INTRODUCTION

Major obstetric haemorrhage is a common cause of maternal morbidity and mortality. In the UK, major haemorrhage occurs in approximately 3.7 per 1000 births. Maternal haemorrhage has fallen to being the sixth leading cause of direct maternal death in the 2006-2008 UK ‘Saving Mothers’ Lives’ national enquiry (mortality rate of 0.39 per 100 000 maternities). It is thought that improvement in the multidisciplinary management of these patients may have contributed to this decline. However, the overall rate in some developed countries appears to be increasing and in less developed countries obstetric haemorrhage remains one of the leading causes of maternal death. World Health Organisation statistics show it complicates up to 10.5% of births, and up to 50% of maternal deaths are attributable to its effects. The recognition of major obstetric haemorrhage can be challenging. Blood loss may be concealed and can be difficult to quantify due to dilution with amniotic fluid. In addition the physiological changes of pregnancy may mask the normal clinical signs of hypovolaemia. The blood flow to the placenta is approximately 700 ml/min at term and hence bleeding can be rapid and may quickly become life threatening.
DEFINITION

There is no consensus on a definition of major obstetric haemorrhage. Up to 1000 ml blood loss is not uncommon in the peripartum period and may be of little clinical significance. Blood loss >1500 ml; a decrease in haemoglobin of more than 4 g/dl; or an acute transfusion requirement of more than 4 units of packed red blood cells are suggested criteria. Definitions based on haemodynamic deterioration are unhelpful as maternal physiology often allows compensation until haemorrhage is advanced. Careful clinical observation and a high index of suspicion are required to detect bleeding early.

AETIOLOGY

Antepartum Haemorrhage

Antepartum haemorrhage (APH) is defined as bleeding from the vagina after 24 weeks gestation and has an estimated incidence of between 2–5% of all pregnancies. Complications include maternal shock; fetal hypoxia; premature labour and fetal death. Causes include:

- Placenta praevia
- Placental abruption
- Uterine rupture
- Trauma

Postpartum Haemorrhage

Postpartum haemorrhage (PPH) can be classified as primary or secondary. Primary PPH occurs during the first 24 hours whilst secondary PPH refers to haemorrhage occurring between 24 hours to 6 weeks after delivery. The 4 ‘T’s pneumonic is useful to aid recall the major causes of primary PPH:

- Tone – uterine atony
- Tissue – retained products of conception
- Trauma – genital tract injury
- Thrombin – inherited or acquired coagulopathy

Uterine atony accounts for the majority of primary PPH (upwards of 80%) and complicates 5% of all deliveries. Risk factors for poor uterine tone include overdistension of the uterus (polyhydramnios, multiple gestation, macrosomia), prolonged or augmented labour, tocolysis, general anaesthesia, multiparity, previous primary PPH and advanced maternal age. Additional causes to consider include abnormal placentation (placenta accreta, increta, percreta) and uterine inversion. Other risk factors include obesity and previous caesarean delivery. Secondary PPH is associated with retained products of conception and puerperal sepsis.

SYMPTOMS AND SIGNS

Many physiological changes occur during pregnancy including a decrease in blood pressure and an increase in baseline heart rate and blood volume. This altered physiology may mask the extent of blood loss until it is severe. Complete circulatory collapse is often rapid when the limits of physiological compensation are reached.

Warning signs of significant maternal haemorrhage that should not be ignored include tachycardia, tachypnoea, hypotension, pallor, poor urine output and pathological CTG changes. The performance of regular observations in conjunction with obstetric early warning scores is encouraged. Attention should be paid to vital sign trends as well as absolute values and a rapid clinical review should be carried out should any warning criteria be met. Tachycardia may be the first and only sign of haemorrhage until 30–40% of the circulating volume has been lost, where after hypotension and peripheral
vasoconstriction ensue. In APH, signs of fetal distress due to uterine hypoperfusion may precede maternal compromise.

The symptoms and signs of hypovolaemia may be more difficult to recognise if there is a language barrier, obesity, pre-eclampsia, dark skin or beta-blockade and hence extra care should be taken in these situations.

**MANAGEMENT OF UNANTICIPATED HAEMORRHAGE**

The management principles include early recognition, prompt resuscitation in conjunction with prompt identification and treatment of the underlying cause. The management strategy will be determined by both maternal and fetal considerations. Often maternal resuscitation will improve fetal condition. Where there is conflict, maternal life should be prioritised over fetal life.

High flow oxygen should be administered and, if antepartum, the patient placed in a full left lateral position to reduce aorto-caval compression and to aid uterine perfusion. Two wide bore intravenous cannulae (at least 16 G) should be sited and blood taken for urgent blood count, clotting studies and cross-match. If a point-of-care device such as a Hemocue® or blood gas analyser is available, a rapid haemoglobin concentration can be obtained.

All fluid that is administered during resuscitation should be warmed where possible and rapid infusion devices are beneficial. The choice of fluid for initial resuscitation includes crystalloid or colloid as well as blood. In significantly haemodynamically compromised women, Group O negative blood, which should be more rapidly available than either type specific or fully cross-match blood, should be considered.

If bleeding continues after the initial resuscitation steps have been undertaken then prompt transfer to the operating theatre should be performed for an examination under anaesthesia. Invasive monitoring may assist with resuscitation.

Senior help should be requested including obstetricians (and paediatricians if a viable fetus is in-situ). The haematology service should be alerted as to the possible need for massive transfusion and the advice of a haematologist is often useful. Blood should be commenced early if bleeding is ongoing to avoid dilutional coagulopathy. Disseminated intravascular coagulopathy can also complicate bleeding, particularly where there is abruption, infection or fetal demise.

**ANAESTHETIC MANAGEMENT**

The main aims of management are rapid resuscitation to restore tissue oxygen delivery while predicting, preventing and correcting haemostatic disorders. Appropriate levels of monitoring (especially invasive arterial blood pressure monitoring) should be considered and instituted early.

If anaesthesia is required for examination and/or surgical intervention and haemodynamic stability is compromised, general anaesthesia is usually indicated. Haemodynamic compromise and coagulopathy should be addressed prior to surgery whenever possible although surgical control may at times be required to enable effective resuscitation. Regional anaesthesia may be contra-indicated due to maternal coagulopathy and risk of neuraxial haematoma as well as haemodynamic compromise. In addition, surgery may be lengthy with the potential for further patient deterioration. Rapid sequence induction is indicated, preferably following antacid prophylaxis (e.g. sodium citrate and ranitidine). Induction of general anaesthesia in a severely hypovolaemic patient may cause a catastrophic fall in cardiac output. Ketamine is a suitable induction agent (1.5 mg/kg IV) as is cautious dosing of either thiopentone or propofol.

If time and the patient’s condition allow, direct arterial monitoring may be established, both as a guide to response and for ongoing blood sampling to guide transfusion therapy. Central venous access may be required, however this is not imperative and can wait until the situation is under control and should not interfere with prompt resuscitation. Central venous access may be necessary for inotrope and vasopressor infusion and central venous pressure monitoring may provide some additional information to help guide fluid management. Although there are few reports of the use of minimally invasive
haemodynamic monitoring devices (e.g. oesophageal Doppler monitoring) in the management of major obstetric haemorrhage, these devices may aid fluid management in the anaesthetised patient. Attention to fluid balance is imperative since over-transfusion and dilution before achieving surgical haemorrhage control is associated with worse outcomes.

**UTEROTONIC DRUGS**

The mainstay of conservative treatment is administration of uterotic drugs. It is often beneficial to have a locally agreed protocol of drug escalation. Drugs that should be considered include:

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<th>Oxytocin</th>
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<tr>
<td>Slow intravenous bolus of 5 IU repeated if required</td>
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<td>Give slowly - causes vasodilation and may be especially harmful in the haemodynamically unstable patient</td>
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<tr>
<td>Following bolus dose, commence infusion, typically using 10 IU/h for 4 hours</td>
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<th>Ergometrine</th>
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<td>Causes nausea and vomiting and may precipitate severe hypertension</td>
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<tr>
<td>Avoid in pre-eclampsia</td>
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<tr>
<td>Typical dose of 500 mcg can be given either intravenously (slowly) or intramuscularly</td>
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<th>Prostaglandin F2 Alpha (e.g. Carboprost)</th>
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<tr>
<td>0.25 mg dose can be given intramuscularly, repeated to a total dose of 2 mg</td>
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<tr>
<td>Side effects include: hypertension, pulmonary hypertension and bronchospasm</td>
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<tr>
<td>Use with caution in asthmatic patients</td>
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<tr>
<td>Intramyometrial administration has a more rapid onset but is an ‘off-label’ use</td>
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<th>Misoprostol</th>
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<td>A prostaglandin E1 analogue</td>
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<td>Often overlooked but can prove useful in combination with the other uterotonic agents</td>
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<tr>
<td>Can be used rectally, orally or sublingually</td>
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<td>The recommended dose is 800 mcg</td>
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**SURGICAL MANAGEMENT**

Regardless of the cause of obstetric haemorrhage, conservative measures may fail to control bleeding. In these cases, invasive procedures must be performed promptly. The primary goals are to deliver the placenta in its entirety and identify any remediable aetiology (for example, genital tract tears). If uterine atony is the identified issue, in addition to uterotonic the surgeon can:

- Perform bimanual uterine compression.
- Perform a uterine compression suture (e.g. B-Lynch suture).
- Provide hydrostatic intra-uterine balloon tamponade (e.g. Bakri tamponade balloon, Rusch urological balloon or Sengstaken-Blakemore tube). The balloon device is inserted via the vagina into the uterus and filled with warm sterile water until the uterus is firm on abdominal palpation. If PPH is controlled it is typically left in-situ for at least 6 hours.
- Perform surgical ligation of uterine, ovarian and/or internal iliac arteries.
- Perform a peripartum hysterectomy.
Obstetricians should consider all available interventions in order to arrest haemorrhage. Severe cases may require hysterectomy and in extreme situations aortic clamping/compression can allow time to control the surgical field. Emergency surgical interventions in patients with PPH can be technically challenging due to the enlarged uterus, engorged vessels, and oedematous tissues. The decision to perform a hysterectomy can be difficult to make as it will take away future fertility options for the mother but it may be life saving.

**RADIOLOGICAL MANAGEMENT**

Advances in interventional radiology have introduced alternative options in the treatment of PPH although it requires the mother to be stable enough to be transferred to a radiology suite if a joint angiography-operating theatre is not available. Embolisation requires fluoroscopic guidance and the availability of an interventional radiologist with appropriate facilities and team. Many hospitals do not have the resources to provide this service out-of-hours. The radiologist can potentially identify the vessels responsible for the bleeding and embolise them. Angiographic occlusion balloon catheters can also be placed to occlude the hypogastric or common iliac arteries as a temporising measure or inserted electively in cases anticipated to be at high risk of haemorrhage (e.g. caesarean section for placenta accreta). Results to date would suggest that interventional radiology may potentially reduce blood loss and there is minimal impact on future fertility, however its use has been associated with adverse fetal and maternal outcomes.

**TRANSFUSION PRACTICE**

Care must be taken to avoid a dilutional coagulopathy with excessive crystalloid or colloid. A significant PPH generally requires the early use of blood products. Recent research in transfusion medicine has pointed towards early transfusion of fresh frozen plasma (FFP), and targeted use of platelets. Packed red blood cells and FFP are given in a ratio of between 1:1 and 1:2 in an effort to avoid dilution of clotting factors and development of a coagulopathy. Regular measurements of haemoglobin and clotting are recommended to guide transfusion requirements as well as close liaison with a haematologist.

Thromboelastography (TEG) and thromboelastometry (ROTEM) are viscoelastic whole blood point-of-care testing devices that evaluate the haemostatic capacity of blood. Their use has been reported in the management of obstetric haemorrhage. Although normal values in pregnancy and labour are only now being established, these devices may have a role in the management of blood product replacement in major obstetric haemorrhage.

It is important to avoid the vicious cycle of hypothermia, acidosis and coagulopathy in the massive transfusion patient. Warmed fluids must be given and care directed to achieving normothermia by the use of devices such as forced air warmers. Correction of electrolyte imbalance may be necessary; this may include hyperkalaemia (secondary to high concentrations of potassium in transfused blood) and hypocalcaemia (chelated by the citrate found in transfused FFP).

**INTRAOPERATIVE CELL SALVAGE**

There are numerous reports of the safe use of intraoperative cell salvage in obstetric patients and it has been recommended in women who refuse traditional blood transfusions as well as in other major haemorrhage situations. It is useful to consider cell salvage in both anticipated and unanticipated massive haemorrhage as this can reduce the exposure to allogeneic blood transfusion (and its associated risks) and is cost-effective. Cell salvage is usually started after the majority of the amniotic fluid has been suctioned to decrease the theoretical risk of amniotic fluid embolism. A leucocyte depletion filter should be used prior to re-infusion of the salvaged blood to remove additional contaminants that the washing process may not clear. In addition it is important to remember that cell salvaged blood contains only red cells with essentially no clotting factors or platelets.
ADDITIONAL DRUGS

Recombinant factor VIIa (Novoseven®) is an expensive and controversial therapy that may be considered and has been reported in obstetric haemorrhage. It has been used primarily as a treatment of uncontrolled haemorrhage in the trauma setting. Recombinant factor VIIa causes a thrombin burst, promoting clotting in open vessels. Its effectiveness is markedly diminished by hypothermia and acidosis and so effective resuscitation towards normal physiology is a prerequisite of its use. The major concern with its use is the potential for thrombotic complications. It is typically given in a dose of 90 mcg/Kg.

Antifibrinolytics are a useful adjunct in the pharmacological management of massive transfusion and PPH. Tranexamic acid is a potentially useful drug that is widely available. It can decrease bleeding and reduce the need for further transfusion without many major side effects. The initial dose is a slow IV bolus of 1g followed by a further 1g 4 hours later.

SUBSEQUENT MANAGEMENT

After controlling the acute situation, attention should be paid to the possibility of rebound hypercoagulation and the risk of thromboembolism. Pregnant women are physiologically hypercoagulable and those women who have received blood products have a further increase in the incidence of thromboembolic disease. Graduated compression stockings should be worn and pharmacological thromboprophylaxis initiated as soon as practical.

IMPORTANT POINTS

- Maternal haemorrhage remains a leading cause of maternal morbidity and mortality, particularly in the developing world.
- PPH can be anticipated or unanticipated. Detection of concealed haemorrhage is vital.
- All mothers should have anaemia diagnosed and treated in the antepartum period.
- Active management of the 3rd stage of labour decreases bleeding.
- There are several uterotonic drugs that can be used in combination.
- Control of bleeding is paramount and management is multidisciplinary.
- Prevention of hypothermia is imperative.
- Intraoperative cell salvage appears safe to use in obstetric patients.
- Interventional radiology may be useful in some cases although there are reports of adverse fetal and maternal outcomes.
- Rebound hypercoagulability is an important cause of death and thromboprophylaxis should be initiated early.
ANSWERS TO QUESTIONS

Question 1

Answer C: Endometritis is a cause of secondary PPH (presents >24 hours after delivery)

Question 2

Suitable pharmacological therapies for uterine atony include: oxytocin, ergometrine, misoprostol and carboprost.

Question 3

A. F: Carboprost can cause bronchospasm and should be used with caution in women with asthma.
B. T: Cell salvage allows autologous blood transfusion. A separate suction should be used for amniotic fluid and a leucocyte depletion filter used when infusing collected blood.
C. F: A suitable transfusion trigger in a healthy, uncompromised mother is a haemoglobin level of <7 g/dl.
D. F: Hypotension is a late sign of haemorrhage when 30-40% of blood volume has already been lost. Maternal tachycardia may be the only sign of early haemorrhage and should be investigated.

WEBLINKS AND FURTHER READING


http://www.aagbi.org/sites/default/files/massive_haemorrhage_2010_0.pdf


Blood Safe eLearning Australia Post Partum Haemorrhage Course
http://www.bloodsafelearning.org.au

Royal College of Obstetricians and Gynaecologists. Postpartum Haemorrhage, Prevention and Management (Green-top guide 52).