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Antenatal screening programmes offered in Wales

Test	Purpose of Test
Early pregnancy ultrasound dating scan	Determine viability, accurately assess gestational age and detect multiple pregnancies.
Fetal anomaly scan	Detect major structural fetal anomalies that are likely to have an adverse effect on the health of the baby.
Blood group and antibodies	Offer antenatal and postnatal anti-D immunoglobulin prophylaxis to Rhesus negative women to reduce the risk of Rhesus alloimmunisation in current and subsequent pregnancies.
Rubella susceptibility screening	Reduce the risk of congenital rubella syndrome in subsequent pregnancies by giving postnatal measles, mumps and rubella (MMR) vaccination.
Hepatitis B	Reduce the risk of mother to baby transmission of the hepatitis B virus by providing a programme of immunisation for babies of affected mothers.
Syphilis screening	Reduce the risk of the fetus contracting congenital syphilis by prompt antibiotic treatment.
HIV	Reduce the risk of mother to baby transmission of the HIV virus by providing various interventions.
Sickle cell and thalassaemia	Identify women who have a higher chance of having a baby with a sickle cell disorder or thalassaemia major and offer maternal laboratory screening and subsequent diagnostic testing.
Down's syndrome screening	Offer diagnostic testing and pregnancy choices if the pregnancy is affected by Down's syndrome.

Preface

This third edition of the Screening Handbook is provided to enable professionals involved in antenatal screening to have easy access to information about antenatal screening. The Antenatal Screening Wales (ASW) standards and protocols are available on www.antenatalscreeningwales.org and should be referred to when planning and providing care.

The revision of the Screening Handbook was discussed with stakeholders in 2009. As a result, this third edition Screening Handbook has been developed for midwives and includes:

Section 1

Basic care pathways for each antenatal screening programme.

Section 2

Background information.

Section 3

Updated clinical information.

Section 4

Additional information.

Section 5

Sources of additional web based information.

Section 1: Screening pathways

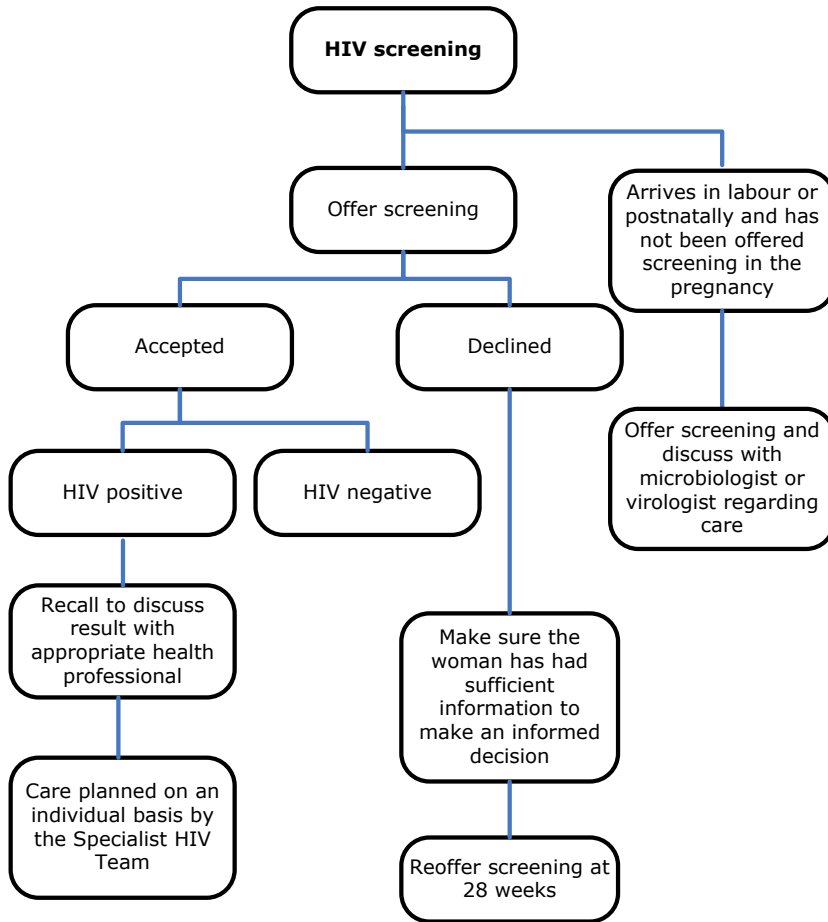
Diagrams provide a simple way to illustrate complex care pathways.

The following pathways are included:

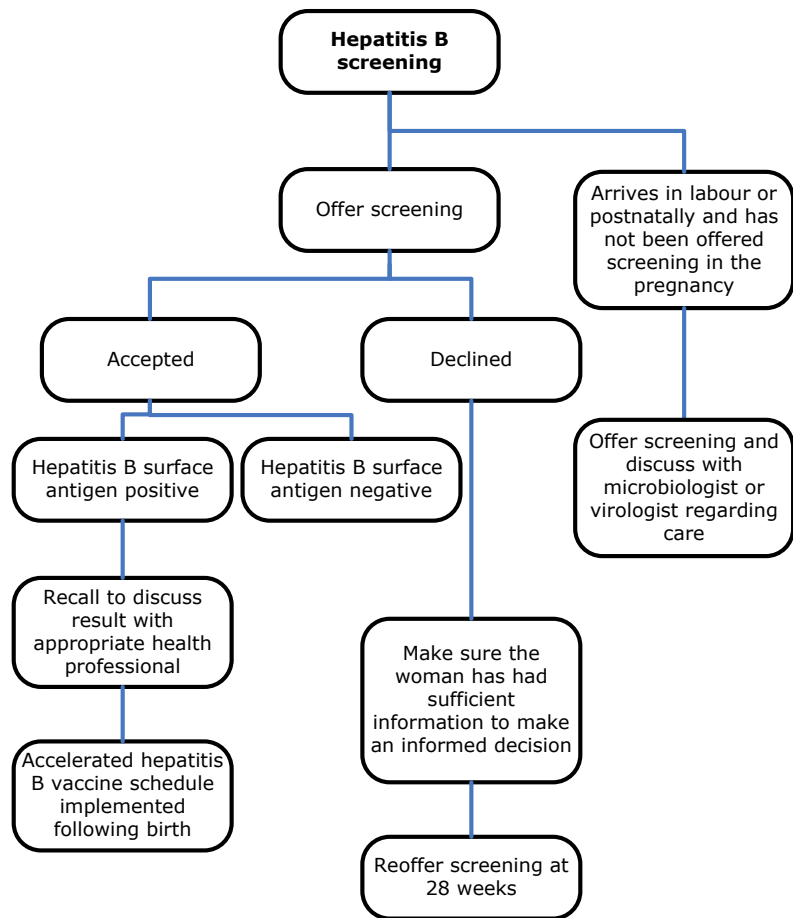
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Detailed and additional relevant pathways are available at: www.mapofmedicine.com/.

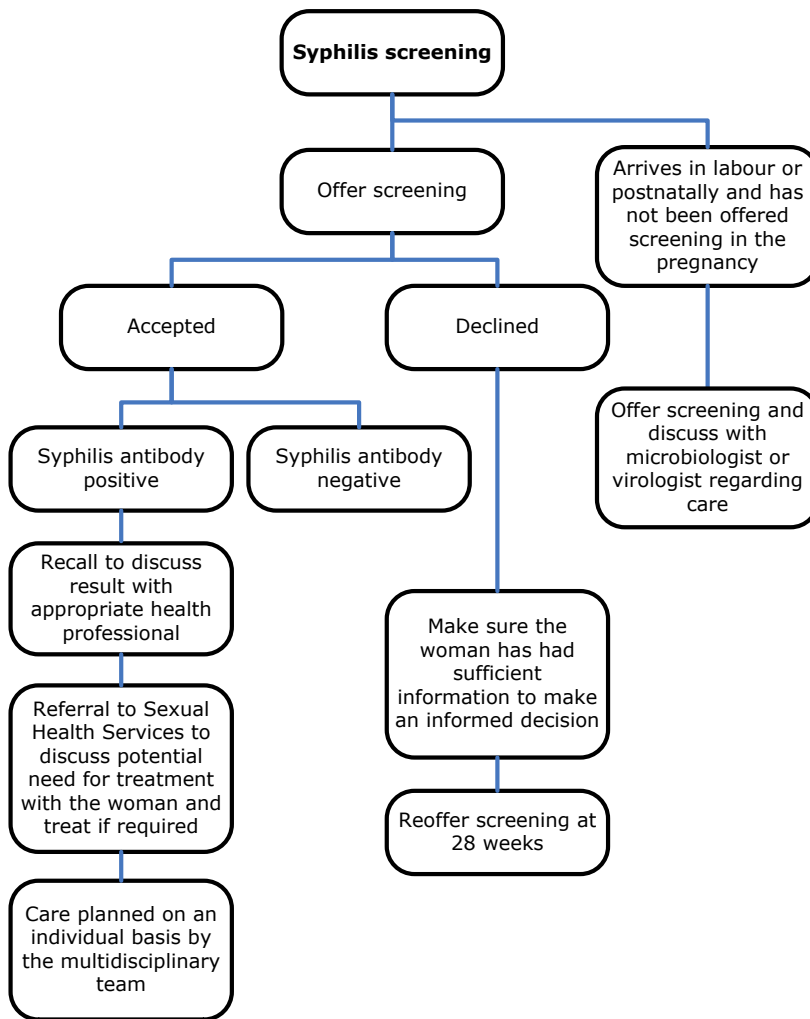
1. HIV antenatal screening pathway



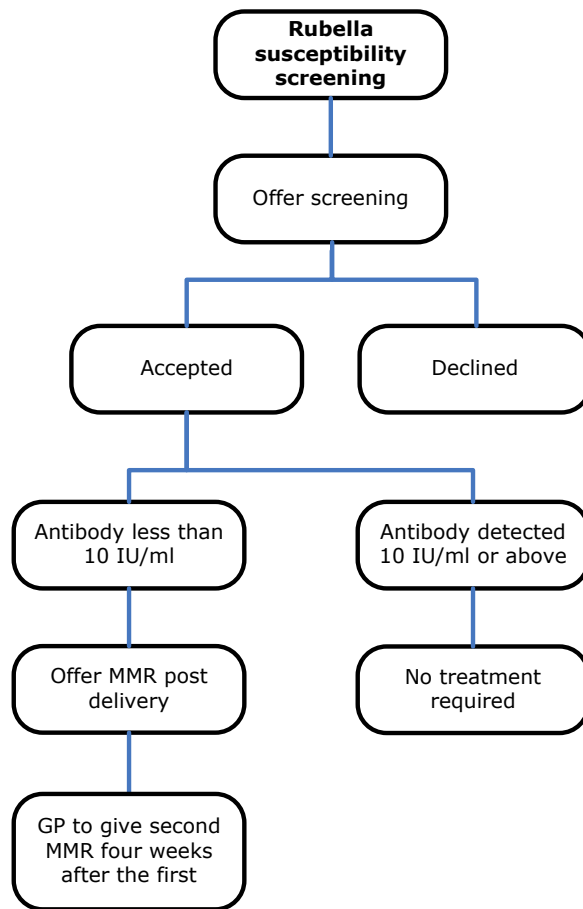
2. Hepatitis B antenatal screening pathway



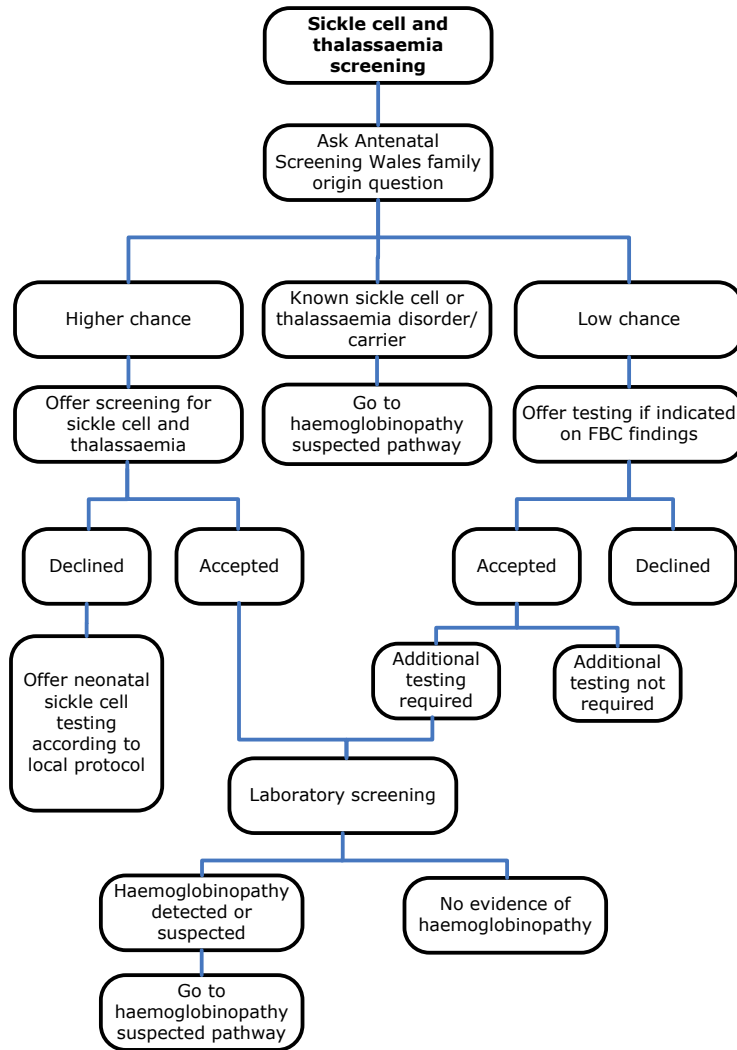
3. Syphilis antenatal screening pathway



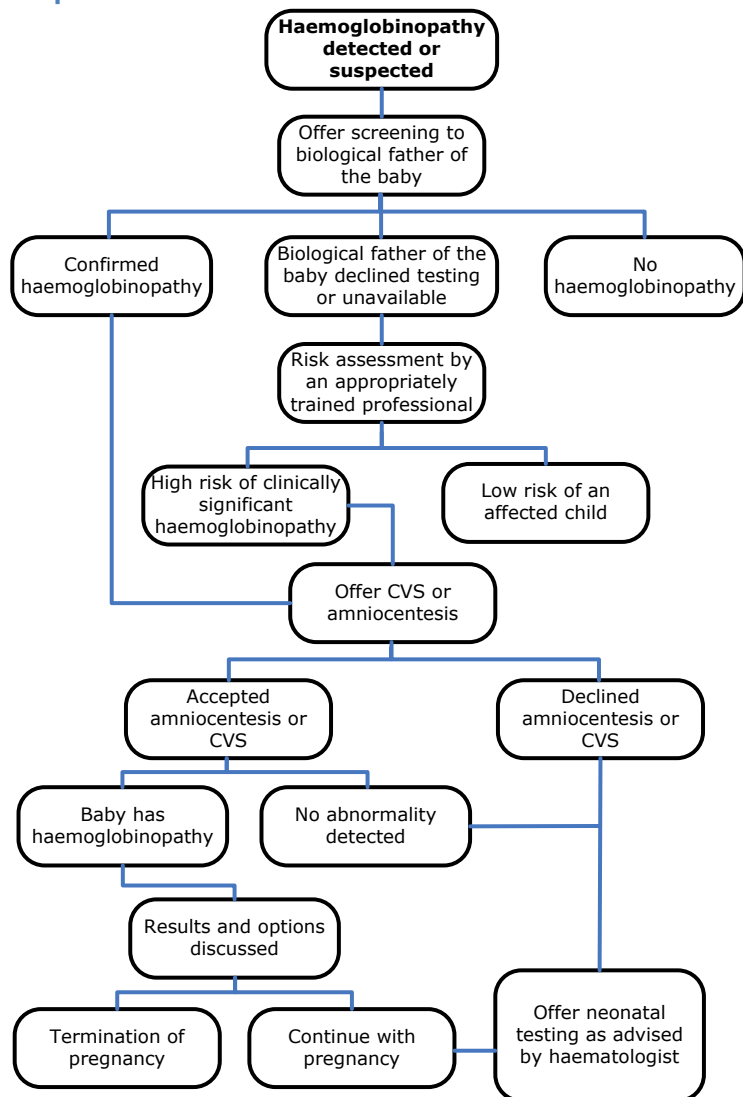
4. Rubella susceptibility antenatal screening pathway



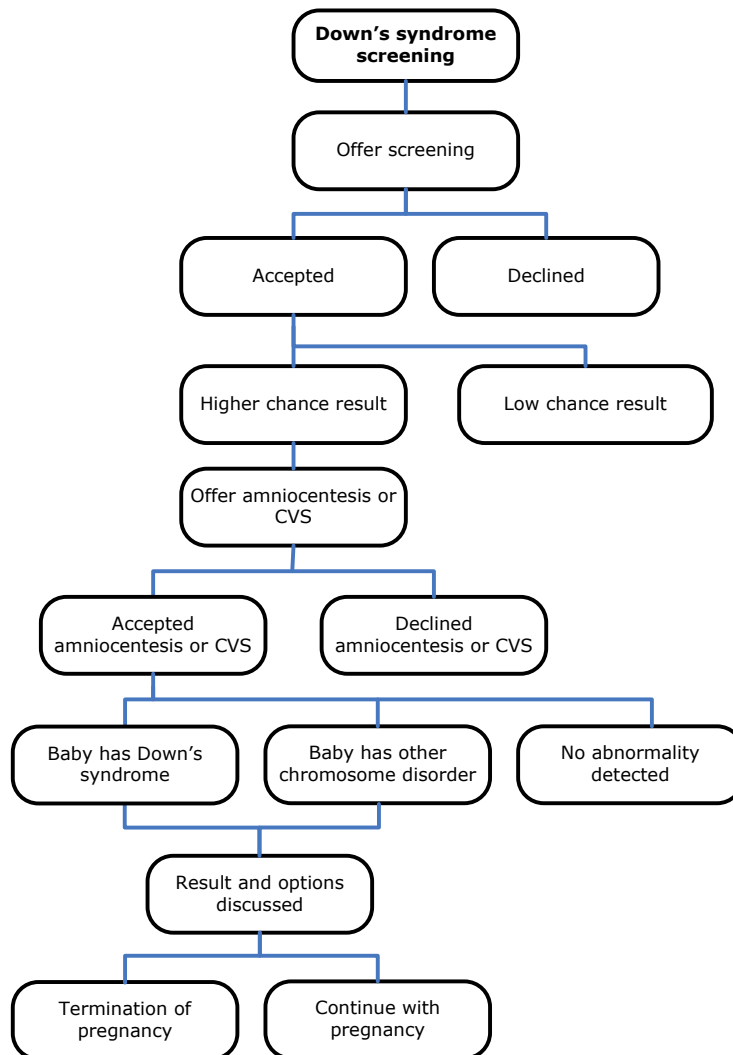
5a. Sickle cell and thalassaemia antenatal screening pathway



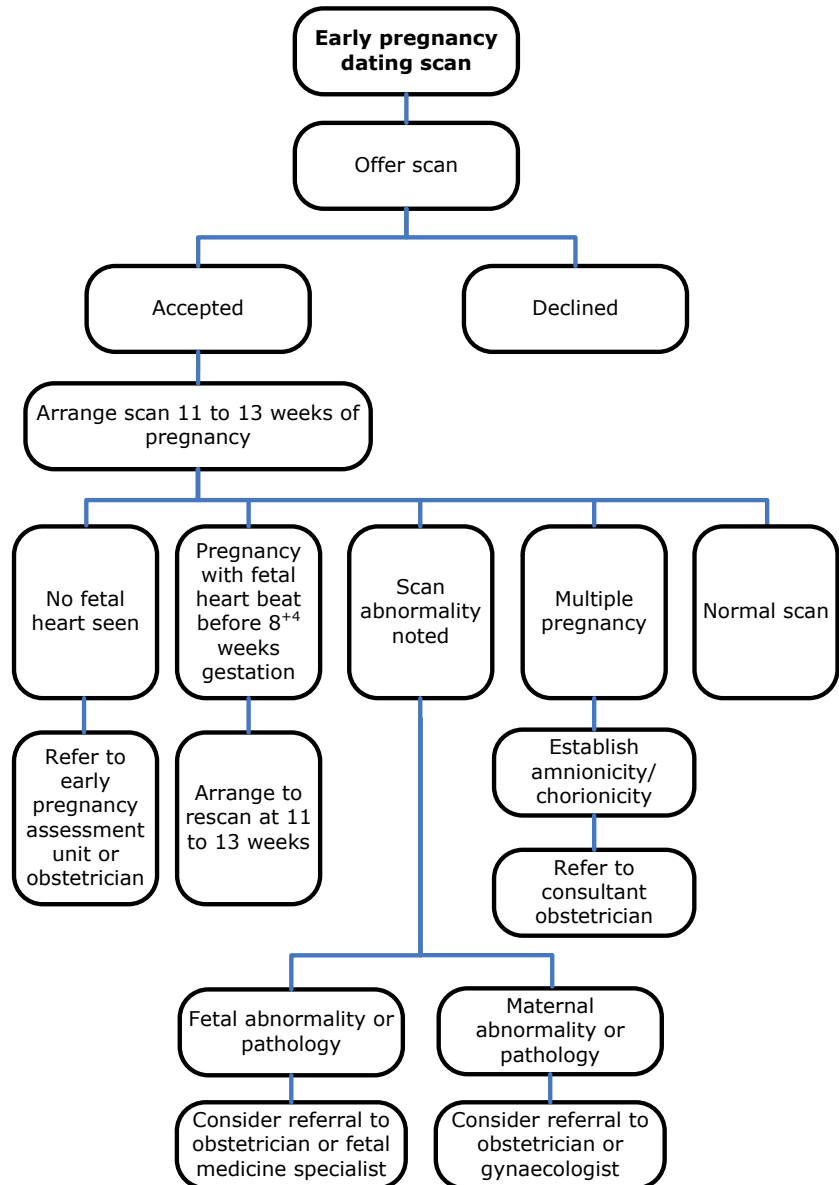
5b. Sickle cell and thalassaemia haemoglobinopathy suspected



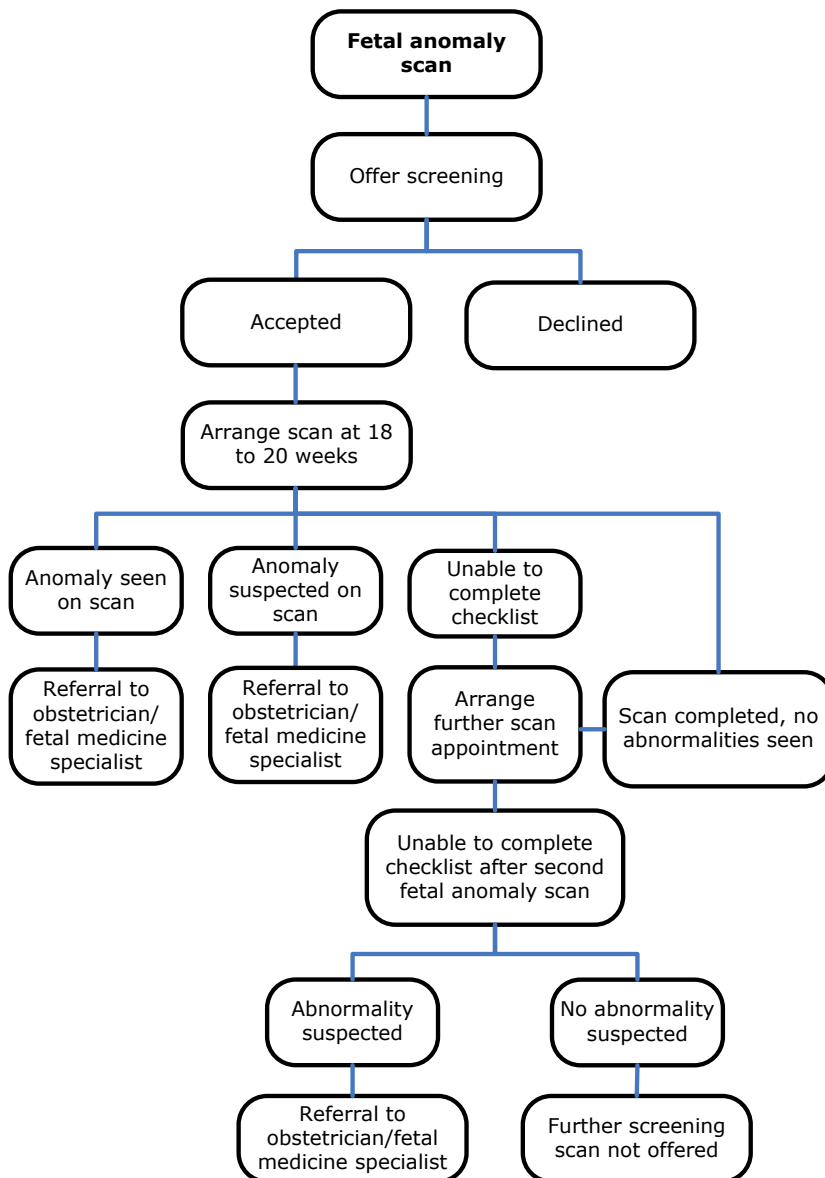
6. Down's syndrome antenatal screening pathway



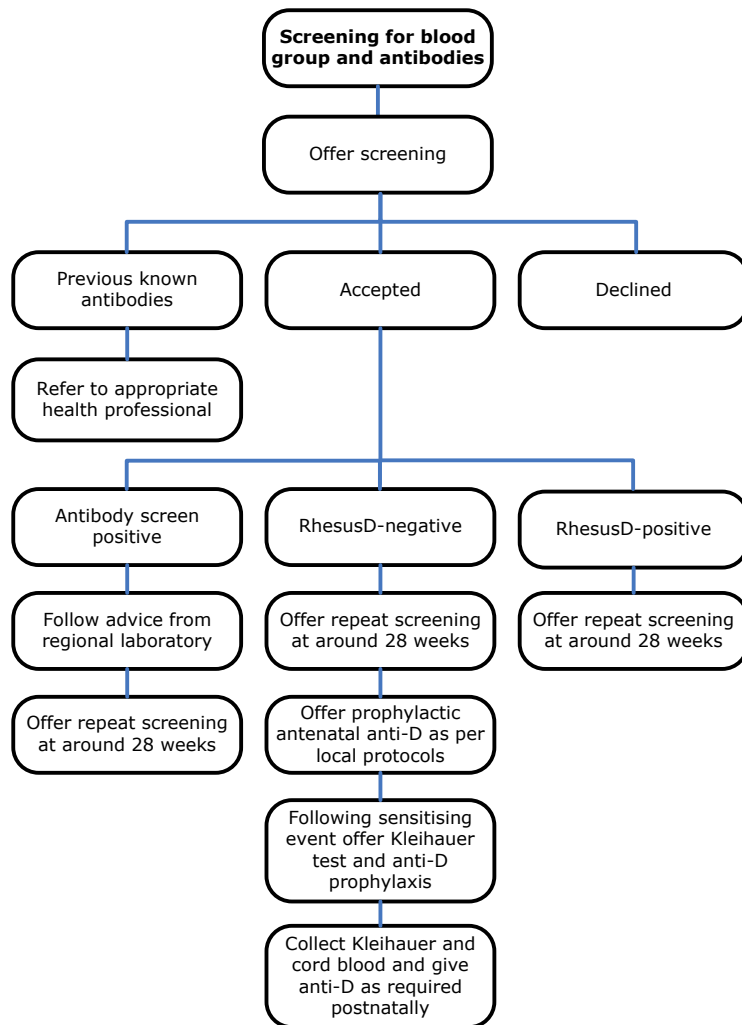
7. Early pregnancy ultrasound scan pathway



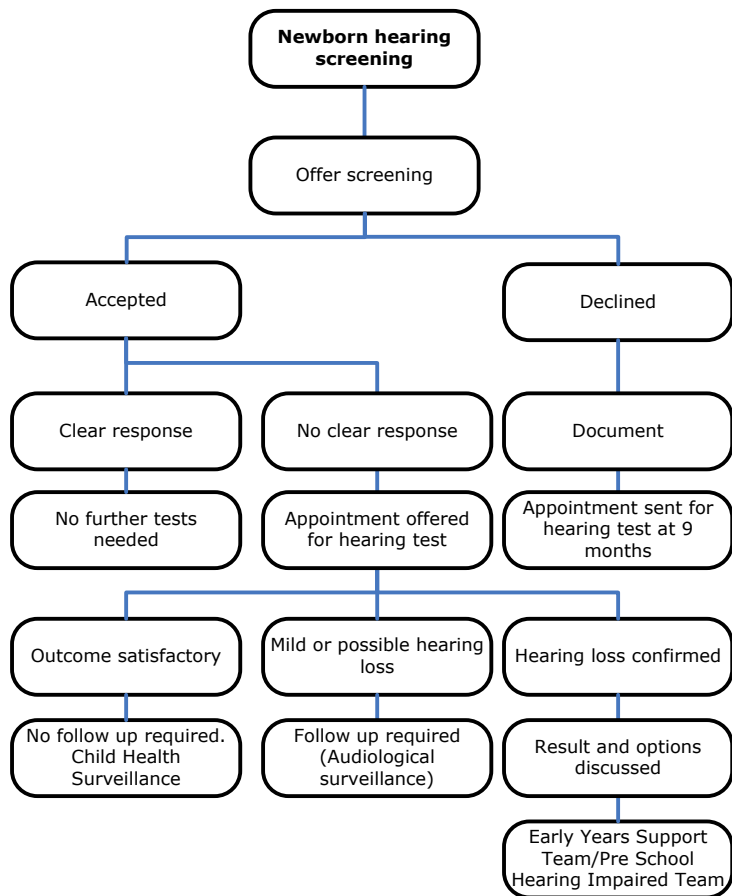
8. Fetal anomaly ultrasound scan screening pathway



9. Blood group and antibody antenatal screening pathway



10. Newborn hearing screening pathway



Section 2: Background information

Introduction to antenatal screening

The maternity services in Wales provide antenatal screening tests to pregnant women as part of their antenatal care. Antenatal screening tests are provided for different reasons and this makes antenatal screening a complex programme with a number of different purposes and unique ethical considerations and implications.

The following definition is used to describe the purpose of antenatal screening in Wales:

- *Antenatal screening is undertaken to detect defined serious conditions present in either the mother or baby that are likely to have an adverse effect on the health of either, and for which an effective intervention is available and warranted.*
- *For some conditions, preventive treatment is available during the antenatal period or after delivery to improve the baby's health.*
- *For others, the condition can be identified during the antenatal period but no preventive treatment is available. With high quality counselling women can make an informed choice about whether they wish to continue the pregnancy and appropriate support, depending on their ultimate choice, can be arranged (Choices, Velindre NHS Trust 2002).*

The UK National Screening Committee

The UK National Screening Committee (UK NSC) was established in 1996 and has a remit to advise Ministers, the devolved National Assemblies and the Scottish Parliament on all aspects of screening policy. Proposals for new screening programmes are assessed against a set of internationally recognised criteria which cover the condition in question, the test, the treatment options and the effectiveness and acceptability of the screening programmes.

The Fetal Maternal and Child Health (FMCH) subgroup of the UK NSC, addresses all aspects of antenatal, newborn and child health screening programmes. This includes reviewing the latest research evidence and, where necessary, the skills of specially convened multidisciplinary expert groups are elicited.

The UK NSC has over a hundred screening policies on conditions that it reviews. The UK NSC reviews all its policies on a regular basis because new evidence from research is being published regularly. As a result of this review process, a screening programme can be recommended, discontinued or amended.

The process for review has four main steps: stakeholder review, knowledge update, external review and UK NSC decision. This review can take up to 24 months depending on the current evidence for review and how contentious the policy is.

As all screening programmes have the possibility of providing harm as well as benefit, the policy recommendations of the UK NSC are important.

The current UK NSC policy position (March 2010) is set out in Tables 1, 2 and 3 as follows:

- Table 1: Systematic population antenatal screening programmes recommended by the UK NSC.
- Table 2: Clinical practice guidelines covered by the National Institute for Health and Clinical Excellence (NICE).
- Table 3: Systematic population screening programmes not recommended by the UK NSC.

Updated information is available on the UK NSC website:

www.screening.nhs.uk/policy

Table 1: Systematic population antenatal screening programmes recommended by the UK NSC

Systematic population screening programmes recommended by the UK NSC		
	Last review by the UK NSC completed	Next review decision by the UK NSC due
Down's syndrome	Jul 2006	2009/10
Fetal anomalies	Jul 2006	2009/10
Hepatitis B	Jul 2006	2010/11
Human immunodeficiency virus	Jul 2006	2009/10
Neural Tube defect	Jul 2006	2009/10
Rubella susceptibility	Jul 2006	2010/11
Sickle cell and thalassaemia	Jul 2006	2009/10
Syphilis	Jul 2006	2010/11
Tay Sachs disease	Jul 2006	2009/10

Table 2: Clinical practice guidelines covered by NICE

Systematic population screening programmes not recommended. Clinical practice guidelines covered by NICE		
	Last review by the UK NSC completed	Next review decision by the UK NSC due
Anaemia	Jul 2006	2009/10
Asymptomatic bacteriuria	Jul 2006	2009/10
Blood Group & RhD status and red cell alloantibodies	Jul 2006	2009/10
Placenta praevia	Nov 2008	2011/12
Pre-eclampsia	Jul 2006	2009/10
Psychiatric illness	Jul 2006	2009/10

Table 3: Systematic population screening programmes not recommended by the UK NSC

Systematic population screening programmes not recommended by the UK NSC		
	Last review by the UK NSC completed	Next review decision by the UK NSC due
Bacterial vaginosis	Jul 2006	2009/10
Chlamydia (pregnancy)	Jul 2006	2009/10
Cystic Fibrosis (pregnancy)	Jul 2006	2009/10
Cytomegalovirus	Jul 2006	2009/10
Domestic violence (pregnancy)	Jul 2006	2009/10
Familial dysautonomia	Jul 2006	2010/11
Fragile X	Jul 2006	2009/10
Genital herpes	Jul 2006	2009/10
Gestational diabetes	Jul 2006	2009/10
Group B streptococcus	Nov 2008	2011/12
Hepatitis C (pregnancy)	Jul 2006	2009/10
HTLV-1	Jul 2006	2009/10
Postnatal depression	Jul 2006	2009/10
Preterm labour	Jul 2006	2009/10
Thrombocytopenia	Jul 2006	2010/11
Thrombophilia (pregnancy)	Jul 2006	2009/10
Toxoplasmosis	Jul 2006	2009/10
Varicella susceptibility	Oct 2009	2012/13
Vasa praevia	Nov 2008	2011/12

Antenatal Screening Wales

In April 2003 the Minister for Health and Social Services agreed that a Managed Clinical Network for antenatal screening should be established in Wales, based on the principles described in the Antenatal Screening Project Report Choices – Recommendations for the Provision and Management of Antenatal Screening in Wales (Velindre NHS Trust 2002). The network is known as Antenatal Screening Wales (ASW) and is hosted by Public Health Wales as part of its Screening Division. ASW does not provide or directly manage any antenatal screening services.

Governance for the work of ASW is provided by the All Wales Multiprofessional Management Group (AWMMG) and three sub groups. There are regular meetings with the Health Board's antenatal screening coordinators and sonographers. The work of ASW is supported and assisted by the Public Health Wales Screening Division, which has extensive expertise in the management and provision of population-based screening programmes. ASW has a small core team supported by administrative staff. Details are available at:

www.antenatalscreening.org.

As part of its initial work, ASW was asked by the Welsh Assembly Government to establish policies, standards and a performance management framework for antenatal screening to support demonstrable improvements in the quality of antenatal screening offered to women. Standards and protocols for antenatal screening were first published by ASW in December 2005 and a revised version published in 2010.

The implementation of service changes to meet the expectations in the original standards has been monitored by the ASW balanced scorecard, which is reported every six months.

An audit framework has been developed to facilitate record keeping and process audits in Health Boards.

Principles of screening

Informed choice

The UK NSC has adopted the principle that individuals should be offered the opportunity for an informed choice before they enter a screening programme. This means individuals should be able to appreciate the risks and benefits of the screening programme for themselves before accepting screening. This principle is particularly important when antenatal screening services are considered as there are moral, ethical, religious and cultural issues which rightly impact on the antenatal screening programme in unique ways.

The purpose, implications, limitations and benefits of screening must be explained to the woman by the midwife before the test is requested or performed. To support pregnant women to understand the screening tests offered to them and their implications, ASW has developed an 'Information for Women' pack which is provided to all Health Boards to supply to women in early pregnancy. These leaflets are also available in a number of languages on www.antenatalscreening.org or from the ASW office.

Consent

Obtaining informed consent is a key legal and ethical principle within screening programmes. Informed consent should be voluntary, following appropriate information and be given by people with capacity to give consent. Within a regularised maternity care framework, great care needs to be taken that 'routine tests' are offered in such a way that the woman has a true opportunity to give informed consent.

The woman's informed verbal consent is required for all antenatal screening tests. Written consent is not required but a record of the woman's verbal consent must be made by the midwife in the maternity notes.

Interpretation of screening test results

It is important that the public and health professionals have realistic expectations of what a screening programme can achieve.

It should be remembered that in any screening programme there is an irreducible minimum of:

- **false positive results** (wrongly reported as having the condition)
- and
- **false negative results** (wrongly reported as not having the condition).

Screening programmes use the following terms to describe elements of the programme:

- **Sensitivity:** The true positive test results that are correctly identified by the screening test as a proportion of the total number of women with a specific disease in a defined population.
- **Specificity:** The true negative test results that are correctly identified by the screening test as a proportion of the total number of women with a specific disease in a defined population.
- **False positives:** A false positive result indicates a positive test when there is, in fact, no disease.
- **False negatives:** A false negative result indicates a negative test when there is actually disease present.
- **Risk (chance):** Risk is usually taken to mean the chance of an event happening. It can be expressed in a number of ways, e.g. percentages, figures, pictorial, etc.

Some antenatal screening tests, e.g. HIV screening tests are very sensitive, which means the result is very likely to be accurate.

Other antenatal screening tests, e.g. Down's syndrome screening tests, can only provide a risk estimation of the event happening.

Screening tests for inherited disorders, e.g. sickle cell and thalassaemia, require samples from the mother and if she has a haemoglobinopathy, a sample from the father of the baby in order to best assess the risk to the fetus.

Ultrasound scanning is different to the other antenatal screening programmes because the test is non-selective in nature. This means that it is impossible to observe only targeted abnormalities. This makes explaining to women the purpose and possible result from ultrasound scans particularly challenging.

Management of the antenatal screening programme

The effective management of the antenatal screening programme is essential. The Health Board's antenatal screening programme should be supported by suitable management arrangements and as recommended in the revised ASW standards and protocols.

Each Health Board should have a named antenatal screening coordinator(s) responsible for the overall programme management and coordination of antenatal screening. These Health Board coordinators are also a valuable source of advice and expertise for midwives who are less familiar with the antenatal screening programme and in particular the care pathways following the identification of a problem, or potential problem, by a screening test.

CARIS

The Congenital Anomaly Register & Information Service for Wales (CARIS) provides information on numbers and rates of congenital anomalies in Wales. Around 5% of live and stillbirths in Wales have some type of congenital anomaly.

Information about CARIS is included in the ASW 'Information for Women' packs.

Data from CARIS is used to help evaluate the detection rate of the Down's screening programme and the detection rates of antenatal ultrasound.

The reporting of cases by health professionals remains essential for the success of the register. Reporting is in the antenatal period and also up to one year of age.

More information on CARIS and how to report to CARIS can be found at: www.wales.nhs.uk/caris

Section 3: Clinical information

HIV (human immunodeficiency virus)

Clinical information

HIV is a retrovirus that attacks and destroys T-lymphocytes, resulting in immune-suppression that eventually leads to acquired immune deficiency syndrome (AIDS). Vertical transmission of the virus from mother to fetus or baby can occur during pregnancy, at delivery or postnatally through breastfeeding.

Two forms of the virus have been identified: HIV-1 and HIV-2. The commonest and most virulent form is HIV-1.

Transmission of HIV

HIV is transmitted through:

- sexual contact
- vertical transmission from an infected mother-to-child during pregnancy, delivery or breastfeeding
- contact with contaminated blood and other body fluids.

HIV infection and pregnancy

- Without intervention mother-to-child transmission rates of HIV are 15 to 25% or higher if seroconversion occurs in pregnancy.
- Drug therapy, a carefully managed delivery, and avoidance of breastfeeding can reduce the risk of vertical transmission to around 1% (Townsend et al. 2008).
- Without intervention about one third of babies who contract HIV die before their first birthday and around half die before the age of two (UNICEF 2008).

Incidence and prevalence

Global/worldwide picture

The World Health Organization (WHO) are the directing and coordinating authority on international health and take the lead within the United Nations (UN) system on the global health sector response to HIV/AIDS. The WHO considers HIV to be pandemic.

An estimated 33.4 million people were living with HIV/AIDS at the end of 2008 (WHO 2010):

- Sub-Saharan Africa – 22.4 million
- South and South-East Asia – 3.8 million
- Latin America – 2.0 million
- Eastern Europe and Central Asia – 1.5 million
- North America – 1.4 million
- Western and Central Europe – 850, 000
- East Asia – 850, 000.

Antiretroviral treatments are not readily available in all regions.

In order to better target much needed interventions, the WHO HIV/AIDS Programme focuses on five strategic directions:

www.who.int/hiv/aboutdept/en/index.html.

- Enable people to know their HIV status;
- Maximise the health sector's contribution to HIV prevention;
- Accelerate the scale-up of HIV treatment and care;
- Strengthen and expand health systems;
- Invest in strategic information to better inform the HIV response.

UK/Wales

- An estimated 83,000 people were living with HIV in the UK (including 23,200 women) at the end of 2008.
- In 2008 there were 6,727 HIV diagnoses in England, 331 in Scotland, 148 in Wales and 92 in Northern Ireland. Half of all people diagnosed in the UK were infected through heterosexual sex, making this the single biggest exposure category. 34% of all new HIV diagnoses were in women.
- 110 new cases of HIV diagnosis were because of mother-to-child transmission in the UK (AVERT 2010).

The number of mother to baby transmissions of HIV has reduced in the UK. In the mid-1990s only about one-third of infected pregnant women were diagnosed, and most of those were aware of their infection status before they became pregnant. By the end of 2003 virtually all UK maternity units had implemented the routine offer of antenatal screening.

Despite the high uptake of this screening programme a number of women in the UK remain undiagnosed by the time of delivery, leading to potentially avoidable cases of mother-to-child transmission.

BHIVA (British HIV Association) produce guidelines for the management of HIV infection and these are regularly updated and available at: www.bhiva.org/.

In general the risk of transmission of HIV from mother-to-child can be greatly reduced by a care plan which includes:

- antiretroviral (ARV) therapy antenatally and intrapartum
- ARV therapy for neonate for four to six weeks after birth
- avoiding breastfeeding
- carefully managed delivery.

Delivery is usually recommended to be by caesarean section but an elective vaginal delivery can be considered in those with no detectable virus in the blood. Some women may decline a caesarean section despite a detectable plasma viral load. It is important that the delivery method should be planned in advance and should take into account the woman's wishes.

Antenatal screening for HIV

Antenatal screening for HIV is to identify pregnant women with the infection and offer treatment and care to reduce mother-to-baby transmission (NICE 2008a). The identification and treatment of HIV also has considerable health benefits for the woman.

The screening programme will not detect infections contracted recently or infections contracted after the antenatal screening test has been taken.

Timing of the tests

Whenever possible, the sample should be taken before 13 weeks of pregnancy but the test can be taken at any time in pregnancy.

If the woman declines screening, the midwife should ensure the woman has received accurate information on which to base her decision.

If a woman declines screening in early pregnancy she should be given further written or verbal opportunity to have this screening test during pregnancy, preferably at the 28 week antenatal appointment. This is so the woman can have a second opportunity to be informed about the benefits of being screened.

If, during pregnancy, the woman changes her partner or is worried that she may have contracted HIV, hepatitis B, or syphilis, the midwife can repeat the test at any time during the pregnancy.

Screening test

Fourth generation screening assays are recommended which detect HIV-1, HIV-2 antibodies and p24 antigen.

Positive results are confirmed in the laboratory before the result is issued, whenever there is a sufficient sample.

Screening test result

A negative HIV screening test result means the woman does not have a detectable HIV infection at time of testing.

Informing a woman of a negative result should be used as an opportunity to remind her of how to protect herself from infection in the future.

The HIV positive result is reliable. Diagnosis of HIV infection is made by the detection of HIV antibodies in the woman's blood.

Screen positive results are tested in the laboratory by three different methods and all methods need to be positive for HIV before a HIV positive result is issued. These are regarded as confirmed positives.

Women should only be given an HIV positive result by a health professional with suitable skills and knowledge. An information leaflet for women who are HIV positive is available at: www.antenatalscreening.org.

Care following a HIV positive result

The type of care required will depend on the woman's viral load and other factors and must be managed by a specialist HIV team.

An appropriate integrated care plan should be developed in accordance with BHIVA guidance (www.bhiva.org/).

Women should be encouraged to be involved in developing their care plan and should receive specialist counselling and support to consider:

- advantages of early treatment
- therapeutic options
- mode of delivery
- accessing voluntary sector support and information
- lifestyle and employment issues
- offering screening to the partner and other children
- method of infant feeding
- the need for neonatal follow up.

Women who have not been offered antenatal screening

Women who do not attend for antenatal care and present during labour, should be offered screening for HIV on admission to the delivery suite.

The midwife or doctor should contact the consultant microbiologist/virologist to ask for a risk assessment and to establish the urgency of testing and management whilst results are awaited.

Women who have not been offered screening for HIV in the antenatal period or intrapartum period must be offered these tests in the immediate postnatal period (within 4 hours of delivery) by the midwife caring for her.

Hepatitis B

Clinical information

Hepatitis B is an infectious disease of the liver caused by the hepatitis B virus (HBV), resulting in both acute and chronic infection.

Hepatitis B can be detected in blood, saliva and semen and transmitted:

- vertically from mother to baby
- through contact with contaminated blood
- through sexual contact.

Possible outcome from a hepatitis B infection:

Adults

- recovery and immunity
- persistently infected or chronic carrier state
- fulminant hepatitis (1% of cases) (Department of Health 2006).

Neonates

- vertical transmission at or around time of delivery is an important cause of the continued high prevalence of this infection in some parts of the world
- chronic infection occurs in up to 70% of those infected perinatally
- this chronic infection may result in complications, including cirrhosis and carcinoma; about 20% of chronic hepatitis B carriers die from liver failure.

Prevalence

Global picture

WHO (2008) has estimated that two billion people have been infected with the hepatitis B virus and over 350 million people worldwide are chronically infected with hepatitis B.

- Hepatitis B is endemic in China and other parts of Asia; most people in the region become infected with hepatitis B during childhood. In these regions, 8% to 10% of the adult population are chronically infected.
- High rates of chronic infections are also found in the Amazon and the southern parts of eastern and central Europe.
- In the Middle East and Indian sub-continent, an estimated 2% to 5% of the general population is chronically infected.
- Less than 1% of the population in Western Europe and North America are chronically infected.
- Liver cancer caused by hepatitis B is among the first three causes of death from cancer in men, and a major cause of cancer in women.

It is recommended by WHO that all infants should receive the hepatitis B vaccine as this is the mainstay of hepatitis B prevention. In the UK there is a selective infant post-exposure vaccination policy, which targets infants at increased risk.

UK/Wales

The hepatitis B immunisation programme in the UK is a minimum of three doses of hepatitis B vaccine for individuals at high risk of exposure to the virus.

Pre-exposure immunisation is used for individuals who are at increased risk of hepatitis B because of their lifestyle, occupation or other factors.

Immediate post-exposure vaccination is used to reduce the risk of infection, especially in babies born to infected mothers or following needlestick injuries (Department of Health 2009).

The prevalence of hepatitis B carriers varies across different ethnic groups and is higher among women from countries where the disease is endemic.

Fifty-three pregnant women were hepatitis B positive in Wales in 2008 (ASW 2009).

Antenatal screening for hepatitis B

The purpose of offering antenatal screening for hepatitis B to pregnant women is to enable the identification of hepatitis B carriers whose babies will be at significant risk of contracting hepatitis B. These neonates can be offered a programme of vaccination.

The screening programme aims to detect women with established hepatitis B infection and not infections contracted after the antenatal screening test has been taken. If the woman contracted hepatitis B in the few months before the blood sample was taken, the test will not be able to detect the infection.

Timing of the tests

Whenever possible, the sample should be taken before 13 weeks of pregnancy but the test can be taken at any time in pregnancy.

If the woman declines screening, the midwife should ensure the woman has received accurate information on which to base her decision.

If a woman declines screening in early pregnancy she should be given further written or verbal opportunity to have this screening test during pregnancy, preferably at the 28 week antenatal appointment. This is so the woman can have a second opportunity to be informed about the benefits of being screened.

If, during pregnancy, the woman changes her partner or is worried that she may have contracted HIV, hepatitis B, or syphilis, the midwife can repeat the test at any time during the pregnancy.

Screening test result

A hepatitis B surface antigen negative result means the woman does not have hepatitis B infection at time of testing.

A hepatitis B positive result is very reliable. If the hepatitis B test is positive, additional tests are undertaken to determine the likely level of infectivity. This will ensure that the recommended neonatal treatment can be made available.

Surface antigen (HBsAg) is present in those currently infected. The presence of another antigen (HBeAg) indicates high infectivity.

Women should only be given a positive hepatitis B result by health professionals with suitable skills and knowledge. An information leaflet for women who are hepatitis B positive is available at: www.antenatalscreeningwales.org.

Care following a hepatitis B surface antigen positive result

The accelerated immunisation schedule and the importance of the baby completing the course should be explained to the mother.

Arrangements should be in place for the required immunisations to be available following delivery.

The care plan may require discussion with the paediatrician and virologist.

Women with chronic hepatitis B infection should be referred, by the lead professional, during the antenatal period for further assessment by a gastroenterologist, hepatologist or infectious disease specialist (dependent on availability of local services).

The woman's GP should be informed by the obstetrician or Health Protection Team once the woman has been informed.

Neonatal immunisation against hepatitis B

Arrangements should be in place for the baby to receive the accelerated immunisation schedule recommended for post exposure prophylaxis.

Babies born to hepatitis B positive mothers should receive hepatitis B vaccination as follows:

- first dose within 24 hours after birth
- second dose at one month
- third dose at two months
- fourth dose at twelve months
- the baby requires a blood test to establish immunity when the course is finished.

Babies born to hepatitis B mothers with high infectivity and babies born to any hepatitis B infected mother where birth weight is less than 1500g should also receive hepatitis B specific immunoglobulin (HBIG) within 24 hours of birth.

Full details of when HBIG is indicated can be found on the HPA website: www.hpa.org.uk.

Green Book – immunisation against infectious diseases (Department of Health 2009).

Syphilis

Clinical information

Syphilis results from infection by the spirochete bacterium, *treponema pallidum*. Humans are the only host, and transmission can occur through sexual contact (adult syphilis) or following transmission across the placenta during pregnancy from an infected mother to her fetus (congenital syphilis).

Transmission of syphilis

Syphilis is passed from person to person through direct contact with a syphilis sore (chancre). Sores occur mainly on the external genitals, vagina, anus or in the rectum. They can also occur on the lips or in the mouth.

Stages of infection and symptoms

- primary - sore (chancre)
- secondary - symptoms include disseminated disease including fever, malaise, maculopapular rash, hepatitis, meningitis, renal damage
- latent - asymptomatic but moderately infectious
- tertiary - 2 to 40 years after infection many major symptoms including cardiovascular syphilis, neurosyphilis.

Congenital syphilis

Congenital syphilis is acquired by horizontal transmission through the placenta.

- if the pregnant woman has untreated syphilis infection, the fetal loss rate is approximately 50%
- those babies that survive experience considerable morbidity.

Incidence

The incidence of infectious syphilis relative to other sexually transmitted infections remained low in Wales until the late 1990s (NPHS Wales 2010).

- The number of cases of infectious syphilis reported in Wales increased from 75 in 2006 to 104 in 2008
- The proportion of cases acquired heterosexually has varied from 22% of all cases in 2002 to 27% in 2005, 39% in 2006, 25% in 2007 and 19% in 2008
- Sixteen cases in 2007 (20%) were also known to be HIV positive.

Antenatal screening for syphilis

The purpose of antenatal screening for syphilis is to identify women with the infection and offer treatment which will reduce the risks of the baby developing congenital syphilis.

The identification and treatment of syphilis also has potential health benefits for the mother.

The screening programme will not detect infections contracted recently or infections contracted after the antenatal screening test has been taken.

Timing of the tests

Whenever possible, the sample should be taken before 13 weeks of pregnancy but the test can be taken at any time in pregnancy.

If the woman declines screening, the midwife should ensure the woman has received accurate information on which to base her decision.

If a woman declines screening in early pregnancy she should be given further written or verbal opportunity to have this screening

test during pregnancy, preferably at the 28 week antenatal appointment. This is so the woman can have a second opportunity to be informed about the benefits of being screened.

If, during pregnancy, the woman changes her partner or is worried that she may have contracted HIV, hepatitis B, or syphilis, the midwife can repeat the test at any time during the pregnancy.

Screening test

The recommended method for initial screening is an automated enzyme immunoassay (EIA) test.

Screening test result

A negative syphilis screening test result means the woman does not have syphilis infection at time of testing.

Syphilis screening tests cannot always distinguish between syphilis and other non communicable diseases, e.g. yaws, pinta, bejel or a previously treated syphilis infection. The laboratory result therefore needs expert interpretation by a consultant microbiologist/virologist before the result is issued.

Women should only be given a syphilis positive result by health professionals with suitable skills and knowledge. An information leaflet for women who are syphilis positive is available at: www.antenatalscreeningwales.org.

Care following a syphilis antibody positive result

Women with a confirmed syphilis positive result should have an urgent referral to a specialist in the GUM/Sexual Health Service for assessment, counselling and possible treatment.

Treatment with antibiotics (if required) should be commenced promptly by the GUM/Sexual Health Service specialist to reduce the risk of fetal damage caused by maternal to fetal transmission of syphilis. The risks to the baby should be explained to the woman.

Rubella

Clinical information

Rubella (German measles) usually presents as a mild infection, with non-specific symptoms:

- erythematous rash
- lymphadenopathy
- arthralgia.

In non-immunised populations rubella is common among children aged four to nine years.

Vaccination provides long-term immunity in 95% of recipients.

Maternal rubella and risk to the fetus

Maternal rubella infection in pregnancy can lead to congenital rubella syndrome (CRS).

Maternal rubella in the first eight to ten weeks of pregnancy results in severe fetal damage in up to 90% of infants.

The risk of fetal damage declines to 10 to 20% for infection at 16 weeks gestation and after this stage fetal damage is rare (Department of Health 2006).

Congenital rubella syndrome

Maternal rubella infection in early pregnancy may result in a miscarriage or CRS.

CRS presents with one or more of the following clinical signs and symptoms:

- cataract and eye defects
- deafness
- cardiac abnormalities

- intrauterine growth restriction
- inflammatory lesions of brain, liver, lungs or bone marrow
- learning disability.

Only two conditions commonly occur in isolation:

- sensorineural deafness
- pigmentary retinopathy.

Incidence

- Before the introduction of routine immunisation, rubella was common among children aged four to nine years. Epidemics of rubella occurred every six to nine years (NPHS Wales 2010).
- Rubella immunisation was introduced in the UK in 1970 for pre-pubertal girls and non-immune women of childbearing age, to protect them from the risks of rubella in pregnancy.
- Before the introduction of rubella immunisation, there were as many as 70 cases of CRS during epidemic years (NPHS Wales 2010).
- A small number of women do not seroconvert following immunisation.
- In Wales, the number of confirmed cases of rubella is low with only nine cases recorded from January 2000 to July 2008. There have been no cases of CRS in Wales in recent years.
- Women living in the UK who were born abroad are more likely to be susceptible to rubella than those born in the UK (Hardelid et al. 2009).

Screening for rubella susceptibility

Screening for rubella susceptibility in pregnancy is to identify women who should be offered immunisation with measles, mumps and rubella vaccine (MMR) following completion of the pregnancy to reduce the risk of CRS in subsequent pregnancies.

Screening test

- Whenever possible, the sample should be taken before 13 weeks of pregnancy.
- The sample is tested using a sensitive quantitative immunoassay capable of reporting results in IU/ml.
- If the woman has a recent history and/or current viral type rash, she should be offered diagnostic testing for rubella and viral studies.

NOTE: The screening test only screens for rubella susceptibility and does not screen for congenital rubella syndrome.

Screening test result

Rubella 'not susceptible' screening result means that rubella antibody levels are 10 IU/ml or greater.

The screening test can give a false impression of immunity, if the woman has a recent or current rubella infection at the time of the screening test.

Women with screening results with antibodies less than 10 IU/ml should be considered susceptible to rubella infection and offered immunisation with MMR post delivery.

Post test counselling is essential to ensure that women who are susceptible to rubella can be advised of the benefit of postpartum vaccination to protect future pregnancies.

Pregnant women should be advised to report any contact with rubella or symptoms of rubella infection to the professionals caring for them.

An information leaflet for women who are susceptible to rubella is available at: www.antenatalscreeningwales.org.

Care following a rubella susceptible result

Women should not be immunised if they are known to be pregnant, however, termination of pregnancy is not recommended following inadvertent immunisation during pregnancy. There is good evidence that immunisation against rubella in pregnancy has an adverse effect on the baby.

When the pregnancy is completed, the first immunisation with MMR must be offered and provided by the maternity service to women who are rubella susceptible.

The midwife should inform the woman that she requires a second MMR vaccination at her GP surgery in four weeks after the first MMR vaccination. This information needs to be documented on the discharge letter.

Women should avoid pregnancy for a least one month following vaccination.

There are no contraindications to breastfeeding following vaccination.

Sickle cell and thalassaemia

Clinical information

Sickle cell disorders

Sickle cell disorders are genetic conditions where an individual inherits unusual types of haemoglobin, one of which is sickle haemoglobin which affect the ability of the haemoglobin to function normally and results in chronic multi-system organ disease. The characteristics of sickle cell disease are chronic anaemia, sequestration of red cells in the spleen and lung, pneumococcal sepsis, stroke and painful crisis.

Polymerisation of haemoglobin within the red blood cell occurs in the presence of deoxygenation, infection, dehydration and stress. This causes the cells to 'sickle', i.e. to change shape from flexible disc shaped cells to ridged structures which sometimes resemble the shape of a farmer's sickle. The cells tend to clump together and block blood vessels causing hypoxia and pain.

There are many different haemoglobin gene variants and some are more clinically significant than others. Significant haemoglobin gene variants include sickle cell, haemoglobin C, haemoglobin D, haemoglobin E, haemoglobin O and haemoglobin Lepore.

The disorder can be disabling and life threatening and symptoms may include:

- chronic haemolytic anaemia
- jaundice
- painful crisis
- organ damage where 'sickling' occurs
- susceptibility to infections
- strokes in childhood.

Sickle cell disorders and pregnancy

There are a number of problems associated with sickle cell disorder during pregnancy, labour and in the immediate postnatal period. All pregnant women with a sickle cell disorder should receive specialist obstetric and haematological care.

Thalassaemia

Thalassaemias are haemoglobin gene variants that affect the production of a globin chain. They are classified according to the chain which is inefficiently produced, i.e. alpha or beta thalassaemia.

Alpha thalassaemia is characterised by an inability to produce the alpha chains, and the more alpha globin genes that are deleted, the more serious the condition. Alpha thalassaemia major is incompatible with extra uterine life.

Beta thalassaemia disorders are characterised by an absence or reduced output of the beta globin chain synthesis and result in a reduced production of haemoglobin causing varying degrees of anaemia. Beta thalassaemia major can be life threatening requiring regular blood transfusion and iron chelation for survival.

People with beta thalassaemia can be treated with regular blood transfusions, iron chelation therapy, and potentially bone marrow transplants.

Without treatment severe symptoms of beta thalassaemia major appear in the first two years of life. Children become severely anaemic between the age of three and eighteen months. Without treatment, children with beta thalassaemia typically do not live beyond early childhood.

All pregnant women with a thalassaemia disorder should receive specialist obstetric and haematological care.

Prevalence

The chances of being a carrier of sickle cell or thalassaemia are higher for certain groups, as illustrated in Table 4.

Table 4: Prevalence of haemoglobinopathies

Ethnic origin	Chance of carrying sickle cell or thalassaemia
West Africa	1 in 4
Cyprus	1 in 7
Afro-Caribbean	1 in 10
Gujarati Indian	1 in 10
Pakistan	1 in 17
Thailand	1 in 20
China/Hong Kong	1 in 20

With population movement, sickle cell and thalassaemia are increasingly common in countries of Northern and Western Europe.

In the UK, it is estimated that 240,000 people are carriers of the sickle cell gene variant and over 12,500 people have a sickle cell disease (Streetly 1997).

Wales

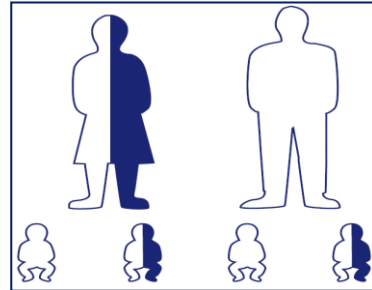
Wales has a low prevalence of sickle cell disorders and thalassaemia major with approximately 15 pregnancies a year predicted to be 'at risk' of the child having either sickle cell disorder or thalassaemia major.

Inheritance of sickle cell or thalassaemia disorders

The vast majority of sickle cell and thalassaemia disorders are inherited in an autosomal recessive manner, which means an individual needs to inherit the gene variant **from both parents** in order to have the clinical features of the condition.

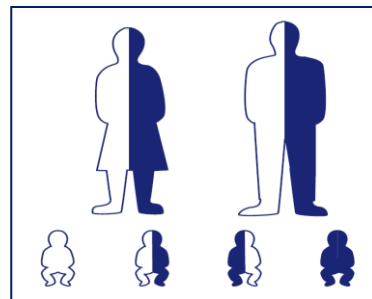
If one parent is a carrier and one is not, there is a 1 in 2 chance of the baby inheriting the haemoglobin gene variant from one parent and a normal gene from the other, i.e. the child would be a carrier (see figure 1).

Figure 1



If both parents carry an abnormal gene (see figure 2.) there is a:

Figure 2



- 1 in 4 chance of the baby inheriting a normal haemoglobin gene from both parents
- 2 in 4 chance of inheriting the sickle cell or thalassaemia gene from one parent and a normal haemoglobin gene from the other, resulting in a carrier state
- 1 in 4 chance of the baby inheriting the sickle cell or thalassaemia gene from both parents.

Screening for sickle cell and thalassaemia

The woman should be offered laboratory screening for sickle cell and thalassaemia in every pregnancy if one or more of the following applies:

- the woman or the biological father of the baby has a family history of sickle cell or thalassaemia
- the woman's family origins or those of the biological father, no matter how many generations back, are from anywhere outside of the UK or Republic of Ireland
- the woman's family origins or those of the biological father are unknown, e.g. the woman was adopted
- the woman has a history of unexplained anaemia.

If the screening process (including screening the biological father of the fetus if required) is performed in a timely manner, CVS rather than amniocentesis may be a preferable option for women who wish to access diagnostic testing.

Laboratory screening

This requires a full blood count sample (FBC) i.e. 4ml of venous blood in an EDTA vacutainer bottle. If a sample for FBC or Hb is being taken, then the request can be added to the FBC request and the same sample used, provided that it is a full sample.

Electrophoresis or HPLC (high performance liquid chromatography) or IEF (iso-electric focusing) identifies most haemoglobin variants present.

The Hb A₂ is measured as part of the FBC and a level above 3.5% is usually diagnostic of beta thalassaemia (normal Hb A₂ is 1.5 to 3.0%).

The screening algorithm used by the laboratory will not detect all haemoglobinopathies.

Correct recording of the woman's and the biological father of the baby's ethnic origin is very important as it is used by the laboratory to interpret the blood results.

Additional tests and investigations and partner sample may be requested as advised by the laboratory.

General guidance on the risk to the fetus and laboratory tests is available in the Handbook for Laboratories and is available at: www.sct.screening.nhs.uk/.

Re-testing in subsequent pregnancies

Haemoglobinopathies are genetic conditions so the result will not change. If the woman has previously been screened, she should still be offered screening in this pregnancy and the laboratory can decide whether to re-issue the original result or re-screen the sample, using the criteria set out in the Handbook for Laboratories.

Iron deficiency anaemia

Reduction in the MCH should be assumed to be due to a haemoglobinopathy and investigated by the laboratory. It may be appropriate for the laboratory to simultaneously investigate pregnant women for iron deficiency, using ferritin but this is not specifically part of the screening protocols.

Screening test result

If no haemoglobinopathies are found the woman should be informed that the chance of her having a child affected by a sickle cell disorder or thalassaemia major is very low.

If haemoglobinopathies are found or suspected the woman should be given the result by an appropriately trained professional.

The chance of the fetus having a clinically significant disorder will depend on whether the biological father of the fetus is also a carrier of sickle cell or thalassaemia. Urgent testing of the biological father of the baby should be offered.

If a blood sample from the biological father of the baby is requested by the laboratory, it is important that the request card includes the following information to enable the maternal and paternal results to be considered together (see figure 3).

Figure 3: Suggested information required on request

Urgent antenatal sample
Name, date of birth and address of the biological father of the baby.
PARTNER OF *** (name and date of birth of the antenatal woman).
Name of lead health professional (i.e. the female partner's lead health professional) and location for report.
Date sample taken.

If this sample is not available the haematologist can advise on the risk to the fetus based on the ethnicity of the biological father of the baby.

The woman may be offered antenatal diagnostic testing after the risk to the fetus has been established by a haematologist.

If antenatal diagnostic testing is declined, neonatal sickle cell testing should be recommended.

Further information on haemoglobinopathies, including patient information on specific conditions is available from the APOGI website: www.chime.ucl.ac.uk/APoGI/.

Down's syndrome

Clinical information

Down's syndrome (also known as Trisomy 21) is the most common chromosomal anomaly and is caused by abnormalities involving the presence of additional genetic material associated with chromosome pair 21.

Adults with Down's syndrome can live partly-independent lives, choosing their friends and partners and working or contributing to society in other ways. They may need help with caring for themselves.

Predisposing factors for Down's syndrome:

- increasing maternal age (see Table 5).
- a family history of Down's syndrome may indicate an increased risk for Trisomy 21 if the trisomy is due to a chromosome translocation. The risk is dependent on the type of translocation and advice should be obtained from the All Wales Medical Genetic Service if there is a family history of Down's syndrome or if the woman has had a previous pregnancy affected by Down's syndrome.

Table 5: Age related chance of having a baby with Down's syndrome

Mother's age when she gives birth (in years)	Chance of having a baby with Down's syndrome
20	1 in 1477
25	1 in 1340
30	1 in 938
35	1 in 353
40	1 in 86
45	1 in 36

Clinical features

People with Down's syndrome are affected in different ways. All have some learning disability. For some people this is mild, for others it is more severe.

Most can lead nearly independent adult lives, but some need more support than others.

Some also have medical conditions, such as heart problems. Many of these conditions can be treated.

About 20% of children with Down's syndrome die before the age of five.

Characteristics of Down's syndrome are variable:

- learning difficulties
- delayed development
- reduced muscle tone (hypotonia)
- broad hands, short fingers, little finger curves inwards
- deep cleft between 1st and 2nd toe with long crease on side of foot
- single palmar crease
- eyes slant upwards and outwards – extra epicanthic fold
- back of head and neck flat
- flat nasal bridge
- Brushfield spots may be visible – grey to white spots resembling grains of salt around the periphery of the iris
- smaller oral cavity, larger protruding tongue
- below average weight and length at birth.

Associated health problems

- congenital cardiac defects – about 45 to 50%

- chest and sinus problems
- feeding difficulties/gastrointestinal problems
- poor temperature control
- poor tongue control
- vision – 70% of children with Down's syndrome need glasses by age seven
- hearing problems – about 50%
- Alzheimer's disease may affect people with Down's syndrome at an earlier age than other people
- Leukaemia, epilepsy, thyroid disorders
- mean life expectancy is 55 to 60 years.

Incidence of Down's syndrome

Overall Down's syndrome usually occurs approximately once in every 500 pregnancies with the incidence increasing with increasing maternal age.

Antenatal screening for Down's syndrome

Antenatal screening for Down's syndrome is to identify pregnant women who have an increased chance of having a baby with Down's syndrome to enable them to decide whether to have diagnostic testing and, if necessary, make choices about continuing the pregnancy.

The screening tests commonly available for Down's syndrome screening involve the use of ultrasound measurements of the fetus and a blood test for biochemical markers to adjust the woman's age related risk.

The screening test which is recommended in the first trimester is the 'Combined Test' (NICE 2008a; UK NSC 2008). This test uses an ultrasound measurement to assess the gestation, a measurement of the fetal neck (the nuchal translucency or NT) with the results from the biochemical markers.

The screening test which is recommended in the second trimester is the 'Quadruple test'. These tests use an ultrasound measurement to assess the gestation and the results from four biochemical markers.

Comparisons between first and second trimester tests are difficult as some cases result in a spontaneous fetal loss before second trimester screening.

Down's syndrome screening risk threshold

The diagnostic follow-up test performed after Down's syndrome screening can result in spontaneous fetal loss, so a careful balance needs to be found between the desire to detect all Down's syndrome cases and to avoid unnecessary fetal loss.

A balance has to be found between a lower detection rate and a higher screen positive rate. This decision is reflected by the risk threshold (or the level at which 'higher chance' is defined) used by the programme.

Small changes in the screen positive rate affect many more pregnancies than a modest change in the detection rate.

The UK NSC has recommended a detection rate greater than 75% for a screen positive rate of less than 3%.

Using a risk threshold of 1 in 150 the:

- Triple test can detect about 70% of affected pregnancies for about a 4% screen positive rate
- Quadruple test can detect about 75% of affected pregnancies for about a 3% screen positive rate
- Combined test can detect about 85% of affected pregnancies for about a 3% screen positive rate.

More information is available in the ROC curve section at: www.fetalanomaly.screening.nhs.uk/dqasspublications.

Samples can be taken for the Triple test between 15⁺³ and 18⁺⁰ weeks (gestation must be confirmed by ultrasound).

Samples taken earlier or later than these gestations cannot be reported.

If the sample is taken at the correct time but the laboratory is unable to report a result, the woman should be offered a discussion to consider whether alternative options are available. This may include offering an amniocentesis based on maternal age or screening by a laboratory able to provide testing in pregnancies up to 20 weeks of pregnancy.

Blood sample requirements

Triple test samples being processed at the Cardiff biochemistry laboratory; require 3mls of venous blood in a serum separator tube (SST).

If blood is being taken for multiple tests at one time, the Down's syndrome screening sample bottle must be filled first as contamination from the EDTA in other blood vacutainers can affect the result.

The sample request form must be fully completed as the information is required to enable accurate risk assessment.

An accurate weight of the woman is required because her weight is used to adjust the serum concentration of the Down's syndrome markers and forms part of the risk calculation.

The Triple test is not suitable for women with multiple pregnancies.

Note: If second trimester screening is offered and there is a history of vaginal bleeding during pregnancy there is potential for this to increase the maternal serum alpha fetoprotein (AFP) and could affect the final risk for Down's syndrome. If timescales allow, it is preferable to delay taking the sample for

one week after the bleeding has stopped as the presumed effect of the bleeding cannot be adjusted for by the laboratory.

Results

About 95 to 97% of women will receive a lower chance Down's syndrome screening result.

Around 3 to 5% of women will receive a higher chance result (result between 1 in 2 and 1 in 150) and should be offered diagnostic tests.

A higher chance result should not usually be given during the weekend or on Friday afternoon unless the woman has access to health professionals who can discuss the result and give accurate information about diagnostic tests.

Care following a higher chance result

An appointment should be made for the woman to discuss the result, with the antenatal screening coordinator or other health professional with suitable skills and knowledge, within 24 hours of the result being given.

The woman should be offered a diagnostic test (i.e. CVS or amniocentesis) appropriate to her gestation.

Ultrasound scans

Introduction

Ultrasound screening scans are to detect fetal problems and to support pregnancy management.

Women should be informed of the limitations of routine ultrasound screening and that detection rates vary by the type of fetal anomaly, the woman's body mass index and the position of the unborn baby at the time of the scan (NICE 2008a).

The detection rates in Table 6 below are derived from a number of major references (see www.fetalanomaly.screening.nhs.uk/).

Table 6: Potential detection rates achieved by ultrasound scanning

Potential Detection Rates	
Anencephaly	98%
Open spina bifida	90%
Cleft lip	75%
Diaphragmatic hernia	60%
Gastroschisis	98%
Exomphalos	80%
Serious cardiac abnormalities	50%
Bilateral renal agenesis	84%
Lethal skeletal dysplasia	60%

Ultrasound when used as a screening test has a number of limitations:

- it may give false reassurance to the woman
- the absence of abnormalities does not guarantee a normal baby as many conditions cannot be diagnosed by ultrasound scans
- some abnormalities may not become detectable by ultrasound until the third trimester

- fetuses with chromosomal abnormalities cannot be **diagnosed** by ultrasound.

Two routine scans should be offered to women.

- An early pregnancy scan before 13⁺⁶ weeks to determine viability, gestational age and detect multiple pregnancies (fetal number and chorionicity/ amnionicity).
- Fetal anomaly scan at 18⁺⁰ to 20⁺⁶ weeks to detect significant structural fetal anomalies.

Test requesting

Accurate demographic and relevant clinical information must be included on the ultrasound request form as this may affect the sonographers' communication with the woman and the interpretation of the scan.

Early pregnancy scan findings

The information from the scan supports pregnancy management and other screening tests:

- measurements to determine the gestational age are required for the Down's syndrome screening programme and to support first trimester screening where available
- using ultrasound derived gestation reduces the need for post term induction of labour (NICE 2008a)
- pregnancy management in multiple pregnancies can be instigated.

Although it is not the primary purpose of the scan, some abnormalities may be observed at the early pregnancy scan.

Major abnormalities:

- anencephaly
- large encephalocele
- renal agenesis – no bladder present
– no amniotic fluid

Anomalies potentially treatable in utero:

- obstructive uropathies

Anomalies associated with abnormal karyotype:

- cystic hygroma
- increased nuchal translucency

Fetal anomaly scan findings

Fetal anomaly ultrasound scans are only able to detect a proportion of structural abnormalities due to the limitations of the test.

The sonographer will try to complete the agreed All Wales scan checklist. There is, however, a number of reasons why it is sometimes not possible and it is helpful if these are explained to the woman before the scan, e.g.:

- maternal habitus or body mass index
- uterine fibroids
- abdominal scarring
- fetal considerations such as a suboptimal fetal position.

If an appropriate image cannot be obtained to allow the standard checklist to be completed the woman will usually be offered one further fetal anomaly scan.

A 'completed fetal anomaly scan' does not mean that all the structures are necessarily normal or that there are no abnormalities, but only means that the scan has been completed to the required standard.

Results

Early pregnancy and fetal anomaly ultrasound scan results are usually discussed with the woman following the scan.

Care following an abnormal scan finding

If the pregnancy is ongoing and a problem is identified, the woman should be seen by an appropriately trained midwife or obstetrician to discuss the findings within 24 hours.

Screening for neural tube defects

The screening test for open spina bifida is the fetal anomaly scan performed between 18⁺⁰ and 20⁺⁶ weeks gestation.

Using raised AFP levels as a screening test for open spina bifida is no longer recommended by the UK NSC and has been discontinued in Wales for a number of years.

The fetal anomaly scan has a 90% detection rate for open spina bifida. In a small number of cases the presentation of open spina bifida is unusual and may not be detected on the scan.

Blood group and antibodies

Clinical information

There are four main blood groups which are group O, group A, group B and group AB (called ABO). There is also another blood group called the Rhesus (RhD) group.

RhD factor is a protein found in red blood cells in about 85% of people and its presence denotes a person is RhD-positive. If it is absent, the person is RhD-negative.

Where the woman is RhD-negative and the baby is RhD-positive there is the possibility of maternal antibodies being produced and passing from the maternal bloodstream into the fetus causing haemolytic disease of the newborn (HDN).

In clinical terms, RhD antibodies are the commonest and most significant, but a number of other red cell proteins (such as Kell, c, Duffy and Kidd) may also cause maternal IgG antibody production, leading to similar problems to those caused by RhD antibodies.

Incidence

The incidence of HDN depends on the proportion of the population who are RhD-negative and this varies within ethnic groups; in the UK it is highest amongst the white population (about 15 to 16%) (NICE 2008b).

RhD alloimmunisation and pregnancy

- RhD alloimmunisation occurs in about 6 in 1,000 births (Moise 2008)
- with prophylactic treatment, the current risk of RhD alloimmunisation in the UK is about 1 in 21,000 births.

In England and Wales, it is estimated that fetal anaemia and HDN could lead to approximately 37 fetal or neonatal deaths, 21 children with minor developmental problems and eight children with major developmental problems (NICE 2008b).

Inheritance patterns

In genetic terms, the RhD-positive allele is dominant (D) and the RhD-negative allele (d) is recessive.

Figure 4

Consequently, there are three possible genetic pairs for Rh alleles as shown in figure 4.

Genes	Blood Type
<i>DD</i>	RhD-positive
<i>Dd</i>	RhD-positive
<i>dd</i>	RhD-negative

There are a number of possible combinations of RhD types in parents but the possibilities outlined here are only those that occur where the woman is RhD-negative, because RhD-positive women are not affected by this issue.

If both of the parents are RhD-negative, all babies will be RhD-negative.

If the woman is RhD-negative and the biological father is RhD-positive, the genetic (and potential clinical) outcomes are dependent upon whether the baby's biological father is homozygous RhD-positive or heterozygous RhD-positive.

- If the father is homozygous RhD-positive (DD), all of his children will inherit one RhD-positive allele from him (and one RhD-negative allele from their mother) and all of the couple's babies will be heterozygous RhD-positive (see figure 5).

Figure 5

	<i>D</i>	<i>D</i>
<i>d</i>	<i>Dd</i>	<i>Dd</i>
<i>d</i>	<i>Dd</i>	<i>Dd</i>

- If the father is heterozygous RhD-positive (Dd), his children will have a 50% chance of inheriting an RhD-positive allele from him and a 50% chance of inheriting an RhD-negative allele from him. Around 55% of RhD-positive men are thought to be heterozygous (see figure 6).

- If the baby inherits the RhD-positive allele from their father, they will be heterozygous RhD-positive.

Figure 6

	<i>D</i>	<i>d</i>
<i>d</i>	<i>Dd</i>	<i>dd</i>
<i>d</i>	<i>Dd</i>	<i>dd</i>

- If the baby inherits the RhD-negative allele from their father and mother they will be RhD-negative.

Screening for blood group and antibodies

Antenatal screening for grouping and maternal RhD antibodies is to:

- identify pregnancies at risk of HDN
- reduce the risk of alloimmunisation by:
 - identifying RhD-negative women who require antenatal anti-D immunoglobulin (Ig) prophylaxis
 - identifying RhD-negative women who require postnatal anti-D immunoglobulin (Ig) prophylaxis.

Screening test

The screening test should be offered and the sample taken before 13 weeks of pregnancy and once again at around 28 weeks of pregnancy regardless of RhD status (British Committee for Standards in Haematology (BCSH) 2008; NICE 2008a).

Antibody screening should be undertaken using an indirect antiglobulin test and a red cell panel conforming to current UK guidelines (NICE 2008a).

If anti-D immunoglobulin has been administered during pregnancy it is important to document this on the request form as this may affect the interpretation of the antibody screen.

Results

RhD-positive

The woman should be informed that she is RhD-positive and will not require anti-D prophylaxis. Further screening for atypical red cell alloantibodies is advised at around 28 weeks of pregnancy (BCSH 2008; NICE 2008a).

RhD-negative

The woman should be informed of the implications of being RhD-negative. All women who are RhD-negative should receive verbal and written information about antenatal and postnatal anti-D prophylaxis and have the opportunity to discuss this treatment with a midwife in the antenatal period.

NICE (2008a) has recommended that routine antenatal anti-D prophylaxis is offered to all non-sensitised pregnant women who are RhD-negative.

Anti-D immunoglobulin should be offered to a RhD-negative mother as a preventative treatment following a potentially sensitising event, e.g.:

- miscarriage
- ectopic pregnancy at any gestation
- threatened miscarriage after 12 weeks gestation
- following invasive procedures such as amniocentesis, CVS or cord blood sampling
- maternal abdominal trauma
- antepartum haemorrhage
- post delivery.

Kleihauer screening should be offered following a potentially sensitising event in pregnancy after 20 weeks gestation or after birth.

Antibody positive results

If antibodies are detected they should be identified and if necessary quantified by the laboratory to assess the likelihood of HDN.

There are a large number of potential antibodies which can cause HDN but anti-D, anti-c and anti-Kell are the antibodies most often implicated in causing HDN.

If significant antibodies are found the woman should be transferred to consultant led care and may need referral to a fetal medicine unit.

Section 4: Additional information

Taking and sending blood samples to laboratories

Patient identification

Correct sample identity is vital and the midwife must ensure they ask the woman to state her name, date of birth and address when taking a sample. These must be identical to the information on the request form and the information on the sample. Health Boards may have additional guidance on ensuring correct sample identity.

Request card completeness

All mandatory fields on the laboratory request must be completed and the health professional requesting the screening test must accurately complete and sign the request form.

Sample transport

Note: Delay in sending samples to the laboratory may mean the sample is not processed.

Blood samples should always be sent straight to the hospital laboratory. Samples stored at room temperature for a prolonged period of time will probably produce an unreliable result.

The midwife should consider whether it would be more appropriate to delay taking samples if it is likely they will arrive at the laboratory on a weekend, or public holiday. If in exceptional circumstances this is not possible, samples can be stored and refrigerated in a specially designed fridge for the following maximum duration as set out in Table 7 overleaf.

Packaging of samples

All Health Boards should have specific guidance for the packaging of samples.

Pathology samples are classified by the United Nations (UN) as Dangerous Goods (Division 6.2 and assigned to UN3373) and must be packaged for transport in a way that meets the requirements of UN packaging instruction P650.

Table 7: Sample storage

Test	Maximum duration and storage requirements
Blood group and antibody screening	24 hours or sample can be stored at 4°C in a specially designed fridge to reach the laboratory within five days.
Sickle cell and thalassaemia screening	24 hours or sample can be stored at 4°C in a specially designed fridge to reach the laboratory within five days.
Screening for HIV, hepatitis B, syphilis and rubella susceptibility	24 hours or sample can be stored at 4°C in a specially designed fridge to reach the laboratory within seven days.
Down's syndrome screening	24 hours or the sample must be centrifuged (spun) by a laboratory within 24 hours of it being taken and stored in a specially designed fridge and must reach Cardiff biochemistry laboratory within six days.

Screening test results

Communicable diseases, sickle cell and thalassaemia and blood group and antibodies screening results should be available to the woman within 15 working days of the sample being taken.

Women with a lower chance Down's syndrome screening result should be informed of the result by the maternity service within 10 working days of the sample being taken.

Where a problem is found the result will be fast-tracked and the information given to the woman as soon as possible and usually within a week of the sample being taken.

Early pregnancy and fetal anomaly ultrasound scan results are usually discussed with the woman following the scan.

Amniocentesis and CVS fact sheet

Amniocentesis and chorionic villus sampling (CVS) are procedures that enable the diagnosis of chromosomal anomalies (most often Down's syndrome) and Mendelian genetic disorders (e.g. inborn errors of metabolism) by obtaining tissue (or fluid) of the same genetic origin as the fetus for diagnostic purposes.

When is the procedure performed?

Amniocentesis

Amniocentesis is usually performed after 15 weeks of pregnancy and most commonly between 15 and 20 weeks of pregnancy.

CVS

CVS can be performed after 10 weeks of pregnancy, but is more commonly performed between 11⁺⁰ and 13⁺⁶ weeks.

What happens during the procedure?

An ultrasound scan is performed before the amniocentesis and CVS to check the position of the baby and the placenta to assess the best location for:

- taking a sample of amniotic fluid in an amniocentesis
- taking a sample of placental tissue in a CVS.

These procedures are performed under continuous ultrasound guidance.

Amniocentesis

A needle is passed through the abdomen and then a syringe is used to withdraw a small amount (15 to 20mls) of amniotic fluid from around the baby. The amniotic fluid in the uterus will be replenished quickly.

Some doctors numb the skin first with a local anaesthetic but the research evidence suggests that local anaesthetic does not

reduce pain scores (RCOG 2005). Therefore, the use of local anaesthesia is not common practice.

CVS

There are two ways of performing a CVS (the choice of route will depend on the position of the placenta and experience of the operator):

1. Transabdominal route (used most commonly)
A local anaesthetic injection is used to numb the abdomen. A needle is pushed through the abdomen and then a syringe is used to withdraw a small amount of placental tissue.
2. Transcervical route (rarely performed)
A speculum is inserted into the vagina and fine forceps or a cannula is inserted through the cervix to the placenta.

A small amount of placental tissue is removed, using either forceps or a suction catheter.

After both procedures the woman may be asked to stay in the clinic for about half an hour to rest. Occasionally the procedure cannot be performed on the day of the appointment due to the position of the baby in an amniocentesis or the position of the placenta or insufficient placental tissue in a CVS. The woman will be offered another appointment.

Discomfort during the procedure

Some women may feel mild cramp like pain, or pressure during the procedure or they may feel no discomfort at all. The amount of discomfort or pain varies among women and from one pregnancy to the next.

Some women may experience mild cramps (like period pains) after the procedure that should subside after 48 hours.

Length of the procedure

Amniocentesis

The whole procedure takes about 10 minutes, but this depends on the position of the baby, the amount of amniotic fluid and the location of the placenta.

CVS

The whole procedure takes about 20 minutes. The sample will be examined to see if there is enough placental tissue to do the test. If not, another sample will be taken. Sometimes CVS may not be performed on the day because it may not be possible to safely access the placenta. This may be due to placental position. Allowing extra days for the placenta to grow, may then make it possible at a later date.

Does the procedure harm the baby?

Amniocentesis

Direct injury to the baby from amniocentesis is very rare with continuous ultrasound guidance. The doctor will avoid placing the needle near the baby, however, it is difficult to stop the baby moving towards the needle. The aspiration needle is fine and pliable.

CVS

Performing CVS after 10 completed weeks of pregnancy has decreased the risk of harm to the baby.

Bringing a partner or friend

A partner, friend or a family member can be with the woman during the procedure. It is not advisable to bring children, as childcare facilities are not provided.

Eating and drinking

A woman will be able to eat and drink as normal before and after the procedure.

Miscarriage rate

Amniocentesis

The risk of causing miscarriage by amniocentesis, derived from research studies, is about 1% (one in 100 procedures) (Tabor et al. 1986 cited in RCOG 2005; RCOG 2006).

CVS

The risk of miscarriage is about 2% (one in 50 procedures) following CVS (RCOG 2006). This is higher than the post amniocentesis miscarriage rate. However, the background risk of miscarriage is higher in early pregnancy; this may contribute to the higher miscarriage rate for CVS.

Local or individual data is of variable quality and the number of procedures performed may not be large enough to reach statistical significance and should not usually be used, particularly if women are seeking reassurance that the miscarriage rate is lower than quoted above.

Causes of miscarriage and when it is more likely to occur

Amniocentesis and CVS

The exact cause of the miscarriage following an amniocentesis or CVS is unknown. Miscarriage following the procedures is thought to be due to infection or bleeding but the mechanisms are not proven.

There is currently no evidence to answer the question frequently asked by women regarding if or when a post amniocentesis miscarriage is likely to occur.

When miscarriages happen clinical experience suggests that miscarriage occurs up to two weeks following the procedure and that the risk diminishes after three weeks. Pregnancy outcomes following amniocentesis and CVS are currently being audited, and more information on this issue may become available.

Activities to prevent miscarriage occurring

It is not possible for the woman to prevent a miscarriage after amniocentesis or CVS. Although there is no evidence, some doctors advise that women should take things easy for a couple of days and avoid intercourse, heavy lifting and strenuous exercise. Resting in bed is not necessary.

Women are advised to arrange for someone to drive them home after the procedure.

Cytogenetic results

Difference between polymerase chain reaction (PCR) marker analysis and karyotyping

Unlike karyotyping, PCR marker analysis is a test that does not require cell culture. PCR results can therefore be obtained quickly. The PCR test usually only looks for defined chromosome problems in the baby. Usually there are two copies of each chromosome. However, in Down's syndrome, there are three copies of chromosome 21 (Trisomy 21), in Edwards' syndrome three copies of chromosome 18 (Trisomy 18) and in Patau's syndrome three copies of chromosome 13 (Trisomy 13). If monosomy X (Turner's syndrome) is suspected, an additional PCR test is performed to look for the sex chromosomes.

The PCR result is usually available within three working days. Occasionally karyotyping results from CVS may be inconclusive because of an abnormal cell line confined to the placenta. This may then require further testing by amniocentesis later in the pregnancy.

PCR result

This test is very accurate, but can only give information about the chromosomes being tested. A result from a rapid test will confirm whether the baby either does or does not have Down's syndrome, Patau's syndrome or Edwards' syndrome. However, other changes involving other chromosomes can occur. Between 2 and 5%, (two to five out of a hundred, depending on the

laboratory) of amniotic fluid PCR samples fail to yield a reportable result, mainly because of maternal cell contamination of the amniotic fluid. More accurate figures should be available from the local laboratory.

Karyotype result

Karyotyping involves culturing or growing the cells floating in the amniotic fluid before they can be examined under the microscope. The cells take about 10 days to grow in the laboratory.

It therefore takes longer to get a result. The test looks at changes in the number and appearance of all the chromosomes. The result from the karyotype test usually comes back within two to three weeks.

On occasions, even though the PCR does not produce a result which indicates Trisomy 21, 18 or 13, there could still be another abnormality in the chromosome make-up that is picked up on karyotyping (if karyotype is offered locally).

Does a normal karyotype mean there is nothing 'wrong' with the baby?

Some chromosome changes are so small that they are invisible even when viewed under the microscope.

The karyotype test will not detect:

- alterations in single genes, such as cystic fibrosis (each chromosome contains thousands of genes);
- microdeletions (loss of small segments of a chromosome); or
- other small changes in chromosomes.

A 'normal' chromosome result therefore means that the baby appears to have normal chromosomes, but this does not rule out all abnormalities.

A baby's physical development is not shown by this test. The fetal anomaly scan is performed to detect structural anomalies in the baby; however, a scan does not detect all structural abnormalities.

Trisomy 21

- Trisomy 21 or Down's syndrome is the most common chromosome abnormality. Down's syndrome occurs when there is an additional chromosome 21.
- Babies with Down's syndrome can have multiple problems such as heart defects, and severe learning difficulties. Some people with Down's syndrome are able to lead semi-independent lives.
- The birth incidence of this condition in an unscreened population is about 1 in 500 live births.

Severity of the condition

Neither the karyotype nor PCR test can tell how severe the condition will be. A fetal anomaly scan may detect physical abnormalities that are associated with Down's syndrome such as heart defects.

Trisomy 18

- Trisomy 18 or Edwards' syndrome is a very rare chromosome abnormality (about 1 in 3,000 to 6,000 live births). It is less common than Down's syndrome. Edwards' syndrome occurs when there is an additional chromosome 18.
- Babies with Edwards' syndrome can have multiple problems such as heart defects, breathing difficulties, kidney problems and severe developmental delay. Life expectancy for the majority of babies with Edwards' syndrome is usually limited to a few weeks and rarely beyond one year of life.

Trisomy 13

- Trisomy 13 or Patau's syndrome is a very rare chromosome abnormality (1 in 4,000 to 10,000 live births).
- It is less common than Down's syndrome. Patau's syndrome occurs when there is an additional chromosome 13.
- Babies with Patau's syndrome can have multiple, severe problems such as heart defects, brain abnormalities and severe kidney abnormalities.
- Most babies do not live beyond the first weeks of life and few survive beyond one year of life.

Sickle cell and thalassaemia

- Sickle cell disorders and thalassaemia major are serious inherited blood conditions. They affect the haemoglobin in the red blood cells.
- If both parents have the sickle cell or thalassaemia gene, there is a high chance (one in four, or 25%) that their baby may have a sickle cell disorder or thalassaemia major.
- Amniocentesis or CVS procedures will be offered in the antenatal period (as early as possible) to detect if the baby has a sickle cell or thalassaemia disorder.

Results handling

The woman should be informed when she is having the procedure about the local arrangements for handling results.

More information is available at: www.antenatalscreening.org

Newborn hearing screening

Clinical information

Sensorineural hearing loss means that either the cochlea in the inner ear, or the hearing nerve (auditory nerve), is not working as well as it should be. Sensorineural hearing loss is permanent.

Conductive hearing loss means that sound cannot pass effectively through the outer and middle ear to the inner ear. Conductive hearing loss is usually temporary (e.g. as in 'glue ear') but may be permanent (e.g. when the external ear has not formed properly).

Prevalence

In Wales, the prevalence of permanent significant bilateral hearing loss is 1.4 per 1,000 babies.

Screening programme

The purpose of newborn hearing screening is to identify babies with a hearing impairment, which is of sufficient severity to potentially cause a disability without additional help and support in infancy. That is, the screening test aims to identify babies with a permanent significant hearing loss in both ears. Early detection of such hearing impairments leads to improved outcomes in speech and language development and in the general well being of the child and family.

Timing of the tests

Well babies

Newborn Hearing Screening Wales aims to test most (75%) babies' hearing within 7 days of birth. Whenever possible, babies will be tested in hospital, but those who are not seen in hospital, or who require a second screening test and have been discharged will be offered a test at home or in a local clinic.

Babies who spend more than 48 hours on the Neonatal Unit are at higher risk of hearing problems.

High risk babies

Babies who spend more than 48 hours on the Neonatal Unit are at higher risk of hearing problems.

They will be screened once only at 36 weeks or as near to discharge as possible. If discharged before 35 weeks, the screening test will be offered at home.

Babies with significant external ear abnormalities will be referred directly for assessment and will not be screened.

Screening tests

- Automated otoacoustic emissions (AOAE) – this test is used for all well babies. A soft-tipped ear piece is put in the baby's ear. A clicking sound is played and the response from the baby's ear is seen on the machine. The ears are tested separately.
- Automated auditory brainstem response (AABR) – this test is used for all high risk babies, and for well babies who have not shown clear responses on the AOAE test on day one and are due to be discharged. Sticky pads are placed on the baby's forehead, neck and shoulder. Headphones are placed over the ears and a clicking sound is played. The response is seen on the machine. Both ears are tested at the same time.

The screener will give verbal and written information about the result straight after the screening test.

Screening test result

Since newborn hearing screening started in Wales in 2003, the screen has been shown to have a sensitivity of 92.5% and a specificity of 98.8%.

If a baby does not have a clear response on the screening test, it does not necessarily mean the baby has a hearing loss.

Clear responses may also not be seen if there is still fluid in the middle ear following the birth, if the baby is unsettled during testing, or if background noise interferes with the test.

The aim of the screen is to identify babies with a hearing loss in both ears. Up to 25% of babies show a clear response in only one ear on the screen.

Well babies with this result will be discharged from the screening programme but the screener will provide information about the options for another test. High risk babies with this result will be referred for assessment.

Referral for further assessment

Well babies with no clear response in either ear and high risk babies with no clear response in either one or both ears after screening will be referred for hearing assessment with an audiologist. The screener will provide the mother with information about the assessment.

Contact telephone numbers:

- South East Wales: 029 2074 3568
- Mid and West Wales: 01656 754085
- North Wales: 01978 727005

Further information is available on the Newborn Hearing Screening website: www.screeningservices.org/nbhs.

Cervical screening

The cervical screening programme is designed to reduce the incidence, morbidity and mortality of cervical cancer through regular screening and early treatment. The programme detects changes in the cells of the cervix, which if not treated, may eventually lead to the development of cervical cancer.

These changes are described as dyskaryosis and are sometimes referred to as pre-malignant changes. The appearances of these cellular changes vary in severity, and cytology results ranging from mild to severe dyskaryosis may be reported. Depending on the severity of these changes the report may either require repeat follow up samples or require referral for further tests at a colposcopy clinic to determine the nature and extent of any disease that may be present, and provide a definitive diagnosis.

Cervical Screening is not a diagnostic test; it identifies women who are at risk of developing cervical cancer if they have a pre-malignant condition that is not treated.

In most cases the pre-malignant disease will be detected before cervical cancer develops and women can be treated at the colposcopy clinic and cured.

In common with all medical tests, individual screening tests can never be 100% effective, so regular repeat screening is recommended to ensure women receive the maximum level of protection.

Women should, therefore, be encouraged at every opportunity to take up their screening invitation and antenatal appointments provide an important opportunity for midwives to mention the importance of the programme.

Human papilloma virus (HPV)

HPV is considered to be the cause of cervical cancer and an immunisation programme for teenagers and young women is in progress.

Timing of the test

The cervical screening policy in Wales advises that all women should be screened every three years starting at age 20 until the age of 65.

Routine cytology tests in pregnancy

If a woman is pregnant and is due for a routine smear test, CSW advises that the test should be postponed, until her baby has been delivered. The test must not, however, be taken immediately postpartum; CSW advises that a minimum period of 12 weeks is allowed to elapse following childbirth before her smear is taken.

Pregnant women who are on early recall for cytology

If a woman is on 'early cytology recall' because a previous mild abnormality has been seen, it is recommended that her repeat sample is delayed until her baby has been delivered and the test repeated at least 12 weeks post delivery.

Women referred to colposcopy in pregnancy

If a woman becomes pregnant after referral for colposcopy, she may attend any assessment appointment offered.

Colposcopy in pregnancy is a safe procedure, which enables the colposcopist to assess and advise on the appropriate management of the woman's condition following her examination.

If a woman requires follow up colposcopy or cytology following previous treatment but is now pregnant, the assessment can be delayed until after delivery.

Further information on cytology and sampling

Guidance is available through the CSW website:
www.screeningservices.org/

Information is available at: www.cancerhelp.org.uk/about-cancer/cancer-questions/what-is-the-hpv-virus

Section 5: Useful websites and references

Additional sources of information

Antenatal Results and Choices (ARC)

Helpline: 0207 631 0285

Email: Info@arc-uk.org

Website: www.arc-uk.org/

Association for Spina Bifida and Hydrocephalus

Telephone: 0845 450 7755

Website: www.asbah.org/

APoGI - Accessible Publishing of Genetic Information

Gives information on inheritance of, and information on haemoglobin gene variants.

Website: www.chime.ucl.ac.uk/APoGI/menu.htm

Avert (Aids Education and Research Trust)

Telephone: 01403 210202

Email: info@avert.org

Website: www.avert.org/

British Liver Trust

Telephone: 0800 652 7330

Website: www.britishlivertrust.org.uk

Children's Liver Disease Foundation

Telephone: 012 212 3839

Website: www.childliverdisease.org/

Cleft Lip and Palate Association (CLAPA)

Telephone: 020 7833 4883

Email: info@clapa.com

Website: www.clapa.com/

Contact a Family

Telephone: 029 2039 6624

Email: wales.office@cafamily.org.uk

DIPEX

Email: info@healthtalkonline.org

Website: www.healthtalkonline.org & www.youthhealthtalk.org

Down's Syndrome Association National Office

Telephone: 0845 230 0372

Email: info@downs-syndrome.org.uk

Website: www.downs-syndrome.org.uk

Fetal Anomaly Screening Programme

Website: www.fetalanomaly.screening.nhs.uk/

Gastroschisis.co.uk

Website: www.Gastroschisis.co.uk

Genetic Interest Group (GIG)

Telephone: 0207 704 3141

Email: mail@gig.org.uk

Website: www.gig.org.uk

MENCAP

Telephone: 029 2074 7588

Helpline: 08088081111

Email: helpline.wales@mencap.org.uk

Website: www.mencap.org.uk

Support and information available 7 days a week

- Monday to Friday 10.00hrs to 18.00hrs
- Saturday and Sunday 10.00hrs to 16.00hrs.

Miscarriage Association

Telephone: 01924 200799

E-mail: info@miscarriageassociation.org.uk

Website: www.miscarriageassociation.org.uk

Multiple Births Foundation

Telephone: 0208 383 3519

Website: www.multiplebirths.org.uk

National Down's Syndrome Society

Website: www.ndss.org/

NHS Direct 24 hour helpline

0845 4647

NHS Website

www.wales.nhs.uk/

Positively Women (information service for women on HIV & AIDS)

Telephone: Administration 020 7713 0444

Helpline: 020 7713 0222 staffed by HIV positive women
10am–4pm MON-FRIEmail: info@positivelywomen.org.uk**Public Health Wales**Website: www.publichealthwales.org/**S.O.F.T. UK**

Telephone: 0121 351 3122

Email: enquiries@soft.org.ukWebsite: www.soft.org.uk**Sickle Cell Society**

Telephone: 020 8961 7795

Email: info@sicklecellsociety.orgWebsite: www.sicklecellsociety.org**NHS Sickle Cell and Thalassaemia Screening Programme**Website: www.sct.screening.nhs.uk/publications**Stillbirth and Neonatal Death Society (SANDS)**

Telephone: 0207 436 5881

Email: helpline@uk-sands.orgWebsite: www.uk-sands.org**The National Childbirth Trust (NCT)**Telephone: Helpline 0300 330 0772 (9am–5pm Monday–
Thursday and 9am–4 pm Friday)Website: www.nct.org.uk**Terrence Higgins Trust**

Telephone 029 2066 6465

Email: info@tht.org.ukWebsite: www.tht.org.uk/**U.K. Thalassaemia Society**

Telephone: 020 8882 0011

Fax: 020 8882 8618

Welsh Assembly GovernmentWebsite: www.wales.gov.uk

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