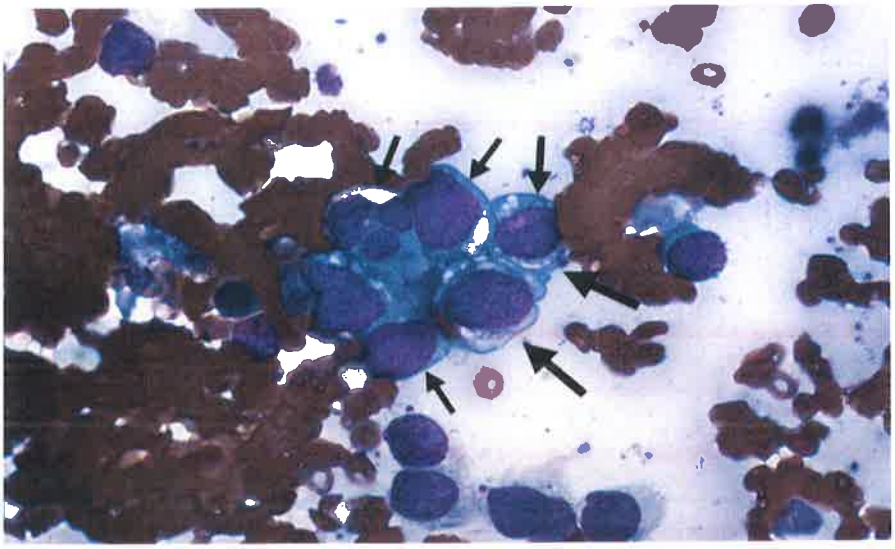
Cell Identification

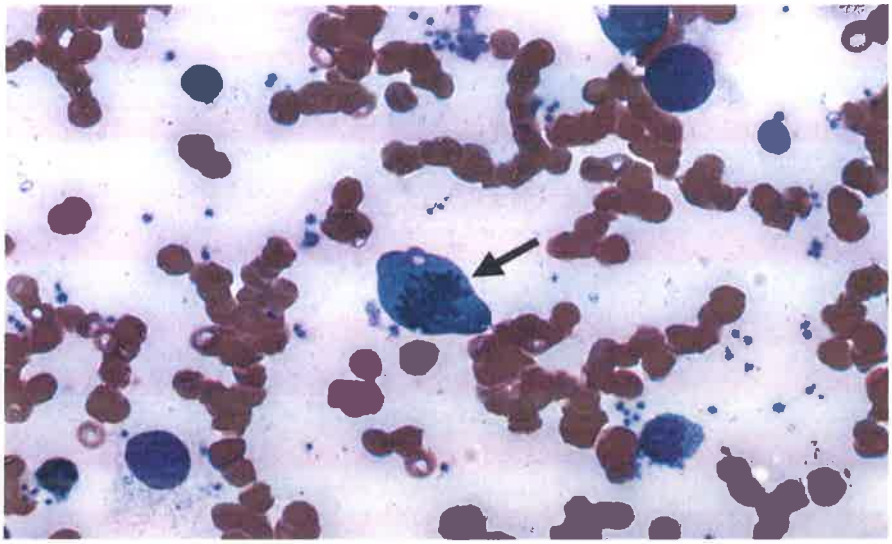


BMD-02

Identification	Participants No.	Participants %	Evaluation
Metastatic tumor cell or tumor cell clump	306	91.9	Educational
Blast cell (includes lymphoblast)	15	4.5	Educational
Immature/abnormal cell, would refer for identification	3	0.9	Educational
Malignant lymphoid cell (other than blast)	2	0.6	Educational
Monocyte, immature (promonocyte, monoblast)	2	0.6	Educational
Stromal cell	2	0.6	Educational
Erythrocyte precursor, abnormal/dysplastic nuclear features (includes pronormoblast, basophilic, polychromatophilic, and orthochromic normoblasts)	1	0.3	Educational
Erythrocyte precursor, normal (includes pronormoblast, basophilic, polychromatophilic, and orthochromic normoblasts)	1	0.3	Educational
Osteoblast	1	0.3	Educational

The arrowed cells are metastatic tumor cells or a tumor cell clump as correctly identified by 91.9% of participants. These malignant cells are larger than hematopoietic cells and form clusters rather than dispersed cells. The cells have a high nuclear:cytoplasmic ratio and hyperchromatic nuclei. These cells also have vacuoles and inconspicuous nucleoli. Blasts, identified by 4.5% of participants, would be somewhat smaller and not cluster.

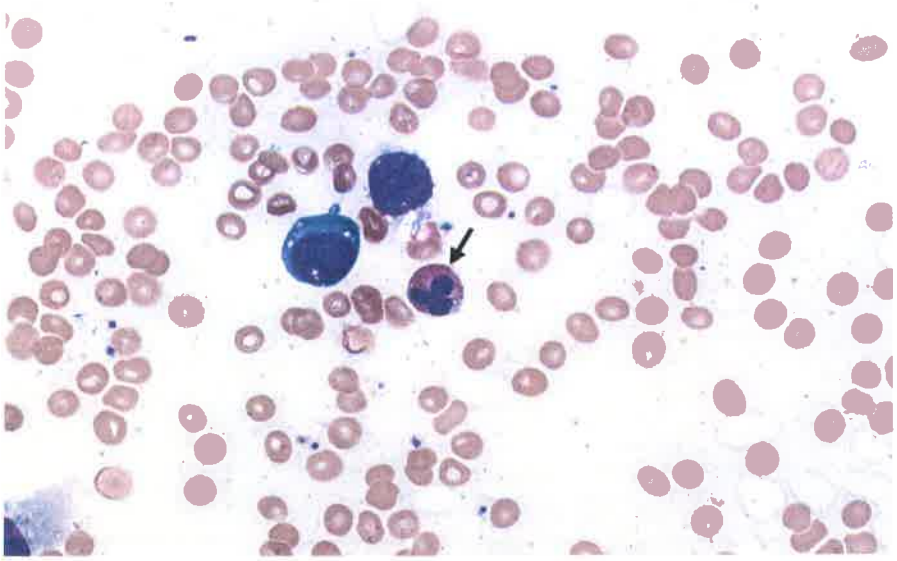
BMD-03



Identification	Participants No.	%	Evaluation
Mitotic figure	332	99.7	Educational
Metastatic tumor cell or tumor cell clump	1	0.3	Educational

The arrowed cell is a mitotic figure as correctly identified by 99.7% of participants. The mitotic figure demonstrates a spindle and separating chromosomes. These forms are often present in tumors with a high proliferative fraction with many dividing cells. The cytoplasm is the deep blue color of the malignant cells.

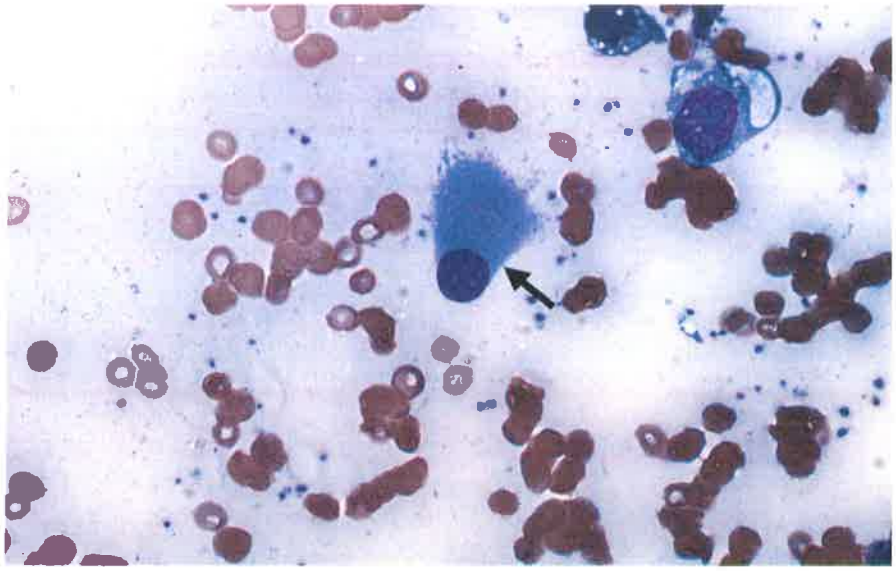
BMD-04



Identification	Participants No.	Participants %	Evaluation
Eosinophil, any stage	313	94.0	Educational
Neutrophil, segmented or band	15	4.5	Educational
Eosinophil, any stage with atypical/basophilic granulation	3	0.9	Educational
Neutrophil with dysplastic nucleus and/or hypogranular cytoplasm	1	0.3	Educational
Neutrophil, toxic (to include toxic granulation and/or Döhle bodies, and/or toxic vacuolization)	1	0.3	Educational

The arrowed cell is an eosinophil as correctly identified by 94.0% of participants. Eosinophils typically have bilobed nuclei (80% of cases) but may have three lobes, as in this example. The cells have coarse orange-red granules. The cells are approximately 10 - 15 um (similar to the size of neutrophils). While this cell has three lobes, it is not a neutrophil, as identified by 4.5% of participants, as it has coarse eosinophilic granules.

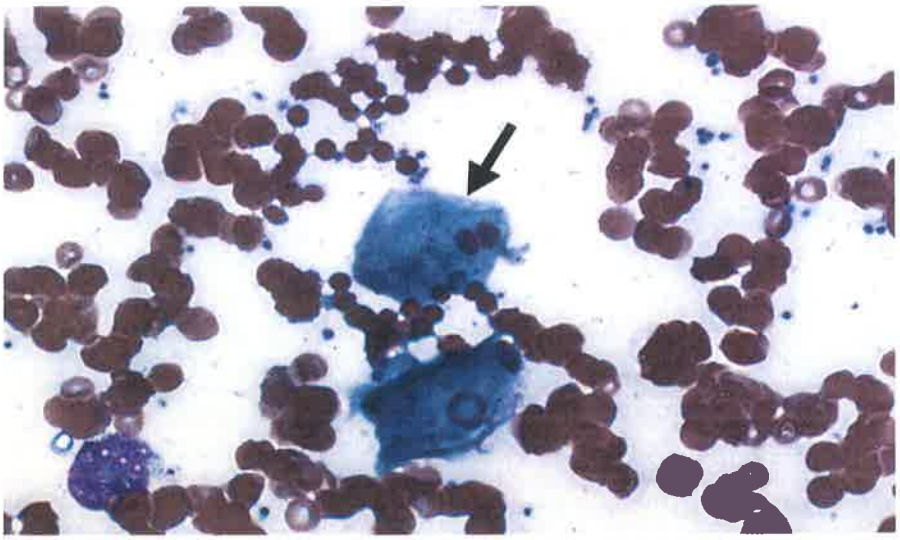
BMD-05



Identification	Participants No.	%	Evaluation
Osteoblast	256	76.9	Educational
Megakaryocyte or precursor, abnormal	18	5.4	Educational
Plasma cell, morphologically mature/abnormal/containing inclusion (eg, Dutcher body, Russell body)	18	5.4	Educational
Macrophage (histiocyte)	16	4.8	Educational
Megakaryocyte or precursor, normal	7	2.1	Educational
Gaucher cell, Pseudo-Gaucher cell	6	1.8	Educational
Histiocyte, sea blue	5	1.5	Educational
Osteoclast	4	1.2	Educational
Metastatic tumor cell or tumor cell clump	2	0.6	Educational
Erythrocyte precursor, normal (includes pronormoblast, basophilic, polychromatophilic, and orthochromic normoblasts)	1	0.3	Educational

The arrowed cell is an osteoblast as correctly identified by 76.9% of participants. Osteoblasts are typically found in bone marrow biopsies with active bony remodeling, such as in children. They are the size of macrophages (histiocytes), identified by 4.8% of participants, but have an eccentric nucleus that almost appears extruded from the cell, unlike plasma cells, identified by 5.4% of participants, which have the nucleus completely within the confines of the cell. As demonstrated here, the cell may resemble a badminton shuttlecock. This cell is not an abnormal megakaryocyte, identified by 5.4% of participants, since abnormal megakaryocytes should not have eccentric nuclei, nor is it a normal megakaryocyte, identified by 2.1% of participants, because those cells have multilobated nuclei. Osteoclasts, identified by 1.2% of participants, have multiple separate nuclei. Gaucher and pseudo-Gaucher cells, identified by 1.8% of participants, should have striated or tissue paper cytoplasm. Sea blue histiocytes, identified by 1.5% of participants, have round or crystalloid blue cytoplasmic inclusions.

BMD-06



Identification	Participants No.	%	Evaluation
Stain precipitate	192	57.8	Educational
Squamous epithelial cell/endothelial cell	67	20.2	Educational
Basket cell/smudge cell	23	6.9	Educational
Macrophage containing cell (hemophagocytosis)	22	6.6	Educational
Macrophage (histiocyte)	9	2.7	Educational
Gaucher cell, Pseudo-Gaucher cell	6	1.8	Educational
Osteoclast	4	1.2	Educational
Lipocyte (adipocyte, fat cell)	2	0.6	Educational
Megakaryocyte or precursor, normal	2	0.6	Educational
Stromal cell	2	0.6	Educational
Metastatic tumor cell or tumor cell clump	1	0.3	Educational
Osteoblast	1	0.3	Educational

The arrowed cell is a squamous epithelial cell as correctly identified by 20.2% of participants. These are artifact seen on slides from slide preparation. They are large (30 - 50 um) with abundant gray-blue cytoplasm and small condensed/absent nuclei. Stain precipitate, as identified by 57.8% of participants, should not have an intact nucleus. Basket/smudge cells, as identified by 6.9% of participants, should not have cytoplasm. Macrophage (histiocyte), identified by 2.7% of participants, and macrophages containing cells, identified by 6.6% of participants, (including Gaucher cells, identified by 1.8% of participants) should have a higher nuclear to cytoplasmic ratio. Osteoclasts, identified by 1.2% of participants, have multiple separate nuclei.

Case Presentation:
This bone marrow aspirate smear is from a 14-year-old boy with a recent diagnosis of Ewing sarcoma. Laboratory peripheral blood data includes: WBC = 2.3 x 10E9/L; RBC = 2.91 x 10E12/L; HGB = 8.6 g/dL; HCT = 26.1%; MCV = 88 fL, and PLT = 91 x 10E9/L.

(BONE MARROW, WRIGHT-GIEMSA)

Case Discussion: Ewing Sarcoma
The bone marrow aspirate shows clumps of malignant cells that are large with deep blue cytoplasm, vacuoles, and large nuclei with variably smooth chromatin and large inconspicuous nucleoli. They are similar in size or slightly larger than myeloid blasts and form clusters. These tumors are part of the differential diagnosis of small round blue cell tumors, which also includes alveolar rhabdomyosarcomas, neuroblastomas, small cell carcinomas, leukemias, and lymphomas. When clusters of cells are present, the neoplasm is more likely to be non-hematopoietic, as hematopoietic cells are usually found as single cells. Staging bone marrows are often performed after the diagnosis, although occasionally these tumors may be first identified in the bone marrow if the peripheral counts are low and a work-up for solid tumor has not been performed.

Question 1: The feature that is most helpful in distinguishing Ewing sarcoma from hematopoietic tumors is:
A. Cell size
B. Clusters of malignant cells
C. Nuclear features
D. Patient age

Ewing sarcoma is a common bone tumor in children (second most common to osteosarcoma) which also occurs in adults. It has a male predominance (3:2 male/female). Common sites of involvement include the tibia, pelvis, femur, and ribs. It can also occur in soft tissue. Patients often present with bone pain which may be present only at night. The painful area may have an associated palpable mass, but pain may also be mistaken for an athletic injury.

Question 2: The most common primary site of disease in Ewing sarcoma is:
A. Bone
B. Brain
C. Lung
D. Mediastinum

Ewing sarcoma is an aggressive cancer with a variable prognosis. The prognosis is good if it is localized but poor if metastatic or recurrent. One quarter of patients have metastases at diagnosis which is the reason why staging bone marrow biopsies are performed. Immunohistochemical markers include NKX2.2. A number of translocations have been identified, including *EWSR1-FLI1* which is seen in 85% of cases.

Question 3: The most common translocation in Ewing sarcoma is:
A. *EWSR1-FLI1*
B. *IGH-BCL2*
C. *IGH-CCND1*
D. *PML-RARA*

Bone marrow involvement is found in approximately 10% of patients. Metastases may also be seen on FDG PET-CT scans which would negate the need for a staging bone marrow biopsy. Treatment involves systemic chemotherapy and local treatment (either surgery or radiation).

Question 4: The prognosis of Ewing sarcoma is best in patients with:
A. Bone marrow metastases
B. Localized disease
C. Recurrence
D. Widespread metastases

Lauren B. Smith, MD
Hematology and Clinical Microscopy Committee

Reference

Grunewald TGP, Cidre-Aranaz F, Surdez, D, et al. Ewing sarcoma. *Nat Rev Dis Primers*. 2018;4(1):5. https://doi.org/10.1038/s41572-018-0003-x

Answers to Questions:

Question 1: B. Clusters of malignant cells

Hematopoietic tumors (leukemias/lymphomas) tend to have single cells on aspirate smears, whereas non-hematopoietic/solid tumors are more likely to forms clusters/clumps.

Question 2: A. Bone

Bone and soft tissue are the most common sites of disease in Ewing sarcoma. The other sites could happen with metastases/recurrence but would not be primary site of disease.

Question 3: A. *EWSR1-FLI1*

The other translocations listed are seen in acute promyelocytic (choice D, PML-RARA), follicular lymphoma and diffuse large B cell lymphoma (choice B, IGH-BCL2), and mantle cell lymphoma and plasma cell myeloma (choice C, IGH-CCND1).

Question 4: B. Localized disease

While patients with localized disease have a 5-year survival of 70 - 80%, the survival rate is only 20 - 30% in patients with metastases or recurrence.

Attestation of Participation of Self-Reported Training*

We the participants below have completed the review of the BMD-A 2021 CAP Program
Product Mailing, Year

Participant Summary/Final Critique report and can self-report this activity towards fulfilling education and maintenance of certification (MOC) requirements. Time spent on activity* _____.

Participant	Date	Participant	Date

_____ _____

Director (or Designee) Signature - I have verified that the individuals listed above have successfully participated in this activity. Date

Retain this page for record-keeping and auditing purposes.

1. Go to www.cap.org
2. Click **Login** and enter your User ID and Password.
   - If you are unsure whether you have an *individual* web account with the CAP, or do not remember your user ID and password, click on **PASSWORD HINT**.
   - If you do not have an *individual* web account, click **CREATE AN ACCOUNT**. Complete and submit the account request form. You will be notified within one business day that your individual account has been activated.
3. Click **Learning** from the top menu bar
4. Click **Transcript** from the menu bar
5. Click **+ Add my own activity**
6. Follow prompts to enter 'Self-Reported Training Activities' including upload of this supporting documentation*.

For assistance, call our Customer Contact Center at 800-323-4040 or 847-832-7000 option 1.

**** CAP Self-Reported Training activities do not offer CE credit but can be used towards fulfilling requirements for maintenance of certification by agencies such as the American Society of Clinical Pathology (ASCP). Please verify with your certifying agency to determine your education requirements. Individuals should report the actual time spent completing the activity.***