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Ectopic pregnancy

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INTRODUCTION

Ectopic pregnancy is defined as a pregnancy in which the implantation of the embryo occurs outside the uterine cavity, most frequently in one of the two fallopian tubes or, more rarely, in the abdominal cavity or the cervix¹. Ectopic pregnancy is one of the frequent emergencies encountered in obstetrics and gynecology and is a common condition throughout the world. It is important to have at least a basic knowledge about this condition and to recognize its symptoms. When an ectopic pregnancy ruptures it is a medical emergency and is a life-threatening condition. One study in Lagos showed that ruptured ectopic pregnancy was responsible for almost 50% of all gynecologic emergencies².

According to the World Health Organization (WHO), incidence in the developing world varies between one ectopic pregnancy per 50–200 pregnancies^{3,4}. A study conducted in Ghana showed incidence rates as high as one ectopic pregnancy in every 44 deliveries⁵. Ectopic pregnancy is a major cause of maternal death around the world, with case fatality rates in the developing world (hospital-based figures) of 1–4%⁴. This is 10 times higher compared with developed countries⁴. In some countries, up to 9% of all maternal deaths are caused by ectopic pregnancies^{4,6,7}.

As is stated in *William's Obstetrics*: 'The risk of death from an extrauterine pregnancy is greater than that for pregnancy that either results in a live birth or is intentionally terminated'⁸. An extrauterine pregnancy is 50 times more likely to result in a maternal death than a first-trimester abortion and 10 times more likely than delivery in the third trimester⁹.

The difficulty with all these figures is that in low-resource settings, the registration of women having an ectopic pregnancy is far from complete. Most of the data mentioned in research and publications are hospital-based figures. Many women with an ectopic pregnancy will survive, and thus not visit a hospital; after tubal abortion, blood loss and symptoms may cease. The incidence of undetected ectopic pregnancy is therefore unknown. Only a limited number of women will be able (due to different factors) to reach a health facility and will be diagnosed correctly and in time with having an ectopic pregnancy. Women who in the worst case die of a ruptured ectopic pregnancy before they can reach a health facility will in most cases not be counted in the maternal mortality figures.

Hence early diagnosis, prior to rupture and hemorrhage, is extremely important. Ideally one should recognize every ectopic pregnancy before it ruptures and becomes a life-threatening condition. The most important thing is to keep in mind that a woman with certain complaints might have an ectopic pregnancy and needs to be seen urgently by a health professional in a clinic preferably with a theatre and a skilled doctor who can perform a salpingectomy.

Early recognition is of course important to prevent maternal death (Figure 1). In addition, early recognition can prevent hemorrhagic shock, excessive tubal damage, acute surgery and blood transfusion. Further, even when a woman survives it might have a major impact on the rest of her life, especially if her fertility is significantly reduced after an ectopic pregnancy¹.

So the best way would be to prevent women from having an ectopic pregnancy.

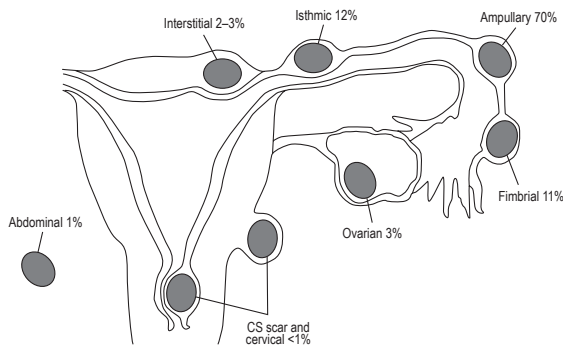


Figure 1 Implantation sites of an ectopic pregnancy

Key points

- Ectopic pregnancy is an emergency condition.
- It is a major cause of maternal death.
- It is important to recognize it at an early stage.

RISK FACTORS AND PREVENTION

As mentioned earlier, ectopic pregnancy is a life-threatening condition and therefore early recognition and proper treatment is very important. However, prevention is even more important. You should always bear in mind that there are several risk factors contributing to developing an ectopic pregnancy. The main risk factors are shown in Table 1^{2,8-11}.

Research in Zimbabwe^{1,12} compared a group of women who had an ectopic pregnancy with women with an intrauterine pregnancy. Previous infection with *Chlamydia trachomatis* was much more common in the group with an ectopic pregnancy. Other studies also showed a relationship with an infection with *Neisseria gonorrhoeae*. Several other studies (descriptive) and some case reports describe a possible role for endometriosis, tuberculosis and *Schistosoma haematobium* infection¹.

A case-control study was carried out in Lagos, Nigeria². Age, marital/socioeconomic status and parity were not significant risk factors for ectopic pregnancy. However, an early age of sexual debut increased the risk of ectopic pregnancy almost two-fold, previous induced abortion increased the risk 14-fold and a sexually transmitted infection (STI) nine-fold. The use of condoms was protective².

In one study, the risk factors for an ectopic to rupture were a previous history of ectopic pregnancy and parity¹³. Other research found that higher β -human chorionic gonadotropin (hCG)

Table 1 Main risk factors for ectopic pregnancy

Pelvic inflammatory disease
Sexually transmitted disease
Multiple sexual partners
Smoking
Previous ectopic pregnancy
Sterilization
Previous induced abortion

levels and higher gestational age were significant risk factors for an ectopic to rupture, but keep in mind that there is no threshold of hCG level for tubal rupture¹⁴.

Intrauterine device

As any contraceptive method reduces the overall pregnancy rates it will also protect against an ectopic pregnancy. So, in general, an intrauterine device (IUD) will not increase the risk of an ectopic pregnancy compared with not using any contraceptive method. However, when a woman with an IUD gets pregnant there is a significantly higher chance of the pregnancy being an ectopic^{11,15}. There might be a bit higher chance of getting an ectopic after the use of an IUD in the past¹⁵. The study conducted in Lagos showed an increased risk of almost four times after the previous use of an IUD; however this seems to be exaggeratedly high².

As you can see by focusing on prevention of STIs and unwanted pregnancies a reasonable number of ectopic pregnancies can be prevented. As with STI and HIV/AIDS prevention, proper sexual education at all ages starting at a young age is most important.

Key points

- Know the risk factors for an ectopic pregnancy: pelvic inflammatory disease (PID), STI, multiple sexual partners, previous ectopic pregnancy, sterilization and previous induced abortion.
- Ectopic pregnancy is linked to STIs.
- Sexual education is important at all ages, in particular at young age.

SIGNS AND SYMPTOMS

The signs and symptoms of an ectopic pregnancy can be subtle or very acute in the case of a ruptured ectopic pregnancy, depending on the amount of

internal hemorrhage. You can make a difference in an acute and a subacute presentation. This difference is caused in most cases by the fact that there is a ruptured or unruptured ectopic pregnancy. In most cases it means the difference between investigating the patient more thoroughly with more extensive diagnostic procedures (if possible) or the need of performing urgent surgery. Some women present after they have had a 'miscarriage': i.e. they lost the so-called decidual cast (decidualized endometrium that is sometimes expelled in ectopic pregnancy and resembles a spontaneous miscarriage).

Acute presentation

Most likely the woman has a ruptured ectopic pregnancy. This is a *medical emergency*. Most women will present at a health facility after having a period of amenorrhea, complaining of (severe) abdominal pain, fainting and often vaginal bleeding. Typically, the pain suddenly became worse. As a result of blood in her abdomen she can also complain of shoulder pain.

Physical examination Her abdomen is painful, rigid with rebound tenderness and guarding. Signs of anemia (paleness) and shock are present in most cases (tachycardia and hypotension).

If a patient presents with the above-mentioned complaints and signs she needs an immediate intravenous (IV) line with fluid substitution while organizing urgent surgery and blood transfusion if she is in severe shock. If she is hemodynamically stable but shows signs of hypotension and anemia she should still have further diagnostics: at least a pregnancy test before operation; if further investigation is not delaying surgery unnecessarily she should have a vaginal ultrasound if available or a vaginal examination and culdocentesis if the diagnosis is not yet clear. If this is not immediately possible at your health facility she needs at least an IV drip and preferably a blood transfusion. She then urgently needs to be transferred to a hospital with a theatre and a surgically skilled doctor.

Subacute presentation

A woman has already had a couple of days of irregular vaginal bleeding, (some) abdominal pain after a period of amenorrhea but is hemodynamically stable.

Physical examination This shows in most cases a clinically stable patient (normal blood pressure and

heart rate) with a painful abdomen which can show signs of an acute abdomen: guarding and rebound tenderness. If you do want to perform a vaginal exam (see Chapter 1 on how to do this), do it carefully, because it can cause an unruptured ectopic to rupture. You may find cervical motion tenderness with a soft small uterus and adnexal tenderness. The patient can be anemic so if she is stable you might want to give her a blood transfusion. As the patient is stable there is time to perform diagnostic tests (see Chapter 9).

The diagnosis of an ectopic pregnancy can however be difficult. Usually women will have experienced a period of amenorrhea, but sometimes the patient thinks she cannot be pregnant: either because she has not yet missed her period or she does not know the exact date, she experiences pathological bleeding due to the ectopic when she expects to have her normal period or she has a levonorgestrel (LNG)-IUD and is amenorrheic. Up to 9% of women with ectopic pregnancy report no pain and one-third lack adnexal tenderness⁸.

Key points

The main symptoms are:

- Amenorrhea
- Abdominal pain
- Abnormal bleeding
- Abdominal and pelvic tenderness
- Shock.

Classic triad of:

- Amenorrhea (98.0%)
- Abdominopelvic pain (92.2%)
- Vaginal bleeding (62.7 %)¹⁰.

Action:

- Acute presentation – immediate surgery.
- Subacute presentation – time to perform diagnostic tests followed in most cases by surgery.

If in doubt:

'Any women with a menstrual irregularity (missed period(s) or lighter period than usual) combined with abdominal pain and adnexal tenderness on one side probably has an ectopic pregnancy'³.

DIFFERENTIAL DIAGNOSIS

As most of the signs and symptoms described above are not specific you should always think of other

causes of the women's complaints (see Chapters 2 and 5 on first trimester of pregnancy and acute pelvic pain).

Differential diagnoses

- Abortion (spontaneous or induced)
- PID
- Bleeding corpus luteal cyst
- Torsion of an ovarian cyst.

And of course any other causes of an acute abdomen which can also present in pregnancy such as for example an appendicitis.

Necessary diagnostics

As already mentioned above, it depends if there is time to perform diagnostic tests. As said, when a patient is in shock and you think she has an (ruptured) ectopic pregnancy, the best thing is to operate on her in an equipped facility as soon as possible. Possibly, there is time to perform a pregnancy test if available; however a negative urinary pregnancy test, at least in the past, did not always rule out an ectopic pregnancy. This is because the threshold of qualitative urinary pregnancy tests differed and were only positive to a minimum of 750 IU of β -hCG/ml of urine. However, with modern tests with a much better threshold of at least 75 IU/ml, false-negative results are still possible but a negative pregnancy test in most cases rules out an ectopic pregnancy. You should check the threshold level of your pregnancy tests. With a negative urinary pregnancy test there can still be a need for surgery due to other causes, so perform a laparotomy when in doubt.

When the patient is (relatively) stable you will have the possibility of performing diagnostic tests. The best way of diagnosing an ectopic pregnancy is by performing a transvaginal ultrasound by a skilled health professional and measurement of β -hCG levels in her blood^{8,9,16}. See how to do a vaginal ultrasound in Chapter 1. However, unfortunately, both these tests are frequently not available in a low-resource setting.

Therefore, we need other tools to help us with the diagnosis. First, when you suspect a woman of having an ectopic pregnancy admit her in the ward. After admittance, don't just leave her there but keep a close eye on her and frequently measure her blood pressure and pulse. Put up an IV line and

give her fluids after taking a blood sample to measure her Hb and for cross-matching. If your hospital/health center does not have blood available, find out if there is a donor available for her. Then perform a urine pregnancy test. If this is positive it makes the suspicion of her having an ectopic pregnancy a bit higher.

Preferably perform an ultrasound; as already mentioned, in the best case, this should be a transvaginal ultrasound. This is the best method of detecting an ectopic pregnancy and in finding out whether the tubal pregnancy has ruptured by showing fluid in the pouch of Douglas^{9,16}. However, you might also be able to diagnose an ectopic with a transabdominal ultrasound.

A study conducted in a reference hospital in Accra, Ghana, showed the impact of introduction of abdominal ultrasound on diagnosing unruptured ectopic pregnancy. The introduction of abdominal ultrasound in the hospital improved the number of unruptured ectopic pregnancies that were diagnosed from 0.3% to 8.5%⁵. Even though this is still only 10% of the unruptured ectopic pregnancies to be diagnosed, it is an important improvement. However, another study performed in 2000 in Cameroun⁷ showed that abdominal ultrasound scanning was not a relevant tool for diagnosing an ectopic pregnancy. It was mentioned that performing an (abdominal) ultrasound can cause delay due to the fact that in many cases ultrasound was performed in a health facility by an untrained health worker. So identification of an ectopic pregnancy with a transabdominal ultrasound can be difficult especially by an untrained or inexperienced health worker and might cause delay.

However, when you perform an ultrasound and you clearly see an intrauterine pregnancy, an ectopic is unlikely, but a heterotopic pregnancy is still possible. This is a combination of both an intrauterine and extrauterine pregnancy, which is very rare. When there is no intrauterine pregnancy, the woman has a positive pregnancy test, and you can see fluid in the pouch of Douglas together with a pelvic mass, the diagnosis of an ectopic pregnancy is very likely⁸.

If β -hCG measurement, ultrasound in many cases and, sometimes, urinary pregnancy tests are not available, there is another possibility of diagnosing a ruptured ectopic pregnancy called *culdocentesis*, where free fluid (or blood) can be produced from the pouch of Douglas vaginally. As the

test is not very difficult to learn or perform, it is a very important diagnostic tool especially in a low-resource setting. In more than 90% of the women having a ruptured ectopic pregnancy culdocentesis will be positive^{9,17,18}.

A positive result means that you will have obtained at least 0.5 ml of non-clotting blood from the pouch of Douglas. Blood from a patient's peritoneal cavity does not clot very easily due to the fact that there are certain proteins in the peritoneal cavity that prevent this. However, clots are still possible especially when a woman has an old ruptured ectopic. In more than 60% of unruptured ectopic pregnancies, non-clotting blood is also aspirated¹⁷. So, in summary, fluid containing some clots or bloody fluid that does not clot are signs of hemorrhage in the patient's abdomen and possibly a ruptured ectopic pregnancy⁸.

Technique of performing a culdocentesis

Carefully perform a bimanual vaginal examination to identify the uterine position and a tubo-ovarian mass (Figure 2). Then perform a speculum examination and identify the cervix. With a tenaculum grasp the cervix and pull and lift it anteriorly so you can see the posterior fornix. Clean with an antiseptic (betadine). Then insert a long needle (16,18 gauge) on a syringe (for example a spinal needle, or any other long needle will do) through the posterior vaginal fornix with traction on your tenaculum and continuous suction on the syringe. You will only have to introduce the needle for a couple of millimeters and if blood is present aspiration should be easy. Complications should be minimal^{8,17}.

Based on the above procedure Lindow and Moore¹⁹ proposed a diagnostic scheme for a low-resource setting; however in their hospital they were able to perform laparoscopy, which in many hospitals in the developing world is not available. See Figure 3 for an adapted diagnostic scheme which will help you when you suspect a patient of having an ectopic pregnancy.

Key points

When you expect your patient of having an (ruptured) ectopic pregnancy:

- When she is in shock, set up an IV line, give fluid substitution and only perform necessary tests such as Hb and cross-matching and perform an urgent laparotomy.

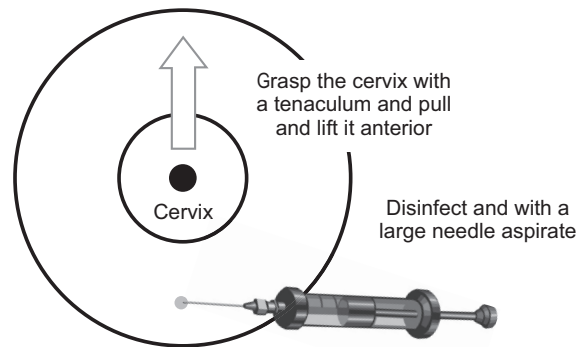


Figure 2 Culdocentesis

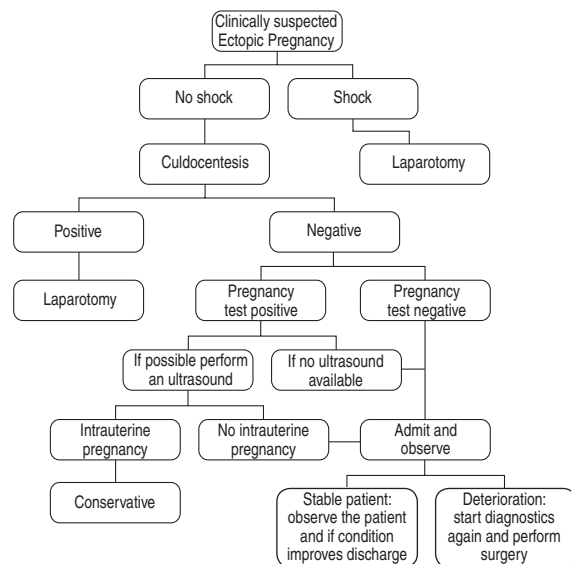


Figure 3 Diagnostic scheme

- Otherwise: perform at least a pregnancy test; be aware of false-negative results. Take her Hb and cross-match, find a donor.
- If possible, perform an ultrasound, preferably vaginal, by a skilled health worker.
- Perform a culdocentesis.

MINIMAL REQUIRED CARE/TREATMENT

Again it is important to differentiate between sub-acute/acute presentation as mentioned above. If you think a patient needs urgent surgery, perform this at your hospital if possible, or otherwise refer the patient as quickly as possible. All patients with an ectopic pregnancy should receive an IV line with fluids, preferably normal saline or, if available plasma expander. Safe transport should be arranged

by the health system. Do not let your patient travel on her own as she might die on the way. As a general measure it is important to have standards of communication and referral in your facility for emergency situations like this.

If surgery is possible, you should perform a laparotomy. Give her a single shot of prophylactic antibiotics such as ampicillin 1000 mg IV plus metronidazole 500 mg IV. Preferably open the abdomen via a Pfannenstiel incision as for cesarean section, otherwise open through a lower midline incision as described for other gynecological procedures. You will in most cases find (clotted) blood in her abdomen. Scoop out if fresh and, if you have set this procedure up in your facility, use it for an autologous transfusion. In cases of an old infected ectopic pregnancy, it is better however not to remove any clots adherent to the bowel or omentum as this might cause a bowel perforation. In this case wash the abdominal cavity out with warm normal saline until you can visualize the uterus and both fallopian tubes. If you see a bleeding at one of the fallopian tubes, put pressure on it with your fingers so you will have time to inspect the rest of her pelvis.

If you have localized the ectopic pregnancy perform a *salpingectomy*. Sometimes it is necessary to also remove her ovary. But if possible try to preserve both ovaries. Here is a description on how to do a salpingectomy:

- After cleaning of the abdominal cavity with normal saline and localization of the ectopic pregnancy put a forceps on the bleeding site to control hemorrhage. If bleeding is severe you might have to do this even before abdominal cleaning by trying to grasp each tube by following them from the uterus with your fingers to check them for bleeding.
- Achieve hemostasis by putting a forceps on the cornual portion (this is the uterine side).
- Grasp the tube with a Babcock forceps and ask your assistant to lift it upwards gently.
- Put a forceps laterally on the mesosalpinx below the fimbria parallel to the tube.
- Ligate the mesosalpinx in forceps below the fimbria using a Heaney stitch (see how to do this in Chapter 19 under abdominal hysterectomy).
- Cut the meso above the forceps and ligate and cut the whole mesosalpinx step-by-step staying closely and parallel to the tube in order to preserve the ovary. Make sure you do not put too

much tissue in one forceps as hemostasis will be incomplete or the meso will tear when tying your suture.

- Finally ligate and cut the cornual portion of the tube.
- Control for hemostasis.
- In most cases you will be able to preserve the ovary. Only in old and infected ruptured ectopic pregnancies might you not be able to identify the respective ovary anymore and will have to remove the whole mass.
- Finally check the contralateral tube for patency and describe your findings in your surgery protocol.
- Wash out/remove as much blood as possible from her abdomen. Document any abnormalities you see in her abdomen. Close her abdomen as mentioned before. Transfuse her if necessary. Admit her in the ward and provide standard postoperative care.

Provide information on contraception and about the risk of recurrence to the women and her partner.

Interstitial pregnancy

Sometimes an ectopic pregnancy will present in the part of the fallopian tube which is embedded in the muscular wall of the uterus. This is called an interstitial or sometimes a cornual pregnancy, which is an incorrect name because this refers to a pregnancy in a horn of a bicornuate pregnancy. As can be seen in Figure 1 this is quite rare.

The standard treatment has been laparotomy and a cornual wedge excision if laparoscopic treatment is not available²⁰. It involves *en block* removal of all involved tissues, which includes wedge resection of the interstitial pregnancy and all the surrounding myometrium. As the pregnancy is embedded in a highly vascularized part of the uterus the risk of significant hemorrhage is very high. In addition, in most resource-poor settings patients with cornual pregnancy present late with more advanced pregnancies or uterine rupture. In both cases hysterectomy is the safest option (see Chapter 19 on how to do that) and cornual wedge resection should be the last option if the patient insists on fertility preservation. She should know however that the procedure can be very dangerous for her due to the high risk of intraoperative hemorrhage and that she has an increased risk of uterine rupture

in subsequent pregnancies, and must deliver in a hospital with a skilled surgeon in her next pregnancy.

Below is a description of how to do a cornual wedge resection for early non-ruptured interstitial pregnancy:

- Open the abdominal wall with a midline incision.
- Place purse-string sutures with one chromic cat-gut in the uterine wall below the pregnancy site. Do not tie it yet.
- Put a clamp on the respective fallopian tube distal to the ectopic.
- Excise the pregnancy including adjacent myometrium and serosa distal to your suture leaving enough myometrium and serosa in between to put a second suture and cover the defect. Carefully tighten your purse-string suture to achieve hemostasis and tie it.
- Put a second purse-string suture distal to your first one and tie it.
- Cover the defect of myometrium and serosa as described in Chapter 19 for myomectomy.
- Close the abdominal wall in layers.

Another safe alternative for the treatment of early non-ruptured interstitial pregnancy is the intramuscular (IM) administration of 50 mg/m² methotrexate, an anti-cancer drug, as a single dose or at maximum a two-dose regimen within 7 days. Ideally, in between, β -hCG levels should be checked (see how to calculate the total amount of methotrexate needed in Chapter 31).

Autologous blood transfusion

A very good method for blood transfusion especially with an ectopic pregnancy can be autologous blood transfusion or in short autotransfusion, especially when blood is scarce or when donors are not readily available. Furthermore, autotransfusion will not have the risk of transferring HIV/AIDS and other blood-borne diseases.

Autotransfusion means that you almost immediately transfuse back the blood that you remove from the patient's abdomen when performing a laparotomy. Especially in low-resource countries it is a very useful and relatively safe procedure.

Different techniques are available and mentioned in different books/literature.

The most important thing to remember is that the procedure should be performed in an aseptic environment and instruments should be sterile.

Do not perform autotransfusion when you think the patient has an abdominal infection, there is a bowel perforation or when a woman is more than 14 weeks pregnant with a ruptured amniotic sac³.

An easy way of performing the transfusion is mentioned in the textbook '*Primary Surgery*' by King *et al.*³. A special tool is used in an article from Benin²¹.

Method 1³

You will need the following equipment:

- A sterile funnel.
- A blood-giving set.
- A sterile tube to connect the end of the funnel with a needle which is connected to a blood-giving set.
- One sterilized stainless soup ladle or a sterile gallipot.
- Cover the top of the funnel with two or three layers of sterile gauze.

Open her abdomen and only make a small hole in her peritoneum and catch up the first blood which is coming out of her abdomen. Try to put a forceps to her parietal peritoneum and lift it up, in order to prevent subcutaneous blood mixing with blood from the peritoneal cavity. Then, finish the incision and scoop out the rest of the blood. Pour the blood through the gauze filter and fill up the blood bag. The gauze and the filter in the drip set will remove the clots.

Method 2

Equipment needed:

- Either a sterile soup ladle or a sterile gallipot.
- A sterile bowl covered with a layer of 2–3 sterile gauzes.
- Large sterile syringes.
- Blood bags and blood-giving sets.

Open her abdomen (see Method 1). Scoop out the blood with the gallipot. Pour it into the bowl and aspirate this with one of the two large syringes. Connect the filled syringe to the blood bag and fill the bag with the blood.

Method 2b Only in emergency situations when no blood-giving set and no anticoagulants are available you might use a method mentioned in research conducted in Nigeria²². Equipment needed: a sterile

IV fluid container (emptied) with an opening in the top of the container big enough to pour in blood and the equipment mentioned in Method 2. When the bowl is filled with blood, pour it directly in the IV-giving set and transfuse it. Do this carefully and prevent splashing and foaming. No complications were seen in this relatively small group of patients. However, it is best to *only use this method in emergency situations when no anticoagulant is available.*

Method 3²¹

This is described in an article from Benin where a special steel funnel is used. The funnel is a 24-cm high conical funnel made of surgical steel. Its open top has a diameter of 6.7 cm and its lower two-thirds are perforated with numerous holes 1 mm in diameter. When you introduce the funnel in the abdomen the blood fills the inside of the funnel. Due to the small holes the blood collected through this funnel is free of clots or particles of diameter >1 mm. The blood can then directly be aspirated with a syringe and connected to a blood bag (see also Method 2).

Important! Transfuse the collected blood immediately back to the patient. If you don't use it immediately, throw the blood away. Do not use it for other patients.

Key points

- If acute presentation of ectopic pregnancy, perform a laparotomy or transfer the patient to the nearest health facility where a safe operation is possible.
- If surgery is not possible, try to stabilize the patient with IV fluids and blood transfusions, if possible. Transfer her as soon as possible.
- Laparotomy with salpingectomy. Try to preserve her ovaries.
- Think of autologous blood transfusion and make yourself familiar with the method.

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