the information given here by consulting more formal texts. However, it will provide a source of reference for material discussed in later sections.

## Learning outcomes

When you have completed this section, you should be able to:

1 Describe how the different body fluids are organized and distributed.

2 Explain the composition and functions of blood.

3 Describe the processes involved and the role of blood in maintaining a constant supply of oxygen to the tissues of the body.

## 2.1 Body fluids and compartments

### Fluids

Water is a major constituent of the body and comprises approximately 60% of an adult's body weight and as much as 70–80% of a child's weight. The remaining body weight is taken up with proteins, fats, sugars and minerals which, when distributed within the water, form the body fluids.

### Compartments

The body fluids are contained in two compartments:

- Within the cells in the intracellular fluid compartment (ICF)
- Outside the cells in the extracellular fluid compartment (ECF).

The extracellular fluid compartment is itself divided into two. It contains:

- Circulating blood plasma, which is confined to the vascular system *and*
- Interstitial fluid which lies outside the blood vessels and surrounds the cells.

The different fluid compartments are separated from each other by membranes that are formed either by the cell walls separating the intracellular and interstitial fluids, or the capillary walls separating plasma from interstitial fluid. Specialized capillary walls in the skin, gut, kidneys and lungs also separate plasma from the body's external environment. See Figure 2.1.

*Figure 2.1: Body fluid compartments*
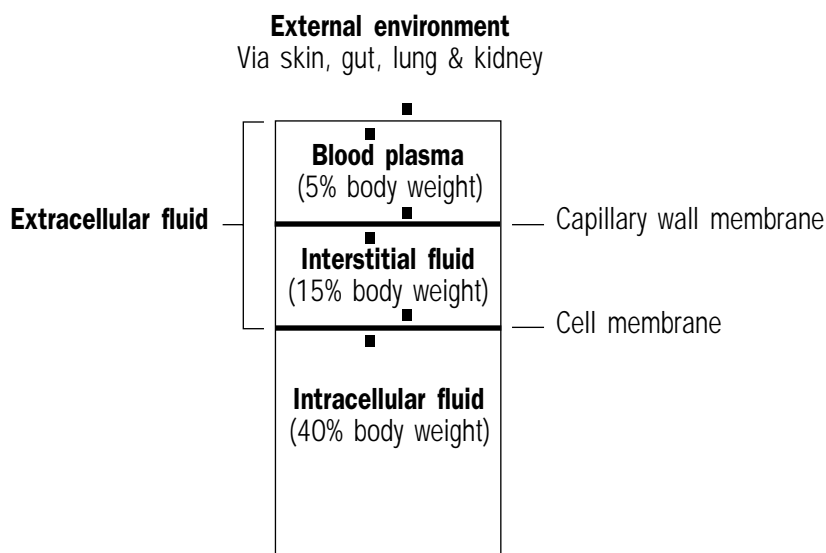


### Fluid movement

There are considerable differences in fluid composition in each of the compartments, as shown in Figure 2.2. However, although the composition of each fluid is rigorously maintained, there is a continuous movement of large amounts of water and other substances between the compartments.

*Figure 2.2: Electrolyte composition of intracellular and extracellular fluids*

| | Plasma (mmol/L) | Interstitial fluid (mmol/L) | Intracellular fluid (mmol/L) |
|---|---|---|---|
| $Na^+$ | 142 | 144 | 10 |
| $K^+$ | 4 | 4 | 160 |
| $Ca^{2+}$ | 2.5 | 1.25 | 1.5 |
| $Mg^{2+}$ | 1 | 0.5 | 13 |
| $Cl^-$ | 102 | 114 | 2 |
| $HCO_{3-}$ | 26 | 30 | 8 |
| $PO_4^{2-}$ | 1 | 1 | 57 |
| $SO_4^{2-}$ | 0.5 | 0.5 | 10 |
| Organic acid | 6 | 5 | 0 |
| Protein | 16 | 2 | 55 |

The type and amount of a substance moving between compartments largely depends on the nature of the membrane separating them and on the forces applied to the substances.

## Forces

There are many varied forces producing movement of substances across membranes. They include:

1 **Diffusion**, in which a substance passes from an area where it has high concentration to an area of lower concentration.

2 **Filtration**, where fluid is forced through a membrane under pressure.

3 **Active transport**, where certain substances are specifically 'pumped' across membranes.

4 **Osmosis**, the process in which freely moving substances, such as water, are drawn across a membrane towards a region where there is a higher concentration of molecules to which the membrane is impermeable. These molecules are termed 'osmotically active'. In body fluids, they include the electrolytes sodium, potassium and chloride, and the proteins. It is the relative concentration of osmotically active particles on either side of the membrane that influences water movement due to osmosis.

## Composition

Plasma and interstitial fluid have a very similar electrolyte composition; the ions of sodium and chloride are the main extracellular electrolyte. However, they differ markedly in their protein content, with plasma containing much greater amounts of protein than interstitial fluid. These are known as the plasma proteins. Plasma proteins are composed of a variety of large molecules to which membranes are normally impermeable, the most abundant of which is albumin.

Intracellular fluid also contains high concentrations of protein, but it differs from plasma and interstitial fluid in that its principal electrolyte is potassium, as shown in Figure 2.2.

## Regulation

Plasma contains many more osmotically active proteins than interstitial fluid. There is therefore a strong tendency for water to move by osmosis into the plasma from the interstitial fluid. This is called the oncotic pressure.

However, there is also a tendency for water to cross in the opposite direction from plasma to interstitial fluid due to the blood pressure in the capillary causing filtration of water across the membrane. This is called the hydrostatic pressure.

The balance between these two opposing forces, oncotic and hydrostatic pressures, determines the net movement of water across the capillary wall and thus has a major influence on the volume of plasma, as shown in Figure 2.3.

*Figure 2.3: Fluid movement across capillary wall*
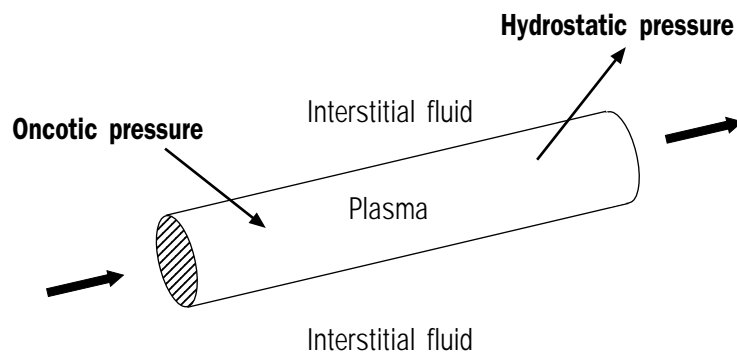


The regulation of the water content and volume of the intracellular compartment is also heavily dependent on osmotic forces, but these are primarily the result of differences in the concentrations of sodium and potassium between the interstitial and intracellular fluids. These concentrations are actively controlled by the sodium-potassium pump in the cell membrane.

## 2.2   Blood

Blood is composed of plasma in which the following highly-specialized cells are suspended (see Figure 2.4):

- ■   Red blood cells (erythrocytes)
- ■   White blood cells (leucocytes)
- ■   Platelets.

All blood cells develop from stem or precursor cells that are produced principally in the bone marrow.

Plasma contains proteins, chemical substances, coagulation factors and numerous metabolic substances. It is capable of clotting.

Figure 2.4: Composition of blood
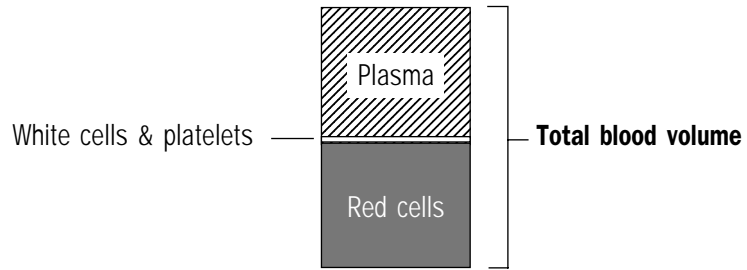


Total blood volume

**Total blood volume**

The volume occupied by both cells and plasma in the vascular system is called the total blood volume.

In an adult, this is approximately 7% of body weight or 70 ml/kg. For example, a 60 kg man would have a blood volume of 70 x 60, which is 4200 ml.

As children have a higher water content, the blood volume is calculated to be 8% of body weight or 80 ml/kg.

It is higher still in the neonate and is calculated to be 85–90 ml/kg (see Figure 2.5).

Figure 2.5: Calculating blood volume

| Age group | Blood volume |
|-----------|--------------|
| Neonates | 85–90 ml/kg |
| Children | 80 ml/kg |
| Adults | 70 ml/kg |

**ACTIVITY 4**

1  *Calculate the blood volumes in adults with the following body weights:*
   - *40 kg*
   - *50 kg*
   - *60 kg*
   - *70 kg*
   - *80 kg*
   - *90 kg*
   - *100 kg*

2  *Repeat this exercise for children whose weights range from 10 kg to 40 kg.*

**Red blood cells**

Red blood cells (erythrocytes) are produced in the bone marrow under the controlling influence of the renal hormone erythropoietin. After entering the bloodstream, they have a life-span of approximately 120 days before being

broken down in the reticuloendothelial system. The red cells contain the iron-containing pigment haemoglobin, whose primary function is to store and transport oxygen.

The haemoglobin molecule is made up of four sub-units, each of which is composed of an iron-containing ring surrounded by a peptide chain. The haemoglobin molecule therefore has four peptide chains which exist in two pairs, as shown in Figure 2.6.

*Figure 2.6: Normal haemoglobin molecule (HbA)*
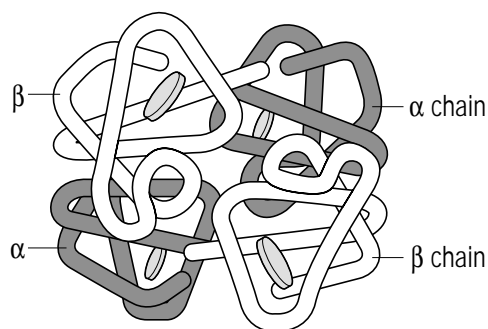


In normal adult haemoglobin (HbA), two of these chains are of one type, alpha-chains, and two of another, beta-chains. Each sub-unit of haemoglobin can reversibly combine with one molecule of oxygen. Thus each molecule of haemoglobin can combine with a maximum of four molecules of oxygen.

Haemoglobin is usually measured in grams per decilitre (g/dl) or grams per millilitre (g/100 ml) of blood. In adult males, a typical level would be approximately 14 g/dl and in adult females 13 g/dl.

Red cells are the most numerous of the cells in blood and normally occupy about 45% of the total blood volume.

## White blood cells

White blood cells (leucocytes) are a family of cells consisting of:

- Granulocytes
- Lymphocytes
- Monocytes.

They are produced in the bone marrow and lymphatic tissue. Their principal role in the blood is to identify, destroy and remove any foreign material that has entered the body. These cells are therefore important in fighting infection and in developing resistance to infection in response to natural exposure or immunization. White cells occupy less than 1% of the total blood volume.

## Platelets

Platelets are small fragments of cells (megakaryocytes), which are produced in the bone marrow and contain enzymes and other biologically active substances (mediators). Their function is to respond to any vascular wall damage by gathering together at the site of injury to form an initial temporary platelet plug and releasing their contents into the blood.

The released contents of platelets are largely responsible for the subsequent coagulation process by activating the blood clotting mechanism that results in the permanent deposition of a fibrin clot at the site of damage, preventing further bleeding.

## Coagulation

### Normal haemostasis

Normal haemostasis is necessary to maintain the blood flow within the vascular system. It involves the interaction of vessels, platelets and coagulation factors and finally the limitation of the clot and fibrinolysis. Bleeding and clotting disorders are the result of the failure of haemostatic mechanisms.

### Primary haemostasis

The vessel wall is the first line of defence for normal haemostasis. In small vessels, vasoconstriction plays an early role in achieving haemostasis. When the vascular endothelium is damaged, platelets will adhere to the exposed collagen, microfibrils and basement membrane.

Once platelets adhere to the subendothelial tissue, they release a variety of mediators. Some of these mediators promote vasoconstriction and all attract other platelets to form an aggregated mass called the primary platelet plug. Platelet factor III is exposed during platelet plug formation and accelerates the formation of thrombin (clot).

### Secondary haemostasis

The coagulation of blood is a series of enzymatic reactions involving plasma proteins, phospholipids and calcium ions that transform the circulating whole blood into an insoluble gel by trapping it within a network of fibrin. This fibrin network extends and anchors the evolving thrombus at the site of damage.

The blood clotting mechanism involves a complex series of steps, or cascades, in which specific plasma proteins called coagulation factors are activated in sequence. Coagulation factors (clotting factors) are often referred to by a number (I, II, III, etc.) and some also have a name: e.g. Christmas Factor (Christmas was the name given to the first patient shown to have a deficiency of what is now known as Factor IX) and anti-haemolytic factor (Factor VIII). See Sections 9.9 and 9.10.

**fibrinogen**: The major coagulant protein in plasma. Converted to (insoluble) fibrin by the action of thrombin.

Two different cascades involving different clotting factors, known as the intrinsic and extrinsic pathways, can be separately triggered in the clotting mechanism, but both ultimately result in the soluble protein **fibrinogen** being converted to a fibrin clot (see Figure 2.7 on p. 28).

### Fibrinolysis

During the normal haemostatic mechanism, the process of limiting the clot occurs through several mechanisms. The most important of these are:

1   Removal of activated clotting factors by blood flow past the clot.

2   Inactivation of clotting factors by circulating inhibitors.

*Figure 2.7: Coagulation and fibrinolyiss*
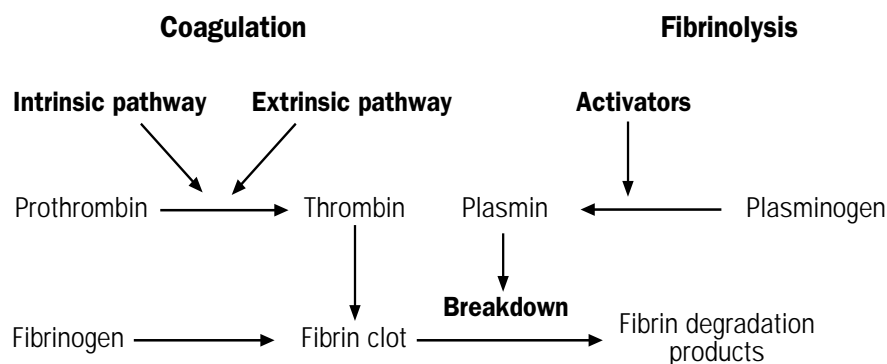
**Coagulation**                    **Fibrinolysis**

**Intrinsic pathway**   **Extrinsic pathway**      **Activators**

Prothrombin ⟶ Thrombin    Plasmin ⟵ Plasminogen

**Breakdown**

Fibrinogen ⟶ Fibrin clot ⟶ Fibrin degradation products

**fibrin degradation products**: Fragments of fibrin molecule formed by the action of fibrinolytic enzymes. Elevated levels in the blood are a feature of disseminated intravascular coagulation.

3   Consumption of platelets and clotting factors by the clotting process.

4   Degradation of the clot by the fibrinolytic enzyme, plasmin (fibrinolysis). Fibrinolysis depends on the sequential activation of specific plasma proteins which results in the formation of the proteolytic enzyme plasmin in the blood. Plasmin's function is to dissolve fibrin clot that is formed in the vessel.

These mechanisms counterbalance the clotting process and prevent uncontrolled coagulation of the blood. If these processes fail, abnormal clotting is produced (thrombosis).

## 2.3   Oxygen supply to the body

One of the most basic physiological functions is to ensure a constant supply of oxygen is delivered to the tissues and organs of the body in order that life can be sustained. To achieve this, four important steps must take place.

1   Oxygen transfer from the lungs into the blood plasma.

2   Oxygen storage on the haemoglobin molecule in the red blood cells.

3   Oxygen transport to the tissues of the body via the circulation.

4   Oxygen release from the blood to the tissues, where it can be utilized.

### Oxygen transfer from lungs to plasma
#### Partial pressure
The air we breathe contains approximately 21% oxygen. The remaining 79% is composed of nitrogen, together with some very small amounts of other gases, including carbon dioxide. The weight (or mass) of these gases exerts a pressure on the body and lungs known as the atmospheric pressure. Each individual gas in air, in proportion to its percentage, contributes a part of the atmospheric pressure. This is known as the partial pressure of the gas. The atmospheric pressure at sea level is 760 mmHg (101 kPa) and thus the partial pressure of oxygen in air is 21% of 760 mmHg, or about 160 mmHg (21 kPa).

## Ventilation

When a breath is taken, the air initially becomes humidified in the upper airway and is then transferred by ventilation to the alveoli of the lungs. Both these effects reduce the partial pressure of oxygen from 160 mmHg (21 kPa) at the mouth down to about 100 mmHg (13.3 kPa) in the alveoli. The major cause of this reduction is diffusion of the metabolic waste gas carbon dioxide from the blood into the lung which has the effect of 'diluting' the partial pressure of oxygen in the alveoli.

## Diffusion

The partial pressure of oxygen in the alveoli constitutes the 'driving force' resulting in the transfer, by diffusion, of oxygen into the blood. Gases diffuse from areas of high pressure to those of low pressure. As already noted, the partial pressure of oxygen in the alveoli is 100 mmHg (13.3 kPa), but it is only 40 mmHg (5.3 kPa) in the pulmonary capillary returning blood from the tissues. Oxygen therefore rapidly diffuses down its pressure gradient across the alveolar-capillary membrane to dissolve into the plasma of the pulmonary blood.

In health, equilibrium is very nearly reached between alveolar and plasma partial pressures and consequently a normal arterial partial pressure of oxygen would be approximately 98 mmHg (13 kPa). See Figure 2.8.

*Figure 2.8: Oxygen transfer*



$pO_2$ in air = 160 mmHg (21 kPa)

$pO_2$ in alveolus = 100 mmHg (13.3 kPa)

$pO_2$ in blood returning to the lung (venous blood) = 40 mmHg (5.3 kPa)

$pO_2$ in blood leaving the lung (arterial blood) = 98 mmHg (13 kPa)
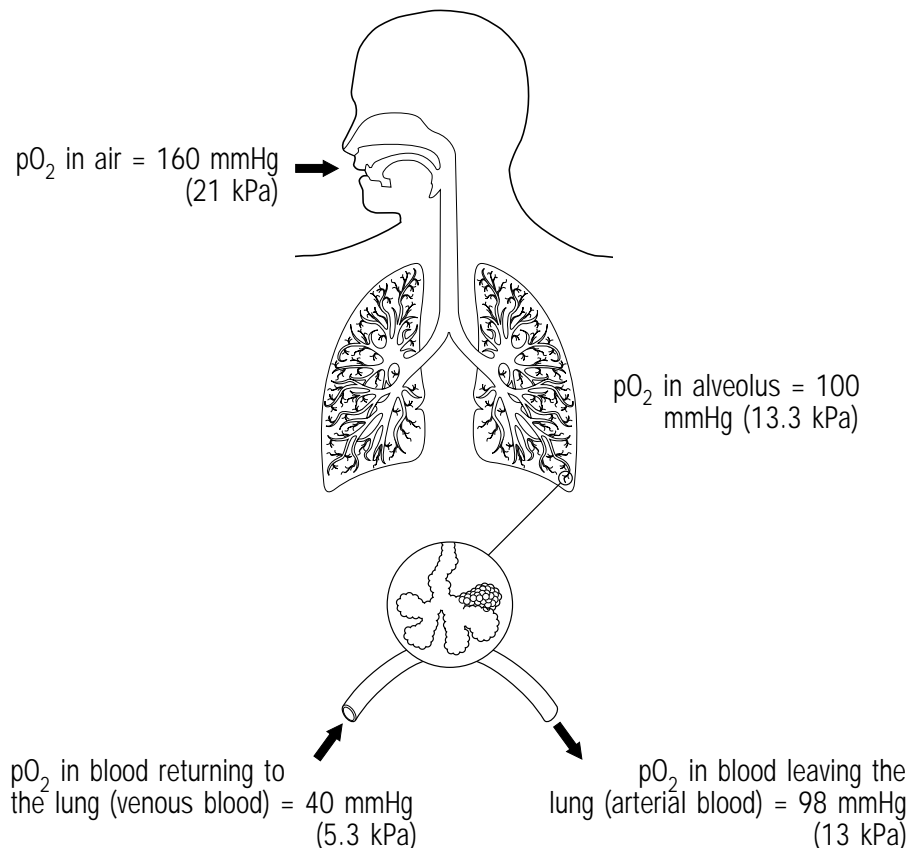
**hypoxic hypoxia**: Reduced supply of oxygen to the tissues due to inadequate supply of oxygen from the lungs to the red cells.

## Disorders

In certain circumstances and disease processes, there may be an abnormal lowering of the arterial partial pressure of oxygen. This is sometimes called **hypoxic hypoxia**. This may be caused by:

- A low partial pressure of oxygen in the inspired air, as occurs when breathing gas containing less than 21% oxygen

- Inadequate ventilation, as in opiate-induced respiratory depression, when carbon dioxide accumulates in the lung reducing the partial pressure of oxygen in the alveoli and consequently that in blood

- Serious mismatching between ventilation and pulmonary blood flow, as can occur in airway collapse or pneumonia (shunt)

- A problem with the diffusion of oxygen across the alveolar capillary membrane in, for example, pulmonary oedema.

## Oxygen storage in blood

### Haemoglobin

Oxygen storage in blood depends almost entirely on the presence of haemoglobin within the red blood cells. Haemoglobin has the ability to combine with oxygen to such an extent that its presence increases the oxygen-carrying capacity of blood by 70 times. Without it, the dissolved oxygen in plasma would be totally inadequate to supply the demands of the tissues.

Each gram of haemoglobin can carry up to a maximum of 1.36 ml of oxygen. When it is in this state, it is fully or 100% saturated with oxygen. Therefore, an individual with a haemoglobin of 15 g/dl which is fully saturated would carry about 20 ml of oxygen (1.36 x 15) for each 100 ml of arterial blood.

### Plasma

Plasma carries only 0.3 ml of oxygen dissolved in each 100 ml, when the individual is breathing air. However, if the inspired oxygen concentration is increased, the amount of oxygen carried by the plasma will also increase.

### Partial pressure and saturation

Once diffusion of oxygen from the alveoli into the plasma of the pulmonary blood has taken place, oxygen at its high partial pressure (98 mmHg/ 13 KPa) rapidly crosses into the red blood cells and binds to the molecules of haemoglobin until they become almost fully saturated. Typically, the haemoglobin in arterial blood is about 97% saturated with oxygen.

The relationship between plasma partial pressures of oxygen and the degree of saturation of haemoglobin is given by the oxygen dissociation curve, shown in Figure 2.9.

This curve embodies the unique ability of haemoglobin to combine with oxygen at high partial pressure in the lung, and then to lose its affinity at lower partial pressures found in the tissues and release its oxygen to them.

Several factors can alter the position of the curve. Some move it to the right, reducing haemoglobin affinity and facilitating oxygen release to the tissues. Others move it to the left, increasing its oxygen affinity and ensuring full saturation of haemoglobin in the pulmonary capillaries.

*Figure 2.9: The oxygen dissociation curve. pH 7.40, temperature 38°C*



The chart data table:

| pO$_2$ (mmHg) | pO$_2$ (kPa) | % saturation of Hb |
|---|---|---|
| 10 | 1.3 | 13.5 |
| 20 | 2.7 | 35.0 |
| 30 | 4.0 | 57.0 |
| 40 | 5.3 | 75.0 |
| 50 | 6.6 | 83.5 |
| 60 | 8.0 | 89.0 |
| 70 | 9.3 | 92.7 |
| 80 | 10.6 | 94.5 |
| 90 | 12.0 | 96.5 |
| 100 | 13.3 | 97.5 |
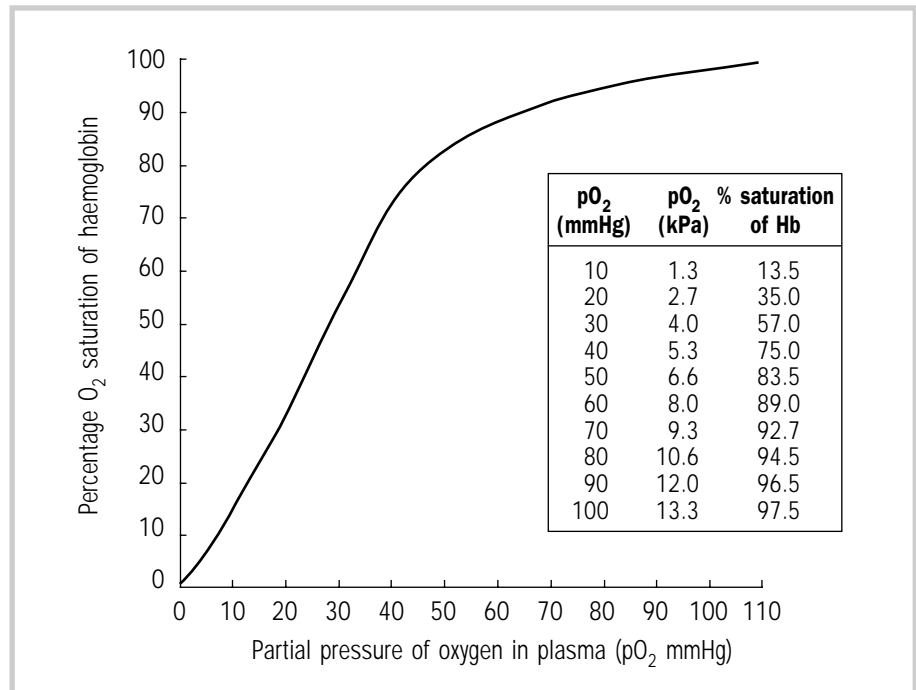
## Disorders

The oxygen-carrying capacity of blood therefore depends on:

- The amount of haemoglobin present in the vascular system
- Its degree of saturation with oxygen.

A reduction in the haemoglobin concentration, as occurs in anaemia, will significantly reduce the overall oxygen-carrying capacity of blood. This is sometimes known as **anaemic hypoxia**. In addition, a failure to adequately saturate the haemoglobin present, because of a disturbance in its affinity for oxygen, will also reduce the oxygen-carrying capacity of blood: e.g. methaemoglobinaemia, carboxyhaemoglobinaemia and some inherited haemoglobinopathies.

**anaemic hypoxia**: Reduced supply of oxygen to the tissues due to low haemoglobin content of red cells in the blood.

## Oxygen transport to the tissues

Once haemoglobin becomes saturated with oxygen in the pulmonary circulation, it must then be transported in the blood flow to the systemic circulation and onwards to the tissue capillaries of the body.

### Control of tissue blood flow

The regulation of blood flow in the circulation is principally controlled by the tissues and organs themselves. Blood entering the capillaries of an organ progressively becomes depleted of its oxygen and nutrients and, at the same time, its levels of carbon dioxide and other products of metabolism increase.

These local changes in blood chemistry control the degree of dilation of the vessels in the organ, which in turn influences its blood flow. If the organ works harder, vasodilatation of its capillaries takes place, increasing its blood flow and consequently the amount of oxygen and nutrients delivered to it.

## Control of cardiac output

Any local increase in blood flow to the tissues or organs must be matched by a corresponding increase in the total amount of blood pumped from the heart, or cardiac output. This is achieved in the following way.

Vasodilatation in the capillaries of an organ causes an increase in the venous blood flow away from that organ. In turn, this increases the total volume of venous blood returning to the heart, or venous return. It is this increase in venous return that is primarily responsible for raising the output of the heart to keep up with the increased demands of the organ for oxygen and nutrients.

As the heart becomes more filled and distended with venous blood, its response is to contract with greater force, which results in an increased cardiac output. This is known as the Frank-Starling mechanism, as shown in Figure 2.10.

*Figure 2.10: The Frank-Starling mechanism*



Within limits, the force of contraction increases in the ventricle
as the filling pressure increases
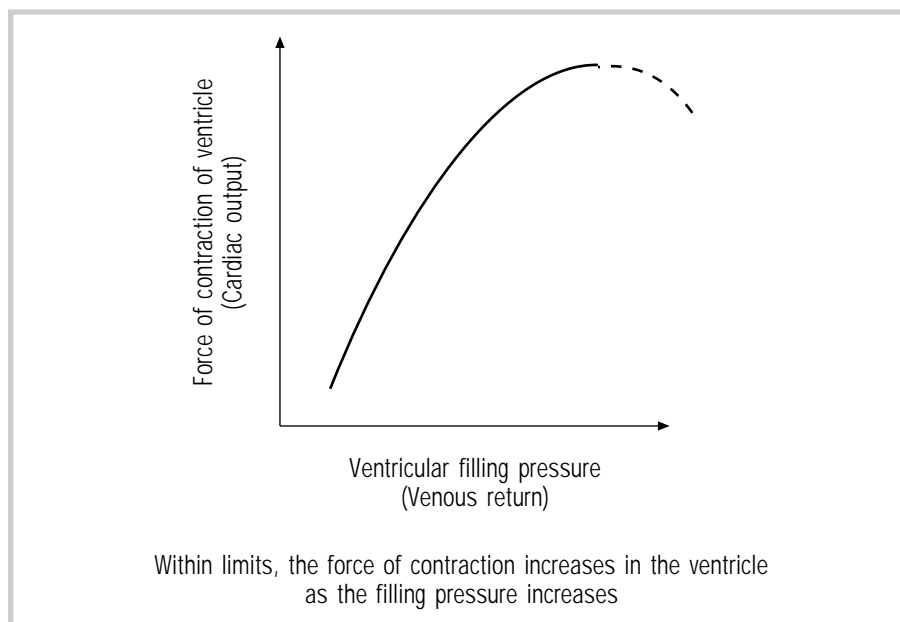
Conversely, if the venous return falls, the heart will become less distended, its force of contraction will reduce and the cardiac output will decrease. The cardiac output therefore automatically adjusts itself to the venous return.

In addition to this mechanism, the cardiac output can be further raised by stimulation of the sympathetic nerves which will also increase the heart's force of contraction and increase the heart rate.

## Venous return

In addition to local changes in blood flow, the maintenance of a sufficient venous return to the heart depends on many other factors, including:

- An adequate circulating blood volume
- The effects of gravity
- The pumping effect of muscles and the thoracic cage
- The mobilization of venous reservoirs of blood by sympathetic nervous stimulation.

The most important factor is an adequate circulating blood volume. If this falls significantly (e.g. in haemorrhage), the venous return will also fall and the ability of the heart to maintain or increase its cardiac output will be impaired.

### Disorders

Despite the overall complexity of the circulation and its regulatory systems, it requires two vital components for it to function at all:

■ An adequate circulating blood volume
■ An efficient 'pump' to generate blood flow.

Without either one, stagnation of blood in the vessels occurs and oxygen transport to the tissues is impaired. This is referred to as **stagnant hypoxia**.

Figure 2.11 on p. 34 shows the relationship between partial pressures and saturation in arterial and venous blood.

**stagnant hypoxia**: Reduced supply of oxygen to the tissues due to reduced blood flow (perfusion).

## Oxygen release to the tissues

The final stage of oxygen delivery involves the release of the stored oxygen in blood to the tissues. Once again, this process is controlled by the tissues themselves and is regulated according to their demand for oxygen.

### Oxygen dissociation

Because oxygen is continuously being utilized in the cells, the partial pressure of oxygen in the tissues is considerably lower than that in arterial blood entering the capillaries. Oxygen therefore diffuses down its pressure gradient from the capillaries into the tissues, resulting in a fall in the partial pressure of oxygen in the capillary plasma.

You can see from the oxygen dissociation curve that a fall in partial pressure of oxygen in plasma reduces the saturation of haemoglobin. Consequently, haemoglobin releases its stored oxygen into the plasma of the capillaries where it can then diffuse into the tissues.

### Shifts in the oxygen dissociation curve

In very active tissues, where the demands for oxygen are highest, there are sharp increases in the levels of carbon dioxide and acids derived from metabolism and in local temperature. These changes also affect the capillary blood and shift the oxygen dissociation curve to the right, reducing the haemoglobin's affinity for oxygen and encouraging its release to the tissues.

When the demands of the tissues for oxygen return to normal, the oxygen dissociation curve shifts back to the left, increasing the affinity of haemoglobin for oxygen and reducing the amount released to the tissues.

Another major factor that influences the position of the oxygen dissociation curve is the presence of the red blood cell metabolite 2,3 diphosphoglycerate (2,3 DPG). When the concentration of this substance increases in the red cell, the dissociation curve shifts to the right, again facilitating the release of oxygen to the tissues, as shown in Figure 2.12 on p. 35.

Once oxygen extraction by the tissues is completed, desaturated blood with a typical partial pressure of oxygen of about 40 mmHg (5.3 kPa), enters the venous circulation and returns to the heart to complete the cycle again.

*Figure 2.11: Oxygen delivery*

**Air partial pressures**

|        | mmHg | kPa  |
|--------|------|------|
| $O_2$  | 158  | 21   |
| $CO_2$ | 0.3  | 0.03 |
| $H_2O$ | 6    | 0.8  |
| $N_2$  | 596  | 79.3 |

Mouth

**Alveolar partial pressures**

|        | mmHg | kPa  |
|--------|------|------|
| $O_2$  | 100  | 13.3 |
| $CO_2$ | 40   | 5.3  |
| $H_2O$ | 47   | 6.3  |
| $N_2$  | 573  | 76.2 |

Right heart

Alveolus

Left heart

**Circulation**

75% saturation

Venous

Capillaries

Arterial

98% saturation

Unloading of oxygen to the tissues

**Venous partial pressures**

|        | mmHg | kPa  |
|--------|------|------|
| $O_2$  | 40   | 5.3  |
| $CO_2$ | 46   | 6.1  |
| $H_2O$ | 47   | 6.3  |
| $N_2$  | 573  | 76.2 |

**Arterial partial pressures**

|        | mmHg | kPa  |
|--------|------|------|
| $O_2$  | 40   | 13.0 |
| $CO_2$ | 46   | 5.3  |
| $H_2O$ | 47   | 6.3  |
| $N_2$  | 573  | 76.2 |

98% saturation



## Disorders

The position of the oxygen dissociation curve and consequently the affinity of haemoglobin for oxygen is affected by pathology that causes major changes to blood's:

- Temperature
- pH
- Carbon dioxide
- 2,3 DPG.

*Figure 2.12: Shifts in the oxygen dissociation curve*



Right shift of oxygen dissociation curve occurs in response to changes in pH, temperature, $CO_2$ and 2,3DPG

Left shift of oxygen dissociation curve occurs in response to opposite changes in these factors
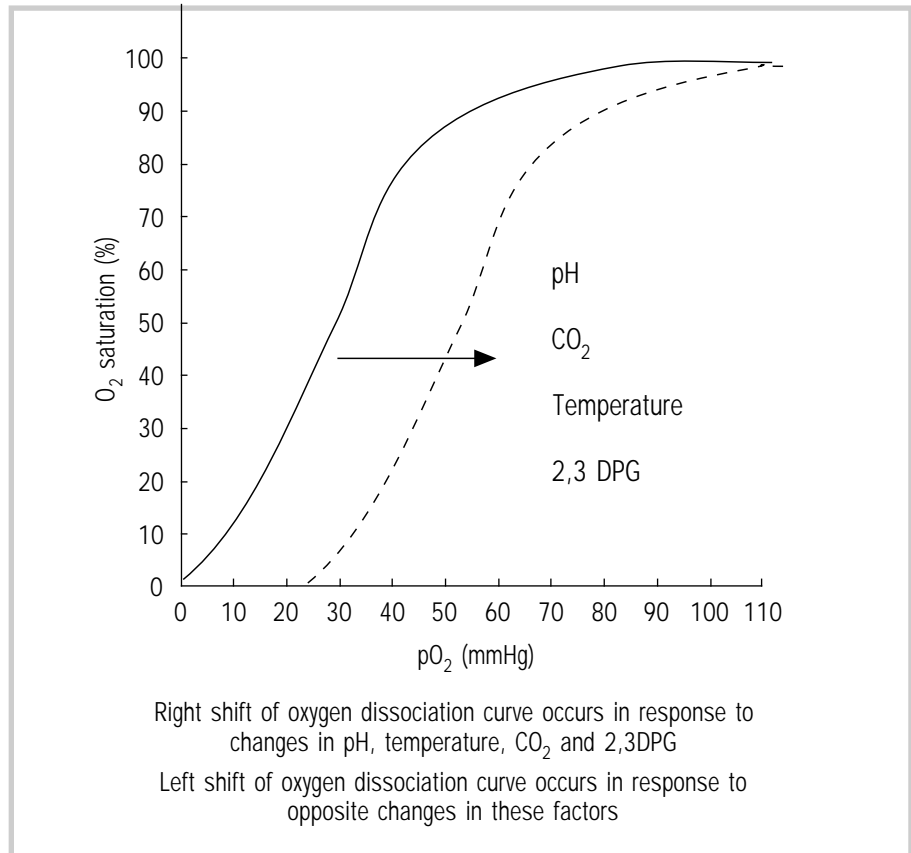
For example, in anaemia and a variety of diseases which result in chronic hypoxia, the levels of 2,3 DPG rise facilitating oxygen release to the tissues. Conversely, in stored banked blood the levels of 2,3 DPG fall, reducing the ability of haemoglobin to release its oxygen.

## Summary: the oxygen supply or flux equation

The overall supply of oxygen to the tissues is dependent on:

■ Haemoglobin concentration

■ Degree of saturation of haemoglobin with oxygen

■ Cardiac output.

These variables are sometimes put in the form of an equation, shown in Figure 2.13, which can be used to calculate the actual amount of oxygen supplied to the tissues. This is called the oxygen supply, delivery or flux equation.

*Figure 2.13: The oxygen supply or flux equation*

| **Oxygen supply** | **= Haemoglobin** | **x 1.36** | **x Saturation** | **x Cardiac output** |
|---|---|---|---|---|
| (ml/min) | (gm/ml) | (ml/gm) | (%) | (ml/min) |

The small fraction of oxygen carried by the plasma has been ignored. The figure 1.36 represents the amount each gram of haemoglobin can carry.

When dealing with clinical situations in which one or more of these variables is altered, it is often useful to consider this equation in order to highlight the effect on the patient's oxygen. It is generally not necessary to make

the detailed calculations, but the equation can be useful in illustrating how the oxygen supply will vary with changes in haemoglobin level, saturation or cardiac output.

Figure 2.14, for example, shows the oxygen supply in health. If the patient develops a chronic anaemia, the reduction in haemoglobin concentration could significantly reduce the oxygen supply, as shown in Figure 2.15.

As the oxygen flux equation shows, however, the supply of oxygen to the tissues can be restored if there is a compensatory increase in cardiac output, as shown in Figure 2.16. This increase in cardiac output is one of the major compensatory mechanisms in chronic anaemia.

A second clinical example is a patient who is suffering from significant chronic obstructive airways disease. One consequence of this disease process can be a failure to maintain the arterial partial pressure of oxygen which, in turn, reduces the degree of saturation of haemoglobin. However, a compensatory increase in the haemoglobin level and cardiac output may occur, both of which attempt to restore the oxygen supply to the tissues.

A similar compensatory increase in haemoglobin level and cardiac output is also seen in patients living at high altitude. This is again due to the reduction in partial pressure of oxygen and saturation of haemoglobin that occurs in this environment.

The effects of acute blood loss and the ensuing compensatory mechanisms are discussed in Section 3: *Anaemia*.

## ACTIVITY 5

*Which other members of the medical and nursing staff in your hospital need a good understanding of the physiology covered in this section? Find out what they know, whether they understand why this knowledge is important and where there are any gaps in their knowledge and understanding.*

*Organize a teaching session for any staff who you feel do not have sufficient understanding of the role of blood in maintaining a constant supply of oxygen to the tissues and organs of the body.*

*Figure 2.14: Normal oxygen supply*

Haemoglobin    Saturation    Cardiac output
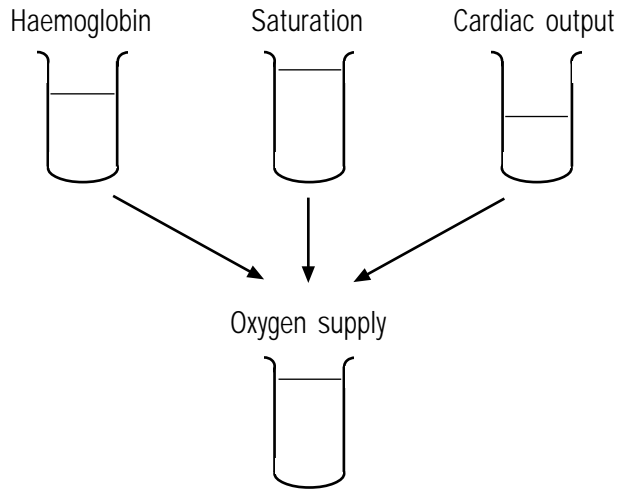
Oxygen supply

*Figure 2.15: Effects of chronic anaemia on oxygen supply*

Haemoglobin    Saturation    Cardiac output
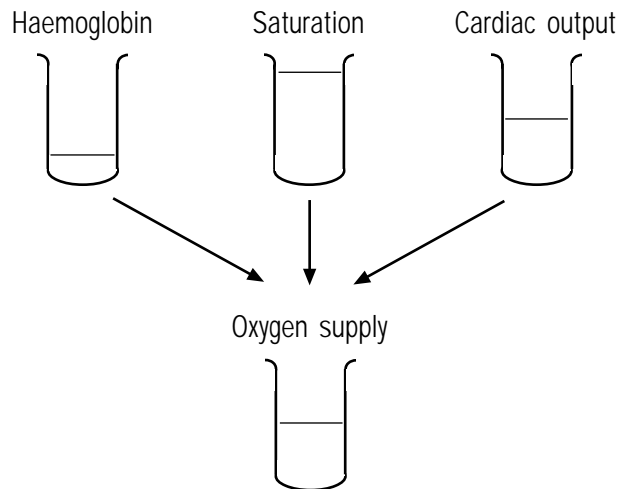
Oxygen supply

*Figure 2.16: Restoration of oxygen supply in chronic anaemic by increased cardiac output*

Haemoglobin    Saturation    Cardiac output

Oxygen supply
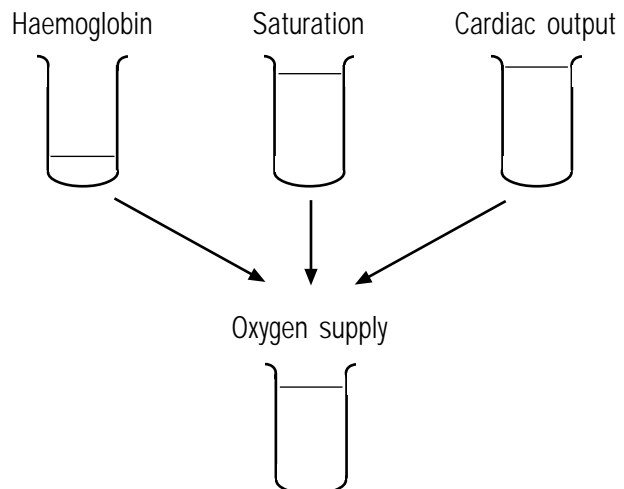
# 3

# Anaemia

## Key points

1 The prevention, early diagnosis and treatment of anaemia, and conditions that cause anaemia, is an important means of minimizing the need for transfusion.

2 Anaemia develops as a result of one or more of the following factors:
- Increased red blood cell loss
- Decreased production of normal red blood cells
- Increased destruction of red blood cells
- Increased demand for red blood cells.

3 Anaemia becomes clinically important when it contributes to a reduction in oxygen supply so that it is inadequate for the patient's needs.

4 The principles of treatment of anaemia are:
- Treat the underlying cause of the anaemia
- Optimize all the components of the oxygen delivery system in order to improve the oxygen supply to the tissues.

5 Blood transfusion should only be considered when anaemia is likely to cause or has already caused a reduction in oxygen supply that is inadequate for the patient's needs.

## Introduction

When an individual becomes anaemic, a variety of physiological changes take place. Central to these changes are the body's own compensatory responses to anaemia that, within limits, help preserve the oxygen supply to the tissues.

The main purpose of this section is to explore these compensatory mechanisms which, when reinforced by appropriate treatment of the anaemia, may be sufficient to make blood transfusion unnecessary.

## Learning outcomes

When you have completed this section, you should be able to:

1. Define anaemia in an individual and distinguish between a normal haemoglobin range and a reference haemoglobin range.

2. List some commonly used methods of determining the red cell or haemoglobin content of the blood.

3. Identify the factors that affect the haemoglobin concentration in a patient and that may alter your interpretation of it.

4. Outline the main causes of anaemia.

5. Describe the effects produced by anaemia and the ensuing compensatory responses, with particular emphasis on acute and chronic blood loss.

6. State the principles of the treatment of anaemia.

7. Outline the measures that can be used to prevent anaemia in a population.

## 3.1 Definitions

### Anaemia

Anaemia in an individual is defined as a haemoglobin (Hb) concentration in blood that is below the expected value, when age, gender, pregnancy and certain environmental factors, such as altitude, are taken into account.

This definition therefore requires a comparison to be made between the individual's haemoglobin concentration and the expected value. To determine the expected haemoglobin concentration of the patient, it is necessary to refer to either of the following haemoglobin ranges:

■ The normal haemoglobin range

■ A reference haemoglobin range.

### The normal haemoglobin range

The normal haemoglobin range is the distribution of haemoglobin concentrations found in a representative, large group of fit and healthy individuals. In principle, therefore, it might be considered as a worldwide standard indicator of good health, varying only with age, gender, pregnancy or altitude of residence.

It has, however, been difficult to establish a normal range of haematological values. Figure 3.1 shows the normal ranges and criteria for defining an individual as anaemic, proposed by WHO, but it is important to remember that some individuals who are apparently normal and healthy will have values outside the range. Published values for 'normal' haemoglobin levels indicate, for example, that many adult females should be considered normal, even though their haemoglobin levels are below 12 g/dl (see p. 43 for haematocrit).

*Figure 3.1: Criteria for anaemia, based on normal haemoglobin range at sea level*

| Age/gender | Normal haemoglobin range (g/dl) | Anaemic if Hb range less than: (g/dl)* |
|---|---|---|
| Birth (full-term) | 13.5–18.5 | 13.5 (Hct 34.5) |
| Children: 2–6 months | 9.5–13.5 | 9.5 (Hct 28.5) |
| Children: 6 months–6 years | 11.0–14.0 | 11.0 (Hct 33.0) |
| Children: 6–12 years | 11.5–15.5 | 11.5 (Hct 34.5) |
| Adult males | 13.0–17.0 | 13.0 (Hct 39.0) |
| Adult females: non-pregnant | 12.0–15.0 | 12.0 (Hct 36.0) |
| Adult females: pregnant | | |
| First trimester: 0–12 weeks | 11.0–14.0 | 11.0 (Hct 33.0) |
| Second trimester: 13–28 weeks | 10.5–14.0 | 10.5 (Hct 31.5) |
| Third trimester: 29 weeks–term | 11.0–14.0 | 11.0 (Hct 33.0) |

* These values simply define anaemia. They are often used as thresholds for investigation and treatment, but are *not* indications for transfusion.

## Reference haemoglobin ranges

A reference haemoglobin range is the distribution of haemoglobin concentrations found in a specific well-defined population, called the reference population. It is developed by sampling the haemoglobin values from a group of individuals who are representative of that population (see Figure 3.2 for examples).

*Figure 3.2: Examples of reference ranges for non-pregnant females*

| Reference range for non-pregnant females | Range | Mean |
|---|---|---|
| Delhi, India | 6.3–14.8 g/dl | 10.5 g/dl |
| Burkina Faso | 9.4–15.0 g/dl | 12.2 g/dl |

If the reference population is composed of predominantly healthy individuals, the reference range will be similar to the normal haemoglobin range. However, the reference range will be lower than the normal range if the reference population has a high prevalence of disorders affecting the haemoglobin concentration, such as iron deficiency, malaria or inherited haemoglobinopathies.

Reference haemoglobin ranges are useful for identifying anaemia in certain populations and in targeting them with appropriate public health measures. When repeated for the same population, reference ranges will also help to assess the effectiveness of these measures.

Reference haemoglobin ranges should not be used as a basis for investigation and treatment in the individual patient. The normal haemoglobin range should be used for this purpose.

## Values and ranges

Haemoglobin concentrations, like other biological variables such as plasma sodium or albumin, show a natural variation even among healthy individuals. For this reason the normal and reference values are expressed as a range: e.g. 9.5–13.5 g/dl. This range, by convention, includes 95% of all the individuals tested, as shown in Figure 3.3.

*Figure 3.3: Haemoglobin range*
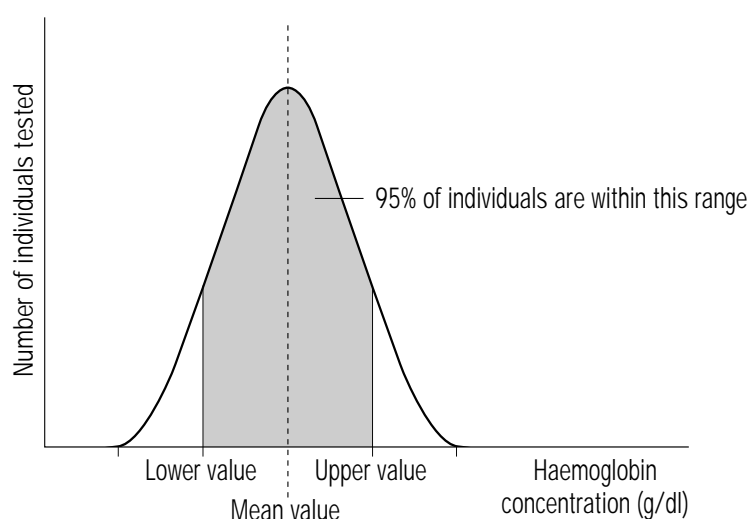
## 3.2 Measuring haemoglobin concentration and haematocrit

### Haemoglobin concentration

Although the clinical features of anaemia may be present in a patient, they are often an unreliable guide to the severity of the anaemia. The clinical assessment of anaemia also tends to vary widely between observers. For this reason, it is essential that there is a means of quickly and reliably obtaining an accurate haemoglobin measurement on a patient's blood sample in hospitals where transfusions are carried out.

Many of the laboratory methods for determining haemoglobin concentration are technically capable of providing results of sufficient quality for clinical use. However, regardless of the method, reliable results depend on good laboratory practice, staff training, the use of standard operating procedures, and regular calibration and maintenance of the equipment. The proper use of internal controls and, if possible, external quality assessment samples is also important.

Figure 3.4 summarizes some commonly used methods of haemoglobin measurement.

*Figure 3.4: Methods of haemoglobin measurement*

| Methods | Comments |
|---|---|
| Methods using a spectrophotometer or photoelectric photometer <br> ■ Haemiglobincyanide <br> ■ Oxyhaemoglobin | All require some type of optical equipment with battery or mains power supply, maintenance, calibration, spares and user training |
| Direct reading haemoglobinometers | |
| WHO Haemoglobin Colour Scale | See below |
| Copper sulphate method | Only useful for screening blood donors |

### WHO Haemoglobin Colour Scale

The WHO Haemoglobin Colour Scale is a simple and inexpensive clinical device that provides a reliable method for screening for the presence and severity of anaemia. It has been designed particularly for use in situations where laboratory-based haemoglobinometry is not readily available.

The Haemoglobin Colour Scale kit consists of a booklet containing a standardized set of colour shades representing a range of haemoglobin values (4 g/dl, 6 g/dl, 8 g/dl, 10 g/dl, 12 g/dl and 14 g/dl). It also contains a pack of special absorbent test-papers. It is accurate to within 1 g/dl when used according to the instructions and using the test-strips supplied in the kit. Its validity cannot be guaranteed if other test-papers are used.

To use the Haemoglobin Colour Scale, a drop of blood from an anticoagulated blood sample or a finger/heel prick is placed on a test-strip. By comparing

the colour of the blood stain with the printed colour standard, as shown in Figure 3.5, it is possible to identify whether the blood is anaemic and, if so, the severity of anaemia in clinical terms.



*Figure 3.5: Using the Haemoglobin Colour Scale*
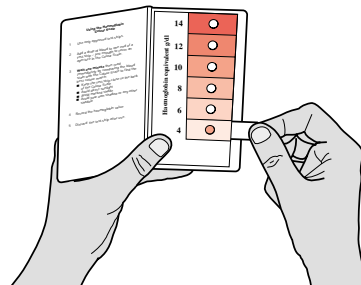
Information on suppliers of the WHO Haemoglobin Colour Scale is available from:

World Health Organization
Blood Safety and Clinical Technology
20 Avenue Appia, CH-1211 Geneva 27, Switzerland
Fax: +41 22 791 4836. E-mail: hbcolourscale@who.int

## Haematocrit or packed cell volume

An alternative method of estimating the red cell content of the blood is to measure the haematocrit or packed cell volume.

**packed cell volume (PCV)**: Determined by centrifuging a small sample of blood in an anticoagulated capillary tube and measuring the volume of packed red cells as a percentage of the total volume.

The **packed cell volume** (PCV) is determined by centrifuging a small sample of blood in an anticoagulated capillary tube and measuring the volume of packed red cells as a percentage of the total volume.

An equivalent measurement, the **haematocrit** (Hct), can be derived by automated haematology analyses from the red cell indices.

For clinical purposes, the terms 'haematocrit' and 'PCV' are used interchangeably.

**haematocrit (Hct)**: Equivalent measurement to PCV, derived by automated haematology analyses from the red cell indices.

The relationship between haematocrit and haemoglobin concentration in a given sample is influenced by the size and haemoglobin content of the red cells. A useful conversion factor is that haematocrit (%) is approximately equal to three times the haemoglobin concentration. Haematocrit values are shown in Figure 3.1.

## 3.3  Clinically important anaemia

It is relatively simple to define a patient as being anaemic by comparing his or her haemoglobin concentration with a normal or reference range. However, in order to judge whether the anaemia is clinically important, a detailed assessment of the individual patient is needed.

As we have seen in Section 2: *Blood, Oxygen and the Circulation*, the haemoglobin concentration of a patient is only one of the critical factors that determines the overall supply of oxygen to the tissues.

The oxygen supply to the tissues also depends on:
- Degree of saturation of haemoglobin
- Cardiac output.

Alterations in the haemoglobin concentration should therefore not be interpreted in isolation, but should be seen in the context of changes or disorders affecting the other variables of oxygen supply.

**Anaemia becomes clinically important when it contributes to a reduction in oxygen supply so that it is inadequate for the patient's needs.**

## 3.4 Interpreting haemoglobin values

The haemoglobin value is a measurement of concentration and is the amount of haemoglobin present in a fixed volume of the patient's blood. It is normally expressed as grams per decilitre (g/dl) or grams per litre (g/L). In this module, all haemoglobin values are expressed in g/dl. The haemoglobin value itself is dependent on:
- Total amount of circulating haemoglobin in the red cells
- Blood volume.

**haemodilution**: Reduced haematocrit (packed cell volume). Acute haemodilution caused by red cell loss and replacement by crystalloid or colloid infusion.

**haemoconcentration**: Elevated haematocrit (packed cell volume) due to a reduction in plasma volume.

A variation in either of these factors will affect the haemoglobin concentration. During pregnancy, for example, an apparent anaemia may exist simply as a result of an increase in plasma volume, but without any reduction in the total amount of haemoglobin present. This is called **haemodilution**. Since the overall capacity of blood to carry oxygen is unchanged, it is not necessarily a pathological state.

Conversely, where there is a reduction in the plasma volume but without any alteration in the total amount of haemoglobin present, a higher than expected haemoglobin concentration will be apparent. This is known as **haemoconcentration** and can occur, for example, in severe dehydration.

The haemoglobin concentration therefore needs to be considered along with other information about the patient's condition to avoid misinterpretation (see Figure 3.6).

### ACTIVITY 6

*What method is used in your hospital laboratory to measure haemoglobin concentrations or otherwise assess the haemoglobin content of blood?*

*Find out from laboratory technical staff whether the results are accurate and reliable and whether any quality control checks are performed. If so, what checks are used and how often are they performed?*

*If you think a more accurate and reliable method could be used or that quality control procedures could be strengthened, talk to senior laboratory technical staff about any improvements that might be needed.*

*Figure 3.6: Alterations of haemoglobin in relation to plasma*



| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| | Normal | Acute blood loss | Chronic blood loss | Haemo-dilution e.g. pregnancy | Haemo-concentration e.g. dehydration |
| **Red cell volume** | Normal | ↓ | ↓ | ↑ | Normal |
| **Plasma volume** | Normal | ↓ | ↑ | ↑↑ | ↓ |
| **Hb level** | Normal | Normal | ↓ | ↓ | ↑ |
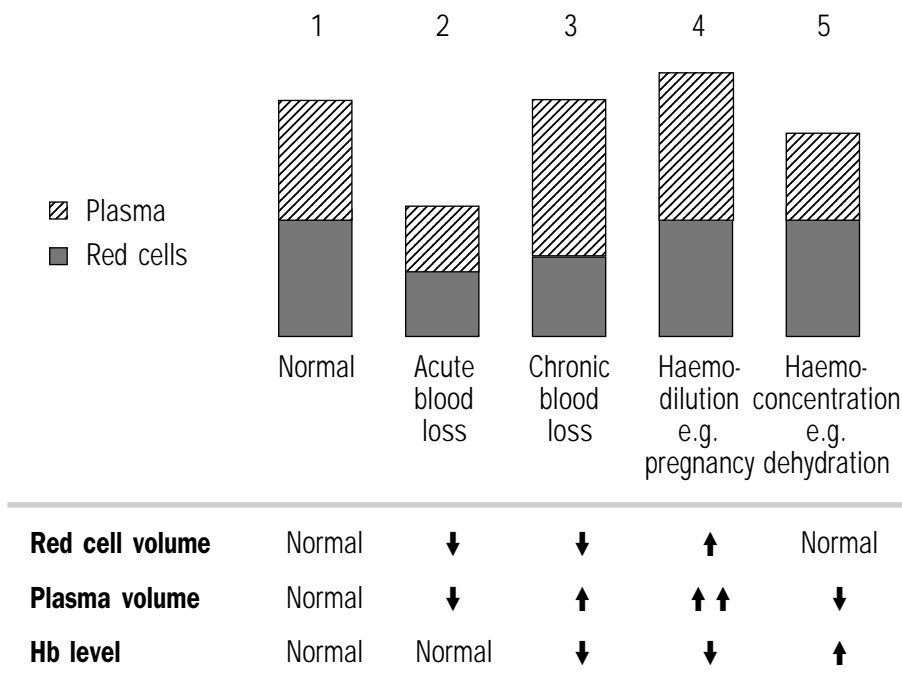
**Column 1** represents the normal situation.

**Column 2** illustrates a patient who loses blood rapidly over a short period of time (haemorrhage). Both red cells and plasma are lost together, but the haemoglobin concentration may initially remain fairly normal.

**Column 3** shows the effect of a slow (or chronic) blood loss over weeks or months. Normal compensatory responses have operated to expand the plasma volume in order to maintain the total blood volume, but the haemoglobin concentration is reduced because red cells have been lost.

**Column 4** illustrates the effect of haemodilution. This picture would be seen in a patient who had received intravenous replacement fluids or as a normal feature in pregnancy.

**Column 5** shows the consequences of dehydration, resulting in haemo-concentration. There is no loss of red blood cells, but blood volume is reduced. The haemoglobin concentration is therefore above normal.

## ACTIVITY 7

*Is there a reference range of haemoglobin concentrations for your country or area? If so, compare it with the normal range.*

*In your locality, what are the most common disorders affecting the haemoglobin concentration that might account for any differences between the two ranges?*

## 3.5   Causes of anaemia

Anaemia is not a diagnosis in itself, but an indication of one or more causes. A simple classification of the processes that can lead to anaemia is shown in Figure 3.7.

*Figure 3.7: Causes of anaemia*

| CAUSES OF ANAEMIA |
| --- |
| **Increased loss of red blood cells**<br>■ Acute blood loss: haemorrhage from trauma or surgery, obstetric haemorrhage<br>■ Chronic blood loss, usually from the gastrointestinal, urinary or reproductive tracts: parasitic infestation, malignancy, inflammatory disorders, menorrhagia |
| **Decreased production of normal red blood cells**<br>■ Nutritional deficiencies: iron, $B_{12}$, folate, malnutrition, malabsorption<br>■ Viral infections: HIV<br>■ Bone marrow failure: aplastic anaemia, malignant infiltration of bone marrow, leukaemia<br>■ Reduced erythropoietin production: chronic renal failure<br>■ Chronic illness<br>■ Poisoning of the bone marrow: e.g. lead, drugs (e.g. chloramphenicol) |
| **Increased destruction of red blood cells (haemolysis)**<br>■ Infections: bacterial, viral, parasitic<br>■ Drugs: e.g. dapsone<br>■ Autoimmune disorders: warm and cold antibody haemolytic disease<br>■ Inherited disorders: sickle cell disease, thalassaemia, G6PD deficiency, spherocytosis<br>■ Haemolytic disease of the newborn (HDN)<br>■ Other disorders: disseminated intravascular coagulation, haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura |
| **Increased physiological demand for red blood cells and iron**<br>■ Pregnancy<br>■ Lactation |

Medical conditions associated with anaemia are discussed in Section 9: *General Medicine.*

Iron deficiency anaemia is the commonest cause of anaemia worldwide. It is important to understand the basic mechanisms of iron metabolism as this is fundamental to the prevention, diagnosis and treatment of anaemia.

### Iron metabolism

Iron is an essential nutrient required by every human cell. Most of the body's iron is in haemoglobin. Iron is absorbed by the intestines, transported in the blood by a carrier protein (transferrin) and stored as ferritin. Humans

do not have an effective mechanism for excreting iron, other than through loss of blood and small amounts through shedding of skin and intestinal cells.

The physiological adjustment of the iron balance in an individual depends on small alterations in intestinal absorption and on sufficient iron in the diet (see Figure 3.8).

*Figure 3.8: Iron absorption*

| Gender | Normal daily iron loss | Maximum iron absorption |
| --- | --- | --- |
| Men | 1 mg/day | 1–2 mg/day |
| Menstruating women | 1.5 mg/day | 1–2 mg/day |
| Pregnant women | 2 mg/day | 1–2 mg/day |

The normal adult's iron content is about 2.4 g of which 65% is in the red cells. Iron forms part of the oxygen-binding site of haemoglobin and is therefore fundamental to the body's oxygen supply (see Figure 2.6). As the red cells are broken down at the end of their normal life span, the iron that is released and recycled provides most of the body's requirements. Only small quantities of iron are absorbed from the gastrointestinal tract (duodenum and jejunum).

A typical adult daily food intake in a developed country contains 10–15 mg of iron, of which 1–2 mg/day (5–10%) is normally absorbed. This is sufficient to meet the replacement needs of healthy adult males and females who are not menstruating. However, when iron requirements are increased for any reason, the body's limited stores can be rapidly depleted. A blood loss of 500 ml removes 250 mg of iron. Chronic or acute bleeding depletes iron stores. Without treatment, they take many months to replenish.

## ACTIVITY 8

*Keep a simple record of the next 25 patients you see. How many are anaemic? What is the cause of anaemia in each patient?*

*Talk to your colleagues to find out whether these cases are typical of the pattern of anaemia in the general population.*

*Are particular groups at greater risk of developing anaemia than the general population? Is there an effective programme of prevention?*

## 3.6  Adaptation to anaemia

Section 2 described how the respiratory and circulatory systems interact with the red blood cells to maintain the supply of oxygen to the tissues. When blood is lost or anaemia occurs for other reasons, these systems adapt to compensate and maintain, as far as possible, the supply of oxygen to essential organs and tissues.

The clinical condition of the patient will depend on:

- Patient's ability to make these compensatory responses
- Degree of red cell insufficiency
- Whether it has occurred rapidly (over hours) or gradually (over months).

Transfusion of whole blood or red cells is often used in the treatment of anaemia and blood loss. However, transfusion can often be avoided because the body's own compensatory mechanisms may maintain adequate oxygen delivery while other treatments take effect. These compensatory responses are now described.

## 3.7 Anaemia due to acute blood loss

**hypovolaemia**: Reduced circulating blood volume.

In acute blood loss, or haemorrhage, there is both a reduction in the total amount of haemoglobin in the circulation and a loss of blood volume, or **hypovolaemia**. In contrast, the blood volume is normally well-maintained in anaemia due to other causes (see Figure 3.6).

### Effects of acute blood loss

As discussed in Section 2, the supply of oxygen to the tissues depends on the transfer of oxygen from the lungs to the blood, its storage in the form of saturated haemoglobin and its transport and delivery to the tissues. It depends on the presence of an adequate level of haemoglobin and an efficient circulation to transport it.

Haemorrhage can interfere with all of these processes by causing:

- Reduced oxygen transfer from the lungs to the red cells
- Reduced oxygen storage by the red cells
- Reduced oxygen transport and delivery to the tissues.

### Reduced oxygen transport

The loss of blood volume from the circulation, or hypovolaemia, causes a reduction in the venous return to the heart. In turn, this reduces the cardiac output and blood pressure. Blood flow to the tissues therefore decreases and the transport of oxygen to them is impaired. This is termed stagnant hypoxia.

### Reduced oxygen storage

The loss of red blood cells reduces the total amount of haemoglobin in the circulation. This reduces the overall oxygen-storage capacity of the blood. It is termed anaemic hypoxia.

Remember that a haemoglobin estimation conducted in the early stages of acute haemorrhage may not be significantly lower than normal and is not a reliable guide to the degree of blood loss. This is because both plasma and red blood cells are lost from the circulation simultaneously. It is only when the plasma volume is restored, either by compensatory mechanisms or fluid therapy, that the haemoglobin concentration (or haematocrit) will begin to fall (see Figure 3.6).

### Reduced oxygen transfer

The reduced cardiac output causes mismatching of the pulmonary blood flow and ventilation in the lung (alveolar dead space), resulting in a decrease in the partial pressure of oxygen in the pulmonary capillaries. This is termed hypoxic hypoxia.

As the partial pressure falls (see Section 2), the degree of saturation of the remaining haemoglobin in the circulation also falls. This reduces the oxygen-carrying capacity of the blood still further.

The consequence of a major uncontrolled haemorrhage is therefore oxygen starvation of the tissues and organs of the body, or tissue hypoxia, as shown in Figure 3.9.

*Figure 3.9: The effect of haemorrhage on the oxygen supply*

↓Haemoglobin  x  ↓Saturation  x  ↓Cardiac output  = ↓↓Oxygen supply to the tissues

## Compensatory responses to acute blood loss

No tissue is able to sustain prolonged periods of hypoxia and the body therefore responds immediately to any significant blood loss with several compensatory mechanisms:

- Restoration of plasma volume
- Restoration of cardiac output
- Circulatory compensation
- Stimulation of ventilation
- Changes in the oxygen dissociation curve
- Hormonal changes
- Synthesis of plasma proteins.

### Restoration of plasma volume

As cardiac output and blood pressure falls, the hydrostatic pressure in the capillaries supplying the tissues of the body also falls. The balance between the oncotic and hydrostatic pressures in the capillaries is therefore altered, allowing an influx of water into the plasma from the interstitial fluid. This mechanism helps to restore the circulating plasma volume. At the same time, water also moves from the intracellular compartment into the interstitial fluid.

### Restoration of cardiac output

The fall in cardiac output and pressure in the heart and major vessels is detected by pressure receptors (baroreceptors) which activate the sympathetic nervous system via the vasomotor centre in the brain. The sympathetic nerves act on the heart, increasing both its rate and force of contraction, helping to restore the cardiac output.

### Circulatory compensation

The sympathetic nerves also act on the vessels supplying the tissues and organs of the body during acute haemorrhage. They cause vasoconstriction of arterioles, particularly in tissues and organs not immediately essential

to life, such as skin, gut and muscle, which reduces the blood flow to them. This has the following effects:

- Preserving blood flow to the essential organs: brain, kidney and heart
- Restoring the arterial blood pressure.

In addition, the sympathetic nerves cause constriction of the veins, or venoconstriction, which transfers blood from the veins into the circulation. Since venoconstriction increases the venous return to the heart, it is another important mechanism for restoring the cardiac output during haemorrhage.

## Stimulation of ventilation

A reduced blood flow and oxygen starvation causes many tissues and organs to convert to anaerobic metabolism, which produces large quantities of lactic acid. The resulting metabolic acidosis, together with the lowered partial pressure of oxygen in blood, is detected by chemoreceptors in the aorta and carotid arteries. These chemoreceptors stimulate the respiratory centre in the brain which responds by increasing the depth and rate of ventilation to restore the partial pressure of oxygen in blood.

## Changes in the oxygen dissociation curve

During haemorrhage, the position of the oxygen dissociation curve moves to the right (see Figure 2.12), largely as a result of acidosis. The effect of this is to reduce haemoglobin's affinity for oxygen in the tissue capillaries, thereby encouraging the release of oxygen and increasing its availability to the tissues.

## Hormonal responses

The secretion of several hormones is increased in response to haemorrhage but, unlike the other compensatory mechanisms, their effects are usually only apparent after several hours or days.

1 Vasopressin (antidiuretic hormone or ADH) is released from the pituitary gland in response to a fall in blood volume. Its principal action is to reduce the amount of water excreted by the kidney. This concentrates the urine and thus conserves body water. Vasopressin also causes vasoconstriction, which may help to increase the blood pressure.

2 Aldosterone production from the adrenal gland is also increased during haemorrhage, triggered by the renin-angiotensin system. Aldosterone acts on the kidney, causing retention of sodium in the body. Together with the water-retaining properties of vasopressin, this helps to restore the volume of the extracellular fluid and, in particular, to re-expand the circulating blood volume.

3 Erythropoietin production from the kidney increases in response to hypoxia caused during haemorrhage. Red blood cell output in the bone marrow is therefore stimulated. This is not an immediate response but, over several days, it will lead to the replacement of cells that have been lost.

4 Other hormones are also released in severe haemorrhage, including:
- Adrenal steroids
- Catecholamines: e.g. adrenaline, noradrenaline.

All have important roles in enabling the body to compensate and respond to the potentially life-threatening situation.

## Synthesis and movement of plasma proteins

Haemorrhage also results in the loss of plasma proteins and platelets from the vascular system. This can lead to alterations in the oncotic pressure of plasma. Although there is rapid mobilization (within 6–12 hours) of pre-formed albumin into the circulation during acute blood loss, complete restoration of plasma proteins levels (by synthesis in the liver) may take several days. The dilution of coagulation proteins and platelets as a result of massive blood loss and fluid replacement can contribute to blood clotting problems (see Section 9: *General Medicine*).

## Clinical features of acute blood loss

The clinical features of haemorrhage in an individual are largely determined by the volume and rate of blood loss. However, they also depend on the patient's capacity to make the compensatory responses described above.

**There are variations in patients' capacity to compensate for a given blood loss. The clinical picture may therefore vary.**

Haemorrhage occurring in an elderly or anaemic patient, particularly where there is co-existing cardiorespiratory disease, is often revealed at an earlier stage than when the same loss occurs in a previously healthy patient.

The clinical picture of acute blood loss can therefore range from minimal signs of hypovolaemia, often detected by a small rise in heart rate when only small amounts of blood are shed, through to haemorrhagic shock when massive uncontrolled bleeding occurs (see Figure 3.10). These features are discussed more fully in Section 13: *Trauma and Acute Surgery.*

*Figure 3.10: Clinical features of major haemorrhage*

### Haemorrhagic shock

- Thirst
- Cool, pale, sweaty skin
- Tachycardia
- Decreased pulse pressure
- Reduced blood pressure
- Increased respiratory rate
- Restlessness or confusion
- Reduced urine output

## 3.8  Anaemia due to chronic blood loss

In chronic blood loss, such as in gastrointestinal losses due to hookworm, there is a continuing loss of blood from the circulation over a long period of time. Anaemia thus develops gradually. There is generally no reduction in the circulating blood volume and **normovolaemia** is maintained (see Figure 3.6, Column 3).

**normovolaemia:** Normal circulating blood volume.

### Effects of chronic blood loss

The body can initially compensate for chronic red cell loss by increasing red blood cell production. However, iron is lost with red cells and this eventually depletes the body's iron stores. Since iron is an essential component of haemoglobin, its deficiency causes a reduction in the level of haemoglobin in the red blood cells being produced.

Chronic blood loss therefore typically gives rise to an iron deficiency anaemia due to impaired production of haemoglobin. The red cells are small (microcytic) and contain little iron (hypochromic). Since the red cells contain less haemoglobin, the oxygen carrying-capacity of blood is reduced.

### Compensatory responses to chronic blood loss

The body responds to chronic blood loss with the following compensatory mechanisms:

- Cardiovascular compensation
- Changes in the oxygen dissociation curve
- Changes in blood viscosity
- Hormonal responses.

#### Cardiovascular compensation

As the oxygen carrying-capacity of blood falls, the amount of oxygen available to the tissues also falls. The tissues respond by vasodilating their blood vessels in order to increase the blood supply to maintain the delivery of sufficient amounts of oxygen. The increased tissue blood flow results in an increased venous return. This increases the cardiac output of the heart through the Frank-Starling mechanism (see Figure 2.10).

Chronic blood loss, and indeed chronic anaemias in general, are therefore largely compensated for by a raised cardiac output. However, in severe chronic anaemia, the heart may be unable to sustain the high cardiac output demanded of it and consequently heart failure can develop.

#### Changes in the oxygen dissociation curve

The other major compensatory response that occurs in chronic anaemia is a shift in the position of the oxygen dissociation curve to the right (see Figure 2.12). This has the effect of reducing haemoglobin's affinity for oxygen in the tissue capillaries, thereby encouraging the release of oxygen and increasing its availability to the tissues. This shift is primarily due to an increase in the red blood cell metabolite 2,3 diphosphoglycerate (2,3 DPG).

### Changes in blood viscosity

As the red blood cell mass becomes reduced in anaemia, the viscosity of blood is lowered. This results in an improved capillary blood flow which enhances the delivery of oxygen to the tissues. Cardiac output also tends to increase as a consequence of reduced blood viscosity.

### Hormonal responses

Many of the same hormonal responses to acute blood loss also occur in chronic blood loss, although the degree of compensation required is considerably less. Thus, red cell production is stimulated by erythropoietin, provided there is sufficient iron available for haemoglobin synthesis, and blood volume is maintained by the action of vasopressin and aldosterone.

## Clinical features of chronic blood loss

Provided that the patient's compensatory mechanisms are effective, chronic anaemia may cause few clinical symptoms or signs until a relatively low haemoglobin concentration is reached. However, the clinical features of anaemia will become apparent at an earlier stage when there is:

- Limited capacity to mount a compensatory response: e.g. significant cardiovascular or respiratory disease
- Increase in demand for oxygen: e.g. infection, pain, fever or exercise
- Further reduction in the oxygen supply: e.g. blood loss or pneumonia.

The clinical features of chronic anaemia are discussed in Section 9: *General Medicine*.

## 3.9 Chronic anaemia due to other causes

There are many causes of anaemia resulting from either:

- Decreased production of either red blood cells or haemoglobin
- Increased destruction of red blood cells.

The underlying causes of these anaemias include:

- Nutritional deficiencies
- Infections
- Malignancy
- Autoimmune diseases
- Inherited disorders of red cells: e.g. haemoglobinopathies
- Aplastic anaemia, myelodysplasia.

Some of these disorders are discussed in more depth in Section 9: *General Medicine*.

Generally, these conditions cause anaemia that develops relatively slowly and so may be compensated for by many of the same mechanisms that occur during chronic blood loss. However, severe acute anaemia may

occur due to medical causes: e.g. haemolysis or splenic sequestration of red cells.

The clinical picture of all chronic anaemias is due to both:

- The anaemia itself: that is, the diminished oxygen-carrying capacity of blood
- Features of the underlying condition (see Section 9: *General Medicine*).

## Acute-on-chronic anaemia

The term 'acute-on-chronic anaemia' is often used to describe a further sudden fall in haemoglobin concentration in a patient who is already chronically anaemic. This situation is often a clinical emergency, especially in young children, and the management may include the need for red cell transfusion (see Section 10: *Obstetrics*, Section 11: *Paediatrics & Neonatology* and Section 13: *Trauma & Acute Surgery*).

## 3.10 Principles of the treatment of anaemia

Anaemia in an individual is abnormal and indicates the presence of some form of pathology which requires investigation and treatment. The haemoglobin concentrations that are commonly used to define anaemia are given in Figure 3.1.

The compensatory mechanisms to anaemia, described in this section, often enable patients to tolerate relatively low haemoglobin concentrations. This is particularly the case in patients with chronic anaemia that has developed slowly over weeks or months. However, if these compensatory mechanisms fail to maintain the oxygen supply to the tissues, decompensation occurs and, without treatment, death will rapidly ensue.

Many factors can precipitate decompensation in an anaemic patient. In general, these are due to one or more of the following:

- Limited capacity to mount a compensatory response: e.g. significant cardiovascular disease
- Increase in demand for oxygen: e.g. superimposed illness, fever or exercise
- Further reduction in the oxygen supply: e.g. blood loss, surgery, pneumonia.

Once decompensation has occurred, the only effective treatment is to raise the oxygen-carrying capacity of the blood by means of a blood transfusion. However, the primary aim should be to treat the anaemia by other means before this point is reached.

**Blood transfusion should only be considered when the anaemia is likely to cause or has caused a reduction in oxygen supply that is inadequate for the patient's needs.**

The management of anaemia will vary according to the cause, time course and degree of compensation to the anaemia. This requires a detailed assessment of the individual patient. However, the general principles of the treatment of anaemias are:

- Treat the underlying cause of the anaemia
- Optimize all the components of the oxygen delivery system to improve the oxygen supply to the tissues.

## Treating the underlying cause of the anaemia

Treatment aimed at the underlying cause of the anaemia will often prevent any further reduction in oxygen-carrying capacity. For example, in a chronic anaemia due to an infestation, eliminating the parasite will prevent further deterioration in the haemoglobin concentration.

## Improving the oxygen supply to the tissues

Remember that the haemoglobin concentration of a patient is only one of the critical factors that determines the overall supply of oxygen to the tissues. The oxygen supply to the tissues also depends on:

- Degree of saturation of haemoglobin with oxygen
- Cardiac output.

Treatment aimed at optimizing all the factors of the oxygen supply system will improve the availability of oxygen to the tissues.

In acute haemorrhage, for example, the oxygen supply will be improved by:

- Restoring the cardiac output with intravenous fluid replacement therapy
- Increasing the inspired oxygen concentration to raise the saturation of haemoglobin
- Transfusion, if necessary, to raise the haemoglobin concentration.

In a chronic iron deficiency anaemia, elevating the haemoglobin level with simple oral iron therapy will improve the supply and availability of oxygen to the tissues.

The specific treatment measures for different types of anaemia are discussed more fully in Section 9: *General Medicine*.

## 3.11 Principles of the prevention of anaemia

**One of the most important means of achieving the appropriate clinical use of blood and blood products is the implementation of effective public health programmes to prevent the conditions that make transfusion necessary.**

Preventive measures can only work successfully with government involvement, especially with the effective organization of the primary health care system.

In many developing countries, the majority of transfusions are given to children under the age of five and women of childbearing age. These groups should be a particular target for preventive measures through the provision of adequate and accessible maternal and child health services.

Details of specific preventive measures can be found in the relevant sections later in the module. However, the prevention of anaemia in a population will often include the following activities.

1 Health education on:
- ■ Nutrition
- ■ Hygiene, sanitation, clean water supplies
- ■ Prevention of malaria: e.g. the use of bednets impregnated with insecticide
- ■ Fire prevention
- ■ Road safety.

2 Supplementation programmes: the administration of iron and/ or folate supplements to targeted groups.

3 Dietary modification: e.g. enhancing iron absorption by increasing dietary vitamin C.

4 Control of viral, bacterial and parasitic infections, including:
- ■ Immunization programmes
- ■ Improvements in sanitation and water supplies
- ■ Eradication of sources of infection: e.g. hookworm, malaria
- ■ Treatment of infection or infestation: e.g. deworming.

5 Food fortification: the fortification with iron of centrally-processed staple foods, such as bread, milk, salt, rice, sugar and fish products may be appropriate in some countries.

---

### ACTIVITY 9

*What measures are taken in your country at national and local level to identify, prevent and treat anaemia in susceptible sections of the population?*

*How effective do you think they are? Can you suggest any ways of improving their effectiveness?*

# 4

# Replacement fluids

## Key points

1  Replacement fluids are used to replace abnormal losses of blood, plasma or other extracellular fluids in:
   - Treatment of patients with established hypovolaemia: e.g. haemorrhagic shock
   - Maintenance of normovolaemia in patients with ongoing fluid losses: e.g. surgical blood loss.

2  Intravenous replacement fluids are the first-line treatment for hypovolaemia. Initial treatment with these fluids may be life-saving and provide some time to control bleeding and obtain blood for transfusion if it becomes necessary.

3  Crystalloid maintenance fluids, which contain dextrose, are not suitable for use as replacement fluids. Only crystalloid solutions with a similar concentration of sodium to plasma (normal saline or balanced salt solutions) are effective as replacement fluids. These should be available in all hospitals where intravenous replacement fluids are used.

4  Crystalloid replacement fluids should be infused in a volume at least three times the volume lost in order to correct hypovolaemia.

5  All colloid solutions (albumin, dextrans, gelatines and hydroxyethyl starch solutions) are replacement fluids. However, they have not been shown to be superior to crystalloids in resuscitation.

6  Colloid solutions should be infused in a volume equal to the blood volume deficit.

7  Plasma should never be used as a replacement fluid.

8  Plain water should never be infused intravenously. It will cause haemolysis and will probably be fatal.

9  In addition to the intravenous route, the intraosseous, oral, rectal or subcutaneous routes can be used for the administration of fluids.

## Introduction

Intravenous fluids have a variety of uses. These include:

■ Providing the normal maintenance fluid requirements of a patient in whom the oral route is unavailable

■ Providing replacement fluids for abnormal losses incurred as a result of surgery, trauma or other pathology

■ Correcting electrolyte disturbances or hypoglycaemia

■ Acting as a vehicle for the administration of certain drugs.

This section focuses on intravenous replacement fluids. It examines the two types, crystalloids and colloids, and discusses their properties, uses, advantages and disadvantages.

## Learning outcomes

When you have completed this section, you should be able to:

1 Explain the difference between maintenance and replacement fluids and be familiar with the characteristics of the crystalloids and colloids in current use.

2 Prescribe the most suitable replacement fluids available for hypovolaemic patients.

3 Contribute to a policy to ensure the availability of essential replacement fluids in your hospital.

## 4.1  Definitions

### Maintenance fluids

**maintenance fluids**:
Crystalloid solutions that are used to replace normal physiological losses through skin, lung, faeces and urine.

Maintenance fluids are fluids used to replace the normal physiological losses that occur in a patient through skin, lung, faeces and urine. Since a considerable proportion of these losses is water, maintenance fluids are mainly composed of water in the form of a dextrose solution. Some electrolytes may also be included in these solutions.

All maintenance fluids are crystalloid solutions. Some examples of crystalloids that are suitable as maintenance fluids are:

- 5% dextrose
- 4% dextrose in sodium chloride 0.18%.

The volume of maintenance fluids required by a patient will vary, particularly with pyrexia, high ambient temperature or humidity, when losses will increase.

Figure 4.1 gives the fluid and electrolyte requirements for adults and children under normal circumstances.

*Figure 4.1: Normal fluid and electrolyte requirements for children and adults*

| Weight | Fluid ml/kg/24 hours | | Sodium mmol/kg/24 hours | Potassium mmol/kg/24 hours |
|---|---|---|---|---|
| **Children** | | | | |
| First 10 kg | 100 | (4*) | 3 | 2 |
| Second 10 kg | 50 | (2*) | 1.5 | 1 |
| Subsequent kg | 20 | (1*) | 0.75 | 0.5 |
| **Adults** | | | | |
| All weights (kg) | 35 | (1.5*) | 1 | 0.75 |

\* These figures represent the fluid requirements in ml/kg/hour

### ACTIVITY 10

*Calculate the normal maintenance fluid requirements in a 16 kg child for a 24 hour period. What are the sodium and potassium requirements for the same child in a period of 24 hours?*

### Replacement fluids

**replacement fluids:** Fluids used to replace abnormal losses of blood, plasma or other extracellular fluids by increasing the volume of the vascular compartment.

Replacement fluids are used to replace abnormal losses of blood, plasma or other extracellular fluids by increasing the volume of the vascular compartment. They are sometimes also called plasma substitutes.

Replacement fluids are used principally in:

- Treatment of patients with established hypovolaemia: e.g. haemorrhagic shock

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- Maintenance of normovolaemia in patients with ongoing fluid losses: e.g. surgical blood loss.

All colloid solutions are replacement fluids. However, only crystalloid solutions that contain a sodium concentration similar to plasma are suitable as replacement fluids.

**balanced salt solution**: Usually a sodium chloride salt solution with an electrolyte composition that resembles that of extracellular fluid.

Some of these crystalloids have a composition resembling extracellular fluid and are known as **balanced salt solutions**: e.g. Ringer's lactate or Hartmann's solution.

Examples of replacement fluids are:
- Crystalloids with a similar concentration of sodium to plasma:
  — Normal saline (sodium chloride 0.9%)
  — Ringer's lactate
  — Hartmann's solution
- All colloid solutions.

## 4.2  Intravenous replacement therapy

In hypovolaemia, the primary goal of treatment is to restore the circulating blood volume in order to maintain tissue perfusion and oxygenation.

The administration of replacement fluids achieves this by increasing the volume of the vascular compartment. A blood transfusion may also become necessary if there is extensive blood loss. However, even in cases of severe haemorrhage, initial treatment with intravenous replacement fluids may be life-saving and will allow time to obtain blood for transfusion.

**Intravenous replacement fluids are the first-line treatment for hypovolaemia.**

## 4.3  Intravenous replacement fluids

### Crystalloids

**crystalloid solution**: Aqueous solution of small molecules which easily pass through capillary membranes: e.g. normal saline, balanced salt solutions.

Crystalloids are composed of crystalline substances such as dextrose or sodium chloride which, when dissolved in water, form a clear solution of electrolytes or sugars.

Crystalloid replacement fluids contain a similar concentration of sodium to plasma. This ensures that they are excluded from the intracellular compartment since the cell membrane is generally impermeable to sodium. However, they readily cross the capillary membrane from the vascular compartment to the interstitial compartment to become rapidly distributed throughout the whole extracellular compartment.

Normally, only a quarter of the crystalloid solution remains in the vascular compartment. For this reason, crystalloids should be infused in a volume at least three times the deficit in order to restore circulating blood volume (intravascular volume).

**Crystalloids should be infused in a volume at least three times the blood volume deficit in order to correct hypovolaemia.**

When large volumes of crystalloid fluid are administered, oedema may develop as a result of the fluid that passes (or 'leaks') from the circulation into the interstitial compartment. Careful monitoring of the patient's clinical condition is therefore essential.

Crystalloid maintenance fluids, which contain mainly dextrose, are not recommended for use as replacement fluids (see Figure 4.2).

*Figure 4.2: Suitability of intravenous fluids as either maintenance or replacement fluids*

| Fluid | Crystalloids composed mainly of dextrose | Crystalloids with high sodium content and balanced salt solutions | Colloids |
|---|---|---|---|
| Maintenance fluids | ✔ | ✗ | ✗ |
| Replacement fluids | ✗ | ✔ | ✔ |

The dextrose rapidly becomes metabolized leaving only water, which readily crosses the capillary and cell wall membranes to become distributed throughout the extracellular and intracellular compartments. Only a very small fraction remains in the vascular compartment, as shown in Figure 4.3.

*Figure 4.3: Distribution of intravenous fluids*
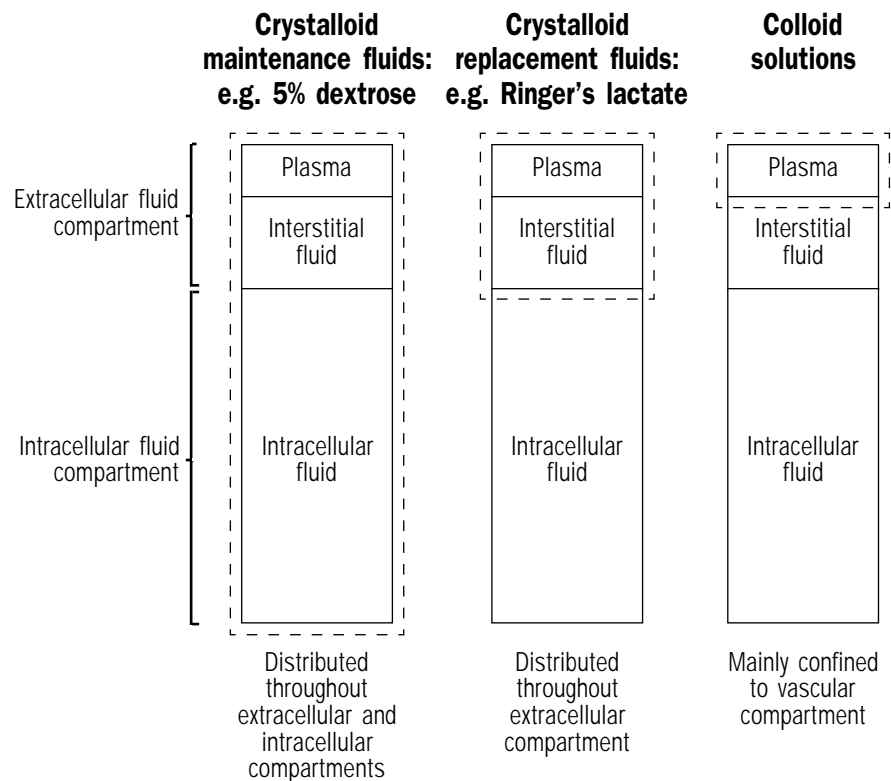


**Dextrose (glucose) solutions do not contain sodium and are poor replacement fluids. Do not use them to treat hypovolaemia unless there is no other alternative.**

## Colloids

Colloid solutions are composed of a suspension of particles that have a much larger molecular weight than crystalloids. These particles are generally too big to pass through the capillary membrane and initially tend to remain within the vascular compartment. The effect of these particles in the circulation is to mimic plasma proteins, thereby maintaining or raising the colloid osmotic pressure of blood.

The molecular weight and number of particles in a colloid solution is important in determining its properties. The larger the particle sizes, the longer the duration of action of the solution in the vascular compartment. Also, the higher the number of particles in the solution, the greater the osmotic effect.

Solutions with an **oncotic pressure** greater than that of plasma have the capacity to draw water from the interstitial compartment into the blood. The increase in blood volume may thus exceed the infused volume (see Figure 4.3).

Colloids can be classified as:

1   Plasma-derived (natural): prepared from donated human blood or plasma (e.g. albumin). These should not be used simply as replacement fluids.

2   Synthetic: prepared from another source (e.g. bovine cartilage).

**Colloids require smaller infusion volumes than crystalloids. They are usually given in a volume equal to the blood volume deficit.**

However, in many conditions where the capillary permeability is increased, they may leak out of the circulation and produce only a short-lived volume expansion. Supplementary infusions will be necessary to maintain blood volume in conditions such as:

■   Trauma
■   Acute and chronic sepsis
■   Burns
■   Snake bite (haemotoxic and cytotoxic).

**Danger: Never infuse plain water intravenously. It will cause haemolysis.**

## The ideal intravenous replacement fluid

The most important property of an intravenous replacement fluid is simply to occupy volume in the vascular compartment. An ideal replacement fluid should do this for a sufficient length of time and without interfering with the normal functions of the blood. Furthermore, it should be:

■   Easily available and inexpensive
■   Non-toxic

**colloid solution**: A solution of large molecules, which have a restricted passage through capillary membranes. Used as a replacement fluid: e.g. gelatines, dextrans, hydroxyethyl starch.

**oncotic pressure**: Osmotic pressure exerted by colloid solutions. Also called 'colloid osmotic pressure'.

■ Free of allergic reactions and risk of infection

■ Totally metabolized or eliminated from the body.

Unfortunately, no fluid yet satisfies all these requirements. It is important, therefore, to be familiar with the properties and characteristics of the replacement fluids used in your hospital and to be able to use them safely.

### The crystalloids or colloids controversy

Much has been written about the crystalloids or colloids controversy, but it can be summarized as follows. Most clinicians agree that, in hypovolaemic patients, it is essential to restore blood volume with replacement fluids. However, they disagree on the type of fluid that should be used.

Both crystalloids and colloids have advantages and disadvantages, as shown in Figure 4.4. However, ensuring that an adequate volume of replacement fluid (of whatever type) is administered to a hypovolaemic patient is more important than the choice of fluid.

*Figure 4.4: The advantages and disadvantages of crystalloids and colloids*

| | **Advantages** | **Disadvantages** |
|---|---|---|
| **Crystalloids** | ■ Few side-effects <br> ■ Low cost <br> ■ Wide availability | ■ Short duration of action <br> ■ May cause oedema <br> ■ Weighty and bulky |
| **Colloids** | ■ Longer duration of action <br> ■ Less fluid required to correct hypovolaemia <br> ■ Less weighty and bulky | ■ No evidence that they are more clinically effective <br> ■ Higher cost <br> ■ May cause volume overload <br> ■ May interfere with clotting <br> ■ Risk of anaphylactic reactions |

**There is no evidence that colloid solutions are superior to normal saline or balanced salt solutions in resuscitation.**

If the supply of infusion fluids is limited, it is recommended that, wherever possible, the crystalloid normal saline (sodium chloride 0.9%) or a balanced salt solution such as Ringer's lactate or Hartmann's solution should be available in all hospitals where intravenous replacement fluids are used.

### Safety

Before giving any intravenous infusion:

1 Check that the seal of the infusion fluid bottle or bag is not broken.

2 Check the expiry date.

3 Check that the solution is clear and free from visible particles.

## 4.4 Other routes of administration of fluids

It is important to remember that there are other routes of fluid administration in addition to the intravenous route. However, with the exception of the intraosseous route, these routes are generally unsuitable in the severely hypovolaemic patient.

### Intraosseous fluids

The intraosseous route can provide the quickest access to the circulation in a shocked child in whom venous cannulation is impossible. Fluids, blood and certain drugs can be administered by this route (see Section 13.6: *The Management of Paediatric Patients*).

### Oral and nasogastric fluids

Oral rehydration can often be used in mildly hypovolaemic patients if the oral route is not contraindicated. Do not use if:

- The patient is unconscious
- The patient has gastrointestinal lesions or reduced gut motility: e.g. obstruction
- General anaesthesia and surgery is planned imminently.

Several proprietary preparations of oral rehydration salts are available in the form of a powder that is reconstituted with clean drinkable water. There are small differences in composition between them. The WHO/UNICEF salt solution formula is shown in Figure 4.5.

*Figure 4.5: WHO/UNICEF formula for oral rehydration fluid*

**Oral rehydration fluid**

**Dissolve in one litre of drinkable water**
- Sodium chloride (table salt)                            3.5 g
- Sodium bicarbonate (baking soda)                  2.5 g
- Potassium chloride or suitable substitute        1.5 g
  (degassed cola drink or banana)
- Glucose (sugar)                                             20.0 g

**Resulting concentrations**
Na$^+$ 90 mmol/L   Cl$^-$ 80 mmol/L   K$^+$ 20 mmol/L   Glucose 110 mmol/L

### Rectal fluids

The rectum may be used for the administration of fluids. It readily absorbs fluids, and absorption ceases with fluids being ejected when hydration is complete. Rectal fluids are administered through a plastic or rubber enema tube which is inserted into the rectum and connected to a bag or bottle of fluid. The fluid rate can be controlled by using a drip giving-set, if necessary.

The fluids used do not have to be sterile. A safe and effective solution for rectal rehydration is 1 litre of clean drinking water to which is added a teaspoon of table salt.

### Subcutaneous fluids

Occasionally, when other routes of administration of fluids are unavailable, a subcutaneous infusion can be used. A cannula or needle is inserted into the subcutaneous tissue (the abdominal wall is a preferred site) and sterile fluids are administered in a conventional manner.

Do not give dextrose-containing solutions subcutaneously as they can cause sloughing of tissues.

## 4.5 Replacement fluids: characteristics

The remainder of this section details some commercially-available intravenous replacement fluids. The composition of replacement fluids and plasma is shown in Figure 4.6 on p. 66.

Some hospitals manufacture intravenous fluids locally. It is important to check the formulation of these products to ensure they are used appropriately.

### ACTIVITY 11

*Check that your own knowledge of crystalloids and colloids is complete and that you are familiar with their characteristics and uses.*

*Organize a teaching session for relevant staff to refresh their understanding of the use and effects of replacement fluids.*

### ACTIVITY 12

*Make a list of the replacement fluids that are available in your hospital. Do you think any alternative or additional replacement fluids should be available in your hospital?*

*Is the supply of replacement fluids inappropriate, inadequate or irregular? If yes, what are the reasons?*
- *National or local policy*
- *Cost*
- *Transportation problems.*

*Consider how you might influence the policy on replacement fluids used in your hospital. Talk to your senior colleagues and develop a plan to work towards the wider provision and effective use of those replacement fluids that you consider to be essential.*

### ACTIVITY 13

*Are there any written guidelines on the use of replacement fluids in your hospital? If yes, are they used appropriately and consistently?*

*If no guidelines currently exist, develop some guidelines in conjunction with senior colleagues. Organize a teaching session for relevant staff and monitor the implementation of the guidelines.*

*Figure 4.6: Composition of replacement fluids and plasma*

| Fluid | Na$^+$ mmol/L | K$^+$ mmol/L | Ca$^{2+}$ mmol/L | Cl$^-$ mmol/L | Base$^-$ mEq/L | Colloid osmotic pressure mmHg |
|---|---|---|---|---|---|---|
| **Crystalloids** | | | | | | |
| Normal saline (sodium chloride 0.9%) | 154 | 0 | 0 | 154 | 0 | 0 |
| Balanced salt solutions (Ringer's lactate/ Hartmann's solution) | 130–140 | 4–5 | 2–3 | 109–110 | 28–30 | 0 |
| **Colloids** | | | | | | |
| Gelatine (urea linked): e.g. Haemaccel | 145 | 5.1 | 6.25 | 145 | Trace amounts | 27 |
| Gelatine (succinylated): e.g. Gelofusine | 154 | <0.4 | <0.4 | 125 | Trace amounts | 34 |
| Dextran 70 (6%) | 154 | 0 | 0 | 154 | 0 | 58 |
| Dextran 60 (3%) | 130 | 4 | 2 | 110 | 30 | 22 |
| Hydroxyethyl starch 450/0.7 (6%) | 154 | 0 | 0 | 154 | 0 | 28 |
| Albumin 5% | 130–160 | <1 | V | V | V | 27 |
| Ionic composition of normal plasma | 135–145 | 3.5–5.5 | 2.2–2.6 | 97–110 | 38–44 | 27 |
| V = varies between different brands | | | | | | |

# Crystalloid solutions

## NORMAL SALINE (Sodium chloride 0.9%)

| | |
|---|---|
| Description | Consists of an isotonic solution of sodium chloride in a near-physiological concentration. 154 mmol/L each of $Na^+$ and $Cl^-$ |
| Unit of issue | 500 ml or 1000 ml bags |
| Infection risk | Nil |
| Storage | In a cool place |
| Dosage | At least 3 times the blood volume lost |
| Plasma half-life | Short, approximately 45 minutes: rapidly distributed throughout extracellular compartment |
| Indications | Replacement of blood volume and other extracellular fluid losses |
| Precautions | ■ Caution in situations where local oedema may aggravate pathology: e.g. head injury <br> ■ May precipitate fluid overload and heart failure |
| Contraindications | Do not use in patients with established renal failure |
| Side-effects | Tissue oedema can develop when large volumes are used |

## BALANCED SALT SOLUTIONS

| | |
|---|---|
| Description | These solutions have a composition that more closely resembles extracellular fluid (see Figure 4.6) and can therefore be infused in large volumes without disturbing the electrolyte balance |
| Examples | ■ Ringer's lactate <br> ■ Hartmann's solution |
| Unit of issue | 500 ml or 1000 ml bags |
| Infection risk | Nil |
| Storage | In a cool place |
| Dosage | At least 3 times the blood volume lost |
| Plasma half-life | Short, approximately 45 minutes: rapidly distributed throughout extracellular compartment |
| Indications | Replacement of blood volume and other extracellular fluid losses |
| Precautions | ■ Caution in situations where local oedema may aggravate pathology: e.g. head injury <br> ■ May precipitate fluid overload and heart failure |
| Contraindications | Do not use in patients with established renal failure |
| Side-effects | Tissue oedema can develop when large volumes are used |

**DEXTROSE AND ELECTROLYTE SOLUTIONS**

| | |
|---|---|
| Examples | ■ 4.3% dextrose in sodium chloride 0.18% |
| | ■ 2.5% dextrose in sodium chloride 0.45% |
| | ■ 2.5% dextrose in half-strength Darrow's solution |
| Description | Dextrose solutions containing some electrolytes; as the concentration of sodium is decreased, an increasing amount of fluid will cross into cells |
| Plasma half-life | Very short: rapidly distributed throughout extracellular and intracellular compartment |
| Indications | Generally used for maintenance fluids, but those containing a higher concentration of sodium can, if necessary, be used as replacement fluids |

**Note**

2.5% dextrose in half-strength Darrow's solution is commonly used to correct dehydration and electrolyte disturbances in children with gastroenteritis.

Several products are manufactured for this use. Not all are suitable. Ensure that the preparation you use contains:
■ Dextrose    2.5%
■ Sodium      60 mmol/L
■ Potassium   17 mmol/L
■ Chloride    52 mmol/L
■ Lactate     25 mmol/L

# Plasma-derived (natural) colloid solutions

Plasma-derived colloids are all prepared from donated blood or plasma. They include:

- Plasma
- Fresh frozen plasma
- Liquid plasma
- Freeze-dried plasma
- Albumin

**These products should not be used simply as replacement fluids**. They can carry a similar risk of transmitting infection, such as HIV and hepatitis, as whole blood. They are also generally more expensive than crystalloid or synthetic colloid fluids.

A description of these products is given in Section 5: *Blood Products*.

# Synthetic colloid solutions

**GELATINES (Haemaccel, Gelofusine)**

| | |
|---|---|
| Description | Consist of molecular chains of gelatine prepared from bovine collagen with an average molecular weight of 30,000 |
| Formulations | ■ Haemaccel: 3.5% gelatine in sodium chloride 0.9%<br>■ Gelofusine: 4% gelatine in sodium chloride 0.9% |
| Unit of issue | 500 ml bags |
| Infection risk | None known at present |
| Storage | At room temperature below 25°C: stable for 5 years |
| Dosage | No known dose limit |
| Colloid osmotic pressure | ■ Haemaccel: approximately 27 mmHg. Expansion of plasma volume equals the volume infused<br>■ Gelofusine: approximately 34 mmHg. Expansion of plasma volume exceeds the volume infused |
| Plasma half-life | Approximately 4 hours: short duration of action, although longer than crystalloids |
| Elimination | Renal excretion |
| Indications | Replacement of blood volume |
| Precautions | ■ May precipitate heart failure<br>■ Caution in renal insufficiency<br>■ Do not mix Haemaccel with citrated blood because of its high calcium concentration |
| Contraindications | Do not use in patients with established renal failure |
| Side-effects | ■ Minor allergic reactions due to histamine release<br>■ Transient increases in bleeding time may occur<br>■ Hypersensitivity reactions may occur including, rarely, severe anaphylactic reactions |

## DEXTRAN 60 AND DEXTRAN 70

| | |
|---|---|
| Description | Consists of macromolecular glucose chains with an average molecular weight of 70,000 |
| Formulations | ■ 3% dextran 60 in sodium chloride 0.9%<br>■ 6% dextran 70 in sodium chloride 0.9%<br>■ 6% dextran 70 in 5% dextrose |
| Unit of issue | 500 ml bottles or bags |
| Infection risk | Nil |
| Storage | At room temperature not exceeding 25°C |
| Dosage | Dextran 60: should not exceed 50 ml/kg body weight in 24 hours<br>Dextran 70: should not exceed 25 ml/kg body weight in 24 hours |
| Colloid osmotic pressure | Approximately 58 mmHg. Expansion of plasma volume exceeds the volume infused |
| Plasma half-life | Approximately 12 hours |
| Elimination | Predominantly renal excretion |
| Indications | ■ Replacement of blood volume<br>■ Prophylaxis of post-operative venous thrombosis |
| Precautions | ■ Coagulation defects may occur<br>■ Platelet aggregation inhibited<br>■ Some preparations may interfere with compatibility testing of blood |
| Contraindications | Do not use in patients with pre-existing disorders of haemostasis and coagulation |
| Side-effects | ■ Minor allergic reactions<br>■ Transient increases in bleeding time may occur<br>■ Hypersensitivity reactions may occur including, rarely, severe anaphylactic reactions. Can be prevented with injection of 20 ml of Dextran 1 immediately before infusion, where available |

## DEXTRAN 40 AND DEXTRAN 110

Not recommended as replacement fluids

## HYDROXYETHYL STARCH (Hetastarch or HES)

| | |
|---|---|
| Description | Consists of macromolecules manufactured from natural starch, with a range of molecular weights: e.g. 450 000 |
| Formulation | 6% hetastarch in sodium chloride 0.9% |
| Unit of issue | 500 ml bags |
| Infection risk | Nil |
| Storage | In a cool place |
| Dosage | Should not usually exceed 20 ml/kg body weight in 24 hours |
| Colloid osmotic pressure | Approximately 28 mmHg. Expansion of plasma volume slightly exceeds the volume infused |
| Plasma half-life | 12–24 hours |
| Elimination | Predominantly renal excretion |
| Precautions | ■ Coagulation defects may occur<br>■ May precipitate fluid overload and heart failure |
| Indications | Replacement of blood volume |
| Contraindications | ■ Do not use in patients with pre-existing disorders of haemostasis and coagulation<br>■ Do not use in patients with established renal failure |
| Side-effects | ■ Minor allergic reactions due to histamine release<br>■ Transient increases in bleeding time may occur<br>■ Hypersensitivity reactions may occur including, rarely, severe anaphylactic reactions<br>■ Serum amylase level may rise (not significant)<br>■ HES is retained in cells of the reticuloendothelial system; the long-term effects of this are unknown |

## PENTASTARCH

■ Similar to hetastarch, but comprises a 10% solution with an average molecular weight of 280 000
■ Shorter half-life of 10 hours
■ Oncotic pressure is approximately 40 mmHg; expansion of plasma volume therefore exceeds volume infused

## SYNTHETIC BLOOD PRODUCTS

Two products, stroma-free haemoglobin and perflurocarbons, are currently under investigation. They are colloids and have the advantage of being able to carry oxygen. Neither is available for clinical use at present.

# 5

# Blood products

## Key points

1   Safe blood products, used correctly, can be life-saving. However, even where quality standards are very high, transfusion carries some risks. If standards are poor or inconsistent, transfusion may be extremely risky.

2   No blood or blood product should be administered unless all nationally required tests are shown to be negative.

3   Each unit should be tested and labelled to show its ABO group and its Rh D group.

4   Whole blood can be transfused to replace red cells in acute bleeding when there is also a need to correct hypovolaemia.

5   The preparation of blood components allows a single blood donation to provide treatment for two or three patients and also avoids the transfusion of elements of the whole blood that the patient may not require. Blood components can also be collected by apheresis.

6   Plasma can transmit most of the infections present in whole blood and there are very few indications for its transfusion.

7   Plasma derivatives are made by a pharmaceutical manufacturing process from large volumes of plasma comprising many individual blood donations. They must be tested to minimize the risks of transmitting infection.

8   Factors VIII and IX and immunoglobulins are also made by recombinant DNA technology and are often favoured because there should be no risk of transmitting infectious agents to the patient. However, the costs are high and there have been some reported cases of complications.

## Introduction

The term 'blood product' refers to any therapeutic substance prepared from human blood.

Blood can be separated into a variety of blood components for different clinical indications. However, many countries have no facilities for component separation and whole blood remains the most widely used product in most developing countries. The use of whole blood may be the safest and most sustainable way of meeting most urgent transfusion requirements. However, where resources are available, the use of blood components offers certain advantages.

This section describes the methods of production of various blood products and summarizes their characteristics and indications for their use. You should be familiar with each of the blood products used in your hospital, whether whole blood, blood components or plasma derivatives.

Since blood transfusion involves the transplant of tissue from the donor to the recipient, there are risks to the recipient of transfusion-transmitted infection and of immunological responses to foreign cells or plasma proteins (see Section 7: *Adverse Effects of Transfusion*).

You should only prescribe blood products when there are clear indications for doing so. Used correctly, they are life-saving. Inappropriate use can endanger life.

## Learning outcomes

When you have completed this section, you should be able to:

1   Describe the main characteristics of each blood product in current use in your hospital.

2   Prescribe the most appropriate blood product available for each patient requiring transfusion.

3   Explain the main factors that may influence the availability and use of blood products.

## 5.1  Definitions

Where the term 'blood' is used in this module, it refers to any blood component in which the main constituent is red blood cells (i.e. whole blood, red cell concentrates or red cell suspension), unless otherwise specified. Definitions of the different blood products are given in Figure 5.1.

*Figure 5.1: Blood products: definitions*

| DEFINITIONS | |
|---|---|
| **Blood product** | Any therapeutic substance prepared from human blood |
| **Whole blood** | Unseparated blood collected into an approved container containing an anticoagulant-preservative solution |
| **Blood component** | 1  A constituent of blood, separated from whole blood, such as:<br>  ■ Red cell concentrate<br>  ■ Red cell suspension<br>  ■ Plasma<br>  ■ Platelet concentrates<br><br>2  Plasma or platelets collected by apheresis*<br><br>3  Cryoprecipitate, prepared from fresh frozen plasma, which is rich in Factor VIII and fibrinogen |
| **Plasma derivative** | Human plasma proteins prepared under pharmaceutical manufacturing conditions, such as:<br>  ■ Albumin<br>  ■ Coagulation factor concentrates<br>  ■ Immunoglobulins |
| * Apheresis: a method of collecting plasma or platelets directly from the donor, usually by a mechanical method | |

## 5.2  Whole blood

Whole blood is obtained from human blood donors by venesection. During donation, blood is collected into a sterile, disposable, plastic pack which contains an anticoagulant-preservative solution. This solution usually contains citrate, phosphate, dextrose and often adenine (CPDA). Their functions are summarized in Figure 5.2.

There are variations in the volume of blood collected and in the type of anticoagulant-preservative solution used in different regions of the world. Glass bottles are still used in some countries for blood collection and storage.

During storage, metabolism continues in the red cells and platelets, while some plasma proteins lose their biological activity. The biochemical and metabolic effects of storage are summarized in Figure 5.3.

*Figure 5.2: Functions of anticoagulant-preservative solution in blood collection pack*

| Solutions | | Functions |
|---|---|---|
| C | Sodium citrate | Binds with calcium ions in blood in exchange for the sodium salt so the blood does not clot |
| P | Phosphate | Supports metabolism of the red cells during storage to ensure they release oxygen readily at tissue level |
| D | Dextrose | Maintains the red cell membrane to increase storage life |
| A | Adenine | Provides energy source |

*Figure 5.3: Effects of storage on whole blood*

**Effects of storage on whole blood**

- Reduction in the pH (blood becomes more acidic)

- Rise in plasma potassium concentration (extracellular $K^+$)

- Progressive reduction in the red cell content of 2,3 diphosphoglycerate (2,3 DPG) which may reduce the release of oxygen at tissue level until 2,3 DPG is restored

- Loss of all platelet function in whole blood within 48 hours of donation

- Reduction in Factor VIII to 10–20% of normal within 48 hours of donation. Coagulation factors such as VII and IX are relatively stable in storage

Whole blood must be collected, tested and processed to high safety standards, as shown in Figure 5.4 on p. 76.

### Advantages
- Requires only simple and inexpensive single collection packs
- No special equipment is needed for processing
- For patients with haemorrhage, whole blood supplies red cells, volume and stable coagulation factors.

### Disadvantages
- For patients at risk of circulatory overload, whole blood contains a higher volume than red cell concentrate.

## 5.3 Blood components

Whole blood may be suitable for transfusion in many clinical situations, such as red cell replacement in acute blood loss where there is also hypovolaemia. However, the separation of whole blood into its constituent components – red cells, platelets and plasma – is widely practised for use when these specific components only are required.

Donor

Whole blood → Test: ABO and Rh D

Test: Infectious disease markers

Quarantine refrigerator          Negative                                    Positive

                                                                Discard:
                                                                unit destroyed

Release

Blood bank refrigerator

Compatibility test

Compatible
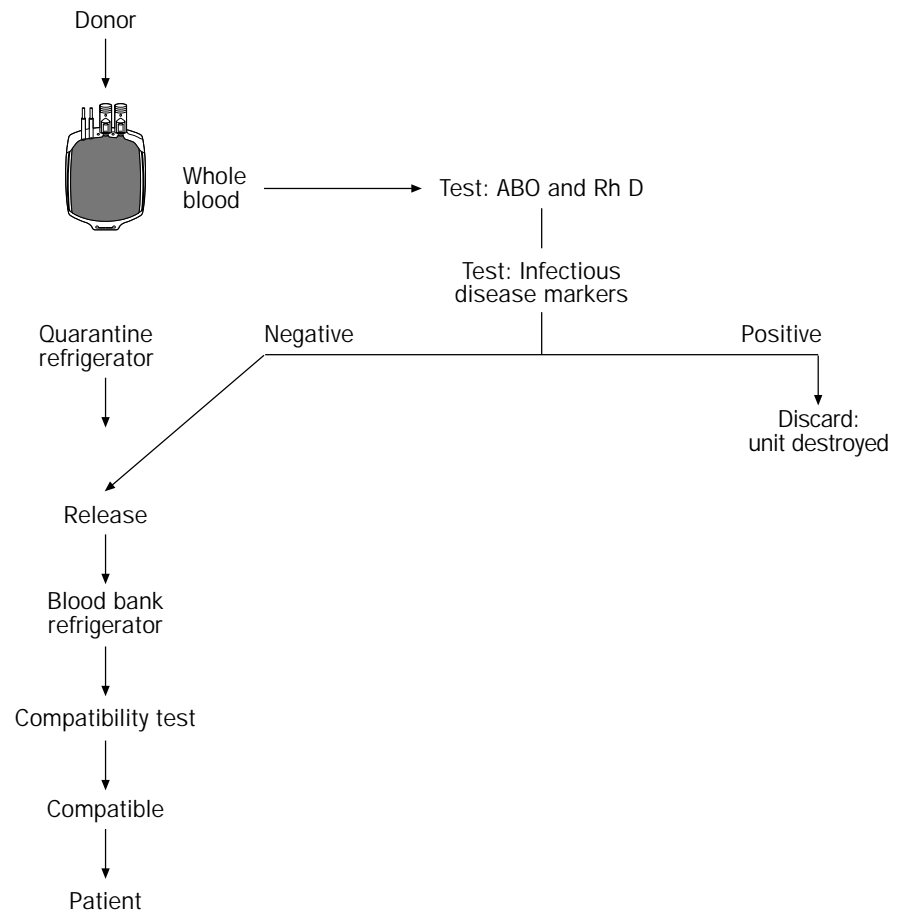
Patient

These components may be processed further by, for example:

■ Leucocyte (white cell) removal

■ 'Pooling' (combining platelets separated from 4–6 donations to produce a therapeutic dose for an adult patient), as shown in Figure 5.5.

The process of separation requires specialized plastic bags, more equipment, a higher level of expertise and more work to ensure the quality of the components produced.

**An infectious agent present in the donated blood may be transmitted to all recipients of the components prepared from a single donation.**

When the plasma is removed from whole blood, the red cells can be used as a red cell concentrate or can be formed into a red cell suspension by the addition of an additive diluent solution.

## Red cell concentrate

Red cell concentrate (also called packed red cells, concentrated red cells or plasma-reduced blood) is the simplest red cell component. It is prepared by allowing the blood to separate under gravity overnight in a refrigerator at a temperature of +2°C to +6°C or by centrifuging the blood pack in a special refrigerated centrifuge.

*Figure 5.5: Blood products*



**Platelet components**
■ 1 donation unit, recovered from 1 donation of whole blood
■ 'Pooled' unit (from 4–6 donation units)
■ 'Single donor' unit, prepared by apheresis

**Red cell components**
■ Red cell concentrate
■ Red cell suspension (red cells + additive solution)
■ Buffy coat depleted red cells
■ Leucocyte-depleted (filtered) red cells

**Plasma components**
■ Fresh frozen plasma
■ Liquid plasma
■ Freeze-dried plasma
■ Cryoprecipitate-depleted plasma
■ Viral-inactivated plasma
■ Cryoprecipitate

**Plasma derivatives**
■ Albumin
■ Coagulation factors
■ Immunoglobulin

The plasma is then removed by transferring it into a second empty plastic pack, which is supplied connected to the primary whole blood bag to ensure sterility, leaving all the red cells in the original blood collection pack (see Figure 5.6 on p. 78).

The red cell concentrate also contains white cells from the donated blood.

***Advantages***
■ Simple and inexpensive to prepare.

***Disadvantages***
■ It has a high ratio of red cells to plasma (high PCV/haematocrit) which increases viscosity, thereby increasing the time required for transfusion through a small gauge needle or cannula
■ The white cells are a cause of febrile non-haemolytic transfusion reactions in some patients.

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*Figure 5.6: Preparation of red cell concentrate*

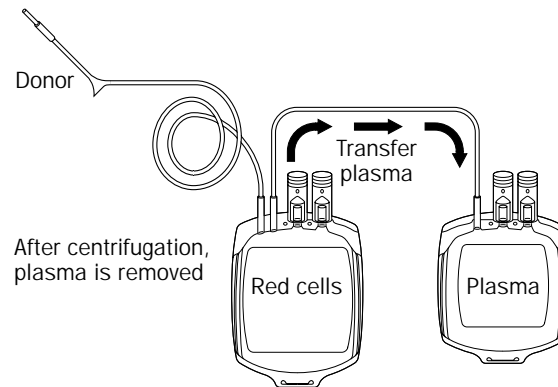**additive solution (red cell additive solution)**: Various proprietary formulas designed for reconstitution of red cells after separation of the plasma to give optimal red cell storage conditions. All are saline solutions with additions: e.g. adenine, glucose and mannitol.

## Red cell suspension

Red cell suspension is prepared by removing the plasma into a second empty plastic pack, as described above. An '**additive**' diluent solution formulated for the best preservation of the red cells is then transferred from a third plastic pack into the original pack (see Figure 5.7).
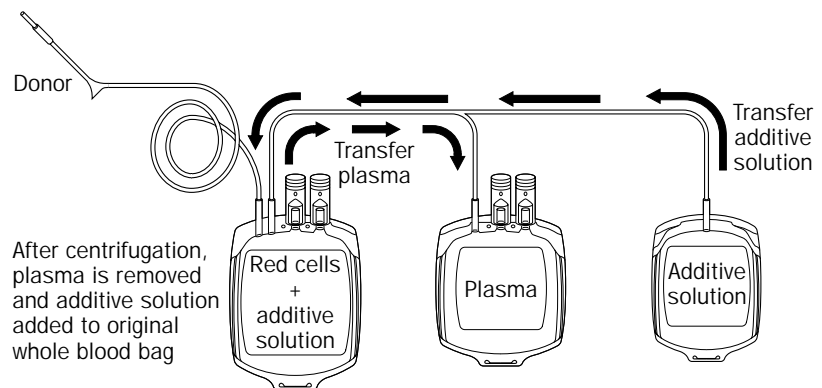


*Figure 5.7: Preparation of red cell suspension*

### *Advantages*

- Lower packed cell volume, which reduces viscosity and is therefore easier to infuse
- Better preservation of the red cells during storage, giving a longer shelf life than whole blood or red cell concentrate
- Permits the use of the separated components (plasma/platelets) for other patients.

### *Disadvantages*

- Cost: a special blood collection set containing three interconnected packs is required
- Expensive equipment (a refrigerated centrifuge) is required.

Figure 5.8 shows the volume of red cell components that can be prepared from a whole blood donation of 450 ml.

## White cells (leucocytes)

White cell transfusions have no proven clinical uses. The removal of white cells from other blood products (leucocyte-depletion) can reduce the incidence of febrile reactions and the risk of transmitting cytomegalovirus (CMV) and other intracellular infectious agents by transfusion.

*Figure 5.8: Volume of red cell components from a whole blood donation of 450 ml*

| Composition | Whole blood | Red cell concentrate/ packed red cells | Red cell suspension in additive solution |
|---|---|---|---|
| Blood | 400–500 ml | 220–340 ml | 280–420 ml |
| Anticoagulant-preservative solution | 63 ml | Minimal | 0 |
| Additive solution | | Small amount of plasma is left to improve viscosity plus some benefit of additive solution | 100 ml |
| Haemoglobin | Minimum 45 g | Minimum 45 g | Minimum 45 g |
| Haematocrit: % | 45–55% | 55–75% | 50–70% |
| Packed red cells: ml | 120–250 ml | 120–250 ml | 120–250 ml |
| Plasma | 200–300 ml | 50–70 ml | 10–20 ml (or less) |
| Maximum storage time at +2°C to +6°C | 21 days: ACD, CPD 35 days: CPDA | 21 days: CPD 35 days: CPDA | 42 days: CPDA + red cell additive solution (e.g. SAG-M, ADSOL) |

ACD  =  Acid Citrate Dextrose
CPD  =  Citrate Phosphate Dextrose
CPDA =  Citrate Phosphate Dextrose Adenine

## 'Buffy coat' depleted red cells

The removal of the white cells from whole blood requires controlled centrifugation so that the red cells settle to the bottom of the blood pack. The white cells (and most of the platelets) remain in a layer called the '**buffy coat**' which forms an interface between the red cells and the plasma.

Where funds are available, specialized bag systems and equipment can be used to remove the buffy coat.

**buffy coat**: The layer of white cells that forms at the interface between the red cells and plasma when blood is centrifuged.

### *Advantages*

■ Red cells are left, containing only about 10% of the white cells in red cell concentrate

■ Less risk of transfusion reactions due to white cell/leucocyte antibody reactions and the transmission of intracellular infection when the red cells are transfused

■ The 'buffy coat' can be used to prepare platelet concentrates.

### *Disadvantages*

■ Cost: special blood packs and equipment are required

■ More skill and operator training is needed.

### Leucocyte-depleted (filtered) red cells or whole blood

Special leucocyte filters can be used to remove virtually all the white cells. It is generally agreed that the best use of filters is made at the time of transfusion (i.e. at the patient's bedside) to avoid any contamination of the sterile blood before it leaves the blood bank.

#### *Advantages*

- Reduces development of immunity to white cells/leucocytes
- Reduces acute transfusion reactions, although removal of the buffy coat is much less expensive and is usually effective for this purpose
- Filtered blood containing less than $1 \times 10^6$ white cells per pack does not transmit cytomegalovirus infection (CMV).

#### *Disadvantages*

- Cost: special blood packs and equipment are required
- More skill and operator training is needed.

## Plasma

Plasma is separated from whole blood by centrifugation or by allowing the red cells to settle under gravity in a blood bank refrigerator. It can also be collected from donors by plasmapheresis (see Section 5.4 below).

The main clinical indication is for the treatment of coagulation disorders with bleeding due to reduced levels of several clotting factors. For this purpose, fresh frozen plasma must be used. This is separated from whole blood and frozen at –25°C or colder within 6–8 hours of donation in order to preserve its labile coagulation factors (Factors V and VIII).

Fresh frozen plasma can be stored for at least one year or longer if low temperatures can be maintained. When plasma is stored at a temperature of 2°C–6°C, the labile clotting activity of Factors V and VIII will decline to 10–20% within 48 hours.

Where facilities exist, plasma from donated blood should be fractionated to ensure a safe, virus-inactivated plasma derivative.

**Plasma is *not* recommended as a replacement fluid to correct hypovolaemia because:**

- **Plasma carries the same risk as whole blood of transmitting HIV, hepatitis viruses B and C and other transfusion-transmissible infections**
- **There is little evidence that plasma offers any additional clinical benefit over crystalloid replacement fluids or colloid fluids in the treatment of hypovolaemia**
- **Plasma is expensive; crystalloid replacement fluids are inexpensive and carry no risk of transmitting infection.**

## Platelet concentrates

Platelets separated from plasma obtained from 4–6 donations of whole blood are often pooled to produce a therapeutic dose of platelets for an adult. National guidelines generally require this dose to contain at least $240 \times 10^9/L$ platelets.

Pooling increases the risk of transmission of infection. A dose of platelets collected from a single donor by plateletpheresis (see Section 5.4 below), avoids exposure to several donations.

## 5.4  Component separation by apheresis

**apheresis**: Procedure that involves withdrawal of blood, ex vivo separation of a component (e.g. plasma and platelets) and reinfusion of the other components.

Apheresis is an alternative method of producing blood components. It is a sterile process in which a donor is connected to a specialized device by which blood is withdrawn and a specific component, usually plasma or platelets, is mechanically separated and collected. The red cells and other components of the blood that are not required are then reinfused back into the donor.

**Plasmapheresis** is the collection of donor plasma by apheresis.

**Plateletpheresis** is the collection of donor platelets by apheresis.

The advantage of apheresis is that relatively large amounts of plasma or platelets can be collected from a donor. Since the red cells are returned to the donor's circulation, this avoids making the donor anaemic and the process can be repeated at frequent intervals.

## 5.5  Plasma derivative production (plasma fractionation)

**plasma derivative**: Human plasma protein prepared under pharmaceutical manufacturing conditions. Include albumin, immunoglobulin and coagulation factor VIII and IX products.

Plasma derivative production, or plasma fractionation, is a pharmaceutical manufacturing process in which large quantities of plasma, obtained from whole blood separation or plasmapheresis, are pooled together and processed into specific products. These products include:

■  Albumin
■  Coagulation factors, such as Factor VIII and Factor IX
■  Immunoglobulin.

It is usual for a single vial of a plasma derivative product such as albumin, produced by a large fractionation plant, to contain plasma from as many as 30 000 different blood donations, as shown in Figure 5.9 on p. 82. A single manufacturing batch of this product may be sent to many countries around the world and be transfused to hundreds of individual patients. This form of transfusion thus has a substantial potential for spreading infection.

The risk of transfusion-transmitted infection can be avoided only by scrupulous quality control and good manufacturing practice throughout plasma fractionation, with the consistent use of effective methods to exclude, remove or inactivate any contaminants at all stages of the process, from blood donor selection through to final viral inactivation of the product.

*Figure 5.9: Plasma derivatives expose many recipients to plasma from many donors*
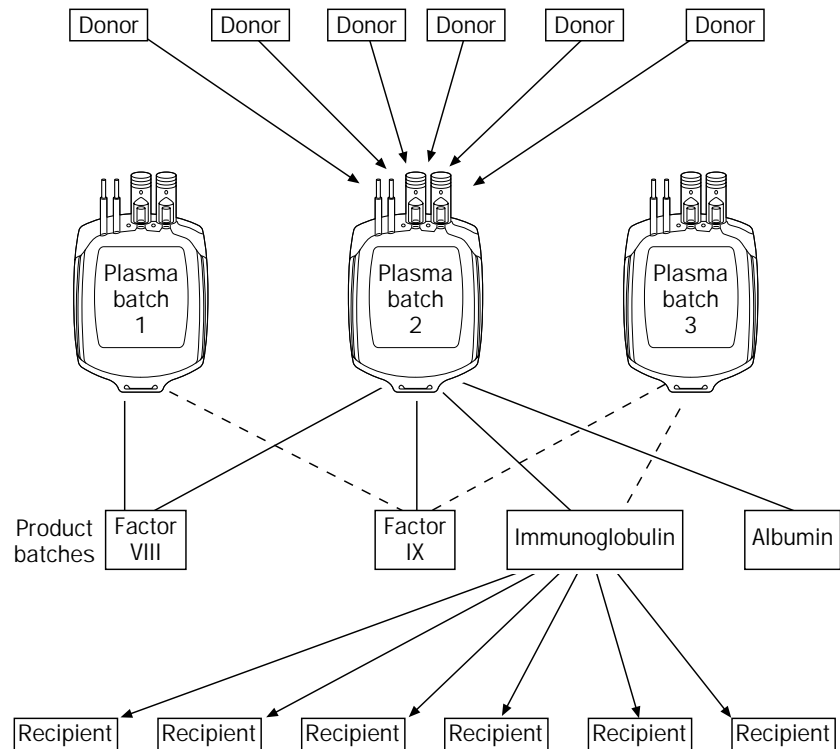
## 5.6 Blood products: characteristics

The remainder of this section summarizes the characteristics of individual blood products.

### ACTIVITY 14

*Check that your own knowledge of blood products is complete and that you are familiar with their characteristics and use.*

*Organize a teaching session for relevant staff to refresh their understanding of the use of blood products.*

### ACTIVITY 15

*Make a list of the blood products available in your hospital.*

*Are there any specific requirements for ordering special components, such as platelet concentrates or leucocyte-depleted red cells? For example, is a specialist consultant's request required or is it necessary to discuss the case with the blood bank?*

# Whole blood

## WHOLE BLOOD (CPD-Adenine-1)

Data for a 450 ml (10%) donation volume. Whole blood may contain an alternative anticoagulant/ additive solution.

| | |
|---|---|
| Description | ■ Up to 510 ml total volume (this volume may vary in accordance with local policies) |
| | ■ 450 ml donor blood |
| | ■ 63 ml anticoagulant |
| | ■ Haemoglobin approximately 12 g/ml |
| | ■ Haematocrit 35 (45%) |
| | ■ No functional platelets |
| | ■ No labile coagulation factors (V and VIII) |
| Unit of issue | 1 donation, also referred to as a 'unit' or 'pack' |
| Infection risk | Not sterilized, so is capable of transmitting any agent present in cells or plasma which has not been detected by routine screening for transfusion-transmissible infections, including: |
| | ■ HIV-1 and HIV-2 |
| | ■ Hepatitis B and C |
| | ■ Other hepatitis viruses |
| | ■ Syphilis |
| | ■ Malaria |
| | ■ Chagas disease |
| Storage | ■ Between +2°C and +6°C in an approved blood bank refrigerator, ideally fitted with a temperature chart and alarm |
| | ■ May be stored up to 35 days if collected in a suitable anticoagulant such as citrate phosphate dextrose with added adenine (CPDA-1) (see Figure 5.2) |
| | ■ During storage at +2°C to +6°C, changes in composition occur resulting from red cell metabolism (see Figure 5.3) |
| Indications | ■ Red cell replacement in acute blood loss with hypovolaemia |
| | ■ Exchange transfusion |
| | ■ Patients needing red cell transfusions where red cell concentrates or suspensions are not available |
| Contraindications | Risk of volume overload in patients with: |
| | ■ Chronic anaemia |
| | ■ Incipient cardiac failure |
| Administration | ■ Must be ABO and Rh compatible with the recipient |
| | ■ Complete transfusion within 4 hours of commencement |
| | ■ Never add medication to a unit of blood |

# Blood components

## RED CELL CONCENTRATE

May also be called 'packed red cells', 'concentrated red cells' or 'plasma-reduced blood'.

| | |
|---|---|
| Description | ■ 150–200 ml red cells from which most of the plasma has been removed |
| | ■ Haemoglobin approximately 20 g/100 ml (not less than 45 g per unit) |
| | ■ Haematocrit 55–75% |
| Unit of issue | 1 donation |
| Infection risk | Same as whole blood |
| Storage | Same as whole blood |
| Indications | ■ Replacement of red cells in anaemic patients |
| | ■ Use with crystalloid replacement fluids or colloid solution in acute blood loss |
| Administration | ■ Same as whole blood |
| | ■ To improve transfusion flow, normal saline (50–100 ml) may be added using a Y-pattern infusion set |

## RED CELL SUSPENSION

| | |
|---|---|
| Description | ■ 150–200 ml red cells with minimal residual plasma to which approximately 110 ml normal saline, adenine, glucose, mannitol solution (SAG-M) or an equivalent red cell nutrient solution has been added |
| | ■ Haemoglobin approximately 15 g/100 ml (not less than 45 g per unit) |
| | ■ Haematocrit 50–70% |
| Unit of issue | 1 donation |
| Infection risk | Same as whole blood |
| Storage | Same as whole blood |
| Indications | Same as red cell concentrate |
| Contraindications | Red cells suspended in additive solution are not advised for exchange transfusion of neonates. The additive solution may be replaced with plasma, 45% albumin or an isotonic crystalloid solution, such as normal saline (see Section 11: *Paediatrics & Neonatology*) |
| Administration | ■ Same as whole blood |
| | ■ Better flow rates are achieved than with red cell concentrate or whole blood |

**LEUCOCYTE-DEPLETED RED CELLS**

| | |
|---|---|
| Description | ■ A red cell suspension or concentrate containing $<5 \times 10^6$ white cells per pack, prepared by filtration through a leucocyte-depleting filter |
| | ■ Haemoglobin concentration and haematocrit depend on whether the product is whole blood, red cell concentrate or red cell suspension |
| | ■ Leucocyte depletion removes the risk of transmission of cytomegalovirus (CMV) |
| Unit of issue | 1 donation |
| Infection risk | Same as whole blood |
| Storage | Depends on production method: consult blood bank |
| Indications | ■ Minimizes white cell immunization in patients receiving repeated transfusion but, to achieve this, all blood components given to the patient must be leucocyte-depleted |
| | ■ Reduces risk of CMV transmission in special situations (see Section 7: *Adverse Effects of Transfusion*) |
| | ■ Patients who have experienced two or more previous febrile reactions to red cell transfusion |
| Contraindications | Will not prevent graft-vs-host disease, although it can improve: for this purpose, blood components should be irradiated where facility is available (radiation dose: 25–30 Gy) |
| Administration | ■ Same as whole blood |
| | ■ A leucocyte filter may also be used at time of transfusion if leucocyte-depleted red cells or whole blood are not available |
| Alternative | Buffy coat-removed whole blood or red cell suspension is usually effective in avoiding febrile non-haemolytic transfusion reactions. The blood bank should express the buffy coat in a sterile environment immediately before transporting the blood to the bedside. Transfusion should start within 30 minutes of delivery with the use, where possible, of a leucocyte filter. Transfusion should be completed within 4 hours of commencement. |

## PLATELET CONCENTRATES (prepared from whole blood donations)

| | |
|---|---|
| Description | Single donor unit in a volume of 50–60 ml of plasma should contain: |
| | ■ At least 55 x $10^9$ platelets |
| | ■ <1.2 x $10^9$ red cells |
| | ■ <0.12 x $10^9$ leucocytes |
| Unit of issue | May be supplied as either: |
| | ■ Single donor unit: platelets prepared from one donation |
| | ■ Pooled unit: platelets prepared from 4 to 6 donor units 'pooled' into one pack to contain an adult dose of at least 240 x $10^9$ platelets |
| Infection risk | ■ Same as whole blood, but a normal adult dose involves between 4 and 6 donor exposures |
| | ■ Bacterial contamination affects about 1% of pooled units |
| Storage | ■ 20°C–24°C (with agitation) for up to 5 days in specialized platelet packs, although some centres use ordinary plastic packs which restrict storage to 72 hours |
| | ■ Longer storage increases the risk of bacterial proliferation and septicaemia in the recipient |
| Indications | ■ Treatment of bleeding due to: |
| | — Thrombocytopenia |
| | — Platelet function defects |
| | ■ Prevention of bleeding due to thrombocytopenia, such as in bone marrow failure |
| Contraindications | ■ Not generally indicated for prophylaxis of bleeding in surgical patients, unless known to have significant pre-operative platelet deficiency |
| | ■ Not indicated in: |
| | — Idiopathic autoimmune thrombocytopenic purpura (ITP) |
| | — Thrombotic thrombocytopenic purpura (TTP) |
| | — Untreated disseminated intravascular coagulation (DIC) |
| | — Thrombocytopenia associated with septicaemia, until treatment has commenced or in cases of hypersplenism |
| Dosage | ■ 1 unit of platelet concentrate/10 kg body weight: in a 60 or 70 kg adult, 4–6 single donor units containing at least 240 x $10^9$ platelets should raise the platelet count by 20–40 x $10^9$/L |
| | ■ Increment will be less if there is: |
| | — Splenomegaly |
| | — Disseminated intravascular coagulation |
| | — Septicaemia |
| Administration | ■ After pooling, platelet concentrates should be infused as soon as possible, generally within 4 hours, because of the risk of bacterial proliferation |
| | ■ Must not be refrigerated before infusion as this reduces platelet function |
| | ■ 4–6 units of platelet concentrates (which may be supplied pooled) should be infused through a fresh standard blood administration set |
| | ■ Special platelet infusion sets are not required |

| | ■ Platelet concentrates should be infused over about 30 minutes |
|---|---|
| | ■ Platelet concentrates prepared from Rh D positive donors should not be given to a Rh D negative potential child-bearing female |
| | ■ Platelet concentrates that are ABO compatible should be given whenever possible |
| Complications | Febrile non-haemolytic and allergic urticarial reactions are not uncommon, especially in patients receiving multiple transfusions. For management, see Section 7: *Adverse Effects of Transfusion* |

## PLATELET CONCENTRATES (collected by plateletpheresis)

| | |
|---|---|
| Description | ■ Volume 150–300 ml |
| | ■ Platelet content 150–500 x $10^9$, equivalent to 3–10 single donations |
| | ■ Platelet content, volume of plasma and leucocyte contamination depend on the collection procedure |
| Unit of issue | 1 pack containing platelet concentrates collected by a cell separator device from a single donor |
| Infection risk | Same as whole blood |
| Storage | Up to 24 hours at 20°C–24°C (with agitation) unless collected using a blood cold chain system validated for longer storage periods; do not store at 4°C |
| Indications | ■ Platelet concentrates collected by apheresis are, generally, equivalent to the same dose of platelet concentrates prepared from whole blood |
| | ■ If a specially typed, compatible donor is required for the patient, several doses may be obtained from the selected donor |
| Dosage | 1 pack of platelet concentrate collected from a single donor by apheresis is usually equivalent to 1 therapeutic dose |
| Administration | Same as for recovered donor platelets, but ABO compatibility is more important: high titre counts of A or B in the donor plasma used to suspend the platelets may cause haemolysis of recipient's red cells |

## FRESH FROZEN PLASMA

| | |
|---|---|
| Description | ■ Pack containing the plasma separated from one whole blood donation within 6 hours of collection and then rapidly frozen to –25°C or colder<br>■ Contains normal plasma levels of stable clotting factors, albumin and immunoglobulin<br>■ Factor VIII level at least 70% of normal fresh plasma level |
| Unit of issue | ■ Usual volume of pack is 200–300 ml<br>■ Smaller volume packs may be available for children |
| Infection risk | ■ If untreated, same as whole blood<br>■ Very low risk if treated with methylene blue/ultraviolet light inactivation (see virus 'inactivated' plasma) |
| Storage | At –25°C or colder for up to 1 year |
| Indications | ■ Replacement of multiple coagulation factor deficiencies, e.g.:<br>— Liver disease<br>— Warfarin anticoagulant overdose<br>— Depletion of coagulation factors in patients receiving large volume transfusions.<br>■ Disseminated intravascular coagulation (DIC)<br>■ Thrombotic thrombocytopenic purpura (TTP) |
| Dosage | Initial dose of 15 ml/kg |
| Administration | ■ Must normally be ABO compatible to avoid risk of haemolysis in recipient<br>■ No crossmatching needed<br>■ Before use, should be thawed in water which is between 30°C and 37°C. Higher temperatures will destroy clotting factors and proteins<br>■ Once thawed, should be stored in a refrigerator at 2°C–6°C<br>■ Infuse using a standard blood infusion set as soon as possible after thawing<br>■ Labile coagulation factors rapidly degrade; use within 6 hours of thawing |
| Precautions | ■ Acute allergic reactions are not uncommon, especially with rapid infusions<br>■ Severe life-threatening anaphylactic reactions occasionally occur<br>■ Hypovolaemia alone is *not* an indication for use |

## LIQUID PLASMA

Plasma separated from a whole blood unit and stored at +4°C. No labile coagulation factors: i.e. Factors V and VIII.

## FREEZE-DRIED POOLED PLASMA

Plasma from many donors pooled before freeze-drying. No virus inactivation step so the risk of transmitting infection is multiplied many times. **This is an obsolete product that should not be used.**

## CRYOPRECIPITATE-DEPLETED PLASMA

Plasma from which approximately half the fibrinogen and Factor VIII has been removed as cryoprecipitate, but which contains all the other plasma constituents.

## VIRUS 'INACTIVATED' PLASMA

Plasma treated with methylene blue/ultraviolet light inactivation to reduce the risk of HIV, hepatitis B and hepatitis C. The 'inactivation' of other viruses, such as hepatitis A and human parvovirus B19 is less effective. The cost of these products is considerably higher than conventional fresh frozen plasma.

## CRYOPRECIPITATE

| | |
|---|---|
| Description | ■ Prepared from fresh frozen plasma by collecting the precipitate formed during controlled thawing and resuspending it in 10–20 ml plasma |
| | ■ Contains about half of the Factor VIII and fibrinogen in the donated whole blood: e.g. Factor VIII: 80–100 i.u./pack; fibrinogen: 150–300 mg/pack |
| Unit of issue | Usually supplied as a single donor pack or a pack of 6 or more single donor units that have been pooled |
| Infection risk | As for plasma, but a normal adult dose involves at least 6 donor exposures |
| Storage | At –25°C or colder for up to 1 year |
| Indications | ■ As an alternative to Factor VIII concentrate in the treatment of inherited deficiencies of: |
| | — Von Willebrand Factor (von Willebrand's disease) |
| | — Factor VIII (haemophilia A) |
| | — Factor XIII |
| | ■ As a source of fibrinogen in acquired coagulopathies: e.g. disseminated intravascular coagulation (DIC) |
| Administration | ■ If possible, use ABO-compatible product |
| | ■ No compatibility testing is needed |
| | ■ After thawing, infuse as soon as possible through a standard blood administration set |
| | ■ Must be infused within 6 hours of thawing |

# Plasma derivatives

Processes for heat treatment or chemical treatment of plasma derivatives to reduce the risk of transmitting viruses are currently very effective against viruses that have lipid envelopes:

- HIV-1 and 2
- Hepatitis B and C
- HTLV-I and II.

Inactivation of non-lipid enveloped viruses such as hepatitis A and human parvovirus B19 are less effective.

## HUMAN ALBUMIN SOLUTIONS

| | |
|---|---|
| Description | Prepared by fractionation of large pools of donated human plasma |
| Preparations | ■ Albumin 5%: contains 50 mg/ml of albumin<br>■ Albumin 20%: contains 200 mg/ml of albumin<br>■ Albumin 25%: contains 250 mg/ml of albumin<br>■ Stable plasma protein solution (SPPS) and plasma protein fraction (PPF): similar albumin content to albumin 5% |
| Infection risk | No risk of transmission of viral infections if correctly manufactured |
| Indications | ■ Replacement fluid in therapeutic plasma exchange: use albumin 5%<br>■ Treatment of diuretic-resistant oedema in hypoproteinaemic patients e.g. nephrotic syndrome or ascites. Use albumin 20% with a diuretic<br>■ Although 5% human albumin is currently licensed for a wide range of indications (e.g. volume replacement, burns and hypoalbuminaemia), there is *no* evidence that it is superior to crystalloid replacement fluids for acute plasma volume replacement |
| Contraindications | Not for use as IV nutrition as it is a very expensive and inefficient source of essential amino acids |
| Administration | ■ No compatibility requirements<br>■ No filter needed |
| Precautions | Administration of 20% albumin may cause acute expansion of intravascular volume with risk of pulmonary oedema |

## COAGULATION FACTORS

### Factor VIII concentrate

| | |
|---|---|
| Description | ■ Partially purified Factor VIII prepared from large pools of donor plasma<br>■ Factor VIII ranges from 0.5–20 i.u./mg of protein. Preparations with a higher activity are available<br>■ Products that are licensed in certain countries (e.g. in the USA and European Union) are all heated and/or chemically treated to reduce the risk of transmission of viruses |
| Unit of issue | Vials of freeze-dried protein labelled with content, usually about 250 i.u. of Factor VIII |
| Infection risk | Current virus inactivated products do not appear to transmit HIV, HTLV and hepatitis C, which have lipid envelopes: the inactivation of non-enveloped viruses such as hepatitis A and parvovirus is less effective<br><br>*See* inactivation of lipid-enveloped and non-lipid enveloped viruses above (p. 90) |
| Storage | Freeze-dried derivatives should be stored at a temperature of 2°C–6°C up to stated expiry date, unless otherwise indicated in manufacturer's instructions |
| Indications | ■ Treatment of haemophilia A<br>■ Treatment of von Willebrand's disease. Use only intermediate purity preparations that contain von Willebrand Factor |
| Dosage | See Figure 9.26 on p. 202 |
| Administration | ■ Reconstitute according to manufacturer's instructions<br>■ Once the powder is dissolved, the solution should be drawn up using a filter needle and infused through a standard infusion set within 2 hours |
| Alternatives | ■ Cryoprecipitate, fresh frozen plasma: (see Section 9: *General Medicine*)<br>■ Factor VIII prepared *in vitro* using recombinant DNA methods is commercially available. It is clinically equivalent to Factor VIII derived from plasma and does not have the risk of transmitting pathogens derived from plasma donors |

**PLASMA DERIVATIVES CONTAINING FACTOR IX**

**Prothrombin Complex Concentrate (PCC)**
**Factor IX Concentrate**

| Description | Contains: | **PCC** | **Factor IX** |
|---|---|---|---|
| | ■ Factors II, IX and X | ✔ | ✔ |
| | ■ Factor IX only | ✔ | |
| | ■ Some preparations also contain Factor VII | ✔ | |
| Unit of issue | Vials of freeze dried protein labelled with content, usually about 350–600 i.u. of Factor IX | ✔ | ✔ |
| Infection risk | As Factor VIII | | |
| Storage | As Factor VIII | | |
| Indications | ■ Treatment of haemophilia B (Christmas disease) | ✔ | ✔ |
| | ■ Immediate correction of very prolonged prothrombin time | ✔ | |
| Contraindications | PCC not advised in patients with liver disease or thrombotic tendency | | |
| Dosage | See Figure 9.26 on p. 202. | | |
| Administration | As Factor VIII | | |
| Alternatives | Plasma | | |

Factor IX produced *in vitro* by recombinant DNA methods will soon be available for treatment of haemophilia B. It offers the same advantages as recombinant Factor VIII

**COAGULATION FACTORS PRODUCTS FOR PATIENTS WITH FACTOR VIII INHIBITORS**

| Description | A heat-treated plasma fraction containing partly-activated coagulation factors |
|---|---|
| Infection risk | Probably the same as other heat-treated factor concentrates |
| Indications | Only for use in patients with inhibitors to Factor VIII |
| Administration | Should be used only with specialist advice |

## IMMUNOGLOBULIN PREPARATIONS

The prevention of infection can have important implications for health and may even reduce the need for transfusion.

Normal human immunoglobulin (NHIG) and so-called 'specific' immunoglobulin products containing higher levels of antibody against specific organisms are used, often together with vaccines (active immunization), to protect against infection. This is called passive immunization. Further information on the use of vaccines and immunoglobulin (active and passive immunization) should be available from your Ministry of Health.

Immunoglobulin preparations are manufactured by cold ethanol fractionation of donated human plasma.

## IMMUNOGLOBULIN for intramuscular use

| | |
|---|---|
| Description | A concentrated solution of the IgG antibody component of plasma |
| Preparations | Standard or normal immunoglobulin: prepared from large pools of donors and contains antibodies against infectious agents to which the donor population has been exposed |
| Infection risk | Transmission of virus infections has *not* been reported with intramuscular immunoglobulin |
| Indications | ■ Hyperimmune or specific immunoglobulin: from patients with high levels of specific antibodies to infectious agents: e.g. hepatitis B, rabies, tetanus<br>■ Prevention of specific infections<br>■ Treatment of immune deficiency states |
| Administration | Do not give intravenously as severe reactions occur |

## ANTI-Rh D IMMUNOGLOBULIN (Anti-D RhIG)

| | |
|---|---|
| Description | Prepared from plasma containing high levels of anti-Rh D antibody from previously immunized persons |
| Indications | Prevention of haemolytic disease of the newborn in Rhesus negative mothers (see Section 10: *Obstetrics*) |

## IMMUNOGLOBULIN for intravenous use

| | |
|---|---|
| Description | As for intramuscular preparation, but with subsequent processing to render product safe for IV administration |
| Indications | ■ Idiopathic autoimmune thrombocytopenic purpura and some other immune disorders<br>■ Treatment of immune deficiency states<br>■ Hypogammaglobulinaemia<br>■ HIV-related disease |

# 6

# Clinical transfusion procedures

## Key points

1 Every hospital should have standard operating procedures for each stage of the clinical transfusion process. All staff should be trained to follow them.

2 Clear communication and cooperation between clinical and blood bank staff are essential in ensuring the safety of blood issued for transfusion.

3 The blood bank should not issue blood for transfusion unless a blood sample label and blood request form have been correctly completed. The blood request form should include the reason for the transfusion so that the most suitable product can be selected for compatibility testing.

4 Blood products should be kept within the correct storage conditions during transportation and in the clinical area before transfusion, in order to prevent loss of function or bacterial contamination.

5 The transfusion of an incompatible blood component is the most common cause of acute transfusion reactions, which may be fatal. The safe administration of blood depends on:
   ■ Accurate, unique identification of the patient
   ■ Correct labelling of the blood sample for pre-transfusion testing
   ■ A final patient identity check to ensure the administration of the right blood to the right patient.

6 For each unit of blood transfused, the patient should be monitored by a trained member of staff before, during and on completion of the transfusion.

## Introduction

This section deals with the practical aspects of ordering and administering blood products and highlights a number of areas in which clinicians and the blood bank need to work together efficiently and effectively to meet the patient's needs. It also emphasizes the importance of systematic procedures to prevent the transfusion of the incorrect blood, which may result in a potentially life-threatening transfusion reaction.

## Learning outcomes

When you have completed this section, you should be able to:

1 Understand the respective roles and responsibilities of clinical staff and blood bank staff in ensuring the safety and availability of blood products for transfusion.

2 Explain the importance of ensuring that only compatible blood products are transfused.

3 Identify any improvements that can be made to procedures in your hospital for the ordering, collection, storage, transportation and administration of blood products, and for monitoring the transfused patient.

## 6.1 Getting the right blood to the right patient at the right time

Once the decision to transfuse has been made, everyone involved in the clinical transfusion process has the responsibility to ensure the right blood gets to the right patient at the right time. Figure 6.1 summarizes the main steps in this process.

National guidelines on the clinical use of blood should always be followed in all hospitals where transfusions take place. If no national guidelines exist, each hospital should develop local guidelines and, ideally, establish a hospital transfusion committee to monitor clinical blood use and investigate any acute and delayed transfusion reactions.

Each hospital should ensure that the following are in place.

1   A blood request form.

2   A blood ordering schedule for common surgical procedures.

3   Guidelines on clinical and laboratory indications for the use of blood, products and simple alternatives to transfusion, including intravenous replacement fluids, and pharmaceuticals and medical devices to minimize the need for transfusion.

4   Standard operating procedures for each stage in the clinical transfusion process, including:
    ■ Ordering blood and blood products for elective/planned surgery
    ■ Ordering blood and blood products in an emergency
    ■ Completing the blood request form
    ■ Taking the pre-transfusion blood sample
    ■ Collecting blood and blood products from the blood bank
    ■ Storing and transporting blood and blood products, including storage in the clinical area
    ■ Administering blood and blood products, including the final patient identity check
    ■ Recording transfusions in patient records
    ■ Monitoring the patient before, during and after transfusion
    ■ The management, investigation and recording of transfusion reactions.

5   The training of all staff involved in the transfusion process to follow standard operating procedures.

Standard operating procedures are usually produced by the blood bank but should be prepared in collaboration with medical and nursing staff. The written procedures should be available to all staff who are involved in the transfusion process.

Responsibility for keeping SOPs up to date and available, and for training staff to use them, should be defined by the hospital transfusion committee or, where none exists, by hospital management.

*Figure 6.1: Steps in the clinical transfusion process*

## GETTING THE RIGHT BLOOD TO THE RIGHT PATIENT AT THE RIGHT TIME

1  Assess the patient's clinical need for blood and when it is required.

2  Inform the patient and/or relatives about the proposed transfusion treatment and record in the patient's notes that you have done so.

3  Record the indications for transfusion in the patient's notes.

4  Select the blood product and quantity required. Use a blood ordering schedule as a guide to transfusion requirements for common surgical procedures.

5  Complete the blood request form accurately and legibly. Write the reason for transfusion so the blood bank can select the most suitable product for compatibility testing.

6  If blood is needed urgently, contact the blood bank by telephone immediately.

7  Obtain and correctly label a blood sample for compatibility testing.

8  Send the blood request form and blood sample to the blood bank.

9  Laboratory performs pre-transfusion antibody screening and compatibility tests and selects compatible units.

10  Delivery of blood products by blood bank or collection by clinical staff.

11  Store blood products in correct storage conditions if not immediately required for transfusion.

12  Check identity on:
   ■  Patient
   ■  Blood product
   ■  Patient's documentation.

13  Administer blood product.

14  Record in the patient's notes:
   ■  Type and volume of each product transfused
   ■  Unique donation number of each unit transfused
   ■  Blood group of each unit transfused
   ■  Time at which the transfusion of each unit commenced
   ■  Signature of the person administering the blood.

15  Monitor the patient before, during and on completion of the transfusion.

16  Record the completion of the transfusion.

17  Identify and respond immediately to any adverse effect. Record any transfusion reactions in the patient's notes.

## Communication between clinicians and the blood bank

The safety of the patient requiring transfusion depends on effective communication between clinical and blood bank staff. Blood bank staff, for example, may not always recognize the problems faced by medical and nursing staff in an emergency when blood may be needed very urgently.

On the other hand, clinicians may not fully understand the problems faced by blood bank staff if they order blood or blood products without completing a blood request form or allow insufficient time for laboratory technicians to prepare them safely for transfusion.

It is essential that there is clear understanding by both clinicians and blood bank staff of each other's role in the transfusion process.

## Clinicians

All clinical staff involved in prescribing and administering blood should know how the blood bank operates and follow agreed procedures for the ordering, collection and administration of blood products. Staff should be trained to follow these procedures and all the basic elements of a quality system need to be in place.

Clinicians should be familiar with the following aspects of the supply of safe blood and blood products.

1 How the hospital blood bank obtains blood, including the different types of blood donor and the potential risks of transmission of infection in the blood available for transfusion.

2 The clinician's responsibility to assist blood bank staff in ensuring that blood is provided at the correct time and in the correct location by:
   ■ Completing a blood request form for every patient requiring transfusion
   ■ Ordering blood in advance, where possible
   ■ Providing clear information on:
      — The products that are being requested
      — The number of units required
      — The reason for transfusion
      — The urgency of the patient's requirement for transfusion
      — When and where the blood is required
      — Who will deliver or collect the blood.

3 The importance of the major blood groups (ABO and Rhesus) and the other dangerous blood group antibodies that may be detected in the patient before transfusion.

4 The responsibilities of blood bank staff in ensuring that blood issued for transfusion is compatible with the patient so there is no risk of dangerous or fatal reactions caused by antibodies to red cells.

5 The responsibilities of clinical staff in ensuring that blood products administered to a patient are compatible and, in particular, the vital importance of:
- Completing all the required details on the blood request form
- Accurately labelling blood sample tubes
- Formally checking the identity of the patient, the product and the documentation at the patient's bedside before transfusion.

6 The importance of the correct storage of blood and blood products both in the blood bank and in the clinical area in order to preserve their function and prevent bacterial contamination, which can be fatal for the patient.

7 The importance of discarding a blood pack that has been allowed to remain for more than 4 hours at room temperature (or whatever time is locally specified) or a pack that has been opened or shows any signs of deterioration.

8 The importance of correctly recording transfusions in the patient's case notes and, in particular:
- The reason for transfusion
- The product and volume that was transfused
- The time of transfusion
- Any adverse events.

## Blood bank staff

It is equally important for all blood bank staff to understand the following issues.

1 The pressures that clinicians are often under when caring for very sick patients who urgently need transfusion.

2 The vital importance of good laboratory practice and accurate records in the blood bank.

3 The need, in an emergency, to use laboratory procedures that are appropriate to the urgency of the situation. Provided ABO compatible blood is given, major haemorrhage is more likely to cause death than a red cell antibody found in the screening test.

Blood bank staff should also recognize that problems arising during an emergency should always be handled immediately in the patient's best interest. If investigation and resolution of the cause of the problem is needed, it should be left until after the emergency has passed.

## Urgent requests for blood

It is particularly important to ensure that there is common agreement and understanding about the language used by both clinical and blood bank staff in order to avoid any misinterpretation of words such as 'immediate', 'urgent' or 'as soon as possible'. It is preferable to agree on categories of urgency, such as:
- Extremely urgent: within 10–15 minutes
- Very urgent: within 1 hour
- Urgent: within 3 hours

- Same day
- *Or* date and time required.

Clinicians and blood bank staff should decide who is responsible for ensuring that, once ready, the blood is transported to the patient as quickly as possible.

### ACTIVITY 16

*What is the procedure in your hospital for making urgent requests for blood and blood products in an emergency?*

*Have there been any occasions in your clinical area when blood or blood products did not arrive from the blood bank at the required time or in the correct location? What were the reasons for this?*

*Listen to some conversations between clinical and blood bank staff about ordering blood. Is the communication courteous, clear and unambiguous?*

*Arrange a meeting of a small group of senior clinical and blood bank staff to agree on the procedures and language to be used to communicate the urgency of requests for blood. Make sure that both clinical and blood bank staff are regularly trained to use them correctly.*
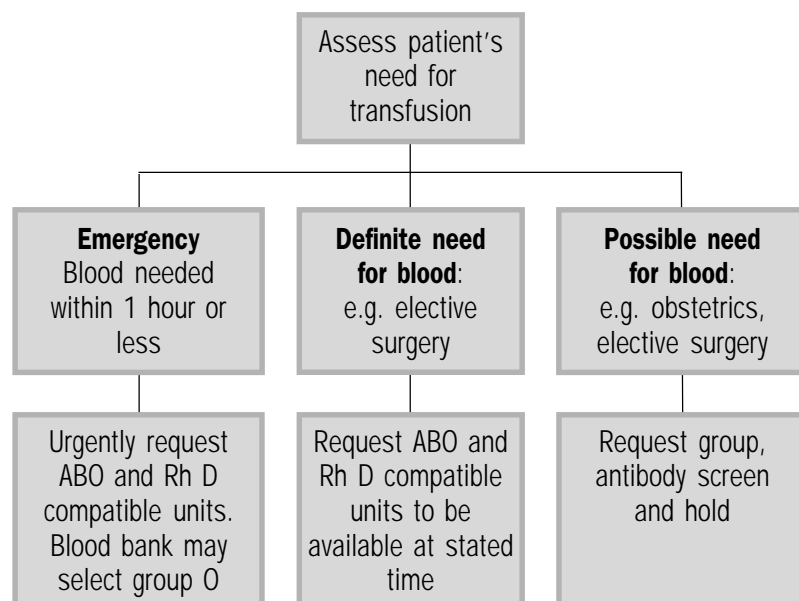
## 6.2  Ordering blood products

When there are clinical and laboratory indications that transfusion is required, the procedure for ordering blood will depend on whether there is:

- Urgent need for blood
- Definite need for blood
- Possible need for blood.

Figure 6.2 provides a simple guide to ordering blood.

*Figure 6.2: Blood ordering policy*

## Informing the patient

Once the decision has been made that transfusion is necessary, it is important to explain the proposed transfusion treatment to the patient or relatives, wherever possible. Record in the patient's notes that you have done so.

Patients or their relatives may be worried about the risks of transfusion and wish to know more about them, as well as the need for transfusion and possible alternatives, such as autologous transfusion or drugs such as erythropoietin (a stimulant for red cell production). Patients of the Jehovah's Witness faith are not allowed by their religious beliefs to receive blood components, but may be prepared to accept plasma fractions or alternative treatments. In some cases, people of other religions or cultural groups may have their own special concerns about giving or receiving blood, and these should be handled sensitively, to the benefit of the patient.

Note that, in many countries, the law defines it as a serious assault to transfuse a patient who has clearly indicated that this is against his or her will, even if you believe the patient's life can only be saved by transfusion. In many parts of the world, the Jehovah's Witnesses have individuals who are trained to work constructively with patients, relatives and hospital staff in these difficult instances.

Research has shown that patients often have no recollection of being informed about treatment options or feel that they have not been given adequate answers to questions that worry them. In some countries, the balance of legal opinion is that a written record that the patient has been given information and that his or her questions have been answered is more valuable in a medico-legal case than the patient's signature on a consent form. However, laws and regulations vary between countries and it is important to be familiar with the local rules.

## Patient identity

Each patient should be labelled using an identity wristband or some other firmly-attached marker with a unique hospital reference number. This number should always be used on the blood sample tube, blood request form and documentation to identify the patient.

When a patient cannot be reliably identified at the time of admission, this hospital reference number should always be used to identify the patient until full and correct details are available and are properly communicated to the hospital blood bank.

## Ordering blood for elective surgery

The timing of requests for blood for elective surgery should comply with local rules and the quantity requested should be guided by the local blood ordering schedule.

### Blood ordering schedule

Since many operations very rarely need blood transfusion, it is unnecessary for a compatibility test (crossmatch) to be performed routinely for every surgical procedure. Considerable time and expense can be saved by avoiding the obligation of units of blood that are unlikely to be used, while still ensuring that blood is readily available for all patients who need it.

Hospitals that regularly carry out surgical procedures should therefore develop and use a blood ordering schedule as a guide to the number of units of blood and blood products that should normally be ordered for each type of operation.

A blood ordering schedule is a table of expected normal blood usage for elective surgical procedures which lists the number of units of blood to be routinely crossmatched for each procedure preoperatively. This should reflect the clinical team's usual use of blood for common procedures, depending on their complexity and expected blood loss. The blood ordering schedule should also include guidance on the use of the group, screen and hold procedure (see p. 111) for patients undergoing procedures for which red cell transfusion is occasionally, but rarely, required.

A blood ordering schedule should always be developed locally by the hospital transfusion committee or, where none exists, by clinicians responsible for prescribing blood, in conjunction with the hospital blood bank. It should be prepared in accordance with national guidance on the adaptation of a model blood ordering schedule for local use.

Each hospital's blood ordering schedule should take account of both local clinical conditions and the supply of blood, blood products and alternatives to transfusion that are available. The availability and use of intravenous crystalloid and colloid solutions is essential in all hospitals carrying out obstetrics and surgery.

The process of developing a blood ordering schedule involves the following steps.

1 Retrospective analysis of requests for blood and blood products over at least a 6-month period.

2 For each surgical procedure, analysis of:
  ■ Type of procedure
  ■ Reason for request of blood
  ■ Number of units tested for compatibility
  ■ Number of units transfused
  ■ Percentage of units used.

3 Calculation of the C:T ratio (crossmatch:transfusion ratio). A realistic objective for surgical procedures is a C:T ratio of approximately 3:1.

4 Surgical procedures with a blood usage of less than 30% should be included in the group and screen (G & S) category.

5 Monitoring and evaluation of the blood ordering schedule by verifying compliance.

Figure 12.11 on p. 272 gives an example of a surgical blood ordering schedule taken from an African country to illustrate the type of information required.

If insufficient blood is available, local practice may be to undertake essential urgent procedures with the patient's haemoglobin at lower levels rather than delay for transfusion or transfer to another hospital.

## Ordering blood in an emergency

In the accident and emergency/casualty department or labour ward, it is often necessary to order blood in an emergency. Following a road accident or other incident, there may be several bleeding and unconscious patients who need blood quickly. In these situations, it is very easy to make mistakes in identifying patients and labelling blood samples. It is therefore essential that the procedures for ordering blood in an emergency are clear and simple and that everyone knows and follows them. Figure 6.3 gives a checklist for ordering blood in an emergency.

*Figure 6.3: Procedure for ordering blood in an emergency*

---

**ORDERING BLOOD IN AN EMERGENCY**

1 In an emergency, insert an IV cannula, use it to take the blood sample for compatibility testing, set up an IV infusion and get the blood sample to the blood bank as quickly as possible.

2 For each patient, the blood sample tube and the blood request form must be clearly labelled with the patient's name and unique hospital reference number. If the patient is unidentified, some form of **emergency admission number** should be used. Use the patient's name only if you are sure you have correct information.

3 If you have to send another request for blood for the same patient within a short period, use the same identifiers used on the first request form and blood sample so the blood bank staff know they are dealing with the same patient.

4 If there are several staff working with emergency cases, one person should take charge of ordering blood and communicating with the blood bank about the incident. This is especially important if several injured patients are involved at the same time.

5 Tell the blood bank how quickly the blood is needed for each patient. Communicate using words that have been previously agreed with the blood bank to explain how urgently blood is needed.

6 Make sure that both you and the blood bank staff know:
   ■ Who is going to bring the blood to the patient or collect it from the blood bank
   ■ Where the patient will be: for example, if your patient is just about to be transferred to another part of the hospital for an X-ray, make sure the blood will be delivered to the X-ray room.

7 The blood bank may send group O (and possibly Rhesus negative) blood, especially if there is any risk of errors in patient identification. During an acute emergency, this may be the safest way to avoid a serious mismatched transfusion.

---

## The blood request form

When blood is required for a transfusion, the prescribing clinician should complete and sign a standard blood request form and enter his/her name in legible capitals.

**All the details requested on the form must be completed accurately and legibly. If blood is needed urgently, also contact the blood bank by telephone.**

The blood request form should provide the following information:

- Date of request
- Date and time the blood is needed
- Where the blood should be delivered
- Patient's family name and given name
- Patient's date of birth
- Patient's gender
- Patient's hospital reference number
- Patient's ward
- Provisional diagnosis
- Reason why transfusion is requested
- Number of units of blood products required *or*
- Whether patient's serum should be grouped, screened and held (see p. 111)
- Urgency of the request
- Name and signature of the person requesting the blood.

Where previous records or a reliable history are available, it helps the blood bank to have the following information:

- Patient's blood group, if known
- The presence of any antibodies
- History of any previous transfusions
- History of any previous transfusion reactions
- Females: number of previous pregnancies and maternal/infant incompatibility
- Other relevant medical history or condition.

It is important to write the reason for transfusion on the blood request form so that the blood bank can select the most suitable product for compatibility testing.

An example of a blood request form is given in Figure 6.4 on p. 105. This includes a compatibility test record which should be completed in the laboratory before the blood is issued. Different hospitals and clinics have varying requirements, so this can only be taken as an example. If a blood request form is not yet used in your hospital, it can be adapted to meet local needs. Remember the absolute essentials are that any request for blood and the patient's blood sample accompanying it must, *at a minimum*, be clearly labelled to:

- Uniquely identify the patient
- Indicate the type and number of units of blood product required
- Indicate the time and place at which they are needed.

*Figure 6.4: Example of a blood request form*

## EXAMPLE OF BLOOD REQUEST FORM

HOSPITAL: _____     Date of request: _____

### PATIENT DETAILS

Family name: _____     Date of birth: _____ Gender: _____

Given name: _____     Ward: _____

Hospital reference no.: _____     Blood group (if known): ABO [____]

Address: _____                                Rh D [____]

_____

### HISTORY

Diagnosis: _____     Antibodies:              Yes/No _____

Reason for transfusion: _____     Previous transfusions: Yes/No _____

Haemoglobin: _____     Any reactions:          Yes/No _____

Relevant medical history: _____     Previous pregnancies: Yes/No _____

### REQUEST

[ ] Group, screen and hold patient's serum          Whole blood [____] units

[ ] Provide product                                 Red cells [____] units

Date required: _____     Plasma [____] units

Time required: _____     Other [____] units

Deliver to: _____

NAME OF DOCTOR (print): _____     SIGNATURE: _____

IMPORTANT: *This blood request form will not be accepted if it is not signed or any section is left blank.*

### LABORATORY USE ONLY

Patient ABO [____]
Rh D [____]

| Donation pack no. | Donor typing | | Compatibility testing | | | | Date of issue | Time of issue |
| | ABO | Rh | AHG | Room temp. saline | Date of match | Time of match | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |

Signature of tester: _____

Blood bank staff are acting correctly if they refuse to accept a request for blood when either the blood request form or the patient's blood sample are inadequately identified or the details do not match. Any failure to follow correct procedures can lead to incompatible transfusions, which may be fatal.

### ACTIVITY 17

*Is a blood request form used in your hospital? If so, does it contain all the points listed above? Compare it with the example given in Figure 6.4 and talk to colleagues about any improvements that could be made to your form or the way it is used.*

*If a blood request form is not yet used in your hospital, talk to senior clinical and blood bank staff about the importance of introducing one, what it should contain and procedures for using it. Also discuss any training that may be required to ensure it is used effectively.*

## Blood samples for compatibility testing

**It is vital that the patient's blood sample is placed in a sample tube that is correctly labelled and is uniquely identifiable with the patient.**

Figure 6.5 outlines the steps involved in taking a blood sample for compatibility testing.

Any national rules or regulations governing the taking and labelling of blood samples must be followed at all times. Where none exist, hospitals should prepare their own procedures. All staff responsible for taking blood samples should be specifically trained for this task.

The blood bank should not accept requests for blood unless *all* the patient's details on the blood sample match those on the blood request form. If the details do not match, they should request a new sample and request form.

### ACTIVITY 18

*Is there a standard operating procedure for taking blood samples for pre-transfusion testing in your hospital? Compare it with Figure 6.5.*

*Is the procedure for taking blood samples correctly followed by all relevant staff?*

*If there is no formal procedure in your hospital or you think that it could be improved, talk to senior colleagues about the importance of ensuring that blood samples are taken correctly and, in particular, labelled accurately.*

*Organize a training session to ensure that all relevant staff understand the critical importance of accurate labelling of the sample tube.*

*Figure 6.5: Procedure for taking blood samples for compatibility testing*

## TAKING BLOOD SAMPLES FOR COMPATIBILITY TESTING

1   If the patient is conscious at the time of taking the sample, ask him or her to identify themselves by given name, family name, date of birth and any other appropriate information.

2   Check the patient's name against:
    - Patient's identity wristband or label
    - Patient's medical notes
    - Completed blood request form.

3   If the patient is unconscious, ask a relative or a second member of staff to verify the patient's identity.

4   Take the blood sample into the type of sample tube required by the blood bank. For adults, this is usually 10 ml, with no anticoagulant.

5   Label the sample tube clearly and accurately at the patient's bedside at the time the blood sample is being taken. The following information should be included on the blood sample tube label:
    - Patient's given name and family name
    - Patient's date of birth
    - Patient's hospital reference number
    - Patient's ward
    - Date
    - Signature of person taking the sample.

    Ensure that the patient's name is spelt correctly. Do not label tubes before obtaining the specimen because of the risk of putting the patient's blood into the wrong tube.

6   If the patient needs further red cell transfusion, send a new blood sample for crossmatching. This is particularly important if the patient has had a recent red cell transfusion that was completed more than 24 hours earlier. Antibodies to red cells may appear very rapidly as a result of the immunological stimulus given by the transfused donor red cells. A fresh blood sample is essential to ensure that the patient does not receive blood which is now incompatible.

## ACTIVITY 19

*Compare your hospital's procedures for ordering blood with those outlined in this section. Can you suggest any improvements that could be made to any of these procedures?*

*In particular, if a blood ordering schedule is not yet used in your hospital for obstetric and surgical procedures, talk to senior clinical and blood bank staff about the importance of developing one as a guide to blood requirements.*

## 6.3 Red cell compatibility testing (crossmatching)

It is essential that all blood is tested before transfusion in order to:

■ Ensure that the transfused red cells are compatible with antibodies in the patient's plasma

■ Avoid stimulating the production of new red cell antibodies in the recipient, particularly anti-Rh D.

All pre-transfusion test procedures should provide the following information about both the patient *and* the units of blood:

■ ABO group and antibodies

■ Rh D type

■ Presence of other red cell antibodies that could cause haemolysis in the patient.

The blood bank plays a central part in ensuring that patients receive compatible blood. Briefly, it is responsible for the following tasks.

1 To ensure that only units of blood that have been tested and found negative for transfusion-transmissible infections are accepted for compatibility testing.

2 To test every blood component to determine its ABO group and Rh D group and label it clearly and correctly with the group.

3 To check that a blood request form has been completed fully by the clinician prescribing blood for a patient and that the details match those on the patient's blood sample.

4 To test the patient's blood sample to determine the ABO and Rh D group and perform an antibody screen.

5 To select the most suitable blood product for the patient.

6 To perform a compatibility test (crossmatch) to test the donor's red cells against the patient's serum and ensure that blood of a safe ABO and Rh D type is supplied for the patient.

7 To label compatible units of blood specifically for the patient and issue them or keep them available for immediate release. Typically, the blood bank will reserve these units for a maximum of 48 hours after the time for which they were requested. If uncrossmatched blood is issued in an emergency, this should be clearly indicated on the compatibility label.

8 To ensure that all other checks and tests have been completed and accurately recorded.

9 To issue the correct products in accordance with local procedures.

### ABO blood group antigens and antibodies
In clinical transfusion practice, the ABO blood groups are by far the most important and can never be ignored in red cell transfusion.

Red cells comprise four main ABO types: O, A, B and AB. Individuals who (genetically) lack antigen A or antigen B have antibodies (IgM class) against the red cell type(s) that they have not inherited.

- A person of group A has antibody to group B
- A person of group B has antibody to group A
- A person of group O has antibody to group A *and* group B
- A person of group AB does not have antibody to group A or B

These antibodies can destroy red cells rapidly in the circulation.

Anti-A + anti-B antibodies occur 'naturally' and are not developed as a result of prior sensitization to the corresponding antigen. However, Rhesus antibodies (anti-Rh D) only appear after a Rhesus negative individual is sensitized by Rh D positive red cells.

## ABO incompatibility: haemolytic reactions

**Safe blood transfusion depends on avoiding incompatibility between the donor's red cells and the antibodies in the patient's plasma.**

Anti-A or anti-B recipient antibodies are almost always capable of causing rapid destruction (haemolysis) of incompatible transfused red cells as soon as they enter the circulation. A red cell transfusion that is not crossmatched carries a high risk of causing an acute haemolytic reaction.

Similarly, if blood is given to the wrong patient, it may be incompatible.

The exact risk depends on the mix of ABO groups in the population. In populations where 30% of unmatched transfusions will be ABO incompatible, at least 10% of these will lead to severe or fatal reactions.

In some circumstances, it is also important that the donor's antibodies are compatible with the patient's red cells.

It is not always essential, however, to give blood of the same ABO group. Figures 6.6 and 6.7 summarize the basic transfusion rules for red cells and plasma in the ABO system.

*Figure 6.6: Transfusion rules for red cells in the ABO system*

| RED CELL COMPONENTS |
| --- |
| In red cell transfusion, there must be ABO and Rh compatibility between the donor's red cells and the recipient's plasma. |
| 1  Group O individuals can receive blood from group O donors only. |
| 2  Group A individuals can receive blood from group A and O donors. |
| 3  Group B individuals can receive blood from group B and O donors. |
| 4  Group AB individuals can receive blood from AB donors, and also from group A, B and O donors. |
| Note: Red cell concentrates, from which the plasma has been removed, are preferable when non-group specific blood is being transfused. |

**PLASMA AND COMPONENTS CONTAINING PLASMA**

In plasma transfusion, group AB plasma can be given to a patient of any ABO group because it contains neither anti-A nor anti-B antibody.

1   Group AB plasma (no antibodies) can be given to any ABO group.

2   Group A plasma (anti-B) can be given to group O and A patients.

3   Group B plasma (anti-A) can be given to group O and B patients.

4   Group O plasma (anti-A + anti-B) can be given to group O patients only.

---

**Severe acute haemolytic transfusion reactions are nearly always caused by transfusing red cells that are incompatible with the patient's ABO type. These reactions can be fatal.**

**They most often result from errors made in identifying the patient when blood samples are being taken or when blood is being administered.**

---

For the treatment of transfusion reactions, see Section 7: *Adverse Effects of Transfusion.*

## Rhesus D antigens and antibodies

Red cells have very many other antigens and those carried by any individual are mainly determined by their genetic make-up. In contrast to the ABO system, individuals rarely make antibodies against these other antigens, unless they have been exposed to them by previous transfusion or during pregnancy and childbirth.

The most important of these is the Rhesus D antigen. Even a single transfusion of Rh D positive red cells to a Rh D negative person will usually provoke production of anti-Rh D antibody. This can cause:

■   Haemolytic disease of the newborn in a subsequent pregnancy

■   Rapid destruction of a later transfusion of Rh D positive red cells.

## Other red cell antigens and antibodies

There are many other minor antigens on the human red cell which may, like the Rhesus D antigen, lead to the development of antibodies if the person lacking the antigen is sensitized by a transfusion of these antigens. These antibodies, which can also cause severe reactions to transfusion, include:

■   Rhesus: C, c, E, e

■   Kell

■   Duffy

■   Lewis.

## Other systems for ensuring red cell compatibility

In some countries, a 'bedside' test is used to determine the ABO group of the patient and of the blood units supplied. This is usually performed

using a simple grouping card that is pre-treated with blood typing reagents and should be supplied with detailed instructions for its use.

Some countries also permit a so-called 'computer crossmatch' that depends on automated systems to ensure absolute accuracy in the identification of both patient and blood units.

Whatever system is used, the principles for ensuring safe transfusion remain the same. There must be clear, agreed procedures, staff should be trained to follow them and all the basic elements of a quality system need to be in place.

### Compatibility problems

If the patient's sample is found to contain a clinically significant red cell antibody, further tests are usually needed to identify the antibody so that blood of a suitable type can be provided. The laboratory may need another blood sample for the tests.

The blood bank staff will always do their best to find blood that is compatible to avoid the risks of a haemolytic transfusion reaction or of stimulating the patient's antibody to a high level. These tests may be complicated and can cause considerable delay in providing red cells.

When this occurs, non-urgent transfusions and surgery that is likely to require transfusion should be delayed until suitable blood is found in order to avoid risks to the patient.

However, when a patient needs transfusion urgently and it is difficult to find compatible red cell units, the doctor responsible for the blood bank should be asked to advise on the risk of a life-threatening reaction if blood is given that is not fully compatible.

This risk must be balanced against the risk of delaying transfusion when the patient's life may be endangered by blood loss that urgently requires restoration of the oxygen-carrying capacity of the blood.

### Group, screen and hold

The 'group, screen and hold' procedure is sometimes also called 'group and save' or 'type and screen'. In the laboratory, the patient's ABO and Rh D type are determined and the patient's serum is tested for IgG antibodies that can damage red blood cells at 37°C. The patient's serum sample is then frozen and stored in the laboratory at –20°C, usually for seven days. If blood is required within this period, the sample is thawed and used to perform an urgent compatibility test.

Using this method, the blood bank will usually need only 15–30 minutes to have blood ready for issue for the patient, provided that blood of a suitable group is available in the blood bank.

This approach avoids the need to hold crossmatched units of blood as an 'insurance' for a patient who is unlikely to need them, while at the same time ensuring that they can be provided quickly if they are required urgently. As a result, the blood bank can make better use of the red cells that it has available.

## 6.4 Collecting blood products prior to transfusion

A common cause of transfusion reactions is the transfusion of a unit of blood that was intended for a different patient. This is often due to mistakes when collecting blood from the blood bank

It is therefore essential that every hospital has a standard operating procedure for the collection of blood from the blood bank and its storage in the clinical area prior to transfusion. This should be followed at all times. An example is given in Figure 6.8.

*Figure 6.8: Procedure for collecting blood from the blood bank*

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**COLLECTING BLOOD PRODUCTS PRIOR TO TRANSFUSION**

1   Bring written documentation to identify the patient.

2   Check that the following details on the compatibility label attached to the blood pack exactly match the details on the patient's documentation:
   - Patient's family name and given name
   - Patient's hospital reference number
   - Patient's ward, operating room or clinic
   - Patient's ABO and RhD group

3   Fill in the information required in the blood collection register.

---

When blood is issued from the blood bank, the time of issue must always be recorded. The person responsible for the blood bank should make sure that blood does not leave the refrigerator until it is issued for transfusion. It only takes about 30 minutes for a unit of blood to reach 10°C and it is rarely necessary to warm blood before transfusing it.

The blood bank will sometimes supply blood that is of a different ABO group from the patient's, but that may still be compatible; for example, red cells of group A are safe for a patient of group AB. In this event, usually due to shortage of a particular group, the blood bank should inform the clinician responsible and also record the fact on the documentation that accompanies the blood units.

## 6.5 Storing blood products prior to transfusion

The 'blood cold chain' is the system for storing and transporting blood and blood products so that they are kept at the correct temperature at all times from collection from the donor to administration to the patient. Any breaks in the blood cold chain increase the dangers for the recipients of blood products and are wasteful of a scarce, valuable resource.

The efficiency and effectiveness of the blood cold chain depend on:

- Well-maintained, regularly monitored equipment to store and transport blood at controlled temperatures, including blood transport boxes, refrigerators, freezers and platelet agitators
- Correct use of this equipment by all staff involved in handling blood products.

Clinical staff are responsible for ensuring that blood products issued by the blood bank for transfusion are kept at the correct temperature until their infusion into the patient.

## Storage conditions

### Red cells and whole blood

Red cells and whole blood must always be stored at a temperature between +2°C and +6°C. They must *never* be allowed to freeze.

The upper limit of 6°C is essential to minimize the growth of any bacterial contamination in the unit of blood. The lower limit of 2°C is essential because red cells that are allowed to freeze become haemolysed. If they are transfused, the presence of cell membrane fragments and free haemoglobin can cause fatal bleeding problems or renal failure.

The solution in the blood bag contains both anticoagulant (sodium citrate) to stop the blood from clotting and dextrose (glucose) to 'feed' the red cells during storage. Storage at a temperature between 2°C and 6°C is essential to make sure the dextrose is not used too quickly.

Whole blood and red cells should be issued from the blood bank in a blood transport box or insulated carrier that will keep the temperature under 10°C if the ambient (room) temperature is greater than 25°C or there is a possibility that the blood will not be transfused within 30 minutes.

Unless required for immediate transfusion, the packs should be stored in the ward or operating theatre blood refrigerator at a temperature between 2°C and 6°C (see p. 120: Warming blood).

**Red cells and whole blood should be infused within 30 minutes of removal from refrigeration.**

Red cells and whole blood that have been out of the correct storage conditions for more than 30 minutes should never be returned to the refrigerator for later use because of the potential for bacterial contamination and the loss of cell function.

### Platelet concentrates

Platelet concentrates must be kept at a temperature of 20°C to 24°C on a platelet agitator to maintain platelet function. Since there is a risk of bacterial proliferation, the storage life is restricted to 3 or 5 days, depending on the type of blood bag used. Platelets that are held at lower temperatures lose their blood clotting capability.

Platelet concentrates should be issued from the blood bank in a blood transport box or insulated carrier that will keep the temperature at about 20°C to 24°C.

Platelet concentrates should be transfused as soon as possible. They should *never* be placed in a refrigerator.

### Fresh frozen plasma

Fresh frozen plasma (FFP) must be stored in the blood bank at a temperature of –25°C or colder until it is thawed before transfusion. As with whole blood or red cells, bacteria can proliferate in plasma that is held at ambient (room) temperature.

Most of the clotting factors are stable at refrigerator temperatures, except for Factor V and Factor VIII. If plasma is not stored frozen at –25°C or colder, Factor VIII falls rapidly over 24 hours. Plasma with a reduced Factor VIII level is of no use for the treatment of haemophilia, although it can be used in other clotting problems (see Section 5: *Blood Products*). Factor V declines more slowly.

Fresh frozen plasma should be thawed in the blood bank in a waterbath between +30°C and +37°C and issued in a blood transport box in which the temperature is maintained between +2°C and +6°C.

FFP should be infused within 30 minutes of thawing. If not required for immediate use, it should be stored in a refrigerator at a temperature of 2°C to 6°C and transfused within 24 hours.

## The blood refrigerator

Once issued by the blood bank, the transfusion of whole blood, red cells and thawed fresh frozen plasma should be commenced within 30 minutes of their removal from refrigeration. If the transfusion cannot be started within this period, they must be stored in a refrigerator at a temperature of 2°C to 6°C.

The temperature inside every refrigerator used for blood storage in wards, operating rooms and other clinical areas should be monitored and recorded every four hours to ensure that the temperature remains within this range.

**All blood refrigerators should be specifically designed for blood storage**. If the ward does not have a refrigerator that is appropriate for storing blood, the blood should not be released from the blood bank until immediately before transfusion.

All staff should be trained to comply with the following procedure.

1   Open the door only when it is necessary to take out or put in blood.

2   Arrange the blood so there is room for cold air to move around inside the refrigerator. The units of blood should be kept in baskets in an upright position or laid flat on the shelf. They should never be packed so tightly that the cold air cannot circulate.

3   Never keep anything except whole blood, red cells or thawed fresh frozen plasma in the blood refrigerator.

4   Never store platelet concentrates in a refrigerator.

5   If a domestic refrigerator is used, never store blood in the door where the temperature is normally higher than inside.

6    Never store blood near the freezer compartment of a domestic refrigerator.

All unused blood products should be returned to the blood bank so that their return and reissue or destruction can be recorded.

### ACTIVITY 20

*Check whether blood is being transported and stored correctly in your clinical area. If it is not, identify any changes needed in the storage and transportation system, including procedures for monitoring and recording the temperature every four hours in all refrigerators used for blood storage. Discuss them with blood bank staff and any staff responsible for using blood and blood products elsewhere in the hospital.*

*Organize a teaching session for staff in your clinical area on the importance of keeping blood products in the correct storage conditions prior to transfusion. Monitor whether blood is being stored correctly and provide any further teaching that may be needed.*

## 6.6   Administering blood products

Every hospital should have a written standard operating procedure for the administration of blood components, particularly for the final identity check of the patient, the blood pack, the compatibility label and the documentation.

### Compatibility label

The blood bank should provide documentation with the blood units stating:

- Patient's family name and given name
- Patient's ABO and Rh D group
- Unique donation number of the blood pack
- Blood group of the blood pack.

A compatibility label, such as the example shown in Figure 6.9, should be attached firmly to each blood pack.

*Figure 6.9: Example of a compatibility label for crossmatched blood*

**THIS BLOOD IS COMPATIBLE WITH:**       Blood pack no. [        ]

Patient's name:

Patient's hospital reference number:

Patient's ward:

Patient's blood group:

Blood group of the blood pack:

Expiry date:

Date of compatibility test:

**RETURN BLOOD PROMPTLY TO BLOOD BANK IF NOT USED**

The compatibility label should show the following information:

- Unique donation number of the blood pack
- Patient's family name and given name
- Patient's hospital reference number
- Patient's date of birth
- Patient's ward
- Patient's ABO and Rh D group
- Blood group of the blood pack
- Expiry date of the blood pack
- Date of the compatibility test.

## Checking the blood pack

The blood pack should always be inspected for signs of deterioration:

- Before it is issued from the blood bank
- On arrival in the ward or operating theatre
- Before transfusion, if it is not used immediately.

If time allows, mix the blood and let it settle until you can see the colour of the plasma layer before checking for each of the following signs of deterioration.

1  Any sign of haemolysis in the plasma indicating that the blood has been contaminated, allowed to freeze or become too warm.

2  Any sign of haemolysis on the line between the red cells and plasma. If you suspect this, gently mix the unit and allow it to 'settle out' before being issued.

3  Any sign of contamination, such as a change of colour in the red cells, which often look darker or purple/black when contaminated.

4  Any clots, which may mean that the blood was not mixed properly with the anticoagulant when it was collected.

5  Any signs that there is any damage or leak in the blood pack or that it has already been opened.

If any discrepancies are found or the pack appears abnormal in any way, the unit must not be transfused and the blood bank must be informed immediately.

**Discoloration or signs of any leakage may be the only warning that the blood contains bacterial contamination and could cause a severe or fatal reaction when transfused.**

Figure 6.10 shows signs of deterioration in blood or plasma. Copy this and put it on a wall near every blood refrigerator in your hospital to remind everyone to check the blood on arrival in the clinical area and before it is transfused.

_Figure 6.10: Checking for signs of deterioration in blood or plasma_



Is the heat seal or clip on the donating tube secure and leak-free?

Are there any leaks? Have you squeezed the bag? Look for blood here

Look for haemolysis in the plasma. Is the plasma pink?

Look for large clots in the plasma

Plasma

Red cells

Look for haemolysis on the line between red cells and plasma

Look at the red cells. Are they normal, or are they purple or black?

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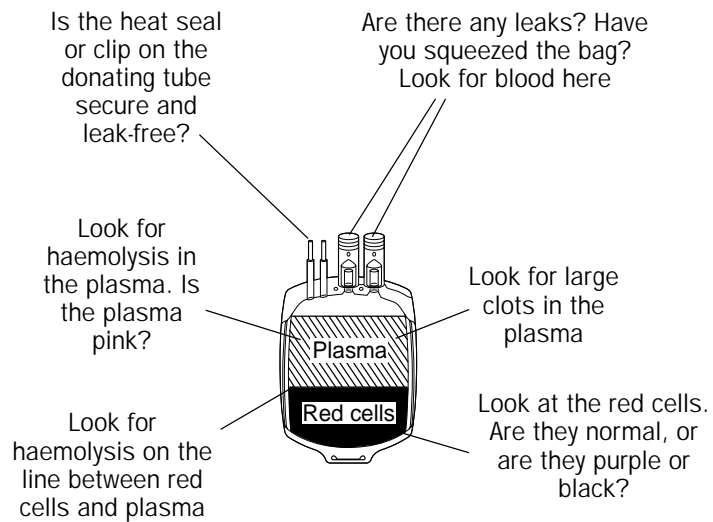
**THE UNIT SHOULD NOT BE TRANSFUSED IF**

The unit has been (or may have been) out of the refrigerator
for longer than 30 minutes

or

If there is any sign that there is a leak or the bag has been opened

or

The plasma is pink or red

or

The red cells look purple or black

---

## Checking the patient's identity and the blood product before transfusion

Before starting the infusion, it is vital to make the final identity check in accordance with your hospital's standard operating procedure.

The final identity check should be undertaken _at the patient's bedside_ immediately before commencing the administration of the blood component. It should be undertaken by two people, at least one of whom should be a registered nurse or doctor.

Figure 6.11 shows the procedure for checking the patient's identity with:

- Blood pack
- Compatibility label
- Patient's notes.

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**The final check at the patient's bedside is the last opportunity to detect an identification error and prevent a potentially incompatible transfusion, which may be fatal.**

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*Figure 6.11: Checking the patient's identity and the blood product before transfusion*

## THE FINAL PATIENT IDENTITY CHECK

1 Ask the patient to identify himself/herself by family name, given name, date of birth and any other appropriate information.

 If the patient is unconscious, ask a relative or a second member of staff to state the patient's identity.

2 Check the patient's identity and gender against:
 ■ Patient's identity wristband or label
 ■ Patient's medical notes.

3 Check that the following details on the compatibility label attached to the blood pack exactly match the details on the patient's documentation *and* identity wristband:
 ■ Patient's name
 ■ Patient's hospital reference number
 ■ Patient's ward, operating room or clinic
 ■ Patient's blood group.

4 Check that there are no discrepancies between the ABO group and Rh D group on:
 ■ Blood pack
 ■ Compatibility label.

5 Check that there are no discrepancies between the unique donation number on:
 ■ Blood pack
 ■ Compatibility label.

6 Check that the expiry date on the blood pack has not been passed.

7 Examine the pack before transfusion. Do not administer the transfusion if the pack is damaged or there is any evidence of signs of deterioration:
 ■ Leakage
 ■ Unusual colour
 ■ Signs of haemolysis.

## ACTIVITY 21

*Is there a written procedure in your hospital for the final patient identity check immediately before the administration of blood or blood products? If yes, compare it with the procedure outlined in Figure 6.11.*

*If there is no written procedure or you feel that the existing procedure could be improved, talk to senior colleagues about the importance of ensuring that all staff systematically check the patient's identity with the blood product before commencing the transfusion.*

*Organize a training session for all relevant staff and monitor whether the procedure is being followed correctly.*

# Time limits for infusion

**There is a risk of bacterial proliferation or loss of function in blood products once they have been removed from the correct storage conditions.**

## Whole blood or red cells

The administration of whole blood or red cells should be started within 30 minutes of removing the pack from the storage temperature of +2°C to +6°C. It should be completed within 4 hours of starting the transfusion. These time limits have been determined for temperate climates where temperatures in hospital buildings are generally between 22°C and 25°C. If the ambient (room) temperature is very high, shorter 'out-of-refrigerator times' should be used.

## Platelet concentrates

Platelet concentrates should be administered as soon as they have been received. The infusion of each concentrate should be completed within about 20 minutes.

## Fresh frozen plasma

Fresh frozen plasma should be infused as soon as possible after thawing to avoid loss of labile clotting factors. In an adult, 1 unit (200–300 ml) should generally be infused within about 20 minutes.

Figure 6.12 summarizes the time limits for the infusion of blood products.

*Figure 6.12: Time limits for the infusion of blood components*

| TIME LIMITS FOR INFUSION | | |
|---|---|---|
| | **Start infusion** | **Complete infusion** |
| Whole blood/red cells | Within 30 minutes of removing pack from refrigerator | Within 4 hours (or less in high ambient temperature) |
| Platelet concentrates | Immediately | Within 20 minutes |
| Fresh frozen plasma | Within 30 minutes | Within 20 minutes |

## Disposable equipment for blood administration

Cannulae for infusing blood products:

- Must be sterile and must *never* be reused
- Use flexible plastic cannulae, if possible, as they are safer and preserve the veins
- A doubling of the diameter of the cannula increases the flow rate of most fluids by a factor of 16.

## Whole blood, red cells, plasma and cryoprecipitate

These products should be infused through a new, sterile blood administration set containing an integral 170–200 micron filter.

The set should be changed at least 12-hourly during blood component infusion. In a very warm climate, it should be changed more frequently and usually after every four units of blood, if given within a 12-hour period.

## Platelet concentrates
A fresh blood administration set or platelet transfusion set, primed with saline, should be used to infuse platelet concentrates.

## Paediatric patients
Special paediatric sets should be used for paediatric patients, if possible. These allow the blood or other infusion fluid to flow into a graduated container built into the infusion set. This permits the volume given, and the rate of infusion, to be controlled simply and accurately. See p. 241 for infusion sets for infants.

# Filtration of red cells and platelets

## Microaggregate filters
Microaggregate filters are expensive and there is no evidence from controlled trials that they offer clinical benefit. Common, but unproven, indications are for massively transfused patients, transfusion for multiple trauma and during cardiopulmonary bypass.

Some patients who require long-term red cell replacement have febrile transfusion reactions and microaggregate filtration of stored red cells may reduce or prevent these reactions.

## Leucocyte-depleting filters
Leucocyte-depleting filters are very expensive and the effective clinical indications for their use are very restricted and still the subject of research. They effectively delay the onset of febrile transfusion reactions in red cell transfusion-dependent patients and can prevent reactions to later transfusions, if less expensive alternatives are not successful (see Section 7: *Adverse Effects of Transfusion*).

The use of leucocyte-depleted red cells and platelets can reduce the development of anti-leucocyte antibodies in multiply-transfused patients, but only if all transfused blood components are filtered. Many clinicians believe this delays or avoids '**refractoriness**' to platelet therapy, but there remains controversy about whether clinical outcomes are improved by the use of leucocyte-depleted blood components, other than when they are used to prevent the transmission of CMV.

**refractory:** A poor response to platelet transfusion. Usually due to a clinical factor: e.g. fever, infection, DIC, splenomegaly, antibiotics. Also occurs if the platelet components transfused are defective.

# Warming blood

There is no evidence that warming blood is beneficial to the patient when infusion is slow. Cold blood can cause spasm in the vein used for infusion. Dry warm towels applied locally may help, but take care not to burn the skin. Case reports suggest that, at infusion rates greater than 100 ml/minute, cold blood could be a contributing factor in cardiac arrest. However, keeping the patient warm is probably more important than warming the infused blood.

Warmed blood is most commonly required in:

- Large volume rapid transfusions:
  — Adults: greater than 50 ml/kg/hour
  — Children: greater than 15 ml/kg/hour
- Exchange transfusion in infants
- Patients with clinically significant cold agglutinins.

Blood should only be warmed in a blood warmer. Blood warmers should have a visible thermometer and an audible warning alarm and should be properly maintained. Older types of blood warmer may slow the infusion rate of fluids.

Blood should never be warmed in a bowl of hot water as this could lead to the haemolysis of the red cells and liberation of $K^+$ which could be life-threatening.

## Pharmaceuticals and blood products

No medicines and no infusion solutions other than normal saline (sodium chloride 0.9%) should be added to any blood component. These may contain additives such as calcium which can cause citrated blood to clot. Dextrose solution (5%) can lyse red cells. If there is an adverse reaction during the transfusion, it may be impossible to determine whether this is due to the blood, to the added drug or to an interaction of the two.

If an intravenous fluid other than normal saline, or a colloid solution, has to be given at the same time as blood components, it should preferably be given through a separate IV line to avoid any risk of these problems.

## Recording the transfusion

The following information should be recorded in the patient's notes.

1   Whether the patient and/or relatives have been informed about the proposed transfusion.

2   The reason for transfusion.

3   Signature of the prescribing clinician.

4   Pre-transfusion checks of:
   - Patient's identity
   - Blood pack
   - Compatibility label
   - Signature of the person performing the pre-transfusion check.

5   The transfusion:
   - Type and volume of each component transfused
   - Unique donation number of each unit transfused
   - Blood group of each unit transfused
   - Time at which the transfusion commenced
   - Signature of the person administering the blood component.

6   Any transfusion reactions.

### Recording the reason for transfusion

Before administering blood products, it is important to write the reason for transfusion in the patient's case-notes. If the patient later has a problem that could be related to the transfusion, the records should show who ordered the products and why.

The reason for transfusion should usually comply with national or local guidelines, but remember that it is the clinician who is responsible for prescribing and giving a transfusion. The record you make in the patient's case-notes is your best protection if there is any medico-legal challenge later on.

## 6.7  Monitoring the transfused patient

Ensuring the patient's safety is the most important aspect of caring for a patient during transfusion. It is essential to take baseline observations and to ensure that the patient is being monitored during and after the transfusion in order to detect any adverse event as early as possible. This will ensure that potentially life-saving action can be taken quickly and efficiently.

Adverse reactions can occur with all blood components so it is equally important to monitor patients receiving FFP, cryoprecipitate or platelet concentrates as those receiving whole blood or red cells.

Severe reactions most commonly present during the first 15 minutes of a transfusion. It is therefore very important that all patients and, in particular, unconscious patients should be monitored during this period and for the first 15 minutes of each subsequent unit.

Before commencing the transfusion, it is essential to:

- Explain the procedure to the patient and check for understanding of the explanation
- Encourage the patient to notify a nurse or doctor immediately if he or she becomes aware of any reactions such as shivering, flushing, pain or shortness of breath or begins to feel anxious
- Ensure that the patient is in a setting where he or she can be directly observed.

If the patient appears to be experiencing an adverse reaction, stop the transfusion and seek urgent medical assistance. Record vital signs regularly until the medical officer has assessed the patient.

The transfusion of each unit of the blood or blood component should be completed within four hours of the pack being punctured. If a unit is not completed within four hours, discontinue its use and dispose of the remainder through the clinical waste system. In the case of a suspected transfusion reaction, do not discard the blood pack and blood administration set, but return them to the blood bank for investigation.

Change the blood administration set after 12 hours if the patient requires ongoing transfusion support.

Figure 6.13 summarizes the observations that should be made and recorded before, during and after the transfusion.

*Figure 6.13: Procedure for monitoring the transfused patient*

**MONITORING THE TRANSFUSED PATIENT**

1  **For each unit of blood transfused**, monitor the patient at the following stages:
- Before starting the transfusion
- As soon as the transfusion is started
- 15 minutes after starting transfusion
- At least every hour during transfusion
- On completion of the transfusion
- 4 hours after completing the transfusion.

2  At each of these stages, record the following information on the patient's chart:
- Patient's general appearance
- Temperature
- Pulse
- Blood pressure
- Respiratory rate
- Fluid balance:
    — Oral and IV fluid intake
    — Urinary output.

3  Record:
- Time the transfusion is started
- Time the transfusion is completed
- Volume and type of all products transfused
- Unique donation numbers of all products transfused
- Any adverse effects.

4  Monitor the patient particularly carefully during the first 15 minutes of the transfusion to detect early signs and symptoms of adverse effects.

## Acute transfusion reactions

Any adverse reaction thought to be related to the transfusion should be assessed and managed as described in Section 7: *Adverse Effects of Transfusion*, which summarizes the symptoms and signs that may indicate that a reaction is occurring. The clinical details and actions taken should be recorded in the patient's case-notes.

### ACTIVITY 22

*Is there a written procedure for monitoring patients before, during and on completion of a transfusion? Can you suggest any ways of improving it? Do staff follow it correctly? For example, do they consistently perform the 15-minute check after the start of each unit? Do transfusions always take place in areas where patients can easily be observed?*

*Identify any changes needed to ensure that all patients are systematically monitored during transfusion in order to ensure the early recognition and*

*management of a transfusion reaction. Discuss your ideas with senior colleagues and with the hospital transfusion committee if one exists in your hospital.*

*Organize a teaching session for all staff involved in monitoring patients during transfusion. Observe whether the procedure is being followed correctly. Provide any further teaching that may be required and continue to monitor practice.*

## 6.8 Specialized procedures

### Therapeutic apheresis

Therapeutic apheresis means the removal of blood or a blood component in order to benefit the patient's condition. The simplest procedure is therapeutic venesection in which 200–450 ml of whole blood is withdrawn periodically. This may be indicated as part of the treatment of some patients suffering from haemochromatosis or polycythaemia.

More commonly, either cells or plasma are removed using a cell separator.

Methods for the more selective removal of plasma constituents such as cholesterol or auto-antibodies are still at the experimental stage of development.

Good venous access is essential as a rapid blood flow is required for processing. Some apheresis machines can operate using a single vein, but separate cannulae are usually required for blood withdrawal and return.

### Plasma exchange

Therapeutic plasma exchange combined with other medical treatment contributes effectively to the management of the conditions shown in Figure 6.14.

*Figure 6.14: Indications for therapeutic plasma exchange (plasmapheresis)*

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**Indications for therapeutic plasma exchange**

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- Hyperviscosity syndromes: e.g. myeloma, Waldenström's macroglobulinaemia
- Rapidly progressive glomerulo-nephritis: e.g. Wegener's granulomatosis
- Goodpasture's syndrome
- Guillain-Barré syndrome (intravenous immunoglobulin therapy is equally effective)
- Familial hypercholesterolaemia
- Thrombotic thrombocytopenic purpura

---

Plasma exchange has been used in many other conditions such as myasthenia gravis, pemphigus, Systemic Lupus Erythematosis (SLE), other auto-immune disorders and maternal Rh D sensitization during pregnancy. Its effectiveness has not been proved in these conditions and, in many cases, objective monitoring is difficult.

The potential risk and the high cost of plasmapheresis should be taken into account before using it in these conditions.

The replacement fluid used for plasma exchange is usually 4.5% albumin, saline or a mixture of these. Fresh frozen plasma (FFP) may occasionally be needed to correct a deficiency of coagulation factors at the end of a plasma exchange. Apart from the single indication of thrombotic thrombocytopenic purpura and closely related conditions, FFP should not otherwise be used in plasma exchange.

## Thrombotic thrombocytopenic purpura

This rare and serious condition often responds to the infusion of fresh frozen plasma. Because large volumes of FFP may have to be given over a long period, plasma exchange, using FFP to replace the patient's plasma, is often used. Fresh frozen plasma should be used as an exchange fluid only in this specific indication because of the risks.

## Cytapheresis (removal of blood cells)

Leucapheresis may help to alleviate symptoms and signs caused by very high cell counts in leukaemic patients (usually chronic granulocytic leukaemia), until chemotherapy takes effect. Plateletpheresis is occasionally used in patients with very high platelet counts causing bleeding or thrombosis. Erythrocytapheresis (red cell exchange) is occasionally needed in the management of malaria, sickle-cell crisis or following a transfusion error in which Rh D positive blood is given to an Rh D negative female of child-bearing age.

Figure 6.15 summarizes possible complications of therapeutic apheresis.

*Figure 6.15: Complications of therapeutic apheresis*

**Complications of therapeutic apheresis**

- Anaphylactic reactions to FFP
- Volume overload
- Hypovolaemia
- Air embolism
- Haemolysis
- Extracorporeal clotting
- Citrate toxicity
- Coagulopathy
- Vasovagal attacks

## Progenitor cell (stem cell) collection by apheresis

Progenitor cells (autologous or allogeneic) can be collected from the peripheral blood by apheresis. This procedure is an effective alternative to the aspiration of bone marrow and avoids the need for the patient or donor to have a general anaesthetic.

This procedure must be carried out by a specialist team, because careful planning and coordination is needed for the preparation of the patient, the collection of the cells and the laboratory procedures to process, store and prepare the patient's cells for reinfusion.

# 7

# Adverse effects of transfusion

## Introduction

Blood transfusion can be associated with various adverse effects. Some of these reactions are acute and arise during or shortly after the transfusion, but the clinical effects of others are delayed, sometimes by months or years.

The safety of blood and blood products varies widely in different areas of the world. However, even with the highest standards of donor selection, blood collection, screening, processing and storage, there remains a risk of transfusion-transmitted infection and other adverse effects.

Consequently, the decision to transfuse must be based on a careful assessment of the risks and benefits to the patient, and with the knowledge and skills to recognize and treat any adverse reactions or complications that may arise.

In addition to this Section, read Section 1: *The Appropriate Use of Blood and Blood Products* and Section 6: *Clinical Transfusion Procedures* which give a more detailed account of the factors that influence blood safety.

## Learning outcomes

When you have completed this section, you should be able to:

1   Identify the different types of transfusion reactions.

2   Recognize, manage and treat different types of transfusion reactions.

3   Investigate and report on transfusion reactions.

4   Carry out appropriate preventive measures to avoid specific transfusion reactions.

## 7.1 Transfusion reactions

Transfusion reactions can be classified in simple categories in order to help you to recognize them, understand their underlying causes and when they may occur, and know how to prevent, manage and record them.

### Acute complications of transfusion

Acute transfusion reactions occur during or shortly after (within 24 hours) the transfusion. They can be broadly classified in the following three categories according to their severity and the appropriate clinical response.

#### Category 1: Mild reactions
■ Mild hypersensitivity: allergic, urticarial reactions

#### Category 2: Moderately severe reactions
■ Moderate–severe hypersensitivity (severe urticarial reactions)
■ Febrile non-haemolytic reactions:
   — Antibodies to white cells, platelets
   — Antibodies to proteins, including IgA
■ Possible bacterial contamination (early signs)
■ Pyrogens

#### Category 3: Life-threatening reactions
■ Acute intravascular haemolysis
■ Bacterial contamination and septic shock
■ Fluid overload
■ Anaphylactic reactions
■ Transfusion-associated lung injury

### Delayed complications of transfusion

Delayed complications of transfusion essentially fall into two categories.

#### Transfusion-transmitted infections
■ HIV-1 and HIV-2
■ HTLV-I and II
■ Viral hepatitis B and C
■ Syphilis
■ Chagas disease
■ Malaria
■ Cytomegalovirus
■ Other rare infections: e.g. human parvovirus B19 and hepatitis A

#### Other delayed complications of transfusion
Other delayed complications of transfusion which occur days, months or even years after the transfusion has been completed, include:

- Delayed haemolytic reaction
- Post-transfusion purpura
- Graft-vs-host disease
- Iron overload (in patients who receive repeated transfusions)

## 7.2  Initial management and investigation

When an acute reaction first occurs, it may be difficult to decide on its type and severity as the signs and symptoms may not initially be specific or diagnostic. However, with the exception of allergic urticarial and febrile non-haemolytic reactions, all are potentially fatal and require urgent treatment.

It is essential to monitor the transfused patient closely in order to detect the earliest clinical evidence of an acute transfusion reaction. Figure 6.13 on p. 123 outlines the procedure for monitoring the transfused patient.

**In an unconscious or anaesthetized patient, hypotension and uncontrolled bleeding may be the only signs of an incompatible transfusion.**

**In a conscious patient undergoing a severe haemolytic transfusion reaction, signs and symptoms may appear within minutes of infusing only 5–10 ml of blood. Close observation at the start of the infusion of each unit is essential.**

### Initial management of acute transfusion reactions

**If an acute transfusion reaction occurs, first check the blood pack labels and the patient's identity. If there is any discrepancy, stop the transfusion immediately and consult the blood bank.**

Figure 7.1 on pp. 130–131 summarizes the signs and symptoms, possible causes and management of the three broad categories of acute transfusion reaction to aid in immediate management.

### ACTIVITY 23

*Find out from hospital records and the blood bank the incidence and types of acute transfusion reactions that were reported in the last year.*

### ACTIVITY 24

*Compare any guidelines in your hospital on the initial management of acute transfusion reactions with the example given in Figure 7.1.*

*If there are no guidelines or you think they could be improved, prepare some draft guidelines and discuss them with senior colleagues. Once they have been agreed, organize a teaching session for all relevant staff. Monitor whether the guidelines are being followed correctly. Provide any further teaching that may be required and continue to monitor practice.*

*Figure 7.1: Guidelines for the recognition and management of acute transfusion reactions*

| CATEGORY | SIGNS | SYMPTOMS | POSSIBLE CAUSE |
|---|---|---|---|
| **CATEGORY 1:**<br>**MILD** | ■ Localized cutaneous reactions:<br>— Urticaria<br>— Rash | ■ Pruritus (itching) | ■ Hypersensitivity (mild) |
| **CATEGORY 2:**<br>**MODERATELY SEVERE** | ■ Flushing<br>■ Urticaria<br>■ Rigors<br>■ Fever<br>■ Restlessness<br>■ Tachycardia | ■ Anxiety<br>■ Pruritus (itching)<br>■ Palpitations<br>■ Mild dyspnoea<br>■ Headache | ■ Hypersensitivity (moderate–severe)<br>■ Febrile non-haemolytic transfusion reactions:<br>— Antibodies to white blood cells, platelets<br>— Antibodies to proteins, including IgA<br>■ Possible contamination with pyrogens and/or bacteria |
| **CATEGORY 3:**<br>**LIFE-THREATENING** | ■ Rigors<br>■ Fever<br>■ Restlessness<br>■ Hypotension (fall of ≥20% in systolic BP)<br>■ Tachycardia (rise of ≥20% in heart rate)<br>■ Haemoglobinuria (red urine)<br>■ Unexplained bleeding (DIC) | ■ Anxiety<br>■ Chest pain<br>■ Pain near infusion site<br>■ Respiratory distress/shortness of breath<br>■ Loin/back pain<br>■ Headache<br>■ Dyspnoea | ■ Acute intravascular haemolysis<br>■ Bacterial contamination and septic shock<br>■ Fluid overload<br>■ Anaphylaxis<br>■ Transfusion-associated lung injury |

**Note**: If an acute transfusion reaction occurs, first check the blood pack labels and the patient's identity. If there is any discrepancy, stop the transfusion immediately and consult the blood bank.

In an unconscious or anaesthetized patient, hypotension and uncontrolled bleeding may be the only signs of an incompatible transfusion.

In a conscious patient undergoing a severe haemolytic transfusion reaction, signs and symptoms may appear very quickly – within minutes of infusing only 5–10 ml of blood. Close observation at the start of the infusion of each unit is essential.

## IMMEDIATE MANAGEMENT    131

### CATEGORY 1: MILD
1 Slow the transfusion.

2 Administer antihistamine IM (e.g. chlorpheniramine 0.1 mg/kg or equivalent).

3 If no clinical improvement within 30 minutes or if signs and symptoms worsen, **treat as Category 2**.

### CATEGORY 2: MODERATELY SEVERE
1 Stop the transfusion. Replace the infusion set and keep IV line open with normal saline.

2 Notify the doctor responsible for the patient and the blood bank immediately.

3 Send blood unit with infusion set, freshly collected urine and new blood samples (1 clotted and 1 anticoagulated) from vein opposite infusion site with appropriate request form to blood bank and laboratory for investigations.

4 Administer antihistamine IM (e.g. chlorpheniramine 0.1 mg/kg or equivalent) and oral or rectal antipyretic (e.g. paracetamol 10 mg/kg: 500 mg – 1 g in adults). Avoid aspirin in thrombocytopenic patients.

5 Give IV corticosteroids and bronchodilators if there are anaphylactoid features (e.g. broncospasm, stridor).

6 Collect urine for next 24 hours for evidence of haemolysis and send to laboratory.

7 If clinical improvement, restart transfusion slowly with new blood unit and observe carefully.

8 If no clinical improvement within 15 minutes or if signs and symptoms worsen, **treat as Category 3**.

### CATEGORY 3: LIFE-THREATENING
1 Stop the transfusion. Replace the infusion set and keep IV line open with normal saline.

2 Infuse normal saline (initially 20–30 ml/kg) to maintain systolic BP. If hypotensive, give over 5 minutes and elevate patient's legs.

3 Maintain airway and give high flow oxygen by mask.

4 Give adrenaline (as 1:1000 solution) 0.01 mg/kg body weight by slow intramuscular injection.

5 Give IV corticosteroids and bronchodilators if there are anaphylactoid features (e.g. broncospasm, stridor).

6 Give diuretic: e.g. frusemide 1 mg/kg IV or equivalent

7 Notify the doctor responsible for the patient and the blood bank immediately.

8 Send blood unit with infusion set, fresh urine sample and new blood samples (1 clotted and 1 anticoagulated) from vein opposite infusion site with appropriate request form to blood bank and laboratory for investigations.

9 Check a fresh urine specimen visually for signs of haemoglobinuria (red or pink urine).

10 Start a 24-hour urine collection and fluid balance chart and record all intake and output. Maintain fluid balance.

11 Assess for bleeding from puncture sites or wounds. If there is clinical or laboratory evidence of DIC (see Section 9.11), give platelets (adult: 5–6 units) **and** either cryoprecipitate (adult: 12 units) *or* fresh frozen plasma (adult: 3 units). Use virally-inactivated plasma coagulation products, wherever possible.

12 Reassess. If hypotensive:
  - Give further saline 20–30 ml/kg over 5 minutes
  - Give inotrope, if available.

13 If urine output falling or laboratory evidence of acute renal failure (rising $K^+$, urea, creatinine):
  - Maintain fluid balance accurately
  - Give further frusemide
  - Consider dopamine infusion, if available
  - Seek expert help: the patient may need renal dialysis.

14 If bacteraemia is suspected (rigors, fever, collapse, no evidence of a haemolytic reaction), start broad-spectrum antibiotics IV, to cover *pseudomonas* and gram positives.

Figure 7.2 indicates the drugs and dosages that may be needed in managing acute transfusion reactions.

Figure 7.2: Drugs that may be required in the management of acute transfusion reactions

| TYPE OF DRUG | RELEVANT EFFECTS | EXAMPLES | | NOTES |
|---|---|---|---|---|
| | | **Name** | **Route and dosage** | |
| Intravenous replacement fluid | Expand blood volume See Section 4.2 | Normal saline | If patient hypotensive, 20–30 ml/kg over 5 minutes | Avoid colloid solutions |
| Antipyretic | Reduce fever and inflammatory response | Paracetemol | Oral or rectal 10 mg/kg | Avoid aspirin-containing products if patient has low platelet count |
| Antihistamine | Inhibits histamine mediated responses | Chlorphen-iramine | Intramuscular or IV 0.1 mg/kg | |
| Bronchodilator | Inhibits immune mediated bronchospasm | Adrenaline | 0.01 mg/kg (as 1: 1000 solution) by slow intramuscular injection | Dose may be repeated every 10 minutes according to blood pressure and pulse until improvement occurs |
| | | Consider salbutamol | By nebuliser | |
| | | Aminophylline | 5 mg/kg | |
| Inotrope | Increases myocardial contractility | Dopamine | IV infusion 1 microgm/kg/minute | ■ Dopamine in low doses induces vasodilation and improves renal perfusion |
| | | Dobutamine | IV infusion 1–10 microgm/kg/minute | ■ Doses above 5 microgms/kg/minute cause vaso-constriction and worsen heart failure |
| Diuretic | Inhibits fluid reabsorption from ascending loop of Henle | Frusemide | Slow IV injection 1 mg/kg | |
| ■ Platelets<br>■ Cryoprecipitate<br>■ Fresh frozen plasma | | | | See Section 5.6 |

## Investigating acute transfusion reactions

Figure 7.3 outlines the procedure for investigating acute transfusion reactions.

*Figure 7.3: Procedure for investigating acute transfusion reactions*

### INVESTIGATING ACUTE TRANSFUSION REACTIONS

1  Immediately report all acute transfusion reactions, with the exception of mild hypersensitivity (Category 1), to the doctor responsible for the patient and to the blood bank that supplied the blood.

   If you suspect the patient is having a severe life-threatening reaction, seek help immediately from the duty anaesthetist, emergency team or whoever is available and skilled to assist.

2  Record the following information on the patient's notes:
   - Type of transfusion reaction
   - Length of time after the start of transfusion that the reaction occurred
   - Volume, type and pack numbers of the blood products transfused.

3  Take the following samples and send them to the blood bank for laboratory investigations:
   - Immediate post-transfusion blood samples (1 clotted and 1 anticoagulated: EDTA/Sequestrene) from the vein opposite the infusion site for:
     — Full blood count
     — Coagulation screen
     — Direct antiglobulin test
     — Urea
     — Creatinine
     — Electrolytes
   - Blood culture in a special blood culture bottle
   - Blood unit and giving-set containing red cell and plasma residues from the transfused donor blood
   - First specimen of the patient's urine following the reaction.

4  Complete a transfusion reaction report form.

5  After the initial investigation of the reaction, send the following to the blood bank for laboratory investigations:
   - Blood samples (1 clotted and 1 anticoagulated: EDTA/Sequestrene) taken from the vein opposite the infusion site 12 hours and 24 hours after the start of the reaction
   - Patient's 24-hour urine sample.

6  Record the results of the investigations in the patient's records for future follow-up, if required.

## 7.3 Acute transfusion reactions

### Category 1: Mild reactions

Urticaria and itching are not uncommon reactions following transfusion. They arise as a result of hypersensitivity with local histamine release to proteins, probably in the donor plasma.

### Signs and symptoms

Localised cutaneous reactions (urticaria and rash), often accompanied by pruritus (intense itching), occur within minutes of commencing the transfusion. The symptoms usually subside if the transfusion is slowed and antihistamine is given.

### Management

1. Slow the transfusion.

2. Give an antihistamine: e.g. chlorpheniramine 0.1 mg/kg by intramuscular injection.

3. Continue the transfusion at the normal rate if there is no progression of symptoms after 30 minutes.

4. **If there is no clinical improvement within 30 minutes or if signs and symptoms worsen, treat the reaction as a Category 2 reaction**.

### Prevention

If a patient has previously experienced repeated urticarial reactions, give an antihistamine such as chlorpheniramine 0.1 mg/kg IM or IV 30 minutes before commencing the transfusion, where possible.

### Category 2: Moderately severe reactions

Fever or rigors during the transfusion of blood or platelet concentrates may affect 1–2% of recipients, particularly those who depend on regular transfusions. They are caused by cytokines released from leucocytes in stored blood components and by the reaction of infused white cells with antibodies in the patient's plasma, resulting in the release of pyrogens.

It is important to routinely record the patient's temperature, pulse, respiration and blood pressure before starting the transfusion to avoid confusion due to pre-existing fever.

Signs and symptoms usually occur 30–60 minutes after the start of the transfusion.

### Signs
- Flushing
- Urticaria
- Rigors
- Fever
- Restlessness
- Tachycardia

## Symptoms

- Anxiety
- Pruritus (itching)
- Palpitations
- Mild dyspnoea
- Headache

## Management

1 Stop the transfusion. Replace the infusion set and keep the IV line open with normal saline.

2 Notify the doctor responsible for the patient and the blood bank immediately.

3 Send the blood unit with infusion set, freshly collected urine and new blood samples (1 clotted and 1 anticoagulated) from the vein opposite the infusion site with an appropriate request form to the blood bank for investigations (see Figure 7.3 on p. 133).

4 Administer antihistamine IV or IM (e.g. chlorpheniramine 0.01 mg/kg or equivalent) and an oral or rectal antipyretic (e.g. paracetamol 10 mg/kg: 500 mg – 1 g in adults). Avoid aspirin in thrombocytopenic patients.

5 Give IV corticosteroids and bronchodilators if there are anaphylactoid features (e.g. broncospasm, stridor).

6 Collect urine for the next 24 hours for evidence of haemolysis and send to the laboratory.

7 If there is a clinical improvement, restart the transfusion slowly with a new unit of blood and observe carefully.

8 **If there is no clinical improvement within 15 minutes or the patient's condition deteriorates, treat the reaction as a Category 3 reaction.**

Febrile reactions are quite common, but fever is associated with other adverse reactions to transfusion and it is important to eliminate these other causes, particularly acute haemolysis and bacterial contamination, before arriving at a diagnosis of a febrile reaction. Fever may also be caused by the patient's underlying condition: e.g. malaria.

## Prevention

If the patient is a regular transfusion recipient or has had two or more febrile non-haemolytic reactions in the past:

1 Give an antipyretic 1 hour before starting the transfusion: e.g. paracetamol 10–15 mg/kg orally. Do not use aspirin in a patient with thrombocytopenia.

2 Repeat the antipyretic 3 hours after the start of transfusion.

3 Transfuse slowly, where possible:
   - Whole blood and red cells: 3–4 hours per unit
   - Platelet concentrates: up to 2 hours per concentrate.

4   Keep the patient warm.

5   If this fails to control the febrile reaction and further transfusion is needed, use buffy coat removed or filtered red cells or platelet concentrates to remove the leucocytes.

## Category 3: Life-threatening reactions

The most common causes of life-threatening transfusion reactions are:

- Acute intravascular haemolysis
- Bacterial contamination and septic shock
- Fluid overload
- Anaphylactic shock
- Transfusion-associated lung injury (TRALI)

### Signs

- Rigors
- Fever
- Restlessness
- Shock
- Tachycardia
- Haemoglobinuria (red urine)
- Unexplained bleeding (DIC)

### Symptoms

- Anxiety
- Chest pain
- Respiratory distress/shortness of breath
- Loin/back pain
- Headache
- Dyspnoea

### Management

1   Stop the transfusion. Replace the infusion set and keep IV line open with normal saline.

2   Infuse normal saline to maintain systolic BP (initial 20–30 ml/kg). If hypotensive, give over 5 minutes and elevate patient's legs.

3   Maintain airway and give high flow oxygen by mask.

4   Give 1:1000 adrenaline 0.01 mg/kg body weight by intramuscular injection.

5   Give IV corticosteroids and bronchodilators if there are anaphylactoid features (e.g. broncospasm, stridor).

6   Give diuretic: e.g. frusemide 1 mg/kg IV or equivalent

7   Notify the doctor responsible for the patient and the blood bank immediately.

8   Send blood unit with infusion set, fresh urine sample and new blood samples (1 clotted and 1 anticoagulated) from vein opposite infusion site with appropriate request form to blood bank and laboratory for investigations.

9   Check a fresh urine specimen visually for signs of haemoglobinuria (red or pink urine).

10  Start a 24-hour urine collection and fluid balance chart and record all intake and output. Maintain fluid balance.

11  Assess for bleeding from puncture sites or wounds. If there is clinical or laboratory evidence of DIC (see Section 9.11), give:
    ■ Platelet concentrates (adult: 5–6 units)

    **and**

    ■ Either cryoprecipitate (adult: 12 units) **or** fresh frozen plasma (adult: 3 units).

    Use virally-inactivated plasma coagulation products, wherever possible.

12  Reassess. If hypotensive:
    ■ Give further saline 20–30 ml/kg over 5 minutes
    ■ Give inotrope.

13  If urine output falling or laboratory evidence of acute renal failure (rising $K^+$, urea, creatinine):
    ■ Maintain fluid balance accurately
    ■ Give further frusemide
    ■ Consider dopamine infusion
    ■ Seek expert help: the patient may need renal dialysis.

14  If bacteraemia is suspected (rigors, fever, collapse, no evidence of a haemolytic reaction), start broad-spectrum antibiotics IV, to cover *pseudomonas* and gram positives.

## Acute intravascular haemolysis

Acute intravascular haemolytic reactions are caused by infusing incompatible red cells. Antibodies in the patient's plasma haemolyse the incompatible transfused red cells. Even a small volume (5–10 ml) of incompatible blood can cause a severe reaction and larger volumes increase the risk. For this reason, it is essential to monitor the patient at the start of the transfusion of **each** unit of blood (see Figure 6.13 on p. 123).

The most common cause of an acute intravascular haemolytic reaction is an ABO incompatible transfusion. The antibodies concerned are either IgM or IgG directed against the A or B antigens on the transfused red cells, causing acute intravascular haemolysis.

The infusion of ABO-incompatible blood almost always arises from:
    ■ Errors in the blood request form
    ■ Taking blood from the wrong patient into a pre-labelled sample tube

- Incorrect labelling of the sample tube sent to the blood bank
- Inadequate checks of the blood against the identity of the patient before starting a transfusion.

Antibodies in the patient's plasma against other blood group antigens of the transfused blood, such as Kidd, Kell or Duffy systems, can also cause acute intravascular haemolysis.

### Signs
- Fever
- Rigors
- Tachycardia, hypotension
- Breathlessness
- Haemoglobinuria, oliguria
- Signs of an increased bleeding tendency due to disseminated intravascular coagulation (DIC)

In the conscious patient undergoing a severe haemolytic reaction, signs and symptoms usually appear within minutes of commencing the transfusion, sometimes when less than 10 ml have been given.

In an unconscious or anaesthetized patient, hypotension and uncontrollable bleeding due to DIC may be the only signs of an incompatible transfusion.

### Symptoms
- Pain or heat in limb where infusion cannula is sited
- Apprehension
- Loin or back pain.

### Management
1 Stop the transfusion, replace the giving set and keep the IV line open with normal saline.

2 Maintain the airway and give high concentrations of oxygen.

3 Support the circulation:
- Give intravenous replacement fluids to maintain blood volume and blood pressure
- Inotropic support of the circulation may be required: e.g. dopamine, dobutamine or adrenaline 1:1000 by intramuscular injection, 0.01 ml/kg body weight.

4 Prevent renal failure by inducing a diuresis:
- Maintain blood volume and blood pressure
- Give a diuretic, such as frusemide 1–2 mg/kg
- Give a dopamine infusion at 1 microgram/kg/minute.

5 If DIC occurs:
- Give blood components, as guided by clinical state and coagulation tests (see Section 9: *General Medicine*)
- Regularly monitor the coagulation status of the patient.

6  Investigations:

- Recheck the labelling of the blood unit against the patient
- Send patient blood sample for:
  — Full blood count
  — Coagulation screen
  — Direct antiglobulin test
  — Urea
  — Creatinine
  — Electrolytes

  The direct antiglobulin test will be positive and serum bilirubin raised

- Examine the patient's urine sample and send to the laboratory for testing for haemoglobinuria
- Return the blood unit and infusion set for checking of group and compatibility testing
- Repeat electrolytes and coagulation screening 12-hourly until the patient is stable.

## Prevention

Ensure that:

1  Blood samples and request forms are labelled correctly.

2  The patient's blood sample is placed in the correct sample tube.

3  The blood is checked against the identity of the patient before transfusion.

## Bacterial contamination and septic shock

It is estimated that bacterial contamination affects up to 0.4% of red cells and 1–2% of platelet concentrates.

Blood may become contaminated by:

- Bacteria from the donor's skin during blood collection (usually skin *staphylococci*)
- Bacteraemia present in the blood of a donor at the time the blood is collected (e.g. *Yersinia*)
- Errors or poor handling in blood processing
- Manufacturing defects or damage to the plastic blood pack
- Thawing frozen plasma or cryoprecipitate in a waterbath (often contaminated).

*Pseudomonas* species are typical contaminants in the last three instances.

Some contaminants, particularly *Pseudomonas* species, grow at 2°C to 6°C and so can survive or multiply in refrigerated red cell units. Rapid growth in contaminants can occur when the unit is allowed to warm. The risk therefore increases with the time out of refrigeration.

*Staphylococci* grow in warmer conditions and proliferate in platelet concentrates at 20°C to 24°C, limiting their storage life.

Signs usually appear rapidly after starting infusion, but may be delayed for a few hours. A severe reaction may be characterized by sudden onset of high fever, rigors and hypotension. Urgent supportive care and high-dose intravenous antibiotics are required.

## Fluid overload

When too much fluid is transfused, the transfusion is too rapid or renal function is impaired, fluid overload can occur resulting in heart failure and pulmonary oedema. This is particularly likely to happen in patients with chronic severe anaemia, and also in patients with underlying cardiovascular disease, for example ischaemic heart disease.

## Anaphylactic reactions

Anaphylactic-type reactions are a rare complication of transfusion of blood components or plasma derivatives. The risk of anaphylaxis is increased by rapid infusion, typically when fresh frozen plasma is used as an exchange fluid in therapeutic plasma exchange. Cytokines in the plasma may be one cause of bronchoconstriction and vasoconstriction in occasional recipients. A rare cause of very severe anaphylaxis is IgA deficiency in the recipient. This can be caused by any blood product since most contain traces of IgA.

Anaphylaxis occurs within minutes of starting the transfusion and is characterized by cardiovascular collapse and respiratory distress, without fever. It is likely to be fatal if it is not managed rapidly and aggressively.

## Transfusion-associated acute lung injury

Transfusion-associated acute lung injury (TRALI) is usually caused by donor plasma that contains antibodies against the patient's leucocytes. Donors are almost always multiparous women.

In a clear-cut case of TRALI, which usually presents within 1 to 4 hours of starting transfusion, there is rapid failure of pulmonary function with diffuse opacity on the chest X-ray. There is no specific therapy. Intensive respiratory and general support in an intensive care unit is required.

## 7.4 Delayed complications of transfusion: transfusion-transmitted infections

Blood donors may carry infectious agents in their blood, sometimes over prolonged periods and without necessarily demonstrating any clinical symptoms or signs of disease. The following infections may be transmitted by transfusion:

- HIV-1 and HIV-2
- HTLV-I and HTLV-II
- Hepatitis B and C
- Syphilis (*Treponema pallidum*)
- Chagas disease (*Trypanosoma cruzi*)
- Malaria
- Cytomegalovirus (CMV).

Other rare transfusion-transmissible infections include:

- Human parvovirus B19
- Brucellosis
- Epstein-Barr virus
- Toxoplasmosis
- Infectious mononucleosis
- Lymes disease.

The possibility has been raised that blood could transmit a new variant of Creutzfeldt-Jakob disease (CJD). Initially labelled 'new variant CJD' (nvCJD), it is now known as 'variant CJD' (vCJD). It is the subject of intense investigation, but there is no evidence of transfusion-associated transmission of CJD or its variant. (See WHO *Weekly Epidemiological Record*, 1998, 73: 6–7).

## Screening for transfusion-transmissible infections

Because of the risk of transfusion-transmitted infection, blood should be collected only from donors who have been selected in accordance with national screening criteria. Every unit of blood should be screened for:

- HIV-1 and HIV-2 (anti-HIV-1, anti-HIV-2) antibody
- Hepatitis B (HBsAg) surface antigen
- *Treponema pallidum* antibody (syphilis).

**No blood or blood product should be released for transfusion until these and all other nationally required tests are shown to be negative.**

Screening for other infectious agents should comply with national policies that should reflect the prevalence of the infection in the potential blood donor population.

Where possible, these should include screening for:

- Hepatitis C
- Chagas disease, in countries where the seroprevalence is significant
- Malaria, in low-prevalence countries. This only applies to donors who have travelled to malarial areas. Malaria screening tests are being evaluated but are not yet sufficiently specific for use in the routine screening of blood donations.

## Human immunodeficiency virus (HIV)

### Acute 'seroconversion' illness

After exposure and infection, viraemia is not detectable for a few days. Thereafter, high titres of virus (i.e. antigen) are detectable for several weeks. During this period, if sufficiently high doses of virus are involved, about one third of infected individuals are reported to experience an acute illness with features of influenza, often with elevated counts of atypical lymphocytes. The individual's blood is highly likely to be infectious at this time.

### The 'window period'

Using the present anti-HIV antibody tests, antibody to HIV becomes detectable approximately 21 days after exposure to infection. Viral DNA and a viral protein, designated p24 antigen, is detectable 7 days earlier than the antibody.

The period when there is viraemia and no detectable evidence of antibodies is often called the 'window period'. Blood taken in this period is usually infectious, but the virus cannot be detected by current screening tests for antibody to HIV. The value of an additional test for an HIV antigen (p24 antigen) has not been proven, although it may allow detection of HIV a few days earlier where there is a high incidence of new HIV infection in a blood donor population that is not carefully selected.

### Epidemiology

There are wide variations in the prevalence of HIV infection between and within countries, and even within small localized areas. Global estimates of HIV-positive individuals are of little help in assessing the risks of transmission by blood transfusion in a given locality and the prevalence of infection in each potential donor population group should therefore be determined.

### Prevention

Prevention initially relies on the selection of low-risk voluntary non-remunerated blood donors and the exclusion of unsuitable donors. Screening tests for HIV are required to enable infected donated blood to be identified and discarded. Confidentiality and the further management of seropositive blood donors through referral for counselling is essential.

## HTLV-I and II

The prevalence of HTLV-I infection is high in some parts of the world, notably the southern part of Japan and parts of the Caribbean. The virus can cause neurological disorders and a rare form of adult T-cell leukaemia. There is usually a delay of many years between infection and the development of illness, but it is likely that only a small proportion of those infected become ill. HTLV-I is transmissible by the transfusion of cellular blood components.

The link between HTLV-II infection and disease is less clear.

### Prevention

Donated blood should be screened where there is epidemiological evidence of HTLV infection or an indication of disease.

## Hepatitis B

The hepatitis B carrier state is highly prevalent in many areas of the developing world, in some areas affecting more than 10% of the potential blood donor population. Transmission by blood may be followed by acute hepatitis, followed either by resolution or by chronic hepatitis. The longer-term consequences are cirrhosis and primary liver cancer.

Infection by hepatitis B virus may lead to clinical or subclinical infection.

It is thought that, in subclinical cases, up to 25% of children and 5–10% of adults become chronic carriers of hepatitis B surface antigen (HBsAg).

### Prevention
All donated blood should be screened for HBsAg prior to transfusion.

Regular recipients of blood products should be vaccinated against hepatitis B.

## Hepatitis C
Antibody tests to detect hepatitis C infection were introduced in 1991 and have been progressively improved. However, these tests remain expensive and different tests may give conflicting results on occasions. Like any blood screening tests, tests should therefore be validated in each country before they are adopted for use.

Hepatitis C infection is usually asymptomatic. About half the affected patients develop chronic hepatitis and a substantial proportion eventually develop severe liver damage.

### Prevention
All donated blood should be screened for hepatitis C, wherever possible.

## Other hepatitis viruses
Hepatitis A has, on very rare occasions, been transmitted by processed blood products (plasma derivatives).

A recently identified virus has been referred to as GB-virus-C or 'hepatitis G'. It appears to be present in about 2% of healthy donors but there is no evidence at present as to whether it is a cause of hepatitis or of any other illness.

## Syphilis
Syphilis is caused by infection with the bacterium *Treponema pallidum*. It is essentially a sexually (venereal) transmitted disease, although it can be spread by close contact with mucous-membrane lesions, and can be transmitted by transfusion. Although a positive syphilis test is not an indication of HIV infection, it is a marker that the blood donor may have a high risk of exposure to other sexually-transmitted infections, including HIV, and should therefore not be accepted to donate blood.

### Prevention
All donated blood should be screened for serological evidence of *Treponema pallidum* infection. A further safeguard is that the storage of donated blood for 72 hours at 2°C to 6°C virtually eliminates the risk of infection as the organism is very sensitive to low temperatures.

## Chagas disease
Chagas disease, caused by *Trypanosoma cruzi*, is transmissible by transfusion. Current estimates suggest that about 18 million people are infected in Latin American countries.

The trypanosoma is transmitted by triatomine insects, triatoma species such as '*triatoma infestans*', although others are involved. The vector lives in low-standard housing in both urban and rural areas.

Blood transfusion is the second most common cause of transmission and up to 50% of blood units that are antibody-positive will transmit the infection. The infection is subclinical in the indeterminate phase, but then leads to a chronic phase which results in irreversible changes, including:

- Cardiomyopathy
- Mega-oesophagus
- Megacolon.

### Prevention

Efforts to eliminate Chagas disease have been successful in reducing the infection by up to 83% in younger age groups. This has been achieved by vector control and the testing of donated blood to exclude infected units. However, different testing assays may give differing results and more than one test may be needed. Most countries in Latin America currently test for Chagas disease using at least two testing assays.

An effective alternative is to add crystal violet, 125 mg, to each unit of stored red cells which inactivates the trypanosoma. However, the procedure for adding crystal violet must safeguard the bacterial sterility of the blood and this is difficult to achieve in practice. It also leads to the staining of skin and mucous membranes.

## Malaria

All blood components can carry the *Plasmodium* parasite and therefore have the potential to transmit malaria. In non-endemic countries, transfusion-transmitted malaria is rare (less than one case per million units of blood transfused). However, the mortality rate is high, often because the diagnosis is not suspected.

### Prevention

In endemic areas, the examination of all donated blood for malaria parasites is not practical. Prevention therefore depends on either:

1 Prophylaxis with antimalarials in the recipient of the blood, if the index of suspicion is high.

2 Pre-treatment of the donor with antimalarials, if indicated.

In many circumstances, neither of these options may be very practical. Therefore, where prophylaxis is not routinely used, it is important to maintain a high index of suspicion and to treat symptoms of malaria in recipients of blood early with the locally-recommended antimalarial regime.

In non-endemic areas, strict donor selection criteria should be used to exclude donors who have recently been in endemic malarial areas or who have had malaria.

## Cytomegalovirus (CMV)

Globally, a very high proportion of blood donors have antibody to CMV.

Transfusion-transmitted CMV is usually only of concern in immune-compromised patients and is of proven clinical importance in:

■ Premature infants, especially those weighing less than 1200–1500 g who are born to CMV antibody-negative mothers

■ CMV antibody-negative bone marrow recipients who receive CMV seronegative grafts.

### Prevention

Immune-compromised patients, premature infants and CMV antibody-negative bone marrow recipients receiving CMV seronegative grafts should receive donations that do not contain detectable antibody to CMV.

Leucocyte-depleted blood components, fresh frozen plasma and cryoprecipitate do not transmit CMV.

## Other rare transfusion-transmissible infections

Other rare infections that have been reported as rare infections transmitted through transfusion include human parvovirus B19, brucellosis, Epstein-Barr virus, toxoplasmosis, infectious mononucleosis and Lymes disease.

### Prevention

Prevention depends on careful blood donor selection criteria to exclude unsuitable donors.

## Creutzfeldt-Jakob disease (CJD) and variant CJD (vCJD)

Creutzfeldt-Jakob disease is a rare and fatal degenerative neurological disorder. The disease has been transmitted from humans to humans by infected extracts of pituitary growth hormone and by grafted cornea and dura mater tissue, and by contaminated neurosurgical instruments.

Although there has been no proven or even probable instance of transmission by blood transfusion or blood products, there is concern about the possibility. It is reassuring that there are no reports of CJD to date among haemophiliacs, who are highly exposed to blood products.

A new variant of CJD (vCJD), occurring in younger patients, has recently been reported. Most of the laboratory and epidemiological studies of blood infectivity and the transmissibility of infection have been made on the sporadic form of CJD, but clinical and neuropathological observations suggest that vCJD may have distinctive biological features. Further studies of vCJD cases are needed in order to determine whether the infectious agent can be transmitted by blood.

### Prevention

Individuals suffering from the following diseases should be permanently excluded from blood donation:

■ Creutzfeldt-Jakob disease and variant CJD

■ Gerstmann-Sträussler-Scheinker disease (GSS)

■ Fatal familial insomnia (FFI)

■ Dementia.

On the basis of current scientific knowledge, it is also essential to exclude the following groups from donating blood:

- Donors who have been treated with extracts derived from human pituitary glands (growth hormone and gonadotrophin)
- Donors with a familial history of CJD, GSS or FFI
- Donors who have received a human cornea or dura mater graft.

## 7.5  Other delayed complications of transfusion

Apart from transfusion-transmitted infections, other delayed transfusion complications may not present immediately but only become apparent days or sometimes months after transfusion. These include:

- Delayed haemolytic transfusion reaction
- Post-transfusion purpura
- Graft-versus-host disease (GvHD)
- Iron overload
- Immunosuppression.

Their presentation and treatment are summarized in Figure 7.4.

*Figure 7.4: Other delayed complications of transfusion*

| COMPLICATION | PRESENTATION | TREATMENT |
|---|---|---|
| Delayed haemolytic reactions | 5–10 days post-transfusion:<br>■ Fever<br>■ Anaemia<br>■ Jaundice | ■ Usually no treatment<br>■ If hypotension and oliguria, treat as acute intravascular haemolysis |
| Post-transfusion purpura | 5–10 days post-transfusion:<br>■ Increased bleeding tendency<br>■ Thrombocytopenia | ■ High dose steroids<br>■ High dose intravenous immunoglobulin<br>■ Plasma exchange |
| Graft-vs-host disease | 10–12 days post-transfusion:<br>■ Fever<br>■ Skin rash and desquamation<br>■ Diarrhoea<br>■ Hepatitis<br>■ Pancytopenia | ■ Supportive care<br>■ No specific treatment |
| Iron overload | Cardiac and liver failure in transfusion-dependent patients | ■ Prevent with iron-binding agents: e. g. desferrioxamine |

## Delayed haemolytic transfusion reactions

### Cause

In patients who have previously been immunized to a red cell antigen during pregnancy or following transfusion, the level of antibody to the blood group antigen may be so low that it cannot be detected in the pre-transfusion blood sample. About 1% of previously-pregnant women have red cell antibodies that are undetectable by routine methods. After transfusion of red cells bearing the relevant antigen, a rapid secondary immune response raises the antibody level so that, after a few days, transfused red cells bearing that antigen are destroyed. Most red cell haemolysis is extravascular.

### Signs and symptoms

The signs of a delayed haemolytic transfusion reaction appear 5–10 days after transfusion:

- Fever
- Anaemia
- Jaundice
- Occasionally haemoglobinuria.

Severe, life-threatening delayed haemolytic transfusion reactions with shock, renal failure and DIC are rare.

### Management

1  Usually, no treatment is required. However, if hypotension and renal failure occur, treat as for acute intravascular haemolysis.

2  Investigations:
- Recheck the patient's blood group
- Direct antiglobulin test is usually positive
- Raised unconjugated bilirubin.

### Prevention

Delayed haemolytic reactions can be prevented by careful laboratory screening for red cell antibodies in the patient's plasma and the selection of red cells compatible with these antibodies. However, some reactions are due to rare antigens (i.e. anti-Jk$^a$ blood group antibodies that are very difficult to detect pre-transfusion).

## Post-transfusion purpura

### Cause

Post-transfusion purpura is a rare but potentially fatal complication of transfusion of red cells or platelet concentrates, most often seen in female patients. It is caused by antibodies directed against platelets in the recipient, causing acute, severe thrombocytopenia 5–10 days after transfusion.

### Signs and symptoms

- Signs of bleeding
- Thrombocytopenia, defined as a platelet count of less than $100 \times 10^9$/L.

## Management

The management of post-transfusion purpura becomes clinically important at a platelet count of 50 x $10^9$/L, with a danger of hidden occult bleeding at 20 x $10^9$/L.

1 Give high dose corticosteroids.

2 Give high dose IV immunoglobulin, 2 g/kg or 0.4 g/kg for 5 days.

3 Plasma exchange.

4 Investigations:
- Monitor the patient's platelet count: normal range is 150 x $10^9$/L to 440 x $10^9$/L
- Give platelet concentrates which are of the same ABO type as the patient's.

Unmatched platelet transfusion is generally ineffective. Recovery of platelet count after 2–4 weeks is usual.

## Prevention

Expert advice is essential and only platelets that are compatible with the patient's antibody should be used.

# Graft-versus-host disease

## Cause

Graft-versus-host disease is a rare and potentially fatal complication of transfusion. It occurs in immunodeficient patients, such as recipients of bone marrow transplants, and in non-immunodeficient patients transfused with blood from individuals with whom they have a compatible tissue type (HLA: human leucocyte antigen), usually blood relatives.

It is caused by donor T-lymphocytes proliferating and attacking the recipient's tissues.

## Signs and symptoms

Graft-versus-host disease typically occurs 10–12 days after transfusion and is characterized by:
- Fever
- Skin rash and desquamation
- Diarrhoea
- Hepatitis
- Pancytopenia.

## Management

The disease is usually fatal. Treatment is supportive; there is no specific therapy.

## Prevention

Graft-versus-host disease is prevented by gamma irradiation of cellular blood components to stop the proliferation of transfused lymphocytes.

## Iron overload

### Cause

There are no physiological mechanisms to eliminate excess iron and thus transfusion-dependent patients can, over a long period of time, accumulate iron in the body resulting in haemosiderosis.

### Signs and symptoms

Excess iron deposits in tissues may result in organ failure, particularly of the heart and liver.

### Management and prevention

Iron-binding agents, such as desferrioxamine, are widely used to minimize the accumulation of iron in these patients. The aim is to keep serum ferritin levels at <2000 μg/litre (see Section 9: *General Medicine*).

## Immunosuppression

Blood transfusion alters the recipient's immune system in several ways and immunosuppression has been a concern in the following two areas:

1 That tumour recurrence rates may be increased: prospective clinical trials have not shown a difference in the prognosis for transfused versus non-transfused patients or for recipients of autologous, as opposed to homologous blood.

2 That transfusion increases the risk of postoperative infection by reducing the immune response: so far, most clinical trials have failed to prove that this occurs.

## 7.6  Massive or large volume blood transfusions

The term 'massive transfusion' can be defined as the replacement of blood loss equivalent to or greater than the patient's total blood volume with stored blood in less than 24 hours (70 ml/kg in adults, 80–90 ml/kg in children or infants: see Figure 2.5).

Massive (or large volume) transfusions generally arise as a result of acute haemorrhage in obstetric, surgical and trauma patients. See Sections 10, 12 and 13.

The initial management of major haemorrhage and hypovolaemia is to restore the blood volume as rapidly as possible in order to maintain tissue perfusion and oxygenation. This requires infusing the patient with large volumes of replacement fluids and blood until control of the haemorrhage can be achieved.

Morbidity and mortality tend to be high among such patients, not because of the large volumes infused but, in many cases, because of the initial trauma and the tissue and organ damage secondary to haemorrhage and hypovolaemia.

> **It is often the underlying cause and consequences of major haemorrhage that result in complications rather than the transfusion itself.**

However, the administration of large volumes of blood and intravenous fluids may itself give rise to a number of problems. These are summarized in Figure 7.5.

*Figure 7.5: Complications of massive or large volume transfusion*

### Complications of massive or large volume transfusion

- Acidosis
- Hyperkalaemia
- Citrate toxicity and hypocalcaemia
- Depletion of fibrinogen and coagulation factors
- Depletion of platelets
- Disseminated intravascular coagulation (DIC)
- Hypothermia
- Reduced 2,3 diphosphoglycerate (2,3 DPG)
- Microaggregates

## Acidosis

During blood storage, red cell metabolism generates acids which results in a small but significant reduction in its pH. If acidosis is present in a patient receiving a large volume transfusion, it is much more likely to be the result of inadequate treatment of hypovolaemia than due to the effects of transfusion.

### Management

Under normal circumstances, the body can easily neutralize this acid load from transfusion and the routine use of bicarbonate or other alkalizing agents, based on the number of units transfused, is unnecessary.

## Hyperkalaemia

The storage of blood will result in a small increase in extracellular potassium concentration, which will increase the longer it is stored. This rise is rarely of clinical significance, other than in neonatal exchange transfusions.

### Management

See Section 11: *Paediatrics & Neonatology* for neonatal exchange transfusion.

### Prevention

Use the freshest blood available in the blood bank and which is less than 7 days old.

## Citrate toxicity and hypocalcaemia

Citrate toxicity is a rare problem, but it is most likely to occur during the course of a large volume transfusion of whole blood. Citrate binds calcium

which reduces the body's ionized calcium level. Hypocalcaemia, particularly in combination with hypothermia and acidosis, can cause a reduction in cardiac output, bradycardia, and other dysrhythmias.

## Management

Following transfusion, the anticoagulant citrate is usually rapidly metabolized to bicarbonate. It is therefore unnecessary to attempt to neutralize the acid load of transfusion. There is very little citrate in red cell concentrates and red cell suspension.

The routine prophylactic use of calcium salts, such as calcium chloride, is not recommended. However, their use should be considered if there is clinical or biochemical evidence of a reduced ionized calcium.

# Depletion of fibrinogen and coagulation factors

Plasma undergoes progressive loss of coagulation factors during storage, particularly Factors V and VIII, unless stored at –25°C or colder. Red cell concentrates and plasma-reduced units lack coagulation factors which are found in the plasma component. In addition, dilution of clotting factors and platelets will occur following administration of large volumes of replacement fluids.

Massive or large volume transfusions can therefore result in disorders of coagulation.

## Management

In order to avoid the indiscriminate use of fresh frozen plasma and cryoprecipitate, use these products only when there is clinical or laboratory evidence that they are needed.

If there is prolongation of the **prothrombin time (PT or INR)**, give ABO-compatible fresh frozen plasma in a dose of 15 ml/kg.

If the **APTT** is also prolonged, heat-treated Factor VIII/fibrinogen is recommended in addition to the fresh frozen plasma. If none is available, give 10–15 units of ABO-compatible cryoprecipitate, which contains Factor VIII and fibrinogen.

# Depletion of platelets

Platelet function is rapidly lost during storage of blood and there is virtually no platelet function after 48 hours.

## Management

Platelet concentrates should only be given when:

- Patient shows clinical signs of microvascular bleeding: i.e. bleeding and oozing from mucous membranes, wounds, raw surfaces and catheter sites
- Patient's platelet count falls below 50 x 10$^9$/L.

Give sufficient platelet concentrates to stop the microvascular bleeding and to maintain an adequate platelet count.

**prothrombin time ratio (PTR)**: A test of the blood clotting system. Prolonged by deficiencies of coagulation factors VIII, X, V, II and fibrinogen. *See* INR.

**international normalized ratio (INR)**: Measures the anticoagulant effect of warfarin. Sometimes called the prothrombin time ratio (PTR).

**activated partial thromboplastin time (APTT)**: A test of the blood coagulation system. Prolonged by deficiency of coagulation factors XII, XI, IX, VIII, X, V, II and fibrinogen. Also referred to as partial thromboplastin time (kaolin) (PTTK).

Platelet transfusion should be considered in cases where the platelet count falls below 20 x $10^9$/L, even if there is no clinical evidence of bleeding, because there is a danger of hidden bleeding, such as into the brain tissue.

### Prevention
The prophylactic use of platelet concentrates in patients receiving large volume blood transfusions is not recommended.

## Disseminated intravascular coagulation
Disseminated intravascular coagulation (DIC) is the abnormal activation of the coagulation and fibrinolytic systems, resulting in the consumption of coagulation factors and platelets (see Section 9.11: *Acquired Bleeding and Clotting Disorders* and Section 10.3: *Major Obstetric Haemorrhage*).

DIC may develop during the course of a massive blood transfusion, although its cause is most likely to be related to the underlying reason for transfusion, such as hypovolaemic shock, trauma or obstetric complications, rather than the transfusion itself.

### Management
Treatment should be directed at correcting the underlying cause and at correction of the coagulation problems as they arise.

## Hypothermia
The rapid administration of blood or replacement fluids directly from the holding refrigerator can result in a significant reduction in body temperature. Hypothermia can result in various unwanted effects (see *Avoiding Hypothermia* in Section 12.3).

### Management
If there is evidence of hypothermia, every effort should be made to warm blood and intravenous fluids during large volume transfusions.

## Reduced 2,3 diphosphoglycerate (2,3 DPG)
The presence of 2,3 DPG in blood facilitates the release of oxygen from the haemoglobin molecule to the tissue. Levels of 2,3 DPG in stored blood are usually well maintained with modern anticoagulant additive solutions.

## Microaggregates
White cells and platelets can aggregate together in stored whole blood, forming microaggregates. During transfusion, particularly a massive transfusion, these microaggregates embolize to the lung and their presence there has been implicated in the development of adult respiratory distress syndrome (ARDS). However, ARDS following transfusion is most likely to be primarily caused by tissue damage from hypovolaemic shock.

### Management
Filters are available to remove microaggregates, but there is little evidence that their use prevents this syndrome. The use of buffy coat-depleted packed red cells will decrease the likelihood of ARDS.

# Part 2

# Transfusion in clinical practice

# 8

# Clinical decisions on transfusion

Part 2 focuses on clinical situations that may require the transfusion of whole blood or blood products, as follows:

Section 9     *General Medicine*

Section 10     *Obstetrics*

Section 11     *Paediatrics & Neonatology*

Section 12     *Surgery & Anaesthesia*

Section 13     *Acute Surgery & Trauma*

Section 14     *Burns*

Section 8 is a very brief section that introduces Part 2 and provides a simple guide to assessing and confirming the need for transfusion.

## Key points

1   **Used correctly, transfusion can be life-saving. Inappropriate use can endanger life.**

2   **The decision to transfuse blood or blood products should always be based on a careful assessment of clinical and laboratory indications that transfusion is necessary to save life or prevent significant morbidity.**

3   **Transfusion is only one element in the patient's management.**

4   **Prescribing decisions should be based on national guidelines on the clinical use of blood, taking individual patient needs into account. However, responsibility for the decision to transfuse ultimately rests with individual clinicians.**

## 8.1 Assessing the need for transfusion

The decision to transfuse blood or blood products should always be based on a careful assessment of clinical and laboratory indications that transfusion is necessary to save life or prevent significant morbidity.

Transfusion is only one element of the patient's management. Figure 8.1 summarizes the main factors in determining whether transfusion may be required in addition to supportive management and treatment of the underlying condition.

## 8.2 Confirming the need for transfusion

Prescribing decisions should be based on national guidelines on the clinical use of blood, taking individual patient needs into account. They should also be based on knowledge of local patterns of illness, the resources available for managing patients and the safety and availability of blood and intravenous replacement fluids. However, responsibility for the decision to transfuse ultimately rests with individual clinicians.

Figure 8.2 on p. 158 provides a simple checklist to assist you in confirming decisions about the need for transfusion.

*Figure 8.1: Assessing the need for transfusion*

## FACTORS DETERMINING THE NEED FOR TRANSFUSION

**Blood loss**
- External bleeding
- Internal bleeding – non-traumatic: e.g. peptic ulcer, varices, ectopic pregnancy, antepartum haemorrhage, ruptured uterus
- Internal bleeding – traumatic: chest, spleen, pelvis, femur
- Red cell destruction: e.g. malaria, sepsis, HIV

**Haemolysis**
For example:
- Malaria
- Sepsis
- DIC

**Cardiorespiratory state and tissue oxygenation**
- Pulse rate
- Blood pressure
- Respiratory rate
- Capillary refill
- Peripheral pulses
- Temperature of extremities
- Dyspnoea
- Cardiac failure
- Angina
- Conscious level
- Urine output

**Assessment of anaemia**
*Clinical*
- Tongue
- Palms
- Eyes
- Nails

*Laboratory*
- Haemoglobin or haematocrit

**Patient's tolerance of blood loss and/or anaemia**
- Age
- Other clinical conditions: e.g. pre-eclampsic toxaemia, renal failure, cardiorespiratory disease, chronic lung disease, acute infection, diabetes, treatment with beta-blockers

**Anticipated need for blood**
- Is surgery or anaesthesia anticipated?
- Is bleeding continuing, stopped or likely to recur?
- Is haemolysis continuing?

*Figure 8.2: Confirming the need for transfusion*

## PRESCRIBING BLOOD: A CHECKLIST FOR CLINICIANS

Before prescribing blood or blood products for a patient, ask yourself the following questions.

1   What improvement in the patient's clinical condition am I aiming to achieve?

2   Can I minimize blood loss to reduce this patient's need for transfusion?

3   Are there any other treatments I should give before making the decision to transfuse, such as intravenous replacement fluids and oxygen?

4   What are the specific clinical or laboratory indications for transfusion for this patient?

5   What are the risks of transmitting HIV, hepatitis, syphilis or other infectious agents through the blood products that are available for this patient?

6   Do the benefits of transfusion outweigh the risks for this particular patient?

7   What other options are there if no blood is available in time?

8   Will a trained person monitor this patient and respond immediately if any acute transfusion reactions occur?

9   Have I recorded my decision and reasons for transfusion on the patient's chart and the blood request form?

Finally, if in doubt, ask yourself the following question:

10   If this blood was for myself or my child, would I accept the transfusion in these circumstances?

# 9

# General medicine

## Key points

1   Patients with chronic anaemia may have few symptoms, but chronic anaemia increases the need for transfusion when the patient experiences sudden loss of red cells from bleeding or haemolysis or during pregnancy or childbirth.

2   Iron deficiency is the commonest cause of chronic anaemia. However, a patient's anaemia may have several causes: e.g. nutritional deficiency, malaria, HIV, parasitic infestation, haemoglobin disorders or malignancy.

3   Transfusion is rarely needed for chronic anaemia. Many transfusions are given that do not benefit the patient, could do harm and could have been avoided. Simple preventive measures and the use of oral iron replacement can greatly reduce the prevalence of iron deficiency anaemia and reduce the need for transfusion.

4   Treat suspected malaria as a matter of urgency. Starting treatment promptly may save the patient's life. In endemic malarial areas, there is a high risk of transmitting malaria by transfusion. It is therefore important to give the transfused patient routine treatment for malaria.

5   Provided the blood supply is safe, in β thalassaemia major, haemoglobin levels should be maintained at 10–12 g/dl by periodic small transfusions. Specific precautions against infections and iron overload should be used.

6   In cases of disseminated intravascular coagulation, rapid treatment or removal of the cause, together with supportive care, is essential. Transfusion may be required until the underlying cause has been dealt with.

## Introduction

This is the first of six sections focusing on clinical situations that may require transfusion of whole blood or any therapeutic substance prepared from whole blood.

You should already have studied Sections 1–8 and it is recommended that, before working through this section, you revise Section 3: *Anaemia* which covers the following topics.

3.1 Definitions

3.2 Measuring haemoglobin and haematocrit

3.3 Clinically important anaemia

3.4 Interpreting haemoglobin values

3.5 Causes of anaemia

3.6 Adaptation to anaemia

3.7 Anaemia due to acute blood loss

3.8 Anaemia due to chronic blood loss

3.9 Chronic anaemia due to other causes

3.10 Principles of the treatment of anaemia

3.11 Principles of the prevention of anaemia.

Section 9 is not intended to be a substitute for standard books on medicine and haematology, but aims to help you to:

■ Manage patients so as to avoid the need for transfusion, wherever possible

■ Know when transfusion is necessary.

## Learning outcomes

When you have completed this section, you should be able to:

1 Recognize the clinical features of chronic anaemia and its main causes.

2 Recognize the clinical features of acute anaemia that indicate that transfusion may be necessary.

3 Select the appropriate diagnostic tests from those that are available to you and know how and when to use them to help identify the presence of anaemia.

4 Decide whether and when transfusion is necessary, taking into account the risks associated with the blood products that are available.

5 Select the most appropriate blood product available and the correct dose regime.

## 9.1  Anaemia

A patient with anaemia may present with symptoms. Alternatively, the anaemia may be detected by, for example, a screening programme or during the investigation of some other condition.

The presence of anaemia indicates a nutritional deficiency and/or some pathological condition. Iron deficiency is by far the commonest cause of anaemia worldwide. It is the main, but not the only cause of anaemia in which the **red cell 'indices'** are all reduced and microscopic examination of the patient's blood film shows small red cells (**microcytosis**) often varying in size (**anisocytosis**) with reduced haemoglobin staining (**hypochromia**).

Anaemia requires investigation and further treatment. It is important to remember the following points.

1   Diagnosis and management should be based on knowledge of the epidemiology of anaemia and relevant conditions in the locality.

2   The approach to diagnosis and management should be planned to make the most effective possible use of the health care resources available and so help to make effective treatment available to the maximum number of individuals in need.

3   The type of anaemia is often a strong pointer to the underlying cause and also to the treatment required to correct the anaemia.

### Clinical features

The rate at which anaemia develops usually determines the severity of symptoms.

**Moderate** anaemia may cause no symptoms, especially when due to a chronic process. Nevertheless, it reduces the patient's reserves to adjust to an acute event such as haemorrhage, infection or childbirth.

**Severe** anaemia, whether acute or chronic, is an important factor in reducing the patient's tissue oxygen supply to critical levels. In this situation, urgent treatment is required and the need for transfusion should be assessed.

#### *Acute blood loss*

The clinical features of haemorrhage are determined by the volume and rate of blood loss and by the patient's capacity to make the compensatory responses described in Section 3.7: *Anaemia due to Acute Blood Loss.*

Following a haemorrhage, a fit person may show minimal signs and symptoms. A similar rate of blood loss may lead to decompensation and hypoxia in a patient who is elderly, has severe cardiovascular or respiratory disease or who is already anaemic when the haemorrhage occurs.

The clinical picture of acute blood loss can therefore range from nothing more than modest tachycardia to the full features of haemorrhagic shock (see Figure 9.1, Section 10: *Obstetrics* and Section 13: *Trauma & Acute Surgery).*

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**red cell indices**:
- Mean cell volume (MCV)
- Mean cell haemoglobin (MCH)
- Mean cell haemoglobin concentration (MCHC).

**microcytosis**: Red cells smaller than normal. A feature of iron deficiency anaemia.

**anisocytosis**: Abnormal degree of variation in the size of red cells observed in the blood film.

**hypochromia**: Reduced iron content in red cells, indicated by reduced staining of the red cell. A feature of iron deficiency anaemia.

**Major haemorrhage**

- Thirst
- Tachycardia
- Reduced blood pressure
- Decreased pulse pressure

- Cool, pale, sweaty skin
- Increased respiratory rate
- Reduced urine output
- Restlessness or confusion

### Chronic anaemia

Provided that the patient's compensatory mechanisms are effective, chronic anaemia may cause few clinical symptoms or signs until a very low haemoglobin concentration is reached. However, the clinical features of anaemia may become apparent at an earlier stage when there is:

- A limited capacity to mount a compensatory response, e.g. significant cardiovascular or respiratory disease
- An increase in demand for oxygen, e.g. infection, pain, fever or exercise
- A further reduction in the oxygen supply, e.g. blood loss or pneumonia.

### Acute-on-chronic anaemia

The term 'acute-on-chronic anaemia' is often used to describe a further sudden fall in haemoglobin concentration in a patient who is already chronically anaemic. This situation is often a clinical emergency, especially in young children, obstetrics and emergency surgery. Management may include the need for red cell transfusion (see Section 10: *Obstetrics*, Section 11: *Paediatrics & Neonatology* and Section 13: *Trauma & Acute Surgery*).

### Clinical assessment

Clinical assessment should determine the type of anaemia, its severity and the probable cause or causes. Figure 9.2 shows symptoms and signs that may be revealed by the history and physical examination.

### History

The patient's history may reveal features that are:

1 Due to anaemia.

2 Related to the underlying cause.

For example, a family history of anaemia, or a history that suggests the patient has been anaemic since childhood, should alert you to the possibility of a haemoglobinopathy (see Section 9.8). The patient's place of residence, diet, parity and obstetric history, history of bleeding, occupation, social habits and travel history may point to causes of anaemia such as nutritional deficiency, drugs, alcohol abuse, malaria or parasitic infection. Low socio-economic status is a strong predictor of nutritional anaemia.

### Physical examination

In the physical examination, look for:

*Figure 9.2: Clinical assessment of anaemia*

## HISTORY

**Non-specific symptoms of anaemia**

- Tiredness/loss of energy
- Light-headedness
- Shortness of breath
- Ankle swelling
- Headache
- Worsening of any pre-existing symptoms, such as angina

**History and symptoms relating to the underlying disorder**

- Nutritional deficiency: poor dietary history
- Pharmaceutical drug history
- Low socio-economic status
- Family history, ethnic origins (haemoglobinopathy)
- History suggesting a high risk of exposure to HIV infection
- Fever, nightsweats (malaria, other infections)
- History of malaria episodes; residence in or travel to malaria endemic area
- Obstetric/gynaecological history, menorrhagia or other vaginal bleeding, type of contraception
- Bleeding from urinary tract
- Bleeding gums, epistaxis, purpura (bone marrow failure)
- Gastrointestinal disturbance: melaena, upper GI bleeding, diarrhoea, weight loss, indigestion

## PHYSICAL EXAMINATION

**Signs of anaemia and clinical decompensation**

- Pale mucous membranes
- Rapid breathing
- Tachycardia
- Raised jugular venous pressure
- Heart murmurs
- Ankle oedema
- Postural hypotension

**Signs of the underlying disorder**

- Weight loss or underweight for height and age
- Angular stomatitis, koilonychia (iron deficiency)
- Jaundice (haemolysis)
- Purpura and bruising (bone marrow failure, platelet disorders)
- Enlarged lymph nodes, hepatosplenomegaly (infection, lympho-proliferative disease, HIV/AIDS)
- Lower leg ulcers (sickle cell anaemia)
- Skeletal deformities (thalassaemia)
- Neurological signs (vitamin $B_{12}$ deficiency)

1   Signs of anaemia and clinical decompensation.

2   Signs of the underlying cause.

Examination of the patient may reveal signs of malnutrition, angular stomatitis and koilonychia associated with iron deficiency, jaundice due to haemolysis, neurological abnormalities due to vitamin $B_{12}$ deficiency, fever and sweating accompanying malaria or bruises and haemorrhages suggesting a bleeding disorder.

---

**Remember that a patient may have several causes of anaemia, such as nutritional deficiency, HIV, malaria, parasitic infestation, haemoglobinopathy or malignancy.**

---

## Laboratory investigations

Once a clinical diagnosis of anaemia has been made, a full blood count, examination of the blood film and red cell indices will enable the cause to be determined in most cases (see Figure 9.3).

1   **Microcytic, hypochromic red cells** are features of both iron deficiency and thalassaemia. 'Pencil' cells (elliptical cells) are much more common in iron deficiency anaemia.

2   A blood film with **abnormal red cells**, varying widely in both size and shape, and especially target cells, suggests thalassaemia. Other features are misshapen microcytes, hypochromic **macrocytes** and red cell fragments, and basophilic stippling. Nucleated red cells are often present and, in a splenectomized patient, are numerous.

3   **Hypersegmented neutrophils** are a feature of vitamin $B_{12}$ and folate deficiency.

4   **Macrocytic red cells** can be due to the presence of rapid red cell production by the bone marrow, deficiency of $B_{12}$ or folate (a megaloblastic bone marrow), or reduced red cell production. They are also seen in liver disease.

5   **Normochromic, normocytic red cells** commonly result from chronic disorders or infection.

6   A **leucoerythroblastic film** (with abnormal red cells and white cells) suggests myelodysplasia or malignancy.

Figure 9.4 on p. 166 shows the causes of common red cell abnormalities associated with anaemia that may be observed in the blood film.

The main feature of severe iron deficiency is lowered red cell indices. The peripheral blood film shows faintly stained red cells, usually of more variable size and shape than normal. If a second deficiency (e.g. of folic acid) is also present, the film may additionally show some larger red cells (macrocytes). When there are two distinct populations of red cells, this is called a **dimorphic blood film**.

**macrocytosis**: Red cells larger than normal. A feature of the red cells in, for example, anaemia due to deficiency of folic acid, vitamin $B_{12}$.

**dimorphic blood film**: A blood film that shows both microcytic, hypochromic, red cells *and* macrocytic red cells, suggesting deficiency of iron and folate (or folate and vitamin $B_{12}$).

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Figure 9.3: Initial clinical assessment, laboratory investigation and management of anaemia

**Clinical assessment**

↓ ↓

History → ← Physical examination

↓

Determine haemoglobin/haematocrit

↓ ↓

Anaemic → → Not anaemic

↓

Identify other causes of presenting complaint

**Further initial investigations**

- Full blood count (Hb, Hct, blood film) + white cell count and other relevant indices
- Reticulocyte count
- Thick and thin blood film for parasites or rapid diagnostic test
- Faecal occult blood test

↓

Provisional diagnosis: iron deficiency anaemia

Diagnosis uncertain

↓

Treat cause of anaemia

Further investigations: see Figure 9.5

↓

Give course of oral iron, if indicated

↓

Check haemoglobin at 4–8 weeks

↓ ↓

Patient responding. Haemoglobin rising: reticulocytosis on blood film. Diagnosis probably correct.

Patient not responding: review diagnosis

Reassess diagnosis and see Figure 9.5 to confirm/identify cause & type of anaemia

↓

Is the patient taking the oral iron? → Yes

↓

Continue iron treatment for at least 3 months

No → Reinforce advice to take oral iron

| BLOOD FILM | RED CELL INDICES | CAUSE |
|---|---|---|
| Microcytic, hypochromic with abnormal red cells | Low MCV, MCH, MCHC | Acquired<br>■ Iron deficiency<br>■ Sideroblastic anaemia<br>■ Anaemia of chronic disorder<br><br>Congenital<br>■ Thalassaemia<br>■ Sideroblastic anaemia |
| Macrocytic, normochromic | Increased MCV | With megaloblastic marrow<br>■ Deficiency of vitamin $B_{12}$ or folic acid<br>With normoblastic marrow<br>■ Alcohol excess<br>■ Myelodysplasia |
| Macrocytic polychromasia | Increased MCV | Haemolytic anaemia |
| Normocytic, normochromic | Normal MCV, MCH, MCHC | ■ Chronic disorder<br>— Infection<br>— Malignancy<br>— Autoimmune disorders<br>■ Renal failure<br>■ Hypothyroidism<br>■ Hypopituitarism<br>■ Aplastic anaemia<br>■ Red cell aplasia<br>■ Marrow infiltration |
| Leucoerythroblastic | Indices may be abnormal due to early and numerous forms of red and white cells | ■ Myelodysplasia<br>■ Leukaemia<br>■ Metastatic cancer<br>■ Myelofibrosis<br>■ Severe infections |

**Note:** MCV is reliable only if calculated using a well-calibrated electronic blood cell counter

### Further investigations

Figure 9.5 shows the further investigations that may be required in order to distinguish iron and folate deficiency from other conditions which show similar characteristics, such as β thalassaemia. These include measures of the level of iron stores: e.g. the plasma ferritin level or plasma iron and total iron-binding capacity.

Figure 9.5: Further
laboratory investigations to
confirm/identify cause &
type of anaemia

## HYPOCHROMIC ANAEMIA: INVESTIGATION & DIFFERENTIAL DIAGNOSIS

| Investigation | Iron deficiency | Chronic inflammation or malignancy | Thalassaemia trait ($\alpha$ or $\beta$) |
|---|---|---|---|
| MCV } MCH } MCHC } | All reduced in relation to severity of anaemia | Normal or moderate reduction | All low in relation to severity of anaemia |
| Serum iron level | Reduced | Reduced | Normal |
| Total iron-binding capacity (TIBC) | Raised | Reduced | Normal |
| Serum ferritin | Reduced | Normal/raised | Normal |
| Bone marrow iron | Absent | Present | Present |
| Haemoglobin electrophoresis | Normal | Normal | Abnormal |
| Response to trial of oral iron treatment | Yes | No | No |

## MACROCYTIC ANAEMIA: INVESTIGATION AND DIFFERENTIAL DIAGNOSIS

Clinical and laboratory investigation should identify the probable cause (dietary deficiency, malabsorption, or another condition). If due to deficiency, measurement of plasma levels of vitamin $B_{12}$ and folate may be required.

**Dietary deficiency or malabsorption**
- Plasma levels $B_{12}$ and folate
- Autoantibody tests: intrinsic factor, gastric parietal cells

**Other causes of a macrocytic blood film, not all associated with anaemia**
- High reticulocyte count, for any reason
- Pregnancy
- Liver disease
- Alcohol excess
- Myelodysplastic conditions
- Hypothyroidism
- Response to folate/$B_{12}$

**Haemolytic anaemia: see pp. 175–177**

**Bone marrow failure: see pp. 184–188**

**reticulocytes**: Young red cells that still contain some RNA: show blue staining on blood film stained with "new methylene blue' with a Romanowsky counterstain. Indicate increased rate of red cell production by bone marrow.

Screening for G6PD deficiency or abnormal haemoglobin may be needed, especially in areas where these conditions are prevalent.

The physical findings, examination of the blood film, a sickle test and haemoglobin electrophoresis will detect most common types of inherited haemoglobinopathies.

The presence of **reticulocytes** (immature red cells) on the blood film indicates that there is rapid production of red cells. The absence of reticulocytes in an anaemic patient should prompt a search for bone marrow dysfunction due to infiltration, infection or primary failure or deficiency of haematinics.

## Management

The treatment of anaemia will vary according to the cause, rate of development and degree of compensation to the anaemia. This requires a detailed assessment of the individual patient. However, the principles of treatment of all anaemias have the following common features.

1 Treat the underlying cause of the anaemia and monitor the response.

2 If the patient has inadequate oxygenation of the tissues, optimize all the components of the oxygen delivery system to improve the oxygen supply to the tissues.

### *Treatment of chronic anaemia*

The principles of treatment of chronic anaemia are shown in Figure 9.6.

*Figure 9.6: Principles of treatment of chronic anaemia*

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**TREATMENT OF CHRONIC ANAEMIA**

1 Exclude the possibility of a haemoglobinopathy.

2 Correct any identified cause of blood loss
- Treat helminthic or other infections
- Deal with any local bleeding sources
- Stop anticoagulant treatment, if possible
- Stop drugs that are gastric mucosal irritants e.g. aspirin, non-steroidal anti-inflammatory drugs (NSAIDs)
- Stop anti-platelet drugs e.g. aspirin, NSAIDs.

3 Give oral iron (ferrous sulphate 200 mg three times per day for an adult; ferrous sulphate 15 mg/kg/day for a child). Continue this treatment for three months or one month after haemoglobin concentration has returned to normal. The haemoglobin level should rise by about 2 g/dl within about 3 weeks. If it does not, review the diagnosis and treatment.

4 Correct identified vitamin deficiencies with oral folic acid (5 mg daily) and vitamin $B_{12}$ (hydroxocobalamin) by injection.

5 Combined tablets of iron and folic acid are useful if there is deficiency of both. Other multi-component preparations for anaemia have no advantages and are often very expensive.

6 Treat malaria with effective antimalarial drugs, taking local resistance patterns into account. Give malaria prophylaxis only where there are specific indications.

7 If evidence of haemolysis, review the drug treatment and, if possible, stop drugs that might be the cause.

8 Check if the patient is on any marrow-suppressing drugs and stop, if possible.

---

### *Treatment of severe (decompensated) anaemia*

The mechanisms that compensate for anaemia are described in Section 3: *Anaemia.* They often enable patients to tolerate low haemoglobin

**decompensated anaemia**:
Severe clinically significant anaemia: anaemia with a haemoglobin level so low that oxygen transport is inadequate, even with all the normal compensatory responses operating.

concentrations if anaemia has developed slowly over weeks or months. However, if these compensatory mechanisms are unable to maintain the oxygen supply to the tissues, decompensation occurs and, without treatment, death may rapidly ensue.

Many factors can precipitate decompensation in an anaemic patient. In general, these are due to one or more of the following:

■ Heart or lung disease that limits the compensatory response

■ Increased demand for oxygen: e.g. infection, pain, fever or exercise

■ Acute reduction in the oxygen supply: e.g. blood loss, pneumonia.

The severely anaemic patient who is decompensated develops clinical features of inadequate tissue oxygen supply, despite supportive measures and treatment of the underlying cause of the anaemia. The clinical signs of hypoxia with severe anaemia may be very similar to those of other causes of respiratory distress, such as an acute infection or an asthmatic attack.

These other causes, if present, should be identified and treated, before deciding to transfuse. Figure 9.7 on p. 170 summarizes the clinical features and possible causes of decompensation.

Figure 9.8 shows the principles of treatment of severe (decompensated) anaemia. The management of specific causes of anaemia is considered in more detail later in this section.

*Figure 9.8: Principles of treatment of severe (decompensated) anaemia*

**TREATMENT OF SEVERE (DECOMPENSATED) ANAEMIA**

1 Treat bacterial chest infection aggressively.

2 Give oxygen by mask.

3 Correct fluid balance. If you give intravenous fluids, take care not to put patient into cardiac failure.

4 Decide whether red cell transfusion is (or may be) needed.

5 If you decide that transfusion is needed, make arrangements for blood to be available (see Section 6: *Clinical Transfusion Procedures*).

6 Use red cells, if available, rather than whole blood to minimize the volume and the oncotic effect of the infusion.

Once decompensation has occurred and the patient is hypoxic, the only effective treatment may be to raise the oxygen-carrying capacity of the blood by blood transfusion. However, the primary aim should be to treat the anaemia by other means before this point is reached.

Blood transfusion should only be considered when the anaemia is likely to cause or has already reduced the oxygen supply to a level that is inadequate for the patient's needs.

**Compensated anaemia**

An adult with well-compensated anaemia may have few or no symptoms or signs.

**Acute decompensation: precipitating factors**

**1 Increased demand for oxygen:**

- Infection
- Pain
- Fever
- Exercise

**2 Reduction in oxygen supply**

- Acute blood loss/haemolysis
- Pneumonia

**Decompensated anaemia**

The patient may rapidly become extremely ill, showing signs of decompensation if, for example, a fever, infection, or further drop in haemoglobin level occurs.

**Signs of acute decompensation**

- Mental status changes
- Diminished peripheral pulses
- Congestive cardiac failure
- Hepatomegaly
- Poor peripheral perfusion (capillary refill greater than 2 seconds)

A patient with these clinical signs needs urgent treatment as there is a high risk of death due to insufficient oxygen carrying-capacity

### Transfusion

In some patients with severe or life-threatening anaemia, red cell transfusion may be an essential first line of treatment. But:

**Transfusion is rarely needed for patients with chronic anaemia. Many transfusions are given that:**

- **Do not give the patient any benefit and may do harm**
- **Could have been avoided by rapid and effective treatment not involving transfusion.**

Figure 9.9 shows the principles of transfusion for patients with severe decompensated anaemia.

*Figure 9.9: Principles of transfusion for patients with severe (decompensated) anaemia*

---

### TRANSFUSION IN SEVERE (DECOMPENSATED) ANAEMIA

1 **Do not transfuse more than necessary. If one unit of red cells is enough to correct symptoms, do not give two units.**

   It is often taught that there is no case for giving a single unit transfusion. However, there are situations when a single unit transfusion may be appropriate. Remember that:
   - The aim is to give the patient *sufficient haemoglobin to relieve hypoxia*
   - The dose should be matched to the patient's size and blood volume
   - The haemoglobin content of a 450 ml unit of blood may vary from 45 g to 75 g.

2 Patients with severe anaemia may be precipitated into cardiac failure by infusion of blood or other fluids. If transfusion is necessary, give one unit, preferably of red cell concentrate, over 2 to 4 hours and give a rapid acting diuretic (e.g. frusemide, 40 mg IM).

3 Reassess the patient and, if symptoms of severe anaemia persist, give a further 1–2 units.

4 It is not necessary to restore the haemoglobin concentration to normal levels. Raise it enough to relieve the clinical condition.

---

## When the patient leaves hospital

1 Once acute problems have been treated and the cause of anaemia determined, give the patient clear instructions on the dose and length of treatment required. For iron deficiency, oral iron (ferrous sulphate 200 mg three times per day) should be given for three months to restore iron stores. A combined iron–folate preparation should be prescribed if there is suspicion of folate deficiency.

   Encourage patients to continue the treatment for the whole course, even if symptoms of anaemia resolve.

   Give advice relevant to the patient's situation and diagnosis on how to prevent further episodes of anaemia.

2 If possible, see the patient again after 1–2 months. Check that the clinical condition has improved and that the haemoglobin level is rising.

3 If the patient is not responding, check:
   - Is the patient taking the treatment?
   - Is the diagnosis correct?

4 Some adult patients may only tolerate half the standard dose of iron (i.e. ferrous sulphate 100 mg three times a day by mouth).

## 9.2 Deficiency of haematinics

Nutritional deficiency is the commonest cause of iron deficiency. Other major causes are gastrointestinal blood loss and menstrual losses in women (see Section 3: *Anaemia*). Hookworm is the most frequent specific cause of gastrointestinal blood loss worldwide. Other helminthic infections associated with blood loss include *Schistosoma mansoni* and *japonicum* (bilharziasis) and severe *Trichuris trichura* infection (threadworm). Iron deficiency due to blood loss can also be caused by gastrointestinal lesions such as peptic ulcers, hiatus hernia, malignant disease and haemorrhoids (see Figure 3.7 on p. 46).

Malabsorption can contribute to iron deficiency, but is usually not the sole cause.

For anaemia in pregnancy, see Section 10: *Obstetrics*.

### Clinical features
In addition to the clinical features common to all anaemias, iron deficiency may specifically be associated with:

- Koilonychia
- Angular stomatitis
- Glossitis.

### Laboratory investigations
See Figures 9.3, 9.4 and 9.5. Iron deficiency is characterized by a microcytic hypochromic anaemia on the peripheral blood film. Indirect measures of iron status such as plasma iron and transferrin saturation lack specificity.

Plasma ferritin is useful in the detection of iron deficiency; concentrations below 12 mg/L are indicative of absent iron stores. In the presence of infection, a higher ferritin level may occur (up to 50 mg/L) in iron deficiency.

Iron deficiency is the only condition in which there is microcytic, hypochromic anaemia with reduced iron stores in the marrow. Staining bone marrow for iron is a very useful test.

### Management
The principles of the management of iron deficiency are as follows.

1 Replace iron stores.

2 Remove or treat the cause of anaemia.

The diagnosis of iron deficiency can be confirmed by the response to iron: e.g. ferrous sulphate 200 mg three times a day. This consists of a rise in reticulocyte count beginning on day 3–5 and peaking at day 8–10, and a rise in haemoglobin at the rate of 0.5–1.0 g/dl/week. This maximal response will occur if the underlying cause of iron deficiency has been identified and treated.

Between 10% to 20% of patients are unable to take the standard dose of iron because of gastrointestinal side-effects. However, many of these patients will manage to take a smaller dose. There are many different iron

preparations, but simple dose reduction seems to be as effective for most patients who do not tolerate a full dose.

Iron tablets should be continued for at least 3 months after the haemoglobin becomes normal in order to replenish the iron stores. Iron preparations for intramuscular or intravenous administration have not been advised in many countries, because of concern about adverse reactions. Newer preparations may be safer and are used by some clinicians.

### Transfusion

Red cell transfusion is rarely indicated in the management of iron deficiency, although it may need to be considered for patients with severe anaemia and signs of inadequate oxygenation.

## Vitamin B$_{12}$ and folate deficiency

Both B$_{12}$ and folate are needed for DNA synthesis. Deficiency therefore affects all rapidly dividing cells of the body, including the bone marrow. Insufficiency of either vitamin B$_{12}$, folic acid or both causes characteristic changes in the bone marrow, which are described as **megaloblastic**, and in the red cells, which are macrocytic.

**megaloblasts**: Precursors of abnormal red cells. Usually due to deficiency of vitamin B$_{12}$ and/or folate and develop into macrocytic red cells (enlarged red cells).

Leafy vegetables are rich sources of folate but this vitamin is easily destroyed by boiling them for 15 minutes. A lack of dietary folate combined with prolonged cooking of vegetables means that, in developing countries, there is often insufficient dietary folate. Clinical deficiency may only become apparent when extra demands are placed upon folate stores, such as:

- Pregnancy
- Prematurity
- Increased turnover of red cells (e.g. haemoglobinopathies, haemolytic anaemia, malaria).

Animal protein is the major dietary source of vitamin B$_{12}$ which requires intrinsic factor for its absorption across the distal ileum. Deficiency of vitamin B$_{12}$ is usually due to lack of absorption rather than dietary insufficiency. Common causes therefore include:

- Gastric atrophy or resection
- Specific lack of intrinsic factor
- Abnormalities of the small bowel, particularly the terminal ileum.

In contrast, folate deficiency is usually due to inadequate dietary folate.

### Clinical features

In addition to general features of anaemia, neurological symptoms such as ataxia, 'pins and needles' and 'burning feet' may occur in vitamin B$_{12}$ deficiency, but are not a feature of isolated folate deficiency.

Glossitis, anorexia and weight loss are features of both B$_{12}$ and folate deficiency.

### Laboratory investigations

See Figure 9.5.

Vitamin $B_{12}$ and folate deficiency are indistinguishable on the peripheral blood film. Both show macrocytes with an increased mean cell volume (MCV), red cell fragmentation and hypersegmented neutrophils. The reticulocyte count is low. Because $B_{12}$ and folate are needed for DNA synthesis by all cells, severe deficiencies are often associated with a reduction in white cells and platelets (pancytopenia).

In most cases, the diagnosis is obvious from the blood film. In difficult cases, bone marrow examination is confirmatory. Other tests which may be useful include red cell folate assays and tests of $B_{12}$ absorption (Schilling test). Investigations of the gastrointestinal tract may be needed if $B_{12}$ deficiency is suspected.

## Management
The recommended doses of vitamin $B_{12}$ and folic acid are as follows.

### Vitamin $B_{12}$
- 1 mg IM twice weekly for 3 weeks
- Then 1 mg IM every 3 months for life.

### Folic acid
- 5 mg by mouth daily for 3 months
- A higher dose of 5 mg 3 times per day may be needed if malabsorption occurs.

The underlying cause of the deficiency should be treated, if possible. If this is not possible (e.g. folate deficiency in sickle cell disease or hereditary spherocytosis), lifelong folate supplements (5 mg every 1–7 days) will be needed.

---

**Folate treatment of a patient who is also deficient in vitamin $B_{12}$ may precipitate sub-acute combined degeneration of the spinal cord. If there is reason to suspect the possibility of combined $B_{12}$ and folate deficiency, give both folate and $B_{12}$ and, if possible, identify the deficiency by further investigation before starting treatment.**

---

## Transfusion
Because anaemia in these deficiencies occurs gradually over months or years and therapy results in a rise in haemoglobin within a few weeks, patients generally tolerate the condition well. Transfusion is therefore rarely indicated.

Blood transfusion in megaloblastic anaemia can be dangerous because poor myocardial function may make patients likely to develop heart failure.

### Normocytic, normochromic anaemia
The main causes of normocytic, normochromic anaemia, with typical blood film features and red cell indices, are shown in Figure 9.4. The term applies to a diverse group of conditions: transfusion may be required in managing some of them. See Section 9.7: *Bone Marrow Failure*.

## 9.3 Haemolytic anaemias

Haemolytic anaemias are due to abnormalities affecting:

1 Red cell haemoglobin: e.g.
   - Haemoglobinopathies, such as sickle cell disease
   - Enzymopathies, such as glucose-6-phosphate dehydrogenase (G6PD) deficiency.

2 Red cell membrane: e.g.
   - Spherocytosis
   - Elliptocytosis
   - Immune haemolysis
     — Associated with lymphoma
     — Due to autoimmune disorders: e.g. systemic lupus erythematosus
     — Often induced by drugs
     — Idiopathic.

3 Factors extrinsic to the red cells: e.g.
   - Disseminated intravascular coagulation (DIC)
   - Hypersplenism
   - Malaria and other infections
   - Pharmaceutical drugs
   - Other toxins.

### Clinical features

In addition to the general features of anaemia, haemolytic anaemias may be associated with jaundice and signs of the underlying disorder. For example, autoimmune haemolysis may be associated with lymphomas and connective tissue diseases, and DIC with septicaemia or eclampsia.

Chronic haemolytic anaemias can also be complicated by gallstones, leg ulceration and parvovirus-induced aplastic crisis. A family history of haemolytic anaemia may suggest hereditary membrane defects or haemoglobinopathies.

The main clinical features and complications of haemolytic anaemia are shown in Figure 9.10 on p. 176. They include:
   - Anaemia
   - Jaundice
   - Gallstones
   - Features of the underlying cause.

### Laboratory investigations

A falling haemoglobin accompanied by a reticulocytosis and raised unconjugated bilirubin are hallmarks of haemolytic anaemia. The blood film shows reticulocytes and, in severe cases, nucleated red cells.

*Figure 9.10: Clinical features of haemolytic anaemia*
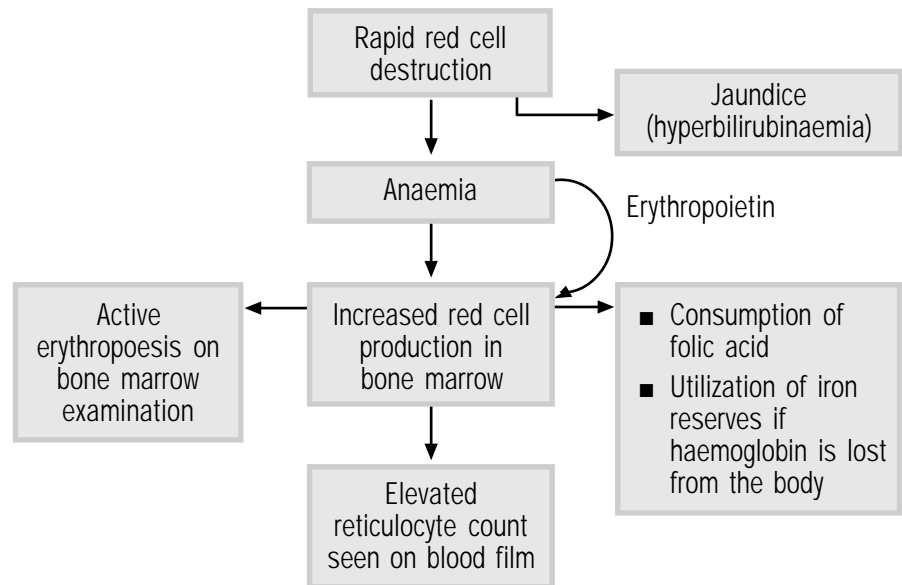
Other features will provide clues to the underlying cause of haemolysis, such as:

- Red cell agglutination in immune haemolysis,
- Helmet cells and red cell ghosts in G6PD deficiency or chemical toxins
- Spherocytes in hereditary spherocytosis
- Red cell fragmentation in DIC.

When appropriate, additional investigations help to confirm the diagnosis, including:

- Direct antiglobulin test (Coombs' test)
- G6PD screen
- Haemoglobin electrophoresis
- Blood cultures.

## Management

Many types of haemolytic anaemia do not reduce haemoglobin to critical levels. The haemolysis will often stop altogether if the underlying cause is treated: e.g.

- Give steroid therapy for autoimmune haemolysis
- Treat infection in G6PD deficiency and DIC
- Stop drugs causing haemolysis.

It is important to ensure that a patient with haemolytic anaemia has adequate stores of folic acid. Give 5 mg/day until the haemoglobin concentration returns to normal. A patient with persistent haemolysis will need long-term, regular folic acid (5 mg every 1–7 days).

## Transfusion

The criteria for transfusion are the same as those for other forms of severe anaemia: i.e. transfusion should be considered only if there is severe and potentially life-threatening anaemia causing haemolysis.

Patients with immune haemolytic anaemias often present very difficult problems in finding compatible blood due to the presence of antibodies and/or complement bound to the patient's red cells. These are detected by the direct antiglobulin test (DAT). These red cell-bound antibodies interfere with the normal laboratory techniques for typing the patient's red cells and for identifying antibodies in the patient's serum that could haemolyse red cells that are transfused.

It is sometimes possible to use special techniques to remove the antibodies bound to the patient's red cells (called antibody elution) so that the type of antibody can be determined.

If the laboratory is unable to do these special tests, the only option may be to test all available ABO and Rh D compatible units of blood for compatibility with the patient and to select those that appear to react least strongly.

Transfusion for immune haemolysis should be restricted to patients with potentially life-threatening anaemia as the transfused red cells may themselves be haemolysed, giving only very transient benefit, and transfusion may worsen the destruction of the patient's own red cells.

## 9.4 Malaria

Human malaria is caused by four species of malaria parasites:

■ *Plasmodium falciparum*
■ *Plasmodium vivax*
■ *Plasmodium malariae*
■ *Plasmodium ovale*.

*P. falciparum* and *P. vivax* account for the vast majority of cases and occur in different proportions in different countries. *P. falciparum* is the dominant species in Africa, South-East Asia and Oceania. *Falciparum* malaria causes severe disease and death if not recognized and treated early.

There are about 300 million cases of malaria each year, with at least one million fatalities. In the symptomatic phase, the parasites grow in the red cells and eventually rupture them, causing haemolysis. Malaria, often combined with other conditions, is one of the major causes of chronic and acute anaemia.

In Africa, Asia and Latin America, efforts to eradicate malaria have largely failed. Most malaria infections seen in developed countries have been acquired in these continents. Methods of controlling transmission (larviciding, spraying houses with residual insecticides, insecticide-treated bednets) have to be used continually. Insecticides become less effective as resistance develops. Candidate vaccines have so far been ineffective in field trials.

**Severe anaemia due to malaria is a significant cause of mortality in children and is the commonest reason for paediatric transfusion in many endemic areas (see Section 11: *Paediatrics & Neonatology*).**

In areas where malaria transmission is very high, there is a significant mortality in children under the age of 5. Because they receive many infected bites each year, survivors develop malarial immunity by the age of 5–10 years, provided that they are not affected by other conditions that impair immunity, such as infections or malnutrition. Pregnant women and visitors (of any age) from non-endemic areas are also at high risk of malaria.

In contrast, where there is low-level malaria transmission, such as in South-East Asia, the population does not have enough exposure to infected bites to develop useful immunity.

In all *P. falciparum* endemic areas, cerebral malaria is a serious cause of mortality. Individuals who return to endemic areas after a period without exposure are also likely to have lost their immunity and be at risk. Travellers who return from an endemic area to a non-malarious country may have undiagnosed *falciparum* malaria.

## Clinical features

Malaria presents as a non-specific acute febrile illness and cannot be reliably distinguished from many other causes of fever on clinical grounds. Typical symptoms include:

- Fever
- Headache
- Myalgia
- Chills
- Rigors
- Sweating.

The diagnosis and treatment of malaria is a matter of urgency since one species in particular, *P. falciparum*, may rapidly lead to death.

The differential diagnosis must consider other infections and causes of fever. The clinical manifestation of malaria may be modified by partial immunity acquired by previous infection or sub-curative doses of antimalarial drugs. Since fever is often irregular or intermittent, history of fever over the last 48 hours is important. Anaemia, splenomegaly, jaundice and hypoglycaemia occur frequently. Diarrhoea and cough may occur.

*P. falciparum* is the species responsible for the severe complications of malaria but, unlike *P. vivax* and *P. ovale*, it is not associated with relapses over some years. Cerebral malaria is the most important lethal complication of *P. falciparum* malaria and only occurs in non-immune people.

Malaria in pregnancy is more severe and is dangerous for mother and fetus. Partially immune pregnant women, especially primagravidae, are also susceptible to severe anaemia due to malaria.

## Laboratory investigations

The following laboratory investigations should be requested:

1. Microscopy of a thick and thin blood film
   - A thick blood film is more sensitive in detecting parasites and should always be done and read
   - A thin blood film is usually read to help to identify the parasite species.

2   Dipstick antigen test, if available: e.g. ParasightF test (*falciparum* malaria only), ICT test (*falciparum* and *vivax* malaria).

These tests are easy to use and are useful where microscopy is not available. The tests have high sensitivity and specificity and positive/negative predictive values for falciparum malaria when compared to microscopy, but the ICT test performs less well for diagnosing *vivax* malaria.

*P. falciparum* infection commonly causes haemolytic anaemia and mild thrombocytopenia. In severe cases, especially in non-immune subjects with >10% of red cells parasitized, there may be raised urea and creatinine indicative of renal failure.

Hypoglycaemia often occurs during quinine treatment, but may also occur in untreated malaria.

## Management

The management of malaria depends on the prompt recognition and treatment of the infection and any associated complications as death can occur within 48 hours in non-immune individuals (see Figure 9.11). Because of the variable resistance patterns of malaria worldwide, the treatment regime must be one that is known to be efficacious for the local strains of malaria.

**When malaria is suspected, treat the patient as a matter of urgency. If laboratory results are likely to be delayed, do *not* wait for them. Start treatment without delay on the basis of the clinical assessment. This may save the patient's life.**

The correction of dehydration and hypoglycaemia may be life-saving, but care must be taken not to precipitate pulmonary oedema by causing fluid overload.

Serious complications may need specific treatments, such as:

- Transfusion or exchange transfusion to correct life-threatening anaemia
- Haemofiltration or dialysis for renal failure
- Anticonvulsants for fits.

The prevention of malaria should be advocated for those at special risk, such as sickle cell patients and non-immune travellers to endemic areas. Preventive measures include the avoidance of bites by the use of repellants and insecticide-treated bednets, and appropriate malaria prophylaxis.

## Transfusion

Anaemia due to malaria is multifactorial and may be superimposed on other causes of anaemia. This can lead to a severe, life-threatening fall in haemoglobin due to haemolysis.

The clinical situations in which transfusions are often prescribed in malaria are different in adults and in children (see Figures 9.11, 10.3 and 11.7).

*Figure 9.11: Guidelines on the general clinical management of malaria*

| CLINICAL FEATURES OF SEVERE *FALCIPARUM* MALARIA | DIAGNOSIS |
|---|---|
| **May occur alone, or more commonly, in combination in same patient**<br><br>■ Cerebral malaria, defined as unrousable coma not attributable to any other cause<br><br>■ Generalized convulsions<br><br>■ Severe normocytic anaemia<br><br>■ Hypoglycaemia<br><br>■ Metabolic acidosis with respiratory distress<br><br>■ Fluid and electrolyte disturbances<br><br>■ Acute renal failure<br><br>■ Acute pulmonary oedema and adult respiratory distress syndrome (ARDS)<br><br>■ Circulatory collapse, shock, septicaemia ('algid malaria')<br><br>■ Abnormal bleeding<br><br>■ Jaundice<br><br>■ Haemoglobinuria<br><br>■ High fever<br><br>■ Hyperparasitaemia<br><br>A bad prognosis is indicated by confusion or drowsiness, with extreme weakness (prostration) | ■ High index of suspicion<br><br>■ Travel history indicative of exposure in endemic area or possible infection through transfusion or injection<br><br>■ Examination of thin and preferably thick films of peripheral blood by microscopy<br><br>■ Dipstick antigen test, if available: e.g.<br> — ParasightF test (*falciparum* malaria only)<br> — ICT test (*falciparum* and *vivax* malaria)<br><br>■ High parasite density in non-immune people indicates severe disease, but severe malaria can develop even with low parasitaemia; very rarely, blood film may be negative<br><br>■ Repeat blood count and blood film every 4–6 hours |

| MANAGEMENT | TRANSFUSION |
|---|---|
| 1 Promptly treat infection and any associated complications, following local treatment regimes<br><br>2 Where index of suspicion, treat urgently on basis of clinical assessment alone, if delays in laboratory investigation likely.<br><br>3 Correct dehydration and hypoglycaemia: avoid precipitating pulmonary oedema with fluid overload.<br><br>4 Specific treatments for serious complications:<br>■ Transfusion to correct life-threatening anaemia<br>■ Haemofiltration or dialysis for renal failure<br>■ Anticonvulsants for fits. | **Adults, including pregnant women**<br>Consider transfusion if haemoglobin <7 g/dl (see Figure 10.3 for transfusion in chronic anaemia in pregnancy)<br><br>**Children**<br>■ Transfuse if haemoglobin <4 g/dl<br>■ Transfuse if haemoglobin 4–6 g/dl and clinical features of:<br> — Hypoxia<br>  — Acidosis<br>  — Impaired consciousness<br> — Hyperparasitaemia (>20%) |

| PREVENTION | |
|---|---|
| ■ Early diagnosis and treatment may prevent the progression of uncomplicated malaria to severe disease and death. In children, progression of disease can be very rapid<br><br>■ Chemoprophylaxis | ■ All measures which reduce risk of inoculation: e.g. insecticide-treated bednets, indoor residual spraying, larviciding, house-screening |

> **In endemic malarial areas, there is a high risk of transmitting malaria by transfusion. It is important to give the transfused patient routine treatment for malaria.**

Adults with severe anaemia due to *falciparum* malaria are likely to require a blood transfusion if the haemoglobin falls to a level where there are clinical features of hypoxia. See Figure 10.3 for indications for transfusion in chronic anaemia in pregnancy.

The haemoglobin level (or haematocrit), together with the clinical features, should guide the decision to transfuse. Typically, transfusion would be indicated at a haemoglobin concentration of 5 g/dl or at 7 g/dl in pregnancy or in the presence of other complicating conditions.

See Section 11.2: *The Management of Paediatric Anaemia* for indications for transfusion in children with severe anaemia due to malaria.

## 9.5  HIV/AIDS

WHO estimates that in the year 2000 there will be at least 30 million people infected with HIV and 5–6 million with AIDS.

Because of the immune suppression that accompanies HIV, many patients have other microbial infections affecting all systems and producing multiple signs and symptoms. These diseases are often caused by organisms that rarely infect persons with normal immunity.

### Anaemia in HIV and AIDS
HIV infection is associated with anaemia due to several causes:

- Normochromic, normocytic anaemia of chronic disease
- Direct suppression of the bone marrow by the virus itself
- Myelodysplasia
- Haemolytic anaemia
- Parvovirus-induced suppression of red cell production
- Bleeding due to thrombocytopenia
- Zidovudine and stavudine-induced megaloblastic changes
- Opportunistic infections infiltrating the bone marrow: e.g. tuberculosis, leishmaniasis, fungi
- Associated malignant diseases: e.g. lymphoma, Kaposi sarcoma.

### Clinical classification of HIV/AIDS
Figure 9.12 on p. 182 summarizes the clinical features and classification of HIV/AIDS.

| **Group I**<br>Initial infection | Symptomatic (e.g. mononucleosis-like syndrome, mild meningocephalitis) as asymptomatic seroconversion |
|---|---|
| **Group II**<br>Chronic asymptomatic infection | Normal tests, but may have anaemia, neutropenia, thrombocytopenia, low CD4 lymphocytes and lymphopenia, hypergammaglobulinaemia |
| **Group III**<br>Persistent generalized lymphadenopathy | Laboratory test abnormalities as in Group II may or may not be present |
| **Group IV**<br>Clinical AIDS and other diseases | 1 Constitutional disease: fever, weight loss, diarrhoea<br><br>2 Neurological disease: either central (e.g. dementia or myelopathy) or peripheral neuropathies<br><br>3 Secondary infectious disease: e.g. *Pneumocystis carinii*, toxoplasmosis, *Cryptococcus*, cryptosporidiosis, atypical *Mycobacteria*, herpes simplex or zoster, oral hairy leucoplakia, histoplasmosis, candidiasis, cytomegalovirus, *Salmonella*<br><br>4 Secondary cancers: e.g. Kaposi sarcoma, non-Hodgkin's lymphoma, squamous carcinoma of the mouth or rectum<br><br>5 Other conditions: clinical problems related to HIV and decreased cellular immunity not included above |

## Management of anaemia in HIV and AIDS

The management of anaemia in HIV infection is based on treating associated conditions. Patients who are HIV positive have good mid-term survival prospects and deserve the same treatment as others to extend and improve their quality of life.

Around 80% of AIDS patients will have a haemoglobin level less than 10 g/dl. HIV has direct effects on the bone marrow that may lead to anaemia and thrombocytopenia, even though the marrow remains cellular. Drugs such as zidovudine (AZT) and combination chemotherapy also suppress red cell production: falling haemoglobin may limit the doses that can be given.

Drug-induced anaemia may respond to changes in drug combinations. Erythropoietin may also improve the haemoglobin level, but is very expensive.

## Transfusion

Blood transfusion may be needed when anaemia is severe and other measures have failed. For the patient with HIV who is suffering from severe symptomatic anaemia, the decision about transfusion should be made

using the same criteria as for any other patient. The patient should be transfused with blood that meets national criteria for blood safety, including screening for transfusion-transmissible infections. It should be remembered that in some areas, transfusion of blood products has been an important *cause* of HIV infection.

## 9.6  Glucose-6-phosphate dehydrogenase (G6PD) deficiency

Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme required for normal red cell metabolism. Deficiency affects about 200 million people worldwide, mainly males, especially in parts of Africa and South-East Asia.

### Clinical features
G6PD deficiency is commonly asymptomatic and can cause jaundice and anaemia precipitated by:

- Infection
- Drugs
- Chemicals (see Figure 9.13).

*Figure 9.13: Drugs and chemicals that may provoke haemolysis*

| May cause clinically significant haemolysis | No significant haemolysis under normal conditions |
|---|---|
| Antimalarials | |
| ■ Pamaquine (plasmoquine) | ■ Chloroquine |
| ■ Pantaquine | ■ Quinine |
| ■ Primaquine | ■ Quinacrine |
| ■ Quinocide | |
| Antipyretics and analgesics | Acetylsalicylic acid |
| Sulfonamides | |
| ■ Cotrimoxazole | |
| ■ Sulphanilimide | |
| Sulfones | |
| ■ Dapsone | |
| ■ Sulphasalazine | |
| Others | |
| ■ Fava beans | ■ Ascorbic acid |
| ■ Nalidixic acid | ■ Chloramphenicol |
| ■ Napthalene (mothballs) | ■ Procaine amide |
| | ■ Probenecid |
| | ■ Pyrimethamine |

Many of the drugs listed in Figure 9.13 can be prescribed in all but the most severely deficient patients. Failure to give the drug may be more hazardous than the haemolysis (often mild) that may be caused.

G6PD deficiency is also a common cause of neonatal jaundice.

The form of G6PD deficiency which occurs around the Mediterranean basin can be very severe and may be provoked by ingestion of fava beans. It can cause massive haemolysis and may lead to:

- Marked anaemia
- Red urine due to haemoglobinuria
- Occasionally renal failure.

### Laboratory investigations

The blood count and film are normal in steady state but, during a haemolytic crisis, red cell fragmentation with helmet cells becomes apparent. Heinz bodies (denatured haemoglobin) may be seen in a reticulocyte preparation. G6PD screening tests (e.g. methaemoglobin reductase) or assays are needed to make a definitive diagnosis.

### Management

This is a self-limiting condition and haemolysis will stop once the cells which are most deficient in G6PD have been destroyed. It is important to remove or treat any identified cause.

### Transfusion

Transfusion is not required in most cases of G6PD deficiency. However, transfusion may be life-saving in severe haemolysis when the haemoglobin continues to fall rapidly.

Exchange transfusions are indicated for neonates who are at risk of kernicterus and are unresponsive to phototherapy (see Section 11.6: *Neonatal Transfusion*).

## 9.7  Bone marrow failure

Bone marrow failure is present when the bone marrow is unable to produce adequate cells to maintain normal counts in the peripheral blood. It usually manifests as pancytopenia – reduced levels of two or three of the cellular elements of blood (red cells, white cells, platelets). Figure 9.14 shows the main causes of bone marrow failure or suppression.

### Clinical features

Anaemia, infection and bleeding depend on the degree to which the production of red cells, white cells and platelets respectively has been reduced.

### Laboratory investigations

In addition to the changes in the peripheral blood described above, an examination of the bone marrow morphology and histology will usually enable a definitive diagnosis to be made.

## CAUSES OF BONE MARROW FAILURE OR SUPPRESSION

- Chemotherapy for malignant disease
- Malignant infiltration of the marrow
- Infections
  — Tuberculosis
  — Typhoid
  — Viruses (hepatitis, human parvovirus B19, HIV)
- Myelodysplasic conditions (cause unknown): a group of conditions, usually progressive and fatal, including:
  — Myelofibrosis
  — Chronic myeloid leukaemia
- Aplastic anaemia of unknown cause
- Toxic effects of drugs and chemicals
- Effect of ionizing radiation

## Management

The principles of management of bone marrow failure or suppression are summarized in Figure 9.15 and an overview is provided in Figure 9.16.

## MANAGEMENT OF BONE MARROW FAILURE OR SUPPRESSION

1. Treat infection.
2. Maintain fluid balance.
3. Give supportive treatment: e.g. nutrition, pain control.
4. Stop potentially toxic drug treatments.
5. Ensure good nutrition.
6. Treat the underlying condition.

   The management of malignant haematological disorders requires:
   - Treatment by clinicians familiar with current chemotherapy regimes
   - Treatment in an environment with facilities for:
     — Diagnosis
     — Chemotherapy
     — Transfusion support
     — Management of the complications of chemotherapy.

## Transfusion of patients with bone marrow failure or suppression due to chemotherapy

The treatment of malignant haematological disease by chemotherapy commonly causes bone marrow suppression that requires transfusion support with red cells and platelets.

*Figure 9.16: Overview of bone marrow failure and suppression*

**Possible causes**
- Drugs
- Poisons
- Infection
- Malignancy
- Unknown

**History**
Exposure to:
- Toxic drugs
- Environmental chemicals
- Infection
- Radiation

Bone marrow failure with reduced production of:
- Red cells
- White cells
- Platelets

**Physical examination**
- Anaemia
- Bruising
- Bleeding
- Fever
- Enlarged lymph glands
- Splenomegaly

Symptoms due to anaemia or thrombocytopenia and infection

- Anaemia
- Bleeding
- Infection

**Laboratory investigations**
Full blood count and film may show:
- Anaemia
- Reduced or abnormal white cells
- Reduced platelets

Bone marrow examination may show features of:
- Leukaemia
- Lymphoma
- Aplasia or hypoplasia
- Malignant infiltration
- Infective infiltration

**Further investigation**
Requires specialist advice and facilities

**General management**
1 Treat infection
2 Maintain fluid balance
3 Analgesics for pain
4 Ensure good nutrition

**Treatment of underlying condition**
1 Chemotherapy for leukaemia or lymphoma *plus*
2 Irradiation therapy for some conditions
3 Bone marrow transplant for some conditions

**Transfusion management**

| | |
|---|---|
| Severe anaemia | Red cell transfusion |
| Bleeding due to thrombocytopenia | Platelet transfusion |

If repeated transfusions are likely to be needed, it is preferable to use leucocyte-reduced red cells and platelets, wherever possible

Chemotherapy, irradiation therapy and bone marrow transplant further suppress bone marrow and increase the need for platelet and red cell transfusion until remission occurs

Patients are often immunosuppressed and may be at risk of graft-versus-host disease (GvHD) which is a potentially fatal complication caused by transfused lymphocytes (see Section 7.5: *Other Delayed Complications of Transfusion*). Blood components from any blood relative have the potential to cause GvHD. Treatment of red cell or platelet preparations by gamma irradiation under controlled conditions inactivates the lymphocytes and reduces the risk of GvHD.

Some immunosuppressed patients are at risk of cytomegalovirus (CMV) infection transmitted by blood transfusion. This can be avoided or reduced by transfusing blood that is tested and contains no CMV antibodies or by using leucocyte-depleted blood components, if these are prepared correctly.

### Red cell transfusion

Anaemia due to the underlying disease and to treatment may become symptomatic and require red cell replacement. A red cell component may be preferable to whole blood as the patient is at risk of circulatory overload. If repeated transfusion is likely to be needed, leucocyte-reduced red cells (see Section 5: *Blood Products*) may reduce the risk of reactions and of alloimmunization.

### Platelet transfusion

Platelet transfusion (see Section 5: *Blood Products*) may be given either to control or prevent bleeding due to thrombocytopenia. The adult 'dose' of platelets should contain at least $2.4 \times 10^{11}$ platelets. This can be provided by infusing the platelets separated from 4–6 units of whole blood or obtained from one donor by plateletpheresis.

Platelets may need to be irradiated, leucodepleted or CMV negative, depending on the needs of the patient and the resources available.

#### Platelet transfusion to control bleeding

A platelet transfusion regime should be set for each patient. The aim is to balance the risk of haemorrhage against the risks of repeated platelet transfusion (infection and alloimmunization).

The presence of clinical signs such as mucosal or retinal haemorrhage, or purpura in a patient with a low platelet count, generally indicates the need for platelet transfusion to control bleeding. It should also prompt a check for causes such as infection in a patient. Often one platelet transfusion will control bleeding, but repeated transfusions over several days may be needed.

Failure to control bleeding may be due to:
- Infection
- Splenomegaly
- Antibodies against leucocytes or platelet antigens
- Failure to control the primary condition.

**HLA**: Human leucocyte antigen

Increasing the frequency of platelet transfusion and occasionally the use of **HLA**-compatible platelet concentrates may help to control bleeding.

#### Platelet transfusion to prevent bleeding (prophylactic transfusion)

Most platelet transfusions are given prophylactically. For stable afebrile patients, platelets are not usually given, provided the count is above

$10 \times 10^9$/L. If the patient has a fever and is suspected or known to have an infection, many clinicians adopt a higher threshold for platelet transfusion of $20 \times 10^9$/L.

If the patient is stable, platelet transfusions should be given to maintain the platelet count at the chosen level; transfusion every 2 or 3 days is often sufficient.

## 9.8   Genetic disorders of haemoglobin

### Normal adult haemoglobin composition

In a normal individual older than 6 months, more than 90% of the haemoglobin is adult type (haemoglobin A). Only small amounts of haemoglobin $A_2$ and F are still present. See Figure 2.6 and Figure 9.17.

*Figure 9.17: Normal adult haemoglobin composition*

| Haemoglobin | % in normal adult | Globin chains |
|---|---|---|
| Haemoglobin A (HbA) | 94%–96% | 2α and 2β (α2β2) |
| Haemoglobin F (HbF) | 0.8% | 2α and 2γ (α2γ2) |
| HbA$_2$ | <3% | 2α and 2δ (α2δ2) |

Figure 9.18 shows the major type of molecular abnormalities and their consequences.

*Figure 9.18: Abnormalities in haemoglobin*

| Molecular abnormality | Consequences |
|---|---|
| Structural variants of haemoglobin e.g. HbS, HbE | Sickle cell disease or trait HbE disease or trait |
| Failure to synthesize haemoglobin normally | Homozygous β thalassaemia (β thalassaemia major) |
| | Heterozygous β thalassaemia (β thalassaemia minor trait) |
| | α thalassaemia 4 α genes lost (hydrops fetalis) |
| | α thalassaemia minor or trait 1, 2 or 3 α genes lost |
| Failure to make normal neonatal switch from fetal haemoglobin (HbF) to adult haemoglobin (HbA) | HPFH: Hereditary persistence of fetal haemoglobin |

In many parts of the world, inherited abnormalities affecting haemoglobin are a common cause of morbidity and mortality. WHO estimates that about 7% of the world's population are carriers of these abnormalities.

Transfusion is important in the management of some of these conditions. There are special problems in transfusing these patients. It is essential to be familiar with them if you work in a region where these conditions occur.

# Sickle cell disease

Sickle cell disease (SCD) is the commonest of the haemoglobinopathies, affecting over 150,000 births per year. Eighty per cent of these are in Africa and most of the remainder are in the Mediterranean region, the Middle East and India.

## Clinical features

Children with sickle cell disease do not develop symptoms until they are 6 months old. By this age, most of the fetal haemoglobin (HbF) has been replaced with sickle Hb (HbS). The symptoms of anaemia are usually less than the haemoglobin concentration would suggest because of the low oxygen affinity of HbS which favours release of oxygen to the tissues.

Beyond six months, the severity of clinical features is variable, related in part to the percentage of HbS. Generally, sicklers have long periods of health punctuated by crises that may be followed by recovery or may lead to long-term morbidity.

### Acute crises

Acute crises include:

- Vaso-occlusive crises, leading to pain and infarction
- Splenic sequestration crises
- Aplastic crises due to infections, such as parvovirus or folate deficiency
- Haemolytic crises (occur rarely).

### Chronic complications

Chronic complications are the result of prolonged or repeated ischaemia leading to infarction. They include:

- Skeletal abnormalities and delayed puberty
- Neurological loss due to stroke
- Hyposplenism
- Chronic renal failure
- Impotence following priapism
- Loss of lung function
- Visual loss.

## Laboratory investigations

The following laboratory investigations should detect anaemia, characteristic abnormalities of the red blood cells and the presence of abnormal haemoglobin.

1 Haemoglobin concentration: Hb of 5–11 g/dl (usually low in relation to symptoms of anaemia).

2 Blood film to detect sickle cells, target cells and reticulocytosis.

3 Sickle solubility or slide test to identify sickle cells.

4 HbF quantitation to detect elevation of HbF which may modify the severity of the disease.

5   Haemoglobin electrophoresis to identify abnormal haemoglobin patterns. In homozygous HbSS, no normal HbA is detectable.

## Management
The main aims are to prevent crises and to minimize long-term damage when a crisis does occur, as shown in Figure 9.19.

*Figure 9.19: Prevention and treatment of sickle crisis*

### PREVENTION OF CRISES

1   Avoid precipitating factors:
    - Dehydration
    - Hypoxia
    - Infection
    - Cold
    - Slowed circulation.

2   Give folic acid 5 mg daily by mouth **long-term.**

3   Give penicillin:
    - 2.4 million iu benzathine penicillin IM **long-term**
    *or*
    - Penicillin V 250 mg daily by mouth **long-term.**

4   Vaccinate against *pneumococcus* and, if possible, hepatitis B.

5   Recognize and treat malaria promptly. Haemolysis due to malaria may precipitate a sickle crisis.

6   Treat other infections promptly.

7   Consider whether regular transfusion is indicated.

### TREATMENT OF CRISES

1   Rehydrate with oral fluids and, if necessary intravenous normal saline.

2   Treat systemic acidosis with IV bicarbonate, if necessary.

3   Correct hypoxia: give supplemental oxygen, if required.

4   Give effective pain relief: strong analgesics, including opiates (i.e. morphine), are likely to be needed.

5   Treat malaria, if infected.

6   Treat bacterial infection with the best available antibiotic in full dose.

7   Give transfusion, if required (see below).

## Transfusion and exchange transfusion in the prevention and treatment of sickle crisis
### Prevention of crises and long-term disability
Regular transfusion of red cells has a role in reducing the frequency of crises in (homozygous) sickle cell disease. This approach has a role in the

prevention of recurrent strokes and may assist in preventing recurrent life-threatening acute lung syndrome and chronic sickle cell lung disease. It may also be a useful approach in patients with very frequent, disabling veno-occlusive crises.

Transfusion is not indicated purely to raise a low haemoglobin level. Patients with SCD are well-adapted to haemoglobin levels of 7–10 g/dl and are at risk of hyperviscosity if the haemoglobin is raised significantly above the patient's normal baseline without a reduction in the proportion of sickle cells.

The aim is generally to maintain a sufficient proportion of normal HbA (about 30% or more) in the circulation to suppress the production of HbS-containing red cells and to minimize the risk of sickling episodes.

Stroke occurs in 7–8% of children with SCD and is a major cause of morbidity. Regular transfusions can reduce recurrence rates for stroke from 46–90% down to less than 10%.

Patients receiving regular transfusion are at risk of iron overload (see p. 196) as well as transfusion-transmitted infections and alloimmunization (see Section 7: *Adverse Effects of Transfusion*).

### Treatment of crises and severe anaemia

Transfusion is indicated in severe acute anaemia (haemoglobin concentration of <5 g/dl or >2 g/dl below the patient's normal baseline) and prompt transfusion in sequestration crisis and aplastic crisis can be life-saving. Aim for a haemoglobin level of 7–8 g/dl only.

### *Sequestration crisis*

Without obvious precipitating cause, there is sudden pooling of blood in the spleen which becomes temporarily greatly enlarged.

The patient presents with the equivalent of hypovolaemic shock due to loss of blood from the circulation into the spleen. The circulating blood volume must be urgently restored with intravenous fluid. Blood transfusion is usually needed.

### *Aplastic crisis*

Aplastic crisis is usually triggered by infection: e.g. parvovirus. There is transient acute bone marrow failure and transfusions may be needed until the marrow recovers.

### Management of pregnancy and anaesthesia in patients with sickle cell disease

See Section 10.2: *Chronic Anaemia in Pregnancy* and Section 12: *Surgery & Anaesthesia*.

1 Routine transfusions during pregnancy may be considered for patients with a bad obstetric history or frequent crises.

2 Preparation for delivery or surgery with anaesthesia may include transfusion to bring the proportion of HbS below 30%.

3 Anaesthetic techniques and supportive care should ensure that blood loss, hypoxia, dehydration and acidosis are minimized.

## Sickle cell trait

Patients with sickle cell trait (HbAS) are asymptomatic, may have a normal haemoglobin level and the red cells may appear normal on a blood film. However, the proportion of HbS can range from 25% to 45%. As a result, crises may be provoked by dehydration and hypoxia. Anaesthesia, pregnancy or delivery may lead to such problems and should be managed with care in known carriers.

## Combined defects: HbS and other genetic defects of haemoglobin

Combined defects include sickle cell/β thalassaemia, with a special tendency to thrombosis and pulmonary embolism in pregnancy. Diagnosis requires haemoglobin electrophoresis and family studies.

## Haemoglobin C, D and E diseases

### Haemoglobin C

Haemoglobin C occurs in West Africa and in populations of West African descent. It is asymptomatic in the trait form but, in the homozygous state gives rise to a mild haemolysis. Mild splenomegaly is common and the haemoglobin concentration is usually above 10 g/dl.

HbC interacts with HbS in the double heterozygous condition, haemoglobin sickle cell disease. This is a severe sickling disorder.

### Haemoglobin D

Haemoglobin D is prevalent in parts of India and is asymptomatic in both the trait and homozygous states. The doubly heterozygous condition with haemoglobin S gives rise to a particularly severe form of SCD.

### Haemoglobin E

Haemoglobin E is common in South-East Asia. The trait form gives rise to mild microcytosis and hypochromia without anaemia. The homozygous state causes mild anaemia and splenomegaly with both hypochromia and target cells on the blood film. Double heterozygous inheritance with HbS leads to a moderate sickling disorder without crises.

It produces a thalassaemia syndrome when combined with a β-thalassaemia mutation. Although most patients can survive long periods without transfusion, the clinical features of HbE/β thalassaemia cover the entire spectrum seen in homozygous beta thalassaemia.

## Thalassaemias

Thalassaemia is a major public health problem in many parts of the world and is particularly important in the Mediterranean region, the Middle East and South-East Asia. The cost of treatment is very high and makes major demands on the blood supply system. Treatment is often unavailable to those most in need.

β thalassaemias are clinically classified according to severity.

1  **Thalassaemia major**: in contrast to sickle cell disease, patients cannot maintain oxygenation of their tissues and require regular transfusion to maintain an adequate haemoglobin level.

2 **Thalassaemia intermedia**: encompasses a much broader pattern than thalassaemia major. The designation itself is a label applied to thalassaemia patients with anaemia and with a transfusion-independent clinical cause whose severity is extraordinarily heterogeneous.

Events such as infections or pregnancy may constitute significant causes for blood transfusion in the non-transfusion dependent patient, or may increase transfusion requirements in the transfusion-dependent patient.

3 **Thalassaemia minor**: generally asymptomatic with a normal or slightly reduced haemoglobin and microcytic, hypochromic red cells.

Thalassaemia is also classified according to the genetic and molecular defect. Figure 9.20 shows both of these classifications and how they relate to each other.

*Figure 9.20: Clinical classification of thalassaemia*

| Condition | Genetic defect | Clinical features |
|---|---|---|
| Homozygous β thalassaemia (β thalassaemia major) | β chain suppression or deletion | Severe anaemia: Hb <7 g/dl. Dependent on transfusion |
| Heterozygous β thalassaemia (β thalassaemia minor trait) | β chain deletion | Asymptomatic. Mild anaemia: Hb >10 g/dl. *But* two parents with β thalassaemia trait have a 1 in 4 chance of a child with β thalassaemia |
| Thalassaemia intermedia | β chain suppression or deletion | Heterogeneous: ranges from asymptomatic to resembling β thalassaemia major: Hb 7–10 g/dl |
| Homozygous α thalassaemia | All 4 α globin chains deleted | Fetus does not survive (hydrops fetalis) |
| α thalassaemia minor | Loss of two or three α genes | Usually mild or moderate |
| α thalassaemia trait | Loss of one or two α genes | Symptomless: mild microcytic, hypochromic anaemia |

The differentiation at presentation between thalassaemia intermedia and major is essential to determining appropriate treatment. Unfortunately the accurate identification of these two phenotypes is often difficult at the onset. Nevertheless, a careful analysis of the clinical, haematological, genetic and molecular data, as shown in Figure 9.21, may assist in planning treatment.

Figure 9.21 gives a summary of diagnostic parameters and clinical manifestations which assist in the differential diagnosis of thalassaemia syndromes.

|  | Major | Intermedia | Minor |
|---|---|---|---|
| Haemoglobin (g/dl) | <7 | 7–10 | >10 |
| Reticulocytes (%) | 2–15 | 2–10 | <5 |
| Nucleated RBC | ++/++++ | +/+++ | 0 |
| RBC morphology | ++++ | ++ | + |
| Jaundice | +++ | +/++ | 0 |
| Splenomegaly | ++++ | ++/+++ | 0 |
| Skeletal changes | ++/+++ | +/++ | 0 |

## Clinical features

### Thalassaemia major

Homozygous β thalassaemia (thalassaemia major) is the clinically most important condition. Red cell production is ineffective and haemolysis of abnormal red cells causes severe anaemia. There is an increase in $HbA_2$ and Hb F, but this does not compensate for the lack of Hb A. Patients are therefore reliant on transfusion to maintain a haemoglobin level sufficient to oxygenate the tissues.

β thalassaemia major presents within the first year of life, with failure to thrive and anaemia. Without effective treatment, it usually leads to death before the age of ten years.

These patients have:

- Severe anaemia becoming evident at 3–6 months of age
- Deformities such as the characteristic bossing of the skull, enlarged maxilla and stunted growth.

Children who are adequately transfused grow normally. However, problems may begin to become evident after about 20 units of blood (250 mg of iron per unit of blood) have been infused. Iron accumulates in the body due to the destruction of red cells, increased absorption and red cell transfusion. This damages the heart, endocrine system and liver, leading to cardiac failure, hormone deficiencies, cirrhosis and eventually death, unless iron chelation therapy is instigated.

## Laboratory investigations

See Figure 9.5 on p. 167.

### Thalassaemia major

The following laboratory findings will be seen in patients with β thalassaemia major.

1  Severe microcytic, hypochromic anaemia.

2  Blood film: red cells are microcytic and hypochromic with target cells, basophilic stippling and nucleated red cells.

3  Haemoglobin electrophoresis: absent HbA with raised HbF and $HbA_2$.

*Thalassaemia intermedia*

The following laboratory findings will be seen in patients with β thalassaemia intermedia, minor or trait:

1   Microcytic, hypochromic anaemia: normal iron, TIBC.

2   Haemoglobin electrophoresis: depends on variant.

## Management of thalassaemia major

The principles of management of β thalassaemia major are summarized in Figure 9.22.

*Figure 9.22: Management of thalassaemia major*

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**MANAGEMENT OF THALASSAEMIA MAJOR**

1   Transfusion (see below).

2   Chelation therapy.

3   Vitamin C: 200 mg by mouth to promote iron excretion, on the day of iron chelation only.

4   Folic acid: 5 mg day by mouth.

5   Splenectomy may be required to reduce the transfusion requirement.

6   Long-term penicillin.

7   Vaccinate against:
   - Hepatitis B
   - *Pneumococcus.*

8   Endocrine replacement for diabetes, pituitary failure.

9   Vitamin D and calcium for parathyroid failure.

---

## Transfusion in thalassaemia major

Planned blood transfusions can save life and improve its quality by helping to avoid the complications of hypertrophied marrow and early cardiac failure. The aim is to transfuse red cells in sufficient quantity and frequently enough to suppress erythropoiesis.

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**Where the risks of transfusion are judged to be small and iron chelation is available, target haemoglobin levels of 10.0–12.0 g/dl may be applied. It is not advisable to exceed a haemoglobin level of 15 g/dl.**

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Because splenomegaly increases anaemia by the pooling and destruction of blood, splenectomy may be required and will usually reduce the transfusion requirement.

Small transfusions are the preferred approach because they need less blood and suppress red cell production more effectively. However, less frequent, larger transfusions may be the best that can be achieved for patients who live far from the place of treatment.

## Repeated red cell transfusions over a long period

Repeated red cell transfusions over a long period cause major difficulties in treating patients with a haemoglobinopathy and other conditions.

### Alloimmunization

Up to 50% of patients who are repeatedly transfused will develop antibodies to red cells that can cause immediate or delayed haemolytic transfusion reactions (see Section 7: *Adverse Effects of Transfusion*). If possible, patients should from the start receive red cells that are matched for those red cell phenotypes, especially Kell and Rhesus D and E, that readily stimulate haemolytic antibodies in the recipient.

### Non-haemolytic febrile transfusion reactions (NHFTR)

Non-haemolytic febrile transfusion reactions (see Section 7: *Adverse Effects of Transfusion*) are very common in long-term recipients of transfusion. Consistent use of leucocyte-depleted red cell transfusions can delay the onset or severity of reactions.

Unpleasant symptoms of these reactions can be reduced by premedication with paracetamol:

**Adults**: 1 g by mouth one hour before transfusion, repeated if necessary after starting transfusion

**Children over 1 month**: 30–40 mg/kg/24 hours in 4 doses.

### Hyperviscosity

Blood viscosity rises exponentially above a haemoglobin of about 12 g/dl. In patients with sickle cell disease, high blood viscosity can precipitate vascular occlusion.

It is therefore important to:

1   Maintain the circulating fluid volume.

2   Transfuse only to a maximum haemoglobin level of 12 g/dl.

Exchange red cell transfusion may be required to achieve a sufficient reduction of HbS red cells without increasing viscosity.

### Iron overload

**desferrioxamine**: An iron-chelating (binding) agent that increases excretion of iron.

Repeated transfusion eventually leads to iron accumulation, damaging the heart, endocrine system and liver. The risks are reduced by giving only essential transfusions. Desferrioxamine, which increases iron excretion, should be given (see Figure 9.23).

### Infection

All blood and blood products should be screened for transfusion-transmissible infections, including HIV 1 and 2, hepatitis B and C, syphilis and other infectious agents. If there are concerns about the safety of blood in your local situation, it is important to balance the risks of transfusion-transmitted infection against the benefits to the patient of being transfused.

### IRON CHELATION FOR TRANSFUSION-DEPENDENT PATIENTS

1 Give subcutaneous infusion of desferrioxamine: 25–50 mg/kg/day over 8–12 hours, 5–7 days per week. Dose adjustment should be conducted on an individual basis.

Young children should be started on a dose of 25–35 mg/kg/day, increasing to a maximum of 40 mg/kg/day after 5 years of age and increasing further up to 50 mg/kg/day after growth has ceased.

2 Give vitamin C up to 200 mg/day orally one hour after initiating chelation.

3 Undertake splenectomy, if indicated (but not before 6 years of age: see below).

**In exceptional cases, under careful monitoring:**
Give desferrioxamine 60 mg/kg by intravenous infusion over 24 hours, using the patient's subcutaneous infusion pump with the butterfly inserted into the drip tubing. *Desferrioxamine should not be put into the blood pack.*

**Or**

Give desferrioxamine 50–70 mg/kg/day in a continuous intravenous infusion via an implanted catheter device. This method should be used only for patients with very high iron levels and/or other iron-related complications.

Close monitoring for ocular and auditory toxicity is strongly recommended. Some patients are unable to take desferrioxamine for medical reasons. The oral iron-chelating agent deferiprone is now licensed and available in Europe as a second-line alternative.

Patients who are not immune to hepatitis B should be vaccinated with hepatitis B vaccine. HAV vaccine should be administered to all anti-HCV positive thalassaemics.

### Venous access
Repeated transfusion carries the risk of thrombosis of peripheral veins and consequent difficulties when further infusions are essential. The patient's veins are his/her lifeline. See Section 13.2: *Initial Assessment and Resuscitation* for guidance on preserving venous access.

### Splenectomy
Splenectomy reduces red cell destruction and transfusion requirements (frequency and quantity). However, it should not be performed in children younger than 6 years because of the high risk of infections after splenectomy.

Vaccinate against *pneumococcus* 2–4 weeks prior to splenectomy. Yearly administration of influenza vaccine is recommended in splenectomized patients. The efficacy and utility of vaccination against *N. meningitidis* is not as clear as for *S. pneumonia*.

Once the spleen has been removed, lifelong penicillin prophylaxis is needed.

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## 9.9   Bleeding disorders and transfusion

Patients who have an abnormality of platelets or the coagulation/fibrinolytic system may suffer from severe bleeding due to childbirth, surgery or trauma.

Recognition that a patient may have a bleeding disorder and the correct diagnosis and treatment can influence the timing and type of elective surgery, reduce the need for transfusion and avoid risks to the patient due to bleeding.

A bleeding tendency may be due to:

- Congenital (inherited) disorder of blood vessels, platelets or coagulation factors
- Use of pharmaceutical drugs
- Trauma
- Haemorrhage
- Obstetric complications
- Nutritional deficiencies
- Immunological disorders.

### Clinical features

Recognition of a bleeding disorder is based on:

- Clinical assessment:
  — History
  — Physical examination
- Knowledge of the probable causes
- Selection of laboratory tests and interpretation of the results
- Occasionally, the response to a trial of treatment.

The clinical features of a bleeding disorder are shown in Figure 9.24.

The clinical history is perhaps the most important single component of the investigation of haemostatic function. Where the family history suggests an inherited disorder, construct a family tree, if possible.

### Laboratory investigations

Laboratory investigations should be performed when a bleeding problem is suspected. This is especially important if the patient is going to have a surgical procedure.

The investigation of the bleeding problem should be as methodical as possible. Figure 9.25 on p. 200 shows a flow chart for the interpretation of the three routine tests in bleeding disorders.

*Figure 9.24: Clinical features of bleeding disorders*

## HISTORY

### Symptoms suggestive of bleeding disorder

- Easy bruising
- Development of purpura
- Nosebleeds
- Excessive bleeding after circumcision, dental extraction or other surgery
- Heavy menses, frequently accompanied by the passage of clots
- Perinatal haemorrhage
- Dark or bloody stools
- Red urine
- Episodes of swollen, painful joints or muscles
- Excessive bleeding after minor scratches
- Bleeding that recurs hours or days after original trauma
- Poor wound healing

### Other symptoms

- Weight loss
- Anorexia
- Fever and night sweats

### Exposure to drugs or chemicals

- Alcohol ingestion
- All current or past drugs used by the patient
- Any exposure to drugs or chemicals at work or in the home

### Family history

- Relatives with a similar condition
- Relatives with any history suggesting bleeding disorder

## PHYSICAL EXAMINATION

### Signs of bleeding or blood loss

- Pale mucous membranes
- Petechial haemorrhages
- Purpura or ecchymoses (bruising)
- Bleeding from mucous membranes
- Muscle haematomas
- Haemarthroses or deformed joints
- Positive faecal occult blood test
- Blood observed at rectal examination

### Other signs

- Splenomegaly
- Hepatomegaly
- Jaundice
- Fever
- Tenderness
- Lymphadenopathy

## INTERPRETATION

Source of bleeding usually suggests most likely cause:

- Bleeding from mucous membranes suggests low platelet count or platelet abnormalities, von Willebrand disease or vascular defects
- Muscle and joint bleeding or bruising suggest haemophilia A or B

**Note:** Skin manifestations of bleeding disorders (i.e. petechial haemorrhages or ecchymoses) are sometimes difficult to see in dark-skinned patients. Examination of the mucous membranes, including the conjunctivae, oral mucosa and optic fundi, for evidence of bleeding, is therefore very important.

*Figure 9.25: Interpretation of tests of haemostasis*



**Screening test**

**Clinical features of a bleeding tendency**

- Skin petechiae
- Bleeding gums
- Excessive bleeding from venepuncture sites
- Retinal haemorrhages

Excessive bleeding from venepuncture sites or surgical wounds associated with:
- Sepsis
- Prolonged hypotension
- Trauma
- Childbirth

Excessive prolonged bleeding after:
- Circumcision, tooth extraction or other surgery
- Episodes of bleeding into joints

**?** Low platelet count or abnormal platelet function

**?** DIC

**?** Warfarin (coumarin) overdose
**?** Haemophilia A or B

**Laboratory investigations: typical results**

| | Thrombocytopenia | Heparin | DIC | Fibrinolytic therapy | von Willebrand disease | Liver disease | Warfarin | Haemophilia A | Haemophilia B | Massive transfusion |
|---|---|---|---|---|---|---|---|---|---|---|
| Platelet count | ↓ | Normal | ↓ | Normal | Normal/↓ | Normal/↓ | Normal | Normal | Normal | ↓ |
| Prothrombin time | Normal | Normal | ↑ | ↑ | Normal | ↑ | ↑ | Normal | Normal | ↑ |
| Activated partial thromboplastin time | Normal | ↑ | ↑ | ↑ | Normal/↑ | ↑ | ↑ | ↑ | ↑ | ↑ |
| Thrombin time | Normal | ↑ | ↑ | ↑ | Normal | ↑ | Normal | Normal | Normal | Normal/↑ |
| Fibrinogen concentration | Normal | Normal | ↓ | ↓ | Normal | ↓ | Normal | Normal | Normal | Normal/↓ |
| Fibrin degradation products | Normal | Normal | ↑ | ↑ | Normal | Normal/↑ | Normal | Normal | Normal | Normal/↑ |

Reversal of prolonged thrombin time by protamine indicates heparin is absent

## 9.10 Congenital bleeding and clotting disorders

### Deficiencies of Factor VIII and IX

#### Clinical features

Haemophilia A and haemophilia B are caused by inherited deficiencies of Factors VIII and IX respectively. These two factors interact to activate Factor X, which is needed for the production of thrombin and hence coagulation. The clinical characteristics of deficiencies of Factors VIII and IX are therefore identical. Both are X-linked recessive disorders affecting males almost exclusively.

The clinical severity of the disorder is determined by the amount of active coagulation factor available. In severe cases, there is spontaneous delayed deep soft tissue bleeding, particularly into joints and muscles. Chronic synovitis eventually supervenes, leading to pain, bony deformities and contractures. Bleeding after circumcision is a frequent mode of presentation in babies. Moderate or mild haemophilia may cause severe bleeding when tissues are damaged by surgery or trauma.

#### Laboratory investigations

Both Factor VIII and Factor IX deficiency cause prolongation of the activated partial thromboplastin time (APTT) with a normal prothrombin time. The abnormal APTT corrects with the addition of normal plasma. Specific factor assays will confirm the level of the deficiency, but require a specialized laboratory service.

#### Management

##### Management of an acute bleed

1 Avoid anti-platelet agents such as aspirin and non-steroidal anti-inflammatory drugs.

2 Do not give intramuscular injections.

3 Administer coagulation factor concentrates to treat bleeding episodes as quickly as possible (see Figure 9.26 on p. 202). Haemarthroses need strong analgesia, ice packs and immobilization initially. **Never incise joint for haemarthrosis**.

4 Do not incise swellings in haemophiliacs.

5 Start physiotherapy early to minimize loss of joint function.

##### Supportive management

1 A team approach to coordinate care (physician, physiotherapist, surgeon) is of great benefit.

2 Home therapy: some patients learn to self-administer factor concentrates at the earliest symptoms of a bleed.

3 Prophylactic administration of factor concentrates, to reduce the frequency of bleeds, helps to preserve joint function. However, the cost of treatment is high.

## DOSAGE OF FACTOR VIII AND ALTERNATIVES FOR TREATMENT OF HAEMOPHILIA A

| Severity of bleed | Required Factor VIII dose | *Supplied as:* Factor VIII concentrate (500 iu/bottle) | *or* Cryoprecipitate* (80–100 iu/pack) |
|---|---|---|---|
| 1  Mild bleed: nose, nose, gums, etc. | 14 iu/kg | 1–2 bottles (adult) | 1 pack/6 kg |
| 2  Moderate bleed joint, muscle, gastrointestinal tract, surgery | 20 iu/kg | 2–4 bottles (adult) | 1 pack/4 kg |
| 3  Major bleed: e.g. cerebral | 40 iu/kg | 4–6 bottles (adult) | 1 pack/2 kg |
| 4  Prophylaxis for major surgery | 60 iu/kg | 6–10 bottles (adult) | 1 pack/1 kg |

**Note**

* Cryoprecipitate containing 80–100 iu of Factor VIII, usually obtained from 250 ml of fresh frozen plasma.

1  For 1, 2, 3 above, repeat dose 12-hourly if bleeding persists or swelling is increasing. With more severe bleeds, it is usually necessary to continue treatment with half of total daily dose 12-hourly for 2–3 days or occasionally longer.

2  For 4, start therapy 8 hours before surgery. Continue 12-hourly therapy for 48 hours post-operatively. If no bleeding occurs, scale down gradually over next 3–5 days.

3  As adjunct to factor replacement in mucosal or gastrointestinal bleeding and surgery, give fibrinolytic inhibitor:

   Tranexamic acid (oral): 500–1000 mg 3 times/day. Do **not** use for haematuria.

4  In an emergency, use fresh frozen plasma to treat bleeding in haemophiliacs (give 3 bags initially) if none of the above are available.

5  Careful assessment of the patient's fluid intake is important to avoid fluid overload when using fresh frozen plasma or large doses of cryoprecipitate.

## DOSAGE OF FACTOR IX FOR TREATMENT OF HAEMOPHILIA B

| Severity of bleed | Required Factor IX dose | *Supplied as:* Factor IX concentrate (500 iu/bottle) | *or* Fresh frozen plasma |
|---|---|---|---|
| 1  Mild bleed | 15 iu/kg | 2 bottles (adult) | 1 pack/15 kg |
| 2  Major bleed | 20–30 iu/kg | 3–6 bottles (adult) | 1 pack/7.5 kg |

**Note**

1  Repeat in 24 hours if bleeding continues.

2  Factor VIII concentrate and cryoprecipitate are not useful for haemophilia B so accurate diagnosis is essential.

3  As adjunct to replacement therapy:

   Tranexamic acid (oral): 500–1000 mg 3 times/day, as for haemophilia A.

### Desmopressin (DDAVP)

Desmopressin releases stored endogenous Factor VIII and von Willebrand factor, so may be useful in mild or moderate haemophilia A. It is not indicated in Factor IX deficiency.

### Replacement with factor concentrates

Prior to viral inactivation of factor concentrates, there was a high risk of transmission of HIV and hepatitis B and C to haemophilia patients. It is therefore imperative to use factor concentrates that are licensed and certified to be virus-inactivated.

If coagulation factor concentrates are not available, use:

- Haemophilia A: Cryoprecipitate
- Haemophilia B: Fresh frozen plasma or liquid plasma.

### Dose regime: Haemophilia A and B

The dosage required depends on an assessment of the severity of the bleed. Use Figure 9.26 to determine the dosage for both adults and children, according to body weight.

## von Willebrand disease

### Clinical features

von Willebrand factor (vWF) is a protein which is involved in platelet adhesion, both to other platelets and to the subendothelium. It also acts as a carrier protein for Factor VIII. Deficiency of von Willebrand factor is inherited as an autosomal dominant condition affecting both males and females. The major clinical manifestation is mucocutaneous bleeding, such as:

- Epistaxis
- Easy bruising
- Menorrhagia
- Bleeding after dental extractions
- Post-traumatic bleeding.

### Laboratory investigations

The abnormality of platelet function is best detected by demonstrating a prolonged bleeding time by the template method. The measurement of deficiencies in Factor VIII coagulant activity and von Willebrand factor itself require specialized laboratory facilities.

### Management

The aim of treatment is to normalize bleeding time by either increasing endogenous vWF levels with desmopressin (DDAVP) or by replacing vWF using an intermediate-purity Factor VIII product that is known to contain some vWF or with cryoprecipitate, which also contains vWF.

### Dose regime

Treat as for mild or moderate bleed of haemophilia A, except that the haemostatic dose may be repeated not 12-hourly, but after 24–48 hours, as von Willebrand factor has a longer half-life than Factor VIII.

1 **Desmopressin (DDAVP)**
   0.3–0.4 µg/kg IV lasts 4–8 hours and avoids the need to use plasma products.

   The dose can be repeated every 24 hours, but the effect is reduced after some days of treatment.

2 **Factor VIII products**
   Reserve for patients unresponsive to desmopressin. It is essential to use a virally-inactivated product that contains vWF. These products are so-called 'intermediate purity Factor VIII concentrates' (see Section 5: *Blood Products*).

3 **Cryoprecipitate**
   Cryoprecipitate is effective, but is not available in virally-inactivated form in most countries.

## 9.11 Acquired bleeding and clotting disorders

### Disseminated intravascular coagulation

Disseminated intravascular coagulation (DIC) is caused by the abnormal and excessive stimulation of the coagulation system, resulting in widespread utilization of coagulation factors, fibrinogen and platelets. This in turn stimulates an overproduction of fibrinolytic enzymes to break down the clots formed, leading to an increase in fibrin degradation products (FDPs).

As the coagulation factors, platelets and fibrinogen are consumed faster than they can be replaced, this results in widespread, uncontrolled bleeding.

Common causes of DIC include:
- Infection
- Malignancy
- Trauma
- Acute leukaemia
- Eclampsia
- Abruptio placenta
- Amniotic fluid embolism
- Retained products of conception
- Retained dead fetus.

### Clinical features

In severe DIC, there is excessive, uncontrolled bleeding. The lack of platelets and coagulation factors causes:
- Haemorrhage
- Bruising
- Oozing from venepuncture sites.

Microvascular thrombi may cause multiple organ dysfunction leading to:

- ■ Respiratory distress
- ■ Coma
- ■ Renal failure
- ■ Jaundice.

## Laboratory investigations

DIC is characterized by:

- ■ Reduced platelet count (thrombocytopenia)
- ■ Prolonged prothrombin time (PT)
- ■ Prolonged activated partial thromboplastin time (APTT)
- ■ Prolonged thrombin time
- ■ Decreased fibrinogen concentration
- ■ Breakdown of products of fibrinogen: fibrin degradation products (FDPs).

In less acute forms of DIC, sufficient platelets and coagulation factors may be produced to maintain haemostasis, but laboratory tests reveal evidence of fibrinolysis (FDPs).

## Management

Rapid and appropriate treatment or removal of the underlying condition is imperative. Most patients with bleeding due to DIC are critically ill and require supportive care.

1   Monitor:
- ■ Prothrombin time
- ■ International normalized ratio (INR)
- ■ Activated partial thromboplastin time
- ■ Platelet count
- ■ Fibrinogen.

2   Identify and treat or remove the cause of DIC.

3   Give supportive care:
- ■ Fluids
- ■ Vasopressor agents
- ■ Renal, cardiac or ventilatory assistance.

## Transfusion

Transfusion support should be given to help control bleeding until the underlying cause has been dealt with and to maintain an adequate platelet count and coagulation factor levels. See Figure 9.27 on p. 206.

## Disorders of vitamin K-dependent coagulation factors

Vitamin K is a fat-soluble vitamin found primarily in green vegetables and liver. It is a cofactor for the synthesis of Factors II, VII, IX and X, which takes place in the liver.

**TRANSFUSION IN DIC**

1 If the PT or APTT is prolonged and the patient is bleeding:

- Replace red cell losses with the freshest whole blood available as it contains fibrinogen and most other coagulation factors

*and*

- Give fresh frozen plasma as this contains labile coagulation factors: 1 pack/15 kg body weight (4–5 packs in adults)
- Repeat FFP according to the clinical response.

2 If fibrinogen is low or the APTT or thrombin time is prolonged, also give cryoprecipitate (to supply fibrinogen and Factor VIII): 1 pack/6 kg (8–10 packs in adults).

3 If the platelet count is less than $50 \times 10^9$/L and the patient is bleeding, also give platelet concentrates: 4–6 packs (adult).

4 The use of heparin is not recommended in bleeding patients with DIC, although it may be mentioned in older textbooks.

**Note**

Doses are based on the preparation of fresh frozen plasma, cryoprecipitate and platelet concentrates from 450 ml donations.

Deficiency of vitamin K-dependent coagulation factors may be present in the following conditions:

- Haemorrhagc disease of the newborn (see Section 11: *Paediatrics & Neonatology*)
- Ingestion of coumarin anticoagulants (warfarin)

  Note: when a patient is taking coumarin, starting other drugs (such as some antibiotics) may cause bleeding by displacing warfarin bound to plasma proteins

- Vitamin K deficiency due to inadequate diet or malabsorption
- Liver disease, leading to underproduction of Factors II, VII, IX: a prolonged prothrombin time is usually a feature of severe liver disease with severe loss of hepatocytes.

### Clinical features

Clinically, these disorders usually present with bleeding from the gastrointestinal or urogenital tracts.

### Laboratory investigations

The prothrombin time is prolonged, often severely so. For patients with liver disease, thrombocytopenia and abnormalities of fibrinogen and fibrinolysis often complicate diagnosis and treatment.

### Management

See Figure 9.28 for the management of deficiency of vitamin-K dependent coagulation factors.

### MANAGEMENT OF DEFICIENCY OF VITAMIN K-DEPENDENT COAGULATION FACTORS

1 Remove the underlying cause of vitamin K deficiency:
   - Stop anticoagulants (warfarin)
   - Treat malabsorption or dietary deficiency.

2 Replace coagulation factors with fresh frozen plasma, as necessary.

3 Reverse warfarin with intravenous vitamin K if the patient is bleeding and the INR is prolonged. Doses of vitamin K exceeding 1 mg may make the patient refractory to further warfarin for up to 2 weeks. If anticoagulation is still needed, consider doses of 0.1–0.5 mg.

## Bleeding problems associated with surgery

See Section 12.1: *Patient Selection and Preparation*.

## Gastrointestinal bleeding

Gastrointestinal bleeding is common and has a significant mortality risk.

### Clinical features

1 Upper gastrointestinal bleeding can present as anaemia due to chronic bleeding, haematemesis (vomiting blood) or melaena (black, altered blood passed from the rectum).

2 Lower gastrointestinal bleeding presents as anaemia with a positive faecal occult blood test or fresh blood in or on the faeces.

3 Peptic ulcer (gastric, duodenal).

4 Oesophageal varices.

5 Gastric carcinoma.

Patients with oesophageal varices, usually due to chronic liver disease, may also have peptic ulcers or erosions.

### Management

The principles of the management of gastrointestinal bleeding are:

1 Resuscitate the patient (see Figure 9.29 on p. 208).

2 Find the source of bleeding (by endoscopy, if possible).

3 Give $H_2$ receptor blockers (e.g. Tagamet, Cimetidine).

4 Stop continued or repeat bleeding by endoscopy or surgical means.

Most patients stop bleeding without surgical or endoscopic intervention. Re-bleeding has a high mortality and is more likely in patients who:
   - Are old
   - Are shocked on admission to hospital
   - Have acute bleeding visible on endoscopy
   - Have gastric (rather than duodenal) ulcer
   - Have liver disease.

## Transfusion

Figure 9.29 provides guidelines on transfusion in gastrointestinal bleeding.

*Figure 9.29: Resuscitation and transfusion in acute gastrointestinal bleeding*

| SEVERITY OF BLEED | CLINICAL FEATURES | IV INFUSION/ TRANSFUSION | END POINT |
|---|---|---|---|
| 1 Mild bleed | Pulse and haemoglobin normal | ■ Maintain intra-venous access until diagnosis is clear<br>■ Ensure blood is available | |
| 2 Moderate bleed | Resting pulse >100/min **and/or** Haemoglobin <10 g/dl | ■ Replace fluid<br>■ Order compatible red cells (4 units) | Maintain Hb >9 g/dl* |
| 3 Severe bleed | History of collapse **and/or** Shock<br>■ Systolic BP <100 mmHg<br>■ Pulse >100/min | ■ Replace fluid rapidly<br>■ Ensure blood is available<br>■ Transfuse red cells according to clinical assess-ment and Hb/Hct | ■ Maintain urine output >0.5 ml/kg/ hour<br>■ Maintain systolic BP >100 mmHg<br>■ Maintain Hb >9 g/dl* |

\* Until you are confident that the patient is not likely to have a further large bleed. The patient may need to be referred for surgical intervention, once resuscitated.

### ACTIVITY 25

*List the common conditions on your adult and paediatric medical wards.*

*What are the commonest reasons for transfusing these patients? Could some transfusions be avoided by more appropriate prevention or treatment of the underlying condition?*

### ACTIVITY 26

*Are any guidelines available in your hospital on the clinical indications for transfusion in medical patients? Are they accurate and comprehensive?*

*If there are no guidelines or you think they could be improved, discuss your ideas with members of the hospital transfusion committee or with senior clinical and blood bank colleagues.*

*Once they have been agreed, organize a teaching session for all relevant staff. Monitor whether the guidelines are being used correctly. Provide any further teaching that may be required and continue to monitor practice.*

# 10

# Obstetrics

## Introduction

Acute blood loss and chronic anaemia in pregnancy are major causes of maternal morbidity and mortality worldwide. Anaemia in pregnancy also increases the likelihood of intrauterine growth retardation, premature birth and fetal loss.

Anaemia in pregnancy and its effects on maternal and perinatal morbidity and mortality can be avoided by effective prevention and treatment. It is therefore essential to identify anaemia and take early corrective measures. This will minimize the risks to mother and child and reduce the need for transfusion if obstetric haemorrhage occurs.

## Learning outcomes

When you have completed this section, you should be able to:

1 Describe the haematological changes in pregnancy.

2 Make an accurate assessment of the obstetric patient and be able to diagnose chronic anaemia.

3 Promote preventive measures to reduce chronic anaemia in the obstetric patient.

4 Provide appropriate treatment for the obstetric patient with chronic anaemia.

5 Provide appropriate treatment for the obstetric patient with acute blood loss.

6 Identify the fetus at risk of haemolytic disease and take measures to prevent haemolytic disease of the newborn (HDN).

## 10.1 Physiological & haematological changes during pregnancy

During pregnancy, the following haematological changes occur.

### Plasma volume

There is a 40–50% increase in plasma volume which reaches its maximum by week 32 of gestation. This is accompanied by a similar increase in cardiac output. These changes:

- Increase blood supply to the uterus
- Increase the excretory capacity of the kidneys
- Help dissipate heat produced by the elevated metabolic rate during pregnancy
- Protect the fetus against impaired placental perfusion as a result of aortal caval compression by the gravid uterus.

### Red blood cells

The mother's red cell mass increases by 18–25% during pregnancy. This occurs more slowly than the increase in plasma volume. The discrepancy between the rate of increase in plasma volume and red cell mass results in a physiological reduction in the haemoglobin concentration during pregnancy (see Figure 3.6 on p. 45). A normal or elevated haemoglobin during pregnancy may be a sign of pre-eclampsia in which plasma volume is reduced.

### Iron metabolism

The mother's iron requirement is increased during the last two trimesters of pregnancy because of the demands of the fetus and the increase in maternal red cell mass. Up to 80% of the increased requirement occurs in the last trimester.

The total iron requirement over the whole pregnancy is approximately 1300 mg, made up of:

- 300 mg for the fetus
- 50 mg for the placenta
- 450 mg for the increase in the maternal red cell mass
- 250 mg for the mother's 'basal' iron losses
- 250 mg for blood loss during a normal vaginal delivery (500 ml).

**Although intestinal iron absorption increases during pregnancy, dietary iron intake is unable to meet the increased iron requirement. This therefore has to be met by the body's iron stores. If these are inadequate, the mother will become anaemic if iron supplements are not given.**

## Non-haematological effects of maternal iron deficiency

Anaemia is a late manifestation of iron deficiency. However, because all cells have iron-dependent enzymes, tissues begin to malfunction even in the early stages of iron deficiency. Iron supplementation therefore results in improved well-being, even before the haemoglobin rises significantly.

In addition to anaemia, maternal iron deficiency may result in the following non-haematological effects.

1   Impaired neuromuscular transmission that may be responsible for increased blood loss at delivery in anaemic women.

2   Abnormal cellular function that may be responsible for the reported association between iron deficiency anaemia and pre-term birth.

3   Poor fetal growth, suggested by the observed correlation between maternal iron deficiency anaemia, high placental weight and increased ratio of placental weight to birthweight.

4   Significantly decreased ferritin levels in newborn infants of iron deficient mothers, indicating reduced iron stores in the first year of life when iron intake is very poor.

5   Behavioural abnormalities in iron deficient infants that have been related to changes in the brain thought to be due to iron deficiency.

## Coagulation and fibrinolytic systems

See Section 2.2: *Blood*.

During pregnancy, a physiological hypercoagulable state develops. There is an increase in both platelet activation and the levels of coagulation factors, particularly fibrinogen, Factor VIII and Factor IX. In addition, the fibrinolytic system is suppressed. The effect is to protect the mother from haemorrhage during labour and delivery. However, these changes also result in an increased susceptibility to thromboembolism.

## Blood loss during delivery

Approximately 500 ml of blood (250 mg iron) is lost during normal vaginal delivery of a single fetus and up to 1000 ml during a Caesarean section.

**This blood loss rarely necessitates transfusion provided that the maternal haemoglobin is above 10.0–11.0 g/dl before delivery.**

The haemoglobin concentration should return to normal by 2 weeks postpartum. If this does not occur, further investigation is required but is almost invariably due to excessive blood loss, iron deficiency or a combination of the two.

## 10.2  Chronic anaemia in pregnancy

Anaemia in pregnancy, as defined by WHO, is a haemoglobin concentration of less than 11 g/dl in the first and third trimesters. In the second trimester, a fall of 0.5 g/dl due to increased plasma volume is allowed and a cut-off value of 10.5 g/dl is used, as shown in Figure 10.1.

*Figure 10.1: Defining anaemia in pregnancy*

| Stage of pregnancy | | Anaemic if less than (g/dl) |
|---|---|---|
| First trimester | 0–12 weeks | 11.0 |
| Second trimester | 13–28 weeks | 10.5 |
| Third trimester | 29 weeks–term | 11.0 |

## Causes of chronic anaemia in pregnancy

Iron deficiency, with or without folate deficiency, is by far the most common cause of anaemia in pregnancy. Remember, however, that pregnant women may also have other causes of anaemia (see Figure 3.7 on p. 46).

### Iron deficiency

The most common cause of iron deficiency anaemia in pregnancy is poor dietary intake. Hookworm and schistosoma infestations can rapidly cause iron deficiency anaemia in individuals whose dietary intake of iron is low and whose body iron stores are already depleted. This is a common situation during pregnancy because of the extra demands for iron.

Maternal iron deficiency anaemia is associated with lower scores on tests of motor and mental development in infancy.

### Short birth intervals

If iron supplementation is not given, it may take up to two years for a woman to regain her pre-pregnancy iron status. Short birth intervals can therefore contribute to iron deficiency anaemia. Iron supplementation replenishes iron stores.

### Folate deficiency

Folate requirements approximately double during pregnancy, especially in the last trimester and during lactation. Body stores of folate are limited and dietary folate may be insufficient. Consequently, anaemia may develop. Folate deficiency may occur alongside iron deficiency anaemia. Consider the possibility of folate deficiency, particularly if there is a poor response to iron supplementation (see Section 9.2: *Deficiency of Haematinics*).

Folate supplements (5 mg/day by mouth) should be given throughout pregnancy to prevent anaemia. This should not be confused with the use of folate to reduce the risk of neural tube defects in infants (e.g. spina bifida). For this latter indication, the prospective mother should be given folate *before* and around the time of conception.

### Vitamin B$_{12}$ deficiency

Deficiency of vitamin B$_{12}$ is due to malabsorption (see Section 9.2: *Deficiency of Haematinics*) or to dietary deficiency.

Dietary deficiency is rare and should be suspected in the following circumstances.

- Patients who decline to eat any animal protein (vegans)
- Patients from populations whose diet contains little or no animal protein.

### HIV infection

If a patient has anaemia with leucopenia, thrombocytopenia, lymphadeno-pathy and oral candidiasis, consider the possibility of HIV infection.

### Malaria

Haemolysis due to malaria is an important cause of severe anaemia in pregnancy. Where malaria is suspected in a pregnant woman, early diagnosis and treatment is essential to minimize the risk of maternal morbidity and mortality and the need for transfusion (see Figure 9.11 on p. 180).

Chloroquine, quinine and sulfadoxine-pyrimethamine combination are considered safe in all three trimesters of pregnancy. However, chloroquine-resistant *falciparum* malaria is widespread and multidrug-resistant *falciparum* malaria also occurs in some countries. It is essential to know the local sensitivity pattern of *falciparum* malaria to guide optimal treatment. Some drugs (mefloquine, halofantrine and artemisinin derivatives) are currently contraindicated during the first trimester of pregnancy because of anxiety associated with their possible use. Mefloquine should be avoided in the second and third trimesters unless there is no alternative. Data on the use of artesunata and other artemisinins in pregnancy are few. However, their use is justified in patients who fail treatment or develop severe malaria.

### Sickle cell disease

Anaemia is usually severe and may be exacerbated by acute sequestration of sickled cells in the spleen or, more commonly, by the aplastic crisis that occurs when bone marrow red cell production slows down during acute infections. Folate deficiency is common in sickle cell disease because red cell production is increased. Because the body does not excrete iron and reutilizes the iron from the red cells, iron deficiency in sicklers is no more common than in the general population.

The avoidance or early treatment of infections, such as urinary tract infections, and the administration of folate are important in the management of sickle cell disease in pregnancy. The pregnant woman should be advised to avoid high altitudes, where possible, in order to promote adequate oxygenation. See Section 9.8: *Genetic Disorders of Haemoglobin*. For sickle cell disease in neonates, see Section 11.3: *Paediatric Transfusion in Special Clinical Situations*.

## Assessment of chronic anaemia in pregnancy

When anaemia is detected, it is important to determine the cause and assess its severity, including any evidence of clinical decompensation (see Figure 9.2 on p. 163 and Figure 10.2). Assessment should be based on:

- Patient's clinical history
- Physical examination
- Laboratory investigations to determine the specific cause of anaemia: for example, serum $B_{12}$, folate or ferritin.

*Figure 10.2: Clinical assessment of anaemia in pregnancy*

**HISTORY**

**Non-specific symptoms of anaemia**
- Tiredness/loss of energy
- Light-headedness
- Shortness of breath
- Headache
- Ankle swelling
- Worsening of any pre-existing symptoms: e.g. angina

**History and symptoms relating to the underlying disorder**
- Nutritional deficiency: poor dietary history
- Short birth intervals
- Previous history of anaemia

**Bleeding during current pregnancy** (see Figure 9.2)

**PHYSICAL EXAMINATION**

**Signs of anaemia and clinical decompensation**
- Pale mucous membranes (palms, nail-beds)
- Rapid breathing
- Tachycardia
- Raised jugular venous pressure
- Heart murmurs
- Ankle oedema
- Postural hypotension
- Altered mental state

**Signs of the underlying disorder** (see Figure 9.2)

**Evidence of blood loss**

### Laboratory investigations

See Section 9.1: *Anaemia* for laboratory investigations for chronic anaemia.

## Prevention and management of chronic anaemia in pregnancy

The prevalence of anaemia and the need for transfusion during pregnancy can be reduced by:

- Prevention and management of nutritional anaemia
- Adequate antenatal care.

### Prevention of nutritional anaemia in pregnancy

The following measures are particularly important in preventing nutritional anaemia in pregnant women.

1 Education about nutrition, food preparation and breast-feeding, with particular emphasis on the effects on the fetus and newborn.

2 The provision of adequate maternal and child health care.

3 Access to family planning information, education and services.

### Dietary sources of iron

Iron deficiency is mainly due to inadequate nutrition. There are two types of dietary iron:

■ Haem iron, which is well-absorbed and is contained in foods of animal origin, such as meat, poultry and fish

■ Non-haem iron, which is poorly-absorbed and is contained in foods of plant origin, such as whole grain cereals, tubers, vegetables and pulses.

The absorption of non-haem iron requires the presence of vitamin C or meat, poultry or fish in the diet.

**The addition of as little as 50 mg of vitamin C to a meal can double iron absorption. This could be provided by an orange, 120 g of papaya or mango, or 100 g of *raw* cabbage.**

### Prophylactic administration of haematinics

Prophylactic administration of haematinics is strongly indicated during pregnancy in countries where iron and folate deficiency is common (see Section 9.2: *Deficiency of Haematinics*).

The optimum *daily* doses to prevent anaemia in pregnant women are:

■ 120 mg elemental iron: e.g. 200 mg tablet of ferrous sulphate

■ 500 μg folate.

A suitable combination tablet, to be taken twice a day, would contain 60 mg of elemental iron and 250 μg of folate. Where this is not available, tablets such as ferrous sulphate, containing 60 mg of elemental iron, should be taken twice a day together with one folic acid tablet (1 mg).

### Treatment of anaemia in pregnant women

When anaemia is already present, especially if severe, higher *daily* therapeutic doses of iron should be given, usually:

■ 180 mg elemental iron

■ 2 mg folate.

Iron treatment should continue for at least another two or three months to build up iron stores to about 200–300 mg, which is equivalent to a serum ferritin of 30 μg/L.

### ACTIVITY 28

*Look back at Section 3: Anaemia. What factors can cause anaemia during pregnancy?*

*Review the records of the last obstetric 25 patients in your hospital. Note the haemoglobin levels recorded during pregnancy.*

- *How many had their haemoglobin level or haematocrit measured during the last trimester?*
- *How many were anaemic?*
- *How many were prescribed iron?*

*Do your findings indicate appropriate care of women during pregnancy? If not, talk to senior colleagues about any steps that could be taken to improve their care.*

## Transfusion

It is important to remember that transfusing an anaemic patient does not treat the cause of the anaemia or correct the non-haematological effects of iron deficiency, such as impaired neuromuscular transmission or the effects on fetal stores of iron, until transfused cells release their iron at the end of their life-span. It is therefore essential to investigate the cause of the anaemia to prevent the need for future transfusions.

**Transfusion does not treat the cause of anaemia.**

**Transfusion does not correct the non-haematological effects of iron deficiency.**

The decision to transfuse blood must not be based on the patient's haemoglobin concentration alone, but also on her clinical needs, including:

- Stage of pregnancy
- Clinical condition.

The indications for transfusion in chronic anaemia in pregnancy are broadly divided into three groups:

- Duration of pregnancy less than 36 weeks
- Duration of pregnancy 36 weeks or more
- Elective Caesarean section.

Figure 10.3 on p. 218 shows an *example* of guidelines on transfusion for chronic anaemia in pregnancy from one developing country. Local guidelines should be developed, reflecting the availability and safety of blood and other local factors.

### ACTIVITY 29

*Are any guidelines available in your hospital on the assessment and management of chronic anaemia in pregnancy? Are they accurate and comprehensive? Are they used systematically by all health workers involved in antenatal care?*

*If there are no guidelines or you think they could be improved, prepare some draft guidelines and discuss them with senior colleagues.*

## DURATION OF PREGNANCY LESS THAN 36 WEEKS

1 Haemoglobin 5.0 g/dl or below, even without clinical signs of cardiac failure or hypoxia

2 Haemoglobin between 5.0 and 7.0 g/dl and in the presence of the following conditions:
   - Established or incipient cardiac failure or clinical evidence of hypoxia
   - Pneumonia or any other serious bacterial infection
   - Malaria
   - Pre-existing heart disease, not causally related to the anaemia

## DURATION OF PREGNANCY 36 WEEKS OR MORE

1 Haemoglobin 6.0 g/dl or below

2 Haemoglobin between 6.0 g/dl and 8.0 g/dl and in the presence of the following conditions:
   - Established or incipient cardiac failure or clinical evidence of hypoxia
   - Pneumonia or any other serious bacterial infection
   - Malaria
   - Pre-existing heart disease, not causally related to the anaemia

## ELECTIVE CAESAREAN SECTION

When elective Caesarean section is planned and there is a history of:
   - Antepartum haemorrhage (APH)
   - Postpartum haemorrhage (PPH)
   - Previous Caesarean section

1 Haemoglobin between 8.0 and 10.0 g/dl: establish/confirm blood group and save freshly taken serum for crossmatching

2 Haemoglobin less than 8.0 g/dl: two units of blood should be crossmatched and available

**Note**
These guidelines are simply an example to illustrate how local guidelines might be constructed. The specific indications for transfusion for chronic anaemia in pregnancy should be based on national guidelines, modified as appropriate to the local situation.

### ACTIVITY 29 (continued)

*Once they have been agreed, organize a teaching session for all staff involved in antenatal care.*

*Monitor whether the guidelines are being used correctly and make regular checks on whether they are being followed. Provide any further teaching that may be required and continue to monitor practice.*

## 10.3  Major obstetric haemorrhage

Acute blood loss is one of the main causes of maternal mortality. It may be a result of excessive bleeding from the placental site, trauma to the genital tract and adjacent structures, or both. Increasing parity increases the risk of obstetric haemorrhage. The prompt recognition and correct management of obstetric haemorrhage reduces the number of maternal deaths in pregnancy.

**Major obstetric haemorrhage can be defined as any blood loss occurring in the peripartum period, revealed or concealed, that is likely to endanger life.**

Major obstetric haemorrhage may result in clear signs of hypovolaemic shock, as shown in Figure 10.4. However, because of the physiological changes induced by pregnancy, the woman may demonstrate few signs of hypovolaemia, even though she may have lost a considerable volume of blood. She may then suddenly collapse unless the blood volume is promptly restored.

It is therefore essential to monitor and investigate a patient with an obstetric haemorrhage, even in the absence of signs of hypovolaemic shock, and staff should be ready and prepared to resuscitate, if necessary.

*Figure 10.4: Signs of hypovolaemia in major obstetric haemorrhage*

### Signs of hypovolaemia

- Tachypnoea
- Thirst
- Hypotension
- Tachycardia
- Increased capillary refill time
- Reduced urine output
- Decreased conscious level

### Causes of major obstetric haemorrhage

Serious haemorrhage may occur at any time throughout pregnancy and the puerperium. Figure 10.5 on p. 220 lists the many clinical conditions in which there is a risk of acute blood loss.

### Management of major obstetric haemorrhage

Obstetric bleeding may be unpredictable and massive.

**At term, blood flow to the placenta is approximately 700 ml per minute. The patient's entire blood volume can be lost in 5–10 minutes. Unless the myometrium contracts on the placental site appropriately, rapid blood loss will continue, even after the third stage of labour is complete.**

*Figure 10.5: Causes of acute blood loss in the obstetric patient*

| | |
|---|---|
| **Fetal loss in pregnancy, which may result in**: | ■ Incomplete abortion<br>■ Septic abortion |
| **Ruptured ectopic pregnancy** | ■ Tubal<br>■ Abdominal |
| **Antepartum haemorrhage, which may be caused by**: | ■ Placenta praevia<br>■ Abruptio placentae<br>■ Ruptured uterus<br>■ Vasa praevia<br>■ Incidental haemorrhage from cervix or vagina: e.g. polyps |
| **Traumatic lesions, including**: | ■ Episiotomy<br>■ Laceration of perineum or vagina<br>■ Laceration of cervix<br>■ Ruptured uterus |
| **Primary postpartum haemorrhage: haemorrhage in excess of 500 ml from genital tract, occurring within 24 hours of delivery**<br>Causes include: | ■ Uterine atony<br>■ Retained products of conception<br>■ Traumatic lesions<br>■ Abnormally adherent placenta: e.g. placenta accreta<br>■ Clotting defects<br>■ Acute uterine inversion |
| **Secondary postpartum haemorrhage: any haemorrhage from uterus, after 24 hours and within 6 weeks of delivery**<br>Causes include: | ■ Puerperal sepsis<br>■ Retained products of conception (membranes or placental tissue)<br>■ Tissue damage following obstructed labour (which may involve cervix, vagina, bladder or rectum)<br>■ Breakdown of uterine wound after Caesarean section |
| **Disseminated intravascular coagulation induced by**: | ■ Intrauterine death<br>■ Amniotic fluid embolism<br>■ Sepsis<br>■ Pre-eclampsia<br>■ Abruptio placentae<br>■ Retained products of conception<br>■ Induced abortion<br>■ Excessive bleeding<br>■ Acute fatty liver |

The patient's life may depend on a rapid response from the obstetric team. Every obstetric unit should have a current protocol for major bleeding incidents and all staff should be trained to follow it.

It is essential to take immediate steps to identify:

■ Any cause of antepartum haemorrhage

■ Presence of uterine atony

■ Retained products of conception

■ Lacerations of the genital tract.

Section 13.2: *Initial Assessment and Resuscitation* provides guidance on initial resuscitation during acute blood loss. Figure 10.6 on p. 222 provides more specific guidelines for the management of major obstetric haemorrhage.

### Intraoperative blood salvage

Intraoperative blood salvage may be life-saving in the management of ectopic pregnancy, where blood is clean. See Section 12.4: *Autologous Blood Transfusion*.

### Bi-manual compression of the uterus

The fingers of one hand are pressed into the anterior fornix, as shown in Figure 10.7. If a good pressure is not obtained as the vagina is lax, the whole fist can be inserted.

*Figure 10.7: Bi-manual compression of the uterus*



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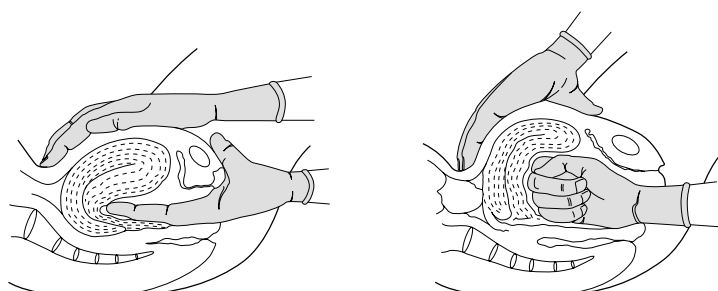
## ACTIVITY 30

*Are any guidelines available in your hospital on the management of major obstetric haemorrhage? Are they accurate and comprehensive? Are they used systematically by all staff involved in obstetric care? Are the necessary drugs readily available and easy to access?*

*If there are no guidelines or you think they could be improved, find out whether any have been produced elsewhere and try to obtain a copy. If none are available, prepare some draft guidelines and discuss them with senior colleagues.*

*Once they have been agreed, organize a teaching session for all obstetric staff.*

*Monitor whether the guidelines are being used correctly and provide any further teaching that may be required.*

*Figure 10.6: Guidelines for emergency management of major obstetric haemorrhage*

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**RESUSCITATE**

1 Administer high concentrations of oxygen.

2 Head down tilt/raise legs.

3 Establish intravenous access with 2 large-bore cannulae (14 g or 16 g).

4 Infuse crystalloid replacement fluids or colloids as rapidly as possible. Restoration of normovolaemia is a priority.

5 Inform blood bank this is an emergency.

   Give Group O negative antibody-screened blood, and/or uncrossmatched group specific blood until fully crossmatched blood is available.

   In areas where the population contains extremely low numbers of women who are Rhesus D negative, use Group O blood.

6 Use a pressure infusion device and warming device, if possible.

7 Call extra staff to help:
   - Senior obstetrician
   - Senior anaesthetist
   - Midwives
   - Nurses
   - Alert the haematologist (if one is available)
   - Ensure assistants are available at short notice.

---

**MONITOR/INVESTIGATE**

1 Send sample to blood bank for matching of further blood, but do not wait for crossmatched blood if there is serious haemorrhage.

2 Order full blood count.

3 Order coagulation screen.

4 Continuously monitor pulse rate and blood pressure.

5 Insert urinary catheter and measure hourly output.

6 Monitor respiratory rate.

7 Monitor conscious level.

8 Monitor capillary refill time.

9 Insert central venous pressure line, if available, and monitor CVP.

10 Continue to monitor haemoglobin or haematocrit.

**STOP THE BLEEDING**

1 Identify the cause.

2 Examine cervix and vagina for lacerations.

3 If retained products of conception and uncontrolled bleeding, treat as DIC (see Figure 10.9).

4 If uterus hypotonic and atonic:
   - Ensure bladder is empty
   - Give IV oxytocin 20 units
   - Give IV ergometrine 0.5 mg
   - Oxytocin infusion (40 units in 500 ml)
   - 'Rub up' fundus to stimulate a contraction
   - Bi-manual compression of the uterus (see Figure 10.7)
   - If bleeding continues, deep intramuscular or intramyometrial prostaglandin (e.g. Carboprost 250 *mg*) directly into uterus (dilute 1 ampoule in 10 ml sterile saline).

5 Consider surgery earlier rather than later.

6 Consider hysterectomy earlier rather than later.

## Disseminated intravascular coagulation

Disseminated intravascular coagulation (DIC) is a cause of massive obstetric haemorrhage. It may be triggered by abruptio placentae, intrauterine death, eclampsia, amniotic fluid embolism and many other causes (see Figure 10.5 on p. 220).

The clinical picture ranges from major haemorrhage, with or without thrombotic complications, to a clinically stable state that can be detected only by laboratory testing (see Figure 10.8).

*Figure 10.8: Laboratory tests for DIC*

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**LABORATORY TESTS**

- Platelet count
- Prothrombin time (PTR or INR)
- Activated partial thromboplastin time (APTT)
- Thrombin time (TT): particularly helpful in establishing presence or absence of DIC
- Fibrinogen: normal concentration at term should be 4.0–6.0 g/L
- Fibrin degradation products (FDPs)

If laboratory tests are available, they will show:
- Reduced coagulation factors (so all coagulation tests are prolonged)
- Low fibrinogen and fibrin degradation products
- Low platelet count: <50 x $10^9$/L
- Fragmented red cells on the blood film

If these tests are not available, the following simple test for DIC can be used.

1 Take 2–3 ml of venous blood into a clean plain *glass* test tube (10 x 75 mm).

2 Hold the tube in your closed fist to keep it warm (i.e. body temperature).

3 After 4 minutes, tip the tube slowly to see if a clot is forming. Then tip it again every minute until the blood clots and the tube can be turned upside down.

The clot will normally form between 4 and 11 minutes but, in DIC, the blood will remain fluid well beyond 15 to 20 minutes.

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**If DIC is suspected, do not delay treatment while waiting for the results of coagulation tests.**

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DIC is always secondary to an underlying process. You should therefore direct treatment towards the precipitating cause. Replacement with blood products is indicated when there is bleeding with acute DIC. The goal is to control the bleeding.

Figure 10.9 on p. 224 summarizes the management of DIC.

Figure 10.9:
Guidelines for the
management of DIC

## MANAGEMENT OF DISSEMINATED INTRAVASCULAR COAGULATION

1 Treat the cause (see Figure 10.5)
   ■ Deliver fetus and placenta
   ■ Evacuate uterus, as indicated for retained or necrotic tissue.

2 Give uterine stimulants to promote contraction: e.g. oxytocin, ergometrine and/or prostaglandin.

3 Use blood products to help control haemorrhage. In many cases of acute blood loss, the development of DIC can be prevented if blood volume is restored with a balanced salt solution: e.g. Hartmann's solution or Ringer's lactate.

   If needed for oxygen perfusion, give the freshest whole blood available (or packed red cells).

4 Avoid the use of cryoprecipitate and platelet concentrates unless bleeding is uncontrollable.

   If bleeding is not controlled and if coagulation tests show very low platelets, fibrinogen, prolonged PT or APTT, replace coagulation factors and platelets with:
   ■ Cryoprecipitate: at least 15 packs, prepared from single donor units, containing 3–4 gm fibrinogen in total.

   If cryoprecipitate is not available, give:
   ■ Fresh frozen plasma (15 ml/kg): 1 unit for every 4–6 units of blood to prevent coagulation defects resulting from use of stored red cell concentrates/suspensions.

   If there is thrombocytopenia, give:
   ■ Platelet concentrates: rarely necessary to control obstetric haemorrhage with DIC in a woman with previously normal platelet production.

   If these blood components are not available, give the freshest whole blood available (ideally no more than 36 hours old).

5 Give broad spectrum antibiotics, as indicated, to cover aerobic and anaerobic organisms.

## Puerperal sepsis and HIV

The HIV epidemic has caused a considerable increase in the incidence of sepsis occurring 1–2 weeks after normal delivery or Caesarean section. Laparotomy for puerperal peritonitis is now a common operation in many developing countries.

Though not haemorrhaging, these patients are invariably anaemic as well as septic and perioperative blood transfusion is frequently indicated.

## 10.4 Haemolytic disease of the newborn (HDN)

For management of the fetus, see Section 11.6: *Neonatal Transfusion.*

Fetal red blood cells can enter the maternal circulation throughout gestation. Under normal circumstances however, feto-maternal bleeding occurs mainly at separation of the placenta during delivery. If the mother lacks blood group antigens from the father that are carried on the fetal red cells, she may produce IgG antibodies against these antigens.

These antibodies may cross the placenta and destroy fetal red cells, particularly in subsequent pregnancies. Maternal antibodies to fetal red cells may also arise as a result of a previous blood transfusion. These will only affect the fetus if its cells carry the offending red cell antigen.

HDN due to ABO incompatibility between mother and infant does not affect the fetus in utero but is an important cause of neonatal jaundice. It is discussed further in Section 11.6: *Neonatal Transfusion.*

HDN due to Rh D incompatibility is an important cause of severe fetal anaemia in countries where a significant proportion of the population is Rh D negative. Rh D-negative mothers develop antibodies to a Rh D-positive fetus, especially when the mother and infant are of the same or compatible ABO blood type. The fetal red cells are haemolysed, causing severe anaemia. The fetus may die in utero or be born with severe oedema, anaemia and jaundice.

Severe neurological damage after birth can be caused by a rapidly rising bilirubin concentration unless this is corrected by exchange transfusion. A skilled specialist team is needed to provide effective antenatal and neonatal care both to the pregnant woman and the newborn.

HDN due to other blood group antibodies can also occur, in particular anti-c (also within the Rh blood group system) and anti-Kell. These two antibodies together with anti-D are the only ones likely to cause significant anaemia in utero requiring fetal transfusion with some very rare exceptions.

### Screening in pregnancy
The ABO and Rh D group of all pregnant women should be determined when they first attend for antenatal care and the mother's serum should also be screened for any IgG antibodies to red cells which can cause HDN or could cause problems in obtaining compatible blood in the event of obstetric haemorrhage.

### Blood group antibodies
If no antibodies are detected at the first antenatal visit, the pregnant woman should have a further antibody check at 28–30 weeks gestation.

If antibodies are detected at an antenatal visit, the levels should be frequently monitored throughout the pregnancy in case they increase. Rising levels may be indicative of HDN developing in the fetus, but do not confirm the blood group of the fetus or the severity of haemolysis.

### Amniotic fluid bilirubin

The level of bilirubin in the amniotic fluid gives an indirect assessment of the severity of fetal haemolysis.

### Ultrasound examination

Ultrasound examination will also show physical indications of developing anaemia before hydrops develops.

### Fetal blood sampling (FBS)

If the techniques are available, fetal blood sampling can, in cases of doubt, identify the blood group and the haemoglobin concentration directly. Transfusion via the umbilical cord (intrauterine transfusion) can then be given to correct anaemia.

## Prevention of Rhesus disease

The prevention of Rhesus disease of the newborn is based on the use of anti-Rh D immunoglobulin in Rh D negative women. Anti-Rh D immunoglobulin prevents the sensitization and production of antibodies in a Rh D negative mother to Rhesus positive red cells that may have entered the maternal circulation.

Approaches to prevention of Rhesus disease include:

- Postpartum administration of anti-Rh D immunoglobulin to those Rh D negative women who give birth to an Rh D positive fetus
- Selective administration of anti-Rh D immunoglobulin antenatally to cover procedures or accidents
- Routine antenatal prophylaxis.

### Postpartum prophylaxis

Postpartum prophylaxis is the most common approach to the prevention of Rhesus disease.

Anti-Rh D immunoglobulin is administered in a dose of 500 mg/IM to a Rh D negative mother within 72 hours of delivery if the fetus is Rh D positive.

A 500 mg dose of anti-Rh D immunoglobulin gives protection for up to 4 ml of fetal red cells. If the Kleihauer or other test is performed and shows more than 4 ml of fetal red cells in the maternal circulation, further anti-Rh D immunoglobulin must be given in a dose of 125 mg/1.0 ml of fetal red cells.

### Selective prophylaxis

If any sensitizing event (see Figure 10.10) occurs during the antenatal period, 250 mg of anti-Rh D immunoglobulin should be administered up to 20 weeks gestation and 500 mg of anti-Rh D from 20 weeks to term.

### Antenatal prophylaxis

Since not all cases of feto-maternal haemorrhage are detected during pregnancy, there is still a risk that maternal sensitization to Rh D positive

**SELECTIVE PROPHYLAXIS IN THE ANTENATAL PERIOD**

- Procedures during pregnancy:
  — Amniocentesis
  — Cordocentesis
  — Chorionic villus blood sampling
- Threatened abortion
- Abortion (particularly therapeutic abortion)
- Antepartum haemorrhage (placenta praevia, abruptio placentae))
- Abdominal trauma
- External cephalic version
- Fetal death
- Multiple pregnancy
- Caesarean section
- Ectopic pregnancy

red cells may occur. For this reason, some countries now recommend that all pregnant women who are Rh D negative should receive routine anti-Rh D IgG prophylaxis.

There are two options for an intramuscular dosage schedule, both of which appear equally effective:

1  500 mg at 28 and 34 weeks.

2  Single larger dose: 1,200 mg early in the third trimester.

### Intrauterine transfusion

If antibodies are detected early in pregnancy, if possible send the patient to a tertiary (referral) centre for evaluation and management.

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**ACTIVITY 31**

*What is the local protocol for following up pregnant women with anti-D antibodies or other antibodies? Is it used appropriately and consistently? Is anti-Rh D immunoglobulin readily available in your obstetric unit?*

*If you feel that the procedures are inadequate or ineffective, talk to the staff to identify ways of improving the follow-up system. Develop a new protocol in conjunction with staff involved in antenatal care and provide any training needed to ensure that it is followed.*

# 11

# Paediatrics & neonatology

## Key points

1   The prevention and early treatment of anaemia is a vital part of the strategy to reduce the need for paediatric transfusion.

2   If hypoxia occurs despite the normal compensatory responses, immediate supportive care is required. If the child continues to be clinically unstable, a transfusion may be indicated.

3   The decision to transfuse should not be based on the haemoglobin level alone, but also on a careful assessment of the child's clinical condition.

4   In patients at risk of circulatory overload, transfusion of red cells is preferable to whole blood. Paediatric blood packs should be used, if available, to decrease exposure to multiple donors.

5   In some conditions, such as haemoglobinopathies (sickle cell disease and thalassaemia) repeated red cell transfusions may be indicated.

6   There are very few indications for transfusing fresh frozen plasma. Inappropriate and ineffective use can transmit HIV and hepatitis and should be avoided.

# Introduction

The incidence of severe anaemia among young children varies widely in different parts of the world. In areas where nutritional deficiencies, malaria, helminthic infections and haemoglobinopathies are prevalent, young children are at high risk of developing severe anaemia. Consequently, blood transfusions are more common in children in these areas. Studies conducted in hospitals in east and west Africa demonstrated that children receive 45–60% of all blood transfusions and that up to 30% of paediatric admissions are for the treatment of severe anaemia.

In many areas, the prevalence of transfusion-transmissible infections such as HIV, hepatitis viruses and Chagas disease, is high among blood donors. The frequent use of blood transfusions in these regions has made transfusion a leading mode of paediatric HIV infection. A study conducted in a large African hospital one year after implementation of HIV testing indicated that 25% of paediatric HIV infections were still attributable to blood transfusion. The appropriate use of safe, quality-assured blood is an important means of reducing the transmission of HIV and other infectious agents.

This section focuses primarily on paediatric anaemia. See Section 3: *Anaemia* and Section 9: *General Medicine* for relevant background material. See also Section 12: *Surgery & Anaesthesia* and Section 13: *Trauma & Acute Surgery* for guidance on surgery, trauma and acute blood loss.

# Learning outcomes

When you have completed this section, you should be able to:

1 Identify the main causes of paediatric anaemia in your locality.

2 Select relevant diagnostic tests from those that are available to you and know how and when to use them to help assess anaemia in children.

3 Recognize the clinical signs of the normal compensatory responses to chronic anaemia in children and the signs of decompensation that may warn of the need to transfuse.

4 Recognize the clinical indications for transfusion and when and how to prescribe it.

5 Suggest ways of improving the use of blood products for paediatric patients in your hospital or clinic.

## 11.1 Paediatric anaemia

Paediatric anaemia is defined as a reduction of haemoglobin concentration or red cell blood volume below the normal values for healthy children.

Normal haemoglobin/haematocrit values differ according to the child's age. The average haemoglobin concentration of full-term infants at birth is approximately 18.0 g/dl. All infants then have a normal 'physiological' decrease in haemoglobin during the first three months of life.

The average haemoglobin concentration in a healthy child from 3 months to 6 years is 11.0–12.0 g/dl. By 7–13 years of age, the average haemoglobin concentration is 13.0 g/dl. The haemoglobin levels of healthy children over 14 years should be the same as those of adults.

According to WHO criteria, infants and children are considered to have anaemia if their haemoglobin concentration falls below the levels shown in Figure 11.1.

*Figure 11.1: Criteria for anaemia in infants and children*

| Age | Haemoglobin concentration (g/dl) |
|---|---|
| Cord blood (term) | ± 16.5 g/dl |
| Neonate: Day 1 | ± 18.0 g/dl |
| 1 month | ± 14.0 g/dl |
| 3 months | ± 11.0 g/dl |
| 6 months–6 years | ± 12.0 g/dl |
| 7–13 years | ± 13.0 g/dl |
| > 14 years | Same as adults, by sex |

### Causes of paediatric anaemia

Anaemia is not in itself a diagnosis, but results from a wide variety of pathological processes. A child with anaemia may be affected by one or more of the causes shown in Figure 11.2. Each should be treated.

**Very young children are at particular risk of severe anaemia. The majority of paediatric transfusions are given to children under three years of age. This is due to a combination of the following factors occurring during a rapid growth phase when blood volume is expanding:**

- **Iron-poor weaning diets**
- **Recurrent or chronic infection**
- **Haemolytic episodes in malarious areas.**

A severely anaemic child with other illness, such as acute infection, has a high risk of mortality. As well as treating the anaemia, it is very important to look for and treat other conditions such as diarrhoeal disease, pneumonia and malaria.

*Figure 11.2: Causes of paediatric anaemia*

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### CAUSES OF PAEDIATRIC ANAEMIA

**Decreased production of normal red blood cells**

- Nutritional deficiencies due to insufficient intake or absorption (iron, $B_{12}$ folate)
- HIV infection
- Chronic disease or inflammation
- Lead poisoning
- Chronic renal disease
- Neoplastic diseases (leukaemia, neoplasms invading bone marrow)

**Increased destruction of red blood cells**

- Malaria
- Haemoglobinopathies (sickle cell disease, thalassaemia)
- G6PD deficiency
- Rh or ABO incompatibility in the newborn
- Autoimmune disorders
- Spherocytosis

**Loss of red blood cells**

- Hookworm infection
- Acute trauma
- Surgery
- Repeated diagnostic blood sampling (particularly among hospitalized infants)

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## Nutritional deficiencies

Even when severe enough to cause anaemia, nutritional deficiencies do not usually result in the need for transfusion. However, they may affect the child's ability to respond to or compensate for a further reduction in haemoglobin concentration due, for example, to acute haemolysis or haemorrhage.

### Iron deficiency anaemia

**Iron deficiency is the most important cause of anaemia worldwide. It is estimated that 50% of children in developing countries have iron deficiency anaemia.**

Iron deficiency anaemia is still highly prevalent in many developing countries. Breast milk contains the ideal nutrients for an infant and breast-feeding is one of the most important ways that a mother can ensure that her infant stays healthy.

Up to the first 4–6 months of life, breast milk is the only food or fluid that an infant requires. Infants who are breast-fed longer than 4–6 months need weaning foods rich in iron and/or vitamin C, such as purees of cooked vegetables and raw fruit. An alternative is dietary supplementation

with iron-fortified formulas or infant foods providing 1 mg/kg/day of elemental iron. High cost limits the use of such products in many areas.

Although local foods can often provide the required levels of iron, iron therapy should always be considered when treating children with anaemia, even if another primary cause, such as malaria or helminthic infection, is identified.

Iron deficiency anaemia can be effectively treated using oral ferrous sulphate 15 mg/kg/day (equivalent to 3 mg/kg/day of elemental iron). This should be continued for 3 months, or at least one month after the child´s haemoglobin concentration returns to normal. Iron injections do not result in a more rapid or superior response than iron administered orally. Iron preparations with other added vitamins or other supplements increase the cost of iron therapy but do not improve efficacy.

It is important to reassess the child's haemoglobin level following treatment, to check whether therapy has been effective.

## Other nutritional deficiencies

Inadequate intake of folate, vitamin $B_{12}$ vitamin C and vitamin A may also contribute to anaemia in children. Nutritional deficiencies are usually caused by inadequate diets and are frequently made worse by infectious processes, such as diarrhoeal diseases, which further compromise the absorption of nutrients.

Where anaemia may be due to multiple causes and specific nutritional deficiencies cannot be diagnosed, the child should be treated for the causes of anaemia that are likely to be common in your environment.

Therapeutic trials of iron, folate and vitamin $B_{12}$, and combinations of these, are indicated. The child's haematological response (haemoglobin or haematocrit, and reticulocyte count, if available) should be monitored.

## Infections causing anaemia

### Malaria

**In endemic areas, malaria is an important cause of severe paediatric anaemia.**

Malaria causes increased red cell destruction and young children who have not yet developed some immunity to the parasite are at particular risk. In addition, continued use of chloroquine in areas with high rates of chloroquine-resistant *P. falciparum* may result in persistent parasitaemia and increased risk of severe anaemia.

Prompt recognition and treatment of the infection and any associated complications may be life-saving since death can occur within 48 hours.

Figure 9.11 on p. 180 summarizes the clinical management of malaria, including indications for transfusion. The treatment regime should take local resistance patterns of malaria into account.

### Other infectious diseases

Chronic or recurrent viral and bacterial infections may result in decreased red cell production. Helminthic and other parasitic infections, such as hookworm, cause increased blood loss.

HIV infection is associated with anaemia, neutropenia, thrombocytopenia and pancytopenia. Treatment of HIV with zidovudine (AZT) is also a cause of anaemia. Treat as normal iron deficiency anaemia.

## Prevention of paediatric anaemia

The most effective and cost-effective means of preventing anaemia-associated mortality and the use of blood transfusion is to prevent severe anaemia by:

■ Early detection of anaemia

■ Effective treatment and prophylaxis of the underlying causes of anaemia

■ Clinical monitoring of children with mild and moderate anaemia.

Strategies to prevent anaemia include:

1 Prevention of iron deficiency in pregnancy by routine supplementation with oral iron tablets.

2 Maternal education at all maternal-child health visits, including:

■ Hygiene (sanitation, hand washing, use of clean or boiled water)

■ Nutrition (foods rich in iron and ascorbic acid)

■ Use of bednets (particularly insecticide-impregnated)

■ Prevention and management of fever illness.

3 Checking of haemoglobin/haematocrit at clinic attendances, particularly when malaria is suspected.

4 Early identification of anaemia and initiation of effective treatment.

5 Iron fortification of foods.

6 Prompt and effective treatment of malaria at the primary health care level and community-based measures, such as malaria control.

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### ACTIVITY 32

*What programmes for the prevention of severe paediatric anaemia exist in your locality? How effective are they?*

*Identify the people who would need to be involved in planning new strategies for the prevention of anaemia and talk to them about how they might be strengthened.*

## 11.2 The management of paediatric anaemia

### Clinical assessment

Clinical assessment of the degree of anaemia should be supported by a reliable determination of haemoglobin or haematocrit.

### Laboratory investigations

An inexpensive, reliable and rapid method for screening children for anaemia in the outpatient setting is essential. The simple diagnostic tests shown in Figure 11.3 can be very helpful in defining the cause of anaemia. See also Section 9.1: *Anaemia*.

*Figure 11.3: Laboratory investigation of paediatric anaemia*

| Laboratory test | Purpose |
| --- | --- |
| Haemoglobin concentration or haematocrit (packed cell volume) | Diagnose presence of anaemia and response to treatment |
| Blood film | Diagnose malaria and help determine the type of anaemia |
| Stool smear | Evaluate presence of parasitic infection |
| Reticulocyte count | Increased reticulocyte level suggests haemolytic anaemia |

### ACTIVITY 33

**Case study**

*A two-year old male has just been admitted to your hospital ward from the outpatient department with a diagnosis of 'anaemia'. Because the outpatient department was so busy, the patient was admitted without any laboratory testing.*

*1  What family and medical history would you elicit?*

*2  What elements of the physical examination would you assess?*

*3  What causes of anaemia are prevalent in your own locality that would need to be investigated?*

### Management of paediatric anaemia

#### Compensated anaemia

The body normally compensates for chronic anaemia by the mechanisms described in Section 3: *Anaemia*. In children, as in adults, this often means that very low haemoglobin levels can be tolerated with few or no symptoms, provided anaemia develops slowly over weeks or months.

The management of a clinically stable child with compensated anaemia requires:

1 Supportive care.

2 Monitoring for clinical decompensation or worsening of anaemia.

3 Treatment of the underlying cause of the anaemia.

4 Recognition, investigation and treatment of other causes of illness and fever.

Figure 11.4 shows normal vital signs, by age.

*Figure 11.4: Normal vital signs, by age*

| Age | Respiratory rate | Heart rate at rest | |
|---|---|---|---|
| | Normal range | Normal range | Average |
| Newborn (term) | 40 ± 15 | 70–190 | 125 |
| 1–11 months | 31 ± 8 | 120–160 | 80 |
| 1–5 years | 25 ± 4 | 110–130 | 80 |
| 6–10 years | 21 ± 3 | 90–110 | 70 |
| 11–15 years | 19 ± 3 | 80–110 | 60 |
| 16+ years | 17 ± 3 | 75–95 | 55 |

## ACTIVITY 34

### Case study (continued)
*The mother brought the child to the clinic because of a 2-day history of fever and diarrhoea. On physical examination, you find:*
- *Patient is alert and in no apparent distress*
- *Pale conjunctiva and palmar creases*
- *Heart rate: 150*
- *Respiratory rate: 30*
- *Blood pressure: 90/60*
- *Temperature: 38.6°C*
- *Brisk capillary refill*
- *No grunting, flaring of nostrils or intercostal recession*
- *No cyanosis*
- *Liver is not palpable*
- *Mucous membranes are dry.*

*1 What investigations would you request?*

*2 What would you do next?*

### Decompensated anaemia
Many factors can precipitate decompensation in an anaemic child and lead to life-threatening hypoxia of tissues and organs. Figure 11.5 summarizes the clinical features and possible causes of decompensation.

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*Figure 11.5: Clinical
features of compensated
and decompensated
anaemia in children*

**Compensated anaemia**

A child with well-compensated anaemia may have:

■ Raised respiratory rate

■ Increased heart rate

but will be:

■ Alert

■ Able to drink or breastfeed

■ Normal, quiet breathing, with abdominal movement

■ Minimal chest movement

**Causes of decompensation**

1 Increased demand for oxygen:

   ■ Infection

   ■ Pain

   ■ Fever

   ■ Exercise

2 Further reduction in oxygen supply

   ■ Acute blood loss

   ■ Pneumonia

**Decompensated anaemia**

**Early signs of decompensation**

■ Laboured, rapid breathing with intercostal, subcostal and suprasternal retraction/recession (respiratory distress)

■ Increased use of abdominal muscles for breathing

■ Flaring of nostrils

■ Difficulty with feeding

**Signs of acute decompensation**

■ Forced expiration ('grunting')/respiratory distress

■ Mental status changes

■ Diminished peripheral pulses

■ Congestive cardiac failure

■ Hepatomegaly

■ Poor peripheral perfusion (capillary refill greater than 2 seconds)

A child with these clinical signs needs urgent treatment as there is a high risk of death due to insufficient oxygen carrying-capacity.

Immediate supportive treatment is needed if the child is severely anaemic with:

- Respiratory distress
- Difficulty in feeding
- Congestive cardiac failure
- Mental status changes.

Severely anaemic children are, contrary to common belief, rarely in congestive heart failure, and dyspnoea is due to acidosis. The sicker the child, the more rapidly transfusion needs to be started.

Figure 11.6 summarizes the management of severe (decompensated) paediatric anaemia.

*Figure 11.6: Management of severe (decompensated) anaemia in children*

**SUPPORTIVE TREATMENT**

1  Position the child and airway to improve ventilation: e.g. sitting up.

2  Give high concentrations of oxygen to improve oxygenation.

3  Take blood sample for crossmatching, haemoglobin estimation and other relevant tests.

4  Control temperature or fever to reduce oxygen demands:
   - Cool by tepid sponging
   - Give antipyretics: e.g. paracetamol.

5  Treat volume overload and cardiac failure with diuretics: e.g. frusemide, 2 mg/kg by mouth or 1 mg/kg intravenously to a maximum dose of 20 mg/24 hours.

   The dose may need to be repeated if signs of cardiac failure persist.

6  Treat acute bacterial infection or malaria.

**REASSESSMENT**

1  Reassess before giving blood as children often stabilize with diuretics, positioning and oxygen.

2  Clinically assess the need for increased oxygen-carrying capacity.

3  Check haemoglobin concentration to determine severity of anaemia.

## Transfusion

Prospective studies of severely anaemic children in Africa showed that transfusion was only associated with improved survival in children with a haemoglobin below 5–6 g/dl and clinical signs of cardiac or respiratory compromise.

Irrespective of transfusion, however, children with severe chronic anaemia are at high risk of death. In a study of hospitalized children in Kenya, 30% of children with haemoglobin concentrations below 5.0 g/dl died within two months of hospitalization.

> **The decision to transfuse should not be based on the haemoglobin level alone, but also on a careful assessment of the child's clinical condition.**

The need for blood transfusion must be assessed with great care in each individual child, taking into account not only the haemoglobin concentration or haematocrit, but also the clinical condition of the patient.

Both laboratory and clinical assessment are essential. A child with moderate anaemia and pneumonia may have more need of increased oxygen-carrying capacity than a child with a lower haemoglobin who is clinically stable.

If the child is stable, is monitored closely and is treated effectively for other conditions, such as acute infection, oxygenation may improve without the need for transfusion.

Figure 11.7 shows the situations in which transfusion is generally indicated for children with severe (decompensated) anaemia.

*Figure 11.7: Indications for transfusion of children with severe (decompensated) anaemia*

---

### INDICATIONS FOR TRANSFUSION

1 Haemoglobin concentration of 4 g/dl or less (or haematocrit 12%), whatever the clinical condition of the patient.

2 Haemoglobin concentration of 4–6 g/dl (or haematocrit 13–18%) if any the following clinical features are present:
- Clinical features of hypoxia:
  — Acidosis (usually causes dyspnoea)
  — Impaired consciousness
- Hyperparasitaemia (>20%).

---

Figure 11.8 outlines the procedure for paediatric transfusion.

### ACTIVITY 35

**Case study (continued)**
*The nurse contacts you at 02.00 hours because the patient is having difficulty breathing. You come in to find the child with:*
- *Laboured breathing*
- *Heart rate: 190*
- *Temperature: 40°C*
- *Capillary refill: 2 seconds*
- *Liver: 3 cm below the costal margin*
- *Haemoglobin concentration: 4.8 g/dl*
- *Rales in both lung fields.*

*1 What may have caused this patient to decompensate?*

*2 What would you do next?*

*Figure 11.8: Procedure for paediatric transfusion*

**TRANSFUSION PROCEDURE**

1 If transfusion is needed, give sufficient blood to make child clinically stable.

 5 ml/kg of red cells or 10 ml/kg whole blood are usually sufficient to relieve acute shortage of oxygen carrying-capacity. This will increase haemoglobin concentration by approximately 2–3 g/dl unless there is continued bleeding or haemolysis.

2 Use a paediatric blood pack and a device to control the rate and volume of transfusion (see Figures 11.9 and 11.10).

3 Although rapid fluid infusion increases the risk of volume overload and cardiac failure, give the first 5 ml/kg of red cells to relieve the acute signs of tissue hypoxia. Subsequent transfusion should be given slowly: e.g. 5 ml/kg of red cells over 1 hour.

4 Give frusemide 1 mg/kg by mouth or 0.5 mg/kg by slow IV injection to a maximum dose of 20 mg/kg if patient is likely to develop cardiac failure and pulmonary oedema. Do not inject it into the blood pack.

5 Monitor during transfusion for signs of:
 ■ Cardiac failure
 ■ Fever
 ■ Respiratory distress
 ■ Tachypnoea
 ■ Hypotension
 ■ Acute transfusion reactions
 ■ Shock
 ■ Haemolysis (jaundice, hepatosplenomegaly)
 ■ Bleeding due to DIC.

6 Re-evaluate the patient's haemoglobin or haematocrit and clinical condition after transfusion.

7 If the patient is still anaemic with clinical signs of hypoxia or a critically low haemoglobin level, give a second transfusion of 5–10 ml/kg of red cells or 10–15 ml/kg of whole blood.

**PRECAUTIONS**

1 The volume of fluid in a transfusion of whole blood may precipitate or worsen cardiac failure. 5 ml/kg of red cells gives the same oxygen-carrying capacity as 10 ml/kg of whole blood and contains less plasma protein and fluid to overload the circulation. A red cell transfusion is preferable to whole blood for a patient at risk of circulatory overload.

2 Reduce the risk of bacterial contamination
 ■ Never re-use a blood pack that has been entered
 ■ Keep the blood pack at 2°C–6°C before transfusion
 ■ Complete the transfusion within 4 hours of commencing it
 ■ Never start to transfuse blood from a pack that has been out of the refrigerator for longer than 30 minutes

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*Four hours later, the transfusion is running, the patient is looking more comfortable and vital signs have stabilized, except for a slight tachycardia. It's late, you're very tired and looking forward to lying down. The nurse tells you that she hasn't given a blood transfusion for some time and she doesn't seem comfortable monitoring the transfusion without instruction.*

*3 What would you tell her to monitor during the transfusion?*

*4 What conditions should prompt her to contact you?*

*Later that day, the patient is looking much better:*
- *Perfusion: good*
- *Conjunctiva: pink*
- *Vital signs: stable*
- *Temperature: 38°C*
- *Two diarrhoeal stools since morning.*

*5 Would you request any other diagnostic tests. If yes, what?*

## Special procedures for paediatric and neonatal transfusion

Infants and children require small transfusions and, wherever possible, specially-designed equipment and appropriate dosage units should be provided and used.

Never re-use an adult unit of blood for a second paediatric patient because of the risks of bacteria entering the pack during the first transfusion and proliferating while the blood is out of the refrigerator.

### Paediatric blood packs

As the actual amount of blood transfused per transfusion episode is small, a unit of blood can be divided into multiple satellite packs of approximately 50–100 ml each, allowing repeat transfusions to be given to the same patient from a single donation unit.

This method can help to reduce the risk of infection since the patient receives blood from only a single individual. Fresh frozen plasma can also be prepared in paediatric blood packs with the same potential benefit. Figure 11.9 shows an example of a paediatric blood pack.

*Figure 11.9: Paediatric blood pack*
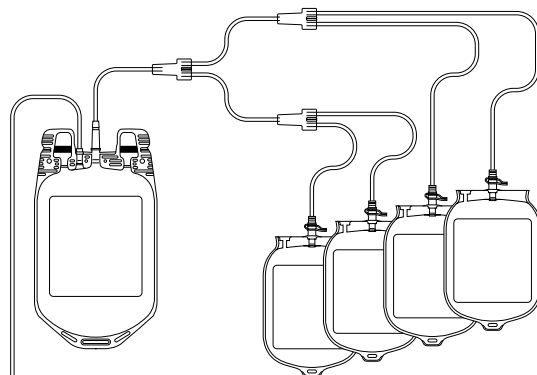
### Infusion devices

Infants and small children require small volumes of fluid and can easily suffer circulatory overload if the infusion is not well-controlled.

If possible, therefore, use an infusion device that makes it easy to control the rate and volume of infusion. Two examples are illustrated in Figure 11.10.

*Figure 11.10: Examples of paediatric infusion devices*
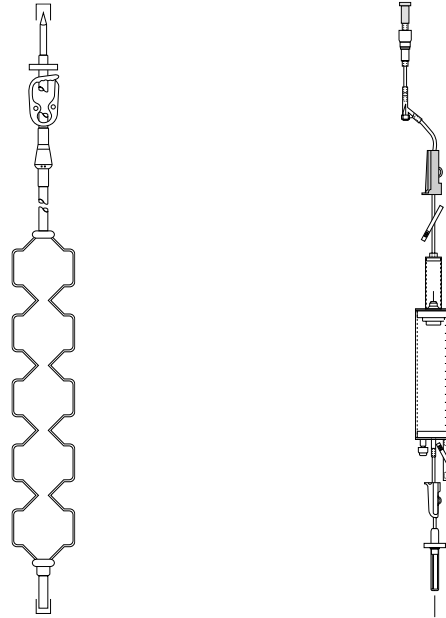


### After the acute phase

Continue treatment of anaemia after transfusion to help haematological recovery. The patient should be discharged with the appropriate medications (see Section 9: *General Medicine*) for the treatment of anaemia. Malaria prophylaxis and iron therapy should be routine in areas where these conditions are common.

## 11.3  Paediatric transfusion in special clinical situations

### Sickle cell disease and thalassaemia

For more detail, see Section 9.8: *Genetic Disorders of Haemoglobin.*

### Sickle cell disease

Children with sickle cell disease do not develop symptoms until they are six months old. By this age, most of the fetal haemoglobin (HbF) has been replaced with sickle haemoglobin (HbS). Transfusions are not necessary to correct the haemoglobin concentration because the oxygen dissociation curve is shifted to the right, oxygen affinity is low and oxygen delivery to the tissues is adequate in the absence of sickling crises (see Figure 2.12). Beyond six months, sicklers have long periods of well-being, punctuated by crises.

The main aim of management is to prevent sickle crises by the measures shown in Figure 11.11.

---

**PREVENTION OF SICKLE CRISIS**

1  Give life-time prophylaxis of bacterial infection:
   Penicillin V by mouth

|  |  |
|---|---|
| Year 1 | 62.5 mg/day |
| 1–3 years | 125 mg/day |
| >3 years | 250 mg/day |

2  Vaccinate against *pneumococcal* infection.

3  Treat infection early.

4  Give folic acid: 1–5 mg/day.

4  Maintain hydration by oral, nasogastric or intravenous fluids during episodes of vomiting and/diarrhoea.

**TREATMENT OF SICKLE CRISIS**

1  Maintain hydration by oral, nasogastric or intravenous fluids.

2  Give supplementary oxygen by mask to maintain adequate oxygenation.

3  Give prompt and effective pain relief.

4  Give antibiotics:
   - If causative organism is not identified, give a broad-spectrum antibiotic: e.g. amoxicyllin 125–500 mg/3 times/day
   - If causative organism is identified, give the most specific antibiotic available.

5  Transfusion or exchange transfusion.

---

Exchange transfusion is indicated for treatment of vaso-occlusive crisis and priapism that does not respond to fluid therapy alone (see Figure 11.16 on p. 249 for calculations for exchange transfusion).

### Thalassaemia

Thalassaemia is one of the most important public health problems in the Mediterranean, Middle East and South-East Asia. It is very difficult to maintain these children in optimum health and the treatment is often not available where the disease is most prevalent.

Children with thalassaemia, unlike those with sickle cell disease, cannot maintain oxygenation of tissues and the haemoglobin has to be corrected by regular transfusion. Also unlike sickle cell disease, the anaemia results from ineffective erythropoiesis rather than haemolysis.

Some children with less severe forms of the disease (see Section 9.8: *Genetic Disorders of Haemoglobin*) can survive untreated, but they will have chronic severe anaemia with characteristic mongoloid faces and skeletal deformities due to expansion of the bone marrow.

In more severe forms, survival is prolonged to the late teens and early twenties by regular transfusion. The problem then becomes one of iron overload derived from the transfused red cells which leads to endocrine and liver problems and ultimately to cardiac failure, which is the major cause of death.

Iron overload can only be prevented by regular treatment with chelating agents such as desferrioxamine, the most efficient, which has to be given parenterally (see p. 196 and Figure 9.23). There are also some recently developed oral agents which have not yet proved to be as effective as desferrioxamine.

In developed countries, the usual approach is the screening of populations and identification of couples at risk, together with the option of termination of affected pregnancies. It is essential that these skills, particularly in counselling and education, should be brought to populations where the carrier rate and the disease is frequent.

## Malignant disorders

See Section 9: *General Medicine.* Leukaemia and other malignancies can cause anaemia and thrombocytopenia. If a child needs repeated transfusions after a period of months, the diagnosis of a malignancy should be considered. A full blood count is the first essential laboratory test.

Treatment with chemotherapy often causes severe anaemia and thrombocytopenia. These infants may need repeated blood and platelet transfusions for several weeks during and after chemotherapy until bone marrow recovery occurs.

## 11.4  Bleeding and clotting disorders

See Section 9.9: *Bleeding Disorders and Transfusion.*

Disorders of haemostasis should be suspected in a child with a history of bleeding problems. Children with coagulation problems (such as haemophilia) may suffer episodes of internal bleeding into joints and muscles, as well as large bruises and haematomas. Children with low platelet counts or defective platelet function are more likely to have petechiae, multiple small bruises (eccymoses) and mucous membrane bleeding (mouth, nose bleeds, gastrointestinal).

## Congenital disorders

See Section 9.10: *Congenital Bleeding and Clotting Disorders* for haemophilia A, haemophilia B and von Willebrand disease.

## Acquired disorders
### Vitamin K deficiency in the neonate
A transient decrease in vitamin K-dependent coagulation factors (II, VII, IX, X) occurs normally in the neonate 48–72 hours after birth, with a gradual return to normal levels by 7–10 days of age. Prophylactic administration

of 1 mg of oil-soluble vitamin K IM at birth prevents haemorrhagic disease of the newborn in full-term and most premature infants. However, despite prophylaxis, some premature infants and some full-term newborns may develop HDN. Infants of mothers taking anticonvulsant drugs (phenobarbitol and phenytoin) are at increased risk. An affected infant has a prolonged PT and PTT, while platelets and fibrinogen levels are normal.

Bleeding as a result of deficiencies of vitamin K-dependent coagulation factors should be treated with 1–5 mg vitamin K intravenously. Transfusion of fresh frozen plasma may be required to clinically correct a significant bleeding tendency.

Late onset disease (more than one week after birth) is often associated with malabsorption of vitamin K. This may be due to intestinal malabsorption and liver disease. It can be treated with water-soluble vitamin K orally.

## 11.5  Thrombocytopenia

A normal neonate's platelet count is 80–450 x $10^9$/L. After one week of age, it reaches adult levels of 150–400 x $10^9$/L. Platelet counts below this level are considered to be thrombocytopenia.

The causes of thrombocytopenia in infants and children are shown in Figure 11.12.

*Figure 11.12: Causes of thrombocytpenia in infants and children*

---

**CAUSES OF THROMBOCYTOPENIA**

- Congenital defects in platelet production or function
- Prematurity (less than 1500 gm)
- Maternal antibodies crossing the placenta and acting against the fetal platelets (neonatal allo-immune thrombocytopenia: NAIT)
- Infections: congenital rubella, CMV, toxoplasmosis, syphilis, neonatal bacterial infections
- Idiopathic thrombocytopenia purpura
- Haemolytic uraemic syndrome
- Drug-induced (phenytoin, carbamazepine, sulfonamides, cotrimoxazole, chloramphenicol)

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### Treatment of thrombocytopenia

The patient with thrombocytopenia due to bleeding typically has petechiae, retinal haemorrhages, bleeding gums and bleeding from venepuncture sites.

The treatment of thrombocytopenia varies according to the cause. Idiopathic thrombocytopenic purpura is usually self-limited, but may be treated with gammaglobulin and corticosteroids. Blood or platelet transfusion may be indicated if life-threatening haemorrhage occurs.

Other acquired disorders should be managed with supportive care, stopping drugs that may be causing the disorder and treating infection. For immune

neonatal thrombocytopenia, intravenous immunoglobulin may be helpful. If available, the transfusion of compatible platelets (e.g. washed platelets collected from the infant's mother) is effective.

### Platelet transfusion for bleeding due to thrombocytopenia
The goal of platelet therapy is to control or stop the bleeding. The clinical response is more important than the platelet count.

Figure 11.13 gives guidelines on the dosage and administration of platelet concentrates.

*Figure 11.13: Guidelines on the transfusion of platelet concentrate in infants and children*

**TRANSFUSION OF PLATELET CONCENTRATES**

**Dose units**: Platelet concentrate from 1 donor unit (450 ml) of whole blood contains about $60 \times 10^9$/L

| Dosage | | Volume | Platelet concentrate |
|---|---|---|---|
| Up to 15 kg | 1 platelet concentrate | 30–50 ml* | $60 \times 10^9$ /L |
| 15–30 kg | 2 platelet concentrate | 60–100 ml | $120 \times 10^9$ /L |
| >30 kg | 4 platelet concentrate | 120–400 ml | $240 \times 10^9$ /L |

* For small infants, the blood bank may remove part of the plasma before transfusion

**ADMINISTRATION OF PLATELET CONCENTRATES**

1 Transfuse immediately on receiving the platelet concentrates.

2 Do not refrigerate.

3 Use a fresh, standard blood infusion set, primed with normal saline.

### Prophylactic platelet transfusion
Many clinicians adopt similar thresholds for neonates as for adults. In a stable thrombocytopenic patient without evidence of bleeding, platelet transfusion is indicated when the platelet count falls below $10 \times 10^9$/L, the point where spontaneous bleeding is more likely to occur. Some clinicians favour a higher threshold of between $20 \times 10^9$/L in a patient who is stable. If the patient is feverish or infected, a threshold of $20–50 \times 10^9$/L may be appropriate.

## 11.6  Neonatal transfusion

There are few clinical trials to provide a firm basis of evidence for clinical guidelines on neonatal transfusion. However, national guidelines have been developed in a number of countries, based on current practice and the opinions of expert clinicians. These may help in the development of local practice guidelines which should reflect local resources and patterns of disease.

## Practice in specialist institutions

Techniques for intrauterine transfusion are now available in specialist neonatal units. Intravascular transfusion of blood components to the fetus is possible from as early as 18 weeks gestation. Exchange transfusions for Rhesus haemolytic disease of the newborn are avoided by effective prophylaxis programmes (see Section 10.4: *Haemolytic Disease of the Newborn*). Very low birth weight (VLBW) babies need component therapy to manage the unique complications of prematurity.

These techniques may be available only in specialist neonatal units.

In developed countries, newborn infants in special care baby units (SCBU) are more likely to be transfused than any other patients. In these units, repeated blood sampling for laboratory tests is a common cause of anaemia that requires 'top-up' red cell transfusion.

Figure 11.14 shows the blood products commonly used in the management of neonatal disorders.

*Figure 11.14: Factors in selecting blood components for nenatal transfusion*

| PRODUCT | INDICATION | SPECIAL REQUIREMENTS FOR NEONATES |
|---|---|---|
| Whole blood | Exchange transfusions for HDN | Freshest blood available (less than 5 days after collection), free of relevant alloantibodies |
| Red cells | 'Top-up' transfusion to raise haemoglobin concentration in symptomatic chronic anaemia, often due to blood sampling in sick premature infants | Small dose unit (paediatric pack from a single donation) to minimize exposure to different donors |
| Specially-processed cellular components | Intrauterine transfusion:<br>■ Risk of GvHD may be greater in premature infants<br>■ Risk of GvHD *is* greater if donor is a blood relative | Avoid graft-versus-host disease:<br>■ Irradiate: 250 Gy<br>■ Do not use donation from blood relative |
| Avoid CMV infection in recipient | CMV infection or reactivation may complicate the management of sick infants. CMV may be transmitted by blood or infection reactivated by allogenic leucocyte transfusion | Use CMV-negative donations<br>***and/or***<br>Leucocyte-depleted component |

## Replacement fluids

The choice of fluids for the resuscitation of infants with septic shock or shock of unknown cause after delivery remains essentially a clinical preference as there are no adequate clinical trials. Many clinicians prefer to use albumin solutions.

If crystalloids are used, particularly in sepsis, about three times the equivalent volume of albumin 4.5% (20 ml/kg) is needed to maintain blood pressure. Some clinicians consider that such large crystalloid infusions risk causing volume overload, hyperchloraemia and pulmonary oedema.

In contrast, a number of reports show that neither albumin nor fresh frozen plasma are superior to crystalloids as a replacement fluid to correct hyperviscosity or polycythaemia in an otherwise healthy neonate. Many neonatologists take the view that albumin infusions should continue to be used in the management of septic shock in neonates and, in some cases, to correct polycythaemia.

## Exchange transfusion

**kernicterus**: Damage to the basal ganglia of the brain, caused by fat-soluble bilirubin. Causes spasticity. Can be caused by haemolytic disease of the newborn.

The main indication for exchange transfusion of a neonate is to prevent neurological complications **(kernicterus)** caused by a rapidly-rising unconjugated bilirubin concentration. This occurs because the immature liver cannot metabolise the breakdown products of haemoglobin. The underlying cause is usually haemolysis (red cell destruction) due to antibodies to the baby's red blood cells.

### Jaundice

Haemolytic disease is the most common and clinically important cause of neonatal jaundice. In many countries where the main cause of haemolytic disease of the newborn was Rh D incompatibility between mother and fetus, the need for exchange transfusion has decreased in recent years because of the following developments.

1   Prevention of Rhesus haemolytic disease of the newborn by the administration of anti-Rh D immunoglobulin to the mother (see Section 10.4: *Haemolytic Disease of the Newborn*).

2   Prevention of kernicterus in less severe jaundice by phototherapy of the infant.

If exchange transfusion is needed, a group O blood unit should be used that does not carry the antigen against which the maternal antibody is directed:

- For HDN due to anti-D: use group O Rh D negative
- For HDN due to anti-Rh c: use group O Rh D positive that does not have the c antigen ($R_1R_1$, CDe/CDe).

For more information on these red cell antigens and antibodies, see *Safe Blood and Blood Products. Module 3: Blood Group Serology* (WHO, 1994).

An exchange transfusion of about two times the neonate's blood volume (about 170 ml/kg: see Figure 11.15 on p. 248) is most effective to reduce bilirubin and restore the haemoglobin level. This can usually be carried out

| Age | Total blood volume |
| --- | --- |
| Premature infants | 100 ml/kg |
| Term newborns | 85–90 ml/kg |
| Greater than 1 month | 80 ml/kg |
| Greater than 1 year | 70 ml/kg |

with one unit of whole blood. A unit of whole donor blood will normally have a haematocrit of 37–45%, which is more than adequate for neonatal needs. The oxygen delivery to tissues of adult haemoglobin HbA is much more efficient than that of the neonate's own fetal haemoglobin (HbF). There is no need to adjust the haematocrit of the unit: if it is raised to 50–60%, there is a risk of polycythaemia and its consequences, especially if the neonate is also receiving phototherapy.

### Guidelines on neonatal exchange transfusion

Figure 11.16 on pp. 249–250 gives guidelines on calculations and the procedure for neonatal exchange transfusion, precautions and possible complications.

## Haemolytic disease of the newborn due to materno-fetal ABO incompatibility (ABO HDN)

See also Section 10.4: *Haemolytic Disease of the Newborn.*

In many parts of the world, particularly in South America, Africa and Asia, HDN due to ABO incompatibility is the most important cause of severe neonatal jaundice and is the most frequent indication for exchange transfusion in the newborn. The diagnosis of ABO HDN is usually made in infants born at term who are not severely anaemic, but who develop jaundice during the first 24 hours of life. ABO incompatibility does not present in utero and never causes hydrops.

Characteristically, the mother is group O with IgG anti-A or anti-B antibodies that can cross the placenta into the fetal blood; the fetal blood group is A or B. The direct antiglobulin test is usually positive with good quality antiglobulin (Coombs') reagents. The blood film shows increased numbers of spherocytes. Treatment should be initiated promptly as these infants can develop jaundice severe enough to lead to kernicterus.

The neonate should receive phototherapy and supportive treatment. Blood units for exchange transfusion should be Group O, with low-titre anti-A and anti-B with no IgG lysins. A two-volume exchange (approximately 170 ml/kg) is most effective in removing bilirubin. If the bilirubin rises again to dangerous levels, a further two-volume exchange should be performed.

### Indirect (unconjugated) hyperbilirubinaemia

The relationship between elevation in serum indirect bilirubin levels and kernicterus among healthy term infants is uncertain. Healthy term infants may tolerate serum bilirubin levels of 25 mg/dl. Infants are more prone to the toxic effects of bilirubin if they have:

## CALCULATIONS FOR NEONATAL EXCHANGE TRANSFUSION

**Partial exchange transfusion for treatment of symptomatic polycythaemia**

Replace removed blood volume with normal saline or 5% albumin

Volume to be exchanged (ml):

$$\text{Estimated blood volume} \times \frac{\text{(Patient's Hct – desired Hct)}}{\text{Patient's haematocrit}}$$

**Two-volume red cell exchange transfusion for treatment of sickle cell crisis and neonatal hyperbilirubinaemia**

Replace calculated blood volume with whole blood or red cells suspended in 5% human albumin

Volume to be exchanged (ml):

$$\text{Estimated blood volume} \times \frac{\text{(Patient's haematocrit (\%)} \times 2)}{\text{Haematocrit of transfused unit (\%)*}}$$

| | * Haematocrit |
|---|---|
| Whole blood | 35–45% |
| Red cell concentrate | 55–75% |
| Red cell suspension | 50–70% |

## TRANSFUSION PROCEDURE

1  Give nothing by mouth to the infant during and at least 4 hours after exchange transfusion. Empty stomach if the infant was fed within 4 hours of the procedure.

2  Closely monitor vital signs, blood sugar and temperature. Have resuscitation equipment ready.

3  For a newborn, umbilical and venous catheters inserted by sterile technique may be used (blood is drawn out of the arterial catheter and infused through the venous catheter). Alternatively, two peripheral lines may be used.

4  Prewarm blood only if a quality-controlled blood warmer is available. Do **not** improvise by using a water bath.

5  Exchange 15 ml increments in a full-term infant and smaller volumes for smaller, less stable infants. Do not allow cells in the donor unit to form a sediment.

6  Withdraw and infuse blood 2–3 ml/kg/minute to avoid mechanical trauma to the patient and donor cells.

7  Give 1–2 ml of 10% calcium gluconate solution IV slowly for ECG evidence of hypocalcaemia (prolonged Q-Tc intervals). Flush tubing with normal saline before and after calcium infusion. Observe for brachycardia during infusion.

8  To complete two-volume exchange, transfuse 170 ml/kg for a full-term infant and 170–200 ml/kg for a pre-term infant.

9  Send the last aliquot drawn to the laboratory for determination of haemoglobin or haematocrit, blood smear, glucose, bilirubin, potassium, calcium, and group and match.

10  Prevent hypoglycaemia after exchange transfusion by continuing infusion of a glucose-containing crystalloid.

**PRECAUTIONS**

1  When exchange transfusion is performed to treat haemolytic disease of the newborn, the transfused red cells must be compatible with the mother's serum since the haemolysis is caused by maternal IgG antibodies that cross the placenta and destroy the fetal red cells. The blood should therefore be crossmatched against the mother's serum using the antiglobulin method that detects IgG antibodies.

2  There is no need to adjust the haematocrit of donor whole blood.

**COMPLICATIONS OF EXCHANGE TRANSFUSION**

1  Cardiovascular
  - Thromboemboli or air emboli
  - Portal vein thrombosis
  - Dysrhythmias
  - Volume overload
  - Cardiorespiratory arrest

2  Fluid and electrolyte disturbances
  - Hyperkalaemia
  - Hypernatremia
  - Hypocalcaemia
  - Hypoglycaemia
  - Acidosis

3  Haematological
  - Thrombocytopenia
  - Disseminated intravascular coagulation
  - Over-heparinization (may use 1 mg of protamine per 100 units of heparin in the donor unit)
  - Transfusion reaction

4  Infection
  - Hepatitis
  - HIV
  - Sepsis

5  Mechanical
  - Injury to donor cells (especially from overheating)
  - Injury to vessels
  - Blood loss

- Acidosis
- Prematurity
- Septicaemia
- Hypoxia
- Hypoglycaemia
- Asphyxia
- Hypothermia
- Hypoproteinaemia
- Exposure to drugs that displace bilirubin from albumin
- Haemolysis.

The goal of therapy is to prevent the concentration of indirect bilirubin from reaching neurotoxic levels. Figure 11.17 shows suggested maximum indirect serum bilirubin concentrations (mg/dl) in pre-term and term infants.

*Figure 11.17: Suggested maximum indirect serum bilirubin concentrations (mg/dl) in pre-term and term infants*

| Birthweight (gm) | Uncomplicated | Complicated* |
|---|---|---|
| <1000 | 12–13 | 10–12 |
| 1000–1250 | 12–14 | 10–12 |
| 1251–1499 | 14–16 | 12–14 |
| 1500–1999 | 16–20 | 15–17 |
| >2000/term | 20–22 | 18–20 |

\* Complicated refers to presence of risk factors associated with increased risk of kernicterus, listed above

Figure 11.18 provides guidelines on the management of indirect hyperbilirubinaemia.

*Figure 11.18: Management of neonates with indirect hyperbilirubinaemia*

### MANAGEMENT OF NEONATES WITH INDIRECT HYPERBILIRUBINAEMIA

1  Treat underlying causes of hyperbilirubinaemia and factors that increase risk of kernicterus (sepsis, hypoxia, etc.).

2  Hydration.

3  Initiate phototherapy at bilirubin levels well below those indicated for exchange transfusion. Phototherapy may require 6–12 hours before having a measurable effect.

4  Monitor bilirubin levels (see Figure 11.17: Suggested maximum indirect serum bilirubin concentrations (mg/dl) in pre-term and term infants).

5  Give exchange transfusion when indirect serum bilirubin levels reach maximum levels (see Figure 11.16: Calculations for neonatal exchange transfusion).

6  Continue to monitor bilirubin levels until a fall in bilirubin is observed in the absence of phototherapy.

Exchange transfusion is necessary when, after phototherapy, indirect bilirubin levels approach those considered critical during the first two days of life and when a further rise is anticipated. Exchange transfusion may not be necessary after the fourth day in term infants or the seventh day in pre-term infants, when hepatic conjugating mechanisms become more effective and a fall in bilirubin can be anticipated.

An exchange transfusion should be at least one blood volume. Exchange transfusion should be repeated if the indirect bilirubin level is not maintained at a safe level.

## Red cell transfusion

The majority of transfusions are given to pre-term infants who are very unwell.

1 To replace blood samples taken for laboratory testing.

2 To treat hypotension and hypovolaemia.

3 To treat the combined effect of anaemia of prematurity and blood loss due to sampling.

Neonates do not have an effective erythropoietin response to anaemia. A baby who requires one blood transfusion will therefore often need to be transfused again within a period of days.

The first transfusion will increase the concentration of HbA, shift the oxygen dissociation curve to the right and lower the oxygen affinity of the circulating haemoglobin (see Figure 2.12). This will depress red cell production further and increase the delay before erythropoiesis is reactivated.

## Specific clinical situations (neonatal)

### Critically ill neonates

1 Record the volume of each blood sample taken. If 10% of the blood volume is removed over 24–48 hours, it should be replaced with packed red cells.

2 These sick neonates may need to have their haemoglobin level maintained in the range of 13–14 g/dl to ensure adequate tissue perfusion.

### Convalescent very low birth weight babies

1 Measure the haemoglobin at weekly intervals. The haemoglobin level will drop 1 g/dl per week on average.

2 Do not transfuse on the basis of the haemoglobin level alone. Although haemoglobin levels of 7 g/dl or less require investigation, transfusion may not be required.

### Neonates with late anaemia

It may be necessary to consider transfusing an infant if anaemia is thought to be the cause of:

1   Poor weight gain.

2   Fatigue while feeding.

3   Tachypnoea and tachycardia.

4   Other signs of decompensation.

## Minimizing the risks and increasing the effective use of neonatal transfusion

The following practical measures reduce the risks of neonatal transfusion and increase its effectiveness.

1   For an infant who is likely to need several 'top-up' transfusions over a period of days or weeks, select red cells in additive solution and prepare paediatric packs from a single unit of blood.

2   Reduce blood loss from diagnostic sampling:
   ■   Avoid unnecessary repeat compatibility testing
   ■   Avoid non-essential laboratory tests
   ■   Where possible, the laboratory should use micro-methods and should select suitable small sample tubes.

3   Avoid transfusing blood donated by blood relatives as the risk of graft-versus-host disease is increased.

### Recombinant erythropoietin

Recombinant erythropoietin is expensive, but a safe and effective stimulator of red cell production. Its role in managing neonatal anaemia is still under evaluation.

## Neonatal allo-immune thrombocytopenia

Neonatal allo-immune thrombocytopenia (NAIT) is a cause of intrauterine cerebral haemorrhage. Screening and prevention programmes are under evaluation. Transfusion of washed, irradiated platelets may help the infant at a period of dangerous thrombocytopenia.

## Fresh frozen plasma

Plasma has the same risk as whole blood of transmitting HIV, hepatitis B, hepatitis C and other transfusion-transmissible infections. Plasma should only be used for specific clinical indications for which it is proved to be effective. These indications are:

1   The correction of clinically important bleeding tendencies due to deficiency of plasma clotting factors – and only when a safer, virus-inactivated product is unavailable.

2   For infusion or exchange transfusion treatment of the rare conditions of thrombotic thrombocytopenic purpura or haemolytic-uraemic syndrome.

Neonatal and paediatric specialists often use plasma for a variety of other reasons but none of these have been proved to be effective by adequate clinical trials.

The inappropriate and ineffective transfusion of plasma is inexcusable. It places the patient at risk of serious transfusion-transmitted infections without offering clinical benefits.

## Polycythaemia and hyperviscosity

Partial exchange transfusion is often used for treatment of symptomatic polycythaemia. Clinicians do not agree about which infants are likely to suffer adverse effects in the neonatal period. Controversy centres on the need to screen all neonates within hours of birth and whether or not early treatment of symptomless babies has any effect on the incidence of late manifestations, such as motor coordination and intellectual performance.

A central venous haematocrit of 65% or more is the generally-accepted screening test. It is strongly recommended that in infants with suspected hyperviscosity, haematocrit values are measured by microcentrifugation since viscosity tests are unavailable to most physicians. Falsely low values for haematocrit may be given by automated haematology analysers.

The formula used to calculate the volume of blood to be exchanged is:

$$\text{Estimated blood volume* x} \frac{(\text{Observed haematocrit} - \text{desired haematocrit})}{\text{Observed haematocrit}}$$

* Assuming the neonatal blood volume to be 85 ml per kg.

The volume exchange is usually around 20 ml per kg. The exchange transfusion should be performed in 10 ml aliquots.

## Suggested practical approach

Healthy term infants appear to be at little risk of polycythaemia and hyperviscosity and need not be screened routinely. In those identified polycythaemic babies with mild or no symptoms, keeping the baby warm and well-hydrated is probably all that is required to prevent microthromboses in the peripheral circulation

All infants with significant symptoms should undergo partial exchange with 4.5% albumin to bring the haematocrit down to a safe level of 50–55%.

### ACTIVITY 36

*Are any guidelines available in your hospital on neonatal transfusion? Are they accurate and comprehensive? Are they used systematically by all health workers involved in neonatal care?*

*If there are no guidelines or you think they could be improved, prepare some draft guidelines and discuss them with senior colleagues.*

*Once they have been agreed, organize a teaching session for all staff involved in neonatal care. Monitor whether the guidelines are being used correctly and make regular checks on whether they are being followed. Provide any further teaching that may be required and continue to monitor practice.*

# 12

# Surgery & anaesthesia

## Key points

1 Most elective surgery does not result in sufficient blood loss to require a blood transfusion.

2 The careful assessment and management of patients prior to surgery will reduce patient morbidity and mortality. This should include:
- Diagnosis, investigation and treatment of anaemia
- Treatment and optimizing coexisting cardiorespiratory disorders
- Detection of coagulation and platelet disorders preoperatively.

3 There is rarely justification for the use of preoperative blood transfusion simply to facilitate elective surgery.

4 Operative blood loss can be significantly reduced by:
- Meticulous surgical technique
- Use of posture
- Use of vasoconstrictors
- Use of tourniquets
- Anaesthetic techniques
- Use of antifibrinolytic drugs.

5 A significant degree of surgical blood loss can often safely be incurred before blood transfusion becomes necessary, provided that the loss is replaced with intravenous replacement fluids to maintain normovolaemia.

6 Autologous transfusion is an effective technique in both elective and emergency surgery to reduce or eliminate the need for homologous blood. However, it should only be considered where it is anticipated that the surgery will result in sufficient blood loss to require homologous transfusion.

7 Blood loss and hypovolaemia can still develop in the postoperative period. Vigilant monitoring of vital signs and the surgical site is an essential part of patient management.

## Introduction

Blood transfusion practices in elective surgery have been shown to be remarkably inconsistent and it is common to find wide variations in blood usage for the same procedure. These differences are not only apparent between countries, but also between hospitals in the same country and even between different theatre teams in the same hospital. Many factors can account for this, including variations in the medical condition of patients presenting for surgery, differences in surgical or anaesthetic techniques, differing attitudes and concerns of both clinicians and patients towards blood transfusion and differences in the cost and availability of blood.

In addition, the decision to transfuse a surgical patient can often be a difficult judgement. There is no one sign or measurement, including a single haemoglobin estimation, which accurately predicts that the oxygen supply to the tissues is becoming inadequate. It is necessary to rely on the careful assessment of a variety of factors and clinical signs, which themselves may be masked or attenuated by the effects of general anaesthesia. Furthermore, patients' individual responses to blood loss vary considerably, often as a result of age or underlying cardiorespiratory disease.

Most elective or planned surgery does not result in sufficient blood loss to require a blood transfusion.

However, there are clearly some procedures during which significant blood loss can be expected and there is always the potential for unexpected blood loss to occur during any type of surgery.

The purpose of this section is to demonstrate how it is often possible to safely minimize blood usage in elective surgery, or to avoid blood transfusion altogether. It also provides guidance on when a blood transfusion is indicated.

## Learning outcomes

When you have completed this section, you should be able to:

1   Assess and treat patients with anaemia, cardiorespiratory and coagulation disorders prior to elective surgery in order to minimize both the potential risks of surgery and the need for blood transfusion.

2   Correctly apply techniques to reduce operative blood loss.

3   Correctly assess the patient's requirement for fluid replacement or blood transfusion.

4   Use autologous blood transfusion techniques appropriately.

5   Maintain appropriate care in the postoperative period.

# 12.1  Patient selection and preparation

Reducing patient morbidity and mortality is a key objective of any surgical or anaesthetic practice. The careful assessment and management of patients prior to surgery can do much to secure this aim. It is the responsibility of the surgeon and anaesthetist who initially assess the patient to ensure he or she is adequately prepared for surgery and anaesthesia. Communication between the surgeon and anaesthetist is vital before, during and after surgery.

## Classification of surgery

It is common to classify surgery into major or minor cases, based on the type of surgical procedure. However, this is not always a reliable guide and there are several other factors which should influence your decision as to the complexity of the case. These are shown in Figure 12.1.

*Figure 12.1: Classification of surgery*

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**Factors affecting classification of surgery**

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- Experience of the surgeon or anaesthetist
- Duration of surgery
- Condition of the patient
- Anaesthetic technique
- Anticipated blood loss
- Availability of 'back-up': e.g. senior assistance, blood supplies, recovery facilities, intensive care unit

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## Anaemia and surgery

### The risks of anaemia

It is common to detect anaemia in patients presenting for elective surgery. Although the compensatory mechanisms described in Section 3: *Anaemia* often enable patients to tolerate relatively low haemoglobin levels, it is essential to investigate and treat the cause of anaemia in the period leading up to elective surgery. There are sound clinical reasons for doing this.

1   The presence of anaemia in a patient is not in itself a diagnosis, but merely an indication that an underlying pathology exists. Treating that pathology or the associated anaemia will improve the general condition of the patient requiring surgery.

2   The compensatory responses to anaemia which normally preserve the oxygen supply to the tissues, may not always be sufficient to maintain oxygenation during surgery. In an already anaemic patient, a further reduction in the oxygen-carrying capacity due to surgical blood loss or the cardiorespiratory depressant effects of anaesthetic agents may lead to a significant impairment of oxygen delivery and decompensation can occur.

3   Ensuring an adequate haemoglobin preoperatively will reduce the likelihood of a blood transfusion becoming necessary if expected or unexpected blood loss occurs during surgery.

## Treating anaemia

Nutritional deficiencies, particularly of iron and folate, together with parasitic and helminthic infestations significantly contribute to the prevalence of anaemia in a population. These and other common causes of anaemia are straightforward to identify and treat. In addition, the medical treatments are often inexpensive and carry little or no risk to the patient.

The screening and treatment of anaemia should therefore be a key component of the preoperative management of elective surgical patients, even if this means postponing surgery until the haemoglobin is adequate. (See Sections 9, 10 and 11 for guidelines on the treatment of anaemia).

**There is little justification for the use of a preoperative blood transfusion simply to facilitate elective surgery, other than in exceptional circumstances.**

## Haemoglobin levels and surgery

The judgement on what is an adequate preoperative haemoglobin level for patients undergoing elective surgery must be made for each individual patient. It should be based on the clinical condition of the patient and the nature of the procedure being planned.

Many practitioners will accept a threshold haemoglobin level of approximately 7–8 g/dl in a well-compensated and otherwise healthy patient presenting for minor surgery. However, a higher preoperative haemoglobin level will be needed in the following circumstances.

1 Where the patient has symptoms or signs indicating that there is inadequate compensation for the anaemia and the oxygen supply to the organs and tissues is insufficient, such as:
   - Evidence of angina
   - Increasing dyspnoea
   - Dependent oedema
   - Frank cardiac failure as a result of the reduced oxygen-carrying capacity of blood.

2 Where the patient may have coexisting cardiorespiratory disease which may limit his or her ability to further compensate for a reduction in oxygen supply due to operative blood loss or the effects of anaesthetic agents. For example:
   - Significant ischaemic heart disease
   - Obstructive airways disease.

3 When major surgery is planned and it is anticipated that operative blood loss may be more than 10 ml/kg.

The presence of one or more of these factors in anaemic patients undergoing surgery has been shown to increase morbidity and mortality. It is therefore unjustified to subject patients to unnecessary risk in elective surgery when it is often a simple process to correct the anaemia preoperatively.

## Preoperative haemoglobin level

Adequate haemoglobin concentration should be ensured before elective surgery if:

1  There is inadequate compensation for the anaemia.

2  There is significant coexisting cardiorespiratory disease.

3  Major surgery or significant blood loss is expected.

## Cardiorespiratory disorders

Coexisting disease processes in a patient, and particularly those affecting the cardiac or respiratory systems, can have a significant influence over oxygen delivery. Treating and optimizing these disorders preoperatively will:

- Improve the overall oxygen supply to the tissues
- Reduce the need for transfusion at operation.

## Coagulation disorders

Undiagnosed and untreated disorders of coagulation in surgical patients may result in excessive operative blood loss, uncontrolled haemorrhage and death of the patient.

Coagulation and platelet disorders can be classified as follows:

- Acquired coagulation disorders, arising as a result of disease or drug therapy: for example, liver disease, aspirin-induced platelet dysfunction or disseminated intravascular coagulation
- Congenital coagulation disorders, for example, haemophilia A or B, and von Willebrand disease.

Although a specific diagnosis may require detailed investigation, the history alone is nearly always sufficient to alert the physician to a potential problem. It is therefore essential that a careful preoperative enquiry is made into any unusual bleeding tendency of the patient and his or her family, together with a drug history.

If possible, obtain expert haematological advice before surgery in all patients with an established coagulation disorder.

### Surgery and acquired coagulation disorders

Bleeding during or after surgery is sometimes a very difficult problem to evaluate. It may simply be caused by a problem following surgical intervention, in which case re-operation may be necessary. Alternatively, it may be due to any one of a number of haemostatic problems, of which the following are the most common:

- Massive transfusion: replacement of blood losses greater than 10 ml/kg, leading to dilution of coagulation factors and platelets
- DIC, which causes:
  — Thrombocytopenia
  — Hypofibrinogenaemia.

Following elective surgery, patients are often treated with heparin to reduce the risk of deep vein thrombosis and pulmonary embolism. This should be considered in assessing a patient with postoperative bleeding.

Figure 12.2 gives a simple guide to the evaluation of bleeding in surgical patients. See also Section 7: *Adverse Effects of Transfusion*.
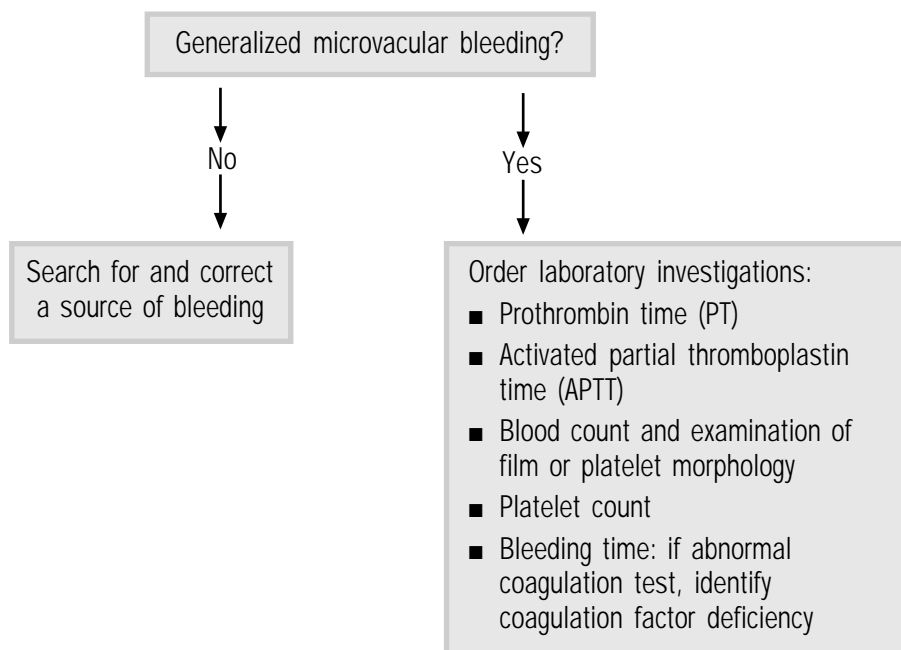
## Surgery and congenital coagulation disorders

Congenital coagulation disorders are discussed more fully in Section 9: *General Medicine*. See Figure 9.26 on p. 202 for the prophylactic measures that can be used to allow surgery to be performed safely in these patients, depending on the local availability of the various drug and blood products.

Start treatment at least 1–2 days prior to surgery and continue for 5–10 days, depending on the risk of postoperative bleeding. Regular assessment of the patient in the perioperative period is essential to detect unexpected bleeding.

## Surgery and thrombocytopenia

A variety of disorders may give rise to a reduced platelet count. Prophylactic measures and the availability of platelets for transfusion are invariably required for surgery in this group of patients; for example, splenectomy in a patient with idiopathic thrombocytopenic purpura (ITP) (see Section 9).

Platelet transfusions should be given if there is clinical evidence of severe **microvascular bleeding** and the platelet count is below 50–100 x $10^9$/L.

## Surgery and the anticoagulated patient

In patients who are being treated with anticoagulants (oral or parenteral) , the type of surgery and the thrombotic risk should be taken into account when planning anticoagulant control perioperatively.

For most surgical procedures, the INR and/or APTT ratio should be less than 2.0 before surgery commences. Figure 12.3 provides guidance on how this can be achieved.

## Other drugs and bleeding

There are several drugs which interfere with platelet function, but the commonest are aspirin and the non-steroidal anti-inflammatory drugs (NSAIDs). Stopping these drugs 10 days prior to surgery can significantly reduce operative blood loss.

**microvascular bleeding**: Bleeding from the mucous membranes; oozing from catheter sites that persists after application of pressure; continuous oozing from surgical wounds and raw tissue surfaces; generalized petechiae or increasing size of eccymoses (bruises). Indicates severe haemostatic failure.

*Figure 12.3: Preparation of
the anticoagulated patient
for surgery*

## PATIENTS FULLY ANTICOAGULATED WITH WARFARIN

### Elective surgery

1   Stop warfarin three days preoperatively and monitor INR daily.

2   Give heparin by infusion or subcutaneously, if required.

3   Stop heparin 6 hours preoperatively.

4   Check INR and APTT ratio immediately prior to surgery.

5   Commence surgery if INR and APTT ratio are <2.0.

6   Restart warfarin as soon as possible postoperatively.

7   Restart heparin at the same time and continue until INR is in the
therapeutic range.

### Emergency surgery

1   Give vitamin K, 0.5–2.0 mg by slow IV infusion.

2   Give fresh frozen plasma, 15 ml/kg. This dose may need to be repeated
to bring coagulation factors to an acceptable range.

3   Check INR immediately prior to surgery.

4   Commence surgery if INR and APTT ratio are <2.0.

## PATIENTS FULLY ANTICOAGULATED WITH HEPARIN

### Elective surgery

1   Stop heparin 6 hours preoperatively.

2   Check APTT ratio immediately prior to surgery.

3   Commence surgery if APTT ratio is <2.0.

4   Restart heparin as soon as appropriate postoperatively.

### Emergency surgery

Consider reversal with IV protamine sulphate. 1 mg of protamine neutralizes
100 iu heparin.

### PATIENTS RECEIVING LOW-DOSE HEPARIN

It is rarely necessary to stop low-dose heparin injections, used in the
prevention of deep vein thrombosis and pulmonary embolism prior to
surgery.

## ACTIVITY 37

*Are any guidelines available in your hospital on the assessment and
management of patients prior to surgery? Are these available to clinicians
who refer patients for surgery? Are they used systematically by all staff?
Are the necessary drugs readily available and easy to access?*

*If there are no guidelines or you think they could be improved, find out whether any have been produced elsewhere, perhaps by the Ministry of Health, and try to obtain a copy. If none are available, prepare some draft guidelines and discuss them with senior colleagues.*

*Once they have been agreed, organize a teaching session for all relevant staff. Monitor whether the guidelines are being used correctly and provide any further teaching that may be required.*

## 12.2  Techniques to reduce operative blood loss

Operative blood loss can be significantly reduced by the following techniques during surgery:

- Meticulous surgical technique
- Use of posture
- Use of vasoconstrictors
- Use of tourniquets
- Anaesthetic techniques
- Use of antifibrinolytic drugs.

### Surgical technique

The training, experience and care of the surgeon performing the procedure is the most crucial factor in reducing operative blood loss. The importance of surgical technique, meticulous attention to bleeding points, appropriate use of diathermy, if available, and the use of haemostatic, e.g. collagen, felt, or warmed packs, cannot be overstated.

### Posture

Positioning the patient to encourage free unobstructed venous drainage at the operative site can not only reduce venous blood loss, but will also improve the operating conditions.

The level of the operative site should be a little above the level of the heart. The Trendelenburg position (head down) is the most appropriate for lower limb, pelvic and abdominal procedures. For head and neck surgery, the head-up posture should be adopted.

If a large vein above the level of the heart is opened to the atmosphere during surgery, there is the potential for air to be drawn into the circulation causing an air embolus. This complication is rare and can be avoided with careful surgery. However, you should bear this in mind when making postural changes to the patient.

### Vasoconstrictors

Infiltration of the skin at the site of surgery with a vasoconstrictor can help to minimize skin bleeding once an incision is made. In addition, if the vasoconstrictor also contains local anaesthetic, some contribution to postoperative analgesia can be expected from this technique.

Bleeding from skin graft donor sites, desloughed areas and tangential excisions can also be reduced by direct application of swabs soaked in a saline solution containing a vasoconstrictor.

One of the most widely-used and effective vasoconstrictors is the catecholamine adrenaline (epinephrine), although several other preparations are available. It should not be necessary to exceed a total dose of 0.1 mg of adrenaline in an adult, equivalent to 20 ml of 1 in 200 000 strength or 40 ml of 1 in 400 000 strength.

Because of the profound systemic actions of both vasoconstrictors and local anaesthetics, do not exceed the recommended dose levels and ensure that these drugs remain at the site of incision and are not injected into the circulation.

Of all the anaesthetic inhalational agents, halothane is the most likely to cause cardiac dysrhythmias when a vasoconstrictor is being used.

Vasoconstrictors should not be used in areas where there are end arteries, such as fingers, toes and penis.

## Tourniquets
When operating on extremities, blood loss can be reduced considerably by the application of a limb tourniquet. To take full advantage of this effect and to provide a bloodless operative field, the limb should first be exsanguinated using a bandage or elevation prior to inflation of a suitable sized, well-fitting tourniquet. The inflation pressure of the tourniquet should be approximately 100–150 mmHg above the systolic blood pressure of the patient.

Towards the end of the procedure, it is good practice to deflate the tourniquet temporarily to identify missed bleeding points and ensure complete haemostasis before finally closing the wound.

Tourniquets should not be used on patients with sickle cell disease or trait (HbSS, HbAS, HbSC) because of the risk of precipitating sickling, or in patients where the blood supply to the limb is already tenuous: for example, severe atherosclerosis.

## Anaesthetic techniques
The anaesthetic technique can make an important contribution to reducing operative blood loss.

Episodes of hypertension and tachycardia due to sympathetic overactivity should be prevented by ensuring adequate levels of anaesthesia and analgesia. Similarly, coughing, straining and patient manoeuvres which increase venous blood pressure should be avoided.

Excessive carbon dioxide retention, or hypercarbia, can cause widespread vasodilatation which will increase operative blood loss. It should therefore be avoided, if necessary by controlling ventilation. The appropriate use of regional anaesthesia, particularly epidural and subarachnoid anaesthetic techniques, can significantly reduce operative blood loss in a variety of surgical procedures.

The use of hypotensive anaesthesia can undoubtedly reduce operative blood loss. However, because of the risks associated with this technique, it is not recommended for the inexperienced anaesthetist or where comprehensive monitoring facilities are unavailable.

## Antifibrinolytic and other drugs

Several drugs, including aprotinin and tranexamic acid, which inhibit the fibrinolytic system of blood and encourage clot stability, have been used in an attempt to reduce operative blood loss. The indications and benefits of these drugs in surgery are not yet clearly defined.

Desmopressin (DDAVP) has been shown to be of value in preventing excessive bleeding when used in haemophiliacs and some acquired bleeding disorders, such as cirrhosis of the liver. It acts by increasing the production of Factor VIII.

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### ACTIVITY 38

*Evaluate the techniques to reduce operative blood loss used in your hospital and check them against those recommended above. Prepare some draft guidelines if none exist or you think they could be improved and discuss them with senior colleagues.*

*Once they have been agreed, organize a teaching session for all anaesthetic and surgical staff. Monitor whether the guidelines are being used correctly and provide any further teaching that may be required.*

---

## 12.3  Fluid replacement and transfusion

Provided that surgical blood loss is replaced with crystalloid or colloid fluids to maintain normovolaemia, a significant degree of loss can often safely be incurred before a blood transfusion becomes necessary. This practice is well-tolerated in the majority of patients, despite the reduction in oxygen-carrying capacity that occurs. The reasons for this are as follows:

1  The supply of oxygen in a healthy, resting adult with a normal haemoglobin concentration is 3–4 times greater than that required by the tissues for metabolism. A safety margin therefore exists between oxygen supply and demand, and this allows some reduction in haemoglobin to occur without serious consequences.

2  When significant blood loss occurs, the fall in the oxygen-carrying capacity of blood together with the reduction in blood volume invoke several compensatory responses which help to maintain the supply of oxygen to the tissues (see Section 3: *Anaemia*).

3  These compensatory mechanisms are facilitated and tissue oxygenation is even better preserved if the normal blood volume is maintained with fluid replacement therapy as blood loss occurs. In particular, ensuring normovolaemia allows the cardiac output to increase, thereby sustaining the oxygen supply in the face of a falling haemoglobin (see the oxygen flux equation in Figure 2.13).

4   The replacement of blood loss with crystalloid or colloid fluids also results in dilution of the blood components, or haemodilution. This reduces the viscosity of blood which improves capillary blood flow and cardiac output, enhancing the supply of oxygen to the tissues.

**A key objective is to ensure normovolaemia at all times during the course of a surgical procedure.**

## Estimating blood loss

In order to maintain blood volume accurately, it is essential to continually assess surgical blood loss throughout the procedure. Using Figure 12.4, an adult weighing 60 kg would have a blood volume equal to 70 x 60, which is 4200 ml.

*Figure 12.4: Calculating blood volume*

| Blood volume | |
| --- | --- |
| Neonates | 85–90 ml/kg body weight |
| Children | 80 ml/kg body weight |
| Adults | 70 ml/kg body weight |

Accurate measurement of blood loss is especially important in neonatal and infant surgery where only a very small amount lost can represent a significant proportion of blood volume. However, whatever methods are used there is always a tendency to underestimate blood loss.

Guessing how much blood is on a swab is a very inaccurate method of estimating blood loss. It is important to weigh swabs while still in their dry state and in their sterile packs and then to weigh the blood-soaked swabs as soon as they are discarded. Subtract the dry weight of any unused swabs from the total dry weight. Then subtract the weight of the blood-soaked swabs to estimate the blood loss (1 ml of blood weighs approximately 1 g).

It is straightforward to assess the amount of blood lost into graduated drains or suction bottles. However if the bottles are ungraduated, the loss can again be calculated by weighing, provided that you know the empty weight of the bottle.

It is also important to estimate blood loss into surgical drapes, together with that pooling beneath the patient and onto the floor.

Remember to note the volume of any irrigation or washout fluids that are used during surgery and which have contaminated swabs or suction bottles. This volume needs to be subtracted from the measured blood loss to arrive at a final estimate.

## Monitoring for signs of hypovolaemia

Many of the autonomic and central nervous system signs of significant hypovolaemia can be masked by the effects of general anaesthesia. The

classic picture of the restless or confused patient who is hyperventilating (air-hunger), in a cold sweat and complaining of thirst is not a presentation under a general anaesthetic. However, many of these signs will still be apparent in the patient undergoing local or regional anaesthesia and in those recovering from general anaesthesia.

Patients under a general anaesthetic may show only very few signs that hypovolaemia is developing. Pallor of the mucous membranes, a reduced pulse volume and tachycardia may be the only initial signs. As volume depletion progresses, a fall in blood pressure will occur and the capillary refill time will be delayed; more than 2 seconds for colour to return to finger pad or nail-bed after it has been briefly compressed is abnormal. In addition, desaturation detected by oximetry or the development of cyanosis, ischaemic or rhythm changes on an ECG, and a falling urine output, may also occur. If capnography is used, hypovolaemia may be manifested by a reduction in end-tidal carbon dioxide as pulmonary perfusion falls. Central venous pressure will fall in hypovolaemia and, if temperature monitoring is used, there will be a increase in the difference between the core and peripheral temperature as vasoconstriction occurs.

See Figure 12.5 for features to be monitored for signs of hypovolaemia.

*Figure 12.5: Monitoring for signs of hypovolaemia*

**Monitoring for hypovolaemia**

- Colour of mucous membranes
- Respiratory rate
- Level of consciousness
- Urine output
- ECG
- CVP, if available and appropriate

- Heart rate
- Capillary refill time
- Blood pressure
- Peripheral temperature
- Saturation of haemoglobin

## Replacement of blood loss

Two methods, shown in Figure 12.6, are commonly used to estimate the volume of surgical blood loss that can be expected (or allowed) to occur in a patient before a blood transfusion becomes necessary:

- Percentage method
- Haemodilution method.

It must be stressed that these methods are simply guides to fluid replacement and transfusion. During surgery, the decision to transfuse will ultimately need to be based on the careful assessment of other factors, in addition to the volume of blood loss. These include:

- Rate of blood loss (actual and anticipated)
- Patient's clinical response to blood loss and fluid replacement therapy
- Signs indicating inadequate tissue oxygenation.

You must therefore be prepared to move away from any guidelines and transfuse at an earlier stage if the situation warrants it.

*Figure 12.6: Methods of estimating allowable blood loss*

### PERCENTAGE METHOD OF ESTIMATING ALLOWABLE BLOOD LOSS

This method simply involves estimating the allowable blood loss as a percentage of the patient's blood volume.

1 Calculate the patient's blood volume. See Figure 12.4: Calculating blood volume.

2 Decide on the percentage of blood volume that could be lost but safely tolerated, provided that normovolaemia is maintained. For example, if 10% were chosen, the allowable blood loss in a 60 kg patient would be 420 ml. If 20% of blood volume were chosen, up to 840 ml could be lost before transfusion became necessary.

3 During the procedure, replace blood loss up to the allowable volume with crystalloids or colloid fluids to maintain normovolaemia.

4 If the allowable blood loss volume is exceeded, further replacement should be with transfused blood.

### HAEMODILUTION METHOD OF ESTIMATING ALLOWABLE BLOOD LOSS

This method involves estimating the allowable blood loss by judging the lowest haemoglobin (or haematocrit) that could be safely tolerated by the patient as haemodilution with fluid replacement takes place:

1 Calculate the patient's blood volume and perform a preoperative haemoglobin (or haematocrit) level.

2 Decide on the lowest acceptable haemoglobin (or haematocrit) that could be safely tolerated by the patient.

3 Apply the following formula to calculate the allowable volume of blood loss that can occur before a blood transfusion becomes necessary.

$$\text{Allowable blood loss} = \text{Blood volume} \times \frac{\text{(Preoperative Hb – Lowest Acceptable Hb)}}{\text{(Average of Preoperative \& Lowest Acceptable Hb)}}$$

4 During the procedure, replace blood loss up to the allowable volume with crystalloid or colloid fluids to maintain normovolaemia.

5 If the allowable blood loss volume is exceeded, further replacement should be with transfused blood.

### Precautions

Whichever method is used to determine the point at which transfusion becomes necessary, a judgement is required to decide on either the percentage of blood volume that can be safely lost or the lowest haemoglobin (or haematocrit) that can be tolerated. This judgement must be based on the clinical condition of each individual patient. The ability of a patient to compensate for a reduction in oxygen supply will be limited by:

- Evidence of cardiorespiratory disease
- Treatment with drugs such as beta-blockers
- Pre-existing anaemia
- Increasing age.

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A healthy adult may be able to sustain losses of up to 30% of blood volume, or a haemoglobin of approximately 9 g/dl, without requiring a blood transfusion, provided that blood volume is maintained. However, an anaemic patient with a history of ischaemic heart disease losing 20% of blood volume, or haemodiluted below 10 g/dl, may decompensate despite maintaining normovolaemia.

It is therefore vital to ensure that either the percentage loss or the lowest acceptable haemoglobin reflect what the patient can safely tolerate. Figure 12.7 gives some guidance.

*Figure 12.7: Guide to estimating allowable blood loss before transfusion, assuming blood volume is maintained*

| Method | Healthy | Average clinical condition | Poor clinical condition |
|---|---|---|---|
| **Percentage method**<br>Acceptable loss of blood volume | 30% | 20% | Less than 10% |
| **Haemodilution method**<br>Lowest acceptable<br>haemoglobin (or Hct) | 9 g/dl<br>(Hct 27) | 10 g/dl<br>(Hct 30) | 11 g/dl<br>(Hct 33) |

## Choice of replacement fluid

As you have seen in Section 4: *Replacement Fluids*, there is some debate about the choice of fluid used for the initial replacement of blood loss in order to maintain blood volume. Crystalloid replacement fluids, such as normal saline or Ringer's lactate solution, leave the circulation more rapidly than colloids. For this reason, at least three times the volume of blood lost should be used: that is, 3 ml of crystalloid to every 1 ml of blood loss. If colloid fluids are used, the amount infused should be equal to the volume of blood lost.

## Maintaining normovolaemia

It is essential that blood volume is maintained at all times. Even if the allowable blood loss is exceeded and no blood for transfusion is readily available, you should continue to infuse crystalloid replacement fluids or colloids to ensure normovolaemia.

## Avoiding hypothermia

A fall in body temperature of a patient can cause several unwanted effects. These include:

- Impairment of the normal compensatory responses to hypovolaemia
- Increase in operative bleeding
- Increase in oxygen demand postoperatively as normothermia become re-established. This may lead to hypoxia
- Increase in wound infection.

For these reasons, every effort should be made to maintain a normal body temperature in the perioperative period, including the warming of intravenous fluids (see Figure 12.8). Remember that heat loss occurs more readily in children.

| Patient | Fluids |
|---------|--------|
| ■ Cover with blankets | ■ Store fluids in warming cabinet |
| ■ Use warming mattress (37°C) | ■ Immerse fluid bags in warm water |
| ■ Humidify anaesthetic gases | ■ Use heat exchangers on infusion set |

*Figure 12.8: Avoiding hypothermia*

### Planning

Whatever the method used to estimate the volume of allowable blood loss, make any necessary calculations prior to surgery and have a clear idea of the volumes involved at the outset.

Staff caring for patients should be aware that a degree of haemodilution and anaemia is to be expected using these techniques, particularly postoperatively.

## Replacement of other fluid losses

If normovolaemia is to be maintained, other fluid losses in addition to blood loss must also be replaced during the operative period.

### Maintenance fluid requirement

The normal loss of fluid through the skin, respiratory tract, faeces and urine accounts for 2.5–3 litres per day in an average adult, or approximately 1.5 ml/kg/hour. This is often known as the maintenance fluid requirement of the patient and this background volume should be infused over the operative period. The maintenance fluid requirement may clearly vary and will be increased in situations such as in hot climates or if the patient is pyrexial or has diarrhoea. It is proportionately greater in children, as shown in Figure 12.9.

*Figure 12.9: Normal maintenance fluids and electrolyte requirements*

| Weight | Fluid ml/kg/24 hrs | Sodium mmol/kg/24 hrs | Potassium mmol/kg/24 hrs |
|--------|--------------------|-----------------------|--------------------------|
| **Children** | | | |
| First 10 kg | 100 (4*) | 3 | 2 |
| Second 10 kg | 50 (2*) | 1.5 | 1 |
| Subsequent kg | 20 (1*) | 0.75 | 0.5 |
| **Adults** | | | |
| All weights (kg) | 35 (1.5*) | 1 | 0.75 |

* These figures represent the fluid requirements in ml/kg/hour

### Maintenance fluid deficit

Since there is usually a period of fasting prior to an operation, a maintenance fluid deficit will occur and this volume should be added to the replacement volume.

### Body cavity losses

During a laparotomy or thoracotomy, evaporation of water can be considerable and these body cavity losses need to be replaced for the duration of opening. On average, 5 ml/kg/hour of fluid for each cavity opened should be infused in addition to the maintenance fluid.

### Continuing losses

If there are continuing fluid losses, such as nasogastric aspirate or drainage fluid, these need to be measured and again added to the volume of replacement fluid.

Figure 12.10 summarizes adult replacement volume requirements for patients undergoing surgery.

*Figure 12.10: Adult replacement volume requirements during surgery*

| Type of loss | Volume | Type of fluid |
|---|---|---|
| **Blood** | | |
| Up to allowable volume | 3 x volume lost | Crystalloid replacement fluid |
| **or** | 1 x volume lost | Colloid |
| When allowable volume exceeded | 1 x volume lost | Blood |
| **+ Other fluids** | | |
| Maintenance fluids | 1.5 ml/kg/hr | Crystalloid maintenance fluid |
| Maintenance deficit | 1.5 ml/kg/hr | Crystalloid maintenance fluid |
| Body cavity losses | 5 ml/kg/hr | Crystalloid replacement fluid |
| Continuing losses | Measure | Crystalloid/colloid |
| **Adult replacement volume = Blood loss + other losses** | | |

### ACTIVITY 39

*What fluid replacement regimes are used in your hospital to ensure that normovolaemia is maintained in surgical patients? How are patients assessed and monitored to ensure that the regime is adequate?*

*If no fluid replacement regime exists, develop one in conjunction with senior colleagues.*

*Similarly, jointly develop some guidelines on monitoring for hypovolaemia and organize a teaching session to ensure that all staff understand how to follow them correctly.*

### ACTIVITY 40

*What methods are used in your hospital to help you to determine the point at which a blood transfusion is necessary in a surgical patient? What are the limitations of these methods?*

*Discuss with senior colleagues any ways in which you think they could be improved and develop some guidelines. Organize a teaching session to ensure that all staff understand how to follow them correctly.*

## Blood transfusion strategies

### Blood ordering schedules

Blood ordering schedules which aid the clinician to decide on the quantity of blood to crossmatch (or group and screen) for a patient about to undergo surgery are widely used (see Section 6.2: *Ordering Blood Products*). Although they provide a useful guide to potential transfusion requirements they are often based solely on the surgical procedure and rarely take into account other factors such as the skills and experience of the surgeon and anaesthetist and the availability of safe blood.

Blood ordering schedules should always be developed locally and should be used simply as a guide to expected normal blood usage. Each hospital transfusion committee should agree a procedure for the prescribing clinician to override the blood ordering schedule when it is probable that the patient will need more blood than is stipulated: for example, if the procedure is likely to be more complex than usual or if the patient has a coagulation defect. In such cases, additional units of blood should be crossmatched as requested by the clinician.

Figure 12.11 on p. 272 shows an *example* of a blood ordering schedule.

### O-Rhesus negative blood

The availability in a hospital of two units of group O Rhesus negative blood, reserved for use only in an emergency, can be a life-saving strategy. Unused units should be regularly replaced well before their expiry date so they can enter the blood bank pool.

### Control of bleeding

When the decision is made to improve the oxygen-carrying capacity of the patient by means of a blood transfusion, if possible transfuse blood when surgical bleeding is controlled. This will maximize the benefits of the transfusion.

### Massive or large volume transfusion

Administering large volumes of blood and intravenous fluids may give rise to a number of problems. These complications and their management are discussed in Section 7.6: *Massive or Large Volume Transfusions.*

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### ACTIVITY 41

*Using the instructions on p. 102, investigate the normal transfusion requirements of surgical patients in your hospital based on the types of procedure performed. In conjunction with senior colleagues and the hospital transfusion committee, if one exists, use this information to plan a blood ordering schedule for your hospital. How does this differ from the example given in Figure 12.11 and for what reasons?*

Figure 12.11: Example of a blood ordering schedule: a guide to expected normal blood usage for surgical procedures in adult patients

| Procedure | Action | Procedure | Action |
|-----------|--------|-----------|--------|
| **General surgery** | | **Obstetrics & gynaecology** | |
| Cholecystectomy | G & S | Termination of pregnancy | G & S |
| Laparotomy: planned exploration | G & S | Normal delivery | G & S |
| Liver biopsy | G & S | Caesarean section | G & S |
| Hiatus hernia | X-M 2 | Placenta praevia/retained placenta | X-M 4 |
| Partial gastrectomy | G & S | Antepartum/postpartum haemorrhage | X-M 2 |
| Colectomy | X-M 2 | | |
| Mastectomy: simple | G & S | Dilatation & curettage | G & S |
| Mastectomy: radical | X-M 2 | Hysterectomy: abdominal or vaginal: simple | G & S |
| Thyroidectomy: partial/total | X-M 2 (+ 2) | | |
| | | Hysterectomy: abdominal or vaginal: extended | X-M 2 |
| **Cardiothoracic** | | | |
| Angioplasty | G & S | Myomectomy | X-M 2 |
| Open heart surgery | X-M 4 (+ 4) | Hydatidiform mole | X-M 2 |
| Bronchoscopy | G & S | Oophorectomy (radical) | X-M 4 |
| Open pleural/lung biopsy | G & S | | |
| Lobectomy/pneumonectomy | X-M 2 | **Orthopaedics** | |
| | | Disc surgery | G & S |
| **Vascular** | | Laminectomy | G & S |
| Aortic-iliac endarterectomy | X-M 4 | Removal hip pin or femoral nail | G & S |
| Femoral endarterectomy | G & S | Total hip replacement | X-M 2 (+ 2) |
| Femoro-popliteal bypass | G & S | Ostectomy/bone biopsy (except upper femur) | G & S |
| Ilio-femoral bypass | X-M 2 | | |
| Resection abdminal aortic aneurysm | X-M 6 (+ 2) | Nailing fractured neck of femur | G & S |
| | | Laminectomy | G & S |
| **Neurosurgery** | | Internal fixation of femur | X-M 2 |
| Craniotomy, craniectomy | G & S | Internal fixation: tibia or ankle | G & S |
| Meningioma | X-M 4 | Arthroplasty: total hip | X-M 3 |
| Head injury, extradural haematoma | G & S | Spinal fusion (scoliosis) | X-M 2 |
| Vascular surgery (aneurysms, A-V malformations) | X-M 3 | Spinal decompression | X-M 2 |
| | | Peripheral nerve surgery | G & S |
| **Urology** | | | |
| Ureterolithotomy | G & S | | |
| Cystotomy | G & S | | |
| Ureterolithotomy & cystotomy | G & S | | |
| Cystectomy | X-M 4 | | |
| Open nephrolithotomy | X-M 2 | | |
| Open prostatectomy (RPP) | X-M 2 | | |
| Transurethral resection prostatectomy (TURP) | G & S | | |
| Renal transplantation | X-M 2 | | |

X-M = Crossmatch          G & S = ABO/Rh group and antibody screen (see p. 111)

(+  ) indicates additional units may be required, depending on surgical complications

*Remember that your hospital's blood ordering schedule should take into account factors such as local clinical conditions, the safety of the local blood supply and the experience of surgeons and anaesthetists.*

*Organize a teaching session for all surgical and anaesthetic staff to ensure that they understand how to use the blood ordering schedule. Set up a simple system to monitor compliance with the schedule and periodically review and, where necessary, revise it.*

## 12.4  Autologous blood transfusion

Autologous transfusion involves the collection and subsequent reinfusion of the patient's own blood or blood products.

It can avoid some of the immunological and disease-transmission problems associated with donor, or homologous blood and, in some circumstances, may also be the only readily available source of blood for transfusion.

Autologous transfusion is an effective technique in both elective and emergency surgery, but you should only consider it in a patient if you anticipate that the surgery will result in sufficient blood loss to require homologous transfusion.

All autologous transfusion methods require careful preparation and planning and it is vital to seek the advice and cooperation of the blood bank or transfusion centre before they are introduced into a hospital.

The principal methods of autologous transfusion are:

1   Preoperative blood donation.

2   Acute normovolaemic haemodilution.

3   Blood salvage.

These techniques can be used alone or in combination to reduce or eliminate the need for homologous blood.

### Preoperative blood donation

Preoperative blood donation involves the collection and storage of the patient's own blood prior to elective surgery. Firstly, it must be established that the surgical procedure is likely to result in sufficient blood loss to require transfusion. A unit of the patient's own blood is then collected every five or more days in the period leading up to surgery. The blood is tested, labelled and stored to the same standard as homologous blood and the patient is prescribed oral iron supplements. On the date of operation, up to 4–5 units of stored blood are then available if transfusion becomes necessary during the procedure.

This technique requires considerable planning and organisation to be effective and experience shows that the initial costs can be higher than those of homologous transfusion. Thought must also be given to the criteria for patient eligibility since not all patients are either fit enough or live close enough to the hospital to make repeated donations.

Unused units of the blood should not be transferred to the homologous pool for the benefit of other patients unless they have been tested for transfusion-transmissible infections, including HIV, hepatitis B, syphilis and other nationally-required tests.

This method of autologous transfusion does not avoid the risk of bacterial contamination as a result of collection or storage problems and does not reduce the risk of procedural errors that can cause incompatibility of blood.

## Acute normovolaemic haemodilution

Acute preoperative normovolaemic haemodilution involves removing a predetermined volume of the patient's own blood immediately prior to the commencement of surgery and its simultaneous replacement with sufficient crystalloid or colloid fluid to maintain the blood volume.

During surgery, the haemodiluted patient will lose fewer red cells for a given blood loss and the autologous blood collected can subsequently be reinfused, preferably when surgical bleeding has been controlled. An additional benefit is that the fresh units of autologous blood will contain a full complement of coagulation factors and platelets.

When using this technique, it is essential to adopt some basic safeguards.

1  There should be criteria to exclude unsuitable patients, such as those who cannot compensate for the reduction in oxygen supply due to haemodilution.

2  The volume of blood to be removed should be carefully assessed and strict attention given to its replacement with a crystalloid (at least 3 ml for every 1 ml blood collected) or colloid (1 ml for every 1 ml blood collected).

3  It is vital to monitor the patient carefully and maintain blood volume and oxygen delivery at all times, particularly when surgical blood loss occurs.

## Blood salvage

Blood salvage is the collection of shed blood from a wound, body cavity or joint space and its subsequent reinfusion into the same patient. Blood salvaging techniques can be used both during elective surgery, for example cardiothoracic procedures, and in emergency or trauma surgery, for example ruptured ectopic pregnancy or ruptured spleen.

In common with other autologous techniques, it should only be considered where sufficient blood loss to require a transfusion has occurred or is anticipated to occur.

Contraindications to salvage include blood contaminated with bowel contents, bacteria, fat, amniotic fluid, urine, malignant cells and irrigants. However, where salvage is being performed as an emergency, these risks must be balanced against the life-saving benefits to the patient.

It is also important not to reinfuse salvaged blood which has been shed for more than 6 hours since haemolysis of red cells is likely to be complete.

Methods of blood salvage include:

■ Gauze filtration
■ Simple suction collection systems
■ Automated suction collection systems.

### Gauze filtration

This method is inexpensive and suitable for the salvage of blood from body cavities. At operation and using an aseptic technique, blood is collected from the cavity using a ladle or small bowl. It is then mixed with anticoagulant, filtered through gauze, as shown in Figure 12.12, and reinfused into the patient. This method of salvage is described in Case History 2.

*Figure 12.12: Blood salvage using gauze filtration*
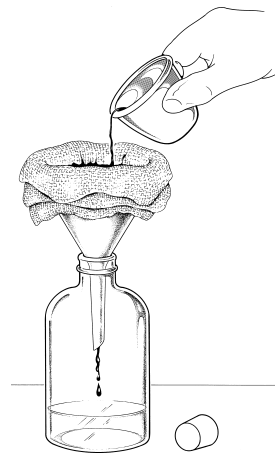


### Manual suction collection system

Commercially available suction systems incorporate suction tubing connected to a specially designed storage bottle containing anticoagulant. At operation, blood is sucked from the cavity or wound directly into the bottle. In certain circumstances blood may also be collected postoperatively via surgical drains using this method. Suction pressure should be as low as possible to avoid haemolysis of red cells.

### Automated suction collection systems

These commercially available systems, often called cell-savers, collect, anticoagulate, wash, filter, and re-suspend red cells in crystalloid fluid prior to reinfusion. Although a significant amount of automation is involved in the process, a dedicated operator of the device is frequently required. The high capital cost of this equipment together with the significant cost of disposable items for each patient may limit its availability.

### ACTIVITY 42

*Assess the different techniques of autologous transfusion in use in your hospital. In conjunction with senior colleagues, develop guidelines on their use if none already exist.*

*Organize a training session for relevant staff and monitor whether these techniques are being used correctly.*

## 12.5 Care in the postoperative period

Blood loss and hypovolaemia can still develop in the postoperative period. Its prevention, early detection and treatment is of prime importance to the patient's welfare and may again reduce the need for an unnecessary transfusion to take place. Particular attention should be paid to:

- Postoperative oxygen
- Monitoring of vital signs and the surgical site, including drains
- Fluid balance
- Analgesia.

Consideration may need to be given to:

- Surgical re-exploration
- Postoperative transfusions
- Haematinics.

### Postoperative oxygen

In the early postoperative period, hypoxia is a common problem, particularly following a general anaesthetic. The effects of hypoxia (see Section 2: *Blood, Oxygen and the Circulation*) will be compounded in a patient with an already reduced haemoglobin level and in whom hypovolaemia may be present.

It is desirable to give supplementary oxygen to all patients recovering from a general anaesthetic.

### Monitoring

The monitoring of patients should continue postoperatively, with particular attention being given to identifying clinical signs of hypovolaemia and blood loss. The patient's wound and drains should be regularly checked for haematoma and bleeding, and abdominal girth measurements may be useful.

### Fluid balance

Ensuring normovolaemia in the postoperative patient is essential. Intravenous fluid replacement, as already described above, should address both measured losses occurring after surgery and the maintenance requirements of the patient.

Replacement should continue until adequate oral intake is established and when significant postoperative bleeding is unlikely.

### Analgesia

Inadequate pain relief is a major cause of hypertension and restlessness postoperatively. Both may aggravate bleeding and increase blood loss. Attention should therefore be given to the provision of satisfactory analgesia throughout the perioperative period.

Where surgery involves a limb, elevation of that part postoperatively will reduce swelling, control venous blood loss and reduce pain.

## Surgical re-exploration

Where significant blood loss continues to occur postoperatively and there is no treatable disturbance of the coagulation status of the patient, early surgical re-exploration should be considered.

## Postoperative transfusion

Staff caring for patients postoperatively should be aware that some degree of haemodilution can be expected in patients who have lost blood during a procedure. For this reason, a haemoglobin level performed postoperatively is very likely to be lower than the preoperative level. This alone is not an indication for a blood transfusion, and the decision to transfuse should only be made following a careful assessment of the patient.

Consideration should be given to the general condition of the patient and, in particular, to coexisting cardiopulmonary disease, signs of inadequate tissue oxygenation and continued blood loss.

## Haematinics

Treating patients in the later postoperative period with iron supplements will optimize the erythropoietic response and restore the haemoglobin level to normal more rapidly.

### ACTIVITY 43

*Are there any guidelines in use covering the postoperative care of surgical patients in your hospital? In conjunction with senior colleagues, develop guidelines on their use if none exist or if you think they could be improved.*

*Organize a training session for relevant staff and monitor whether these techniques are being used correctly.*

### CASE HISTORY 1

**A 67-year-old man was scheduled to undergo a partial gastrectomy. At first presentation three weeks earlier, he was noted to be clinically anaemic, short of breath on mild exertion and had evidence of peripheral oedema. A haemoglobin level was performed which showed an iron deficiency anaemia of 8 g/dl. Investigations showed the cause to be hookworm infestation and he was therefore treated with oral iron and mebendazole. On the day of operation, his haemoglobin level was 12 g/dl and his symptoms had markedly improved. His weight was estimated to be 50 kg.**

**Before the start of the operation, his blood volume was calculated based on his weight. This was estimated to be 3500 ml (50 kg x 70 ml/kg). In view of his general condition and the presence of symptoms when his haemoglobin was only 8 g/dl, it was decided that the lowest acceptable haemoglobin for this man would be 10 g/dl. The anaesthetist then calculated the allowable volume of blood loss that could occur before a blood transfusion became necessary, using the following formula.**

Allowable blood loss = Blood volume x (Preoperative Hb – Lowest Acceptable Hb)

(Average of Preoperative & Lowest Acceptable Hb)

Allowable blood loss = 3500 x (12 – 10)/11

Allowable blood loss = 640 ml

During the course of the procedure, the patient in fact lost only 500 ml of blood and the anaesthetist replaced this with the same volume of colloid. Since the allowable blood loss volume was not exceeded and the patient remained stable, there was no need for a blood transfusion. The anaesthetist was also careful to maintain normovolaemia by giving enough normal saline to account for the maintenance requirements of the patient (1.5 ml/kg/hr) and the fluid deficit incurred as a result of preoperative starvation (1.5 ml/kg for each hour starved). The patient made an uneventful recovery and was advised to continue taking the oral iron supplements.

## CASE HISTORY 2

A 53-year-old woman was undergoing a cholecystectomy when a small tear in the liver inadvertently occurred. Despite efforts to control the ensuing haemorrhage, she lost 850 ml of blood within 10 minutes. It was estimated that her weight was 60 kg and her normal blood volume was approximately 4200 ml. This degree of blood loss therefore represented about 20% of her blood volume.

The anaesthetist replaced the blood loss with 2500 ml of Ringer's lactate and the patient remained stable for a time, apart from a tachycardia of 100/min. However, it soon became apparent that further blood loss was occurring, despite packing of the liver by the surgeon, and the patient's vital signs began to deteriorate. While continuing to replace the blood loss with Ringer's lactate, the anaesthetist asked for the autologous bottles to be made ready since there was no ready access to donor blood. A number of sterilized 500 ml bottles, each containing 2 g of sodium citrate and 3 g of dextrose made up to 120 ml with sterile water, were always kept in theatre and these were brought in.

The surgeon collected the shed blood from the abdominal cavity into a kidney dish, approximately 500 ml at a time. The scrub nurse poured the anticoagulant from one of the bottles into the kidney dish containing the blood, and mixed it well. She then filtered the mixture through five layers of sterile gauze back into the bottle and replaced the stopper. The nurse handed the bottle to the anaesthetist before repeating the process with the next bottle. The anaesthetist then transfused the blood via a normal giving-set. Four bottles of blood were returned to the patient before surgical control over bleeding was eventually regained. The patient subsequently made a full recovery.

Salvaging the patient's own blood can be very effective in both elective and emergency surgery, but it needs preparation. If you cannot make your own anticoagulant as described, use the anticoagulant from a normal venesection bag available from blood banks.

# 13

# Trauma & acute surgery

## Key points

1 The immediate management of acute surgical and trauma patients should be carried out in three phases:
   - Phase 1: Initial assessment and resuscitation
   - Phase 2: Reassessment
   - Phase 3: Definitive management.

2 In Phase 1, the objective is to assess and treat life-threatening conditions and resuscitate the acute surgical or traumatized patient.

3 In Phase 2, the objective is to evaluate the response to resuscitation, plan a management strategy and perform a detailed examination.

4 In Phase 3, the objective is to implement the management strategy and prepare the patient for definitive treatment, usually surgery.

5 The basic principles of resuscitation and management apply to paediatric patients.

## Introduction

Patients presenting with acute surgical conditions and particularly those with multiple injuries can make enormous demands on both the expertise of staff and the facilities provided by a hospital. Hypovolaemia, commonly as a result of haemorrhage, is a major cause of mortality in these patients. Many deaths are potentially avoidable, especially among trauma casualties who are often young and previously healthy and who frequently respond well to appropriate therapy.

The quality and speed of the initial assessment and management of these acutely-ill patients has a major influence on their subsequent outcome. Experts in trauma and life support refer to 'the Golden Hour'; this means that effective management in the first hour after the trauma gives the patient the best chance of survival. Many countries have therefore introduced staff training programmes with the aim of reducing morbidity and mortality by ensuring that an early and systematic approach to the management of these patients is adopted. Central to the success of these programmes are:

- The concentration of resources at the time they are most required, often within the first hour of admission
- The development of a multidisciplinary team approach to care, or trauma teams
- The use of management protocols which reduce the risk of misdiagnosis.

The purpose of this section is to provide a structured approach to the initial management of hypovolaemia of multiple etiology, but with the emphasis on haemorrhage occurring in the injured patient.

## Learning outcomes

When you have completed this section, you should be able to:

1 Assess and treat life-threatening conditions and resuscitate the acute surgical or traumatized patient.

2 Evaluate the response to resuscitation and plan a management strategy.

3 Implement the management strategy and prepare the patient for definitive treatment.

4 Apply the principles of resuscitation and management to paediatric patients.

## 13.1  Management of the acute surgical or traumatized patient

The immediate management of all acutely ill patients presenting to hospital should be carried out in the following three phases:

1  **Initial assessment and resuscitation**
Objectives: to assess and treat life-threatening conditions and resuscitate the patient.

2  **Reassessment**
Objectives: to evaluate the response to resuscitation, determine the extent of other injuries and plan a management strategy.

3  **Definitive management**
Objectives: to implement the management strategy and prepare the patient for definitive treatment.

## 13.2  Initial assessment and resuscitation

This phase is sometimes referred to as the primary survey, the objectives being to rapidly assess the patient and immediately treat any life-threatening conditions before proceeding to the next phase of management. This phase can often be completed in less than a few minutes.

To ensure that clinical priorities are met, initial assessment and resuscitation should be performed in the following sequence.

### Initial assessment and resuscitation

| | |
|---|---|
| **A** | **A**irway control and cervical spine stabilization |
| **B** | **B**reathing |
| **C** | **C**irculation and control of haemorrhage |
| **D** | **D**isorders of the central nervous system |
| **E** | **E**xposure of the whole body |

### A  Airway control

It is vital to ensure that the patient has a clear and unobstructed airway. Noisy or laboured breathing or paradoxical respiratory movements are evidence of airway obstruction, which must be rectified. Vomit, blood or foreign material in the mouth should be removed.

Sometimes a simple chin lift will prevent the tongue of an unconscious patient from obstructing the airway, although other measures to secure the airway may be necessary. These include a forward jaw thrust, insertion of an oro/nasopharyngeal airway, endotracheal intubation, cricothyroid puncture or tracheostomy.

Immobilize the neck of any patient with a suspected cervical spine injury with a rigid collar, or simply hold the head in a neutral position, particularly when manoeuvres to secure the airway take place.

## B Breathing

Note any obvious injuries to the thorax and measure the respiratory rate. If the patient is not breathing or has inadequate respiration, assisted ventilation will be necessary. High concentrations of supplementary oxygen should be administered.

It is essential to conduct a rapid but complete examination of the respiratory system to exclude life-threatening conditions such as a tension pneumothorax or haemothorax. These two conditions require immediate treatment by pleural drainage with an underwater seal. An open chest wound should be initially sealed with an occlusive dressing.

## C Circulation and control of haemorrhage

### Haemorrhage control

Major external haemorrhage should be controlled by direct pressure to the bleeding site. Tourniquets are not recommended as they may increase tissue destruction. Penetrating objects should be left in-situ until formal surgical exploration can be performed.

### Assessment

A rapid assessment of the cardiovascular system must then be made. This should include

- Pulse rate
- Capillary refill time (the time taken for colour to return to the finger pad or nail-bed after it has been briefly compressed; greater than 2 seconds is abnormal)
- Level of consciousness
- Blood pressure.

### Extent of hypovolaemia

An estimate of blood or fluid losses should be made, based on the patient's clinical signs and the nature of the injury or surgical condition. Concealed bleeding can be very difficult to assess and should not be underestimated; for example, blood loss from a closed fractured femur can be as much as 1000 ml, a fractured pelvis up to 3000 ml and a ruptured spleen or ectopic pregnancy may result in loss of the total blood volume.

Trauma also causes soft tissue injury and considerable tissue oedema may develop at the site. This will compound any hypovolaemia present due to blood loss.

Figure 13.1 classifies hypovolaemia into four classes based on the patient's clinical signs and assuming the normal blood volume of an adult to be 70 ml/kg. Although this is a useful guide, it must be stressed that patients may not fit a precise class and variations will occur.

Factors such as age, pre-existing medical disorders and medications will all influence a patient's response to hypovolaemia. The young and fit tolerate it well; the elderly and infirm tolerate it poorly.

*Figure 13.1: Classification of hypovolaemia in the adult*

| | Class I Mild | Class II Progressing | Class III Severe | Class IV End stage |
|---|---|---|---|---|
| % of blood volume lost | Up to 15% | 15–30% | 30–40% | >40% |
| Volume lost in 70 kg adult (ml) | <750 | 750–1500 | 1500–2000 | >2000 |
| Pulse rate | Normal | >100 | >120 | >140 but variable in terminal stages of shock |
| Pulse pressure | Normal | Reduced | Very reduced | Very reduced/ absent |
| Systolic blood pressure | Normal | Normal | Reduced | Very reduced |
| Capillary refill | Normal | Prolonged | Very prolonged | Absent |
| Respiratory rate | Normal | 20–30 | 30–40 | >45 or slow sighing respiration |
| Mental state | Alert | Anxious | Confused | Comatosed/ unconscious |
| Urine output | >30 ml/hr | 20–30 ml/hr | 5–20 ml/hr | <5 ml/hr |

### Intravenous access

Establish intravenous access promptly, preferably with two large-bore cannulae (16 gauge or 14 gauge in an adult or the appropriate size in a child) sited in the antecubital fossae or any large peripheral vein (see Figure 13.2 on p. 284).

Do not place intravenous lines in injured limbs. If there is a suspected risk of the patient having an infection that can be transmitted via blood, or the operator has broken skin on the hands, gloves must be worn during this procedure.

If intravenous access is not possible, the external jugular vein or femoral vein can often be cannulated. Alternatively, consider a venous cutdown (see Figure 13.3 on p. 285).

Central venous access (see Figure 13.4 on p. 286) is rarely indicated for initial resuscitation, but it may later be useful as a guide to fluid replacement. Catheterization of the internal jugular vein should only be performed by a trained person.

While reliable venous access is being obtained, blood should be taken for baseline haematological and biochemical values and for crossmatching.

*Figure 13.2: Intravenous cannulation*

Cephalic vein    Basilic vein    Forearm vein    Great saphenous vein    Scalp veins
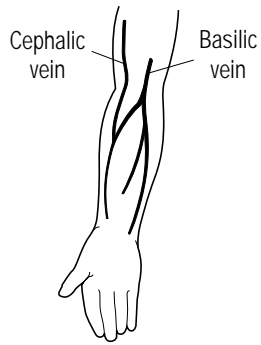
1 Occlude the venous drainage with a tourniquet or finger pressure. This will allow the veins to fill and stand out. Tap the vein to make it stand out.

2 Identify a vein, preferably with a Y-junction. Stretch the skin below the vein. This will stop it moving.

3 Gently push the needle through the skin at the Y-junction. Do not go too deep. Always wear gloves before starting intravenous access.

4 Stop pushing when blood appears in the cannula.

5 Hold the needle steady and push the cannula up the vein.

6 When the cannula is fully in the vein, release the tourniquet and remove the needle.

7 Connect up to the drip set.
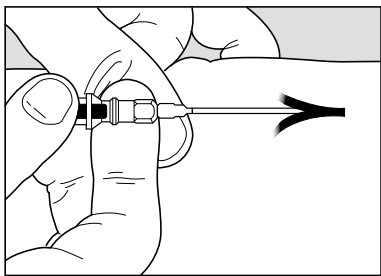
8 Fix the cannula with strapping.
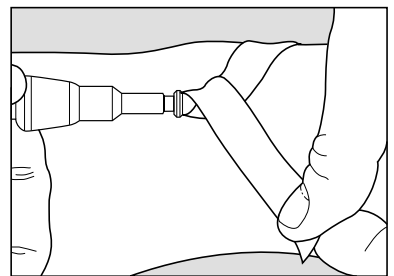
*Figure 13.3: Sites for venous cutdown*

Cephalic vein
Basilic vein

**Antecubital fossa**

Great saphenous vein
Small saphenous vein

**Saphenous vein**

Femoral vein

**Femoral vein**
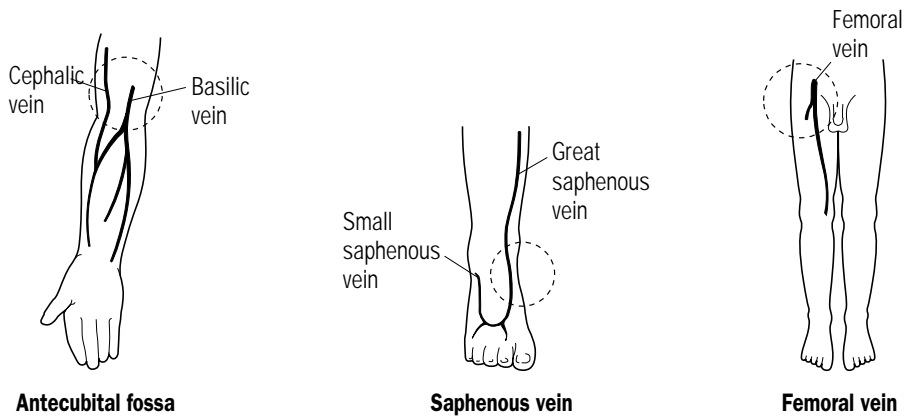
1   Infiltrate skin with local anaesthetic.

2   Make a transverse incision.

3   Expose the vein.
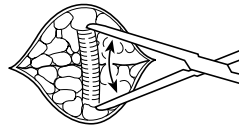
4   Insert sutures loosely at proximal and distal ends of vein.
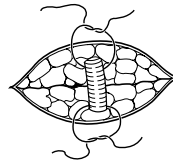
5   Make small incision in vein.
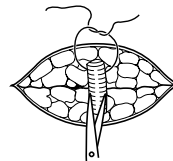
6   Expose the opening in vein and insert cannula.
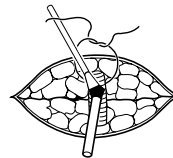
7   Tie upper suture to secure cannula.
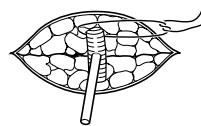
8   Close the wound.
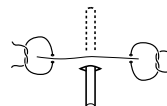
*Figure 13.4: Sites for central venous catheterization*



**Antecubital veins**

Subclavian vein

Axillary vein

Cephalic vein

Brachial veins
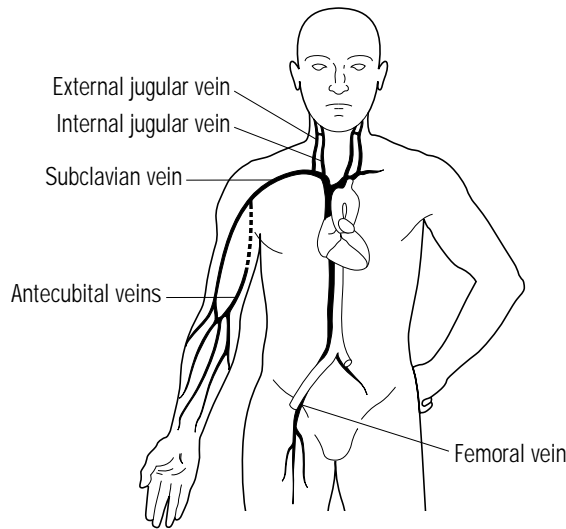
Basilic vein

Median antecubital vein
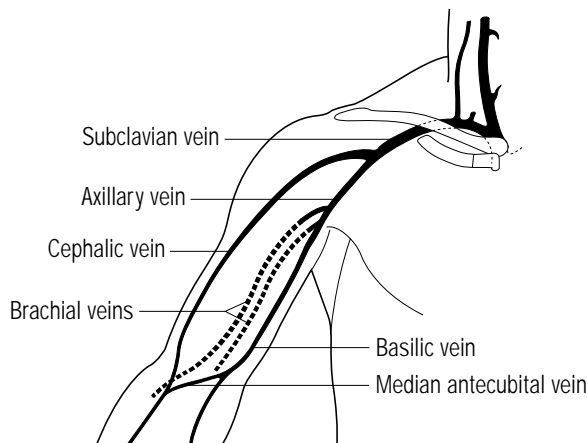
The basilic vein takes a smoother course than
the cephalic and is often the most
successful approach.

**Femoral vein**

Inguinal ligament

Femoral nerve

Femoral artery
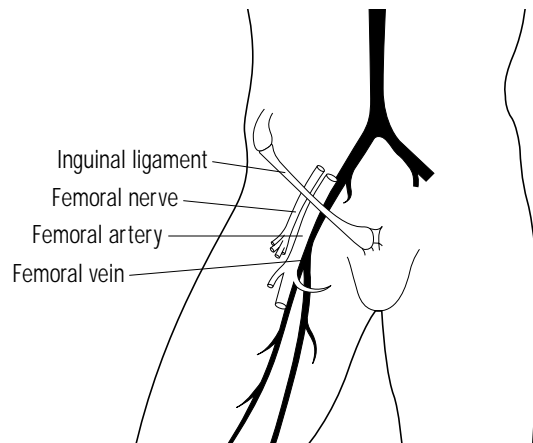
Femoral vein

The skin is entered at a 45° angle 3 cm below the
inguinal ligament and 1 cm medial to the maximal
femoral artery pulsation.

**Internal jugular vein**

Identify the point midway between
a line joining the mastoid and
sternal notch. Insert the needle at
a 45° angle just lateral to this point
and aim the needle at the nipple.

Sternal notch

Subclavian vein

Internal jugular vein

Clavicle

External jugular vein

Mastoid
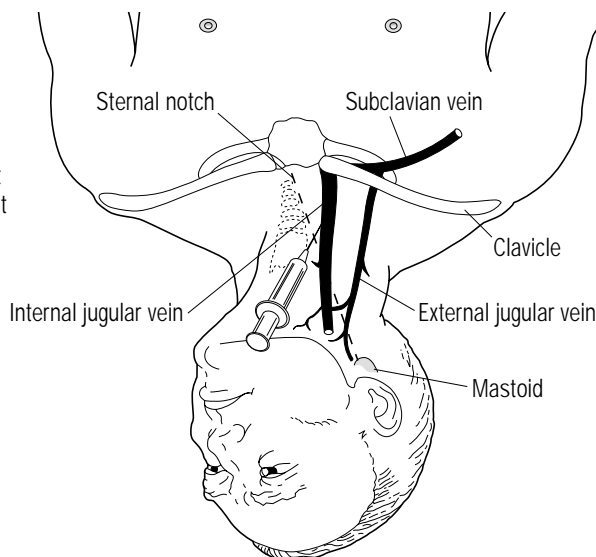
**External jugular vein**

In the head-down position, the
external jugular vein will fill and
become visible. It can then be
cannulated in the normal way.
This vein is extremely useful for
fluid resuscitation and can
often be found when others
have collapsed.

## Fluid resuscitation

The goal of fluid resuscitation is to restore the circulating blood volume rapidly in order that organ perfusion can be maintained. Ideally, seriously-ill or traumatized patients should receive intravenous fluids within minutes of admission to hospital.

The initial choice of fluid is largely unimportant and will often depend on local policy and availability. Either crystalloid replacement fluids or colloids can be used, provided you keep the following points in mind.

1   Select crystalloid solutions that principally expand the extracellular fluid, such as sodium chloride 0.9% or Ringer's lactate solution. Do not use solutions containing only dextrose unless there is no alternative.

2   Because crystalloid solutions rapidly leave the circulation, give crystalloids in a volume at least three times the volume of blood loss.

3   Give colloid solutions in volumes equal to the blood loss as they remain within the circulation for longer.

4   If urgent transfusion is likely to be life-saving, do not wait for fully crossmatched blood, but use uncrossmatched group 0 negative blood, and/or uncrossmatched group specific blood.

The amount of fluid given will depend on the clinical state of the patient and the estimated losses. Give an initial fluid bolus of 10–20 ml/kg of colloid or 20–30 ml/kg of crystalloid to any patient showing signs of greater than 15% blood loss (Class II hypovolaemia and above).

This volume should be given rapidly over a period of approximately five minutes. Whenever possible, the fluid should be warmed to prevent further patient cooling.

Carefully observe the patient's response to this initial fluid bolus since further fluid administration will be guided by this response.

## D Disorders of the central nervous system

Cerebral perfusion becomes impaired when losses of over 30% of blood volume are incurred, and unconsciousness results. The central nervous system should therefore be quickly assessed by ascertaining the level of consciousness and pupillary response to light.

At this stage, conscious level can be assessed by simply grading the patient's response into one of the following categories:

A   **A**lert

V   Responds to **V**erbal commands

P   Responds to **P**ainful stimuli

U   **U**nresponsive

A more detailed neurological examination should be made at a later stage when you undertake a full examination of the patient.

## E Exposure of the whole body

It is particularly important to remove the clothing of all trauma casualties to allow a thorough survey of injuries to take place. However, hypothermia needs to be avoided.

At this stage, insert a urinary catheter and consider gastric decompression via a nasogastric tube, especially in children. However, do not insert a nasogastric tube if a fracture of the anterior cranial fossa is suspected.

## 13.3  Reassessment

Following initial assessment and resuscitation, the purpose of reassessment is to:

1   Evaluate the response to resuscitation.

2   Plan a management strategy.

3   Perform a detailed examination.

## Evaluating the response to resuscitation

It is essential to make a regular reassessment of the patient's clinical condition (Airway, Breathing, Circulation, etc.). This process of reassessment will not only detect any unexpected deterioration in the patient's condition, but will also provide information on the patient's response to resuscitation.

### Cardiovascular features

Signs that normovolaemia is being re-established include the return of a normal pulse rate, peripheral pulses and blood pressure. Further positive signs that the circulation is stabilizing include features of recovering organ perfusion, such as improving conscious level and decreasing capillary refill time.

### Urine output

Since renal function is extremely sensitive to circulatory changes, monitoring urine output is of great importance when assessing patient response to fluid resuscitation. A normal urine output in an adult should be greater than 0.5 ml/kg/hour, and 1 ml/kg/hour in an infant.

### Central venous pressure

Properly-interpreted changes to the central venous pressure (CVP) can provide useful information about the state of the circulation in response to fluid administration.

A low CVP which stays low or continues to fall during resuscitation indicates hypovolaemia and that further fluid is required. A rising CVP suggests restoration of the blood volume, although an abrupt rise in response to a small volume of fluid may indicate imminent overload of the circulation.

### Acid-base status

The development of a metabolic acidosis in a patient is due to anaerobic metabolism and indicates inadequate tissue perfusion. Restoring

normovolaemia, and consequently improving tissue perfusion, will return the body pH towards normal (7.36–7.44). Sequential arterial pH measurements can therefore provide a useful guide to fluid resuscitation.

Figure 13.5 summarizes the signs of normovolaemia being re-established.

*Figure 13.5: Normovolaemia*

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**Signs of normovolaemia being re-established**

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- Decreasing heart rate
- Reduced capillary refill time and return of peripheral pulses
- Increasing urine output
- Normalizing arterial pH
- Return of normal blood pressure
- Improving conscious level
- Slow rise in CVP

---

## Planning a management strategy

Based on the response of the patient to the initial resuscitation and fluid administration, a strategy for further management can now be planned. This can be broadly divided into three groups, which are summarized in Figure 13.6.

*Figure 13.6: Management strategy in the adult based on response to initial fluid administration*

Established hypovolaemia of Class II and above
(greater than 750 ml in a 70 kg adult)

↓

Infuse 20–30 ml/kg of crystalloid or 10–20 ml/kg of colloid

↙            ↓            ↘

| **Rapid improvement** | **Transient improvement** | **No improvement** |
|---|---|---|
| Slow fluids to maintenance levels | Rapid fluid administration | Vigorous fluid administration |
| No immediate transfusion, crossmatch | Initiate blood transfusion | Urgent blood transfusion |
| Regular reassessment | Regular reassessment | Immediate surgery |
| Detailed examination | Detailed examination | |
| Definitive treatment | Early surgery | |

**1 Rapid improvement following initial fluid administration**
A small number of patients respond quickly to the initial fluid bolus and remain stable after it is completed. These patients have usually lost less than 20% of their blood volume.

Management comprises:
- Slow fluids to maintenance levels

- Blood transfusion is not indicated at this stage, but crossmatching is required
- Regular reassessment to detect any deterioration in condition
- Detailed examination of the patient
- Appropriate specialist referral.

## 2  Transient improvement following initial fluid administration

Many patients will show some improvement with the initial fluid bolus, but deterioration of the circulatory parameters recurs when it is slowed. Most of these patients will have lost between 20–40% of their blood volume or are still bleeding.

Management comprises:

- Rapid fluid administration
- Blood transfusion is indicated
- Regular reassessment
- Detailed examination if the patient stabilizes
- Early surgery.

## 3  No improvement following initial fluid administration

Little or no response to the initial fluid bolus will occur in a small, but significant number of patients. A failure to respond to adequate volumes of fluids and blood requires immediate surgical intervention to control exsanguinating haemorrhage.

On rare occasions, failure to respond may be due to heart failure which, in trauma victims is likely to be the result of myocardial contusion or cardiac tamponade.

Management comprises:

- Vigorous fluid administration
- Urgent blood transfusion
- Immediate surgery.

**Patients who show no improvement following initial fluid administration or in whom there is obvious exsanguinating haemorrhage require urgent surgery, together with resuscitation.**

## Performing a detailed examination

As soon as the patient is stabilized, obtain any history that may be available and make a detailed head-to-toe examination of the patient. Then perform appropriate investigations and administer tetanus immunization and prophylactic antibiotics, if necessary.

This phase of the management is sometimes referred to as the secondary survey. Its objectives are to arrive at a diagnosis and avoid missed diagnoses. In some patients, it may only be possible to conduct the secondary survey after surgical control of exsanguinating haemorrhage has been achieved.

**ACTIVITY 44**

*A previously healthy 60 kg man was admitted to casualty having fallen 9 m (30 ft) from the roof that he was repairing. Following initial assessment and resuscitation, a detailed examination revealed the following injuries:*

- *Fractured left os calcis*
- *Compound left tibia and fibula*
- *Compression fractures of the lst and 2nd lumbar vertebrae*
- *Fractures to the 7th, 8th and 9th ribs on the left*
- *Deep 6 cm laceration to the scalp.*

1  *What would you expect his normal blood volume to be?*

2  *What would you estimate his blood loss to be?*

3  *What associated abdominal injury should you consider in this man?*

## 13.4  Definitive management

The objective of this phase is to implement the planned management strategy outlined above. With a few exceptions, the definitive management of haemorrhage is surgery and the aim should be to achieve this within one hour of presentation.

Many of the methods to conserve and manage blood loss during surgery are described in Section 12: *Surgery & Anaesthesia* are equally applicable in the acute surgical or traumatized patient. In addition, administering large volumes of blood and intravenous fluids may itself give rise to a number of problems. These complications and their management are discussed fully in Section 7.6: *Massive or Large Volume Transfusions*.

## 13.5  Other causes of hypovolaemia

Hypovolaemia due to medical and surgical causes other than haemorrhage, such as cholera, diabetic ketoacidotic coma or peritonitis (see Figure 13.7), should be initially managed in a very similar manner to that described earlier in this section.

*Figure 13.7: Some causes of hypovolaemia*

| Medical | Surgical |
|---|---|
| ■ Cholera | ■ Major trauma |
| ■ Diabetic ketoacidosis | ■ Severe burns |
| ■ Septic shock | ■ Peritonitis |
| ■ Acute adrenal insufficiency | ■ Crush injury |

Clearly, the need for blood transfusion and surgical intervention in these patients will depend on the diagnosis. In these cases, additional therapeutic measures such as antibiotics or insulin need to be instigated at this stage.

## 13.6 The management of paediatric patients

The basic principles of management and resuscitation of the hypovolaemic child are the same as for the adult and should proceed as described in this section. However, the following points should be remembered:

1   The normal blood volume is proportionately greater in children and is calculated at 80 ml/kg in a child and 85–90 ml/kg in the neonate (see Figure 13.8). Using a height/weight chart is often the easiest method of finding the approximate weight of a seriously-ill child.

*Figure 13.8: Normal values for paediatric vital signs*

| Age | Pulse rate beats/min | Blood pressure systolic mmHg | Respiratory rate breaths/min | Blood volume ml/kg |
|---|---|---|---|---|
| <1 year | 120–160 | 70–90 | 30–40 | 85–90 |
| 1–5 years | 100–120 | 80–90 | 25–30 | 80 |
| 6–12 years | 80–100 | 90–110 | 20–25 | 80 |
| >12 years | 60–100 | 100–120 | 15–20 | 70 |

2   Venous access in children who are hypovolaemic can be difficult. Useful sites for cannulation include the long saphenous vein over the ankle, the external jugular vein and femoral veins.

3   The intraosseous route can provide the quickest access to the circulation in a shocked child in whom venous cannulation is impossible. Fluids, blood and many drugs can be administered by this route. The intraosseous needle is normally sited in the anterior tibial plateau, 2–3 cm below the tibial tuberosity, thereby avoiding the epiphysial growth plate (see Figure 13.9).

*Figure 13.9: Tibial technique for intraosseous infusion*
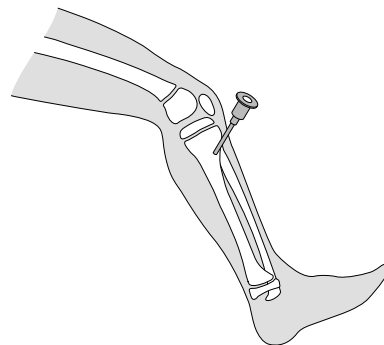


Once the needle has been located in the marrow cavity, fluids may need to be administered under pressure or via a syringe when rapid replacement is required. If purpose-designed intraosseous needles are unavailable, spinal, epidural or bone marrow biopsy needles offer an alternative. The intraosseous route has been used in all age groups, but is generally most successful in children below about six years of age.

4   Recognition of hypovolaemia can be more difficult than in the adult. The increased physiological reserves of the child may result in the vital signs being only slightly abnormal, even when up to 25% of blood volume is lost (Class I and II hypovolaemia).

Tachycardia is often the earliest response to hypovolaemia, but this can also be caused by fear or pain (see Figure 13.10).

*Figure 13.10: Classification of hypovolaemia in children*

| | Class I | Class II | Class III | Class IV |
|---|---|---|---|---|
| Blood volume lost | <15% | 15–25% | 25–40% | >40% |
| Pulse rate | Increased | >150 | >150 | Increased or bradycardia |
| Pulse pressure | Normal | Reduced | Very reduced | Absent |
| Systolic blood pressure | Normal | Reduced | Very reduced | Unrecordable |
| Capillary refill time | Normal | Prolonged | Very prolonged | Absent |
| Respiratory rate | Normal | Increased | Increased | Slow sighing respiration |
| Mental state | Normal | Irritable | Lethargic | Comatosed |
| Urine output | <1 ml/kg/hr | <1 ml/kg/hr | <1ml/kg/hr | <1 ml/kg/hr |

5   Because the signs of hypovolaemia may only become apparent after 25% of the blood volume is lost, the initial fluid challenge in a child should represent this amount. Therefore, 20 ml/kg of crystalloid fluid should be given initially to the child showing signs of Class II hypovolaemia or greater. Depending on the response, this may need to be repeated up to three times (up to 60 ml/kg).

6   Children who have a transient or no response to the initial fluid challenge clearly require further crystalloid fluids and blood transfusion. 20 ml/kg of whole blood or 10 ml/kg of packed red cells should be initially transfused in these circumstances.

7   Due to the high surface-to-mass ratio in a child, heat loss occurs rapidly. A child who is hypothermic may become refractory to treatment. It is therefore vital to maintain the body temperature.

8   Acute gastric dilatation is commonly seen in the seriously ill or injured child. Gastric decompression, usually via a nasogastric tube, is therefore an essential component of their management.

9   After initial fluid resuscitation, and in the absence of a head injury, analgesia should not be withheld. A recommended regime is a 50 microgm/kg intravenous bolus of morphine, followed by 10–20 microgm/kg increments at 10 minute intervals until an adequate response is achieved.

The management of the paediatric patient is summarized in Figure 13.11.

*Figure 13.11: Management of the paediatric patient*



Tachycardia is earliest response to hypovolaemia

Gastric decompression via a nasogastric tube

Heat loss occurs rapidly; keep warm

Consider intraosseous route

Blood volume is 80 ml/kg in the child and 85–90 ml/kg in the neonate

Initially give 20 ml/kg of crystalloid replacement fluid if signs of hypovolaemia
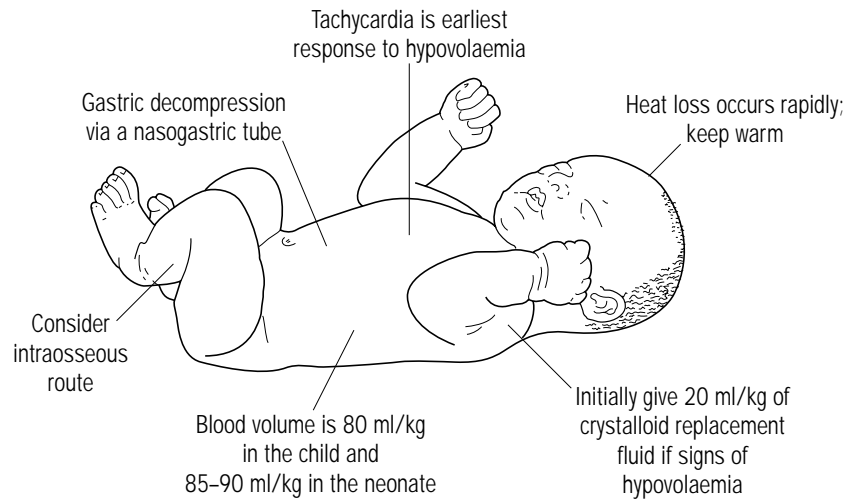
## CASE HISTORY 1

A 36-year-old man was involved in a fight in which he sustained several deep lacerations to his arms, chest and abdomen as a result of being struck with a long-bladed machete knife. The most serious laceration was to the anterior abdominal wall which had exposed the abdominal contents. The man's friend applied pressure to those wounds which were bleeding and covered the abdomen with a clean moist dressing. He was taken to the nearest hospital in the back of a pickup truck, a journey of 14 hours.

On arrival, initial assessment showed him to have a unobstructed airway, with a respiratory rate of 40 breaths/min. The chest was clear and, although lacerations were apparent, none had penetrated the chest wall. He had all the signs of Class III hypovolaemia and he was confused, only opening his eyes and moving with painful stimuli.

The patient was promptly resuscitated with 6 L/min of oxygen via a mask, two large intravenous needles were sited (the hospital had run out of cannulae) and he was given 2500 ml of warmed normal saline over 10 minutes. Blood was taken for crossmatching and a urinary catheter was inserted. There was no residual urine. He had a good response to initial resuscitation and, after 30 minutes, his blood pressure was 90 mmHg, he had passed 50 ml of urine, had regained consciousness and was able to talk coherently.

A full examination revealed that there was no penetration of gut from the abdominal wound, but blood loss was continuing to occur. A reassessment at this stage showed that his circulatory parameters were deteriorating again and he was therefore given a further 1500 ml of normal saline and two units of crossmatched blood over 30 minutes. This stabilized the patient and he was taken to the operating theatre. Anaesthesia and surgery were uneventful and he made a good recovery.

**CASE HISTORY 2**

A 9-year-old girl was admitted to hospital following a serious car accident in which two people were killed. On initial assessment, she was tachypnoeic, although her airway was clear. She had absent air entry on the left side of her chest and it was dull to percussion. Her trachea was not deviated. She was hypovolaemic with a pulse rate of 150/min, an unrecordable blood pressure and a delayed capillary refill time. Her level of consciousness was depressed as she would respond only to painful stimuli by making groaning sounds. Both pupils were responding normally. She was also noted to have a distended abdomen. Her weight was estimated to be 30 kg.

Oxygen was immediately given at 8 L/min via a face mask. Blood was taken for crossmatching while two intravenous cannulae were inserted. She was given an initial fluid bolus of 20 ml/kg (600 ml) of normal saline. As there was no improvement, this was repeated. Her blood pressure improved for a short time, but then again became unrecordable.

She was given a further 20 ml/kg of normal saline, which was followed by two units of uncrossmatched group 0 negative blood. During the resuscitation, the surgeon performed a detailed examination and decided on an immediate laparotomy, preceded by the insertion of a chest drain on the left to drain the haemothorax. At laparotomy, a ruptured spleen was resected.

The child required a further two boluses of 20 ml/kg of normal saline and another unit of blood in theatre before she stabilized. She subsequently made a good recovery and was discharged home.

### ACTIVITY 45

*Develop a simple poster outlining the overall management of acutely-ill patients admitted to your hospital. Apart from the admissions areas, where else would this type of poster be of value in your hospital?*

### ACTIVITY 46

*Develop a fluid resuscitation chart for both adults and children, based on the guidance given in this section and taking into account the type of intravenous replacement fluids available in your hospital.*

### ACTIVITY 47

*Make a list of the essential pieces of equipment needed for the immediate management of acutely-ill patients admitted to your hospital. Are these available in your hospital and are they readily accessible in the main admissions area? Can the resuscitation equipment be easily transported from one area to another in your hospital?*

# 14

# Burns

## Key points

1   The early management of seriously burned patients should follow a similar sequence to the management of other trauma patients.

2   The primary goal of treatment is to restore the circulating blood volume in order to maintain tissue perfusion and oxygenation.

3   Give intravenous fluids if the burn surface area is greater than 15% in an adult or greater than 10% in a child.

4   The use of crystalloid fluids alone is safe and effective for burns resuscitation. Using the correct amount of fluid in serious burns injuries is much more important than the type of fluid used.

5   The most useful indicator of fluid resuscitation is hourly monitoring of urine output.

6   Transfusion should only be considered when there are signs indicating inadequate oxygen delivery

## Introduction

Burns are a major cause of morbidity and mortality worldwide. The early and appropriate management of the seriously burned patient is a significant factor in improving survival. Fluid resuscitation and, if necessary, the use of blood products, is an important component of this management.

## Learning outcomes

When you have completed this section, you should be able to:

1  Assess and treat any life-threatening conditions arising in the burned patient.

2  Assess the severity of the burn in adults and children.

3  Provide adequate fluid resuscitation in burns patients.

4  Provide appropriate continuing care for burns patients.

## 14.1  The management of burns patients

The early management of seriously burned patients should follow a very similar sequence to the management of other trauma patients (see Section 13: *Trauma & Acute Surgery*). It should include:

1   Initial assessment and resuscitation.

2   Reassessment.

3   Definitive management.

The basic principles of first aid and initial resuscitation (Airway, Breathing, Circulation, etc.), are equally applicable in the seriously burned patient. However, it is also important to consider the following additional points.

1   First aiders must first protect themselves from the source of danger, whether it is heat, smoke, chemical or electrical hazard.

2   Evacuate the patient from the source of danger and stop the burning process by removing clothing or washing chemical burns with large amounts of water.

3   Smoke, toxic fumes or heat inhalation can result in damage to both the upper and lower airway. Injury to the upper airway can cause airway obstruction, although this may not develop immediately.

    High concentrations of oxygen, careful endotracheal intubation and mechanical ventilation may therefore be required.

    Figure 14.1 shows features that should alert you to an airway injury. Frequent assessment of the airway and ventilation is essential.

    *Note*: Endotracheal intubation may cause damage, especially when hot air has been inhaled. Consider the use of a laryngeal mask to avoid trauma.

*Figure 14.1: Features of an inhalation injury*

| Definite features | Suspicious features |
|---|---|
| ■ Pharyngeal burns | ■ History of confinement in burning area |
| ■ Sooty sputum | ■ Singed eyebrows and nasal hair |
| ■ Stridor | ■ Cough |
| ■ Hoarseness | ■ Wheeze |
| ■ Airway obstruction | ■ Respiratory crepitations |
| ■ Raised carboxyhaemoglobin level | |

4   Unconscious patients who have received electrical or lightning burns may be in ventricular fibrillation. External cardiac massage or defibrillation can be life-saving in this situation.

5   Cooling the burned area with *large* amounts of cold water can reduce the extent of injury, provided it is done as soon as possible following the burn.

6 Phosphorus burns, often caused by explosives, should be sealed with soft paraffin (Vaseline) or immersed in water to prevent reignition.

7 Other injuries may be present due to an explosion or an attempt to escape the fire. In addition, medical conditions such as a cerebrovascular accident may have precipitated a fall into a fire.

8 Intravenous fluids are required for burns greater than 15% in an adult under 50 years of age, or greater than 10% in a child or adult over 50 years of age.

9 Escharotomy may be required in deep burns to chest, limbs or digits as the effect of resuscitation increases tissue turgor, resulting in constriction of the vessels and limitation of chest movement.

## 14.2 Assessing the severity of burn

The severity of burn is determined by:

■ Burned surface area
■ Depth of burn
■ Other considerations.

### The burned surface area

Morbidity and mortality rises with increasing burned surface area. It also rises with increasing age so that even small burns may be fatal in elderly people.

Burns greater than 15% in an adult, greater than 10% in a child, or any burn occurring in the very young or elderly are considered serious.

### Adults

The 'Rule of 9's' is commonly used to estimate the burned surface area in adults. The body is divided into anatomical regions that represent 9% (or multiples of 9%) of the total body surface, as shown in Figure 14.2 on p. 300. The outstretched palm and fingers approximates to 1% of the body surface area. If the burned area is small, assess how many times your hand covers the area.

### Children

The 'Rule of 9's' method is too imprecise for estimating the burned surface area in children because the infant or young child's head and lower extremities represent different proportions of surface area than in an adult. Figure 14.3 shows a simple method of calculating the burns area in a child.

### Depth of burn

It is important to estimate the depth of the burn to assess its severity and to plan future wound care. Burns can be divided into three types, as shown in Figure 14.4 on p. 301.

*Figure 14.2: Estimating the
burned surface area in the
adult: the Rule of 9's*

Front

4.5%

18%

4.5%    4.5%

1%

9%    9%

Back

4.5%

18%

4.5%    4.5%

9%    9%

Front

A

2%    13%    2%

2%    2%

1%    1%

1%

B    B

C    C

2%    2%

Back

D

2%    13%    2%

2%    2%

1%    1%

E    E

F    F

2%    2%
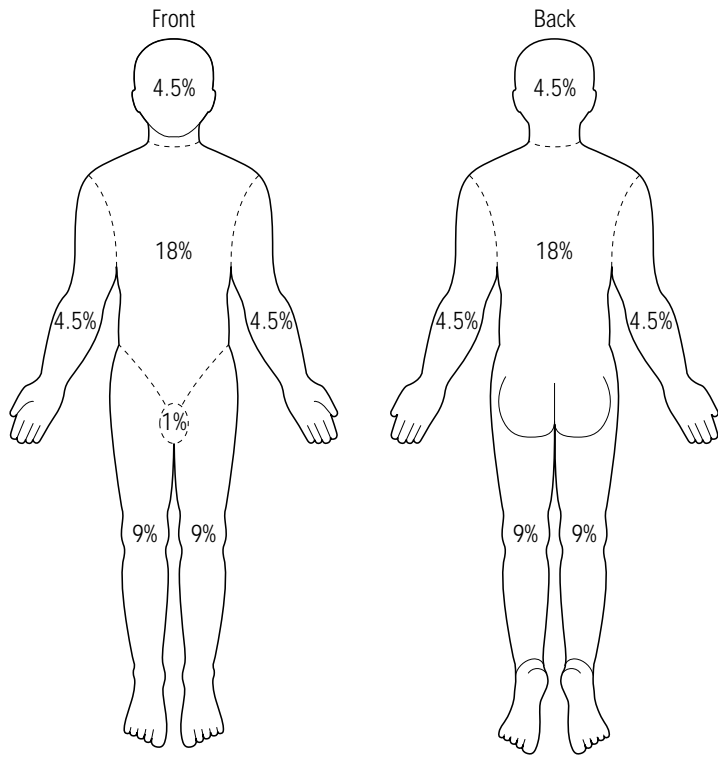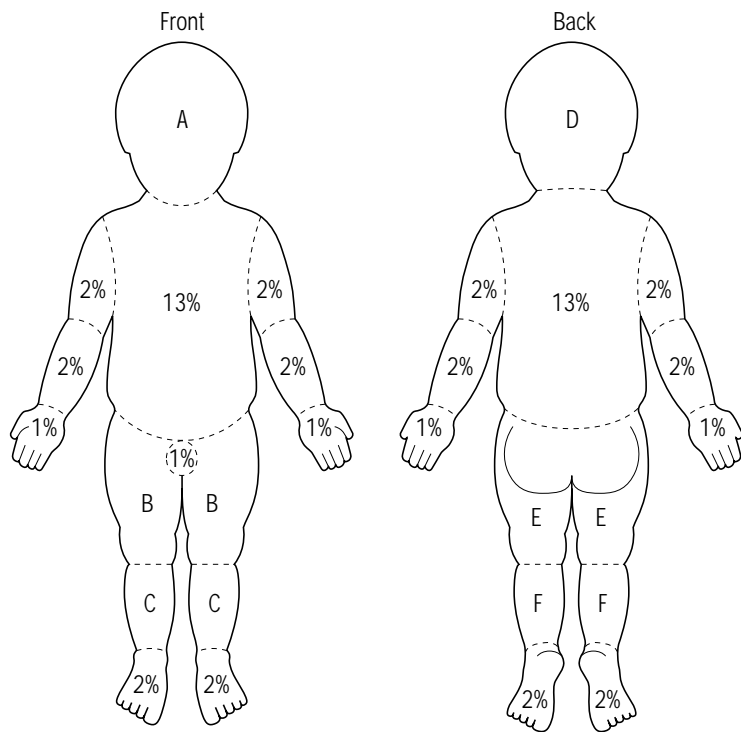
| Area | By age in years | | | |
|------|------|------|------|------|
|  | **0** | **1** | **5** | **10** |
| Head (A/D) | 10% | 9% | 7% | 6% |
| Thigh (B/E) | 3% | 3% | 4% | 5% |
| Leg (C/F) | 2% | 3% | 3% | 3% |

| Depth of burn | Characteristics | Cause |
|---|---|---|
| First degree burn | ■ Erythema<br>■ Pain<br>■ Absence of blisters | ■ Sunburn |
| Second degree (partial thickness) burn | ■ Red or mottled<br>■ Swelling and blisters<br>■ Painful | ■ Contact with hot liquids<br>■ Flash burns |
| Third degree (full thickness) burn | ■ Dark and leathery<br>■ Dry<br>■ Sensation only at edges | ■ Fire<br>■ Electricity or lightning<br>■ Prolonged exposure to hot liquids/objects |

It is common to find all three types within the same burn wound and the depth may change with time, especially if infection occurs. Any full thickness burn is considered serious.

## Other considerations

In addition to the area and depth of burn, the site of burn also determines its severity. Burns to the face, neck, hands, feet, perineum and circumferential burns (those encircling a limb, neck, etc.) are classified as serious.

Patients with an inhalation injury and those with associated trauma or significant pre-burn illness are also at special risk. See Figure 14.5.

*Figure 14.5: Criteria for a serious burn requiring hospitalization*

**Serious burn requiring hospitalization**

■ Greater than 15% burns in an adult

■ Greater than 10% burns in a child

■ Any burn in the very young, the elderly or the infirm

■ Any full thickness burn

■ Burns of special regions: face, hands, feet, perineum

■ Circumferential burns

■ Inhalation injury

■ Associated trauma or significant pre-burn illness: e.g. diabetes

## ACTIVITY 48

### Case study

*A 5-year-old boy, weighing 20 kg, accidentally set his clothes on fire while sitting near a cooking fire. He was wearing a pair of shorts and a shirt.*

His mother heard him scream, came running to investigate and found his clothes alight. She quickly managed to put out the burning clothes.

The child sustained burns to the outer aspect of his left thigh, from mid-thigh level to the side of his buttock and on the left side of his back between the buttock to his armpit. The skin was red, mottled and blistering.

1  How would you initially manage this patient?

2  Using Figures 14.3 and 14.4, estimate:
   ■ The burned surface area.
   ■ The expected depth of the burn.

### ACTIVITY 49

What is the procedure for estimating the burned surface area in your hospital? Are any charts available? Are they being used correctly?

If there are no charts available in your hospital, make copies of those shown in Figures 14.2 and 14.3.

Organise a teaching session for all staff involved in assessing and treating burns patients on how to use these charts to assess the severity of burns. Then monitor whether they are being used correctly and provide any further teaching required.

## 14.3  Fluid resuscitation in burns patients

Severe burns are characterized by a loss of integrity of the capillary wall membrane, resulting in the leakage of plasma-like fluid into the interstitial space, with oedema formation. The increase in capillary permeability that occurs is not just limited to the area of the burn, but takes place throughout the body. If untreated, hypovolaemia will occur leading to a reduced cardiac output, hypotension, oliguria and shock.

This loss of membrane integrity is greatest in the first 8 hours following injury and is only restored after approximately 18–36 hours.

In common with other forms of hypovolaemia, the primary goal of treatment is to restore the circulating blood volume in order to maintain tissue perfusion and oxygenation.

### Calculating fluid requirements
Several different methods to calculate the fluid requirement of burns patients in the first 24 hours are in common use. One of these methods is as follows.

1  Assess the patient:
   ■ Ascertain the time of the burn injury.

- ■ Estimate the weight of the patient.
- ■ Estimate the % burned surface area.

2  Commence oral fluids only (unless other injuries or conditions necessitate intravenous fluid replacement) if the % burned surface area is:
- ■ Less than 15% in adults
- ■ Less than 10% in a child.

3  Give intravenous fluids if the burned surface area is greater than 15% in an adult or greater than 10% in a child.

4  Do not overestimate the burn size as this can result in fluid overload.

5  To calculate the fluid requirements from the time of burn injury, apply the formulae shown in Figure 14.6 on p. 304.

6  During the first 48 hours, the use of a CVP line does not confer a particular advantage over more basic monitoring processes. This can later be reviewed if parenteral nutrition is involved.

## Resuscitation fluids used in burns

The fluid required due to the burn should be given as a replacement fluid, such as a balanced salt solution, e.g. Hartmann's solution or Ringer's lactate.

The fluid required for maintenance should be given as a maintenance fluid such as 4.3% dextrose in sodium chloride 0.18% (see Section 4: *Replacement Fluids*). The use of crystalloid fluids alone is safe and effective for burns resuscitation.

Whole plasma, human albumin solution and colloids have all been used in fluid resuscitation of burns patients. However, there is no clear evidence that they significantly improve outcomes or reduce oedema formation when used as alternatives to crystalloids.

> **There is no justification for the use of blood in the early management of burns, unless other injuries warrant its use.**

Using the correct amount of fluid in serious burns injuries is much more important than the type of fluid used. Figure 14.7 on p. 305 gives an example of fluid requirements from the time of injury for an adult patient weighing 60 kg with 20% burn.

## Monitoring

Any formulae that are used to calculate the fluid requirements of burns patients must only be regarded as a guide. It is essential to monitor and reassess the patient's clinical condition regularly and, if necessary, to adjust the volume of fluid given to maintain normovolaemia.

## FLUID REQUIREMENTS FOR BURNS PATIENTS

### Adults

**First 24 hours**

Fluid required due to burn (ml) = 3 x weight (kg) x % burned area

***plus***

Fluid required for maintenance (ml) = 35 x weight (kg)

Give half this volume in the first 8 hours and the other half over the remaining 16 hours

**Second 24 hours**

Fluid required due to burn (ml) = 1 x weight (kg) x % burned area

***plus***

Fluid required for maintenance (ml) = 35 x weight (kg)

Give this volume over 24 hours

**Note**

The upper limit of burned surface area is sometimes set at 45% for adults as a caution to avoid fluid overload. This limit can be overridden if indicated by the overall monitoring process.

### Children

**First 24 hours**

Fluid required due to burn (ml) = 3 x weight (kg) x % burned area

***plus***

Fluid required for maintenance (ml):

   First 10 kg = 100 x weight (kg)

   Second 10 kg = 75 x weight (kg)

   Subsequent kg = 50 x weight (kg)

Give half this volume in the first 8 hours and the other half over the remaining 16 hours

**Note**

1   The upper limit of burned surface area is sometimes set at 35% for children as a caution to avoid fluid overload. This limit can be overridden if indicated by the overall monitoring process.

2   In children, a very approximate weight guide is:

   Weight (kg) = (Age in years + 4) x 2

   Alternatively use a height/weight chart.

3   Children compensate for shock very well, but may then collapse rapidly.

Figure 14.7: Example of
fluid requirements from the
time of injury for an adult
patient

**EXAMPLE OF FLUID REQUIREMENTS FROM THE TIME OF INJURY:
Adult patient weighing 60 kg with 20% burn**

**First 24 hours**

Replacement fluid: 3 x 60 (kg) x 20 (%)　　3600 ml

*plus*

Maintenance fluid: 35 x 60 (kg)　　2100 ml

Total fluid requirement　　5700 ml

Give half this volume in the first 8 hours and the other half over the
remaining 16 hours.

**Second 24 hours**

Replacement fluid: 1 x 60 (kg) x 20 (%)　　1200 ml

*plus*

Maintenance fluid: 35 x 60 (kg)　　2100 ml

Total fluid requirement　　3300 ml

Figure 14.8 shows the clinical features that should be monitored. Blood
pressure can be difficult to ascertain in a severely burned patient and may
be unreliable.

**Monitoring**

- Blood pressure
- Fluid input/output (hydration)
- Conscious level and anxiety state
- Heart rate
- Temperature
- Respiratory rate/depth

The most useful indicator of fluid resuscitation is hourly monitoring of urine
output. In the absence of glycosuria and diuretics, aim to maintain a urine
output of 0.5 ml/kg/hour in adults and 1 ml/kg/hour in children.

**ACTIVITY 50**

**Case study (continued)**

*Estimate the volume of fluids required for the child described in Activity 48.
Which fluids would you prescribe? Why? How would you assess the adequacy
of the resuscitation?*

**ACTIVITY 51**

*Are there any guidelines available in your hospital on fluid resuscitation for
burns patients? Are they adequate and used appropriately by all staff
involved in prescribing their use?*

*If none exist or you think they are inadequate, develop some draft guidelines and discuss them with senior colleagues.*

*Once they have been agreed and approved, organise a teaching session for all staff involved in the treatment of bums patients. Monitor whether the guidelines are being used correctly and provide any further teaching that may be required.*

## 14.4 Continuing care of burns patients

After initial treatment, consider the following measures in the continuing care of burns patients.

### Anti-tetanus toxoid
Anti-tetanus toxoid is essential in burns patients.

### Analgesia
Give analgesia to severely-burned patients. For initial pain relief, give a 50 microgm/kg intravenous bolus of morphine, followed by 10–20 microgm/kg increments at 10-minute intervals until the pain is just controlled.

**Note**: Do not give intramuscular analgesics for at least 36 hours until the patient has been resuscitated.

Pain may also be reduced by elevating burned limbs and covering partial thickness burns with clean linen to deflect air currents.

### Nasogastric tube
Insert a nasogastric tube if the patient experiences nausea, vomiting, abdominal distension or if the burns involve more than 20%. It may later be used for feeding if this is not possible orally after 48 hours and to administer antacids to protect the gastric mucosa.

Antacids are often required, especially with large burns, and can usually be given orally: e.g. mixture of magnesium trisulphate, cimetidine or ranitidine.

### Urinary catheter
This should be sited early to allow accurate measurement of urine output.

### Temperature
Nursing patients in a room with a temperature above 28°C will help to prevent heat loss.

### Infection control
The profound depression of immunity that occurs in seriously burned patients means that infections and sepsis are common. Strict attention should be given to aseptic techniques when changing dressings and during invasive procedures. Antibiotics are indicated only for contaminated burns.

## Nutrition

Severe burns are characterized by an increase in the body's metabolic rate, together with protein catabolism, weight loss and poor wound healing. Morbidity and mortality can be significantly reduced in these patients by providing a high-protein, high calorie diet. Enteral feeding (orally or via a nasogastric tube) is the safest method.

The approximate daily nutritional requirement of a severely burned patient is 3 g/kg of protein and 90 calories/kg.

Various nutritional regimes have been described to provide this requirement. A straightforward example of one is the 'egg diet': each egg contains about 6 g of protein and 70 calories. A 70 kg patient would therefore require 35 eggs per day to maintain his or her nutritional status.

## Anaemia

Anaemia and hypoproteinaemia commonly develop following extensive burns. These can be minimized by ensuring that burns patients receive a high-protein, high-calorie diet. Vitamin supplements and haematinics should also be administered.

**Blood transfusion should only be considered when there are signs indicating inadequate oxygen delivery.**

## Surgery

Debridement and skin grafting is often required for serious burns. However, extensive debridement can result in considerable blood loss. This can be minimized by limiting the area to be debrided at each procedure and by using techniques to reduce operative blood loss, such as tourniquets (see Section 12.2: *Techniques to Reduce Operative Blood Loss*).

Haematinics should also be administered to these patients between surgical procedures.

## Escharotomy

Escharotomy is the longitudinal splitting of deep circumferential burns to relieve swelling and pressure and restore the distal circulation (limbs and digits). It may also be required as a matter of urgency to relieve airway compression resulting from circumferential chest burns. The procedure is painless and can be performed on the ward under sterile conditions, if necessary.

## Transfer

Seriously burned patients often require long-term special care and are therefore best managed in a specialized burns unit, if available. Patients should only be transferred following stabilization, usually after 36 hours or more.

## Physiotherapy

Physiotherapy is very important to prevent pneumonia, disability and contracture formation and should be started at an early stage.

## 14.5  Burns prevention

It is beyond the scope of this module to include a detailed account of the many important steps that can be taken to prevent burns injuries. However, effective public education campaigns and fire prevention programmes can significantly reduce the incidence or severity of burns.

Education programmes on burns prevention are most effective before and during the cold season. They should include education on the first aid treatment of burns.

### ACTIVITY 52

1  *What are the most common causes of bums in your locality?*

2  *Talk to senior colleagues about ways in which you could contribute to a reduction in the incidence of bums, such as training community health workers to organise a first aid programme in local schools.*

# Part 3

# The appropriate use of blood: putting it into practice

# 15

## Making it happen: what can *I* do?

### Key points

1   Health care providers at any level of the health care system can take the initiative to develop effective strategies to improve the appropriate clinical use of blood.

2   Information needs to be collected in a systematic way in order to evaluate clinical blood use within the hospital.

3   A hospital transfusion committee is an essential component of a strategy to ensure the appropriate clinical use of blood.

4   Guidelines on the clinical use of blood are essential in minimizing unnecessary transfusion and promoting the appropriate use of blood and blood products. Guidelines should be based on systematic reviews of the evidence on clinical effectiveness. Their development requires the involvement of personnel from different departments, specialties and levels of the health care system.

5   The effective implementation of guidelines on the clinical use of blood depends on the education and training of all personnel involved in the clinical transfusion process.

## Introduction

The challenges that now face you as a prescriber of blood are to find ways of improving the availability and effective use of safe blood products and alternatives to transfusion, essential diagnostic tests and treatments for anaemia and volume depletion.

Health care providers at any level of the health care system can take the initiative to develop effective strategies to promote the appropriate clinical use of blood. The goal is to improve transfusion services and the use of blood and blood products within accepted policies and procedures of your country or region.

## Learning outcomes

When you have completed this section, you should be able to:

1   Gather information on ways in which the clinical use of blood can be improved in your hospital, based on a review of existing records, and by talking with colleagues about their experiences and problems.

2   Develop a plan to improve clinical transfusion practice in your own hospital.

3   Promote the establishment of a transfusion committee within your hospital.

4   Promote and contribute to the development, implementation and monitoring of local guidelines on the clinical use of blood.

5   In conjunction with senior colleagues, prepare a plan for the education of relevant staff within your hospital on the clinical use of blood.

## 15.1  Where do I start?

As you have worked through this module, you have no doubt related the information it contains to your own situation. In particular, your work on the activities should have helped you to evaluate practice and procedures in your own hospital and to identify ways in which they might be improved. You may, for example, already have begun to work towards the development of standard operating procedures or clinical transfusion guidelines in relation to your own specialty.

Since this module has been designed for global use, it covers a wide variety of clinical situations, including those where highly technical diagnostics and expensive therapeutics are available. Many hospitals do not have such options, however, and some of the material may not be relevant to your local situation. The key to using the module effectively is therefore to:

1   Assess the safety and adequacy of the supplies of blood, blood products and alternatives to transfusion available in your hospital.

2   Evaluate clinical transfusion practice in your own hospital and Identify any constraints on the appropriate clinical use of blood.

3   Identify how the clinical use of blood could be improved in your hospital through, for example, better organization, education and supervision.

While there may be a need for additional resources, it is important to remember that simple, inexpensive changes can often have a dramatic impact on clinical blood use.

The purpose of this module is to help you, as a prescriber of blood, to understand the importance of avoiding unnecessary or preventable transfusions and to provide you with the tools for doing so. However, reading this module alone will not change practice. You now need to take the initiative, to make something happen and perhaps to convince others that they also need to help make something happen. Nothing will improve if no-one begins the process of change. It's now up to you.

### Identifying the problems

From your work on this module, you may have identified some ways in which you want to modify your own clinical transfusion practice. You may also have identified a need for a wider, more systematic approach to clinical decision-making on transfusion through the development of guidelines on the clinical use of blood and continuing education for staff involved in various aspects of the transfusion process.

You will have realized, however, that you will need the support of clinical colleagues as well as the hospital laboratory, pharmacy and administration and that you may perhaps also need to involve public health programmes that are concerned with the prevention and treatment of anaemia.

The first step is to draw on your own experience to identify what is needed in order to minimize unnecessary transfusions and reduce the risks of transfusion for your patients. Your work on the activities should have

provided a useful starting point for this. Formal and informal discussions with your colleagues will provide further insights into problems that need to be addressed. Key information on the use of transfusion can also be collected from a review of existing records, such as blood request forms.

Challenges and solutions to the prevention of anaemia and the appropriate use of blood vary widely between countries and at different levels of the health care system. Some of the issues that might need to be addressed include:

- Availability of adequate supplies of safe blood for immediate transfusion
- Availability of blood bank personnel and reagents to crossmatch the patient's blood and get the blood to the clinical area when it is required
- Availability of intravenous replacement fluids
- Availability of pharmaceuticals to prevent and treat the causes of anaemia in your area: e.g. iron, antimalarials, anti-helminthics
- Availability of laboratory support to evaluate anaemia among outpatients and inpatients
- Appropriate use of available diagnostic services by practitioners
- Availability of sterile, disposable equipment for blood samples, injection or infusion of intravenous replacement fluids
- Availability of trained staff to ensure the prompt transport of specimens to and from the blood bank, the correct administration of blood products and the monitoring of transfused patients.

### ACTIVITY 53

*Identify the main specialties and categories of personnel who are involved in the clinical transfusion process in your hospital.*

*Through formal or informal discussions, talk to a selection of them about their approaches to prescribing or administering blood and blood products and identify any problems they face in using blood appropriately.*

## Collecting data

As you work towards developing a plan of action, you will realize that you need access to a range of information to enable you to evaluate the effectiveness of clinical transfusion practice in your hospital and identify any areas where improvement is required. A review of hospital records is important to evaluate how patients are assessed prior to transfusion and whether blood is being prescribed appropriately on the basis of both clinical and laboratory indications. It will also help you to assess the effectiveness of the diagnosis and early treatment of anaemia in the primary health care setting.

A review of records should focus on information that is routinely documented in writing in blood bank, haematology and pharmacy records, ward registers, and patient records and charts. Examples of records that could be used in a review of clinical transfusion practice include:

1 Blood bank records:
   ■ Number of units requested by patient category
   ■ Number of units crossmatched
   ■ Number of unfilled requests for blood
   ■ Number of elective surgeries cancelled because of blood shortages
   ■ Number of units issued for transfusion by patient category
   ■ Number of units issued and returned unused
   ■ Number of units discarded
   ■ Number of units issued without screening for infectious disease markers (HIV, hepatitis, syphilis and other nationally-required tests)
   ■ Number of units issued without compatibility testing
   ■ Indications for transfusion that appear to comply with national, regional or hospital guidelines.

2 In-patient records:
   ■ Number of patients transfused by patient category
   ■ Clinical and laboratory indications for transfusion
   ■ Outcome of transfusions:
      — Acute complications of transfusion
      — Delayed complications of transfusion
      — Mortality.

3 Out-patient records (in areas of high prevalence of anaemia):
   ■ Number of patients seen
   ■ Number of patients assessed for anaemia (clinically or by measurement of haemoglobin) during:
      — Prenatal visits
      — Well child visits
      — Sick child visits.

4 Pharmacy records to assess the adequacy and reliability of the supply of:

**Intravenous replacement fluids**
   ■ Crystalloid solutions, including normal saline (0.9% sodium chloride)
   ■ Colloid solutions.

**Drugs used in:**
   ■ Anaemia
   ■ Malaria
   ■ Labour and delivery
   ■ Shock
   ■ Child-spacing (to reduce pregnancy-associated anaemias)
   ■ Haemolytic disease of the newborn (immunoglobulin anti-D).

**Medical devices for:**

- Blood salvage
- Maximization of intravascular volume (pressure cuffs)

**Sterile disposable equipment:**

- Needles
- Syringes
- Blood sample tubes
- Blood giving sets, including cannulae/needles.

Where national, regional or hospital clinical transfusion guidelines are already available, these should define criteria for transfusion that can be used to monitor the use of blood and blood products.

Ensuring the accuracy and completeness of existing records is an important step in the assessment of a hospital's transfusion practices. Often, many records are maintained, but not in a form that is useful for tracing important information. In these circumstances, record-keeping may need to be revised to improve its usefulness. For example, extracting data from a review of patient charts requires considerable time and resources, but if registers are available, it may be possible to modify them to make them more useful for periodic evaluations of transfusion practice.

---

### ACTIVITY 54

*List some examples of clinical and laboratory criteria for the appropriate use of blood that could be used for a review of clinical transfusion practice in your own hospital. Identify the records in your hospital that could be used to assess the proportion of transfusions that meet these criteria.*

*Then identify other sources of information you would need to review in order to evaluate transfusion practice in your hospital.*

*In conjunction with senior colleagues in relevant departments, organize a review of records. Are there significant variations in blood use between different specialties and clinical teams? Is there a need for any additional records or for any modification of the way in which certain records are kept?*

*From the review of records, it should be possible to begin to monitor patterns of clinical blood use in your hospital and identify whether any changes are needed to minimize unnecessary transfusions.*

---

## Monitoring and evaluating the clinical use of blood

As you begin to identify problems and solutions in your hospital, it should be obvious that a regular review is required of transfusion practices, laboratory capacity and the availability of safe blood, intravenous replacement fluids, essential drugs and equipment. Systematic monitoring and evaluation is needed to ensure that:

1  Patients are assessed appropriately.

2   Alternatives to blood products, including crystalloid fluids and colloid solutions are readily available.

3   Blood is not used unnecessarily.

4   Appropriate blood products are used, when necessary.

5   Adequate and reliable supplies of safe blood products are available to meet the demands of the hospital.

Periodic evaluations will be needed on a routine basis with the development of standardized criteria for clinical transfusion practice and hospital services. Clearly defined criteria set a standard for record-keeping in the hospital and facilitate review.

## 15.2  Developing a plan of action

Once you have made a preliminary assessment of the current situation and identified the factors that determine how blood products are being used, the next step is to begin planning any action that may be required to improve clinical transfusion practice in your hospital. You may feel that action is needed at several levels:

■   To modify your own clinical practice

■   To improve practice among members of your clinical team: for example, through teaching and monitoring of practice

■   Within your hospital as a whole, such as the establishment of a hospital transfusion committee or the development of guidelines on the clinical use of blood, if national or local guidelines do not yet exist

■   On a national or regional basis, such as the inclusion of transfusion medicine in the curricula of medical and nursing schools.

You may have tried out some of your ideas already, but others will require more time and effort as well as the cooperation and support of other personnel and departments. It is therefore important to identify priorities. You will almost certainly be unable to put all your ideas into action yourself and it will be necessary to work with others to plan and implement the action that you have identified as being both necessary and feasible.

1   Make a list of everything you want to achieve, but set priorities:

■   Select short-term and long-term goals

■   Set a schedule for achieving these goals, but be realistic about the time that will be needed

■   Don't neglect any possible opportunities. Low-cost solutions are often available.

2   Keep your expectations high and think creatively. How could the situation be improved without more resources or with very limited additional resources? For example:

■   The establishment of a hospital transfusion committee

■   The development of guidelines on the clinical use of blood

■ The development of a blood ordering schedule and standard operating procedures for each stage in the transfusion process

■ Clinical meetings and training sessions for all practitioners involved in the transfusion process

■ The expansion of nutrition education in routine maternal-child health visits

■ Regular reviews of transfusion practice and feedback in regular staff meetings

■ A review of pharmacy drug lists to identify essential replacement fluids, pharmaceuticals, medical devices and equipment and to remove more expensive or unnecessary products.

Bulk purchases of drugs and supplies at a regional or national level tend to be less expensive and provide an opportunity for testing the quality and sterility of drugs, replacement fluids and other supplies. Information on the WHO Drug Management Programme can be obtained from WHO Regional Offices.

3 Plan a strategy for advocacy. Whose commitment and support will be needed to modify clinical practice or record-keeping or to obtain more resources for equipment, consumables or personnel?

■ Hospital medical director

■ Clinical, blood bank, laboratory and pharmacy personnel

■ Hospital managers and administrators

■ Local/regional/national health authorities

■ Medical and nursing schools

■ Non-governmental organizations.

4 Continue to re-evaluate by evaluating resources, resetting priorities and strategies, and setting new time schedules for achieving goals.

## ACTIVITY 55

*Look back at your work on the activities in this module and identify areas where you feel action is required to improve clinical transfusion practice.*

*Make a list of any action you feel is needed and divide your suggestions into two categories.*

*1 Action that you can take. Choose the issues that you think are most important and put them in order of priority. Note down the action that you plan to take and the results that you would expect.*

*2 Action that requires collaboration with others within the hospital or beyond. Identify the people or departments whose support will be needed and note down your suggestions for action, putting them into order of priority and a logical sequence.*

*Prepare a realistic schedule for the planning and implementation of your ideas for action and identify any resources that may be required.*

## 15.3  Hospital transfusion committee

There is no question that everyone at each level of the health care system can make a difference to clinical transfusion practice in their own hospital. Many small and inexpensive innovations can have a significant impact on the appropriate use of blood and the prevention and treatment of anaemia and other conditions that may lead to the need for transfusion. However, there is a limit to what individuals alone can achieve and a bigger force is also needed to change clinical practice and the allocation of resources.

For this reason, every hospital should establish a hospital transfusion committee to monitor and review clinical transfusion practice in that hospital. The hospital transfusion committee should have authority within the hospital structure to determine hospital policy in relation to transfusion and resolve any problems that have been identified. The role of a hospital transfusion committee includes the following functions.

1   To monitor the safety, adequacy and reliability of the supply of blood, blood products and alternatives to transfusion, including intravenous replacement fluids and essential drugs.

2   To establish systems and procedures for effective clinical transfusion practice within the hospital, including the development of a hospital blood ordering schedule, standard operating procedures and guidelines on the clinical use of blood, if none have been developed at national level.

3   To coordinate the education and training of all clinical and blood bank staff involved in the transfusion process.

4   To monitor the usage of blood and blood products in the hospital.

5   To review incidents of severe adverse effects or errors associated with transfusion and identify any corrective action required.

In addition, the committee should review related issues such as the availability of laboratory support and the effectiveness of public health programmes that are required for the effective prevention and treatment of anaemia and blood loss. Reports by hospital staff on their problems and concerns may also help guide a systematic evaluation of a particular aspect of clinical transfusion practice.

The committee should be multidisciplinary and involve all departments in the hospital that are involved in providing and prescribing blood and blood products. These may include:

1   Senior representatives of clinical specialties that prescribe blood.

2   The responsible officer from the hospital blood bank and, where applicable, a representative of the blood transfusion service that supplies blood and blood products to the hospital.

3   The hospital staff member responsible for the supply of intravenous replacement fluids, pharmaceuticals, medical devices and sterile disposable equipment.

4   The senior nurse.

In areas where chronic anaemia is prevalent, members of the primary health care system should also be included on the committee to ensure that strategies for the prevention of anaemia are being implemented effectively and adequately supported. For example, the WHO Haemoglobin Colour Scale (see pp. 42–43) now provides a simple and inexpensive method of screening all women for anaemia during pregnancy.

While the membership of the hospital transfusion committee will be primarily clinical, it may also need to involve other personnel on occasions, such as the hospital administrator/finance officer and the medical records officer.

Health care providers at all levels can take the initiative to heighten awareness of transfusion practices in their hospital and work to establish a transfusion committee. However, the hospital transfusion committee is most likely to be successful if it is led by a respected, senior clinician who is enthusiastic about promoting the appropriate use of blood and blood products.

### ACTIVITY 56

*Identify key personnel who should be represented on a hospital transfusion committee, if one has not yet been established in your hospital.*

*Talk to these people about the importance of having a hospital transfusion committee to monitor and evaluate clinical transfusion practice. Discuss the role of a committee and propose that one should be formally established within your hospital.*

## 15.4  Guidelines on the clinical use of blood

Guidelines on the clinical use of blood usually represent a consensus or 'expert' statement on the clinical and laboratory criteria for the use of blood products and replacement fluids. They serve the following functions.

1  They define optimal standards of patient care for clinicians, blood banks and hospital managers.

2  They serve to protect the scarce resource of blood and contain costs for transfusion services.

3  They outline a commitment to the safe and appropriate clinical use of blood, which facilitates the development of policy, procedures, resource allocation and monitoring of blood use.

Where national or regional guidelines exist, these should form the basis of local guidelines. Where no national guidelines have yet been developed, the hospital transfusion committee should be responsible for preparing simple guidelines with the objective of:

■  Promoting the prevention and early diagnosis and treatment of anaemia

- Promoting the availability and use of replacement fluids
- Defining clinical and laboratory criteria for transfusion in order to minimize the number of unnecessary transfusions
- Ensuring that safe blood is available to patients in a timely manner
- Improving the accuracy and completeness of record-keeping to assist in monitoring clinical blood use.

## Involving the right people

Whether at national or local level, the development and implementation of transfusion guidelines requires the involvement and support of a wide range of personnel including:

1  Health care providers from:
   - Different medical specialties:
     — Surgery
     — Anaesthesia/intensive care
     — Obstetrics/gynaecology
     — Paediatrics
     — Accident and emergency/casualty
     — Internal medicine
     — Haematology/oncology
     — Transfusion medicine
   - Different training backgrounds and varied experiences:
     — Doctors
     — Nurses
     — Mid-level providers, including (clinical officers, physicians' assistants, nurse-anaesthetists, nurse-midwives)

2  Personnel from:
   - Blood transfusion service/hospital blood bank
   - Haematology laboratory.

3  Administrators
   - Hospital managers and administrators
   - Programme managers of maternal-child health, nutrition and malaria control programmes.

4  Non-governmental organizations involved in blood transfusion:
   - National Red Cross or Red Crescent Society
   - Blood donor organizations
   - Associated voluntary organizations: e.g. Haemophilia Association, Thalassaemia Association.

The involvement of individuals from related programmes, such as maternal-child health, nutrition and malaria control will ensure that guidelines are consistent with existing policy and facilitate coordination with primary health care programmes.

It is important to recognize that it takes time to develop comprehensive guidelines on the clinical use of blood, whether they are for national, regional or local use. Where possible, they should be based on the best available evidence of clinical effectiveness. However, the different perspectives, experiences and training of individuals from different specialties and different levels of the health care system are important in defining standards of care for patients. If key data are not available, guidelines may be reached by consensus until more information is available.

Guidelines should be periodically reviewed and revised as new information becomes available.

Guidelines should be developed with the involvement of local and/or national health authorities. The approval of transfusion guidelines by these authorities will help to secure commitment from government and non-governmental organizations, which is essential to their successful implementation.

Guidelines should cover all the activities required to optimize clinical transfusion practice. They may include sections on:

1 Prevention of anaemia and conditions that lead to the need for transfusion, including:
   - Public health measures
   - Early diagnosis
   - Effective treatment (including an essential drugs list).

2 Blood request form.

3 Blood ordering schedule.

4 Standard operating procedures for all stages of the clinical transfusion process, including essential laboratory and blood bank services.

5 Clinical and laboratory criteria for transfusion and alternatives to transfusion in all major specialties.

6 Plans for implementation: strategies for the dissemination, implementation and monitoring of the guidelines.

## ACTIVITY 57

*Look back on your work on activities in this module that suggest the development of guidelines in relation to various aspects of transfusion practice. Make a list of areas where you feel guidelines are required or where existing guidelines may need to be improved.*

*Identify key personnel within your hospital and/or region who could play an important role in the development of guidelines. Arrange a meeting to plan the process of developing, implementing and monitoring guidelines on the clinical use of blood.*

For more detailed guidance on preparing transfusion guidelines, see the WHO document, *Recommendations on Developing a National Policy and Guidelines on the Clinical Use of Blood* (1998).

## 15.5 Education and training on the clinical use of blood

The development and dissemination of guidelines alone is insufficient to alter long-standing practices. The prescribing of transfusion in accordance with the guidelines will also depend on the development of educational programmes for all clinicians, laboratory technical staff and other personnel involved in the transfusion process.

Examples of opportunities for education on the clinical use of blood include:

1 Undergraduate and postgraduate programmes in:
   ■ Medical schools and teaching hospitals
   ■ Medical laboratory technology training institutions
   ■ Schools of nursing
   ■ Paramedical schools.

2 In-service training
   ■ Clinicians
   ■ Nurses
   ■ Hospital blood bank staff.

3 Continuing medical education
   ■ Teaching sessions within the clinical area
   ■ Hospital clinical meetings
   ■ Seminars and conferences
   ■ Medical publications.

Members of the hospital transfusion committee and well-respected clinicians can serve as effective educators in hospital meetings. Reviews of actual clinical practice with meetings for staff to present and discuss the findings of these reviews are a valuable way of sharing experience to help improve practice.

In the longer term, the incorporation of transfusion medicine into undergraduate and postgraduate medical and nursing programmes will be an important means of promoting the appropriate clinical use of blood at all levels of the health care system.

### ACTIVITY 58

*Talk to members of your clinical team to identify any areas where they feel continuing education would be helpful in relation to the clinical use of blood.*

*Then talk to senior colleagues in other departments to identify priorities for education in relation to clinical transfusion practice. What opportunities are there within your own hospital for education on the clinical use of blood? Propose to the hospital transfusion committee that a structured programme of teaching for all relevant staff should be planned to support the development and implementation of clinical guidelines on transfusion.*

*Also suggest that the hospital transfusion committee should make contact with medical and nursing schools to encourage the inclusion of transfusion medicine within undergraduate and postgraduate curricula.*

Now that you have reached the end of this module and have had an opportunity to reflect on transfusion practice in your own clinical area and more widely within your hospital, you should be able to recognize the part that you can play in promoting the appropriate clinical use of blood and blood products. Remember that even small changes in systems, procedures and practice can have significant effects in minimizing unnecessary transfusion and reducing the risks for patients who require transfusion.

You may find it difficult at first to convince some people that change is necessary, particularly when human and financial resources are stretched. Be realistic in making and implementing your plan for action, and recognize the importance of securing the cooperation and support of staff at all levels through sharing information and taking their own experience, ideas and problems into account. While progress may initially be slow, a regular and systematic review of transfusion practices should demonstrate the effectiveness of change and point to any areas where further improvement may be needed.

# Glossary

**Additive solution (red cell additive solution)**
Various proprietary formulas designed for reconstitution of red cells after separation of the plasma to give optimal red cell storage conditions. All are saline solutions with additions: e.g. adenine, glucose and mannitol.

**Albumin**
The main protein in human plasma.

**Anaemic hypoxia**
Reduced supply of oxygen to the tissues due to low haemoglobin content of red cells in the blood.

**Anisocytosis**
Abnormal degree of variation in the size of red cells observed in the blood film.

**Anti-D immunoglobulin**
Human Immunoglobulin G preparation containing a high level of antibody to the Rh D antigen.

**Apheresis**
Procedure that involves withdrawal of blood, ex vivo separation of a component (e.g. plasma and platelets) and reinfusion of the other components. *See* Plasmapheresis.

**Activated partial thromboplastin time (APTT)**
A test of the blood coagulation system. Prolonged by deficiency of coagulation factors XII, XI, IX, VIII, X, V, II and fibrinogen. Also referred to as partial thromboplastin time (kaolin) (PTTK).

**Balanced salt solution (crystalloid)**
Usually a sodium chloride salt solution with an electrolyte composition that resembles that of extracellular fluid: e.g. Ringer's lactate, Hartmann's solution.

**Blood (as a product for treatment)**
In this module, refers to any component containing red cells, except where otherwise specified. *See* Red cell components.

**Blood product**
Any therapeutic product derived from human whole blood or plasma donations.

**Buffy coat**
The layer of white cells that forms at the interface between the red cells and plasma when blood is centrifuged.

**Colloid solution**
A solution of large molecules which have a restricted passage through capillary membranes. Used as an intravenous replacement fluid. Colloid solutions include gelatines, dextrans and hydroxyethyl starch.

**Commercial or professional donor**
A donor who gives blood for money or other form of payment.

**Crystalloid solution**
Aqueous solution of small molecules which easily pass through capillary membranes: e.g. normal saline, balanced salt solutions.

**Decompensated anaemia**
Severe clinically significant anaemia: anaemia with a haemoglobin level so low that oxygen transport is inadequate, even with all the normal compensatory responses operating.

**Desferrioxamine (Desferal)**
An iron-chelating (binding) agent that increases excretion of iron.

**Dextran**
A macromolecule consisting of a glucose solution that is used in some synthetic colloid solutions.

**Dimorphic blood film**
A blood film that shows both microcytic, hypochromic, red cells *and* macrocytic red cells, suggesting deficiency of iron and folate (or folate and vitamin $B_{12}$).

**Disseminated intravascular coagulation (DIC)**
Activation of the coagulation and fibrinolytic systems, leading to deficiencies of coagulation factors, fibrinogen and platelets. Fibrin degradation products are found in the blood. May also cause tissue/oxygen damage due to obstruction of small vessels. Clinically, often characterized by microvascular bleeding.

**Family or replacement donor**
A donor who gives blood when it is required by a member of the patient's family or community. This may involve a hidden paid donation system in which the donor is paid by the patient's family.

**Fibrinogen**
The major coagulant protein in plasma. Converted to (insoluble) fibrin by the action of thrombin.

**Fibrin degradation products**
Fragments of fibrin molecule formed by the action of fibrinolytic enzymes. Elevated levels in the blood are a feature of disseminated intravascular coagulation.

**Gelatine**
A polypeptide of bovine origin that is used in some synthetic colloid solutions.

**Haematocrit (Hct)**
An equivalent measure to packed cell volume, derived by automated haematology analyses from the red cell indices. *See* Packed cell volume.

**Haemoconcentration**
Elevated haematocrit (packed cell volume) due to a reduction in plasma volume.

**Haemodilution**
Reduced haematocrit (packed cell volume). Acute haemodilution caused by red cell loss and replacement by crystalloid or colloid infusion.

**HLA**
Human leucocyte antigen.

**Hydroxyethyl starch (HES)**
A macromolecule made from starch that is used in some synthetic colloid solutions.

**Hypertonic**
Fluid exerting a higher osmotic pressure than normal body fluids.

**Hypochromia**
Reduced iron content in red cells, indicated by reduced staining of the red cell. A feature of iron deficiency anaemia. *See* microcytosis.

**Hypovolaemia**
Reduced circulating blood volume.

**Hypoxic hypoxia**
Reduced supply of oxygen to the tissues due to an inadequate supply of oxygen from the lungs to the red cells.

**Immunoglobulin (Ig)**
Protein produced by B-lymphocytes and plasma cells. All antibodies are immunoglobulins. The main classes of immunoglobulin are IgG, IgM (mainly in plasma), IgA (protects mucosal surfaces) and IgE (causes allergic reactions).

**IgG, IgM, IgA, IgE**
*See* Immunoglobulin.

**Incidence**
The proportion of a defined population becoming newly infected by an infectious agent within a specific period of time.

**International normalized ratio (INR)**
Measures the anticoagulant effect of warfarin. Sometimes called the prothrombin time ratio (PTR).

**Isotonic**
Fluid exerting the same osmotic pressure as normal body fluids.

**Kernicterus**
Damage to the basal ganglia of the brain, caused by fat-soluble bilirubin. Causes spasticity. Can be caused by haemolytic disease of the newborn.

**Kleihauer test**
Acid elution of blood film to allow counting of fetal red cells in maternal blood.

**Macrocytosis**
Red cells larger than normal. A feature of the red cells in, for example, anaemia due to deficiency of folic acid, vitamin $B_{12}$.

**Maintenance fluids**
Crystalloid solutions that are used to replace normal physiological losses through skin, lung, faeces and urine.

**Megaloblasts**
Precursors of abnormal red cells. Usually due to deficiency of vitamin $B_{12}$ and/or folate and develop into macrocytic red cells (enlarged red cells).

**Microcytosis**
Red cells smaller than normal. A feature of iron deficiency anaemia. *See also* Hypochromia.

**Microvascular bleeding**
Bleeding from the mucous membranes; oozing from catheter sites that persists after application of pressure; continuous oozing from surgical wounds and raw tissue surfaces; generalized petechiae or increasing size of eccymoses (bruises). Indicates severe haemostatic failure. *See* Disseminated intravascular coagulation

**Normal saline**
An isotonic 0.9% sodium chloride solution.

**Normovolaemia**
Normal circulating blood volume.

**Oncotic pressure**
Osmotic pressure exerted by colloid solutions. Also called 'colloid osmotic pressure'.

**Oxygen dissociation curve**
Graph depicting the relationship between the oxygen content of haemoglobin and the oxygen content ('partial pressure') in the plasma. See Figure 2.9.

**Packed cell volume (PCV)**
Determined by centrifuging a small sample of blood in an anticoagulated capillary tube and measuring the volume of packed red cells as a percentage of the total volume. *See also* Haematocrit.

**Plasma derivative**
Human plasma protein prepared under pharmaceutical manufacturing conditions. Include albumin, immunoglobulin and coagulation factor VIII and IX products.

**Plasmapheresis**
The method used to remove plasma from the blood by separating the red blood cells, returning them suspended in saline to the patient and retaining the plasma. *See* Apheresis.

**Prevalence**
The proportion of a defined population that are infected with an infectious agent at any particular time.

**Prothrombin time ratio (PTR)**
A test of the blood clotting system. Prolonged by deficiencies of coagulation factors VIII, X, V, II and fibrinogen. *See* International normalized ratio.

**Partial thromboplastin time (PTTK)**
*See* Activated partial thromboplastin time (APTT).

**Red cell components**
Any blood component containing red cells: e.g. red cell concentrate, red cells in additive solution, packed red cells.

**Red cell indices:**
- ■ Mean cell volume (MCV)
- ■ Mean cell haemoglobin (MCH)
- ■ Mean cell haemoglobin concentration (MCHC).

**Refractory**
A poor response to platelet transfusion. The patient's platelet count fails to rise by at least $10 \times 10^9$/L the morning after a platelet transfusion. Usually due to a clinical factor: e.g. fever, infection, DIC, splenomegaly, antibiotics. Also occurs if the platelet components transfused are defective.

**Replacement fluids**
Fluids used to replace abnormal losses of blood, plasma or other extracellular fluids by increasing the volume of the vascular compartment. Used to treat hypovolaemia and to maintain a normal blood volume.

**Reticulocytes**
Young red cells that still contain some RNA: show blue staining on blood film stained with "new methylene blue' with a Romanowsky counterstain. Indicate increased rate of red cell production by bone marrow.

**Rhesus D (Rh D)**
The most immunogenic antigen of the Rhesus blood group system. An important cause of haemolytic disease of the newborn.

**Stagnant hypoxia**
Reduced supply of oxygen to the tissues due to reduced blood flow (perfusion).

**Tissue hypoxia**
Oxygen starvation of the tissues and organs of the body.

**Transfusion-transmissible infection**
An infection that is potentially capable of being transmitted by blood transfusion.

**Transfusion-transmitted infection**
An infection that has been transmitted by blood transfusion.

**Voluntary non-remunerated donor**
A donor who gives blood freely and voluntarily without receiving money or any other form of payment.

**Window period**
The period of time between the moment of infection by a virus (e.g. HIV) and the development of detectable antibodies.

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