Fetal Anomaly Screening- Coverage for Down's, Edward's and Patau's Syndrome

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Key Amendment

Date	Amendment	Approved by
17th Jan 2020	Minor changes throughout document	Maternity Governance

Description of Screening Programme

Down's (Trisomy 21/T21), Edwards' (Trisomy 18/T18) and Patau's (Trisomy 13/T13) syndromes Screening is part of the NHS Fetal Anomaly Screening Programme (FASP). This pathway has been reviewed in line with the national standards for fetal anomaly screening.

The screening policy is to offer screening to assess the risk of the baby being born with Down's, Edwards' or Patau's syndromes. The eligible population is identified through maternity antenatal care services and includes the total number of pregnant women booked for antenatal care excluding women who miscarry, opt for termination or transfer out between booking and testing (ie prior to testing), and women who book later than 14 weeks and 1 day of pregnancy.

For Down's syndrome screening, the eligible population are women with singleton and twin pregnancies <20^{+0} weeks of pregnancy confirmed by ultrasound scan and for Edwards' and Patau's syndromes screening using biochemical markers the eligible population are women with singleton and twin pregnancies ≤ 14^{+1} weeks of pregnancy confirmed by ultrasound scan.

Introduction

Screening for Trisomy T21, 18 and 13 is well established in England. The primary aim of screening is to enable parents to make informed choice concerning their pregnancy outcome. The purpose of this guideline is to ensure that appropriate tests, methods and limitations of screening for the above conditions are outlined.

The test of choice for both singleton and twin pregnancies is first trimester Combined screening. As part of this test, patients can choose from the following options:

- Not to have screening
- To have screening for T21 and T18 / T13
- To have screening for T21 only
- To have screening for T18 / T13 only

For women having first trimester screening (Combined screening), dependant of their screening choice, up to two risks will be reported:

- A risk for T21 and a risk for T18/T13
- A risk for T21 only or T18/T13 only

The test of choice for both singleton and twin pregnancies in second trimester is Quadruple (QUAD) testing. As part of this test, patients can choose from the following options:

- Not to have screening
- To have screening for T21 only

For women having second trimester screening (Quadruple screening), two risks will be reported:

- A risk for T21 only
- A risk for Neural Tube Defect (NTD)

1st trimester screening (Combined test) The optimal time to perform the combined test is between 11 weeks 2 day to 14 weeks 1 day of gestation, which corresponds to a CRL of 45.0mm to 84.0mm. The test uses maternal age, the nuchal translucency ultrasound measurement (NT) and two biochemical tests, free beta HCG and PAPP-A, together with the gestational age calculated from the crown rump length (CRL) measurement, to calculate the risk of the pregnancy being affected by T21 or T18/T13.

If the ultrasound measurement shows that the CRL is less than 45.0mm, the woman should be recalled for a further scan to measure the NT. If the CRL is greater than 84.0mm, the second trimester quadruple test should be offered.

Women should be made aware that whilst the screening programme, dependant on their screening choice, aims to assess the risk of the baby being born with T21/13/18, other complications may also be identified due to out of range results i.e.:

- Low PAPP-A
- Raised AFP

In the event of a low PAPP-A result being identified via combined screening, the pathway for serial growth scans would be triggered including the need for Asprin. The patient will be informed of the result and management plan via a detailed patient information leaflet sent out by the screening team. This is included with the letter from Birmingham Womens Hospital which reports the low risk findings for the chromosomal testing. Please refer to the identification of low PAPP-A pathway and allocation of pregnant women to high risk care and serial growth scans pathway.

Woman should be informed that second trimester blood testing looks at the level of Alpha Fetoprotein (AFP) in the blood as part of the Down's screening process. If the AFP level is raised (above 2.5MoM) it may indicate a problem with the development of the neural tube e.g. Spina Bifida, anencephaly, gastroschisis. It is important to ensure the woman knows that a raised AFP is not a diagnosis of a neural tube defect or abdominal wall defect. It is an incidental finding and may have no adverse effect on the pregnancy. The woman will be offered an early scan from 18 weeks onwards to look at the fetal anatomy.

Likewise an increase of Nuchal Translucency of >3.5mm may indicate potential complications other than Down's syndrome. A local fetal medicine referral should be made and the samples should be marked as 'Fast Track' prior to sending to Birmingham Women's Regional Laboratory.

Women with a previous pregnancy affected by a chromosomal anomaly should be offered the Combined Test in the 1st instance but can opt directly for a Diagnostic test if requested.. Pregnant women should not be offered a diagnostic test for Down's syndrome based on their age-related risk alone (NSC working standards 2007) without prior screening. Diagnostic testing is also not available on the NHS for any woman found to be low risk on screening. Diagnostic testing carries a risk of

miscarriage (1%) for amniocentesis and 1-2% for Chorionic Villus Sampling [CVS]) which needs to be balanced against the risk of having an affected pregnancy. Women who request an invasive test and do not want to have screening for Down's syndrome are able to access the antenatal screening team to discuss this further.

Twin Pregnancy- the combined test will be offered for twin pregnancies. If the nuchal translucency is not measurable on a first attempt a 2nd attempt should be offered within the screening time frame. If a combined test is unable to be performed then a quad test can be offered following specialist discussion (quad testing detection rate is less in twin pregnancy's than in a singleton pregnancy).

For women screened using the combined test, where a dichorionic twin pregnancy is identified, the chances will be reported for each fetus. In a monochorionic twin pregnancy, both fetuses are either affected or unaffected so the chance will be the same and a single 'pregnancy' chance will be reported.

Please note where there are triplets or more, biochemistry cannot be offered as there is no Software programme available to assess risk. In this situation nuchal translucency measurement only will be used to assess the risk calculation.

NB: In cases of vanishing twin, where one sac contains a non-viable fetus, only a nuchal translucency measurement and maternal age will be used to ascertain the risk calculation (biochemistry would be unreliable) unless the woman prefers to have a quadruple screening test at 16 weeks.

Definitions

Title	Definition
Down's Syndrome genetic makeup	The structure of each human cell is made up of 46 chromosomes in 23 pairs. Down's syndrome there is an extra chromosome 21 making 47 in total. This gives three number 21 chromosomes, hence the medical terminology Trisomy 21. The extra genetic material gained from this gives the characteristics of Down's syndrome
Standard or Regular Trisomy 21	Most cases arise when the chromosomes donated by the mother or father have Failed to divide correctly. This type is called Standard or Regular Trisomy 21 and Accounts for 95% of people with this condition. Regular Trisomy 21 is not hereditary but it is known from statistical analysis that if a woman has a child with this type of condition then the risk will be higher of it occurring in the next pregnancy.
Other types of Down's Syndrome	Other types of Down's syndrome occur due to translocation of genetic material between chromosome 21 and another chromosome (e.g. Chromosomes 14 and 21 known as Robertsonian translocation). This type occurs in 4% of cases
Mosaicism	The remaining 1% occurs when there is Mosaicism – where normal and Trisomy 21 cells are found within the individual.
Edwards syndrome	In trisomy 18 there is an extra copy of chromosome 18 in each cell. Complete trisomy 18 is fatal. Babies with partial and mosaic trisomy 18 may survive to adulthood, but this is

	rare.
Patau's syndrome	With trisomy 13 there is an extra copy of chromosome 13 in each cell. Complete trisomy 13 is fatal. Babies with partial and mosaic trisomy 13 may survive to adulthood, but this is rare.
Combined test (CT)	This screening combines a nuchal translucency (NT) scan with biochemical testing, and gives results at an earlier gestation
Quadruple screening	This is a single blood test using four biochemical markers.

Prevalence

Down's syndrome occurs in approximately 1:1000births. (NDSCR, 2010) This figure is similar in all populations and is an overall population risk. The incidence rises sharply with maternal age. It affects both boys and girls equally. Approximately 70% of Down syndrome babies are born to women under 35 therefore maternal ages should not be the sole screening factor.

Table to show incidence of Trisomy 21 with rising maternal age

Age of mother	**Risk**	**Risk in percentage**
20 years	1:1500	0.066
30 years	1:800	0.125
35 years	1: 270	0.37
40 years	1:100	1.0
45 and over	1:50 and greater	2.0

Detection Rate Of Screening Tests

These figures are provided by Birmingham laboratory quarterly and by DQASS (Down's syndrome screening Quality Assurance Support Service).

FASP (2015) defines the national cut off set at 1 in 150 at term for both first and second trimester screening tests. A woman with a risk of 1 in 150, or greater (1 in 2 – 1 in 150), of having a pregnancy

affected by T21, T18/T13 in the first trimester or T21 only in the second trimester will be considered to be in the 'higher risk' group and offered an invasive test.

Excludes increased nuchal translucency (NT) measurement only – FASP policy (2015) stipulates all women who accept first trimester screening must have all components of the screening test completed-NT and biochemistry.

Detection Rates (DR) performance thresholds: **for singleton pregnancies**

- T21 Standardised DR 85%
- T13/18 Standardised DR 80%
- T21/ 13/18 Standardised DR 80%
- Quadruple Standardised DR 80%
-
- Detection Rates (DR) performance thresholds: **for twin pregnancies**
- T21 Standardised DR 85% For Monochorionic
- T13/18 Standardised DR 80% For Monochorionic
- T21/T13/ T18 Standardised DR 80% for Monochorionic
- T21 Standardised DR 85% For Diamniotic
- T13/18 Standardised DR 80% For Diamniotic
- T21/T13/ T18 Standardised DR 80% for Diamniotic
- Quadruple Standardised DR 80% in Monochorionic twin pregnancies
- Quadruple Standardised DR 40-50% in Diachorionic Twin pregnancies

Process of Screening

1) 1st Contact and Booking appointment with Community Midwife (ideally before 10 weeks)

- Information offered about screening for T21/13/18 ("Screening tests for you and your baby booklet-NHS screening programmes"). This will provide the opportunity for further discussion before embarking on screening
- The screening pathway for both screen positive and screen negative results
- The decisions that need to be made at each point along the pathway and their consequences
- The fact that screening does not provide a definitive diagnosis and a full explanation of the risk score obtained following testing
- Balanced and accurate information about the above conditions.

All pregnant women should be offered screening for T21/13/18. This offer and acceptance/decline should be documented in the pregnancy hand held notes and the Maternity information system (NSC leaflet 'Screening Tests for You and Your Baby' should be given at the point of offer). Women should understand that it is their choice to embark on screening. Ideally a cooling off period should elapse between the offer and decision.

2) A dating scan appointment is generated from the Community Midwives referrals to the appropriate hospital.

3) On attending the dating scan appointment the trained ultra-sonographer will re-offer combined screening.

4) If screening is accepted the Nuchal translucency will be measured as part of the Combined Test.

5) CT bloods taken directly after the USS which will be documented in the hand held records.

6) If Nuchal Translucency is unable to be measured at that appointment, a second appointment within the screening window should be offered. If the pregnancy is greater than 14+1 a Quad test will be offered and appointment for the Quad clinic will be generated with the patient still present.

7) It is the responsibly of the person taking screening bloods for either combined or quad tests to deliver the sample to the laboratory. The person who is responsible for the individual screening clinics should also ensure that the blood samples have been delivered to the laboratory in a timely manner. The air pod transporting system for blood samples should not be used.

8) Following completion of screening process information will be given as to how results will be reported.

Management of Screening Test Results:

Low chance results:

Results reviewed on a daily basis by the screening team. All women should be notified of their screening test result by letter within two weeks of the test being taken. The paper copy of the report will be filed in the Hospital Maternity notes and documented on the Maternity Information System.

Community Midwife to document low risk result in the pregnancy hand held records at the next appointment.

High chance results:

Birmingham Women's Hospital Regional laboratory directly informs the Screening team of the high chance result via the antenatal screening results generic email account. In turn the screening team will acknowledge receipt of the high chance result with a return email. Women are informed of the result within 3 working days of the receipt of result and offered a face to face discussion with a relevant specialist midwife.

The midwife will discuss the options available:

- Whether to have no further testing
- Whether to have a diagnostic test.
- Private Non Invasive Prenatal Testing (NIPT) should be mentioned as an option if high ~~risk~~ chance results alone and no additional anomalies have been noted on scan. Currently this is not an NHS funded test and therefore the woman will be required to organise this independently. However it is expected that NIPT will be available, funded by the NHS, later this year as an option for patients who receive 'increased chance' results following combined or quad screening.

Discussion should include sufficient information to ensure that the woman is aware of the purpose, benefits, limitations and risks of undergoing a diagnostic test.

If diagnostic testing is declined the woman continues with her pregnancy and the pregnancy outcome is obtained for audit purposes. A paediatric alert is completed to alert the paediatric/maternity team providing subsequent care including NIPE in the post-natal period.

Results to be documented in pregnancy hand held records and on the maternity information system.

Diagnostic Testing:

Chorionic Villi sampling (CVS) - 10+0-13+6 weeks

- Woman's decision is documented in the pregnancy hand held notes

- Referral to tertiary Fetal Medicine Unit -Birmingham Women's Hospital via e-mail.
- Following referral for diagnostic testing, Birmingham FMU will share information with the Screening Team to ensure appropriate pregnancy management/delivery of the baby and monitoring of screening outcomes.

Amniocentesis - 15 weeks onwards

- Woman's decision is documented in the pregnancy hand held records.
- Appointment to be made at WRH ideally within 3 working days of women receiving high risk results (gestation dependent).
- Please refer to Amniocentesis policy-WAHT-OBS-066 for full process.
- If appointments unavailable at WHAT within a reasonable timeframe please refer to the tertiary Fetal Medicine Unit at Birmingham Women's Hospital via email.

Management of Diagnostic Test Results:

Normal result:

- The woman will continue with pregnancy and outcome is obtained at delivery.

Abnormal result:

- Abnormal results are reported by the Regional Cytogenetic Laboratory (Birmingham Women's Hospital) to the Antenatal Screening Team via email (read receipt in place).
- The woman is given the opportunity to discuss the results with health professionals who are knowledgeable about Down's, Edwards' and Patau's syndromes. This will include the offer of a termination of pregnancy or continuing support through pregnancy.
- If the woman chooses not to undergo termination of pregnancy and continues with her pregnancy a referral to appropriate paediatric and support services should be made (see appendix 3-Paediatric alert referral) for on-going care.
- If termination of pregnancy is chosen, this should be undertaken in line with the Abortion Act 1967 and Medical Management of Termination (14+0-20+) policy and WAHT-GYN-001/ Medical management of termination (20+ weeks).
- Abnormal results will be reported to West Midlands Congenital anomaly register (WMCAR) now (NCARDRS) by the Antenatal Screening team via e-mail

Failsafe Mechanisms:

Worcester Royal Hospital, Evesham and the Alexandra Hospital

- The designated Midwife in charge of the combined/quad clinic will generate a list of all Combined and Quad test samples. This list is sent to the local laboratories and screening team via secure email. (see appendix 3 -Fail Combined and Quad failsafe list).
- On receipt of the sample the local laboratory will return the list to the screening team via email acknowledging receipt of all samples.
- The screening team will be informed of any missing samples. These will be followed up as a matter of urgency.

- In exceptional circumstances, if a blood sample is taken in a community clinic, the health care professional taking the blood must inform the screening team and Biochemistry so they are aware the sample is expected.
- All results (high and low risks) are checked daily, via direct access to Birmingham Clinical Chemistry results system, against the check lists to ensure all patients have received a reportable result.
- At Kidderminster Treatment Centre, The blood samples are sent directly to Birmingham Women's Laboratory via courier who signs the failsafe list to confirm all blood samples have been collected.

All screening results (even if declined) are checked and will be documented in the pregnancy hand held records at the routine16/40 Community midwife appointment. If there is no documented evidence of results then it is the responsibility of all healthcare professionals at every point of contact to ensure that a reportable screening result is documented. If there is any uncertainty regarding these results the Antenatal Screening Coordinator should be informed to investigate further.

Training-Ultra sonographers

All professionals involved in the provision of ultrasound screening for Down's, Edwards' and Patau's syndromes should comply with the training requirements detailed in the FASP ultrasound practitioner's handbook':

NHS FASP recommends that any person undertaking a Fetal Anomaly ultrasound scan on pregnant women, for the purpose of screening and diagnosis of a related condition should hold, as a minimum, one of the following:

- Completion of NT and CRL online screening resources (CEM 21) annually
- Certificate/Diploma (as appropriate) in Medical Ultrasound (CMU/DMU) of the College of Radiographers (CoR) with evidence of appropriate continuous professional development (CPD)
- Post Graduate Certificate in Medical Ultrasound (PgCert) approved and validated by a Higher Institute of education and accredited by the Consortium for Sonographic Education (CASE) or equivalent. The qualification should be relevant to obstetric ultrasound practice
- Royal College of Obstetricians and Gynaecologists (RCOG) Royal College of Radiologists (RCR) Diploma in Obstetric Ultrasound or the Advanced Training Skills Module (ATSM)

http://www.fetalanomaly.screening.nhs.uk/Combinedscreeningresources

The NSC Continuing Professional Development website for Antenatal and Newborn Screening

www.e-lfh.org.uk

Appendix 1 Roles and Responsibilities

Multi-disciplinary Team Members	**Roles and Accountability**
Antenatal Screening Coordinator **(ANSCO)**	[illegible] [illegible] [illegible] [illegible] training of local staff with respect to screening [illegible] [illegible] are identified [illegible] [illegible]
Midwives and Obstetricians	[illegible] [illegible] [illegible]
Named Community Midwife	[illegible] [illegible] [illegible]
UltraSonographer/Midwife	[illegible]

sonographer	[illegible] [illegible] [illegible]
Phlebotomist/MCA	[illegible] [illegible] [illegible] • Samples taken at Kidderminster Hospital are collected and signed for by courier and taken directly to Birmingham Women's Hospital Regional Laboratory
Local Biochemistry Laboratory	[illegible] [illegible] [illegible] (evidence of arrival in laboratory) [illegible] [illegible]
Birmingham Women's Hospital Regional Biochemistry Laboratory	[illegible] [illegible] [illegible] identified [illegible] [illegible] [illegible]

Antenatal Screening Group	Governance Group and Divisional Quality Committee. arrangements are in place to support vulnerable. Assist in the composition of audit reports and oversee the clinical management and quality of the Trust's screening programme
Maternity Clinical Governance Group	programme

Appendix 2: Contact Details

NAME	ROLE	CONTACT NUMBER
Emma Davis **Nicola Wilcox** **Sadie Stringer** **Cassie Taft**	**Antenatal and Newborn Screening Team, based at Worcester Royal Hospital**	**01905 768945** **wah-tr.antenatalscreeningresults@nhs.net**
FETAL MEDICINE UNIT-BIRMINGHAM	**TERTIARY REFFERAL UNIT**	**0121 6272683** **f.medicine@nhs.net**
CLINICAL CHEMISTRY LAB-BIRMINGHAM	**DOWN'S SCREENING LAB**	**0121 6272730** **bwh-tr.clinchem@nhs.net**

Appendix 3

Combined and Quad Test Sample Checklist

For attention of Tracy Stock or Charlotte Dixon (WRH)
For attention of Claire Todd, Lisa Richardson or Tina Waldron (ALEX)

Copies of this form must be emailed to wah-tr.AntenatalScreeningResults@nhs.net
wah-tr.dutyBMS@nhs.net
The lab will email confirmation of receipt of all samples to screening team generic email account.

Date	Name	Hospital Number	Date of Birth	Where Sample was Taken	Received in Lab	Result letter Sent

Checked by midwife 1 …… **Checked by midwife 2 ……**

Received in lab by / confirmation emailed by …….. Signature……