Bone Marrow Aspiration and Biopsy

Overview

The procedure known as trepanning, or trephination, of bone is the oldest surgical practice that continues to have clinical relevance in modern times. The method dates as far back as the Neolithic period and initially entailed the drilling of cranial bones as a form of medical intervention for headaches and mental illnesses. However it was not until 1905, when the Italian physician Pianese reported bone marrow infiltration by the parasite *Leishmania*, that this procedure was applied toward clinical evaluation.\[1\]

In the present day, inspection of the bone marrow is considered one of the most valuable diagnostic tools to evaluate hematologic disorders.\[2\] Indications have included the diagnosis, staging, and therapeutic monitoring for lymphoproliferative disorders such as chronic lymphocytic leukemia (CLL), Hodgkin and Non-Hodgkin lymphoma, hairy cell leukemia, myeloproliferative disorders, myelodysplastic syndrome and multiple myeloma. Furthermore, evaluation of cytopenia, thrombocytosis, leukocytosis, anemia, and iron status can be performed.

The application of bone marrow analysis has grown to incorporate other, nonhematologic, conditions. For example, in the investigation for fever of unknown origin (FUO), specifically in those patients with autoimmune deficiency syndrome (AIDS), the marrow may reveal the presence of microorganisms, such as tuberculosis, *Mycobacterium avium intracellulare* (MAI) infections, histoplasmosis, leishmaniasis, and other disseminated fungal infections. Furthermore, the diagnosis of storage diseases (eg. Niemann-Pick disease and Gaucher disease\[3\] ), as well as the assessment for metastatic carcinoma and granulomatous diseases (eg, sarcoidosis) can be performed. Bone marrow analysis may reveal toxic effects of certain offending medications or substances, such as alcohol, or nutritional deficiencies, such as copper/zinc or vitamin B-12/folate.

Bone marrow analysis can also be performed in patients with idiopathic thrombocytopenia purpura (ITP), incidental elevated serum paraprotein levels, iron deficiency anemia, polycythemia vera, essential thrombocytosis, or infectious mononucleosis; but these conditions are often more appropriately diagnosed by routine laboratory evaluation.\[4\]

Bone marrow consists of stem cells, which are large, "primitive," undifferentiated cells supported by fibrous tissue called stroma. There are 2 main types of stem cells and, therefore, the bone marrow consists of 2 types of cellular tissue. One type of stem cell is involved in producing blood cells and the other is involved in producing stromal cells, which are responsible for the supporting stroma. For more information about the relevant anatomy, see Bone Marrow Anatomy.

Sampling of the marrow consists of either aspiration of the cellular component and/or acquirement of tissue fragments. Aspiration of the marrow, as shown below, has been primarily utilized for cytologic assessment, with analysis directed toward morphology and obtainment of a differential cell count. Further sampling allows for material to be directed toward other ancillary test such as cytogenetics, molecular studies, microbiologic cultures, immunohistochemistry, and flow cytometry. Biopsies, on the other hand, allow for studies of the marrow’s overall cellularity, detection of focal lesions, and extent of infiltration by various pathologic entities.\[5, 6, 7\]
Bone marrow aspiration.

For patient education information, visit eMedicineHealth's [Osteoporosis Center](http://emedicine.medscape.com/content/osteoporosis) and [Cancer Center](http://emedicine.medscape.com/content/cancer), as well as [Bone Marrow Biopsy](http://emedicine.medscape.com/article/207575-overview).

## Preliminary Assessment

An initial review of the patient's clinical background is necessary to determine whether a bone marrow evaluation is warranted.

### Medical history

- Travel history: exposure to parasites (leishmaniasis), fungi (histoplasmosis, *Cryptococcus*), mycobacteria
- Immune compromise or immune deficiency status: This may contribute to a high infection risk, such as in patients with [human immunodeficiency virus (HIV)](http://emedicine.medscape.com/article/207575-overview) infection, underlying autoimmune deficiency (eg, Wiskott Aldrich Syndrome), and/or the use of immunosuppressive agents
- Risk of bone fragility: Previous surgeries, chemotherapy, and radiation therapy can increase the risk of bone fragility, as well as pathologic processes that may contribute to bone resorption (eg, [osteoporosis](http://emedicine.medscape.com/article/207575-overview), [multiple myeloma](http://emedicine.medscape.com/article/207575-overview))
- Previous diagnosis of malignancies: These are a risk for metastasis to bone, especially breast and prostate cancer
- Glycogen storage diseases
- Risk for hematologic anomalies: Contributing factors include a patient's nutrition status, alcoholism, medications, and history of a coagulation factor deficiency
- **Allergies:** Testing and/or knowledge of a patient's allergy status are preventive measures to the potential allergens exposed during bone marrow sampling, such as latex, anesthetics (eg, lidocaine), antiseptics (eg, povidone-iodine)

### Clinical presentation

Perform a thorough physical examination to assess the patient for signs of malignancy, infections, lesions associated with hemorrhagic injury, as well as disorders of hemostasis and coagulation.

Laboratory tests should initially include complete blood cell (CBC) counts, a reticulocyte count, peripheral blood smears, prothrombin time/international normalized ratio (PT/INR), and activated partial thromboplastin time (aPTT).

Other studies take into account the clinical presentation and may consist of the following: serum iron studies, serum ferritin study, vitamin B-12 and folate levels, peripheral flow cytometry, quantitative polymerase chain reaction (PCR) of known translocations (BCR-Abl, JAK-2), erythrocyte sedimentation rate (ESR), serum protein electrophoresis, platelet function studies, coagulation mixing study, fibrin D-dimers, serum fibrinogen levels, serum bilirubin levels, and radiographs.\(^8\)

Obtain informed patient consent that provides procedural information and potential complications (eg, hemorrhage, infections, pain). This will minimize any apprehension that the patient may have.

## Collection Site

The safe and preferred sites for bone marrow aspiration and/or biopsy are described below.

### Aspiration and biopsy

- **Posterior superior iliac crest:** This is the most commonly employed site for reasons of safety, a decreased risk of pain, and accessibility. The posterior superior iliac crest site is localized to the central crest area. See the image below.
• Anterior superior iliac crest: This is an alternative site when the posterior iliac crest is unapproachable or not available due to infection, injury, or morbid obesity. The anterior superior iliac crest site is localized to the center prominence, under the lip of the crest. This location is generally not preferred due to the dense cortical layer, which makes obtaining samples more difficult and smaller in size, as well as creates a risk for an increased painful event.

Aspiration only

• The sternum is sampled only as a last resort in those older than 12 years and in those who are morbidly obese, but it should be avoided in highly agitated patients. To decrease the risk of penetrating the underlying soft-tissue organs, the sternal site is limited to a region that spans between the second and third intercostal spaces.

• The tibia is sampled only for infants younger than 1 year, and the procedure is conducted under general anesthesia. This site is localized to the proximal anteromedial surface, below the tibial tubercle. The tibial location is not utilized in older patients because the marrow cellularity is not consistent. [5, 9]

Procedure

Aspiration sampling is generally performed before marrow biopsy of the posterior/anterior iliac crest due to the fact the biopsy technique induces elevated thromboplastic substances. The consequence of this is a reduction in the effectiveness of an aspiration sampling. [6, 10, 11]

Aspiration

• The patient is placed in the lateral decubitus position, with the top leg flexed and the lower leg straight. Alternatively, the patient may be placed in the prone position.

• Palpate the iliac crest, and mark the preferred sampling site with a pen.

• Aseptic technique is employed, including sterile gloves and gown.

• The site is prepared with an antiseptic (eg, povidone-iodine or chlorhexidine gluconate), scrubbed, and draped, exposing only the site to be sampled. See the images below.

• The skin and the underlying tissue to the periosteum are infiltrated with a local anesthetic (eg, approximately 10 mL of 1% Xylocaine [lidocaine]). A 10-mL syringe with a 25-gauge needle is used to inject an initial 0.5 mL directly under the skin, raising a wheal. A 22-gauge needle is used to penetrate deeper into the subcutaneous tissue and the underlying periosteum, an area roughly 1 cm in diameter. See the image below.
Adequacy of the anesthesia is tested by gently prodding the periosteum with the tip of the needle and questioning the patient for any painful sensation. It is important to be aware of changes in the patient's comfort level throughout the procedure to not only decrease the patient's anxiety level, but to minimize movements that may affect the efficacy of the procedure. Having a family member present may help to alleviate the patient's anxiety. To ensure sufficient pain control is being managed well, the person performing the procedure should talk to the patient, discuss the steps taken throughout the process, and listen to the manner as well as the content of the patient's response.

A skin incision is made with a small surgical blade, through which the bone marrow aspiration needle, with a stylet locked in place, is inserted. See the image below.

Once the needle contacts the bone, it is advanced by slowly rotating clockwise and counterclockwise until the cortical bone is penetrated and the marrow cavity is entered. Contact with the marrow cavity is usually noted by a sudden reduction in pressure. The depth of the penetration should not extend beyond an initial 1 cm. See the image below.

Once within the marrow cavity, the stylet is removed. Using a 20 mL syringe, approximately 0.3 mL of bone marrow is aspirated. A volume greater than 0.3 mL may dilute the sample with peripheral blood and thus is not recommended. The material collected for bone marrow slides is generally not mixed with an anticoagulant, and it is processed immediately by a technologist; this avoids any cellular morphologic artifacts. If there is to be a delay in slide preparation, place the sample in an EDTA (ethylenediaminetetraacetic acid) anticoagulant-containing tube, preferably a pediatric-sized tube to avoid exposure to excess anticoagulant.

If additional marrow is needed for ancillary studies, subsequent specimens are obtained by attaching a separate syringe, collecting 5 mL at a time. The samples are then transferred into an anticoagulant-containing tube that is appropriate to the requested study: heparin for cytogenetic analysis; either heparin or EDTA for immunophenotyping; formalin for a Cytoblock preparation; and, glutaraldehyde for ultrastructural examination.

The marrow needle is removed, and pressure is applied to the aspiration site with gauze until any bleeding has stopped (see Postprocedure Care).

Once the aspiration is completed, the specimen is processed by the hematopathology technician.

**Bone marrow biopsy**

Any of several needle models can be utilized; however, the Jamshidi needle is considered the most popular. This disposable needle is tapered at the distal end to help retain the specimen for improved extraction.

- Patient preparation is to be followed in the manner previously described for bone marrow aspiration. Some kits allow for aspiration and biopsy to be obtained from the same needle, which is convenient for the patient. However, if the latter is used, it is important to change the needle position slightly to a different area of bone.
after aspiration is obtained. Otherwise, aspiration artifact is created where the marrow has been aspirated out of the core.

- The needle, with stylet locked in place, is held with the palm and index finger and repositioned so that a new insertion site is created for biopsy sampling. Once the needle touches the bone surface, the stylet is removed. See the images below.

Using firm pressure, slowly rotate the needle in an alternating clockwise-counterclockwise motion, and advance it into the bone marrow cavity to obtain an adequate bone marrow specimen measuring approximately 1.6-3 cm in length.

- Rotate the needle along its axis to help loosen the sample, pull back approximately 2-3 mm, and advance the needle again slightly, at a different angle, to help secure the specimen.
- Following this procedure, slowly pull the needle out, while rotating in an alternating clockwise and counterclockwise motion.
- Remove the specimen from the needle and introduce a probe through the distal cutting end. If the aspirate was unsuccessful (ie, a “dry tap”), the core biopsy may be used to make touch preparations (see Slide Preparation). This must be performed before placing the specimen in formalin.
- Place the specimen in formalin solution for histologic processing. See the images below.
Bone marrow biopsy specimen in fixative solution.

- The marrow needle is removed, and pressure is applied to the site with gauze until any bleeding has stopped (see Postprocedure Care).

**The Sternum**

Note: With this site, only aspiration is to be performed, and it is only to be performed on adolescent and adult patient populations.

- The second to third intercostal level of the sternum is palpated, and the selected sample site is marked with a pen. Note: The area chosen should be to one side of the midline as the marrow cellularity is considered to be diminished at that location.
- The designated area is prepared with an antiseptic scrub and draped.
- Aseptic technique is employed, including sterile gloves and gown.
- Local anesthetic is used to infiltrate from the skin to the periosteum.
- After small cut is made in the skin with a surgical blade, the aspiration needle with the stylet locked in place, is inserted until the needle touches the bone.
- With the same technique described in the above section (see Procedure: Posterior/Anterior Iliac Crest), advance the needle into the marrow cavity, obtain the specimen, and remove the needle. Note: Unlike other sites, the attached guard is not to be removed; rather, it is adjusted to allow for the maximum depth of needle penetration to 0.5 cm. This prevents needle slippage that can result in injury to the underlying mediastinal organs.
- Core biopsies are not to be performed from the sternum.

**Unilateral Versus Bilateral Iliac Crest Biopsy**

Controversy exists in the application of bilateral iliac biopsies. However, recent studies have indicated that this technique increases the probability of detecting focal lesions, such as in the case of carcinoma and lymphoma staging, where 11-16% of cases may be missed with unilateral biopsies.[12]

Wang et al reported an improvement in identifying bone malignancy in the following pathologic cases[13]: Hodgkin disease by 19.5%, sarcomas by 14%, carcinomas by 11.5%, and non-Hodgkin lymphoma by 4.6%. Unilateral iliac sampling was considered sufficient in patients diagnosed with multiple myeloma, chronic myeloproliferative disorders, and myelodysplastic syndromes.[13]

**Postprocedure Care**

After the procedure, firm pressure is applied for 5 minutes to several layers of sterile gauze placed over the wound site. Remove residual antiseptic to avoid further skin irritation by the solution.

If hemorrhage from the wound persists, then place the patient in the supine position, with gauze over the wound site, so that consistent pressure can be applied for a minimum of 30 minutes. Rarely, bleeding may be present; if that is the case, consider placing a pressure dressing, again with the patient in a supine position, for an additional 1 hour.[10]

The patient is to be discharged with orders that the wound dressing is to be maintained in a dry state for 48 hours. The wound site is to be checked frequently, and if persistent bleeding or worsening pain occurs, these findings are to be reported to the clinician’s office.

**Slide Preparation**

This stage in bone marrow preparation should be performed by trained personnel, such as a hematopathology technician. Thin-spread preparations of aspiration-collected samples, placed onto glass slides, can be prepared in numerous ways, all of which have the aim to retain and evaluate marrow particles. These spicules of fat droplets (not prominently seen in pediatric cases) and fragmented bone are likely to have adherent cellular material and thus be a target for morphologic evaluation. See the images below.

- An aspirate smear (or wedge) is the most simplistic of the methods, similar in presentation as a peripheral blood smear. A drop of the acquired specimen is placed 1 cm from the edge that opposes the frosted "labeled" end and, with a second glass slide placed at a 30º angle, the sample is pushed toward the opposing side in one rapid smooth stroke. Excess sample can be removed by tilting the glass slide onto gauze or pipetting the extraneous fluid.
Squash (or crush) preparations are prepared on glass slides by placing marrow particles on a slide and pressing the particles with another slide. These preparations are used to better observe cellular interactions as the architecture of the marrow unit is preserved. One report has shown that the crush technique is better for the evaluation of the percentage composition of bone marrow cells, whereas the wedge technique may be better to identify cellularity.[14]

The cover slip method produces samples that have been concentrated more than the squash preparation. The aspirate particles are selected from a petri dish and directly placed onto a glass cover slip. In a manner similar to the squash method, a second cover slip is gently applied to crush the sample. Each cover slip is then stained individually. Thus, enhanced removal of contaminating peripheral blood is performed, again with retention of the marrow unit architecture.

At times, biopsy touch prints are useful, especially if the aspirate is dry and the only sample available is the bone marrow biopsy. In touch preparations, the hematopathology technician gently touches the tissue fragment onto a glass slide; this can provide morphologic details similar to that of an aspirate.

Marrow particles can be collected in aggregate as a clot and processed in a similar manner to that of tissue. The solid component is concentrated by placing the specimen in a finely meshed bag that retains the tissue fragments, but which allows excess fluid to escape.

Bone marrow aspiration and biopsy slide preparation.

Bone marrow aspiration and biopsy slides before staining.

Standard stains used for the initial evaluation include Wright or May-Grunwald-Giemsa staining which enhance cytologic detail. Other special stains can be utilized for various purposes such as Prussian blue for iron in cases of suspected hemosiderosis or for the ringed sideroblasts of myelodysplastic syndromes. Myeloperoxidase, Sudan Black B, and leukocyte alkaline phosphatase are used in the categorization of acute myeloid leukemias. Periodic acid-Schiff (PAS) stain enhances depiction of cells that are implicated in glycogen storage diseases.[4, 10, 15]

Morbidity/Mortality

In 2002 the British Society of Haematology initiated an annual survey to assess the various types and incidence of bone marrow biopsy adverse events.[16] Bain summarized results of a 7-year (1995 to 2001) retrospective study and identified 26 adverse events among approximately 54,890 biopsies, with an overall annual incidence of 0.05%. The most common side effects in order of decreasing frequency were the following: hemorrhage, needle breakage, and infections. Risk factors for hemorrhage included concurrent anticoagulation therapy or underlying myeloproliferative/myelodysplastic syndrome, in which platelet function was affected. Two cases were fatal and were attributed to sepsis and massive hemorrhage.[16]

Four years later, a prospective study by Bain revealed 15 adverse events in a single year, with an overall incidence
of 0.07%, not significantly different from the previous study's results.[11] However, although hemorrhage was still considered the most commonly encountered side effect, this study revealed that pain, anaphylactic reaction, and fractures were prominent secondary consequences. Two fatality cases, attributed to laceration of blood vessels, were reported from 20,323 bone marrow aspiration and biopsy procedures.[11]

**Special Concerns**

- **General anesthesia** is required for pediatric cases, some sternal bone marrow sampling cases, and in those patients who are highly anxious.
- Sternal bone marrow aspiration has a higher risk of complications than other sites due to the delicate bone structure (approximately 1 cm thick in adults). Penetration of the underlying mediastinal organs can result in mediastinitis, pulmonary embolism, pneumothorax, cardiac tamponade, and cardiac tissue injury. For these reasons, biopsies are not to be performed from the sternum.
- Awareness of anatomic variations and pathologies that may affect bone density (eg, osteoporosis, multiple myeloma) can prevent further complications and injuries.
- Thrombocytopenia is not a contraindication to bone marrow aspiration and biopsy.
- Corrective action is required for coagulation disorders before bone marrow sampling.
- Application of sterile techniques is required in the prevention of infections.
- **Dry tap,** or the lack of specimen obtainment during the aspiration sampling process, is most commonly due to technical problems such as misalignment of the needle. Other conditions that should be considered and may contribute to the decision of obtaining a biopsy are recent radiation therapy exposure, aplastic anemia, myelofibrosis, or bone infiltrative neoplasm.
- Knowing that tissue shrinkage can occur at an approximate rate of 25% after processing, the desired biopsy sampling size should initially be greater than 1.5 cm, preferably 2-3 cm in length (pediatric samples may be as small as 0.5 cm). Such a size will allow for the evaluation of 5 or 6 intertrabecular spaces, which is considered sufficient sampling for a diagnosis.[5, 6, 17]
- Rarely, chronic pain may occur at the site of bone marrow sampling, thus requiring further clinical management.

**Medical-Legal Pitfalls**

- Failure to prevent, recognize, or initiate rapid response to excessive bleeding or, rarely, to an anaphylaxis anesthetic event during the bone marrow sampling procedure
- Failure to use proper safety techniques, such as having a guard device to prevent needle slippage, specifically during sternal aspiration.
- Failure to identify complications in sampling an iliac crest that results in penetration of the underlying gastrointestinal tract as well as blood vessels—the latter which runs the risk of the development of massive retroperitoneal hemorrhage and gluteal compartment syndrome[18]

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**References**


