# COMMON LABORATORY INVESTIGATIONS IN OBSTETRICS AND GYNAECOLOGY

*It is sometimes difficult to know which laboratory tests are necessary and then how to interpret them.*

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Laboratory investigations in obstetrics and gynaecology practice have much in common with those in other medical disciplines. However, there is a range of laboratory tests which are requested more frequently and one should be familiar with these 'panels'. Patients with a family history or past history of various medical conditions, or those with complications on presentation, will obviously require specific and additional laboratory tests which must be discussed with the relevant pathologist and gynaecologist.

## TESTS COMMON TO ALL DISCIPLINES

- Full blood count
- Urea and electrolytes
- Glucose
- Lipids
- Calcium
- Liver enzymes
- Vitamin $B_{12}$ and folate
- Iron profile
- Thyroid function
- HIV diagnosis and monitoring.

These 'universal' tests are often requested as screening laboratory tests in asymptomatic patients. The advantages lie in the ability to detect asymptomatic abnormalities. The choice will depend on various factors, e.g. age, risk profile, dietary history, associated diseases and current therapy.

## ROUTINE LABORATORY TESTS IN OBSTETRICS

- Pregnancy tests
- Full blood count
- Rubella
- Blood groups
- Rapid plasma reagin (for syphilis)
- Hepatitis B
- HIV
- Alpha fetoprotein and Down's screen (α-fetoprotein, β-human chorionic gonadotrophin (HCG) and unconjugated oestriol)
- Glucose tolerance test
- Midstream urine
- Papanicolaou cervical smear.

## Pregnancy tests

The biochemical diagnosis of early pregnancy is now taken for granted with the advent of the monoclonal antibody technique. There are numerous rapid home kits that detect HCG in urine or whole blood. Few practitioners are aware that only four decades ago the test was based on injecting a patient's urine into frogs and noting its effects on egg or sperm production stimulated by the presence of HCG in the sample.

The current assays have excellent sensitivities and specificities for HCG. However, it is recommended that these rapid tests have both positive and negative controls incorporated in the assay. Serum-based laboratory tests for HCG have the advantage of offering quantitative levels (usually at the same cost to the patient as a qualitative test) and the option of performing additional assays (e.g. progesterone, follicle-stimulating hormone (FSH), prolactin) that may be required on the sample.

## Haemoglobin (anaemia in pregnancy)

Apart from an altered physiological state in pregnancy characterised by an expanded plasma volume and reduced blood haemoglobin concentration manifesting as a normochromic normocytic anaemia, the mother is at greater risk of a nutritional anaemia of especially iron (microcytic anaemia) and folate (macrocytic anaemia).

Other incidental findings on routine antenatal full blood count screening could include, for example, a thalassaemia or sickle cell trait or hereditary spherocytosis. Later in pregnancy a haemolytic anaemia may be found in pre-eclamptic and eclamptic mothers as part of the HELLP syndrome (Haemolysis, Elevated Liver enzymes and Low Platelets).

## Antenatal blood group and irregular antibody screening

ABO and rhesus grouping can be readily obtained if not already known.

A pregnant rhesus-negative woman needs regular testing throughout the pregnancy either to monitor the titre of a known irregular antibody (commonly anti-D) or to detect the development of an irregular antibody.

A screen for irregular antibodies in those who are rhesus positive can also be of value in detecting obstetrically significant irregular antibodies, e.g. Kell antibodies.

## Screening for infectious diseases in pregnancy

Although not always possible, the ideal time to assess and manage potential pregnancy complications is in the preconception period. Prevention of infections during pregnancy is important for both the mother and the developing fetus.

Available vaccines that should be considered include measles, mumps, rubella, varicella and hepatitis B. Mumps in the first trimester may be associated with fetal death, while measles may lead to preterm birth and possible miscarriage. The congenital rubella syndrome (deafness, cataracts, cardiac defects and mental retardation) may occur in 20 - 85% of infants in women with rubella during the first trimester. Vaccines are best administered before conception. In addition, preconception treatment of HIV, tuberculosis, *Neisseria gonorrhoeae, Chlamydia trachomatis* and *Treponema pallidum* will help to decrease complications during pregnancy. Screening for cytomegalovirus and toxoplasmosis may also be indicated to avoid risk factors in specific settings.

## Prenatal screening

The following are considered basic antenatal tests:

### Urine culture

Asymptomatic bacteriuria — defined as the presence of more than 100 000 colony-forming units ($> 10^5$ CfU) per ml of urine in the absence of urinary symptoms — occurs in 6 - 7% of pregnant women. The significance of this finding is that acute pyelonephritis, with its associated complication of poor pregnancy outcome, occurs in 20 - 40% of pregnant

patients with untreated asymptomatic bacteriuria. It is estimated that a reduction (4 - 0.8%) in pyelonephritis in pregnancy can be achieved by a policy of routine prenatal screening with urine cultures and treatment of asymptomatic bacteriuria.

### Serological tests

- Rubella antibody titres
- Syphilis serology (RPR)
- Hepatitis B surface antigen
- HIV antibody (ELISA).

## Alpha fetoprotein and Down's screening

Down's screening is the commonest prenatal genetic test requested. Although the risk of trisomy 21 increases with increased maternal age, 80% of all affected babies are born to women under the age of 35 years. The triple test ($\alpha$-fetoprotein, $\beta$-HCG, unconjugated oestriol), ideally performed between 16 and 18 weeks' gestation (range 15 - 20 weeks), will detect up to 70% of affected pregnancies. The major disadvantage of this test is the high number of false positives, which lead to unecessary amniocenteses. The $\alpha$-fetoprotein component of the test will provide information on the risk of neural tube defects (NTDs).

Recently, screening even earlier in pregnancy (10 - 13 weeks and 6 days) has become possible with the first trimester screening programme (free $\beta$-HCG and pregnancy-associated plasma protein A). The sensitivity and specificity of the test are improved dramatically with ultrasonographic measurement of the nuchal translucency (a sonolucent space at the back of the fetus's neck in the first trimester) and the identification of the nasal bones. Measurement of the nuchal translucency is a very specific technique that was accredited by the Fetal Medical Foundation prior to its inclusion in the risk calculation programme.

## Glucose tolerance tests

Approximately 7% of all pregnancies are complicated by gestational

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diabetes mellitus (GDM) (prevalence ranging from 1% to 14%, depending on the population group and diagnostic criteria). Women with clinical characteristics of a high risk for GDM (obesity, history of GDM, glycosuria or a family history of diabetes) should be tested on presentation. If initial screening is normal, they should be retested between 24 and 28 weeks of gestation. Women of average risk should be tested at 24 - 28 weeks' gestation. A fasting glucose level of > 7.0 mmol/l or a random glucose of > 11.0 mmol/l confirmed on a subsequent day is sufficient for the diagnosis of diabetes. A glucose tolerance test is not necessary in this setting.

There are various protocols for glucose loading, which include a 50 g glucose challenge followed by a plasma glucose level 1 hour later. This can be performed on non-fasted subjects and will identify 80% of GDM patients, who are subsequently tested by a formal oral glucose tolerance test (OGTT).

The formal OGTT protocols include a 75 g or 100 g loading test with sampling intervals ending at 2 or 3 hours post challenge. The cut-off at 2 hours using either the 75 g or 100 g load is 8.6 mmol/l, which differs significantly from that in the non-pregnant patient.

## ROUTINE TESTS IN GYNAECOLOGY

Of the panel of hormonal assays, many tests are common for more than one gynaecological disorder; however, some of the assays are reserved for specific complaints.

### Irregular cycles/polycystic ovarian disease

FSH, luteinising hormone (LH), prolactin, thyroid-stimulating hormone (TSH), fasting insulin/glucose.

### Hirsutism

Testosterone, dehydroepiandrosterone sulphate (DHEAS), androstendione, cortisol, 17-OH-progesterone.

### Menopausal screen

FSH, LH, oestradiol.

### Ovulatory status

Mid-luteal progesterone, LH, oestradiol.

### TSH/T$_4$

The advent of ultrasensitive TSH assays has enabled screening of thyroid disease by a single test. Raised levels require evaluation of hypothyroidism (free T$_4$, thyroid antibodies) and suppressed levels suggest thyrotoxicosis (free T$_4$, free T$_3$, thyroid antibodies).

In patients in whom Sheehan's syndrome (pituitary disorder) is suspected, the TSH is of no value; a free T$_4$ level is a better indicator of the hypothyroidism.

### Gonadotrophins (FSH, LH)

These levels vary during the menstrual cycle and ideally should be assessed on day 3 of the cycle. The interpretation of the levels must take cognisance of the phase in the cycle. Gonadotrophins should not be measured if patients are taking the contraceptive

pill or medroxyprogesterone acetate (Provera), as levels will be suppressed. Another common case for suppressed levels is early pregnancy.

FSH levels > 20 mIU/ml are consistent with a perimenopausal state and should be assessed with the clinical history.

The LH:FSH in polycystic ovarian syndrome of greater than 2 must not be confused with the pre-ovulatory LH surge at mid-cycle. The oestradiol level on the same sample will help distinguish the conditions.

### Androgen profile

This is usually reserved for patients with hirsutism, severe acne, or virilising features. Family history, menstrual abnormalities and rate of development of signs and symptoms will dictate the extent of investigations. The current profile will assist in identifying the source of androgens (ovary or adrenal).

### Fasting insulin, glucose

Insulin resistance is associated with polycystic ovarian disease (PCOD) (also with obesity, some endocrinopathies, early diabetes), and therapy with metformin has improved menstrual and ovulatory function in most of these patients.

### Ovulatory tests: progesterone

In a 28-day cycle, the day 21 progesterone level will indicate whether ovulation occurred in that cycle. To identify ovulation biochemically during the cycle (as opposed to after the event), serial LH and oestrodiol levels should be determined.

### Prolactin

Raised prolactin levels with or without galactorrhoea may be associated with infertility and menstrual abnormalities. Galactorrhoea with normal prolactin levels indicates increased breast tissue sensitivity to the hormone, and imaging of the pituitary gland is not necessary. Causes of raised prolactin include stress, physical examination, therapy, hypothyroidism, macroprolactinaemia, and hypothalamic-

pituitary pathology. A raised level must be confirmed on repeat testing in a non-stressed state.

### Future investigations

Genetic tests for carrier status of various abnormalities are currently available (cystic fibrosis, haemoglobinopathies, Tay-Sachs, Gaucher's, haemochromatosis). As the range expands, there will be increased pressure on the practitioner for screening. Techniques are available for separation of fetal cells from maternal blood; the potential will soon arise to perform genetic testing directly on fetal cells, with minimal invasiveness.

### CONCLUSION

Laboratory tests play an important role in obstetrics and gynaecology, as in any other discipline of medicine. Their role in antenatal screening is of particular relevance because many women in poor countries are attended to by health professionals for the first time in their lives during the first pregnancy.

In the face of increasing cost-containment pressures from managed care measures, the practitioner must balance this against the benefits of the various preclinical diagnostic tests available.

For more information on laboratory tests: **www.labtestsonline.org**

### IN A NUTSHELL

Knowledge of laboratory tests is critical to clinical management.

Preconception and antenatal screening is essential.

Reproductive hormonal levels are influenced by factors such as stage of cycle, maternal age and therapy.

## SINGLE SUTURE

### PATIENTS WITH PERIPHERAL VASCULAR DISEASE UNDERESTIMATE THEIR RISK OF CARDIAC DISEASE

This interesting paper compared patients' perceptions of their risk of cardiovascular disease (CVD) and the benefits of CVD risk factor reduction between patients with peripheral arterial disease (PAD), patients with coronary artery disease (CAD) and patients with no disease. All groups reported that the risks of myocardial infarction, stroke and death were higher for a patient with CAD than for a patient with PAD.

Compared with other patients, those with PAD underestimated the high risk of cardiovascular events associated with PAD and the benefits of cholesterol-lowering therapy. This may help to explain the low rates of CVD risk factor control previously reported in patients with PAD.

It would probably help if the attending doctor explained that all vessels start with the heart, and that if the peripheral vessels are damaged, there is a good chance that those in the heart are also not too healthy.

McGrae M, et al. Arch Intern Med 2003: **163:** 2157-2162.