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Management of the third stage of labour

(for the *Optimal Intrapartum Care* series edited by Mercedes Bonet, Femi Oladapo and Metin Gülmezoglu)

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Abstract

The physiology of the third stage of labour is described. Active management reduces the risk of postpartum haemorrhage, due to the use of a uterotonic agent. Intramuscular Oxytocin 10 IU has the highest efficacy and lowest side effect profile; although ergometrine, carbetocin and misoprostol are also effective. The appropriate uterotonic in different settings such as home birth by unskilled attendants, and at caesarean section is discussed. For the latter, there is less consensus on the optimal dose / route of oxytocin; this topic remaining on the research agenda. Delayed cord clamping enables transfusion of blood to the neonate and is recommended rather than early clamping. Controlled cord traction should only be performed by skilled birth attendants and confers minimal advantage in preventing retained placenta. The importance of early recognition of postpartum haemorrhage, and preparedness, is emphasised. An approach to medical and surgical management of postpartum haemorrhage is presented.

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1. Background

1.1 The third stage labour

The **third stage of labour** is the time between the birth of the fetus and the expulsion of the placenta. **Postpartum haemorrhage** is traditionally defined as over 500mls blood loss. This can be further subdivided into primary (blood lost in the first 24hrs) or secondary (blood lost from 24hr to 6 weeks), and into minor (500-1000mls) and major or severe (>1000mls) [1]. These definitions have been questioned due to the high prevalence of the 500mls loss especially at caesarean birth. Furthermore, whilst a blood loss of 500mls is unpredictable and usually caused by atony, the larger, life threatening blood losses of 1000 or 2000mls are far more predictable as they are mostly due to emergency CS, uterine rupture and placental abnormalities.[2] Thus, it is suggested that measures of PPH-related morbidity are used for the outcomes of clinical trials and audits.[3]

The 500ml definition has been used to suggest the point at which **PPH treatment should commence**. However, the time at which midwives and doctors commence treatment appears to depend more on the speed of loss, underlying maternal risk factors, and clinical signs than volume.[4] This pragmatic approach, which tailors clinical PPH management to the individual, is appropriate so long as PPH treatment is initiated by 500mls in vaginal birth or 1000mls in a CS. Repeated studies demonstrate the inaccuracy of visual estimation, especially at higher blood loss volumes. Visual estimation can be improved by teaching and charts,[5] but it is recommended that blood loss volume is assessed using gravimetric assessment (weighing blood and approximating 1g weight to 1ml of blood), supplemented with blood collection in a 'V' shaped drape.[6]

1.2 Physiology of the third stage of labour

1.2.1 Cord blood flow and effect of clamping

In utero, fetal blood moves continuously between the placenta and the fetus with around 1/3 of the blood being in the placenta at any one time. The main channel is from the fetal heart down the aorta, through the paired umbilical arteries up the umbilical cord, through the placenta and back to the fetal heart down the umbilical vein. In the transition phase, immediately after birth, the fetus takes its first breath, drawing blood and air into its lungs and thus changing the pressure dynamics. The umbilical arteries also constrict. The combined effect is to draw blood into the fetus from the placenta, and halt the blood pumping out of the fetus into the placenta. In nature, this process would take some minutes as the baby draws blood from the placenta reservoir according to its needs. Newborns still attached to the placenta put onto scales immediately after birth slowly gain weight as they draw the blood in – but at a variable rate and volume.[7]

Immediate cord clamping has two effects on the fetus. The abrupt blocking of the umbilical arteries retains blood in the fetus, but suddenly diverts blood flow to other body organs like the brain and kidneys. The blocking of the umbilical vein however, traps oxygenated blood in the placenta and prevents the fetal heart and lungs receiving the extra blood that they need. The combined effect of immediate cord clamping on the fetus is to reduce red cell mass, oxygenation, blood pressure, blood volume, haemoglobin levels and haematocrit.[8] The consequences of these changes are discussed below.

1.2.2 Placental detachment and retained placenta

As with much of biological function, the third stage of labour is a thing of great wonder, managing to simultaneously both detach the placenta whilst blocking off the 500 mls/min blood flow to the placenta bed. In the 1990s, ultrasound studies allowed researchers to visualise the hidden process of the third stage for the first time.[9,10] This revealed, for the first time, that there were different phases of separation. In the **first phase**, the baby has left the uterine cavity, but the placenta remains attached to the uterine wall. The myometrium behind the placenta is thin and uncontracted, in contrast to the remainder of the uterus which is contracted and thickened. It is the duration of this first phase that largely determines the length of the third stage. The **second phase** starts when the retroplacental myometrium starts to contract, usually starting from the cervical end of the placenta.[11] The contraction of this retroplacental myometrium, as with any other muscle, leads to its shortening and thickening. This not only shears away the relatively inflexible placenta from the underlying myometrium, but also simultaneously obstructs the perforating radial arteries which carry the maternal blood to the underside of the placenta. This *physiological ligature* is the prime cause of haemostasis after childbirth and provides effective haemostasis even in women with marked clotting disorders. Conversely, any relaxation of this retroplacental myometrium will release the ligature and allow blood to once again flow through the radial vessels and cause postpartum haemorrhage.

In the **third phase** the placenta is detached and squeezed through the cavity into the lower segment and out.

Abnormalities of each of these phases can lead to retained placenta. If the retroplacental myometrium fails to contract then the placenta remains attached to it, and the this is known as *placenta adherens*. If the retroplacental myometrium contracts well, but expulsion of the placenta is prevented by a small area of placenta embedded deeply into the myometrium, then this is called *partial accreta.* If the placenta is both detached and expelled from the uterus, but remains in the lower segment, trapped behind a contracted cervix, then this is the relatively benign condition of *trapped placenta*. The three types are shown in figure 1.

2. Routine care in the normal third stage of labour

Active management of the third stage of labour (AMTSL) was originally introduced as a package to prevent PPH. Repeated studies have now shown the efficacy of AMTSL on third stage outcomes. Severe blood loss is reduced by nearly 70% and with it the rates of anaemia, transfusion and need for therapeutic uterotonics.[12]

The main component of AMTSL was originally the uterotonic, with controlled cord traction to prevent trapping of the placenta. Early clamping of the cord was already routine care at that time that AMSTL was first introduced, but was hardly mentioned in the original reports.[13] Since then, it has become clear that it is only the uterotonic that has any meaningful effect on blood loss – controlled cord traction is largely unnecessary and early cord clamping appears harmful to the newborn.

2.1 Umbilical cord clamping

Although the WHO has long advocated deferred cord clamping (DCC; also known as ‘delayed’ or ‘optimal’ cord clamping), the culture in Europe has been to immediately clamp the cord. However,

high quality trials are now available that clearly show how important that placenta blood transfer is for newborn and infant health. For the healthy term infant 3 minutes DCC leads to significantly higher haemoglobin for 6 weeks postnatally and iron stores for the first 3 months.[14] The importance of the improved iron stores for neurological development is seen in the long-term follow up studies. At 4 years of age children randomised to 3 minutes DCC had improved fine motor, social and communication skills.[15] And the importance of DCC appears to be greater in babies born prematurely or who need resuscitation at birth. Systematic review of 18 randomised trials show that DCC (of various lengths) in babies under 32 weeks reduces neonatal mortality by 32% and transfusion by 10%.[8] Clinical trials are more difficult in babies who need resuscitation, but a recent RCT from Nepal found that resuscitation with an intact cord led to improved neonatal oxygenation, higher APGAR scores, lower heart rate than those with immediate cord clamping.[16] Studies have used a variety of methods to facilitate placental transfusion: small bedside resuscitaires have been developed, whilst the transfusion can be accelerated through cord milking or lowering the baby beneath the level of the placenta. There is no good evidence to support one method over another. However, bedside resuscitation would appear to be optimal as it allows the transfusion to occur naturally at a pace dictated by fetal needs and prevents the enforced and psychologically traumatic separation of the baby from its parents.[17]

2.2 Controlled cord traction

Controlled cord traction (CCT) was originally introduced to prevent retained placenta as a complication of retained placenta use. This hypothesis was tested in a large WHO randomised trial which found minimal benefit of CCT when intramuscular oxytocin was used for prophylaxis.[18] It shortened the duration of the third stage but had no effect on rates of PPH or retained placenta. Around 6% of those in the 'no CCT' arm still required traction to deliver the placenta.

Interestingly, in one of the study countries there was a significantly higher rate of retained placenta in the controlled arm. That country had a lot of service delivery problems, but had also continued to use intramuscular Syntometrine™ (oxytocin 5IU and ergometrine 500mcg) rather than oxytocin for prophylaxis. Thus, CCT, whilst unnecessary with oxytocin, may still be important in those who receive Syntometrine™ (or ergometrine alone as well, presumably) for prophylaxis.

2.3 Uterotonics

Oxytocin alone has been long-established as the leading uterotonic for prophylaxis. The use of a combined preparation of oxytocin 5iu and ergometrine 500mcg (Syntometrine™) has been popular in some countries, combining the immediate effect of oxytocin with the prolonged action of ergometrine. Randomised trials do suggest that it may be more effective than oxytocin alone, but at the 'cost' of relatively high rates of hypertension (1.7%) and nausea/vomiting (18%).[19] Thus, considering that the drug is being used in normal, healthy women, most of whom would not have had a PPH even without prophylaxis, there is a wide consensus to use the drug with the least side-effects: oxytocin.

It has been usual practice to administer prophylactic oxytocin intramuscularly. Recent randomised trials however demonstrate that oxytocin is more effective when administered intravenously (iv) than intramuscularly (im). In the Dublin randomised trial, women who received 10 units of oxytocin iv rather than im had half the rate of severe PPH rate and 70% less need for need for blood transfusion.[20] Subgroup analysis found that the benefits were only seen in the nulliparous women

and those who were induced, groups which also had higher rates of PPH. Injecting just 3iu of oxytocin intravenously over 15 seconds causes a rapid, transient drop in blood pressure by 10-40% [21] and has been implicated in maternal deaths - so it was very reassuring that they saw no such effects in this study.

Carbetocin, a synthetic long-acting version of oxytocin, had been hoped to provide the extended action of ergometrine without the side effects and studies using it iv for prophylaxis at CS had showed promise.[22] However, a large randomised trial of im heat-stable carbetocin versus im oxytocin has shown that there is absolutely no difference in efficacy between them.[23] The one potential benefit is that this new version of carbetocin is heat stable, which may increase the effectiveness 'on the ground' in settings where the reliability of the cold chain cannot be assured.

Oral misoprostol tablets have been widely studied as an option for prophylaxis, but a large RCT found them less effective than oxytocin and with more side effects.[24] Some have combined it with oxytocin to achieve rapid but prolonged effects. A recent network meta-analysis of all randomised trials found that although Syntometrine™ and combined misoprostol + oxytocin are probably the most effective agents for prophylaxis, they are both associated with most side effects.[25]

2.4 Conclusion

The uterotonic is the most important component of AMTSL. Early cord clamping appears to be harmful and CCT is of little benefit (except possibly when ergometrine is a component of the uterotonic). The ideal uterotonic for prophylaxis is probably im oxytocin 10iu, as it combines efficacy with a low side effect profile. For those at higher risk, iv oxytocin (given slowly over at least 1 minute) is probably the best option if given slowly as it has fewer side effects than oxytocin combined with ergometrine or misoprostol.

Physiological management remains an option for those at low risk, especially where there is rapid access to effective treatment if needed. An attractive option is that of secondary prevention, where physiological management is combined with early treatment. This strategy reduces the number receiving prophylaxis by over 90% without obvious harm.[26] This targeted approach might be good option both for the mother and the health systems. Further larger studies are awaited to see the effect on rarer outcomes.

3. Adapting third stage management for particular situations

3.1. Adaptations of management for low resource settings

The components of Active Management of Third Stage Labour (AMTSL) described in the previous section which includes intramuscular oxytocin, delayed cord clamping and controlled cord traction (CCT) may not all be feasible in low resource settings.[27]

In such settings, many women deliver at home with traditional birth attendants (TBAs), who are not usually skilled in administering injections or performing controlled cord traction. In addition, many women deliver in primary care clinics which may not always have a professional nurse on duty with the requisite skill. Oxytocin may not consistently be available due to poor functioning of the cold chain since it requires refrigeration.

In such settings, it is therefore often necessary to modify management of the third stage. The need for delayed cord clamping is particularly important to reduce infant anaemia in the context of endemic undernutrition.[28] Attention to aseptic cord-cutting is important to prevent neonatal

tetanus which remains a cause of newborn mortality in some countries.[29] Similarly, there is an imperative to prevent PPH due to high prevalence of maternal anaemia from undernutrition and communicable diseases such as malaria, as well as a higher risk of maternal mortality.[30]

In such settings the following is recommended:

- *Early suckling of the baby on the breast* to promote physiological oxytocin release.
- *Administration of a suitable uterotonic to contract the uterus* after the birth of the baby. Several alternatives to standard im oxytocin have been shown to be effective in reducing PPH compared to placebo[25,31]:
    - The Uniject device is a pre-assembled syringe unit with 10 IU oxytocin that TBAs can administer, the disadvantage being the logistics of distribution, refrigeration and disposal of devices.[32]
    - Oral Misoprostol 400 to 600 mcgms. Currently the latter is available, affordable, heat stable and easy to administer. There are case series of its use by TBAs, and also of self-administration by women who were supplied the medication at an antenatal clinic visit.[33,34,35]
    - Heat stable carbetocin has potential value due to the lack of cold chain requirement but requires skill with injection which would be available in most level of facilities.[23] However, for use by TBAs at home, pre-assembled syringe devices similar to the Uniject would need to be manufactured.
- *Delayed cord clamping.*
- *Cutting the cord with a sterile instrument*. Several TBA training programmes supply them with delivery kits which include a sterile razor blade and sterile threads to tie the cord. Again, women attending antenatal clinics can be supplied with such kits in the event of home birth. Of note, routine tetanus immunisation during antenatal care has assisted in the reduction of neonatal tetanus in low resource settings.[29]
- *Passive delivery of the placenta*. CCT should not be employed by non-skilled attendants in home birth due to the associated risk of cord snapping or uterine inversion. It is a skill that trained midwives should have and can be performed at primary care clinics staffed by such personnel.[28]

3.2 Management issues at Caesarean Section (CS)

The same principles of management of the third stage after vaginal delivery apply to caesarean section, notably use of uterotonic drugs to contract the uterus, delayed cord clamping and CCT for placental delivery. In addition, skin to skin contact and early suckling to aid uterine contraction, can be performed at CS. This can only occur for uncomplicated CS under regional anaesthesia. The three elements of management will be described separately:

- *Administration of uterotonic*. Oxytocin is the preferred prophylactic uterotonic, although it is acknowledged that most of the research has been for vaginal delivery rather than CS.[25,31] The precise dose and route of administration remain contentious. During CS, there is iv access and the anaesthetist (doctor or other health care worker providing anaesthesia) administers medications according to instruction from the surgeon or anaesthetic protocol.

  The recent WHO guidance states that 10 IU oxytocin should be administered iv or im [31]. However, oxytocin causes hypotension following rapid iv boluses. In some cases, this has proved fatal, although it is recognised in these reports that spinal anaesthesia and pre-

existing hypovolaemia may have contributed to fatality.[36] The pharmacokinetic research demonstrates that the lowest dose of oxytocin iv bolus which is effective to contract the uterus is less than 5IU and such doses have less hypotensive effect.[36] The recent WHO guidance qualifies its recommendation for 10 IU im/iv by indicating that, at CS, consideration should be given to dividing the 10 IU dose into a smaller iv bolus accompanied by an infusion. This is also the protocol in SA where 2.5 IU are given by slow iv bolus and the remaining 7.5 IU by infusion.[37] The RCOG green top guideline specifies 5IU IV (RCOG 2016).[38] Guidance varies also about the dose placed in an infusion from 5 IU to 40 IU. Prophylactic oxytocin Infusions have been less researched but are recommended by many guidelines for the duration of the actual surgery, and for continuation in the postnatal ward after the patient leaves theatre to maintain uterine contraction.

Previous anaesthetic publications recommended 'the rule of 3': 3IU iv after delivery of baby, followed by additional 3 IU if poor uterine contraction, and 3 IU in the drip as an infusion.[39,40] However, a recently published new international consensus statement by an association of obstetric anaesthetists recommended 3 IU iv at intrapartum CS but only I IU at elective CS, in both cases accompanied by infusions from 3 to 15 IU.[41]

There is minimal research on im administration of oxytocin or other uterotonics at CS which may be the optimal route (deltoid injection); this route may minimise hypotension effects whilst maintaining uterine contraction.[37]

Carbetocin, ergometrine and syntometrine have a more prolonged action than oxytocin and this may be valuable to reduce post CS bleeding from uterine atony after the patient has left theatre. Like oxytocin, all also have side-effects with rapid iv injection.

There are a few small trials where tranexamic acid (TXA) has been administered at CS together with standard uterotonic for PPH prophylaxis with some success; this needs to be explored further.[42] The WOMAN trial which was the largest one to investigate TXA for efficacy and thrombotic side effects, was for vaginal delivery but not CS, for which thrombotic risk is intrinsically greater.[43]

In summary, although there is agreement that an uterotonic agent is necessary to prevent PPH at CS, and that oxytocin is the drug of choice; there is a need for consensus amongst obstetricians and anaesthetists on the safe effective dose and routes. It is an area for further multidisciplinary research involving anaesthetists and obstetricians.

- *Delayed cord clamping*. Similar to guidance for vaginal delivery, delayed cord clamping is recommended.
- *Controlled cord traction to deliver the placenta.* This is recommended in preference to manual removal of placenta, the latter being associated with increased blood loss.[28,44]

3.3 High risk birth

The management of third stage of labour needs to be adjusted in certain situations and a risk assessment is necessary to identify such scenarios.

- Women at increased risk of PPH after delivery.[38] This includes: grand multiparity, previous PPH, multiple pregnancy, prolonged labour, chorioamnionitis, abruptio placentae, operative vaginal delivery etc. Whilst there is minimal evidence for additional PPH prophylaxis in such cases, it is reasonable to consider this by, for example administering a 20 IU oxytocin infusion in combination with the standard oxytocin prophylaxis. The Gallos network analysis did show benefit in reducing blood loss from certain drug combinations so other uterotonics,

such as ergometrine, or misoprostol can be considered as alternative prophylactic adjuncts, provided not contra-indicated.[25] Women with severe anaemia prior to delivery may also be considered for additional PPH prophylaxis.

- Women suspected to have a morbidly adherent placenta at CS. Controlled cord traction is avoided and if spontaneous delivery of the placenta does not occur, the placenta may be left in situ or consideration given to hysterectomy as dictated by the clinical situation.[45]
- Women with cardiac conditions especially fixed output conditions such as tight mitral stenosis. Lithotomy position must be avoided, and meticulous monitoring of fluid balance is required to prevent pulmonary oedema.[46] Ergot derivatives for preventing or treating PPH must be avoided. Nevertheless. uterotonics in the form of low dose oxytocin are important to prevent PPH.[47]

4. Dealing with complications

4.1 Third stage complications

Maternal complications associated with the third stage of labour after vaginal delivery include uterine atony, genital tract trauma, retained placenta (or placental fragments) and uterine inversion; all of which can cause PPH and also predispose to uterine sepsis. At CS, PPH may be due to uterine atony, trauma including rupture, adhesions, and placental problems (praevia, morbid adherence etc). Although rare, amniotic fluid embolism causing severe coagulopathy is another cause of PPH.

PPH is estimated to occur in 6.6% of deliveries and is a major cause of maternal mortality globally accounting for 27.1 % of maternal deaths.[48] Mortality is higher in low resource settings due to both an increase in PPH incidence and case fatality rate.[30] PPH also contributes to significant morbidity in all settings as evidenced by Severe Acute Maternal Morbidity or Near Miss studies.[49]

4.1.1 Postpartum haemorrhage after vaginal delivery

This chapter will not provide details of PPH management which can be found in a previous dedicated edition on PPH (November 2019). A summary is provided in figure 2. Whereas there is high quality evidence for medical treatment of PPH with uterotonics or TXA; there is a dearth of such evidence for many of the mechanical or surgical measures and the sequence in which they should be employed. Most protocols or guidance are based on review of case series, mortality audit findings and expert opinion.

Important features of management include:

- Recognition of excessive blood loss. Blood loss is often underestimated and signs of shock such as reduction in blood pressure may only occur after 1.5 to 2 litres blood loss. This means that active treatment starts ‘too late’ when coagulopathy has developed, and all known treatment measures are more difficult to enact. Late recognition of the extent of blood loss is compounded when bleeding may be concealed such as in abruptio placentae or paravaginal haematomas.
- Adequate resuscitation with crystalloids, colloids and blood products.[50]
- Performing initial measures such as emptying bladder, oxytocin infusion and bimanual compression whilst awaiting more experienced help.
- Rigorous examination to find the cause or causes (more than one cause may occur)

- Stepwise treatment of the identified cause with progression from medical measures (uterotonics, TXA) to first aid measures such as bimanual or aortic compression and non-pneumatic anti-shock garment (NASG) to surgical measures (removal of placenta, repair of genital tract tears, examination in theatre, balloon tamponade, laparotomy with compression sutures, artery ligations, uterine artery embolisation (UAE) or hysterectomy as a last resort) as required and without delays.[51,52,53] In the rare case of uterine inversion, immediate replacement of the uterus followed by oxytocin infusion is required.
- Team work with a team leader, participants knowing their role and sufficient personnel to perform the multiple actions required.[54]
- Addressing the woman and her family with respect to inform them of the situation and reassure them that you are providing her with lifesaving treatment
- Addressing specific problems related to low resource setting where there may be a lack of skilled personnel, non - availability of blood products, lack of specialist radiology or haematology services, and a need to refer such patients to higher levels of care with resultant delays which can be fatal.[27] The NASG has been documented to decrease mortality when applied before/during transport and to stabilize women to overcome delays due to the problems in low resource settings.[55]

4.1.2 Prolonged third stage

Third stage is said to be prolonged if the placenta is undelivered within 30 minutes with AMTSL and 60 mins with physiological management. It may be due to entrapment of a detached placenta at the level of the cervical os ('trapped placenta') in which case it requires a simple manual removal. However, if the placenta is still attached to the uterine wall ('placenta adherens') it requires a full manual removal with the attendant's hand placed high into the uterus to detach the placenta from its site. This is normally an uncomplicated procedure but, if morbidly adherent ('partial accreta'), can lead to difficult removal and massive bleeding (see figure 1).

Numerous studies have been conducted to examine the efficacy of the injection of oxytocin into the umbilical vein but have found no consistent benefit.[56]

In the absence of PPH, attempts to remove the placenta can be done at 30 mins or 60 mins according to the definition above. However, in the presence of PPH urgent removal is required and the steps outlined above should be followed.

4.1.3 Bleeding at CS

PPH at CS is most commonly defined as blood loss equal or greater than 1000mls, since blood loss at CS is intrinsically greater than after vaginal delivery. It can be due to uterine atony, surgical adhesions, uterine tears, bleeding from the placental site in cases of placenta praevia or morbidly adherent placenta, and amniotic fluid embolism. The combination of anterior placenta praevia with previous lower segment CS increases the risk of morbidly adherent placenta considerably.

The ASOS study, a WHO systematic review and mortality audits from some countries have all shown high case fatality rates from CS particularly in low resource settings. These studies also demonstrate the alarming number of deaths from bleeding after CS.[57]

Similar to PPH after vaginal delivery, the evidence base for medical management of PPH at CS is of much higher quality than that for surgical modalities of treatment.

Important features of management include:

- Recognition of PPH. This is problematic at CS due (a) to contamination of blood with liquor making it difficult to assess blood loss, (b) falls in BP being misinterpreted as an effect of regional anaesthesia, (c) blood loss from the uterus coming out of the vagina under the surgical drapes may not be appreciated, and (d) importantly after abdominal closure, internal CS bleeding into the peritoneal cavity may not be recognised until much blood has been lost
- Active and effective resuscitation usually done by the anaesthetist who needs to communicate with the surgeon about the patient's condition
- Identifying the cause of the bleeding; posterior uterine tears can be missed, as can bleeding from adhesions during wound closure
- Medical and surgical modalities as described under PPH after vaginal delivery, with early recourse to uterine compression suture for intractable uterine atony, and other surgical or radiological measures.[52]
- Ensuring thorough assessment of vital signs and signs of bleeding after CS in a staffed recovery area so that if any signs, she will not be signed out to a ward but returned to theatre,
- Addressing specific problems related to low resource setting which are similar to those described above. Specifically, for CS, there is unlikely to be facilities for UAE and at district hospitals no one availability with skill for hysterectomy. The uterine tourniquet, compression sutures, and packing before closing and referring to higher level of care will then be necessary. When bleeding occurs post CS when the woman is in recovery or on the ward, the NASG can provide stabilization while waiting to return to the surgery or transfer to higher level of care.

4.2 Ensuring preparedness for third stage management and emergencies

In order to perform appropriate evidence-based management of the third stage of labour, facilities should follow a defined protocol, all staff should be trained and supplies should be available. In addition, this should apply to management of third stage complications which are mostly emergencies.

Training

Active and passive management of the third stage of labour should be taught at undergraduate level to student doctors and nurses and be an essential competency for all. Similarly, management of third stage emergencies, notably PPH, should be part of this training. In the workplace drills/scenario training should be conducted regularly to maintain competencies and ensure preparedness for emergencies.[58] In situations where many women deliver at home with a TBA or equivalent in attendance, they require training to provide a uterotonic such as misoprostol, to recognise PPH and retained placenta, and perform preliminary measures for PPH such as emptying the bladder, administering misoprostol, and baby suckling.[59]

Available supplies.

Oxytocin needs to be available and refrigerated, requiring an effective cold chain. However, facilities need alternative uterotonics and TXA, for sequential management of PPH. At primary care level, a PPH box containing uterotonic drugs, resuscitation fluids, iv infusion sets, blood collection bottles and urinary catheters, enables more efficient management when an emergency occurs. The introduction of PPH care bundles need intervention studies to evaluate effectiveness.[60] Operational managers of ward areas need to ensure that supplies are available and accessible. Blood product availability will vary according to the type of facility. Larger regional and tertiary hospitals are likely to have blood banks with a full range of blood products. District hospitals and many regional hospitals will have un-crossmatched packs of O negative and O positive blood stored in a fridge which can be administered rapidly for a severe PPH. In such settings the use of fresh dried plasma which is a pharmacy shelf item acts as a source of clotting factors. Some African countries such as Rwanda, Ghana and SA are utilising drones to fly blood products to remote areas

WHO Surgical Safety Obstetric Checklist.

Running the multidisciplinary check list at CS, before anaesthesia, before surgical incision and before leaving theatre alerts personnel to potential risks at CS and encourages preparedness. There is some evidence that indicates reduction of adverse event when used.[61]

Transport, referrals and clinical support

In academic and tertiary level hospitals, junior staff can call a more senior experienced doctor to assist with an intractable complex PPH and initiate a 'Massive Obstetric Haemorrhage' response so the multidisciplinary team can be assembled. However, in many low resource settings where care is tiered and organised around levels of care there are challenges. For example, a district hospital in a rural area would not have a specialist anaesthetist or obstetrician on site or available. The work would be performed by general doctors or non-doctor equivalents. This cadre can be trained to perform most of the procedures required for PPH short of hysterectomy, temporise the patient and then refer to the next level of care. Balloon tamponade, and the uterine tourniquet placed at laparotomy together with active resuscitation and uterotonics are all measures that can improve condition prior to transfer.[62,63] On site ambulances would assist urgent referral and Air transport could assist in remote areas. There is evidence that the NASG assists in treating shock during transfer.[55] TBAs need links with facilities and have mobile phones and working relations with nearest hospital for advice and urgent referrals.

In summary, the health system and its staff need to be fully prepared and equipped to manage the third stage appropriately to prevent PPH and other complications. This includes TBAs performing home births in low resource settings. Preparedness for emergencies involves Scenario / drills training, ensuring availability of essential supplies, and ensuring clinical support mechanisms, referral channels and emergency transport systems work effectively.

***Summary*:**
The third stage of labour is the time between birth of the fetus and expulsion of the placenta, and involves uterine contraction, placental detachment and expulsion. Active management aims to prevent postpartum haemorrhage (PPH) whilst avoiding retained placenta, both complications associated with maternal mortality. Research shows that the most important component of active management is the uterotonic agent. The uterotonic of choice, with highest efficacy and lowest side effect profile is 10 IU intramuscular Oxytocin after vaginal birth, although ergometrine, carbetocin and misoprostol have all been shown to be effective in preventing PPH. Misoprostol is preferable in the context of home delivery by unskilled attendants with no refrigeration facility or skill for injection. At caesarean section, there is less consensus on the optimal dose and route of oxytocin with suggestions that the 10 IU be divided between lower dose slow intravenous injection and an infusion. Carbetocin, due to its prolonged action and heat stable formulation offers many benefits but currently is not widely available. Delayed cord clamping enables transfusion of blood to the neonate and is now recommended rather than early clamping. Controlled cord traction should only be performed by skilled birth attendants and confers minimal advantage in preventing retained placenta, unless ergometrine was given as prophylactic uterotonic. The importance of early recognition of postpartum haemorrhage, and being prepared (ensuring availability of uterotonics, infusion fluids and blood, health workers with the necessary skills, and simulation training) is emphasised. An approach to medical and surgical management of postpartum haemorrhage is presented.

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ADW has received grants for PPH research from the NIHR and Gynuity Health Projects. He is the inventor of the PPH Butterfly, a first aid device to treat PPH. The patent is held by the University of Liverpool, but Prof Weeks could in the future receive royalties if it were to be commercialised. He is also one of the inventors of the LifeStart bedside resuscitation trolley, but the commercial developer of this pays a sum per sale into a charity fund in lieu of royalties. He has also developed the BabySaver tray, a low cost bedside resuscitation kit. This is not patented, but the IP is held jointly by the University of Liverpool and the Sanyu Africa Research Institute. SF reports no conflicts of interest.

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Figure 1

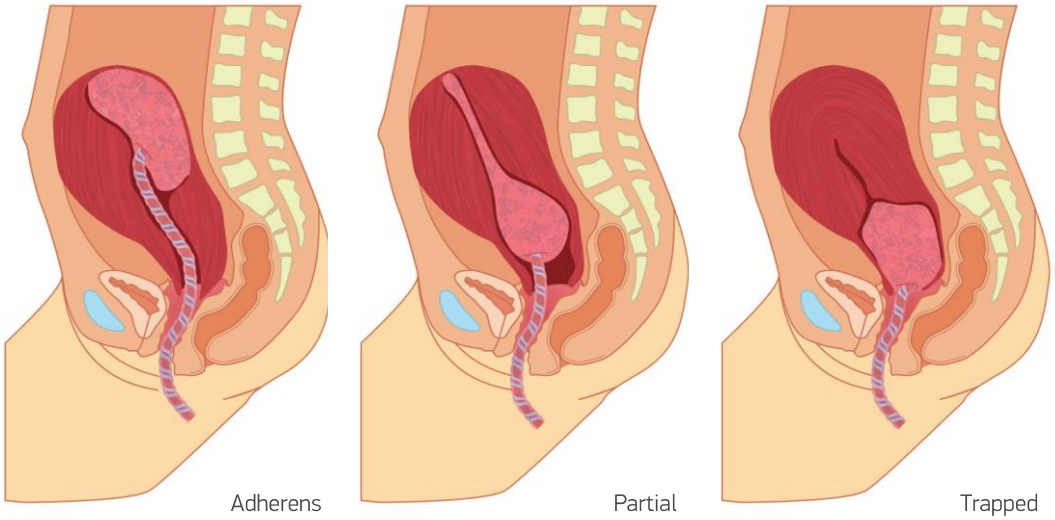

Figure 1. Types of retained placenta (courtesy Achier Akol).

Figure 2

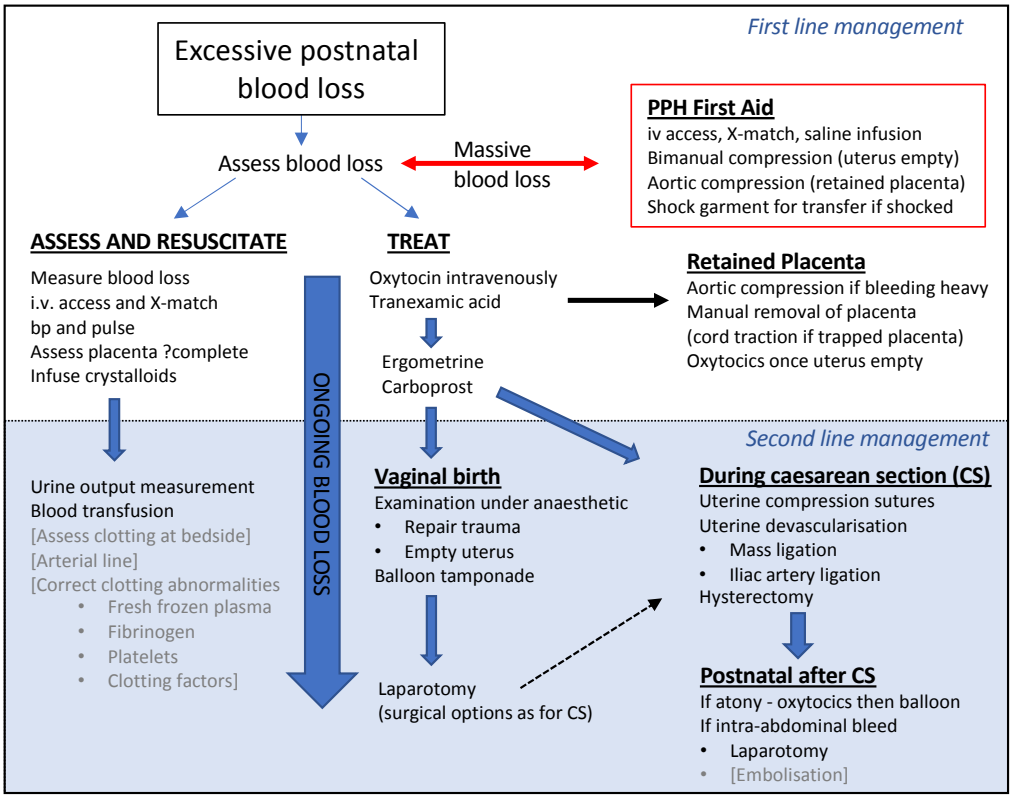

Figure 2. Flow chart for PPH management showing first and second line management options. Text in grey represents higher cost options often unavailable in low income settings.

Highlights

- The normal third stage of labour depends on contraction of the retroplacental myometrium.
- Routine management includes prophylactic uterotonics and delayed cord clamping (DCC)
- At home birth, unskilled attendants can use misoprostol with DCC but without cord traction
- Reducing haemorrhage deaths requires preparedness, simulation training and management algorithms.

Practice points

1. Although 10 IU intramuscular oxytocin is the preferred medication for active management of third stage labour, alternative routes and doses, or alternative medications must be considered in different settings such as at Caesarean section or home birth.
2. Delaying cord clamping for 3 minutes has both short and long-term benefits for babies, especially those needing resuscitation.
3. Intramuscular carbetocin is as effective as intramuscular oxytocin for PPH prophylaxis, and is being made available at low cost in a heat stable preparation for low income settings.
4. All maternity facilities need to be prepared for third stage management and its complications by ensuring correct supplies, trained staff and regular scenario training

Research agenda

1. What is the appropriate safe effective dose of uterotonic for PPH prophylaxis at Caesarean section?
2. Does the use of an intrapartum oxytocin infusion reduce the efficacy of oxytocin prophylaxis and treatment, and is there a more effective alternative?
3. Should additional prophylaxis be given to women assessed to be high risk for PPH after vaginal delivery?
4. How can deferred cord clamping be optimised at birth in babies requiring resuscitation?
5. In what situations is balloon tamponade effective for the treatment of PPH?

MCQs

1. For home delivery by an unskilled birth attendant, the following management for the third stage should be recommended :

(a) No uterotonic agent should be given
(b) Oral misoprostol can be administered
(c) Delayed cord clamping
(d) Controlled cord traction
(e) Early suckling of the neonate

Answers: (a) F, (b) T, (c) T, (d) F, (e) T

Explanation to the answers to question 1

Network analysis demonstrates that use of several uterotonic agents individually (oxytocin, ergometrine, misoprostol, carbetocin) significantly reduce the risk of PPH so a uterotonic agent should be given at home birth by the birth attendant, with the chosen agent being one that can be safely administered in this setting.[25,31]
Oral misoprostol can be administered in the home setting; it is easy to administer, does not require refrigeration and there are several studies where it has been employed in this context.[33,34,35]
Delayed cord clamping has been shown to have benefit for the fetus and is practicable in low resource emergency settings. [8,16]
Evidence shows minimal benefit from CCT, unless following ergometrine. It is a skilled procedure and it is recommended that it should not be performed by an unskilled birth attendant.[18,28]
Early suckling at the breast stimulated endogenous oxytocin release which enable uterine contraction and is also beneficial for the neonate (skin to skin and enables breast feeding)

2. At caesarean section for PPH prophylaxis:

(a) Oxytocin can be administered intramuscularly
(b) The placenta should be removed manually
(c) Misoprostol is the medication of choice
(d) There is no consensus on the appropriate does of intravenous oxytocin
(e) Rapid iv boluses of oxytocin can cause maternal hypertension

Answers: (a) T, (b) F, (c) F, (d) T, (e) F

Explanation to the answers to question 2

Network analysis shows im oxytocin is effective for preventing PPH in third stage and, although most research is on vaginal delivery, there is no pharmacological reason why it should not have same efficacy at CS.[25,37] One systematic review shows increased blood loss with manual placental removal compared to controlled traction after placental separation.[28,44] Network analysis shows oxytocin to be the uterotonic of choice in terms of efficacy and side effect profile.[25] Also, the parenteral route is indicated at CS, and misoprostol has no parenteral preparation. International obstetric guidelines and anaesthetic consensus documents differ on preferred route and dose of oxytocin.[31,38,39,40,41,46] Rapid iv boluses of oxytocin at CS have been shown by pharmacokinetic studies and in some case reports to cause maternal hypotension (not hypertension).[36]

3. Studies have shown that the benefits of deferring cord clamping for 3 minutes include:

(a) Reduced rates of PPH in the mother
(b) A 10% reduction in mortality in healthy term babies born vaginally

(c) Improved motor skills at 4 years of age in healthy term babies born vaginally.
(d) A 30% reduction in mortality in premature babies
(e) Improved Apgar scores in babies needing resuscitation

Answers: (a) F, (b) F, (c) T, (d) T, (e) T

Explanation to the answers to questions 3

Deferred, or delayed cord clamping is now recommended by all major guidelines internationally. There appears to be no benefit to the mother, but the transfer of oxygenated blood to the baby in the first minutes after birth appears to have major effects on the baby. The oxygen in the placental blood improves oxygenation and resuscitation,[16] whilst the increased haemoglobin reduces infant anaemia. It is probably the improved iron stores (important for neurone growth) that leads to the improved neurological function seen in the long-term follow-up studies of babies randomised to early or delayed cord clamping.[15] The optimal delay is not known, but the studies showing improved long-term outcomes were all conducted using a delay of 3 minutes.[14] Randomised studies of delayed cord clamping in premature babies together show a 30% reduction in mortality.[8] The reason is likely to be a combination of improved oxygenation, improved blood pressure, a more stable transition to respiration, higher blood volume and haemoglobin. There are no studies that show an effect of delayed cord clamping on the neonatal mortality of healthy term infants. Neonatal mortality is very rare in this group, and so, even if there were to be a reduction in mortality with delayed cord clamping, it would take an enormous randomised trial to show it and this has not been done.

4. Regarding placental detachment during the third stage of labour:

(a) Ultrasound can be used to differentiate different types of retained placenta
(b) Retained placenta is associated with use of ergometrine for PPH prophylaxis
(c) Umbilical vein oxytocin injection is an effective treatment for retained placenta
(d) The myometrium behind the placenta is the first part of the myometrium to contract
(e) The use of controlled cord traction reduces maternal PPH when oxytocin is used for prophylaxis

Answers: (a) T, (b) T, (c) F, (d) F, (e) F

Explanation to the answers to questions 4

The large WHO controlled cord traction study found no difference overall in PPH rates between those who had CCT and who didn't in women given intramuscular oxytocin for 3rd stage management.[18] Intriguingly, however, there was a small subgroup who were mistakenly given a combination oxytocin/ergometrine in the study who needed the CCT to prevent retained placenta. This hints that CCT may be necessary in this subgroup. The ergometrine risk is supported by the Begley study in which women who had PPH prophylaxis with intravenous ergometrine and CCT had very high rates of retained placenta compared to those with physiological management.[64]

Ultrasound studies have provided an insight into the mechanisms of retained placenta and show that the retroplacental myometrium is last part of the myometrium to contract, and results in the shearing off of the placenta. Failure of this area to contract is the cause of one of the three types of

retained placenta, '*placenta adherens*'. Several studies have tried to deliver oxytocin to this area of the uterus by injecting oxytocin into the umbilical vein so that it reaches the myometrium through the placenta. Despite early promise however, large double-blind studies have been unable to replicate the results.[56]