**Introduction**

Ectopic pregnancy occurs when a fertilized egg implants outside of the uterine cavity, most commonly in the fallopian tube. The incidence has increased from 0.5% of pregnancies in the 1970s to 2% today. This is likely due to a rise in pelvic inflammatory disease and increased use of assisted reproductive techniques.

Although mortality has declined significantly, ectopic pregnancy still accounts for 2-4% of pregnancy-related deaths and is the leading cause of death in the first trimester. It can lead to life-threatening hemorrhage if rupture occurs. Therefore, timely diagnosis and management are critical.

As pharmacists, we can assist in identifying patients at high risk, recognizing potential signs and symptoms, facilitating rapid diagnostic testing, and recommending appropriate pharmacological treatment options. For example, pharmacists can ensure that eligible patients receive methotrexate for medical management and can counsel them on side effects and monitoring parameters. We can also advocate to make Rho(D) immune globulin readily available for administration to Rh-negative patients.

Recent advances in minimally invasive surgery have made laparoscopic salpingectomy and salpingostomy standard. Newer protocols have also allowed more patients to be candidates for outpatient methotrexate therapy. However, diagnosis remains challenging due to variable presentations. Ongoing research on diagnostic algorithms and risk assessment tools is needed to improve detection.

This subtopic will cover risk factors, pathophysiology, signs and symptoms, diagnostic evaluation, differential diagnoses, and current evidence-based medical and surgical treatment options for ectopic pregnancy.

**Clinical Presentation**

Ectopic pregnancy occurs when a fertilized egg implants outside of the uterus, most commonly in the fallopian tubes. The clinical presentation of ectopic pregnancy can vary, but the following are typical signs and symptoms, risk factors, and demographic information associated with this condition:

Signs and Symptoms:

* Abdominal pain: Sharp or stabbing pain on one side of the abdomen or pelvis.
* Vaginal bleeding: Light to heavy bleeding that may be different from a normal menstrual period.
* Amenorrhea: Missed menstrual period.
* Shoulder pain: In some cases, ectopic pregnancy can cause referred pain to the shoulder due to blood irritating the diaphragm.
* Weakness, dizziness, or fainting: These symptoms may indicate internal bleeding and hypovolemia.

Risk Factors:

* Previous ectopic pregnancy: Women who have had one ectopic pregnancy are at an increased risk of having another.
* History of pelvic inflammatory disease (PID): Inflammation and scarring of the fallopian tubes increase the risk of ectopic pregnancy.
* Previous tubal surgery: Surgical procedures on the fallopian tubes, such as tubal ligation or reversal, can lead to ectopic pregnancy.
* In vitro fertilization (IVF) or other assisted reproductive technologies: The use of fertility treatments increases the risk of ectopic pregnancy.
* Maternal age: Ectopic pregnancy is more common in women over the age of 35.
* Smoking: Tobacco use has been associated with an increased risk of ectopic pregnancy.

Demographic Information:

* Ectopic pregnancy can affect women of reproductive age, typically between 15 and 44 years old.
* The incidence of ectopic pregnancy is higher in certain populations, such as women of African descent and those with lower socioeconomic status.

Common Pitfalls or Misdiagnoses:

* Misdiagnosis as a normal pregnancy: Ectopic pregnancy symptoms can mimic those of a normal pregnancy, leading to a delay in diagnosis.
* Misdiagnosis as a miscarriage: Vaginal bleeding and abdominal pain can be attributed to a miscarriage, leading to a missed diagnosis of ectopic pregnancy.
* Atypical symptoms: Ectopic pregnancy may present with atypical symptoms, such as vague abdominal discomfort, making it challenging to identify.

Clinical Insights:

* Early diagnosis of ectopic pregnancy is crucial to prevent complications like tubal rupture and severe internal bleeding.
* Providers should maintain a high index of suspicion for ectopic pregnancy, especially in women with risk factors and presenting with abdominal pain and vaginal bleeding.
* Transvaginal ultrasound is the preferred imaging modality for diagnosing ectopic pregnancy, particularly when the hCG levels are low.

In summary, ectopic pregnancy presents with abdominal pain, vaginal bleeding, and other associated symptoms. It primarily affects women of reproductive age, particularly those with risk factors such as previous ectopic pregnancy, PID, and tubal surgery. Prompt recognition and diagnosis are essential to prevent adverse outcomes.

**Pathophysiology**

Ectopic pregnancy occurs when a fertilized egg implants and grows outside the uterus, typically in the fallopian tubes. The pathophysiology of ectopic pregnancy involves the following processes:

1. Abnormal embryo transport: The fertilized egg fails to move properly through the fallopian tube and into the uterus. This can occur due to structural abnormalities, scarring, or inflammation in the fallopian tubes, hindering the embryo's transit.
2. Implantation in an abnormal location: Instead of implanting in the thick lining of the uterus (endometrium), the embryo implants and begins to grow in the fallopian tube or in other rare sites, such as the ovaries, cervix, or abdominal cavity.
3. Insufficient blood supply: As the embryo grows, it requires a blood supply to sustain its development. However, the fallopian tubes and other ectopic sites are not designed to support a growing embryo, leading to inadequate blood flow and limited nutrient availability.

Clinical Manifestations and Relationships to Pathophysiology:

The pathophysiological processes of ectopic pregnancy contribute to the following clinical manifestations:

* Abdominal pain: As the embryo grows in an abnormal location, it stretches and distends the fallopian tube or other structures, causing pain. The pain is often localized on one side of the abdomen or pelvis.
* Vaginal bleeding: The abnormal implantation can disrupt blood vessels, leading to bleeding from the site of implantation. This bleeding may be lighter or heavier than a normal menstrual period.
* Signs of hypovolemia: In some cases, ectopic pregnancy can result in internal bleeding, leading to symptoms such as weakness, dizziness, and fainting.

Clinical Insights:

* Pharmacists should be aware of the increased risk of ectopic pregnancy in patients with risk factors such as a history of pelvic inflammatory disease, previous tubal surgery, or assisted reproductive technologies.
* Medications used to treat ectopic pregnancy, such as methotrexate, work by inhibiting cell division and promoting the regression of the abnormal pregnancy. Pharmacists should be familiar with the appropriate dosing, monitoring, and potential side effects of these medications.
* Early identification of ectopic pregnancy is crucial to prevent complications. Pharmacists can play a role in educating patients about the signs and symptoms of ectopic pregnancy and the importance of seeking medical attention promptly.

In summary, the pathophysiology of ectopic pregnancy involves the abnormal transport and implantation of the embryo, leading to inadequate blood supply and growth in an abnormal location. Understanding the underlying disease processes can help pharmacists recognize the clinical manifestations of ectopic pregnancy and contribute to the appropriate management and care of affected patients.

**Diagnostic Approach**

Diagnosing ectopic pregnancy requires a comprehensive approach that combines clinical evaluation, laboratory tests, and imaging studies. The following diagnostic methods are commonly used:

History and Physical Examination:

* Obtain a detailed medical history, including menstrual history, previous pregnancies, contraceptive use, history of pelvic infections, and any risk factors for ectopic pregnancy.
* Perform a thorough physical examination, including abdominal and pelvic examinations, to assess for signs of tenderness, mass, or abnormal findings.

Pregnancy Test:

* Perform a urine or serum pregnancy test to confirm pregnancy. Positive results indicate the need for further evaluation.

Quantitative Human Chorionic Gonadotropin (hCG) Measurement:

* Measure the serum hCG level, which is typically increased in early pregnancy. Serial hCG measurements can be useful in assessing the trend and rate of increase.
* Ectopic pregnancies may have lower and slower-rising hCG levels compared to normal intrauterine pregnancies. However, hCG levels alone cannot definitively diagnose ectopic pregnancy.

Transvaginal Ultrasound (TVS):

* TVS is the imaging modality of choice for diagnosing ectopic pregnancy due to its high sensitivity and ability to visualize the reproductive organs with greater detail.
* TVS can identify the location of the pregnancy and assess for signs of ectopic pregnancy, such as an empty uterus, gestational sac outside the uterus, or presence of fluid in the pelvic cavity.
* Additional ultrasound findings suggestive of ectopic pregnancy include an adnexal mass, lack of gestational sac growth, or presence of an embryo or yolk sac outside the uterus.

Discriminatory Zone:

* The discriminatory zone refers to the minimum level of hCG at which an intrauterine gestational sac should be visible on ultrasound.
* If the hCG level is above the discriminatory zone (usually around 1500 to 2000 mIU/mL), an intrauterine pregnancy should be visible on ultrasound.
* If the hCG level is below the discriminatory zone and no intrauterine pregnancy is visualized, ectopic pregnancy should be strongly considered.

Culdocentesis:

* Culdocentesis involves the aspiration of fluid from the cul-de-sac, which is the space behind the uterus.
* Culdocentesis may be performed in cases of suspected ectopic pregnancy with significant pelvic fluid to assess for the presence of blood or other abnormalities.

Clinical Insights:

* Prompt diagnosis of ectopic pregnancy is crucial to prevent complications like rupture and internal bleeding.
* In cases of unstable or hemodynamically compromised patients, immediate surgical intervention may be necessary.
* Risk stratification is important for stable patients, considering factors such as hCG levels, ultrasound findings, and the presence of symptoms.
* Serial hCG measurements and repeat ultrasound examinations may be necessary in cases of indeterminate initial findings.

In summary, the diagnostic approach for ectopic pregnancy involves a combination of history taking, physical examination, laboratory tests (such as hCG measurement), and imaging (typically transvaginal ultrasound). The interpretation of diagnostic tests, along with clinical information, aids in the accurate diagnosis of ectopic pregnancy. Differentiating between intrauterine and ectopic pregnancies is crucial for appropriate management and timely intervention.

**Management – Overview**

The management of ectopic pregnancy depends on various factors such as the patient's clinical stability, the location of the ectopic pregnancy, and the patient's desire for future fertility. The key principles of treatment include:

1. Early Diagnosis: Prompt recognition and diagnosis of ectopic pregnancy are crucial to prevent complications like tubal rupture and severe internal bleeding.
2. Medical Management: Methotrexate, a folic acid antagonist, is the first-line medication used for the non-surgical management of ectopic pregnancy. It stops the growth of the ectopic pregnancy and allows the body to reabsorb it. This approach is suitable for stable patients with low hCG levels, no evidence of tubal rupture, and no fetal cardiac activity.
3. Surgical Management: Surgical intervention may be necessary in cases of unstable patients, hemodynamic instability, or rupture of the ectopic pregnancy. Different surgical approaches include laparoscopic salpingostomy (removal of the ectopic pregnancy while preserving the fallopian tube) or salpingectomy (removal of the affected fallopian tube).
4. Rho(D) Immune Globulin (RhIg): Rh-negative women who receive medical or surgical management of ectopic pregnancy should receive RhIg to prevent sensitization to Rh-positive blood in case of fetal-maternal bleeding.
5. Follow-up and Emotional Support: Patients who have undergone medical or surgical management of ectopic pregnancy should receive appropriate follow-up care and emotional support. This includes monitoring hCG levels to ensure they return to non-pregnant levels and providing counseling regarding future fertility options.

Clinical Insights:

* The choice of treatment depends on several factors, including the patient's stability, desire for future fertility, and the presence of complications such as rupture.
* Methotrexate is effective in selected cases but requires close monitoring of hCG levels and potential side effects.
* Surgical intervention is necessary in unstable patients or cases of rupture, and it may involve removal of the affected fallopian tube.
* Non-pharmacological interventions involve providing emotional support, counseling, and follow-up care to address the psychological impact of ectopic pregnancy.

In summary, the management of ectopic pregnancy involves early diagnosis, consideration of medical or surgical interventions based on the patient's stability and desire for future fertility, administration of RhIg in Rh-negative patients, and appropriate follow-up care. The choice of treatment depends on individual patient factors and requires a multidisciplinary approach to ensure the best possible outcomes for the patient's health and emotional well-being.

**Pharmacotherapy**

Initial Management:

Methotrexate (First-Line Therapy):

* Indication
  + Stable vital signs
  + hCG concentration <5000 mIU/mL
  + Patient will follow up with provider
  + No fetal heartbeat on ultrasound
* Contraindications
  + Unstable Hemodynamically
  + Presence of free peritoneal fluid on ultrasound
  + Ectopic pregnancy larger or equal to 3.5 cm
  + Fetal heart beat on ultrasound
  + high hCG levels (>5000 mIU/mL)
    - Those with contraindications to medical therapy ACOG recommend surgical management

* Mechanism of Action: Methotrexate inhibits the growth of trophoblastic cells by interfering with DNA synthesis and cell division, leading to the resolution of the ectopic pregnancy.
* Dosage and Administration: Methotrexate is typically administered as a single intramuscular (IM) injection.
  + Single Dose
    - IM: 50 mg/m2 on day 1; maximum dose has not been established; some experts do not exceed 100 mg. Measure serum hCG level on days 1, 4 and 7; if the hCG decrease from day 4 to 7 is <15%, administer a second 50 mg/m2 dose on day 7 and measure serum hCG level again on day 14; if the hCG decrease from day 7 to 14 is <15%, administer a third 50 mg/m2 dose
  + Multiple Dose
    - 50 mg/m2 on days 1 and 4
      * Measure serum hCG level on days 1, 4, and 7; if the hCG decrease from day 4 to 7 is <15%, administer a third 50 mg/m2 dose and measure serum hCG level again on day 11
      * if hCG decrease from day 7 to 11 is <15%, administer a fourth 50 mg/m2 dose and measure serum hCG level on day 14.
      * Consider surgical management if hCG does not adequately decrease after 4 doses

* Monitoring Parameters: Serial measurements of hCG levels are crucial to monitor the response to treatment. Liver function tests, complete blood count, and renal function should be monitored regularly.
* Side Effects: Common side effects include nausea, vomiting, stomatitis, and dizziness. Methotrexate can also cause bone marrow suppression, hepatotoxicity, and pulmonary toxicity.
* Contraindications: Methotrexate is contraindicated in patients with significant liver or kidney disease, immunodeficiency, active pulmonary disease, or a history of significant alcohol intake.
* Clinical Pearls: Methotrexate is most effective in patients with low hCG levels (<5,000 mIU/mL), ectopic pregnancies smaller than 3.5 cm, and no signs of rupture. Clear instructions regarding contraception should be provided during and after treatment due to the teratogenic effects of methotrexate.

Mifepristone:

* Mechanism of Action: As a progesterone receptor antagonist, mifepristone leads to decidual breakdown and pregnancy failure. It may augment the efficacy of methotrexate.
* Dosage and Administration: A single 600 mg oral dose given on day 1 or 2 of treatment.
* Monitoring Parameters: Serial quantitative β-hCG measurements.
* Side Effects: Common side effects include nausea, vomiting, diarrhea, headache, dizziness, and hot flashes.
* Contraindications: Mifepristone is contraindicated in patients with hemorrhagic disorders or inherited porphyrias.
* Clinical Pearls: Limited data suggest mifepristone plus methotrexate provides higher treatment success rates than methotrexate alone. However, combined regimens also have more side effects.

Gefitinib:

* Mechanism of Action: Gefitinib is an epidermal growth factor receptor inhibitor that may augment methotrexate efficacy by inhibiting trophoblastic growth.
* Dosage and Administration: A single 250 mg oral dose given on day 1 or 2 of methotrexate treatment.
* Monitoring Parameters: Serial quantitative β-hCG measurements.
* Side Effects: Diarrhea and skin rash are common. Hepatotoxicity and pulmonary fibrosis are rare but serious adverse effects.
* Contraindications: None known.
* Clinical Pearls: Data do not support routine use of gefitinib with methotrexate, as combination regimens have more side effects without clear benefit over methotrexate alone.

Alternative Therapies:

1. Surgical Management:

* Indication
  + Hemodyanimcally unstable
* Salpingostomy: This procedure involves making a small incision in the affected fallopian tube and removing the ectopic pregnancy while preserving the fallopian tube. It may be considered in cases where future fertility is desired.
* Salpingectomy: Salpingectomy involves the complete removal of the affected fallopian tube. It is typically performed when the fallopian tube is severely damaged, ruptured, or when future fertility is not a concern.

Non-Pharmacological Interventions:

* Emotional Support: Ectopic pregnancy can have significant emotional implications for patients. Providing counseling and support during the treatment process is crucial to address the psychological impact of the condition.

In Summary:  
The pharmacotherapy for ectopic pregnancy primarily involves the use of methotrexate as the first-line therapy. Surgical management, such as salpingostomy or salpingectomy, may be considered in specific cases. It is crucial to closely monitor patients receiving methotrexate for potential side effects and to provide appropriate counseling and emotional support throughout the treatment process. The choice of treatment depends on factors such as patient stability, desire for future fertility, and the presence of complications.

**Key Guidelines and Evidence**

Here is a summary of the key guidelines and evidence for the management of ectopic pregnancy:

Clinical Guidelines

* ACOG Practice Bulletin No. 94 (2008): Medical Management of Ectopic Pregnancy  
  This guideline provides recommendations on criteria for using methotrexate as first-line treatment for ectopic pregnancy. Key criteria include hemodynamic stability, no signs of rupture, willingness and ability to comply with monitoring, ectopic mass <3.5 cm, and no fetal heart activity on ultrasound.

Landmark Trials

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|  | Randomized trial in 132 patients with unruptured tubal ectopic pregnancy | Single-dose methotrexate compared to  laparoscopic salpingostomy in | Success rates 88% with methotrexate vs 94% with surgery. Fewer adverse effects with methotrexate. |
| Cochrane Review, 2007 | Meta- Analysis of  35 studies on the treatment of tubal ectopic pregnancy | Systemic methotrexate in a fixed multiple dose intramuscular regimen has a non significant tendency to a higher treatment success than laparoscopic salpingostomy (1 RCT, n=100, OR 1.8, 95% CI 0.73, 4.6)    One single dose intramuscular methotrexate is significantly less successful than laparoscopic salpingostomy (4 RCTs, n=265, OR 0.38, 95% CI 0.20, 0.71)    With a variable dose regimen treatment success rises, but shows no evidence of a difference compared to laparoscopic salpingostomy (OR 1.1, 95% CI 0.52, 2.3).    The efficacy of systemic single dose methotrexate alone is significantly less successful than when combined with mifepristone (2 RCTs, n=262, OR 0.59, 95% CI 0.35, 1.0). | |

**Clinical Scenarios**

Clinical Scenario :

A 38-year-old woman presents to the emergency department with severe abdominal pain and dizziness. She reports a positive pregnancy test and has a history of previous ectopic pregnancy. On examination, she appears pale, and her blood pressure is low. FAST (Focused Assessment with Sonography for Trauma) ultrasound reveals free fluid in the abdomen.

Learning Point: Recognizing the signs of hemodynamic instability and potential internal bleeding in ectopic pregnancy.

Management Considerations:

1. Immediate resuscitation: Initiate fluid resuscitation and monitor vital signs closely. Hemodynamically unstable patients may require blood transfusion and immediate surgical intervention and medical therapy is contraindicated.
2. Consultation with a gynecologist and general surgeon: Notify the gynecologist and general surgeon for urgent evaluation and potential surgical management.
3. Surgical intervention: In the presence of hemodynamic instability and signs of rupture, immediate surgical intervention with laparotomy may be necessary. The surgeon will aim to control bleeding, remove the ectopic pregnancy, and address any internal injuries.

These clinical scenarios highlight the importance of recognizing key findings, considering the patient's stability, and involving appropriate specialists in the management of ectopic pregnancy.

**Tips for Board Exam Questions**

1. Ectopic pregnancy should be suspected in women of reproductive age presenting with lower abdominal pain, vaginal bleeding, and a positive pregnancy test. Understand the risk factors associated with ectopic pregnancy, such as a history of pelvic inflammatory disease, tubal surgery, or previous ectopic pregnancy.
2. Transvaginal ultrasound is the preferred imaging modality for diagnosing ectopic pregnancy. Recognize the sonographic findings suggestive of ectopic pregnancy, such as an empty uterus, extrauterine gestational sac, or adnexal mass. Familiarize yourself with the discriminatory zone and its significance in interpreting hCG levels and ultrasound findings.
3. Be aware of the management options for ectopic pregnancy. Methotrexate is the first-line medical therapy for stable patients with specific criteria. Understand the dosing, monitoring parameters, and potential side effects associated with methotrexate. Surgical management, such as salpingostomy or salpingectomy, may be necessary in unstable patients or cases of rupture.

**Subtopic Summary**

Ectopic pregnancy is a potentially life-threatening condition that requires prompt recognition and management. Key learning points include suspecting ectopic pregnancy in women of reproductive age presenting with abdominal pain, vaginal bleeding, and a positive pregnancy test. Risk factors, such as a history of pelvic inflammatory disease or tubal surgery, should be considered. Transvaginal ultrasound plays a crucial role in diagnosing ectopic pregnancy by identifying sonographic findings such as an empty uterus, extrauterine gestational sac, or adnexal mass. Understanding the discriminatory zone and interpreting hCG levels aid in diagnosis. Management options include medical therapy with methotrexate for stable patients and surgical intervention for unstable patients or ruptured ectopic pregnancies. Close monitoring, appropriate follow-up, and providing emotional support are essential for patient care.

**References and Bibliography**

1. American College of Obstetricians and Gynecologists. ACOG practice bulletin no. 94: Medical management of ectopic pregnancy. Obstet Gynecol. 2008;111(6):1479-1485.
2. Royal College of Obstetricians and Gynaecologists. Diagnosis and Management of Ectopic Pregnancy. Green-top Guideline No. 21. 2016.
3. Society of Obstetricians and Gynaecologists of Canada. SOGC clinical practice guideline: Medical management of ectopic pregnancy. J Obstet Gynaecol Can. 2008;30(7):692-695.
4. Lipscomb GH, Stovall TG, Ling FW. Nonsurgical treatment of ectopic pregnancy. N Engl J Med. 2000;343(18):1325-1329.
5. Barnhart KT, Gosman G, Ashby R, Sammel M. The medical management of ectopic pregnancy: a meta-analysis comparing "single dose" and "multidose" regimens. Obstet Gynecol. 2003;101(4):778-784.
6. Mol F, Mol BW, Ankum WM, van der Veen F, Hajenius PJ. Current evidence on surgery, systemic methotrexate and expectant management in the treatment of tubal ectopic pregnancy: a systematic review and meta-analysis. Hum Reprod Update. 2008;14(4):309-319.
7. van Mello NM, Mol F, Opmeer BC, et al. Salpingotomy versus salpingectomy in women with tubal pregnancy (ESEP study): an open-label, multicentre, randomised controlled trial. Lancet. 2014;383(9927):1483-1489.
8. Barnhart KT, Sammel MD, Rinaudo PF, Zhou L, Hummel AC, Guo W. Symptomatic patients with an early viable intrauterine pregnancy: HCG curves redefined. Obstet Gynecol. 2004;104(1):50-55.
9. Mol F, van Mello NM, Strandell A, et al. Salpingotomy versus salpingectomy in women with tubal pregnancy (ESEP study): an open-label, multicentre, randomised controlled trial. Lancet. 2014;383(9927):1483-1489.
10. Practice Committee of the American Society for Reproductive Medicine. Medical treatment of ectopic pregnancy: a committee opinion. Fertil Steril. 2013;100(3):638-644.
11. Elson CJ, Salim R, Potdar N, Chetty M, Ross JA, Kirk EJ on behalf of the Royal College of Obstetricians and Gynaecologists (RCOG). Diagnosis and management of ectopic pregnancy: Green-top guideline No. 21. BJOG. 2016;123(13):e15-e55. doi:10.1111/1471-0528.14189 [PubMed 27813249]
12. Stovall TG, Ling FW. Single-dose methotrexate: an expanded clinical trial. Am J Obstet Gynecol. 1993;168(6, pt 1):1759-1762; discussion 1762-5. [PubMed 8317518]
13. Barnhart K, Hummel AC, Sammel MD, Menon S, Jain J, Chakhtoura N. Use of "2-dose" regimen of methotrexate to treat ectopic pregnancy. Fertil Steril. 2007;87(2):250-256. doi:10.1016/j.fertnstert.2006.06.054 [PubMed 17097649]
14. Tulandi T. Ectopic pregnancy: methotrexate therapy. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed March 10, 2023.
15. Horne AW, Tong S, Moakes CA, Middleton LJ, Duncan WC, Mol BW, Whitaker LHR, Jurkovic D, Coomarasamy A, Nunes N, Holland T, Clarke F, Doust AM, Daniels JP; GEM3 collaborative. Combination of gefitinib and methotrexate to treat tubal ectopic pregnancy (GEM3): a multicentre, randomised, double-blind, placebo-controlled trial. Lancet. 2023 Feb 25;401(10377):655-663. doi: 10.1016/S0140-6736(22)02478-3. Epub 2023 Feb 1. PMID: 36738759.
16. Barnhart KT, Gosman G, Ashby R, Sammel M. The medical management of ectopic pregnancy: a meta-analysis comparing "single dose" and "multidose" regimens. Obstet Gynecol. 2003;101(4):778-784.

**Clinical Scenarios**

Clinical Scenario 1:

A 32-year-old female presents to the emergency department with lower abdominal pain and vaginal bleeding. She has a positive pregnancy test and reports a missed period. On physical examination, she appears stable with mild tenderness in the lower abdomen. An ultrasound reveals an empty uterus and a complex adnexal mass.

Learning Point: Suspecting an ectopic pregnancy in the presence of a complex adnexal mass.

Management Considerations:

1. Confirm the diagnosis: Ectopic pregnancy should be suspected in women of reproductive age with a positive pregnancy test, abdominal pain, and vaginal bleeding. In this scenario, the complex adnexal mass raises suspicion for ectopic pregnancy.
2. Assess stability: Evaluate the patient's vital signs and overall stability. If the patient is hemodynamically unstable, immediate surgical intervention may be necessary.
3. Serial hCG monitoring: Measure serial hCG levels to assess the trend. In ectopic pregnancies, hCG levels may rise more slowly or plateau compared to normal intrauterine pregnancies.
4. Consultation with a gynecologist: Consider involving a gynecologist for further evaluation and management. They may recommend additional imaging, such as repeat ultrasound or magnetic resonance imaging (MRI), to determine the location and viability of the pregnancy.
5. Surgical management: If the patient deteriorates clinically or has signs of rupture, emergent surgical intervention with salpingostomy or salpingectomy may be required.
6. Medical management: If the patient is stable and the ectopic pregnancy is unruptured, methotrexate therapy may be considered as a first-line medical treatment option. However, in the presence of a complex adnexal mass, methotrexate may not be the preferred option due to potential tubal rupture risk.

Clinical Scenario 2:

A 38-year-old woman presents to the emergency department with severe abdominal pain and dizziness. She reports a positive pregnancy test and has a history of previous ectopic pregnancy. On examination, she appears pale, and her blood pressure is low. FAST (Focused Assessment with Sonography for Trauma) ultrasound reveals free fluid in the abdomen.

Learning Point: Recognizing the signs of hemodynamic instability and potential internal bleeding in ectopic pregnancy.

Management Considerations:

1. Immediate resuscitation: Initiate fluid resuscitation and monitor vital signs closely. Hemodynamically unstable patients may require blood transfusion and immediate surgical intervention.
2. Consultation with a gynecologist and general surgeon: Notify the gynecologist and general surgeon for urgent evaluation and potential surgical management.
3. Surgical intervention: In the presence of hemodynamic instability and signs of rupture, immediate surgical intervention with laparotomy may be necessary. The surgeon will aim to control bleeding, remove the ectopic pregnancy, and address any internal injuries.
4. Blood type and crossmatch: Ensure blood samples are obtained for type and crossmatch in preparation for potential blood transfusion during surgery.
5. Preoperative imaging: Consider obtaining a computed tomography (CT) scan of the abdomen and pelvis to further evaluate the extent of internal bleeding and to assess the condition of surrounding organs.
6. Intraoperative findings: During surgery, the surgeon may identify the source of bleeding, such as a ruptured fallopian tube, and perform salpingectomy if the tube is severely damaged.
7. Postoperative care: Provide appropriate postoperative pain management, monitor for any signs of postoperative complications, and provide emotional support to the patient.

These clinical scenarios highlight the importance of recognizing key findings, considering the patient's stability, and involving appropriate specialists in the management of ectopic pregnancy.

**Tips for Board Exam Questions**

1. Ectopic pregnancy should be suspected in women of reproductive age presenting with lower abdominal pain, vaginal bleeding, and a positive pregnancy test. Understand the risk factors associated with ectopic pregnancy, such as a history of pelvic inflammatory disease, tubal surgery, or previous ectopic pregnancy.
2. Transvaginal ultrasound is the preferred imaging modality for diagnosing ectopic pregnancy. Recognize the sonographic findings suggestive of ectopic pregnancy, such as an empty uterus, extrauterine gestational sac, or adnexal mass. Familiarize yourself with the discriminatory zone and its significance in interpreting hCG levels and ultrasound findings.
3. Be aware of the management options for ectopic pregnancy. Methotrexate is the first-line medical therapy for stable patients with specific criteria. Understand the dosing, monitoring parameters, and potential side effects associated with methotrexate. Surgical management, such as salpingostomy or salpingectomy, may be necessary in unstable patients or cases of rupture.

**Subtopic Summary**

Ectopic pregnancy is a potentially life-threatening condition that requires prompt recognition and management. Key learning points include suspecting ectopic pregnancy in women of reproductive age presenting with abdominal pain, vaginal bleeding, and a positive pregnancy test. Risk factors, such as a history of pelvic inflammatory disease or tubal surgery, should be considered. Transvaginal ultrasound plays a crucial role in diagnosing ectopic pregnancy by identifying sonographic findings such as an empty uterus, extrauterine gestational sac, or adnexal mass. Understanding the discriminatory zone and interpreting hCG levels aid in diagnosis. Management options include medical therapy with methotrexate for stable patients and surgical intervention for unstable patients or ruptured ectopic pregnancies. Close monitoring, appropriate follow-up, and providing emotional support are essential for patient care.

**References and Bibliography**

1. American College of Obstetricians and Gynecologists. ACOG practice bulletin no. 94: Medical management of ectopic pregnancy. Obstet Gynecol. 2008;111(6):1479-1485.
2. Royal College of Obstetricians and Gynaecologists. Diagnosis and Management of Ectopic Pregnancy. Green-top Guideline No. 21. 2016.
3. Society of Obstetricians and Gynaecologists of Canada. SOGC clinical practice guideline: Medical management of ectopic pregnancy. J Obstet Gynaecol Can. 2008;30(7):692-695.
4. Lipscomb GH, Stovall TG, Ling FW. Nonsurgical treatment of ectopic pregnancy. N Engl J Med. 2000;343(18):1325-1329.
5. Barnhart KT, Gosman G, Ashby R, Sammel M. The medical management of ectopic pregnancy: a meta-analysis comparing "single dose" and "multidose" regimens. Obstet Gynecol. 2003;101(4):778-784.
6. Mol F, Mol BW, Ankum WM, van der Veen F, Hajenius PJ. Current evidence on surgery, systemic methotrexate and expectant management in the treatment of tubal ectopic pregnancy: a systematic review and meta-analysis. Hum Reprod Update. 2008;14(4):309-319.
7. van Mello NM, Mol F, Opmeer BC, et al. Salpingotomy versus salpingectomy in women with tubal pregnancy (ESEP study): an open-label, multicentre, randomised controlled trial. Lancet. 2014;383(9927):1483-1489.
8. Barnhart KT, Sammel MD, Rinaudo PF, Zhou L, Hummel AC, Guo W. Symptomatic patients with an early viable intrauterine pregnancy: HCG curves redefined. Obstet Gynecol. 2004;104(1):50-55.
9. Mol F, van Mello NM, Strandell A, et al. Salpingotomy versus salpingectomy in women with tubal pregnancy (ESEP study): an open-label, multicentre, randomised controlled trial. Lancet. 2014;383(9927):1483-1489.
10. Practice Committee of the American Society for Reproductive Medicine. Medical treatment of ectopic pregnancy: a committee opinion. Fertil Steril. 2013;100(3):638-644.