

# MEDICAL PRACTICE

## Gynaecology in General Practice

### Pregnancy Diagnosis

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The diagnosis of early pregnancy can usually be established with reasonable certainty by careful history and examination even as early as two weeks after the first missed period, and there are few cases where doubt remains after eight to ten weeks amenorrhoea. Diagnosis rarely presents any difficulty after the twelfth week of gestation, unless the dates are incorrect, the patient is unduly obese or difficult to examine, or the pregnancy is not developing normally. Pregnancy may supervene during an episode of physiological or hormonal amenorrhoea, such as after delivery or in women who have recently stopped taking oral contraceptives. In these circumstances the appearance of other symptoms and signs of pregnancy are delayed in relation to the period of amenorrhoea.

#### Early Symptoms

The early symptoms of pregnancy—including early morning nausea or sickness, frequency of micturition, constipation, and breast tenderness—are often equivocal, but certain of the clinical signs are particularly helpful to confirm or refute the diagnosis. Dilatation of the superficial veins in the breasts is usually the earliest readily detected sign and is often evident by the sixth to eighth week. Epithelial congestion results in a blueish-violet appearance of the vagina and cervix and cervical softening (especially in primigravidae). The uterus becomes softened, and enlargement—which initially may be asymmetric—is progressive. Pulsation in the lateral fornices due to dilatation and tortuosity of the uterine arteries is usually easily detected and is a reliable sign; eliciting it requires no undue pressure or manipulation.

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#### Biological and Immunological Tests

Chorionic gonadotrophin is produced by trophoblastic tissue. In pregnancy raised serum levels are associated with increased urinary excretion. The excretion of human chorionic gonadotrophin (HCG) is significantly raised within one week of the first missed period, reaches a peak by the tenth week, and falls thereafter to the twentieth week (Fig. 1). In the second half of pregnancy levels fluctuate but remain raised until after delivery. Biological and immunological tests depend on the detection of increased quantities of chorionic gonadotrophins, and reliable positive results may be expected within four weeks of conception.

Positive results are also obtained if there are high levels of luteinizing hormone in the urine. This is particularly likely to

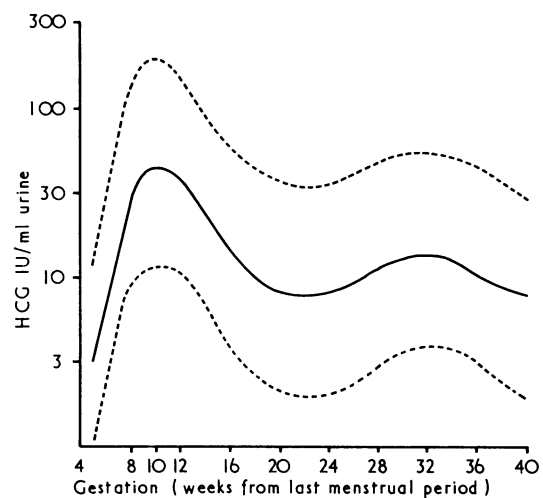


FIG. 1—Urinary excretion of human chorionic gonadotrophin in normal pregnancy based on a haemagglutination inhibition technique. The solid line indicates mean values and interrupted lines  $\pm 1$  standard deviation (From data of McGregor *et al.*<sup>3</sup>)

occur in perimenopausal women, and in such cases positive results should be interpreted with caution. It is usually recommended that urine from women of this age should be diluted with an equal amount of water before testing.

#### IMMUNOLOGICAL TESTS

It is now no longer necessary to have access to animals to perform biological pregnancy tests, since in recent years immunological tests have been introduced and have reached a high degree of reliability. The latter require no special skill or equipment and results are obtained quickly. They are ideal for use in the doctor's surgery and the time taken up need be hardly more than that involved in referring a patient to a hospital laboratory. Furthermore, since the result can be available immediately an additional consultation may be avoided. Reliable results have been reported when tests were undertaken by paramedical personnel in a group practice.<sup>1</sup>

When correctly performed errors occur in only about 2% of normal pregnancies. Reliable results, however, are dependent on following the manufacturers' instructions implicitly. Some of the tests are more susceptible than others to errors in technique and certain pitfalls are worth special comment. The urine specimen may be unsuitable for testing because of the presence of turbidity, debris, infection, or of protein or blood, which influence some of the tests (see Table). The presence of traces of detergent, either in the urine container or equipment, is a common cause of error. The test reagents may be at fault because of improper storage, or pipettes may be contaminated. The test may also be affected by failure to observe instructions concerning the measurement of reagent, because of excessive mixing or agitation, or by not reading the test at the correct time. It is advisable to set up positive and negative controls with each batch of tests.

Immunological tests depend on an HCG antibody-antigen reaction. They involve the use of an HCG antiserum and either latex particles or red blood cells coated with HCG (Fig. 2).

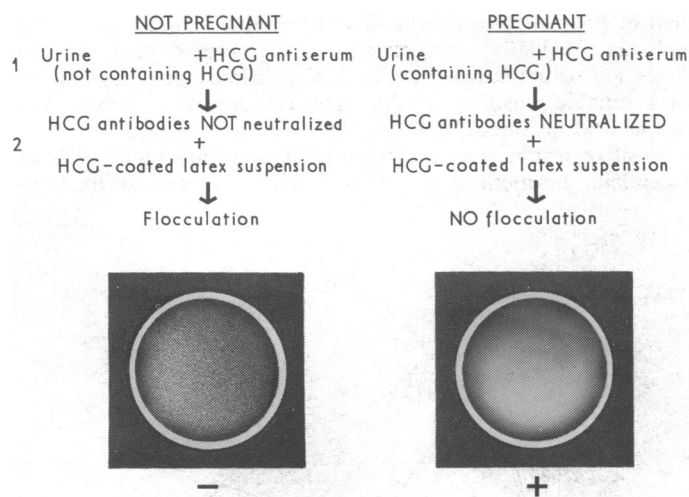


FIG. 2—The principle of latex-flocculation ("slide") tests for pregnancy.

#### Latex-flocculation Inhibition Tests

Latex-flocculation inhibition tests are the most suitable for use in general practice (see Table). The tests are performed in two stages: firstly, urine is added to an HCG antiserum. If the urine contains no HCG the antibody is unaffected. If it contains HCG the antibody is neutralized. Secondly, the subsequent addition of polystyrene latex particles coated with HCG results in flocculation only if unneutralized antibody is

#### Commercially Available slide Tests for Pregnancy

Test	Positive Result	Sensitivity (i.u. HCG/ml)	Influenced by Protein or Blood in Specimen	Storage	
				Temperature	Use
Pregnosticon Planotest (Organon)	No flocculation after two minutes (From 12 days after missed period)†	2.5	—	+4°C	Up to two years Can be used direct from refrigerator
Gravindex (Ortho)	No flocculation after two minutes (From 13 days after missed period)†	3.5	+(if protein 100mg/ or per 100ml or more)	+4°C	Up to one year Warm before use
Preporex (Wellcome)	No flocculation after two minutes (From 14 days from missed period)†	3-5	+	+4°C	Up to two years Warm before use
DAP (Warner)	Flocculation after two minutes (From 4 days after missed period)†	2	—	+4°C	

†Manufacturers' statements

available. Thus a *negative* pregnancy test is indicated by *flocculation* and a *positive* test by *failure to flocculate*. The DAP test differs in that the latex particles are coated with antibody and flocculate when urine containing HCG is added.

The latex tests are all performed on slides and results are obtained in two minutes. Sensitivity varies and this influences both how soon after conception the test is likely to become positive and the incidence of false-positive or false-negative results. In some of the earlier tests there was difficulty in reading the end point, but this has now largely been overcome. Latex tests are not generally suitable for quantitative assays, though some manufacturers describe semiquantitative techniques.

#### Haemagglutination Inhibition Tests

In haemagglutination inhibition tests (Pregnosticon, Pregnosticon-all In, Prepuerin, U.C.G.) red blood cells rather than latex particles are coated with HCG. The test procedure is similar to the latex-flocculation test, the end point being agglutination of the red cells. The reaction is complete only after two to ten hours, depending on the test, though negative results are often evident before the recommended period has elapsed.

This type of test is performed in a test tube and is more time consuming, though an "all-in" test carried out by adding urine and distilled water to an ampoule containing dried reagents has recently become available. The sensitivity of haemagglutination tests is generally greater than that of latex tests and semiquantitative results using serial dilutions are more readily obtained.

#### Hormonal "Tablet" Tests

Administration of relatively large doses of a combined oestrogen/progestogen preparation for a short period may induce withdrawal bleeding. While in most cases failure to bleed is associated with pregnancy, tests of this type are unreliable. If a pregnancy test is indicated because the diagnosis remains in

doubt after competent clinical assessment the more reliable immunological method is preferable. The possibilities of an abortifacient effect and of a fetal teratogenic risk resulting from administration of these potent hormone preparations in early pregnancy have been raised, but in women no firm evidence of such effects is available.

### Radiology

Calcification of the fetal bones starts as early as eight to ten weeks gestation, but it is rarely detected in utero by radiological examination before 14 to 16 weeks. Even then special care is necessary to achieve satisfactory results.

Because of the potential hazards of x-rays to the fetus, radiology as an aid to pregnancy diagnosis is rarely indicated. It is occasionally of value in the middle trimester, when clinical signs are difficult to elicit because of obesity or the presence of tumours, and particularly after 20 weeks gestation, when immunological pregnancy tests occasionally give false-negative results. Radiology may also be of value if some pathological condition of pregnancy such as hydatidiform mole is suspected.

### Ultrasound

Detection of fetal heart sounds with instruments dependent on the Doppler effect (Doptone, Sonicaid) is possible by 12 to 14 weeks gestation. The necessary equipment is now available in many antenatal clinics and should be accessible to those practitioners who work in collaboration with maternity units. This application of ultrasonics should not be confused with sonar scans. The latter enable delineation of fetal parts in the early weeks of pregnancy, but require special facilities, which are not widely available.

### Special Diagnostic Problems

#### BLEEDING

Bleeding following an episode of amenorrhoea is one of the commonest clinical problems encountered in general practice. Symptoms of pregnancy may be equivocal or absent, and the diagnosis rests between a hormone disturbance or a pathological condition of pregnancy.

#### ABNORMALITIES OF PREGNANCY

When bleeding is due to abortion the pregnancy test remains positive as long as active trophoblastic tissue is present, even if the fetus has been expelled. Thus, initially at least, differential diagnosis between threatened, inevitable, and incomplete abortion usually rests on the clinical findings rather than the laboratory investigations.

Hydatidiform mole is usually, but not invariably, associated with a positive pregnancy test. A positive test with urine diluted 1:200 is virtually diagnostic of hydatidiform mole.

In the case of ectopic gestation the amount of trophoblastic activity is often quite small, and a negative pregnancy test does not exclude the diagnosis.

#### OTHER ABNORMALITIES

##### *Hormonal Amenorrhoea*

In most cases of hormonal amenorrhoea there are no clinical signs of pregnancy and the uterus is of normal size and firm in consistency, with the cervical canal closed. Diagnosis of the cause of amenorrhoea in women nearing the menopause may be difficult, but is especially so if examination is ham-

pered by obesity. In such patients pregnancy tests performed on undiluted urine may give false-positive results. It is often only by repeated examination that the diagnosis of pregnancy can be confidently confirmed or refuted.

##### *Metropathia*

Metropathia haemorrhagica may also cause diagnostic problems because of the association of short episodes of amenorrhoea with uterine enlargement due to myohyperplasia. But the pregnancy test is usually negative.

##### *Fibroids*

Fibroids may simulate the uterine enlargement of pregnancy but the mass is usually firm and irregular and other symptoms and signs of pregnancy are absent.

##### *Ovarian Cyst*

An ovarian cyst may be mistaken for an enlarged soft uterus. In a patient seen for the first time the presence of a large cyst may cause confusion, but the absence of fetal parts, movements, or heart sounds usually establishes the diagnosis and x-ray examination shows no fetal skeletal parts.

##### *Pseudocyesis*

Pseudocyesis may occur, particularly in women nearing the menopause or with an unfulfilled desire for pregnancy. Insistence of the patient on subjective symptoms and the presence of abdominal distension make a trap for the unwary, but the distension is due to gas and the distinction from true pregnancy is usually made very simply by percussion of the abdomen.

### Conclusion

The diagnosis of pregnancy usually rests on careful clinical history and examination. Ancillary tests should not be regarded as an alternative and can be interpreted sensibly only in association with the clinical evidence. In general practice they are indicated in certain special circumstances—for example, when much depends on a firm and early diagnosis if there is a possibility of therapeutic abortion or if social or domestic decisions, such as marriage, change of employment, or emigration, depend on the result. Occasionally medical procedures such as vaccination or radiology may have to be deferred if pregnancy is suspected. If there is genuine doubt whether the patient is pregnant, and the doubt is not likely to be resolved in a reasonable period of time—as for example, in a patient approaching the menopause or in case of extreme obesity—ancillary tests may be indicated. Similarly, some gynaecological disorder may be present and confuse the diagnosis, as in amenorrhoea or oligomenorrhoea resulting from hormonal dysfunction or administration of hormones—for example, oral contraceptives. Irregular bleeding may result in confusion between abortion and such conditions as metropathia haemorrhagica. Finally, some abnormal condition such as bleeding in early pregnancy may suggest the possibility of death of the conceptus, and therefore indicate the use of ancillary tests. In the case of persistent or irregular bleeding associated with threatened or inevitable abortion or with hydatidiform mole quantitative tests may be more helpful.

### References

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- McGregor, W. G., Cale, C. W., Simmons, E., and Knight, G. L., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1966, 73, 775.