# VPBS-A 2022 EDUCATION

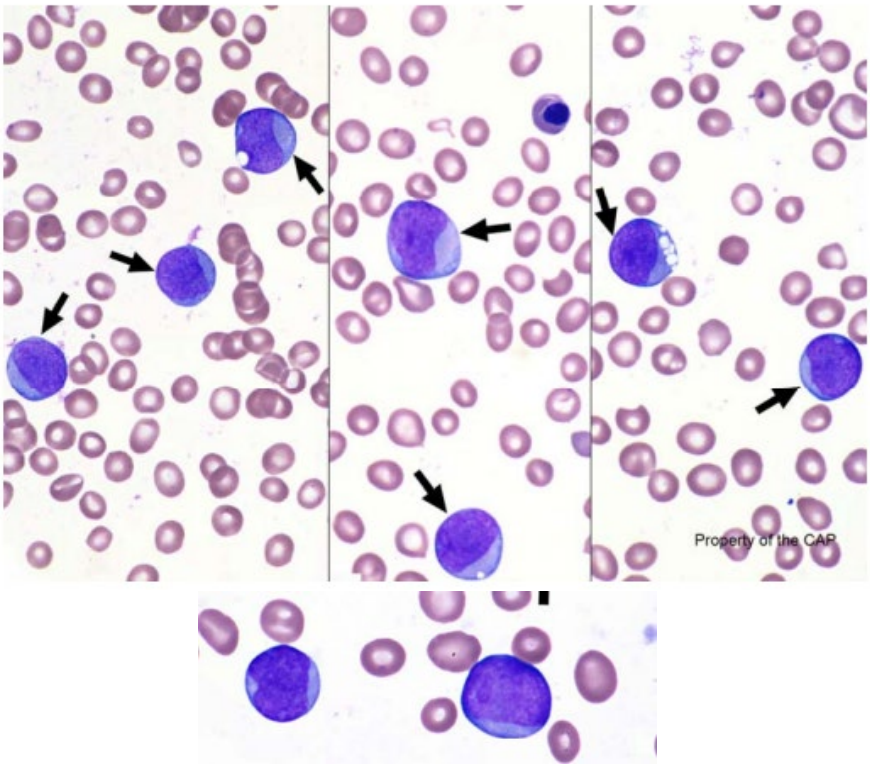
We missed an educational challenge on the peripheral blood smear survey from January. It was totally my fault. The cells that I called Blasts, CAP wanted them to be labeled as Malignant Lymphoid Cells. The patient's diagnosis was "Malignant B-cell Lymphoma," which is why they wanted them called malignant cells and not blasts. The report summary did say that the cells would have been classified as Blasts if the patient didn't have a previous diagnosis (so I can't feel too bad ☺). I looked back through last year's FH9 (heme) and VPBS (diff) surveys and did notice a pattern, so that is what is being presented in this education. Moral: read the history closely. The CAP discussion is included at the end. Please read this document and then mark that you have done so for the educational challenge.

## FH9-A 2021

**Case History**

This peripheral blood smear is from a 76-year-old Japanese woman diagnosed with bladder cancer and with a history of T-cell lymphoproliferation. Laboratory data include: WBC = 51.2 x 10E9/L; RBC = 3.69 x 10E12/L; HGB = 12.2 g/dL; HCT = 35.9%; MCV = 97 fL; MCHC = 34.2 g/dL; PLT = 108 x 10E9/L; and RDW = 16%. Identify the arrowed object(s) on each image.

**BCP-10**




These were classified as BLASTS. Notice the history listing the previous diagnosis as "T-cell lymphoproliferation." It does NOT list it as lymphoma, and the cells are quite large.

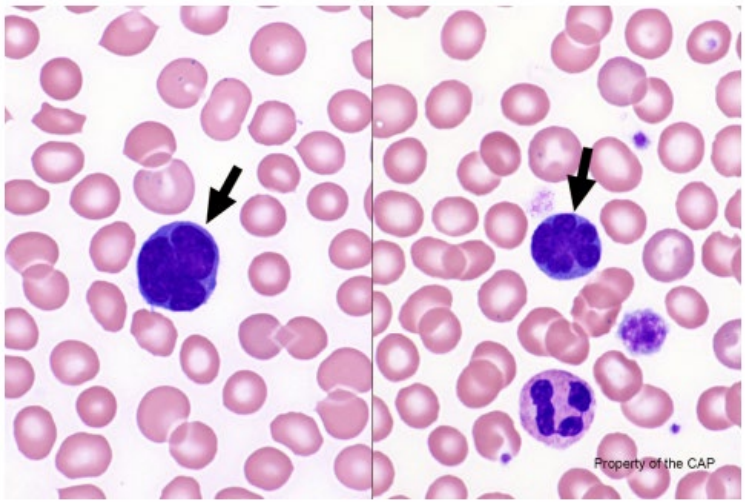
# VPBS-A 2022 EDUCATION

## FH9-B 2021

**Case History**

This peripheral blood smear is from a 76-year-old Japanese woman diagnosed with bladder cancer and history of mature T-cell leukemia/lymphoma. Laboratory data include: WBC = 51.2 × 10E9/L; RBC = 3.69 × 10E12/L; HGB = 12.2 g/dL; HCT = 35.9 %; MCV = 97 fL; MCHC = 34.2 g/dL; PLT = 108 × 10E9/L; and RDW = 16 %. Identify the arrowed object(s) on each image.

**BCP-20**




These were classified as MALIGNANT LYMPHOID CELLS. Notice the inclusion of the word "lymphoma" in the patient's history presentation. These are also "flower cells," which are a widely seen form of lymphoma cells. These are also smaller and more lymph-like than the blasts from FH9-A.

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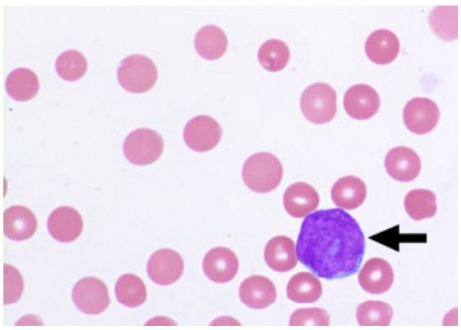
## FH9-C 2021

**Case History**

This peripheral blood smear is from a 21-year-old man who was recently diagnosed with B-lymphoblastic leukemia (WBC at diagnosis 233.0 x 10E9/L) and is on day 5 of initial chemotherapy. Laboratory data include: WBC = 14.2 x 10E9/L; RBC = 2.92 x 10E12/L; HGB = 8.5 g/dL; HCT = 23.9%; MCV = 82 fL; MCHC = 35.5 g/dL; PLT = 12 x 10E9/L; and RDW = 16%.

**BCP-24**



This was classified as BLAST. The diagnosis calls it a "lympoblastic leukemia." It is also a very ugly cell whose nucleus takes up the entirety of the cell.

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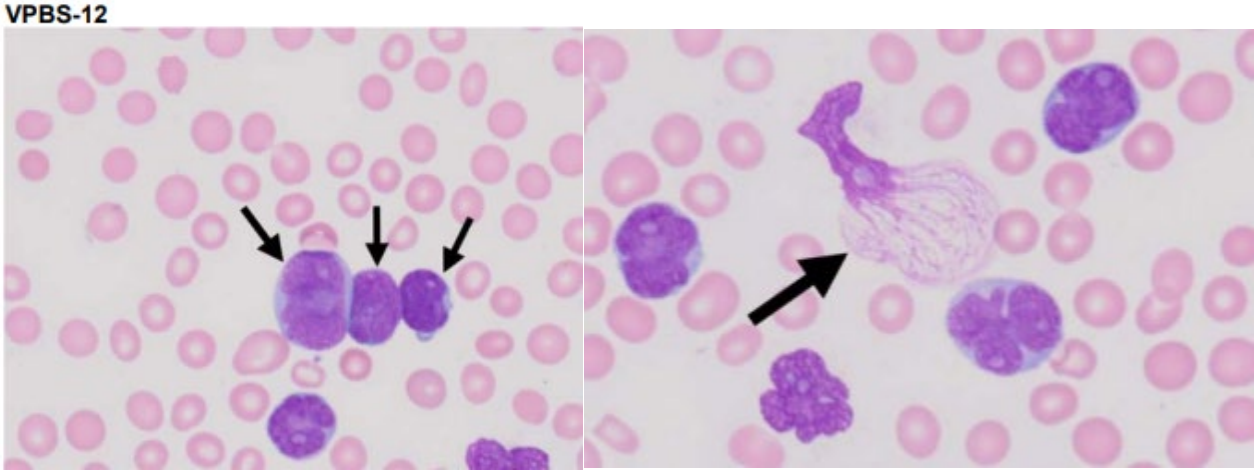
# VPBS-A 2022 EDUCATION

## VPBS-A 2021

**Clinical History for VPBS-07 – VPBS-12**

This peripheral blood smear is from a 23-year-old man with a bulky mediastinal mass and a history of T-lymphoblastic leukemia. Laboratory data include: WBC = 154.6 x 10E9/L; RBC = 3.14 x 10E12/L; HGB = 9.8 g/dL; HCT = 28.2%; MCV = 92 fL; PLT = 18 x 10E9/L; and RDW = 22%.

**VPBS-12**



These were classified as BLASTS. Again the history calls out "lymphoblastic leukemia." And again the cells are huge, and the nucleus takes up almost the entire cell.

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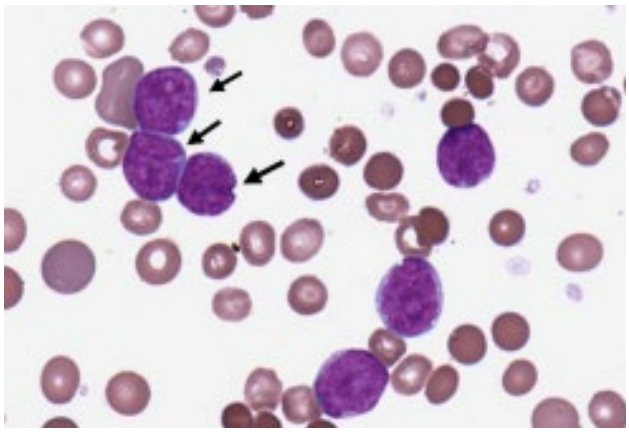
## VPBS-A 2022 (This year's survey)

**Clinical History for VPBS-02 – VPBS-06**

This peripheral blood smear is from a 63-year-old man with a history of malignant B-cell lymphoma, now presenting with fatigue. Laboratory data include: WBC = 66.8 x 10E9/L; RBC = 2.11 x 10E12/L; HGB = 6.3 g/dL; HCT = 18.9%; MCV = 90 fL; PLT = 221 x 10E9/L; and RDW = 17%.



These were classified as MALIGNANT LYMPHOID CELLS. This time the history points out the history of "B-cell lymphoma." Hence these are lymphoma cells. If you compare them to the blasts, they are a bit smaller and a bit darker, but very similar. This is why we have to look closely at the history.

So the main take-away is follow the clues they give first! Below, you can read what CAP said.

## VPBS-01

### Clinical History for VPBS-02 – VPBS-06

This peripheral blood smear is from a 63-year-old man with a history of malignant B-cell lymphoma, now presenting with fatigue. Laboratory data include: WBC = 66.8 x 10E9/L; RBC = 2.11 x 10E12/L; HGB = 6.3 g/dL; HCT = 18.9%; MCV = 90 fL; PLT = 221 x 10E9/L; and RDW = 17%.

(PERIPHERAL BLOOD, WRIGHT-GIEMSA)

**Please click on the hyperlink below to view the DigitalScope images for this case.**
https://www.digitalscope.org/LinkHandler.axd?LinkId=0f4ed923-1162-423b-a4e9-c65ca60e6303

**To access the online Hematology Glossary, please click the hyperlink below:**
https://documents.cap.org/documents/cap-hematology-and-clinical-microscopy-glossary.pdf

### Summary of Participant Survey Results

The following is a statistical summary of all results submitted by participating laboratories. These are provided to allow participants to see their responses in the context of their peers. These results may identify findings or topics for further education or review. Survey results are not intended to represent the correct or desired responses for proficiency testing purposes and the SD and CV% should not be interpreted as acceptable reporting limits. Participants are encouraged to review discrepant results with their medical director.

| WBC Differential - % | N | MEAN | SD | CV% | MEDIAN | MIN | MAX |
|---|---|---|---|---|---|---|---|
| Neutrophils (segmented or bands) | 1302 | 4.0 | 1.9 | 45.8 | 4 | 0 | 10 |
| Lymphocytes | 1271 | 37.8 | 32.9 | 86.9 | 27 | 0 | 100 |
| Lymphocytes, reactive | 575 | 1.2 | 3.5 | * | 0 | 0 | 21 |
| Monocytes | 810 | 1.0 | 1.2 | * | 1 | 0 | 5 |
| Eosinophils | 533 | 0.0 | 0.0 | 0.0 | 0 | 0 | 0 |
| Basophils | 559 | 0.0 | 0.0 | 0.0 | 0 | 0 | 0 |
| Metamyelocytes | 564 | 0.1 | 0.3 | * | 0 | 0 | 1 |
| Myelocytes | 528 | 0.0 | 0.0 | 0.0 | 0 | 0 | 0 |
| Promyelocytes | 537 | 0.0 | 0.0 | 0.0 | 0 | 0 | 0 |
| Blasts | 892 | 33.4 | 36.6 | * | 14 | 0 | 98 |
| nRBC/100 WBC | 1220 | 3.1 | 1.7 | 54.5 | 3 | 0 | 8 |

| WBC Differential - 10E9/L** | N | MEAN | SD | CV% | MEDIAN | MIN | MAX |
|---|---|---|---|---|---|---|---|
| Neutrophils (segmented or bands) | 1209 | 2.660 | 1.189 | 44.7 | 2.67 | 0.00 | 6.55 |
| Lymphocytes | 1188 | 25.244 | 21.960 | 87.0 | 18.04 | 0.00 | 84.64 |
| Lymphocytes, reactive | 533 | 0.848 | 2.355 | * | 0.00 | 0.00 | 14.03 |
| Monocytes | 747 | 0.665 | 0.793 | * | 0.67 | 0.00 | 3.35 |
| Eosinophils | 496 | 0.003 | 0.030 | * | 0.00 | 0.00 | 0.45 |
| Basophils | 517 | 0.000 | 0.000 | 0.0 | 0.00 | 0.00 | 0.00 |
| Metamyelocytes | 484 | 0.005 | 0.052 | * | 0.00 | 0.00 | 0.66 |
| Myelocytes | 487 | 0.000 | 0.000 | 0.0 | 0.00 | 0.00 | 0.00 |
| Promyelocytes | 495 | 0.000 | 0.000 | 0.0 | 0.00 | 0.00 | 0.00 |
| Blasts | 832 | 22.336 | 24.555 | * | 9.35 | 0.00 | 82.00 |

*When low results are reported on an analyte, a high coefficient of variance (CV%) may result. When the mean value is very low, the CV% may be exaggerated.

**Please see discussion on "Calculating Absolute Counts" that appears in this PSR.

## VPBS-01, cont'd.

### Other cells: *All cells not listed on results form and cells not differentiated by your laboratory*

| Cells not listed/differentiated | N = 289<br>Freq |
|---|---|
| Malignant lymphoid cell (other than blast)/lymphoma cell | 151 |
| Immature/abnormal lymphoid cell | 16 |
| Basket cell/smudge cell | 13 |
| Atypical mononuclear cell | 8 |
| Malignant prolymphocyte | 3 |
| Myeloid precursor | 1 |
| Would refer for identification | 97 |

### Platelet Estimate

| Intended Response: Adequate/normal platelets | N = 1318<br>Freq | <br>% |
|---|---|---|
| Decreased platelets | 10 | 0.8 |
| Adequate/normal platelets | 1304 | 98.9 |
| Increased platelets | 3 | 0.2 |
| Unable to quantitate - platelet clumps present | 1 | 0.1 |

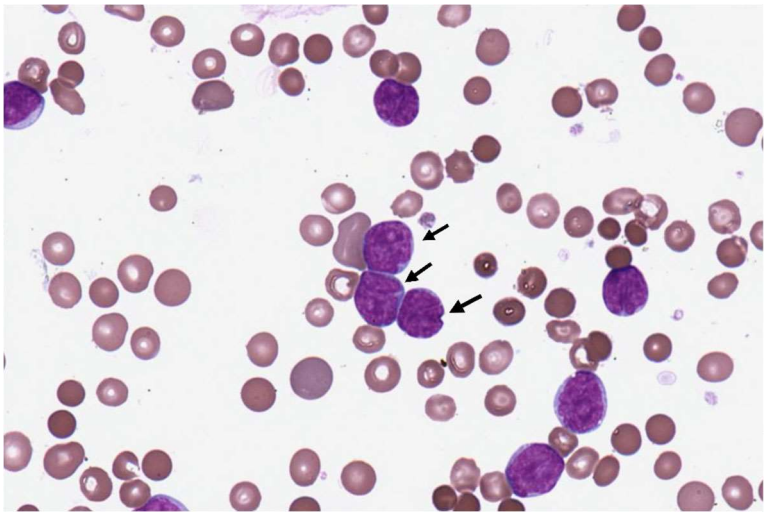
*Note*: For proficiency testing purposes only, platelet counts of < 140 x 10E9/L are considered decreased and > 450 x 10E9/L are considered increased.

| Red Cell Morphology | Total Responses N = 4490<br>Freq | Total Responses N = 4490<br>% Total Response | Total Unique Kits N = 1320<br>% Unique Kits |
|---|---|---|---|
| Polychromatophilic (non-nucleated) red blood cell | 1183 | 26.4 | 89.6 |
| Spherocyte | 1163 | 25.9 | 88.1 |
| Echinocyte (burr cell, crenated cell) | 498 | 11.1 | 37.7 |
| Nucleated red blood cell, normal or abnormal morphology | 430 | 9.6 | 32.6 |
| Macrocyte, oval or round (excluding polychromatophilic red blood cell) | 331 | 7.4 | 25.1 |
| Microcyte (with increased central pallor) | 295 | 6.6 | 22.4 |
| Stomatocyte | 163 | 3.6 | 12.3 |
| Target cell (codocyte) | 113 | 2.5 | 8.6 |
| Ovalocyte (elliptocyte) | 62 | 1.4 | 4.7 |
| Acanthocyte (spur cell) | 52 | 1.2 | 3.9 |
| Howell-Jolly body | 42 | 0.9 | 3.2 |
| Erythrocyte, normal | 38 | 0.9 | 2.9 |
| Fragmented red blood cell (schistocyte, helmet cell, keratocyte, triangular cell) | 36 | 0.8 | 2.7 |
| Teardrop cell (dacrocyte) | 28 | 0.6 | 2.1 |
| Rouleaux | 27 | 0.6 | 2.0 |
| Basophilic stippling (coarse) | 12 | 0.3 | 0.9 |
| Red blood cell agglutinates | 6 | 0.1 | 0.5 |
| Bite cell (degmacyte) | 4 | 0.1 | 0.3 |
| Pappenheimer bodies (iron or Wright stain) | 3 | 0.1 | 0.2 |
| Blister cell/Prekeratocyte | 1 | 0.0 | 0.1 |
| Erythrocyte with overlying platelet | 1 | 0.0 | 0.1 |
| Hemoglobin C crystal | 1 | 0.0 | 0.1 |
| Immature or abnormal cell, would refer for identification | 1 | 0.0 | 0.1 |

## Committee Comments on the CBC and Peripheral Blood Whole Slide

The provided CBC data indicate normocytic anemia and leukocytosis. Red blood cells show anisocytosis with polychromatophilic red blood cells, spherocytes, and nucleated red blood cells present. Leukocytes are increased, consisting of numerous malignant lymphocytes. Smudge cells are readily identified. Platelets are adequate and demonstrate normal morphology.

**VPBS-03**



| Identification | Participants Freq | % | Evaluation |
|---|---|---|---|
| Malignant lymphoid cell (other than blast) | 682 | 51.4 | Educational |
| Blast cell | 532 | 40.1 | Educational |
| Lymphocyte | 38 | 2.9 | Educational |
| Immature or abnormal cell, would refer for identification | 36 | 2.7 | Educational |
| Lymphocyte, reactive (includes plasmacytoid and immunoblastic forms) | 33 | 2.5 | Educational |
| Lymphocyte, large granular | 1 | 0.1 | Educational |
| Monocyte | 1 | 0.1 | Educational |
| Myeloblast with Auer rod | 1 | 0.1 | Educational |
| Neutrophil, promyelocyte | 1 | 0.1 | Educational |
| Plasma cell, morphologically mature/abnormal/containing inclusion (eg, Dutcher body, Russell body) | 1 | 0.1 | Educational |

The arrowed cells are malignant lymphoid cells (other than blast), as correctly identified by 51.4% of participants. 2.7% of participants selected immature/abnormal cell, would refer as the identification which is an acceptable answer. Lymphoma cells can exhibit a variety of appearances depending on the lymphoma subtype, and definitive diagnosis can be difficult. These cells can exhibit a variety of sizes, shapes, and nuclear and cytoplasmic characteristics. Cell size ranges from 8 to 30 µm, and the N:C ratio varies from 7:1 to 3:1. It is critical to obtain an accurate clinical history, since knowledge of a previous diagnosis of lymphoma greatly aids in the identification of these cells. Supplemental studies, such as immunophenotyping, are often necessary to arrive at a diagnosis. In blood smears, it may be difficult to distinguish reactive lymphocytes from lymphoma cells. The most important distinction between these cells is the difference in their N:C ratios. The N:C ratio tends to be low in reactive lymphocytes, while it is high in lymphoma cells. In addition, reactive lymphocytes are characterized by their wide range of morphologic appearances within the same blood smear. In contrast, while lymphoma cells can exhibit a wide range of morphologic appearances, any individual case tends to show a more monotonous population of the abnormal cells as seen in this image.

40.1% of participants incorrectly identified the arrowed cells as blast cells. A blast is a large, round-to-oval cell, 10 to 20 µm in diameter. In the blood film, the cell may appear flattened or compressed by adjacent red blood cells. The nuclear-to-cytoplasmic ratio is high, varying from 7:1 to 5:1. The blast often has a round to oval nucleus, but sometimes it is indented or folded. The blast cell has fine, lacy or reticular chromatin. One or more prominent nucleoli may be seen. The cytoplasm is variably basophilic and typically agranular. The

morphologic features of a blast cell do not permit determination of the cell lineage, ie, myeloblast versus lymphoblast. The one exception is the presence of Auer rods, which are diagnostic of myeloid lineage (ie, "myeloblast"). Other cells may have the appearance of a blast, including some lymphoma cells. In the absence of Auer rods, immunophenotyping by flow cytometry, immunohistochemistry on tissue sections, or, less commonly, cytochemical staining (eg, peroxidase or Sudan black) is required to determine the lineage of a given blast cell.

As blasts are quite variable in appearance, it is often impossible to correctly classify an individual cell based on the morphology alone. Blasts may rarely be morphologically indistinguishable from lymphoma cells. For identification purposes, one should classify individual cells exhibiting this type of morphology as blast cells when additional confirmatory information is unavailable. While there can be significant morphologic overlap between blasts and malignant lymphoid cells, the more condensed chromatin of the cells pictured, as well as the history of a malignant B-cell lymphoma, make 'malignant lymphoid cell, other than blast' the best answer in this case.

2.9% of participants incorrectly identified the arrowed cells as lymphocytes. While most normal lymphocytes are fairly homogeneous, they do exhibit a range of normal morphology. Lymphocytes are small, round to ovoid cells ranging in size from 7 to 15 µm with round to oval nuclei, absence of nucleoli, and an N:C ratio ranging from 5:1 to 2:1, while the cells pictured here are larger with more irregular nuclear contours and conspicuous nucleoli. Despite the fact that both normal and malignant lymphoid cells can have a high N:C ratio, several morphologic features, including increased cell size, irregular nuclear contours, and conspicuous nucleoli should aid in differentiating the malignant lymphoid cells pictured from normal lymphocytes. In addition, the history of a malignant B-cell lymphoma should serve as a clue to the identity of the cells in these images.

2.5% of participants incorrectly identified the arrowed cells as lymphocytes, reactive. The key distinguishing feature of reactive lymphocytes is their wide range of cellular sizes and shapes, as well as nuclear sizes, shapes, and chromatin patterns. These lymphocytes are reacting to an immune stimulus and are frequently increased in viral illnesses. These round to ovoid to irregular cells range from 10 to 25 µm in size with an N:C ratio that varies from 3:1 to 1:2.

The most common type of reactive lymphocyte resembles a larger lymphocyte and corresponds to a Downey type II cell. These cells have round to oval nuclei, moderately condensed chromatin (giving it a smeared appearance), and absent or indistinct nucleoli. They contain abundant pale gray-blue cytoplasm. Granules, if present, are usually small and few in number. Frequently, these reactive lymphocytes have an amoeboid cytoplasm that partially surrounds adjacent red cells and has a darker-staining, furled margin. Basophilia radiating out from the nucleus may also be present.

Immunoblasts and immunoblastic-like reactive lymphocytes are large cells (15 to 20 µm) with round to oval nuclei. They have finely to moderately dispersed chromatin with abundant parachromatin and one or more prominent nucleoli. These may resemble lymphoma cells or blasts. Their cytoplasm is moderately abundant and stains deeply basophilic. The N:C ratio is high (3:1 to 2:1). These reactive lymphocytes correspond to Downey type III cells.

Another type of reactive lymphocyte is referred to as a Downey I cell. These cells are rare. These cells possess scant to moderate amounts of basophilic cytoplasm. The nuclei often appear indented, folded, or lobulated. The chromatin is condensed. A few small vacuoles may be present. Granules may also be apparent.

Plasmacytoid lymphocytes resemble plasma cells and are intermediate in size (10 to 20 µm) and round to oblong in shape. They have round nuclei that are centrally placed or slightly eccentric. The chromatin is slightly to moderately coarse and forms small dense masses or a meshwork of strands resembling that of plasma cells. Nucleoli are generally not visible, but some cells may have one or two small irregular nucleoli. The cytoplasm is moderately abundant, homogeneous, and light blue to deep slate-blue, and it may show a perinuclear clear zone, or hof.

The cells present in these images are monotonous and large in size with high N:C ratios and irregular nuclear contours. These features should aid in the distinction between reactive lymphocytes and malignant lymphocytes. In addition, the history of a malignant B-cell lymphoma should serve as a clue to the identity of the cells in these images.