PATHOLOGISTS
LANCET LABORATORIES
Key to Diagnostic Excellence

Newsletter

The bone marrow aspirate and trephine biopsy (BMAT) procedure:

2nd Quarter 2019

Introduction:
Lancet Laboratories offers a bone marrow aspirate and trephine biopsy procedure service. We have a team of medical officers who perform the procedure for in-patients and out-patients in the greater Johannesburg area. Our other centres in Pretoria, Bloemfontein, Durban and Cape Town also offer the service. This newsletter provides an overview on the process.

Why do a bone marrow aspirate and trephine biopsy (BMAT)?

1. Diagnostic purposes
   * Unexplained high or low blood cell counts
   * Haematological cancers – Leukemia; Lymphoma; Myeloma
   * Unexplained fever
   * Unexplained enlarged spleen
   * Assess iron levels if biochemical iron studies are not informative
   * Evaluation of suspected deposition and storage diseases (e.g., amyloidosis, Gaucher disease)
2. Staging of certain cancers
   * Lymphoma
   * Metastatic cancers
3. Monitoring
   * Follow up after/during chemotherapy
   * Re-staging after treatment
   * Toxicity and efficacy of cancer treatments

How do you book a bone marrow procedure?

1. In-patient: The ward can book through the Lancet Laboratories depot at the respective hospitals, or directly with the bone marrow administration team (Johannesburg – 011 242 7382/011 358 0640)
2. Out-patient booking: this is coordinated with the bone marrow administration team (number provided above). Either the patient, nurse or doctor can make this booking.
3. Theatre patients: this is also coordinated with the bone marrow administration team (number as above).
4. Information which is necessary for the booking includes the presumptive diagnosis and indication for the marrow, if the patient is on any anticoagulant therapy (e.g. warfarin).

How is a BMAT done?

1. The requesting clinician will inform the patient that the procedure is required and the Lancet Laboratory nursing staff will obtain INFORMED WRITTEN CONSENT. The Lancet Laboratory doctor doing the BMAT procedure will discuss the process, including the indication for the procedure and possible risks and complications. Risks of the procedure include bleeding and infection at the site, but these are rare.
2. Positioning of the patient:
   a. Posterior Superior Iliac Spine – patient is lying prone or lateral
   b. Anterior Superior Iliac Spine – patient is lying supine
   c. Sternal – patient is lying supine

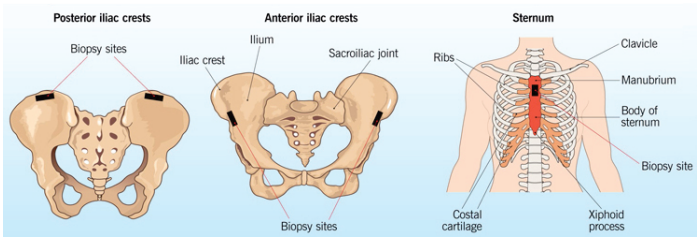

FIGURE 1 COMMON SITES FOR BONE MARROW EXAMINATION IN ORDER OF PREFERENCE

1. For in-patients sedation can be given intravenously. Heart rate and oxygen saturation monitoring is essential if sedation is given. For outpatients, oral dormicum can be prescribed for the procedure.
2. The area is then cleaned to create a sterile surgical field.
3. Local anaesthetic (2% lignocaine) is infiltrated subcutaneously and onto the periosteum
4. The local anaesthetic takes about 5 minutes to take effect.
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6. The local anaesthetic takes about 5 minutes to take effect.
7. A skin incision (<5mm) is then made.
8. Aspirate – the bone marrow needle is inserted through the subcutaneous tissue, and pushed through the cortical bone layer until the tip is in the spongy bone. Using a 20ml syringe, approximately 10 to 15ml of bone marrow is aspirated and used to make slides for cytology; to fill heparin and EDTA tubes for flow cytometry and/or cytogenetic testing; and to fill cultures bottles if indicated.
9. Trephine biopsy – the bone marrow needle is advanced 10 to 20mm deeper into the spongy bone to extract a trephine core of marrow.
10. The area is then covered with a gauze dressing and is recommended to stay on for 48 hours, to prevent infection
11. The patient should lie down on the area where the dressing is for 20 minutes after the procedure, to prevent the formation of a haematoma
12. The samples are then taken to the main laboratory at Lancet Laboratories, Richmond for processing by the haematology laboratory technical staff and analysis and interpretation by the pathologists.

The Procedure:

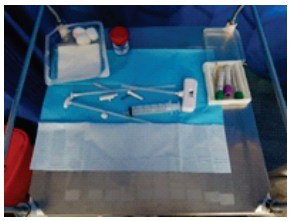

Figure 1: Equipment used

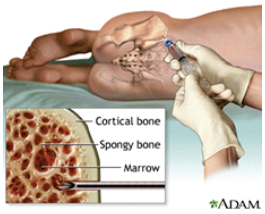

Figure 2: Anatomical representation of BMAT

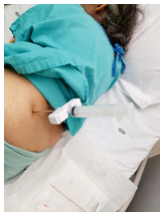

Figure 3: BMAT on a patient

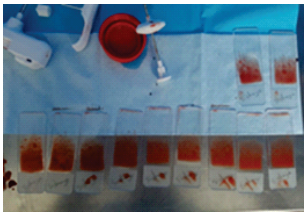

Figure 4: Aspirate on glass slides

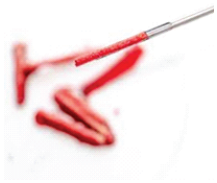

Figure 5: Trephine biopsy

Scope of tests performed:

1. **Bone marrow aspirate:**
   * Is used to assess marrow cellularity.
   * Each haemopoietic lineage is assessed for morphology and is also quantitated (i.e. erythropoiesis, granulopoiesis, megakaryopoiesis, lymphocytes, plasma cells)).
   * Detection of abnormal cells, e.g. blasts, abnormal lymphocytes, occasionally clumps of metastatic cells etc.
   * It is also used to assess iron storage and to detect abnormal/pathological sideroblasts.

2. **Bone marrow trephine biopsy:**
   * The trephine biopsy is used to make a more accurate assessment of marrow cellularity than the aspirate.
   * It is used to assess marrow architecture (maintained, disrupted or effaced).
   * It is best used for assessing megakaryocyte numbers and distribution.
   * Assessment of focal lesions (for example, suspected granulomatous disease, lymphoma, and metastatic infiltrate).
   * It is also used to assess the presence and degree of reticulin and collagen fibrosis.
   * Bone structure and bone marrow blood vessels are also evaluated
   * Immunohistochemistry can be done to further aid in diagnosis.

3. **Flow cytometry:**
   * Is performed to aid in immunophenotyping of haematological malignancies and lymphoproliferative disorders.
   * It is useful in proving clonality, quantifying the clonal population, identifying minimal residual disease (MRD), and detecting relapsed disease.

4. **Bone marrow Cultures:**
   * Mycobacterial, anaerobic, aerobic and fungal cultures can be done on the aspirate sample if indicated.
   * Cultures are often requested in patients presenting with pyrexia of unknown origin (PUO), or in patients with suspected disseminated tuberculosis.

5. **Cytogenetics:**
   * Cytogenetics is one of the molecular tools used in the workup of a patient with a haematological condition.
   * Karyotyping identifies the number and structure of the chromosomes. It is used to detect changes in large regions of chromosomes (translocations, large deletions, or aneuploidies).
   * Only those cells that are proliferating and dividing (i.e. only cells in the metaphase of the cell cycle), are evaluated and 20 cells in metaphase are typically reviewed.

6. **Fluorescent in-situ hybridisation (FISH) analysis:**
   * FISH is the analysis of chromosomes regardless of the phase of the cell cycle. This allows detection of abnormalities even in non-dividing (i.e. interphase) cells.
   * FISH is particularly useful in screening for BCR-ABL1 fusion in myeloproliferative neoplasms, confirming a specific lymphoma diagnosis (e.g. BCL2-IGH in follicular lymphoma or MYC-IGHG1 in Burkitt lymphoma), detection of translocation, inversions or aneuploidy (e.g. t(8;21), inv(16) or MLL rearrangement in AML) and is of value in prognostic panels (e.g. in CLL and in Multiple Myeloma).

7. **Polymerase Chain Reaction (PCR):**
   * Detection of rearrangement of immunoglobulin heavy and light chain loci, and T-cell receptor (TCR) providing evidence of clonality in suspected lymphomas/lymphoproliferative disorders.
   * Detection of leukaemia-related and lymphoma-related chromosomal rearrangements by demonstration of gene juxtaposition or fusion.
   * Detection of gene mutations relevant to diagnosis e.g. JAK-2 in Polycythaemia Vera, Essential Thrombocythaemia and Primary Myelofibrosis.
   * It is also used in prognostic stratification (e.g. detection of ETV6-RUNX1, which is associated with a good prognosis in ALL and FLT3-ITD, which is associated with a poor prognosis in AML).
   * Minimal residual disease (MRD) detection (e.g. detecting FLT3-ITD, PML-RARA or CEBPA mutations in AML patients).

8. **Myeloid Next Generation Sequencing (Myeloid NGS):**
   * Allows massively parallel sequencing of thousands or millions of fragments of DNA simultaneously, thus giving results in a relatively short period.
   * It is used to assess for single gene mutations, including substitutions and insertions and deletions that may have diagnostic, prognostic, and/or therapeutic significance in Acute Myeloid Leukaemia (AML), Myelodysplastic Syndromes (MDS), Myeloproliferative Neoplasms (MPN), or MDS/MPN overlap disorders such as Chronic Myelomonocytic Leukemia (CMML).
   * Importantly, NGS is quantitative and thus an “allelic burden” can be determined.

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