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\(^1\)
3. Fertility rate in 2006 of women aged 15 to 44 years
   - 68.6 live births per 1000 women\(^1\)
4. Mean duration of pregnancy is 280 days or 40 weeks\(^2\)
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\(^3\)
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\(^2\)
   - Estimate EDD by subtracting 3 months and adding 7 days to date of first day of last normal menstrual period (Naegele's rule)\(^2\)
8. Gestational age
   - Estimates pregnancy duration from first day of LMP at 3 weeks before implantation\(^2\)

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\(^4\),\(^5\),\(^6\)
   - 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\(^4\),\(^5\),\(^6\)
   - 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 hCGβcf, hCGβn, and hCGn exist which can prevent a positive result (very rare)\(^7\).
     - 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\(^7\).

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.
  - If hCG fails to increase appropriately in 2 days
    - Ultrasound to look for nonviable and ectopic pregnancy
  - Abnormally elevated hCG:
    - Multiple gestation
    - Gestational trophoblastic neoplasia
  - 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
   - 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
     - Leading cause of first trimester maternal death
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.
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 β-hCG elevation can result from:
     - Hepatic cirrhosis
     - Duodenal ulcer
     - Inflammatory bowel disease

**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
     - 0.8mg for anemia
   - 4 mg/day recommended for high risk patients
     - Prior neural tube defects
4. Prenatal care
Early prenatal care has not been verified by rigorous research to consistently result in improved fetal outcomes. Early care is felt to promote improved reproductive health outcomes, including improved maternal health during current pregnancy as well as subsequent pregnancies. 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)
   - Healthy People 2020
     - Objective is to achieve a maternal mortality of no more than 11.4 maternal deaths per 100,000 live births

References


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