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<th><strong>Title</strong></th>
<th>Bleeding in early pregnancy</th>
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INTRODUCTION

Vaginal bleeding commonly occurs in pregnancy. More than 20% of pregnant women with successful deliveries experienced vaginal bleeding during the antenatal course. Two of the most important differential diagnoses for patients presenting because of bleeding in early pregnancy are miscarriage and ectopic pregnancy.

ASSESSMENT OF BLEEDING IN EARLY PREGNANCY

For patients admitted to the ward through the Accident & Emergency Department, the general condition should be assessed before taking history and performing examination. Resuscitation of the patients should be performed as appropriate.

History should be directed to establish the possibility of pregnancy. Associated symptoms including abdominal pain and passage of tissue mass should be asked. Risk factors of ectopic pregnancy like history of previous ectopic pregnancy, pelvic inflammatory disease, tubal surgery, use of assisted reproduction techniques should be explored.

Abdominal examination is an indispensable assessment. Apart from helping to make the diagnosis, presence of free fluid or peritoneal signs often indicates surgical treatment. The value of performing routine vaginal examination is challenged. However, vaginal examination would be important for patients with severe vaginal bleeding or abdominal pain. Removal of products of conception from the cervix may stop bleeding. It will also ameliorate vasovagal shock as a result of distension of the cervical os. There are other advantages of vaginal examinations. Local causes of vaginal bleeding like cervical ectropion and cervical polyp can be diagnosed. Opportunistic screening for carcinoma of cervix can also be done. The authors are of the opinion that a vaginal examination should be done.

To make a definitive diagnosis, most patients would need further investigations. A negative pregnancy test would rule out pregnancy related complications. The single most useful investigation for a patient with bleeding in early pregnancy is transvaginal ultrasound examination. The other important investigation is the serum human chorionic gonadotrophin (hCG) level.

MISCARRIAGE

Miscarriage is the preferred term for pregnancy loss before 24 weeks. This should replace the term ‘abortion’ in a series of related conditions. (Table 1) The term silent miscarriage is better because
‘missed miscarriage’ is considered ‘a mouthful to enunciate’. The other alternative term is ‘delayed miscarriage’ but this term could imply fault on the part of the woman or her doctors.

**Threatened Miscarriage**

The amount of bleeding is usually not heavy. There is usually no abdominal pain and the uterine size is corresponding to the gestational age. Pelvic ultrasound should be done to confirm the foetal viability by detecting the foetal pulsation. Cardiac activity can be documented at around 5 weeks and 5 days’ gestation. However, a substantial proportion of pregnancies miscarried after detection of cardiac activity. In one series of patients after assisted reproduction treatment, 12.2% of pregnancies miscarried afterward. The efficacy of treatment of patients with threatened miscarriage with progesterone is inconclusive.

**Silent Miscarriage**

The clinical features are very similar to threatened miscarriage. Some patients have no symptoms at all. The uterine size may be smaller than the gestational age. The ultrasound diagnostic criteria are listed in Table 2. The confirmation by a second opinion or repeat ultrasound examination after one week is recommended because of the consequence of misdiagnosing a viable pregnancy as miscarried. After a diagnosis of silent miscarriage is made, there are three options to further management. Expectant management for 1-2 weeks is the preferred management because this would minimise the risk of terminating a viable pregnancy. Also, expectant management is probably the most cost effective. The National Institute for Health and Clinical Excellence (NICE) suggested that an ultrasound examination should be done if bleeding and pain have not started or bleeding or pain are persisting and/or increasing after 3 weeks. If bleeding and pain of the patient have subsided, a pregnancy test should be done at the end of 3 weeks. It is important to note that this recommendations are not supported by sufficient clinical studies. Medical treatment is the second accept-

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Table 1. Recommended Terminology for Early Pregnancy Loss and Related Conditions

<table>
<thead>
<tr>
<th>Old Terminology</th>
<th>Recommended Terminology</th>
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<tr>
<td>Spontaneous abortion</td>
<td>Miscarriage</td>
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<tr>
<td>Threatened abortion</td>
<td>Threatened miscarriage</td>
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<tr>
<td>Inevitable abortion</td>
<td>Inevitable miscarriage</td>
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<tr>
<td>Incomplete abortion</td>
<td>Incomplete miscarriage</td>
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<tr>
<td>Complete abortion</td>
<td>Complete miscarriage</td>
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<tr>
<td>Missed abortion</td>
<td>Silent miscarriage</td>
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<tr>
<td>Septic abortion</td>
<td>Miscarriage with infection</td>
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Adapted from RCOG Green Top Guideline No. 25.

Table 2. Diagnostic Criteria for Silent Miscarriage

<table>
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<th>Ultrasound Findings</th>
<th>Management</th>
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<tr>
<td>Transvaginal Scan</td>
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<tr>
<td>CRL &lt;7mm with no visible heartbeat</td>
<td>Perform a second scan a minimum of 7 days after the first</td>
</tr>
<tr>
<td>CRL ≥7mm with no visible heartbeat</td>
<td>Seek a second opinion on the viability and/or perform a second scan a minimum of 7 days after the first</td>
</tr>
<tr>
<td>MSD &lt;25mm with no visible foetal pole</td>
<td>Perform a second scan a minimum of 7 days after the first</td>
</tr>
<tr>
<td>MSD ≥25mm with no visible foetal pole</td>
<td>Seek a second opinion on the viability and/or perform a second scan a minimum of 7 days after the first</td>
</tr>
<tr>
<td>Transabdominal Scan</td>
<td></td>
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<tr>
<td>Visible foetal pole with no visible heartbeat</td>
<td>Record the size of the CRL, perform a second scan a minimum of 14 days after the first</td>
</tr>
<tr>
<td>Visible intrauterine with no visible foetal pole</td>
<td>Record the size of the MSD, and perform a second scan a minimum of 14 days after the first</td>
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Adapted from NICE Clinical Guideline 154. CRL: Crown-rump Length; MSD: Mean Sac Diameter
able option. This is also cost effective and avoids the risk of evacuation of uterus. Eight hundred micrograms of misoprostol can be administered vaginally. The dose can be repeated if there is no bleeding or abdominal pain the next day. NICE suggested that a pregnancy test should be done after 3 weeks. Again, this recommendation is only based on expert recommendation. The third option is surgical evacuation of the uterus, either through electric vacuum aspiration or manual vacuum aspiration. A comparison of the three options can be found in table 3. The final decision should be made by the patient in the absence of contraindications. Tissue mass obtained in the course of treatment should be sent for histological assessment to confirm intrauterine pregnancy and exclude unsuspected gestational trophoblastic disease.

### Table 3. Three Options of Management of Miscarriage

<table>
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<th>Expectant Management</th>
<th>Medical Management</th>
<th>Surgical Management</th>
</tr>
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<tr>
<td><strong>Treatment</strong></td>
<td>-</td>
<td>Vaginal misoprostol single dose 800 micrograms</td>
<td>Evacuation under MAC or GA</td>
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| **Contraindications**  | • Evidence of infection  
                        • Haemodynamic instability  
                        • Suspicion of ectopic pregnancy | • Evidence of infection  
                        • Haemodynamic instability  
                        • Allergy to misoprostol  
                        • Suspicion of ectopic pregnancy | - |
| **Advantages**         | Non-invasive         | Less invasive      | Quickest, highest success rate. Shortest duration of bleeding. |
| **Disadvantages**      | Increased need for blood transfusion, unplanned admission and intervention.  
                        Longer duration of bleeding. | Compared to surgical treatment:  
                        - Gastrointestinal side effects  
                        - Longer duration of pain and bleeding  
                        - More unplanned admissions | Anaesthetic and surgical risks. |
| **Success Rate**       | 14-47% (silent miscarriage);  
                        85% in 2 weeks (incomplete miscarriage) | 85% | 95% |
| **Anti-RhD prophylaxis for non-sensitised RhD-negative women** | No, if spontaneous miscarriage occurs and no intervention needed | No | Yes  
At least 250 IU anti-D Ig |
| **Cost**               | Most cost effective  | Second most cost effective | Most costly |

MAC: Monitored anaesthesia care

### Intrauterine Pregnancy of Uncertain Viability

A woman is considered to have an intrauterine pregnancy of uncertain viability if transvaginal ultrasonography shows an intrauterine gestational sac with no embryonic heartbeat and no findings of definite pregnancy failure. NICE suggested that an ultrasound examination can be repeated in a week following a transvaginal scan. The findings of a prospective observational multicentre study supported this recommendation.

### Incomplete Miscarriage

The patient usually has a history of passage of tissue mass apart from vaginal bleeding. There may also be history of abdominal pain. The cervical os is open and the uterine size is usually smaller than the gestational age. There is no consensus on the ultrasound diagnostic criteria for incomplete miscarriage. Measurement of endometrial thickness or volume cannot differentiate between retained products of gestation and decidua. The value of morphological criteria are also not sufficiently evaluated. The same three options are useful for management after the diagnosis is
made. Expectant management is probably more successful for incomplete miscarriage when compared to silent miscarriage. The same is probably also true for medical miscarriage. To keep the local protocol simpler, the same protocol used for silent miscarriage can be used although a lower dose for incomplete miscarriage should suffice.

Ectopic pregnancy remains one of the important causes of maternal mortality. The same is probably also true for medical miscarriage. To keep the local protocol simpler, the same protocol used for silent miscarriage can be used although a lower dose for incomplete miscarriage should suffice.

Complete Miscarriage
The presentation is very similar to incomplete miscarriage but usually, both pain and bleeding should have subsided. The cervical os is closed and the uterine size should be smaller. Ultrasound examination should reveal no signs of any pregnancy tissue within the uterine cavity. This diagnosis should be made only if there is evidence supporting the prior presence of an intrauterine pregnancy like previous ultrasound evidence or histological evidence of intrauterine pregnancy.

Pregnancy of Unknown Location
This is a descriptive term applied to women with a positive pregnancy test who have no evidence of either an intrauterine or ectopic pregnancy on transvaginal ultrasound examination. An algorithm to manage patients in this state can be found in figure 1.

ECTOPIC PREGNANCY
Ectopic pregnancy remains one of the important causes of maternal mortality. When an ectopic pregnancy ruptures, the patient develops hypovolemic shock and may die without timely intervention. Fortunately, most patients present before rupture. The classic symptoms of ectopic pregnancy include missed period, vaginal bleeding and abdominal pain. Risk factors should be explored. Significant physical findings include abdominal tenderness, cervical motion tenderness, adnexal mass or tenderness. In a recent review of literature, it was found that all components of patient history and symptoms showed limited clinical value. Similarly, normal findings did not decrease the likelihood of an ectopic pregnancy. Transvaginal ultrasound examination is the most important modality of investigation. The likelihood ratio of ectopic pregnancy in the presence of
Figure 2. Management of Ectopic Pregnancy

Adapted from NICE Clinical Guideline 154.

Expectant management

- **Suitable for expectant management**
  - hCG < 1,000 IU/L
  - hCG on decreasing trend
  - No haemoperitoneum
  - Minimal symptoms
  - Negative foetal cardiac pulsation
  - Patient’s wish (+) compliance to follow up

Blood tests: Complete blood picture, liver & renal function tests, hCG

- **Normal ALT, Cr, WBC, Pt and Serum hCG < 5,000IU/L**

Medical treatment (Methotrexate IMI 50mg/m²)

- **Unsuitable for expectant management**
  - hCG <1,500IU/L, offer medical treatment as first line treatment
  - May be safer to check a second hCG level to confirm the absence of a normal rise when USG findings are probably diagnostic only

USG diagnostic or probably diagnostic of ectopic pregnancy

- **Suitable for medical treatment**
  - No significant pain
  - An unruptured ectopic pregnancy with an adnexal mass smaller than 35mm with no visible heart beat
  - No intrauterine pregnancy (as confirmed on ultrasound scan)
  - Able to return for follow up

- **Unsuitable for medical treatment**
  - Ectopic pregnancy with an adnexal mass of 35mm or larger
  - Ectopic pregnancy with a foetal heartbeat visible on ultrasound scan
  - Significant abdominal pain
  - Unable to return for follow up
  - Medical treatment not acceptable to the woman
  - hCG ≥ 5,000IU/L

Medical vs. Surgical (hCG 1,500-5,000IU/L)

- **Suitable for expectant management**
  - hCG ≤ 1,000 IU/L
  - hCG on decreasing trend
  - No haemoperitoneum
  - Minimal symptoms
  - Negative foetal cardiac pulsation
  - Patient’s wish (+) compliance to follow up

Laparoscopy

- **No risk factors for infertility or no fertility**
  - Patient to check pregnancy test at 3 weeks and reassess if positive

- **Risk factors for infertility e.g. contralateral tube damage**
  - Weekly hCG till normal

Salpingectomy

Salpingotomy
an adnexal mass and the absence of an intrauterine pregnancy was reported to be 111 (95% confidence interval [CI], 12-1028). Presence of extrauterine gestational sac with yolk sac and/or embryo is considered definitive evidence of ectopic pregnancy. The presence of an inhomogeneous adnexal mass or extrauterine sac-like structure should be considered as probably ectopic pregnancy. This distinction is important to avoid inadvertently giving methotrexate to an early intrauterine pregnancy.

Checking serum hCG level is important in pregnancy of unknown location. The concept of discriminatory zone has been described but the pitfalls of using it to diagnose ectopic pregnancy should be avoided. It only suggests that the pregnancy may not be viable. The pregnancy may even be proven to be viable later. In a retrospective study, there were at least 8 patients in whom no intrauterine pregnancy was observed when the hCG level was more than 2,000 IU/L. On follow up, seven of them delivered a live birth and the other pregnancy was ongoing at 35 weeks at the time of report. Serial hCG would be more helpful. In fact, the use of discriminatory zone was not described in the NICE guideline. Apart from making the diagnosis, the level of hCG can also help to triage a patient for the different options of management.

There are also three options in the management of ectopic pregnancy. An algorithm to manage patients suffering from ectopic pregnancy can be found in figure 2. Expectant management has been reported to be effective in more than a third of patients. They included patients in whom there is no immediate indication to perform surgery and the hCG level lower than 1,500 IU/L. A lower cut-off of 1,000 IU/L was recommended in the previous RCOG guideline. This option was not mentioned in the current NICE guideline.

Medical treatment with systemic methotrexate is a cost effective option compared to surgery. In general, it is useful for asymptomatic patients with early ectopic pregnancy. The inadvertent administration of methotrexate to an undetected intrauterine pregnancy is the worst nightmare of medical treatment. It is thus safer to confirm the absence of a normal rise in hCG for patients with a diagnosis of probable ectopic pregnancy before administration of methotrexate.

Laparoscopic salpingectomy should be the surgery of choice for ectopic pregnancy. This can avoid the risk of persistent ectopic pregnancy whilst the reproductive outcome is similar.

Molar pregnancy and cervical ectopion are other causes of bleeding in early pregnancy.

Laparoscopic salpingectomy should be the surgery of choice for ectopic pregnancy. This can avoid the risk of persistent ectopic pregnancy whilst the reproductive outcome is similar.
CONTINUING MEDICAL EDUCATION

OTHER DIAGNOSES

There are other causes of bleeding in early pregnancy.

Molar pregnancy is a condition which can be associated with serious sequelae. This is the reason why all tissue mass obtained in the course of management should be sent for pathological examination.

Cervical ectopy is more commonly found. It was found in more than 10% of patients. Cervical polyp was found in 2% of patients. In fact, in many of these patients, a normal intrauterine pregnancy was found. The ectopy or the polyp could be the cause of the bleeding and the easiest way to make the diagnosis is to perform a vaginal speculum examination.

OTHER MANAGEMENT ISSUES

It is important to give anti-D rhesus prophylaxis at a dose of 250 IU (50 micromg) to all non-sensitised rhesus negative women who have a surgical procedure to manage an ectopic pregnancy or a miscarriage. There is no need for patients who receive solely medical management for an ectopic pregnancy or miscarriage to have a threatened miscarriage or have a complete miscarriage or have a pregnancy of unknown location.

Different patients can have very different reactions after suffering from bleeding in early pregnancy. The doctor should be very sensitive towards the possibility of developing emotional distress and consider appropriate intervention as necessary.

CONCLUSION

Bleeding in early pregnancy is a common condition. The most important differential diagnoses include miscarriage and ectopic pregnancy. Apart from history and physical examination, ultrasound examination and measurement of serum hCG are mostly required to make a diagnosis and guide management.

About the Authors

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REFERENCES

This continuing medical education service is brought to you by MIMS. Read the article ‘Bleeding in Early Pregnancy’ and answer the following questions. This MIMS JPOG article has been accredited for CME by the Hong Kong College of Obstetricians and Gynaecologists.

CME ARTICLE 1 POINT

Bleeding in Early Pregnancy
Answer True or False to the questions below.

1. There is no need to perform pelvic examination in patients suffering from bleeding in early pregnancy because of the accuracy of ultrasound examination.
2. Delayed miscarriage is a better term than silent miscarriage because most patients would have some symptoms and therefore cannot be ‘silent’.
3. Silent miscarriage can be diagnosed if foetal pulsation is not detected after 6 weeks maturity.
4. Expectant management is the preferred management for silent miscarriage because the risk of terminating a viable pregnancy would be minimised with other treatments.
5. It is proven that repeating a vaginal scan after 7 weeks is the most cost effective approach for intrauterine pregnancy of uncertain viability.
6. Endometrial thickness of less than 1 cm confirmed the diagnosis of complete miscarriage.
7. The presence of an inhomogenous adnexal mass or extrauterine sac-like structure and absence of an intrauterine gestational sac confirm the diagnosis of ectopic pregnancy.
8. An hCG level of more than 2,000 IU/L without evidence of intrauterine gestation on transvaginal ultrasound examination is not compatible with a normal intrauterine pregnancy.
9. Expectant management is not an option for the management of ectopic pregnancy.
10. Laparoscopic salpingotomy should be considered the surgical treatment of choice because of the superior reproductive outcome.

Name in BLOCK CAPITALS: __________________________________________
Signature: _________________________________________________________
Date: ____________________________________________________________

Please mail your completed answer sheet back to:
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Hong Kong College of Obstetricians & Gynaecologists
Room 805, Hong Kong Academy of Medicine Jockey Club Building
99 Wong Chuk Hang Road, Aberdeen, Hong Kong

CME Answers for MIMS JPOG Jan/Feb 2016
HKCOG CME Article: Fertility Preservation in Young Female Cancer Patients

Answers

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