The bone marrow is widely distributed throughout the skeletal system. Although marrow elements can be found in virtually all bones, the vast majority of haematopoietically active marrow is found in the long bones, ribs, vertebrae, and flat bones, particularly in the pelvis. In an adult, the estimated marrow volume is about 1,700 mL and thus the marrow is one of the largest organs in the body, similar in size to the liver and brain.

The primary function of the bone marrow is hematopoiesis. Daily red cell production rate is estimated at $2 \times 10^{11}$, WBC (neutrophil) production rate at $0.85-1.6 \times 10^{10}$, and platelet production at $1 \times 10^8$. Additional marrow elements include osteoclasts and osteoblasts, marrow stromal cells, mast cells, and fat cells, all of which play a role in hematopoiesis.

Marrow elements are not exclusively confined to the bone marrow cavities. In unusual situations marrow elements can be identified in other organs (extramedullary hematopoiesis). Most commonly this would be in the liver and spleen. But foci have been identified in other organs, and even in implanted hearts.

This chapter is an introduction to this remarkable organ, and subsequent ones will be concerned with the various marrow elements that can be found in both normal and pathologic conditions. We’ll present how the marrow is sampled, patterns of disease, and the importance of bone marrow differentials. Finally, there is a discussion of the future of hematology, through the lens of artificial intelligence and machine learning.
Bone Marrow Sampling and Specimen Processing
Extramedullary Hematopoiesis
Bone Marrow Environment
Bone Marrow Smear Examination and Differential
Artificial Intelligence in Hematology
Evolution of Bone Marrow Sampling

Archaeologic evidence indicates that trepanning, a surgical procedure involving scraping or actual drilling of the skull to access the dura, the thick membrane located immediately beneath the inner table of the skull, was performed at least 10,000 years ago. The indications were varied, ranging from trauma to epilepsy to an attempt to cure “madness,” but it is obvious from the available evidence that some patients did survive the procedure.

Aspiration of bone marrow for scientific evaluation was first performed in the 19th century, accessing the proximal femoral epiphysis with a needle driven through the cortex using a hammer. Smears were prepared and the cells identified and evaluated. By the end of the 19th century various cell types were defined using what has become the Wright-Giemsa stain. Abnormal cells, such as myeloblasts containing Auer rods were also identified.

By the 1920s marrow for diagnostic purposes was obtained by sternal puncture. Anirkin (as cited by Parapia) reported 27 cases with no complications where marrow was obtained using a lumbar puncture needle. Several specialized sternal puncture needles were subsequently developed with guards to avoid puncturing the inner sternal cortex and marrow aspiration and biopsy became more common. By 1943, following several deaths due to the biopsy needle being driven through the inner cortex and penetrating the heart or other mediastinal structures, the sternal approach to obtaining a bone marrow specimen fell into disuse. In 1948 Limarzi and Bedinger (as cited by Parapia) reported their experience with a needle using an improved guard to prevent puncture of the inner cortex. This needle, developed at the University of Illinois and therefore referred to as the “Illinois Needle” was easy to use and very safe; the Illinois Needle or one of its modifications is the standard instrument used today to obtain a sternal marrow specimen.

Beginning about 1950, the iliac crest, which contains about 50% of the hematologically active marrow, became the preferred site to sample. Several biopsy instruments were developed for this site. In 1971, Khosrow Jamshidi patented his design where the distal portion of the needle lumen is radially tapered towards the cutting tip allowing the biopsy material to expand as it enters the lumen, avoiding crush artifact (see Figure 3).

His initial work, published with Swaim, established the Jamshidi Needle or one of several modifications as the currently preferred biopsy instrument for sampling the iliac crest. The evolution of this technology has resulted in an approach to evaluation and classification of bone marrow disorders that is still used today. Comprehensive lists suggesting indications for examination of the bone marrow have also been published.

Indications for a Bone Marrow Examination

Bone marrow examination is a common procedure in diagnostic hematology, and the availability of newer diagnostic techniques such as flow cytometry and molecular/cytogenetic analytic techniques have increased the frequency of marrow sampling. On the other hand, advances in technology have also decreased the need to examine the marrow to establish the diagnosis of conditions such as
pernicious anemia. A typical list of current indications for a bone marrow examination includes:

- Unexplained anemia, leukopenia, or thrombocytopenia
- Unexplained polycythemia, leukocytosis, or thrombocytosis
- Unexplained organomegaly or lymphadenopathy
- Evaluation for possible metastatic disease
- Unexplained findings from radiographic imaging
- Monitoring response to therapy for established disease states
- Fever of unknown origin
- Obtaining material for ancillary diagnostic studies

Obtaining a Bone Marrow Specimen

Obtaining a bone marrow specimen that is both optimal for diagnosis and accommodates the special studies often required today requires an on-site team of highly trained medical technologists. A bone marrow examination is a team effort.

There are several preferred marrow sampling sites, as shown in Figure 5. The most common is the posterior iliac crest. The patient can be positioned in either the prone or the lateral decubitus (fetal) position. In special cases, the anterior iliac spine is an acceptable biopsy site—particularly if the patient has a large decubitus ulcer, the site cannot be properly sterilized or the fat pad is so thick that bony landmarks cannot be palpated. There are several online videos available illustrating the technique employed and they can be easily accessed by doing a search on “bone marrow biopsy procedure technique” or a similar phrase using your favorite browser search engine. Any of these demonstrate how to obtain the specimen but do not adequately portray the immediate processing steps performed by the attending medical technology team in order to ensure that all of the potential information it contains can be accessed. Table 1 lists the various samples that can be collected during a bone marrow procedure.

There are a few points to emphasize regarding obtaining the specimen from the posterior iliac crest:

- Sufficient local anesthetic should be used to allow the operator to drag the tip of the biopsy needle
In adults and older children, the usual bone marrow sites are the posterior-superior iliac crest, the anterior iliac spine, and the sternum. The preferred site is the posterior iliac crest, which allows for both an aspirate and a biopsy sample. If the posterior site is inaccessible due to patient immobility, markedly thickened fat pad, or inability to be sterilized (e.g., presence of a large decubitus ulcer, etc.), the anterior iliac crest is the preferred site. The sternum is hematopoietically active throughout life but the bone marrow sample should only be an aspirate—biopsying the sternum risks penetration through the bone into the heart.

In infants and children under the age of two, the optimum site is the tibial tubercle. Even in the smallest premature babies the tibia can be easily positioned without disturbing the infant. The tibia is also a safer site in very small pre-term infants, since it avoids any proximity to vital organs. Other less commonly used sites are the spinous processes of the vertebrae, the femur, and the humerus.
A is a CT of the pelvis. When sampling the posterior iliac crest, the bone marrow biopsy needle should be inserted at about a 15° angle, ensuring that the marrow cavity will be followed. B is a Jamshidi needle removed after sampling the posterior iliac crest. A probe inserted into the beveled end is used to push out the core biopsy. A close-up of the Jamshidi needle and the core biopsy is shown in C. The core biopsy is touched repeatedly with a glass slide (D) to make imprints ("touch preps"). An H&E slide of the trephine biopsy specimen is seen in E. The dark blue area of the biopsy image is a piece of cartilage. F shows imprint preparations made by lightly touching the core biopsy multiple times with a clean glass slide. Such touch preparations should always be done and may be the only air-dried sample available if there is a dry tap. G is a split screen photomicrograph of two bone marrow biopsy sections, one fixed in formalin (left) and the other in Zenker’s (right). Formalin fixation is associated with tissue shrinkage and loss of cellular detail when compared to use of a non-formalin fixative such as Zenker’s.
across the periosteal surface as it is removed in order to prevent loss of a portion of the biopsy core as the needle traverses the periosteum and subcutaneous tissues.

- With proper attention to the anatomy, a large-caliber biopsy needle (8- or 12-gauge) can be used and the specimen obtained is superior for diagnostic purposes to one obtained with a smaller needle.

- The CT image in Figure 6-A illustrates that the biopsy needle should be aligned at about a 15° angle and directed at the anterior iliac spine, ensuring that the marrow cavity will be followed. This can be facilitated by guiding the biopsy needle with one hand and placing the fingers of the other hand on the anterior iliac spine to serve as a “target.”

- When the biopsy needle has been advanced to the proper depth it should be vigorously rotated several times in each direction before removal in order to free the retained core from the marrow. The tip of the Jamshidi needle is tapered and has a cutting edge.

- The biopsy core should be at least 2 cm in length and should include more than the immediate subcortical marrow, which is frequently hypocellular. Cortical bone is generally white and homogeneous; cartilage has a smooth, glistening appearance. The marrow itself is generally pink-red.

Sternal Bone Marrow Aspiration
The most common reason for obtaining a bone marrow specimen via the sternal approach is when a patient has received cranio-spinal axis radiation. In this case the iliac crest marrow will be hypocellular and non-representative. In some morbidly obese patients it may not be feasible to obtain marrow from the iliac crest as posterior iliac crest landmarks may be obscured. A better option may be the anterior iliac crest or a sternal aspirate.

Figure 7-B shows the procedure at the time of aspiration. The biopsy point is the mid-sternal body. This is identified as a point approximately two fingerbreadths (2 cm) below the manubrio-sternal junction (the Angle of Louis). It is important to use a needle with a guard (such as the Illinois Needle) so that the needle tip is located in the marrow space and does not penetrate the internal cortex of the sternum. The external sternal cortex is about 2 to 3 mm in thickness.

The guard is initially positioned so that the needle tip cannot be advanced beyond the outer cortical periosteum. The needle guard is then repositioned approximately two complete turns (720° of rotation) and the needle is then advanced until the guard is again in contact with the underlying skin. This should position the needle tip within the marrow cavity. Repeated aspirates can be obtained as with an iliac crest specimen if special studies are desired (Figure 8).

Protocols for Collection and Processing of Bone Marrow
There are two general protocols for collection and processing of iliac crest marrow. In 1978 Byrnes, et al. published a method for collection and on-site processing that is still in use today. This protocol provides the most comprehensive approach to the anatomic examination of the marrow.
Figure 8. Bone Marrow Aspirate Collection Protocol

Table 1: Bone Marrow Preparations for Morphologic Evaluation

<table>
<thead>
<tr>
<th>Type of Preparation</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Smears, without Anticoagulation</td>
<td>Particle placed between two slides or a slide and a coverslip; particle is crushed or pushed across slide to make the smear</td>
</tr>
<tr>
<td>Direct Smears, with Anticoagulation</td>
<td>Anticoagulant added to aspirate and then particles are removed with a pipet and smeared, as above</td>
</tr>
<tr>
<td>Centrifugation and Buffy Coat Smear</td>
<td>Anticoagulated marrow is centrifuged into layers (Figure 14); buffy coat particle concentrates are mixed with plasma and then smeared similar to a peripheral blood preparation, producing cells evenly distributed over entire slide</td>
</tr>
<tr>
<td>Particle (Clot) Section</td>
<td>Clotted particles collected after making smears, placed in fixative, and processed for histology</td>
</tr>
<tr>
<td>Bone Marrow Biopsy Section</td>
<td>Core bone marrow biopsy fixed, decalcified, and processed for histology</td>
</tr>
<tr>
<td>Touch Imprints</td>
<td>Glass slide is gently and repeatedly touched to the bone biopsy; the slide is allowed to air-dry and then stained</td>
</tr>
</tbody>
</table>
specimen. With the development of new diagnostic tools that provide more information for the diagnosis of primary bone marrow neoplasms and for pertinent cytogenetic studies, integrated reporting protocols have been developed that require extraction of multiple marrow samples, which are each handled differently at the bedside. Each of these protocols will be discussed (Figures 8, 9, and 10).

The protocol defined by Byrnes requires the on-site preparation of both trephine biopsy imprints and direct marrow aspirate smears along with subsequent centrifugation of the residual liquid marrow. Initial specimen processing has multiple simultaneous steps and although a single operator can perform them all, the assistance of trained medical technologists or nurses is valuable.

There are a few points to emphasize regarding on-site specimen processing:

- The initial marrow aspirate volume should be no more than 1.5 to 2 cc in order to prevent dilution by sinusoidal blood.
- A 3-cc sample for the initial pull is appropriate if next generation sequencing (NGS), PCR, or multi-parameter flow cytometry is needed to quantify minimal/measurable residual disease (MRD) in patients with acute lymphoblastic leukemia (ALL). These studies are best done on the initial pull (see discussion, page 14).
- Imprints of the marrow trephine biopsy (Figure 6) and direct smears of the marrow aspirate (Figure 9) are prepared at the bedside.
- The trephine biopsy should be expressed onto a 4 X 4 inch telfa pad (not a gauze sponge) in order to remove any liquid blood and allow for optimal imprint smears or “touch preps” (Figure 6). This is the only specimen that cytologically represents marrow cellularity and the relationship of marrow elements as they will be seen in histologic sections of the biopsy.
- Direct smears of the marrow aspirate can be prepared at the bedside from aspirate material remaining in the syringe. As shown in Figure 9, the marrow is injected onto a tilted piece of plate glass or a glass slide. Blood runs down the glass, leaving marrow particles behind. Either particle crush smears (Figure 9) or push smears (Figure 11) are made before the blood clots.
- The aspirate sample is rich in thromboplastin and

Bone Marrow Aspirate Specimen Handling

Figure 9. Direct Smears Performed at Bedside

The photos above show the steps in a direct smear preparation. A portion of the aspirate is expelled onto a glass plate (A) or even another glass slide (B). Blood runs down the glass, leaving a few spicules behind that can be scooped up with the edge of a clean slide. “Squash preparations” as shown in image D can be made or a push smear, as shown in Figure 11. The excess clotted blood can be collected on a telfa pad and placed in fixative for histologic evaluation. Images B, C, and D from Trejo-Ayalaa RA et al. “Bone marrow aspiration and biopsy. Technique and considerations”. Revista Médica del Hospital General de México. 2015;78:196-201. Used with permission.
Instead of making direct smears at the bedside, some bone marrow protocols add anticoagulation to the marrow before it clots. The liquid specimen is then taken to the lab and individual marrow spicules are harvested and then smeared on a slide, either using “squash” preps (Figures 9-C and 9-D) or the push slide method shown in Figure 11, below. Anticoagulation can add artifacts to the smears, however. Photographs A and B are petri dishes containing anticoagulated marrow. Spicules are readily identified. Individual spicules can be collected using a pipet (B) and then smears are made.

Direct aspirate smears can be made using a “squash” technique, as shown in Figure 9-D or by a push technique, as shown in A through D. A spicule is transferred to the slide (A) and then a coverslip, held by a Dieffenbach’s serrifine forceps, is placed at an angle on top of the liquid sample (B and illustration D). Blood and marrow spread out along the bottom of the coverslip and then it is pushed with uniform pressure toward the opposite end of the slide. Photograph E shows an unstained smear prepared with crush technique, as shown in Figure 9-D on the previous page. There is less smear uniformity compared to the push technique in C. Photograph F shows the final Wright-Giemsa stained particle smear with a uniform feather edge and central spicule. After smears are made, the remaining blood is collected and placed in fixative for histologic processing.
Photographs A and B are low- and high-power views of the lateral edge of a smear. Large cells may accumulate there, such as leukemic cells and metastatic tumor. For this reason, it is important to examine not just the central part of the smear where cells are more abundant but also the edges.

Photographs A and B show bone marrow particle preparation. After direct smears are prepared, the plate glass is scraped down to the telfa pad and the bone marrow particles are collected into a biopsy bag for fixation. If the specimen is anticoagulated, remaining blood and spicules can be collected for histology processing as well.

will rapidly clot. A portion is placed in an EDTA tube at the same time that direct smears are being made using the material remaining in the syringe. The tube should be rapidly inverted to prevent clotting. This anticoagulated sample can be used to make additional smears or centrifuged to make buffy coat smears, as shown in Figure 14.

• Direct smears are useful because they are free of any artifacts induced by anticoagulants. Nevertheless, it may be more convenient to bring the sample down to the laboratory for processing, and adding anticoagulant to the marrow is required for transport (Figure 10).

• One of the key reasons for optimally preparing clot-free marrow smears (this also applies to concentrate smears described on the next page) concerns the importance of scanning the margins of the smears. Larger cells tend to accumulate along the margins and thus rarely encountered cells (blasts, metastatic tumor cells) may gather there. Examining a smear free of clots optimizes the chance to identify these rare but important cells (Figures 12-A and 12-B show large leukemic cells along margins of the smear).

• If special studies (cytogenetics, flow cytometry, cell surface marker studies, cultures for infectious agents) are needed, this will require a separate aspiration biopsy from the same general site; otherwise the aspirate volume from a single pull would be too large to do these studies plus prepare adequate marrow smears for conventional cytology, the primary basis for classification of marrow abnormalities (Figure 8).

• Residual marrow particles can be gently scraped from the telfa pad and collected in a tissue bag for fixation and processing. Such particle sections can be stained with H&E, iron, PAS, and other histochemical or immunohistochemical stains (Figure 8).

• The trephine biopsy as well as marrow particles should be placed in a non-formalin-based fixative to prevent shrinkage and preserve cellular detail. Figure 6-G compares a marrow specimen fixed in formalin and Zenker’s fixatives. Mercury-based fixatives such as Zenker’s and B5 produce the best cytologic detail but due to expense and environmental concerns, other fixatives may be preferred, such as zinc-formalin.

• After fixation, decalcification, and processing, the trephine biopsy is sectioned at 4 µ and stained with hematoxylin-eosin for evaluation. Specimen processing usually requires around 24 hours.

• The aspirate can be centrifuged to produce buffy
Centrifuged bone marrow aspirate separates into four distinct layers: fat-perivascular (F-PV) layer, plasma (P) layer, myeloid-erythroid (M-E) layer, and residual blood (RBC) containing marrow particles. The fat is rich in histiocytes and is an optimal specimen for estimating bone marrow iron stores. Smears are made from the M-E layer, which provide a rich source of nucleated cells that may be easier to read than a traditional direct smear.

**Buffy Coat Centrifugation Technique**

This method is not in widespread use but provides beautiful smears with well-separated cells dispersed over the entire slide. Morphology is excellent and staining is uniform. The liquid aspirate is centrifuged and the marrow separates into four distinct layers: fat/perivascular layer, plasma layer, myeloid/erythroid (M-E) layer, and residual blood containing marrow particles. The fat is rich in histiocytes and is an optimal specimen for estimating marrow iron stores. Smears of the concentrated M-E layer are often more uniform and easier to read than direct smears but cellular details and cell-to-cell interactions are better preserved in well-prepared direct smears.

Evaluation of the centrifuged marrow specimen can provide additional information about overall marrow cellularity:

- In a normal centrifuged bone marrow aspirate, the fat-perivascular (F-PV) layer represents about 2-5%, the plasma (P) layer about 40-65%, the myeloid (M-E) layer about 5%, and the residual blood cell (RBC) layer about 30-50% of the specimen.
- Using a micro-pipette, the fat layer is removed from the centrifuged specimen and smears prepared that can be stained with Wright-Giemsa stain and iron. Histiocytes are often concentrated in this layer and it is easier to evaluate marrow iron stores from this specimen.
- The M-E layer is mixed 2:1 with the plasma layer and marrow concentrate smears are prepared from this specimen. The difference between direct and concentrated smears is illustrated in Figure 14-D and 14-E. Photograph 14-D is the direct smear and 14-E is the concentrate smear from the same patient.
- Examples of centrifuge results are shown above—normocellular marrow, hypocellular marrow (aplastic anemia), and hypercellular marrow (chronic myelogenous leukemia). Notice how the proportion of each layer changes.
coat smears (see Figure 14).

- Diagnoses often require specialized testing such as FISH, PCR, and gene expression profiling. Fresh tissue or unstained slides may be needed.
- If no aspirate can be obtained (dry tap), a portion of the marrow biopsy can be placed in RPMI medium and used for flow cytometry and other analyses.

Minimal/Measurable Residual Disease
Patients with acute lymphoblastic leukemia may have a complete remission after treatment (defined as <5% blasts), but that does not mean all the leukemic cells have been eliminated. The body may harbor as many as $10^{10}$ malignant cells in the bone marrow that are not detectable using conventional morphology alone. Minimal or measurable residual disease (MRD) refers to the threshold for detecting leukemic cells in the bone marrow. The most frequently used methods for MRD quantification include multiparameter flow cytometry and PCR assays for specific fusion genes such as BCR-ABL1. The most sensitive method is next-generation sequencing (NGS) to detect clonal rearrangements in immunoglobulin and T-cell receptor genes. Determining the MRD is important because the number of residual leukemic cells has prognostic significance; there is a strong correlation between MRD and risk of relapse. Current recommendations are to perform MRD studies using the initial pull of marrow of up to 3 mL, rather than the third pull, which would be too dilute.

Managing the Patient After the Procedure
This discussion will assume the iliac crest has been used as the biopsy site. In general, an iodine-containing antiseptic is used as a bone marrow biopsy is considered to be a minor surgical procedure. This should be removed with an alcohol-saturated swab and a bandage applied. The patient is then positioned in the supine position (face up) until primary hemostasis is achieved. A good general time estimate is 10 minutes. After the site is inspected to ensure there is no further bleeding, the patient can be discharged and instructed to avoid heavy lifting or exertion for 24 hours, similar to instructions given after a blood donation. The bandage can be removed at that time. Potential complications of this procedure are bleeding and local infection, both extremely uncommon, even in patients with either inherited or acquired coagulation disorders. The patient should be instructed to contact their health care professional if signs of these complications occur.

Pediatric Bone Marrow Examination
The most common reason for conducting a bone marrow examination in the pediatric population is when the diagnosis of acute leukemia is suspected. In the past, especially in very young infants, marrow was obtained from the tibial tubercle by aspiration (bottom of Figure 5). Today most bone marrow specimens in children older than two years are obtained from the iliac crest. Needles are appropriately smaller and often general anesthesia is used. In some instances, particularly in children under 12 months of age, the tibial tubercle is still used as the source. Rarely the spinous process of one of the prominent vertebral segments (C7, L1, L2) can be used. Steps for processing the specimen are similar to those described for adults.

Bone Marrow Results Reporting
Regardless of the institution-specific format used, the final report of a bone marrow examination should integrate results from evaluation of the peripheral blood smear, the bone marrow aspiration, the bone marrow trephine biopsy, and all pertinent ancillary studies such as flow cytometry, cytogenetics, molecular cytogenetics, and microbiologic culture results, if applicable. This is similar to the synoptic reporting format that is now the standard for reporting non-hematologic malignancies. Comprehensive tables listing specific items to include are detailed by Kottke-Marchant as well as others and supported by guidelines published by such organizations as the College of American Pathologists and the International Council for Standardization in Haematology.

Table 2: Potential Components of a Comprehensive Bone Marrow Report

<table>
<thead>
<tr>
<th>Clinical Information, Morphology, and Ancillary Tests</th>
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<tbody>
<tr>
<td>Clinical History</td>
</tr>
<tr>
<td>Indication for Procedure</td>
</tr>
<tr>
<td>Pertinent Previous Test Results</td>
</tr>
<tr>
<td>Routine Laboratory Results</td>
</tr>
<tr>
<td>Complete Blood Count (concurrent)</td>
</tr>
<tr>
<td>Peripheral Smear Microscopy (concurrent)</td>
</tr>
<tr>
<td>Bone Marrow Clot Section Microscopy</td>
</tr>
<tr>
<td>Bone Marrow Biopsy Section Microscopy</td>
</tr>
<tr>
<td>Bone Marrow Aspirate Smear Microscopy</td>
</tr>
<tr>
<td>Routine Special Stains (PAS, Iron)</td>
</tr>
<tr>
<td>Microbiology Culture</td>
</tr>
<tr>
<td>Immunohistochemistry Stains</td>
</tr>
<tr>
<td>Flow Cytometry</td>
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<tr>
<td>Conventional Cytogenetics</td>
</tr>
<tr>
<td>FISH</td>
</tr>
<tr>
<td>Qualitative &amp; Quantitative PCR</td>
</tr>
<tr>
<td>Gene Expression Profiling</td>
</tr>
<tr>
<td>Molecular Genetics</td>
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<tr>
<td>Next-Generation Sequencing</td>
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</table>
This is an example of a multipage comprehensive bone marrow report that combines routine laboratory findings (CBC), morphology of peripheral blood and marrow (including a 200-cell differential), conventional cytogenetics, flow cytometry, and special stains. Different pathologists signed out different parts of the report and a single pathologist created the final comprehensive report.

**Introduction**

The hematopoietic system is composed of blood cells and their precursors. The bone marrow is a highly specialized tissue that produces blood cells. The bone marrow contains various cell types, including hematopoietic stem cells, which are responsible for the production of blood cells.

**Diagnosis**

**Bone Marrow**

Hypercellular (Cellularity = 100%) with marked immaturity (blasts = 98%)

Suppressed myeloid and erythroid maturation.

Adenocarcinoma of the prostate consistent with T-Lymphoblastic Leukemia/Lymphoma, T-LBL.