

Protocol for Pregnancy of Unknown Location (PUL)

For patients who have had an ultrasound without visualization of an intrauterine pregnancy (IUP) and who have an indeterminate last menstrual period (LMP), the following PUL protocol will be followed:

Assess pregnancy desire at the time of unknown location diagnosis. If the pregnancy is desired or uncertain, practice careful conservative management. If the pregnancy is undesired, practice expedient active management.*

A serum BhCG will be obtained urgently.

If the first BhCG is below the discriminatory zone** of 3500 mIU/mL, a second BhCG will be obtained in 48 hours.

If the first BhCG is above 3500 mIU/mL and nothing is seen on ultrasound, this is highly suspicious of ectopic pregnancy. If there are qualifying circumstances (e.g., uterine fibroids, cesarean section scars) and radiology is suspicious that the pregnancy was just difficult to see, a second BhCG may be obtained in 48 hours. If no qualifying circumstances exist for not visualizing the pregnancy, and the patient is hemodynamically stable and asymptomatic, the patient should be referred for treatment with methotrexate. Any signs of instability, free fluid in the cul-de-sac, a visible ectopic with fetal cardiac activity on ultrasound or adnexal tenderness on bimanual exam warrant urgent referral.

If the first BhCG was above 10,000 mIU/mL the patient will be urgently referred to the emergency room for surgical management.

The following minimum rates of increase of BhCG are expected over 48 hours:***

- 49% for an initial BhCG level of less than 1,500 mIU/mL
- 40% for an initial BhCG level of 1,500–3,000 mIU/mL

* Flynn AN, Schreiber CA, Roe A, Shorter JM, Frarey A, Barnhart K, Sonalkar S. Prioritizing desiredness in pregnancy of unknown location: An algorithm for patient-centered care. *Obstet Gynecol* 2020;136:1001-5. DOI: 10.1097/AOG.0000000000004124.

** The discriminatory zone is the BhCG level at which an intrauterine pregnancy (IUP) should be visible on ultrasound. This may vary by institution and by the quality of the ultrasound machine, however with a cutoff of 3500 mIU/mL, 99% of IUPs should be visible.

*** Barnhart KT, Guo W, Cary MS, et al. Differences in Serum Human Chorionic Gonadotropin Rise in Early Pregnancy by Race and Value at Presentation. *Obstet Gynecol*. 2016;128(3):504-511. doi:10.1097/AOG.0000000000001568

- 33% for an initial BhCG level of greater than 3000 mIU/ml

A patient with an adequate rise in BhCG will be counseled on their pregnancy options. Those with an inadequate rise will be referred to the hospital for treatment as described above. In all cases of being sent to the hospital, the records will be sent with the patient.