Prenatal tests

Your clinician (Obstetrician, General Practitioner or Midwife) will request some tests to check that all is well with your pregnancy. Some are optional and may depend on whether you can afford them or not.

The tests include the following:

Routine tests to check your health and risks to the pregnancy

- Your A, B, O and Rhesus blood group and antibodies (to see if your baby is at risk of anaemia or jaundice because your blood group differs from the baby's father's);
- Your haemoglobin level (to check if you are anaemic);
- Antibodies against Rubella (German measles), HIV, hepatitis B and syphilis (to see if your baby is at risk of sustaining an infection before birth);
- Your blood glucose level (in some cases) (to check if you have diabetes, which might be underlying or brought on by the pregnancy);
- Your blood pressure (to check if you have hypertension, which might be underlying or brought on by the pregnancy as in a condition called pre-eclampsia);
- Your urine (to check for a bladder infection, or for protein in your urine (which might also indicate pre-eclampsia or underlying kidney disease);
- A swab (in some cases) to check whether a bacterium called group B streptococcus is present in your vagina (this could cause a serious infection in the baby if born vaginally);
- A basic ultrasound scan to determine exactly how far you are pregnant, whether the baby is in the uterus (womb) and alive, whether there are twins or not, to check the amniotic fluid volume around the baby and the position of the placenta (afterbirth).

Routine tests to check whether your baby is at increased risk for physical or mental problems.

The vast majority of babies develop normally but every pregnancy carries a small risk that the fetus (unborn baby, still in the mother's womb) is not developing normally. It is important to realize that no test or combination of tests is fool-proof and that one can ever guarantee you will give birth to a baby without any abnormality.

The following risk factors indicate that the chance of carrying a fetus with an abnormality is higher than average and it is important that you inform your doctor of any of the following:

	Yes or No
I am 35 years old or more	
I have epilepsy (fits, seizures, convulsions) and take medication for it	

I have diabetes	
I take medication for a chronic condition	
I have used over-the-counter medication/herbal remedies/traditional medicine during this pregnancy	
I took medication for a chronic condition within 3 months before falling pregnant	
I did not take vitamin supplements before I fell pregnant	
I have had a previous pregnancy with an abnormal fetus	
I have lost a previous pregnancy at a late stage	
I have had more than 1 previous miscarriage	
I or my partner or one of our family members was born with an abnormality	
I or my partner or one of our family members suffer from mental impairment	
I or my partner or one of our family members had a termination (abortion) for an abnormal pregnancy	
There is a genetic (inherited, familial) condition in my or my partner's family	
I have smoked during this pregnancy	
I have used alcohol during this pregnancy	
I have used recreational drugs during this pregnancy (Marijuana, TIK, methamphetamine, heroin, cocaine etc…)	

Available tests include prenatal screening tests and prenatal diagnostic tests. These tests are optional, but may provide valuable information for the management of the pregnancy.

Screening and diagnostic tests

Screening tests are tests that can be done on everyone who wants it, but they do not give a definitive answer about whether a condition (for example Down syndrome) is present or absent. They only give an indication of the likelihood of the condition being present, expressed either in numbers (risk of 1 in xxx) or as low, intermediate, or high risk. The majority (but not all) of affected individuals would have a "high risk" result on their screening test. The proportion of individuals with the abnormality who are identified by the test is called the sensitivity or detection rate. The proportion of normal individuals that received a "high risk" result is called the false positive rate. The abnormal fetuses that had a "low risk" result are missed by the screening test and called false negative results. Ideally, a screening test needs a high sensitivity (although it is never 100%) and low false positive rate (although it is never 0%).

Diagnostic tests on the other hand give a definitive answer about whether this condition is present or absent. Diagnostic tests have some features that make them unsuitable for use on a wide scale, such as risk or cost associated with the test or limited availability. The choice of a specific diagnostic test depends on the specific condition that one wants to detect or exclude. Options for diagnostic tests include ultrasound examinations by an expert (e.g. for physical defects in the fetal body parts) or invasive procedures where a needle is passed through the mother's skin and into the womb to obtain samples (specimens) for genetic or infective testing (chorionic villus sampling to obtain a piece of placental tissue, amniocentesis to draw some of the fluid that surrounds the fetus, cordocentesis to draw blood from fetal blood vessels in the umbilical cord which is located outside the fetal body but connects the fetus to the afterbirth). All invasive tests carry a risk of miscarriage (approx. 1:200). More information regarding specific invasive tests can be provided by your obstetrician or genetic counsellor.

The following screening tests are available.

Screening tests for physical abnormalities

1. **Blood test (biochemical screening):**

   Maternal serum Alpha-Feto-Protein (MSAFP) is a blood test done between 15 and 19 weeks and helps to detect fetal spina bifida (open spine) as the level of this chemical substance is increased when the fetal spine is not closed. It does not add value if the anatomy scan will be performed by an expert but does help when done by the general obstetrician. MSAFP can detect 60% of fetuses with spina bifida with a 5% false positive rate. If the MSAFP result is abnormal, it is essential to have a detailed assessment by an expert.

2. **Ultrasound examination:**

   The detection rate for abnormalities of the fetal body parts varies. It strongly depends on the scanning conditions, the expertise of the operator and the time available for the scan. Defects in certain organs are far more difficult to detect than defects in other parts. Some defects only appear late in pregnancy and some can only be seen after birth. The detection rate is considerably lower if technical limitations result in poor image quality. This can be related to maternal overweight, early or late stage of the pregnancy, reduced or increased amount of fluid around the baby, presence of more than one baby, unfavourable fetal or placental position, presence of fibroids (benign growths of the muscle fibres of the womb) or abdominal scars etc.

   It is impossible to detect all fetal abnormalities before birth. As a general rule of thumb, only about 50% of serious abnormalities are detected by a routine anatomy scan (and 50% not). When experts perform such a scan, the detection rate is significantly higher (around 75%) as they have undergone extensive special training and therefore are more experienced than general obstetricians. An expert scan is usually far more expensive than a routine scan since experts also use more expensive equipment and spend more time on the examination. The number of experts in the country is insufficient to cover all pregnancies. It is therefore generally advisable that their services are predominantly used for pregnancies with risk factors or when the routine scan by the obstetrician raises any concern.

Screening tests for genetic diseases.

The main aim is to detect fetuses at high risk of Down syndrome as this is the most common of the genetic conditions with significant consequences. A host of different tests are available and they can also be used in a variety of combinations. In general, the more expensive the tests, the higher the detection rate AND the lower the false positive rate. This translates in a lower chance of a missed diagnosis of Down syndrome AND a lower chance of receiving a "high risk" result which raises the need for further tests, possibly even invasive diagnostic procedures.

1. **Blood tests (biochemical screening based on levels of specific chemical substances in the mother's blood):**

- Maternal blood test for PAPP-A and free β-HCG, done at 8-14 weeks (early is best**).**
- Maternal blood test for AFP, HCG and estriol (Triple test), done at 15-20 weeks.
- A scan is needed before any of these blood tests to check exactly how far you are pregnant and to exclude twins or miscarriage. These blood tests have a 60% sensitivity for Down syndrome (i.e. can detect 6 out of 10 fetuses with Down syndrome) and a 5% false positive rate, at a risk cut-off of approx. 1:300.
- Cell free DNA testing, also called NIPT (Non-Invasive Prenatal Testing). This test is very accurate for Down syndrome (more than 99% sensitivity and less than 1% false positive rate). It can be performed any time after 10 weeks, but also requires a scan beforehand to exclude problems such as a major physical fetal abnormality, a multiple pregnancy or miscarriage. NIPT is currently very expensive and not covered by most medical schemes. It can test for many other genetic conditions apart from Down syndrome and therefore requires quite extensive counselling beforehand.

2. **Ultrasound assessments (sonogram, scan, sonar):**

- "Simple NT scan", done at 11 – 13 weeks and 6 days. The name "NT" refers to the measurement of the nuchal translucency thickness, a fluid collection in the fetus' neck which is thickened in most fetuses with Down syndrome. This has a 70% detection rate and a 5% false positive rate at a risk cut-off of 1:300 when done by an experienced practitioner.
- "Extended NT scan", done at 11 – 13 weeks and 6 days. This includes not only the NT measurement but also assessment of the nasal bone, fetal blood flow patterns and detailed fetal anatomy. The sensitivity of this sort of scan for Down syndrome is about 85% and the false positive rate 5% for a risk cut-off of 1:100 to 1:200. There are very few people in this country trained to do this.
- "Routine fetal anatomy scan" by your obstetrician, done at 18 – 22 weeks. This has only about 40% sensitivity for Down syndrome, in other words it would NOT detect the majority of fetuses with Down syndrome.
- "Genetic sonogram" by an expert, done at 18-22 weeks. This is a more detailed ultrasound examination including a long list of subtle ultrasound markers of a fetal chromosomal abnormality. This has roughly 75% sensitivity and a 10% false positive rate.

3. **Combinations:**

- Maternal blood test in the first AND second trimester. The combined detection rate for Down syndrome is 80-85% and false positive rate 5% for a risk cut-off of approx. 1:300 after the second sample (if the two samples are seen as independent tests however, the false positive rate would double to 10%).

- Maternal blood test in the first trimester together with a "simple NT" scan". This is called "the early combination test" and has a sensitivity of 85% for Down syndrome and 5% false positive rate at a risk cut-off of 1:300.
- Maternal blood test in the first trimester together with an "extended NT scan" by an expert. This can have a sensitivity of 95% for a false positive rate of around 3%.

SUMMARY of screening options

Test	**Detection rate for Down syndrome**	**Detection rate for physical fetal abnormalities**
First trimester		
Biochemistry (PAPP-A, b-HCG)	60%	0%
Simple NT scan	70%	30%
Extended NT scan	85%	40%
Combination test (Simple NT)	80%	30%
Combination test (Extended NT)	95%	40%
NIPT	99%	0%
Second Trimester		
Biochemistry (Triple test, incl MSAFP)	60%	60% for open spina bifida
Biochemistry first AND second trimester	80%	60% for open spina bifida
Fetal anatomy scan by general obstetrician or sonographer	40%	45-50%
Expert scan	75%	75%

If money wasn't an issue and there were more than enough experts in the country, the very best screening would be a combination of NIPT WITH an expert NT scan AND an expert fetal anatomy scan AND a repeat expert scan in the last trimester. This combination could theoretically detect 99% of all Down syndrome fetuses, a whole list of other genetic conditions as well as the majority of physical fetal abnormalities. This approach, even though some patients may choose this, is however very expensive (costs amounting to more than R15 000 per pregnancy) and is simply not available for all pregnancies for the foreseeable future. This is not only the situation in South Africa but also in many developed countries. For this reason, alternative screening strategies can be considered as acceptable, with some form of triaging according to risk.

In low risk pregnancies: First AND second trimester blood test (with Down syndrome risk recalculated after the second one) PLUS a first AND second trimester scan by the general obstetrician. Referral to an expert is recommended if the first or combined blood test results show a risk of Down syndrome higher than 1:300, if the MSAFP level is raised or if the obstetrician is concerned about anything on the scans. The expert will then reassess all findings and advise on further testing or management, as indicated. If the scans are normal and referral to an expert is not planned or possible, NIPT is advised if the risk for Down syndrome is higher than 1:1000. Screening results lower than that are usually only communicated telephonically and not followed by further testing.

In high risk pregnancies: First trimester blood test + extended NT scan if available. If this demonstrates a low risk (<1:1000), no further testing is recommended. If it indicates a high risk for Down syndrome (>1:100), an invasive test (usually amniocentesis or chorionic villus sampling) is offered. If an intermediate risk (1:100 – 1:1000) is found, the possibilities would include a diagnostic test, NIPT or reassessment by an expert genetic sonogram. If the high risk patient has no access to an extended NT scan, then NIPT can be considered with an expert second trimester scan if needed.

Information that will be given to you after the screening

- The risk that your fetus has Down syndrome, based on the test result(s)
- Any other conditions for which there is an increased risk, based on your history or the test result(s)
- Any physical abnormality detected in any of the fetal organs or structures
- Any ultrasound "soft markers" that may affect the health of the fetus and require further assessment
- The fetal gender, only if you wish to know this

Genetic counselling

These options can be confusing. If you require more information, and especially if you have a family history of a genetic condition, a session with a genetic counsellor is advisable. This session will include a detailed family and pregnancy history, and provision of detailed information on the pros and cons of the different screening options, as well as any other knowledge required to make a fully informed decision. Where there is a family history of a rare genetic condition or in more complex situations, referral to a medical geneticist (rather than a counsellor) may be indicated.

Glossary

Sensitivity = Detection Rate	The chance of detecting an abnormality if it is present (e.g. a 60% sensitivity for Down syndrome means that out of 10 babies with Down syndrome, 6 would show up with a "high risk" result and 4 would show up with a low risk result)
False positive rate	The chance of a "high risk" result if the baby is in fact normal (e.g. a 5% false positive rate would mean that 1 in 20 normal pregnancies would have a high risk result on the screening test)
False negative result	The chance that an abnormal baby would have presented with a "low risk" result – this will often result in the abnormality only being diagnosed after birth

Background risk

The background risk for Down syndrome at the time of screening, according to your age alone, is depicted in this table:

Maternal age (years)	*Gestational age* (weeks)					
	10	*12*	*14*	*16*	*20*	*40*
20	1/983	1/1068	1/1140	1/1200	1/1295	1/1527
25	1/870	1/946	1/1009	1/1062	1/1147	1/1352
30	1/576	1/626	1/668	1/703	1/759	1/895
31	1/500	1/543	1/580	1/610	1/658	1/776
32	1/424	1/461	1/492	1/518	1/559	1/659
33	1/352	1/383	1/409	1/430	1/464	1/547
34	1/287	1/312	1/333	1/350	1/378	1/446
35	1/229	1/249	1/266	1/280	1/302	1/356
36	1/180	1/196	1/209	1/220	1/238	1/280
37	1/140	1/152	1/163	1/171	1/185	1/218
38	1/108	1/117	1/125	1/131	1/142	1/167
39	1/82	1/89	1/95	1/100	1/108	1/128
40	1/62	1/68	1/72	1/76	1/82	1/97
41	1/47	1/51	1/54	1/57	1/62	1/73
42	1/35	1/38	1/41	1/43	1/46	1/55
43	1/26	1/29	1/30	1/32	1/35	1/41
44	1/20	1/21	1/23	1/24	1/26	1/30
45	1/15	1/16	1/17	1/18	1/19	1/23

Snijders RJ, Sundberg K, Holzgreve W, Henry G, Nicolaides KH. Ultrasound Obstet Gynecol. 1999 Mar;13(3):167-70.