

# Ectopic Pregnancy

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**E**ctopic pregnancy refers to a pregnancy located away from the normal position, that is an extrauterine pregnancy. Although uncommon, it is associated with a high morbidity and even mortality. This article summarises the current state-of-the-art management of tubal pregnancy.

## EPIDEMIOLOGY

The incidence of ectopic pregnancy is difficult to estimate because of the difficulty in deciding the denominator. According to a territory-wide audit in Hong Kong, the incidence was 0.77% of all reported pregnancies.<sup>1</sup> The real incidence may be even lower because of possible under-reporting of spontaneous miscarriage and pregnancy terminations. The incidence in Hong Kong appears to be lower than that reported in other populations: 2% in the United States in 1992<sup>2</sup> and 1.88% in Northern Europe in 1993.<sup>3</sup>

In many developed countries, there are reports of an increasing

trend.<sup>4</sup> The exact cause for this rise is controversial. It may be related to an increase in pelvic inflammatory disease (PID), local variation in contraceptive use and the use of assisted reproduction techniques (ART). It may, however, also be related to the improved diagnostic techniques that allow earlier diagnosis of ectopic pregnancy.<sup>5</sup> It is uncertain whether the same trend is observed elsewhere in Asia.

The increasing use of ART is associated with an increased incidence of ectopic pregnancies. The incidence of heterotopic pregnancies – the coexistence of an intrauterine and extrauterine gestation – is also increasing;<sup>6</sup> the incidence is thought to be 1:30,000. This is derived by multiplying the incidence of ectopic pregnancy by that of dizygotic twinning. Following ART, the incidence is as high as 1 to 3%.<sup>6</sup>

## AETIOLOGY

An abnormal fallopian tube is considered the basic pathology underlying ectopic pregnancy. Previous

tubal surgery, sterilisation, PID and previous ectopic pregnancy substantially increase the risk for a subsequent ectopic pregnancy. Ovulation induction may also increase the risk because of the effect of hormone fluctuations on tubal function.<sup>7</sup> The mechanism behind the development of ectopic pregnancy following in vitro fertilisation (IVF) is unclear. It may be related to accidental transfer of the embryo to the tube, or migration of the embryo into the fallopian tube following replacement.<sup>5</sup>

## DIAGNOSIS

Ectopic pregnancy is a potentially life-threatening condition, thus early diagnosis is vital. With the availability of minimal access surgery (see later), the early diagnosis of ectopic pregnancy is even more important. The earlier the diagnosis is made, the more appropriate is minimal access surgery.

Patients with ectopic pregnancy are still occasionally admitted to hospital in shock as a result of rupture and haemoperitoneum.

Diagnosis is usually not difficult under these circumstances.

Patients may however, present with the classic combination of abdominal pain and amenorrhoea. A history of syncope and pain radiating to the shoulder are other common complaints. Physical examination may reveal abdominal tenderness with a varying degree of peritonism, which is also the cause for cervical excitation tenderness. Occasionally, an adnexal mass may be felt.

More commonly patients present with subtle symptoms and signs and a clinical diagnosis of ectopic pregnancy remains difficult. It has been suggested that, based on clinical features alone, only half of all cases of ectopic pregnancy can be diagnosed.<sup>8</sup> Therefore, it is important to maintain a high index of suspicion in all women of reproductive age with the possibility of pregnancy. This is especially true in patients at high risk of ectopic pregnancy.

New generation commercially available pregnancy testing kits are very sensitive. Typically, they have a detection limit of 25-50 iu/L for urinary human chorionic gonadotrophin (HCG). There is no need for an early morning urine sample. Thus for practical purposes, a negative pregnancy test virtually excludes the possibility of ectopic pregnancy. Older, less sensitive pregnancy testing kits should not be used.

Traditionally, pelvic ultrasound has been used to demonstrate an intrauterine sac, thus excluding ectopic pregnancy. With the transvaginal approach, which allows the use of a transducer with a higher frequency and therefore higher resolution, the sensitivity of pelvic ultrasound in identifying an intrauterine gestation is greatly enhanced. An intrauterine pregnancy can be identified as early as 33 to 34 days after the missed period.<sup>5</sup> However, heterotopic pregnancy is known to occur following ART and one must be especially vigilant in this group of patients. Ectopic pregnancy can also be picked up as a live embryo within a sac in the adnexa, tubal ring, or presence of fluid in the Pouch of Douglas.

In the absence of the typical symptoms of ectopic pregnancy and an intrauterine gestational sac visible on ultrasound, a serum HCG assay is helpful. If the level is less than the discriminatory zone, eg. <2000 iu/L, the pregnancy may be an early intrauterine pregnancy that cannot yet be seen with ultrasonography.<sup>9</sup> It is useful to repeat the HCG assay after a further 48 hours. The absence of a normal increase will imply the presence of an ectopic pregnancy or miscarriage. A diagnostic algorithm should be established based on the local data available.<sup>10</sup> An example of algorithm can be found in a review written by Fylstra.<sup>11</sup>

For patients in whom the diagnosis remains uncertain, diagnostic laparoscopy should be carried out. If ectopic pregnancy is confirmed, surgical treatment can be performed laparoscopically. The role of laparoscopy is probably more important in patients at risk of heterotopic pregnancy because of the limitations of HCG assay.

Other tests like serum progesterone, and dilatation and curettage have been proposed useful in the diagnosis of ectopic pregnancy. The utility of such tests however, depends on the experience and availability in local centres.

## TREATMENT

Ectopic pregnancy may resolve spontaneously in a limited group of patients (<50%). The risk of rupture however, remains until complete resolution of the pregnancy. The wait-and-see approach should thus not be adopted routinely although it may be appropriate in some circumstances.<sup>12</sup> If the initial HCG level is very low (< 1000 iu/L) expectant management is probably appropriate.

## Surgery

Surgery remains the mainstay of treatment for tubal ectopic pregnancy. For patients in shock, immediate laparotomy with salpingectomy following initial resuscitation is the treatment of choice. In haemodynamically stable patients,

laparoscopic surgery is the gold standard of treatment. It has been shown by randomised trials to be associated with less blood loss, a reduced need for analgesia, a shorter duration of operation time, shorter hospital stay, shorter convalescence time and is also less costly. In a recent audit exercise of the Hospital Authority of Hong Kong, 62.2% of patients suffering from ectopic pregnancy were treated laparoscopically.<sup>13</sup> However, among the nine hospitals that participated in the audit, the proportion of patients with ectopic pregnancy treated laparoscopically varied widely, from 16.7 to 87.9%. Although this may be related to patient characteristics, a more likely explanation is the availability of trained staff in different hospitals. Only 12.8% of the patients were haemodynamically unstable, and thus considered unsuitable for laparoscopic intervention. Moreover, the operating time was reported to be longer in the laparoscopic group (1.2 hours versus 1.01 hours) – this suggests that the majority of procedures were performed by surgeons relatively inexperienced in laparoscopic techniques.

In the past decade, there has been a swing away from conservative surgery back to radical surgery. According to guidelines issued by the Royal College of Obstetricians and Gynaecologists (UK)<sup>14</sup>, salpingectomy is preferred to salpingotomy when the contralateral tube

is healthy. It has been shown that the incidence of intrauterine and extrauterine pregnancy remains the same even when the involved tube is conserved. However, conservative surgery runs the risk of persistent ectopic pregnancy and surprisingly, the risk of persistent ectopic pregnancy was consistently higher with the laparoscopic approach. The reason for this increase is uncertain but may be related to spillage of trophoblastic tissue during retrieval of the specimen.<sup>15</sup>

#### Medical Treatment

Medical treatment has also been reported, most commonly with methotrexate. The medication can be given either locally or systemically, as a single dose or in repeated doses. In general, local treatment and a single systemic dose are less successful. In selected patients, systemic treatment using multiple doses has been shown to be as efficacious as surgical treatment.<sup>16</sup> Patients need to be monitored with serum HCG levels until complete resolution of the pregnancy. Side effects of the treatment, and its applicability to only a limited number of patients plus the need for prolonged serum HCG monitoring preclude it from being the first-line treatment.<sup>14</sup> It is best indicated for early, small ectopics with low HCG levels. Absolute contraindications to medical therapy include breast feeding, overt or laboratory evidence of immunodeficiency, alco-

holism, alcoholic liver disease, other chronic liver disease, pre-existing blood dyscrasias, known sensitivity to methotrexate, active pulmonary disease, peptic ulcer disease, other hepatic or renal or haematological dysfunction. Relative contraindications include a gestational sac  $\geq 3.5$  cm and embryonic cardiac motion.<sup>17</sup>

#### FUTURE PROGNOSIS AND CONTRACEPTION

The risk of subsequent ectopic pregnancy is increased by 10 to 30% following the first episode. This variation is probably due to the different characteristics of individual patients. Nevertheless patients should be informed of the risk so that early diagnosis or exclusion can be facilitated in future pregnancies.

It is now well established that most intrauterine contraceptive devices (IUCD) do not increase the risk of ectopic pregnancy. This is true for all devices including the levonorgestrel releasing device. Progestasert is probably the only exception. However, the proportion of ectopic pregnancy in relation to intrauterine pregnancy, when patients do conceive, is increased. This is due to the effectiveness of IUCDs in preventing intrauterine pregnancy. The absolute incidence of ectopic pregnancy is actually reduced. The same explanation holds for the use

of progestogen only pills.<sup>18</sup> Thus, ectopic pregnancy does not constitute a contraindication to the use of either method *per se*.

## CONCLUSION

Ectopic pregnancy remains an important clinical condition. Early diagnosis is vital to reduce morbidity and mortality, and to facilitate treatment with minimal access surgery. Awareness of the risk factors, use of a sensitive pregnancy test, transvaginal ultrasound and human chorionic gonadotrophin assays all contribute to earlier diagnosis. Surgical treatment remains the mainstay of treatment, with laparoscopic salpingectomy the gold standard. The patient should be informed of the increased risk of ectopic pregnancy in future pregnancies.

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## • PAEDIATRICS •

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