

# Diagnosis of Pregnancy

## Background

1. About 6 million pregnancies diagnosed in US each year
2. Between 4 and 4.3 million live births in US each year from 2000-2007<sup>1</sup>
3. Fertility rate in 2006 of women aged 15 to 44 years
  - 68.6 live births per 1000 women<sup>1</sup>
4. Mean duration of pregnancy is 280 days or 40 weeks<sup>2</sup>
5. Accurate early dx of pregnancy can help:
  - Manage pregnancy complications
  - Improve pregnancy outcomes
  - Affect delivery decisions
6. Early diagnosis important
  - In 2005 there were 25,894 fetal deaths of 20 weeks' gestation or more as well as 28,384 infant deaths<sup>3</sup>
7. Screening tests in pregnancy are dependent upon accurate expected date of delivery (EDD)
  - Elevated human chorionic gonadotropin (HCG) in maternal serum or urine is the earliest and most reliable evidence of pregnancy<sup>2</sup>
  - Estimate EDD by subtracting 3 months and adding 7 days to date of first day of last normal menstrual period (Naegele's rule)<sup>2</sup>
8. Gestational age
  - Estimates pregnancy duration from first day of LMP at 3 weeks before implantation<sup>2</sup>

## Diagnostics

1. History
  - Amenorrhea
  - Irregular menses (if regular prior)
  - Sexual activity (regardless of use of contraception)
  - Patient suspicion of pregnancy
2. Common symptoms of pregnancy
  - Amenorrhea
  - Nausea/vomiting
  - Breast tenderness
  - Urinary frequency
  - Fatigue
3. Physical findings in early pregnancy
  - Pregnancy more likely if these signs are present
  - Their absence does not rule out pregnancy
    - Uterus becomes enlarged and globular
    - **Chadwick sign**
      1. Bluish-violet discoloration of mucous membranes of vulva, vagina, cervix due to congestion

- Breasts fuller, tender, areola darken
- **Hegar sign and Goodell sign**
  1. Softening of uterus (Hegar) and cervix (Goodell) on bimanual exam.
- Cervical mucus changes (becomes thicker due to progesterone effect)
- Uterine artery pulsation may be palpated through lateral vaginal fornices on bimanual examination
- Auscultation of fetal heart tones is diagnostic of pregnancy
  1. Usually not before 10 weeks gestation

## Diagnostic Testing

### 1. Urine hCG and Home pregnancy tests (HPT)

- Detect hCG in urine
- Popular for home and office use due to ease and quick result
- Many brands report >99% “sensitive” for early detection, though this may be misleading<sup>4,5,6</sup>
- Sensitivity varies
  - Brand of kit
  - User technique
  - Timing of test relative to missed menses
    1. Ranges from 79% at time of missed menses to 97% 1 week after missed menses<sup>4,5,6</sup>
- Specificity
  - Excellent, very low false positive rate
- Inaccurate test results
  - False negative:
    1. Operator error (read test too early)
    2. Dilute urine
    3. Extremely high hCG levels (can saturate detection antibodies so that a negative result occurs-Hook effect)
    4. hCG variability after 5 weeks gestation
      1. Increased levels of hCG $\beta$ cf, hCG $\beta$ n, and hCGn exist which can prevent a positive result (very rare)<sup>7</sup>.
  - False positive:
    - Germ cell tumors
    - Peri- and post-menopausal women (pituitary source)
    - If test is read beyond the “read time,” this could allow enough time for antigen-antibody binding to induce a faintly positive result<sup>7</sup>.

### 2. Serum hCG concentration

- Used to verify pregnancy
- Qualitative or quantitative
  - Qualitative serum hCG generally considered positive at level >5 mIU/ml

- Quantitative testing is used to assess doubling time
    - Produced by placental trophoblasts
    - Can be detected in serum as early as 7 to 9 days after LH surge
  - In normal pregnancy, hCG concentration doubles every 29 to 53 hours during the first 30 days after implantation
  - Serum hCG levels are 50–100 mIU/mL at the time of the first missed menstrual period
    - Peak levels are reached 60–80 days after last menstrual period (30,000–100,000 mIU/mL)
    - Levels then decrease to a constant of 5,000–10,000 mIU/mL at about 120 days and persist until delivery<sup>2</sup>.
  - If hCG fails to increase appropriately in 2 days
    - Ultrasound to look for nonviable and ectopic pregnancy<sup>2,8,9,10</sup>
  - Abnormally elevated hCG:
    - Multiple gestation
    - Gestational trophoblastic neoplasia<sup>2</sup>
  - Clearance of hCG
    - Can take anywhere from 9 to 35 days after miscarriage or delivery of fetus to completely clear from serum
    - Median of 19 days to achieve a non-detectable serum level.
- 3. Transvaginal ultrasound commonly used to verify pregnancy
  - Helpful in determining viability and location of pregnancy
  - Gestational sac on transvaginal ultrasound examination is usually visible at 4.5-5 weeks gestation
    - Corresponds to serum hCG of 1000-1500 mIU/mL
  - Yolk sac is first anatomic structure to appear within gestational sac
    - Begins at 5th week of gestation
    - Confirms intrauterine pregnancy
  - Fetal pole with cardiac activity first detected at 5.5-6 weeks EGA
- 4. Fetal heart tones
  - Can be heard first with Doppler at 10-12 weeks EGA
  - May be auscultated by fetoscope at 18-20 weeks
- 5. Uterine size
  - May be used to detect pregnancy and estimate gestation age by bimanual exam<sup>2</sup>
  - 6-12 weeks EGA
    - Uterus enlarges from small pear size to large grapefruit size
  - 12 weeks EGA
    - Fundus of the uterus palpated immediately above symphysis pubis
  - 16 weeks EGA
    - Fundus half way between symphysis pubis and umbilicus
  - 20 weeks EGA
    - Fundus at level of umbilicus
  - Height of the fundus in centimeters beginning at 20 weeks EGA corresponds to weeks of gestation

- Measurement, in centimeters, is taken from top of symphysis pubis to the top of fundus and corresponds to weeks of gestational age +/- 2 weeks

### Differential Diagnosis

1. Signs and symptoms of pregnancy, positive pregnancy test, no intrauterine pregnancy
  - Ectopic pregnancy must be ruled out
    - Patient may have vaginal bleeding and/or abdominal pain/cramping<sup>9</sup>
    - Leading cause of first trimester maternal death<sup>11</sup>
2. Gestational trophoblastic disease
3. Ovarian tumors
  - Ruled out by serial quantitative hCG
    - Tumors do not induce hCG doubling like a normal pregnancy does
  - And/or ultrasound exam
4. Menopause
  - Rare cause of positive pregnancy test due to mildly elevated hCG from pituitary sources.<sup>12</sup>
5. Uterine myoma
  - May be confused with gravid uterus
  - Often firm and irregular
6. Signs and symptoms of pregnancy, negative pregnancy test
  - Non-pregnant, non-neoplastic causes of  $\beta$ -hCG elevation can result from:
    - Hepatic cirrhosis
    - Duodenal ulcer
    - Inflammatory bowel disease<sup>2</sup>

### Therapeutics

1. Accurate EDD is critical for appropriate prenatal care
2. Early ultrasound (before 24 weeks)
  - If irregular periods or last menstrual period (LMP) date is unknown or unsure
  - May help establish EDD and confirm viability of pregnancy
3. Folic acid
  - Administer as early as possible
    - Even for non-pregnant females interested in getting pregnant
  - Dose at least 0.4-0.8 mg daily, for most patients<sup>13</sup>
    - 0.8mg for anemia
  - 4 mg/day recommended for high risk patients
    - Prior neural tube defects<sup>14</sup>
4. Prenatal care

- Early prenatal care has not been verified by rigorous research to consistently result in improved fetal outcomes<sup>15</sup>
  - Early care is felt to promote improved reproductive health outcomes
    - Improved maternal health during current pregnancy as well as subsequent pregnancies<sup>16</sup>
  - Initial laboratory and physical examination by prenatal provider
  - Rh status if bleeding occurs to evaluate need for Rh Immune globulin (Rhogam)
5. Long-term care
- During pregnancy monthly to weekly visits to patient's prenatal provider
  - Administered care is determined by risk and complications during prenatal course

## Follow-Up

1. Return to office
  - Follow-up determined by prenatal care provider
2. Recommendations for early follow-up
  - Return for persistent pain, fever, and/or vaginal bleeding early in pregnancy
3. Referral for complicated prenatal course
  - Referral for surgical treatment, genetic evaluation or management of co-morbid conditions may be necessary
4. Admit to hospital
  - Immediate hospital admission may be necessary for first trimester bleeding
  - Complications later in pregnancy are managed by prenatal provider and often require hospitalization

## Prognosis

1. Prognosis for pregnancy is excellent
  - Risk of death from complications of pregnancy for the 8-year period from 1998-2005 was 14.5 per 100,000 live births (increased from 7.1 in 1998)<sup>17</sup>
  - Healthy People 2020
    - Objective is to achieve a maternal mortality of no more than 11.4 maternal deaths per 100,000 live births<sup>18</sup>

## References

1. National Center for Health Statistics. Fast Stats: Births and Natality. <http://www.cdc.gov/nchs/fastats/births.htm>. Accessed March 10, 2011.
2. Cunningham, F.G. et al. (Eds). Williams Obstetrics, McGraw-Hill, 2010.
3. Berg, CJ et al. Pregnancy-related mortality in the United States, 1998 to 2005. *Obstet Gynecol.* 2010;116(6):1302-09

4. Cole LA, et al. Accuracy of home pregnancy tests at the time of missed menses. *Am J Obstet Gynecol.* 2004; 190(1):100-5.
5. Cole LA, et al. Sensitivity of over-the-counter pregnancy tests: comparison of utility and marketing messages. *J Am Pharm Assoc (2003).* 2005; 45(5):608-15.
6. Wilcox AJ, et al. Natural limits of pregnancy testing in relation to the expected menstrual period. *JAMA.* 2001;286(14):1759-61
7. Cervinski MA and Gronowski, AM. Reproductive-endocrine point-of-care testing: current status and limitations. *Clin Chem Lab Med.* 2010;48(7):935-942.
8. Check, J.H. et al. Slow rising serial gonadotropins predict poor pregnancy outcome despite sonographic viability. *Clinical and Experimental Obstetrics and Gynecology.* 2003; 30(4):193-194.
9. Seeber, BE and Barnhart, KT. Suspected ectopic pregnancy. *Obstetrics and Gynecology.* 2006; 107(2 Pt 1):399-413.
10. Silva, C. et al. Human chorionic gonadotropin profile for women with ectopic pregnancy. *Obstetrics and Gynecology.* 2006; 107:605.
11. Berg, CJ et al. Preventability of pregnancy-related deaths: results of a state-wide review. *Obstetrics and Gynecology.* 2005;106(6):1228-34
12. Cole LA, Khanlian SA, Muller CY. Normal production of human chorionic gonadotropin in perimenopausal and menopausal women and after oophorectomy [Int J Gynecol Cancer.](#) 2009 Dec;19(9):1556-9
13. U.S. Preventive Services Task Force. Folic Acid for the Prevention of Neural Tube Defects. <http://www.uspreventiveservicestaskforce.org/uspstf/uspsnrfol.htm>. Accessed March 10, 2011.
14. American College of Obstetricians and Gynecologists. ACOG Committee Opinion number 313, September 2005. The importance of preconception care in the continuum of women's health care. *Obstet Gynecol* 2005; 106:665
15. The Cochrane Library. Does prenatal care improve birth outcomes: a critical review. *Database of Abstracts of Reviews of Effects* 2006; issue 4.
16. Recommendations To Improve Preconception Health and Health Care – United States. A Report of the CDC/ATSDR Preconception Care Work Group and the Select Panel on Preconception Care. *MMWR* 2006: 55 (RR-6).
17. Maternal Mortality and Related Concepts. National Center for Health Statistics. *Vital Health Stat* 2007;3(33).
18. Healthy People 2020. Maternal, Infant, and Child Objectives: Reduce the rate of maternal mortality. <http://www.healthypeople.gov/2020/objectiveslist.aspx?topicid=26>. Accessed March 10, 2011.

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