## RISK FACTORS FOR ECTOPIC PREGNANCY

Apologies for my absence – am on APLS. Got this from Up To Date. Ladies, please note. Vaginal douching – bad!

RISK FACTORS FOR ECTOPIC PREGNANCY — Risk factors for ectopic pregnancy can be divided into those that confer high, moderate, or low risk (show table 1) [8,9]. However, the characteristics that place a woman at risk for ectopic pregnancy are not completely independent of one another.

## High risk factors

**Tubal pathology** — The major cause of ectopic pregnancy is disruption of normal tubal anatomy from factors such as infection, surgery, congenital anomalies, or tumors. Anatomic distortion can be accompanied by functional impairment due to damaged ciliary activity.

Previous ectopic pregnancy — Women who have had conservative treatment for ectopic pregnancy are at higher risk (15 percent overall) for recurrence. This risk is related to both the underlying tubal disorder that led to the initial ectopic pregnancy and to the choice of treatment procedure. As an example, a study of surgical and medical therapy of ectopic pregnancy reported the rates of recurrent ectopic pregnancy after single dose methotrexate, salpingectomy, and linear salpingostomy were 8, 9.8, and 15.4 percent, respectively, among patients who attempted to conceive [1].

**Tubal surgery** — The association between tubal reconstructive surgery and subsequent ectopic pregnancy depends upon the condition of the tube, the type of surgery, and the surgeon's expertise. The tubal surgery itself is not the main cause of ectopic pregnancy; rather, the underlying tubal damage resulting from prior pelvic inflammatory disease or a prior ectopic pregnancy is the major culprit. Although tubal surgery is a high risk factor for ectopic pregnancy, most women with tubal damage would not conceive with either an intrauterine or ectopic pregnancy in the absence of tubal reconstructive surgery.

**In-utero diethylstilbestrol (DES) exposure** — Women with a history of in-utero DES exposure have a ninefold-increased risk of ectopic pregnancy due to abnormal tubal morphology and, possibly, impaired fimbrial function [10]. (See "Outcome of diethylstilbestrol exposed individuals").

Tubal sterilization — The estimated failure rate during the first year after tubal sterilization ranges from 0.1 to 0.8 percent; approximately one-third of these pregnancies are ectopic (show table 2). The risk of sterilization failure was illustrated by a longterm, multicenter, prospective cohort study that followed 10,685 women after tubal sterilization [11]. These women had 47 ectopic pregnancies with a 10 year cumulative rate of 7.3 per 1000 procedures. The major additional findings from this analysis were:

- The risk of ectopic pregnancy was higher in women sterilized before the age of 30
- Bipolar coagulation was more likely to result in ectopic pregnancy than postpartum partial salpingectomy (31.9 versus 1.2 ectopic pregnancies per 1000 procedures)
- The annual rate of ectopic pregnancy for all methods combined was similar in the first three years and in the fourth through tenth years after sterilization

The high risk of ectopic pregnancy after bipolar coagulation may be due to formation of a tuboperitoneal fistula at the coagulated segment of the tube that allows spermatozoa to escape and reach the oocyte.

Intrauterine contraceptive devices — Most contraceptive methods lower the overall risk of ectopic pregnancy, as well as intrauterine pregnancy, by preventing ovulation or

conception [12]. However, women with an IUD who become pregnant are at high risk that the pregnancy is ectopic (show table 2).

The absolute risk of ectopic pregnancy varies by the method of contraception. The lowest rates are observed with the copper-containing intrauterine contraceptive device (IUCD) and the levonorgestrel-releasing IUCD; their ectopic pregnancy rates are one-tenth of those in women not using contraception [13,14]. By comparison, the progesterone-containing IUCD is associated with a higher absolute rate of ectopic pregnancy than that seen in women not using any contraception, perhaps because its action is limited to a local effect on the endometrium [13]. (See "The intrauterine contraceptive device" section on Ectopic pregnancy).

## Moderate risk factors

Previous genital infections — Pelvic infection (eg, nonspecific salpingitis, chlamydia, gonorrhea), especially recurrent infection, is a major cause of tubal pathology and, therefore, the increasing incidence of ectopic pregnancy [8]. As an example, a retrospective cohort study evaluated the risk of hospitalization for ectopic pregnancy in 11,000 Wisconsin women who had one or more chlamydial infections between 1985 and 1992 [15]. The odds ratios for ectopic pregnancy after two and after three or more episodes of chlamydial infection were 2.1 and 4.5, respectively [15]. (See "Pathogenesis of and risk factors for pelvic inflammatory disease in adults").

Infertility — The incidence of ectopic pregnancy is higher in the infertility population, although this could reflect the increased incidence of tubal abnormality in this group of women. Several reports have also suggested an association between fertility drugs and ectopic pregnancy, which may be related to altered tubal function secondary to hormonal fluctuation. As an example, one large multicenter study found that women taking clomiphene citrate doubled their risk of ectopic pregnancy from 3 to 6 percent [16]. The incidence of ectopic pregnancy after treatment with gonadotropin appears to be slightly higher as well [17,18].

Multiple sexual partners — A lifetime number of sexual partners exceeding one is associated with a moderate risk of ectopic pregnancy. This is related to the increased risk of pelvic inflammatory disease in woman with a history of multiple sexual partners. (See "Pathogenesis of and risk factors for pelvic inflammatory disease in adults").

## Low risk factors

In vitro fertilization — In vitro fertilization (IVF) has been associated with an increased risk of both ectopic and heterotopic pregnancy (see "Heterotopic pregnancy" below) [19,20]. However, US registry data from 2002 showed an overall rate of ectopic pregnancy of 2.1 percent [21]. This rate is comparable to the ectopic pregnancy rate of 19 per 1000 pregnancies reported for the United States [2].

Cervical and interstitial pregnancies are other forms of ectopic pregnancy that are encountered more often following IVF (see "Cervical pregnancy" below, and see "Interstitial pregnancy" below). (See "In vitro fertilization").

Smoking — Cigarette smoking in the periconceptional period increases the risk of ectopic pregnancy in a dose-dependent manner [9,22]. This may be the result of impaired immunity in smokers, thus predisposing them to pelvic inflammatory disease, or to impairment in tubal motility.

 $Vaginal\ douching$  — Regular vaginal douching is associated with an increased risk of both pelvic inflammatory disease and ectopic pregnancy [23].

Age - A young age (ie, less than age 18) at the first sexual encounter slightly increases the risk of ectopic pregnancy [24]. However, there is also an increasing

proportion of ectopic pregnancies among women in the older age groups [25,26]. A Norwegian study reported the overall rate of ectopic pregnancy in the population was 1.8 percent; however, women over the age of 35 years had a rate of 4.1 percent, which was eight times higher than that seen in younger age groups [26]. This high incidence in older women may be a reflection of cumulative risk factors over time.

Oral contraceptives — Women taking oral contraceptive pills are at very low risk of conceiving either an intrauterine or ectopic pregnancy. The number of ectopic pregnancies as a proportion of all pregnancies occurring in contraceptive users is shown in Table 2 (show table 2).