MFine Diagnostics

Pregnancy Loss

Investigation Packages

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Introducing the Most Comprehensive Pregnancy Loss Workup Packages

Pregnancy Loss can occur due to a wide array of factors including genetic, anatomic, endocrine related,antiphospholipid antibody syndrome, immunological and environmetal factors . Benefits of comprehensive evaluation of pregnancy loss: Helps in identifying the cause. Allows estimation of recurrence risk. Allows optimization of obstetric care May help affected couples make informed reproductive choices.

Placental Histopatholgy & Fetal Autopsy DNA Storage

- Detects fetal pathology
- Report Interpretation by expert clinical geneticists
- Identification of placental lesions Confirmatory genetic testing possible

Molecular Cytogenetic Study

- Chromosomal abnormalities are a common cause of fetal loss: Autosomal trisomies: 60-70% Monosomy X: 10-15% Triploidy: 10-15% Other chromosomal abnormalities: 10-15%
- Cytogenomic SNP microarray is recommended first-tier test for intrauterine fetal demise or stillbirth.
- It does not require live cells & offers increased resolution for CNVs.

Molecular Autopsy Exome Sequencing

- The exome accounts for 1-2% of the human genome but harbors approximately 85% of pathogenic variants.
- Whole exome sequencing can detect causative genetic variants in genes associated with missed abortion, congenital anomalies.
- Advanced pipeline allows CNV detection.

Molecular Cytogenetics Packages

QF PCR EXTENDED

- Fully automated, DNA based method, no sample culture required
- Covers Triploidies and most common aneuploidies-Trisomy 13,18,21, 15,16, 22, sex chromosomal anueploidies
- Detects MCC
- Reflex testing by MLPA for 20 common microdeletions and micro duplications if QFPCR report is negative.
- TAT : 5 Days

POC PREMIUM-CMA 315K

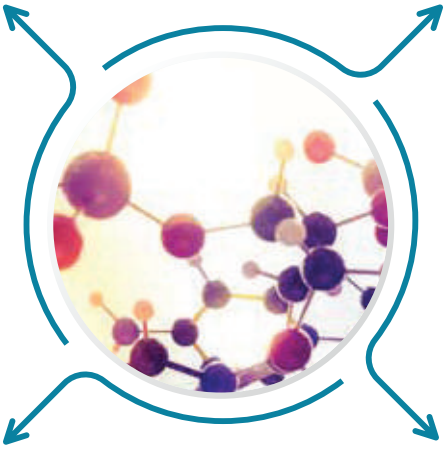
- Fully automated, DNA based method, no sample culture required.
- Whole genome coverage (18,018 CNV 148,450 SNP) probes
- Resolution of 1MB for losses & 2MB for gains
- Increased coverage density targeting 396 empirically selected regions relevant for prenatal loss (25 markers / 100kb)
- Can detect low level of mosaicism
- A minimum resolution of and 5MB for LOH/AOH
- Detects MCC
- TAT- 10 Days

Molecular Autopsy by WES

Next-generation whole-exome sequencing (WES) based autopsy, allows for the simultaneous genetic analysis of an individual's entire library of ~22,0000 genes, is an attractive, cost-effective, and time conducive (~3 weeks) technique for a comprehensive post-mortem genomic study

Benefits of Molecular Autopsy.

Molecular autopsy have a high diagnostic rate



It provides a precise mutational cause rather than a broad etiological classification. This level of precision is essential for accurate genetic counseling and for the pursuit of preventative options in future pregnancies such as preimplantation and prenatal diagnosis.

It complements classical autopsy as molecular autopsy since the latter helps refine the phenotype associated with the molecular variations.

It can also be done in the first trimester using chorionic villus sampling or with properly collected POC sample

Facts In Box:

Guidelines from ACMG, ACOG ,SMFM recommends Chromosomal Microarray as the first line test in case of RPL, still birth and for fetuses with structural abnormalities.

In cases of Recurrent Pregnancy Loss(RPL), couple karyotyping can help identify the balanced translocation carriers which increases the chance of recurrence.

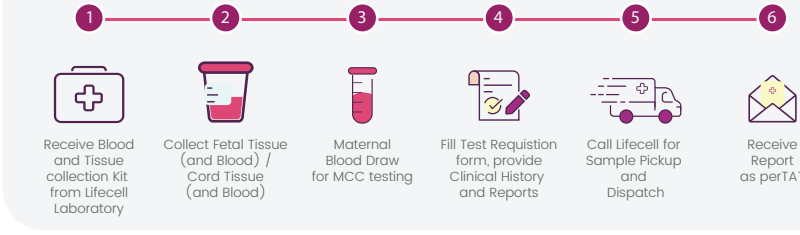
Sample Type & Requirements:

Products Of Conception (POC) or Chorionic Villi Sampling (CVS)

- 1 cm (sterile) fetal tissue and/or villi in tissue culture media provided by lab.
- Preferred fetal tissue sample sites include buttocks or thigh. If fetal tissue is not available placental villi can be utilized. Separate villi from maternal blood and deciduas to reduce the chance for maternal cell contamination.

Please note: Formalin fixed or degraded sample cannot be used.

Product of Conception (POC) Testing - Process flow



Fetal Autopsy

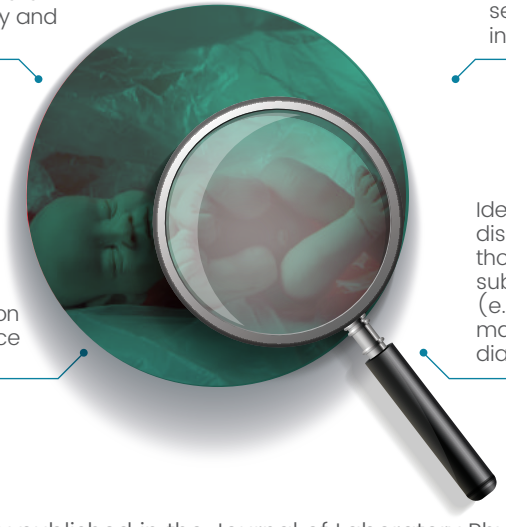
An autopsy is the single most useful investigation and provides information that changes or significantly adds to the clinical diagnosis in nearly half of cases and also helps prevent the recurrence of future adverse events.

LifeCell Diagnostics' Fetal Autopsy-Scope, a post-mortem testing package to detect fetal pathology in the second trimester (11+0–23+6 weeks gestation) that helps establish the immediate cause or factors that may have contributed to the pregnancy loss.

Benefits of Fetal Autopsy Scope

Provides information for audit purposes (e.g. antenatal diagnosis, pregnancy and intrapartum care)

Identify the immediate cause of second trimester intrauterine death



Identify evidence of genetic disease and to allow determination of the likely recurrence risk

Identify concomitant diseases, particularly those with implications for subsequent pregnancies (e.g. growth restriction, malformation, maternal diabetes)

According to a study published in the Journal of Laboratory Physicians and as per the guidelines provided in Child Health Division (Ministry of health & Family Welfare, Government of India), a fetal autopsy is recommended in the following scenarios.

Fetal Autopsy is Essential
Congenital malformations
Recurrent fetal death
Hydrops fetalis - Abnormal accumulation of fluid in fetal compartments
Intrauterine growth restriction (IUGR). Where no cause in detectable
Suspected infections

Fetal Autopsy is Desirable
Temination of pregnancy due to congenital anomalies
Intrauterine fetal death (IUFD)
Inevitable abortion
Termination due to increased risk of chromosomal anomalies

Sample & Documentary Requirements

- The entire fetus and umbilical cord, along with the placenta (ifrequested), should be immersed in 10% buffered formalin and sent in appropriately labeled containers.
- For fetuses of 20 weeks gestational age or above, a death certificate should be sent.

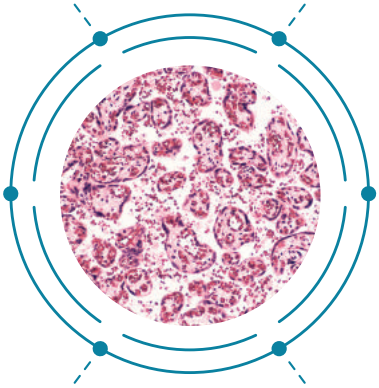
The documents that have to be submitted include:

- An informed consent form (signed by parents)
- A death certificate for fetuses of 20 weeks gestational age or above.
- A sample release form (attested by the doctor/medical director of the hospital to approve the transport of the sample)
- Photocopy of ID proof of the parents
- A test requisition form with clinical details of the mother and fetus/neonate.

Placental Histopathology

LifeCell's Placenta-Scope includes a thorough macroscopic & microscopic analysis of the placenta in order to determine the exact etiology for an adverse perinatal event. It, therefore, helps parents take the right precautions to avoid recurrence of such an event & also, avoid additional costly medical evaluation.

Benefits of Placenta-Scope



- Helps to prove the exact etiology for perinatal death and thus, acts as a legal shield to the obstetrician
- Placental examination provides a specific explanation for an adverse fetal or maternal outcome.
- Provides reports that adhere to RCOG Guidelines & Amsterdam Placental Workshop Group Consensus Statement
- Detects conditions associated with a high probability of recurrence & conditions associated with fetal neurological impairment.
- Turn Around Time of 7 days
- Provides information that can guide the management of future pregnancies.

Sample Type and Requirements

- This test requires the entire placenta along with the umbilical cord for examination.
- The placental specimen is collected by a LifeCell paramedic in an appropriately labelled sturdy plastic container with a tight-fitting lid, containing 10% buffered formalin.
- A test requisition form with the complete clinical details of the mother & the baby/fetus should be submitted along with the sample

Please note: Specimens are not sent in formalin shall not be accepted for processing.

Facts In Box:

ACOG recommends that screening for thrombophilia should be performed on patients with more than 3 miscarriages, late miscarriage and foetal death (Practice bulletin no. 124: Inherited thrombophilias in pregnancy. Obstet Gynecol. 2011;118:730–740).

Biochemical Thrombophilia Workup

- Thrombophilia is a broad medical term which describes a multifactorial condition where the blood has an increased tendency to clot and is considered hypercoagulable.
- The Thrombophilia Workup is a comprehensive combination of tests designed to provide evidence of inherited deficiencies of naturally occurring anticoagulants, Antithrombin, Protein C, and Protein S. Lupus anticoagulant and antibodies associated with anti-phospholipid syndrome are included in the panel.

Hereditary Thrombophilia Panel

- Thrombophilia is linked to recurrent pregnancy loss, foetal growth restriction, late miscarriages, stillbirth and preeclampsia.
- Inherited thrombophilias include factor V Leiden mutation, factor II mutation, protein C deficiency, protein S deficiency, antithrombin deficiency and methylenetetrahydrofolate reductase mutations.
- This panel analyzes multiple genes that are associated with hereditary thrombophilia simultaneously to find the cause and guide prognosis.

Test Catalogue

Code	Test	TAT	Sample Type
GEN0209	QFPCR Extended(13,18,21,15,16,22,X,Y) with reflex MLPA for 20 micro deletions and duplications	5 Days	1. Fetal Tissue/Villi/ Genomic DNA in Tissue Culture Media provided by Lab 2. Maternal Blood in EDTA tube for MCC testing
GEN0736	Integrated QFPCR (Reflex Couple KT if QFPCR is positive; reflex CMA315k if QFPCR is negative.)	10 - 12 Days	
GEN0746	Chromosomal Microarray(CMA315k) and Couple Karyotyping Combo	10 Days	1. Fetal Tissue/Villi/ Genomic DNA in Tissue Culture Media provided by Lab 2. Maternal Blood in EDTA tube for MCC testing 3. Couple PVB in SodiumHeparin tube
GEN0032	Chromosomal Microarray (Cytoscan Optima CMA 315k)	10 Days	1. Fetal Tissue/Villi/ Genomic DNA in Tissue Culture Media provided by Lab 2. Maternal Blood in EDTA tube for MCC testing
GEN0226	Whole Exome Sequencing (WES)	21 Days	
FAPHDNAST	Fetal Autopsy with PlacentoScope and DNA Storage	30 Days	Fetal origin tissue in Tissue Culture vial, Fetus, cord and Placenta in 10% Formalin
FADNAST	Fetal Autopsy with DNA Storage	30 Days	Fetus and cord in 10% Formalin
P0049	PlacentoScope-Placetal Histopathology	7 Days	Placenta and cord in 10% Formalin
RPL+KT	RPL with couple Karyotyping (Anti Cardiolipin Antibody IgM & IgG, Anti Phospholipid Antibody IgM & IgG, Lupus Anticoagulant, Torch Panel, Couple KT)	10 Days	Serum,Sodium fluoride tube, Sodium heparin tube,EDTA BLOOD
RPLBIOT	RPL- Biochemical Thrombophilia Workup (PT,APTT, Lupus Anti-Coagulant, Anti Cardiolopin Antibody, Beta2 glycoprotein antibody, Anti phospholipid antibody, Lupus Anti-Coagulant, Protein C and Protein S activity, Homocystine)	7 Days	Serum, Citrate Plasma.
GEN0532	Hereditary Thrombophilia Panel (PROCR (20q11.22), F2 (11p11.2), F5 (1q24.2), F12 (5q35.3), F13A1 (6p25.1), FGB (4q31.3), GP1BA (17p13.2), MTHFR (1p36.22), SERPINC1 (1q25.1), SERPINE1 (7q22.1), PROS1 (3q11.1))	21 Days	Blood in EDTA vial