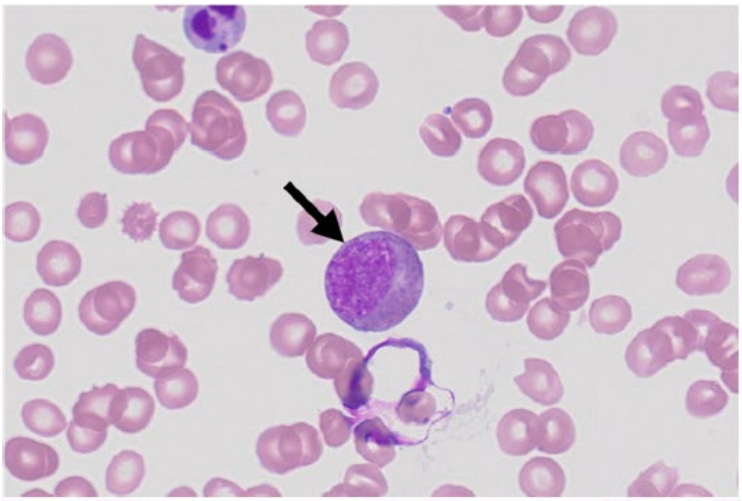
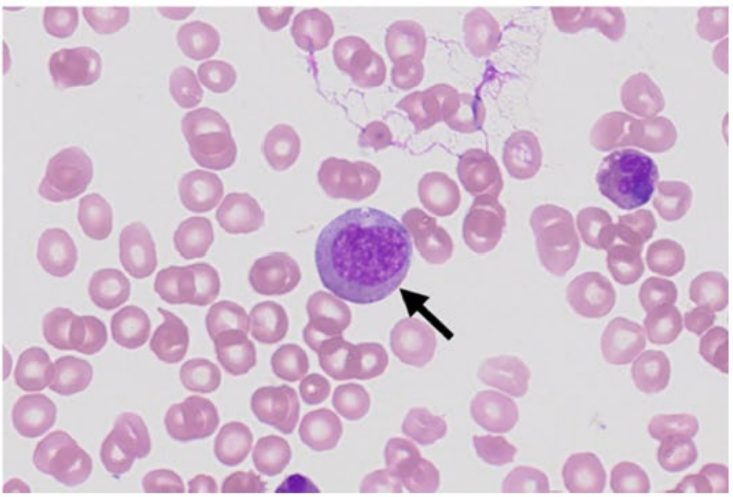
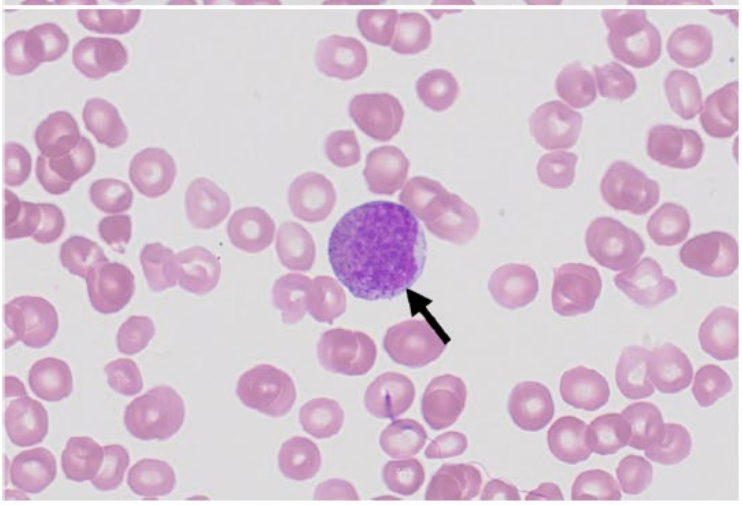
Identify the cell in the images below. Why do you choose that?

This peripheral blood smear is from a 54-year-old man who presents with anemia, lymphadenopathy, and an abdominal mass. Laboratory data include: WBC = 20.3 x 10E9/L; RBC = 2.85 x 10E12/L; HGB = 8.8 g/dL; HCT = 24.6%; MCV = 86 fL; PLT = 21 x 10E9/L; and RDW = 17%.







1st hint: it's definitely a myeloid precursor.

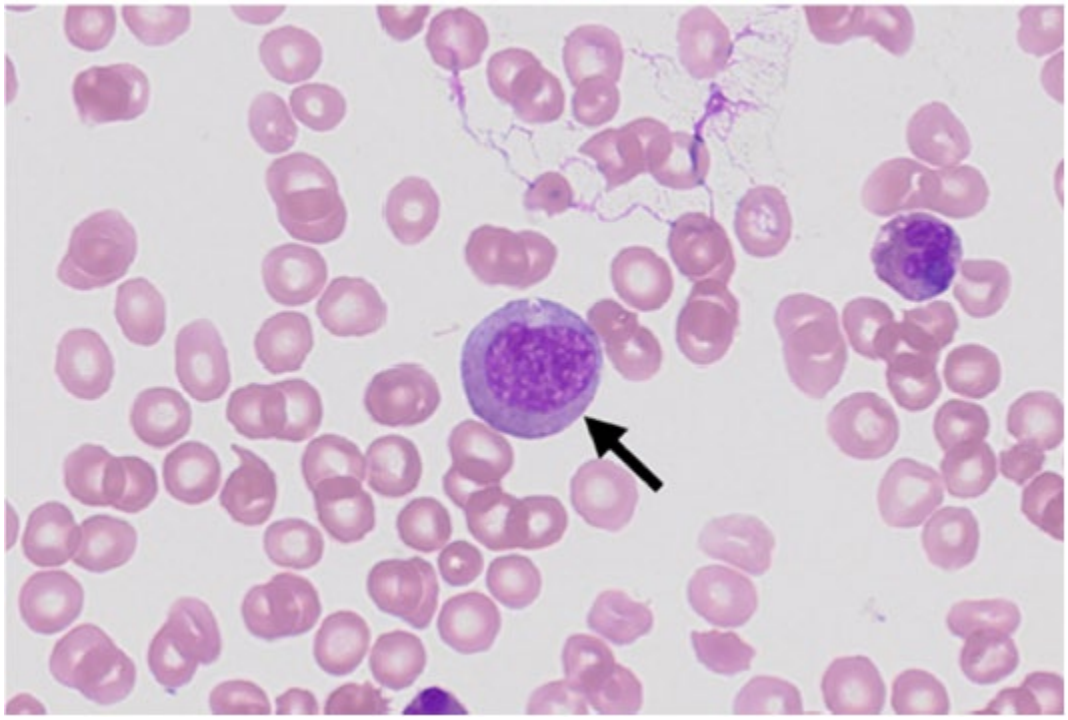
2nd hint: the granules are mostly red in color without large dark granules.

3rd hint: there is a cleared/blue space outside the nucleus where the Golgi Body (Golgi apparatus) is visibly exiting.

4th hint: The nucleus is quite round, even with a flattening side in some cases, and contains no visible nucleoli.

5th hint: the N:C ratio is about 1:1 or 1:2.

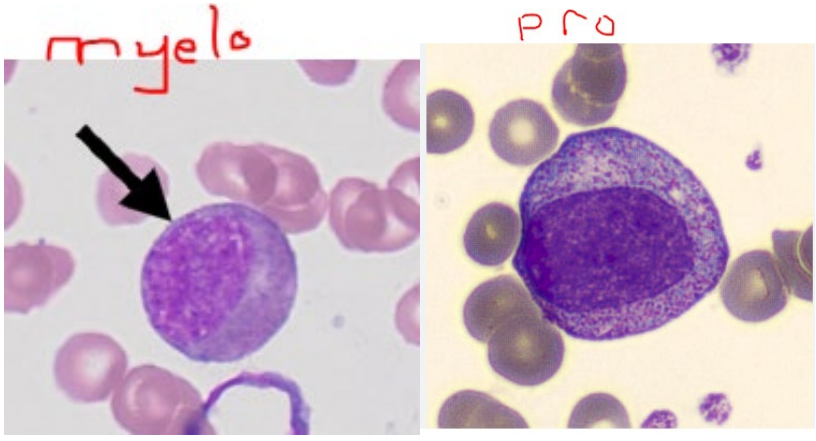
What's your best guess before the next page? 😊



The cell is a myelocyte!!!

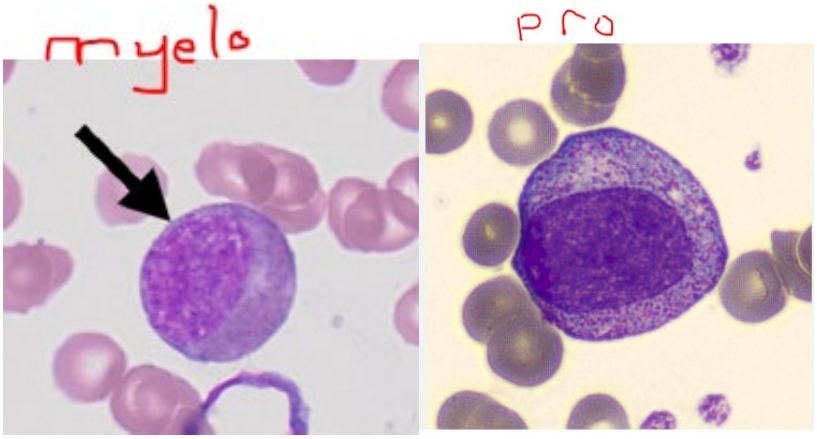
When we identified the cell, we called it a promyelocyte. This isn't a bad guess by any means, and 34% of survey participants also called these cells "promyelocytes." The very large size and deep red of the granules, as well as a nucleus that takes up ¾ of the cell in 2 of the 3 images led to our id of the cell as a promyelocyte. There are, however, some key characteristics which land these cells solidly in the "myelocyte" category.

First, compare these images taking care to notice the size and color of granules.



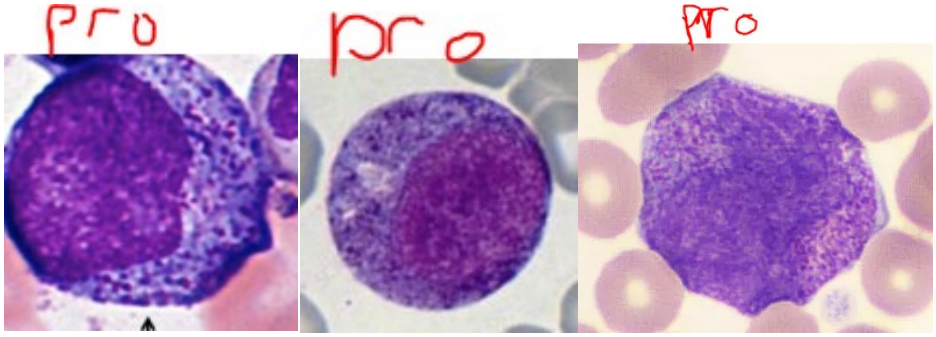
Similar, but the granule size is larger in the pro and the color is darker (or more "azurophilic"). Note also the darker blue cytoplasm in the pro vs. red in the myelo.

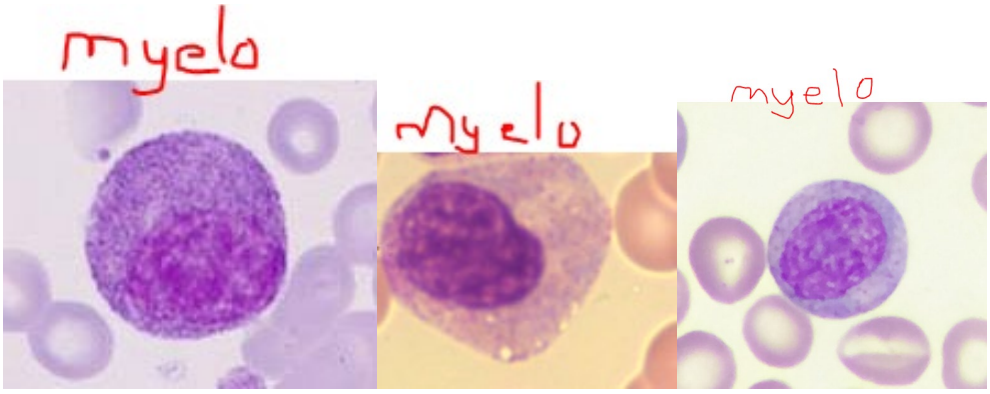
You will notice in both of these images a perinuclear hof (clearing that is slightly blue or clear immediately beside the nucleus). If you look at the pro, you will notice that too is slightly larger and is obscured by some of the large granules. It is smaller and easier to see in the myelocyte. This is because in the pro, this space likely includes the Golgi apparatus as well as the Endoplasmic Reticulum. In the myelocyte, this is typically the only what's left of the Golgi apparatus. It's not an easy-to-use differentiation tool, but there is a difference.



Look also at the chromatin of the nucleus. The myelocyte looks a bit more clumped with darker areas and cleared areas (which happens as the cell matures). The chromatin of the promyelocyte is much smoother and more evenly spread out (and also technically a little larger).

I did pick two images that were fairly similar for a reason. Depending on our moods that day, we could almost call either of these cells a myelo or a pro. I'm trying to give a few helpful hints in distinguishing them. Sometimes it is way easier.



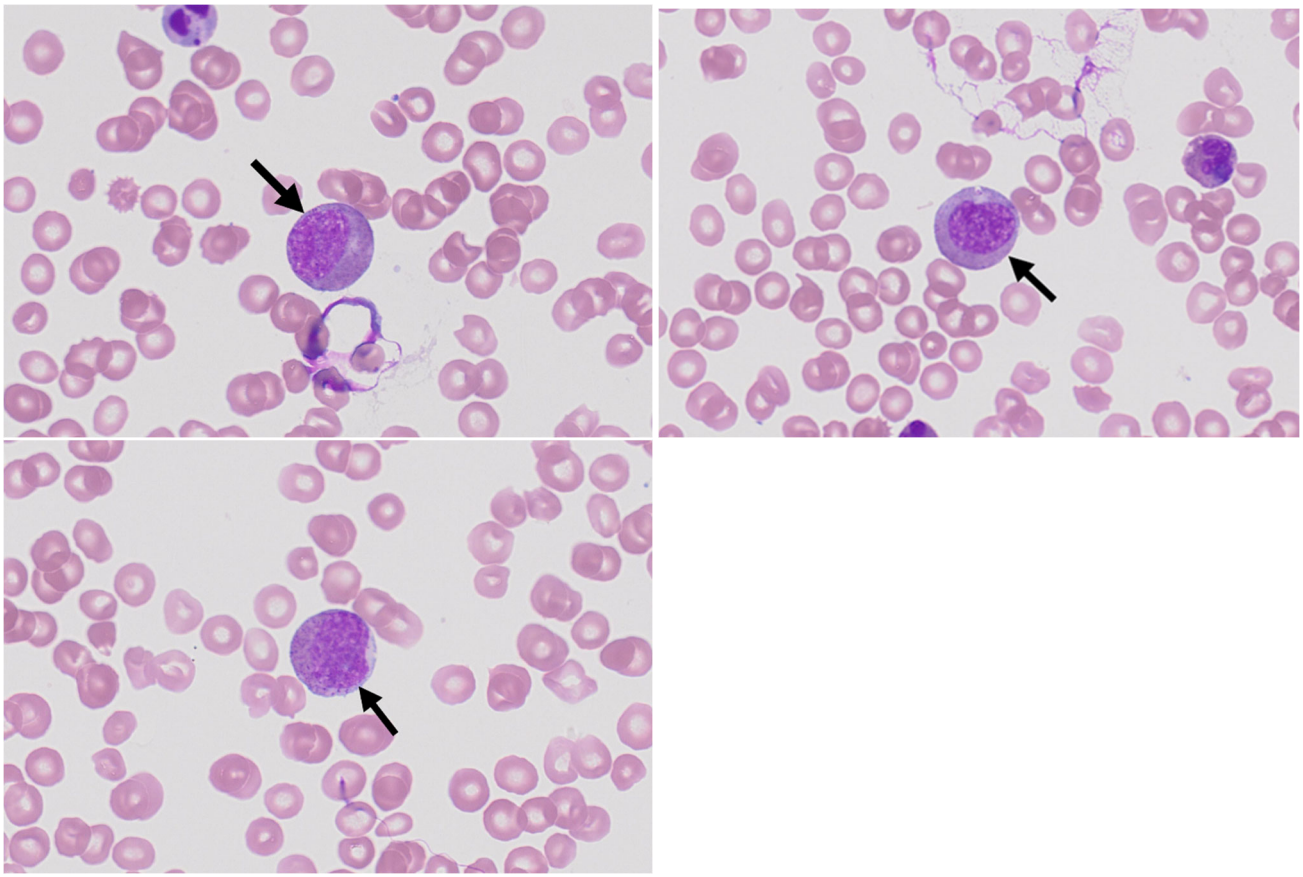


I was always taught, and I think it is important to remember, that if you are really on the fence when dealing with myeloid precursors to err on the side of caution. Lean towards the more mature differentiation unless the major clues of the less mature cell are present.

The following pages are the explanation from the participant summary.

Following that is part 2 of the educational response dealing with RBC morphology.

VPBS-17



Identification	Participants Freq	%	Evaluation
Neutrophil, myelocyte	854	67.0	Educational
Neutrophil, promyelocyte	311	34.4	Educational
Neutrophil, metamyelocyte	33	2.6	Educational
Immature or abnormal cell, would refer for identification	29	2.3	Educational
Blast cell	9	0.7	Educational
Neutrophil, promyelocyte, abnormal with/without Auer rod(s)	9	0.7	Educational
Malignant lymphoid cell (other than blast)	8	0.6	Educational
Lymphocyte, large granular	5	0.4	Educational
Monocyte, immature (promonocyte, monoblast)	5	0.4	Educational
Lymphocyte, reactive (includes plasmacytoid and immunoblastic forms)	4	0.3	Educational
Eosinophil, any stage	2	0.2	Educational
Bite cell (degmacyte)	1	0.1	Educational
Fragmented red blood cell (schistocyte, helmet cell, keratocyte, triangular cell)	1	0.1	Educational
Lymphocyte	1	0.1	Educational
Metastatic tumor cell or tumor cell clump	1	0.1	Educational
Neutrophil with dysplastic nucleus and/or hypogranular cytoplasm	1	0.1	Educational
Neutrophil, segmented or band	1	0.1	Educational

The arrowed cells are myelocytes, as correctly identified by 67.0% of participants. The transition from promyelocyte to myelocyte occurs with the end of production of azurophilic (primary) granules and the

beginning of production of lilac or pale orange/pink (specific) granules. Myelocytes are usually confined to the marrow where they constitute approximately 10% of the nucleated cells. In pathologic states, myelocytes are seen in blood. The myelocyte is smaller than the earlier precursors, usually 10 to 18 µm. The cells are round to oval in shape and have a nuclear-to- cytoplasmic ratio of 2:1 to 1:1. The nucleus is slightly eccentric, lacks a nucleolus, and begins to demonstrate chromatin clumping; one side often shows slight flattening.

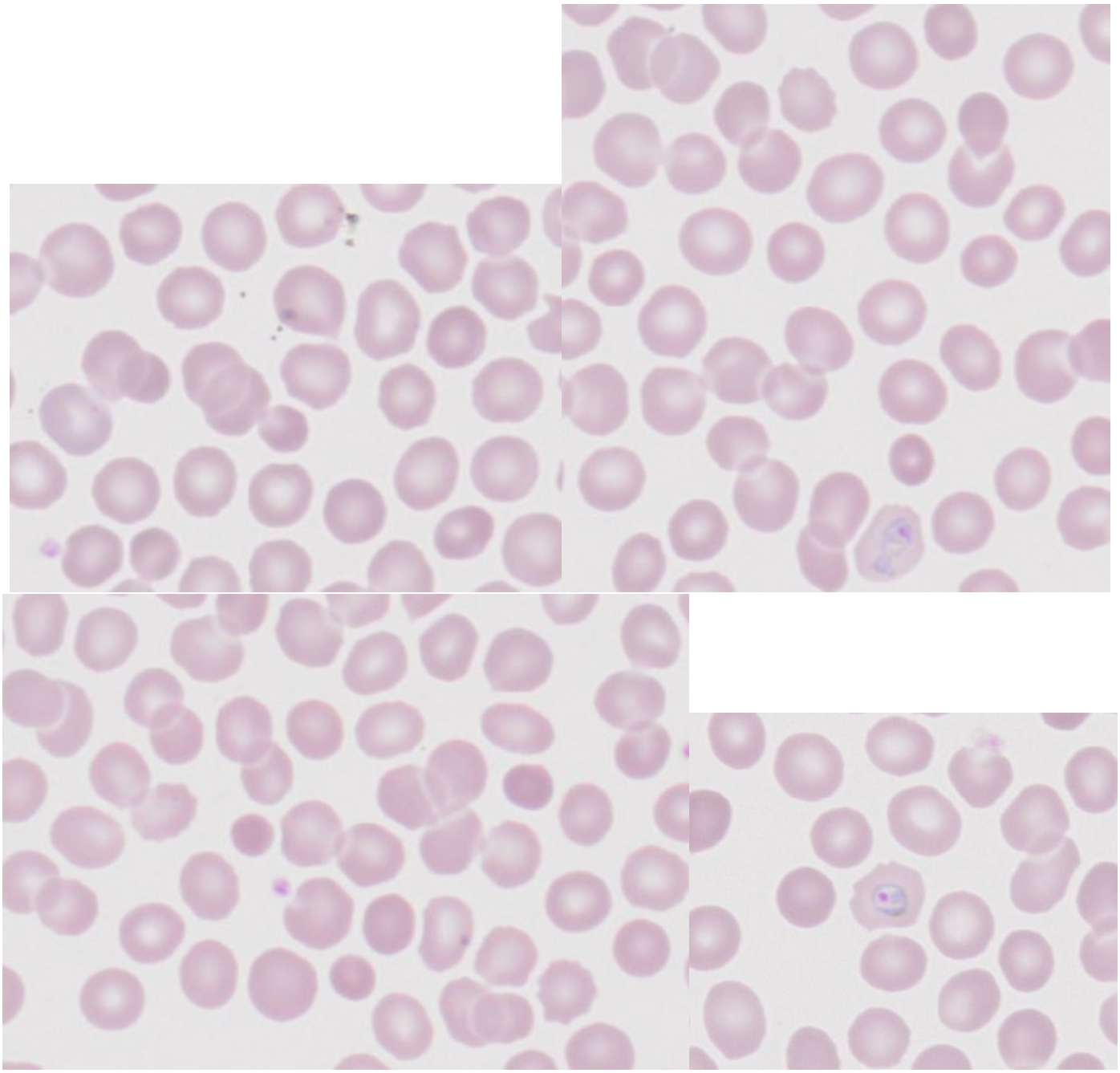
Sometimes a clear space or hof is seen adjacent to the nucleus, indicating the location of the Golgi apparatus. The cytoplasm is relatively more abundant than in earlier precursors and is amphophilic. Both azurophilic and specific granules are present in the cytoplasm with specific granules coming to predominate as maturation progresses.

2.3% of participants identified the arrowed cells as "Immature, would refer for identification". This is an acceptable answer for laboratories that always refer abnormal cell identification to an outside laboratory with a different CLIA number. In addition to blasts, immature cells also include promyelocytes and myelocytes.

24.4% of participants identified the cells as promyelocytes. In contrast to the myelocyte, the N:C ratio of a promyelocyte usually ranges from 5:1 to 3:1. The nucleus is round-to-oval, has fine chromatin, and contains distinct nucleoli. The cytoplasm is basophilic, more plentiful than in a myeloblast, and contains multiple distinct azurophilic (primary) granules. A paranuclear hof or cleared space is typically present.

2.6% of participants identified the cells as metamyelocytes. Myelocytes can be differentiated from metamyelocytes by nuclear morphology. In metamyelocytes, the nuclear chromatin is condensed, and the nucleus is indented to less than half of the maximal nuclear diameter (ie, the indentation is smaller than half of the distance to the farthest nuclear margin). The cytoplasm is amphophilic containing rare azurophilic or purple (primary) granules and many fine lilac or pale orange/pink specific granules.

Can you name some red cell morphology features seen in these images?



We did successfully identify the malaria present (Plasmodium sp.)! We also successfully noted the polychromasia present (hard to see in the images above). What we missed notating, though, was the presence of spherocytes. Did you catch them in the images above (3 of the images)? If it is an abnormal cell morphology that is significant (i.e. spherocyte, schistocyte, sickle, target) is is probably important to call at least occasional if not 1+.

They were present enough that the CAP pathologists commented on them, so we should have noted them on our result form.

Here is the diagnosis of the patient with the previous RBC images as well as the comments from the CAP survey committee.

Clinical History for VPBS-08 – VPBS-12

This peripheral blood smear is from a 32-year-old man who serves as a missionary in Africa presenting with fever and chills. Laboratory data include WBC = 6.7 x 10E9/L; RBC = 4.52 x 10E12/L; HGB = 12.9 g/dL; HCT = 39.8 %; MCV = 88 fL; PLT = 41 x 10E9/L; and RDW = 16%.

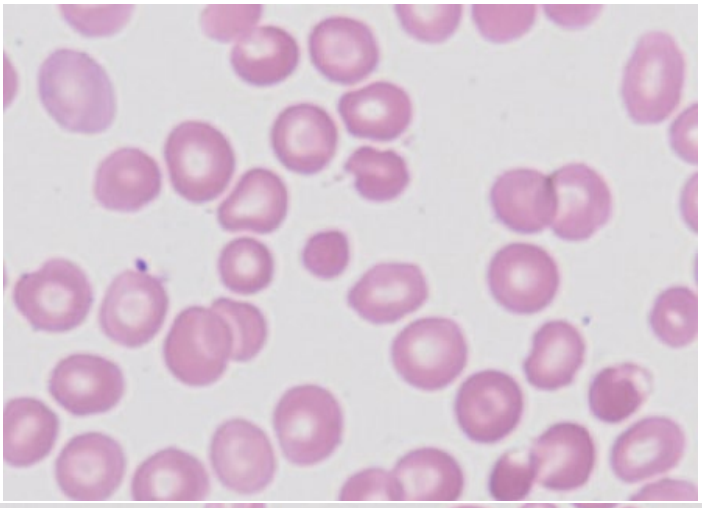
Committee Comments on CBC and Peripheral Blood Whole Slide Image

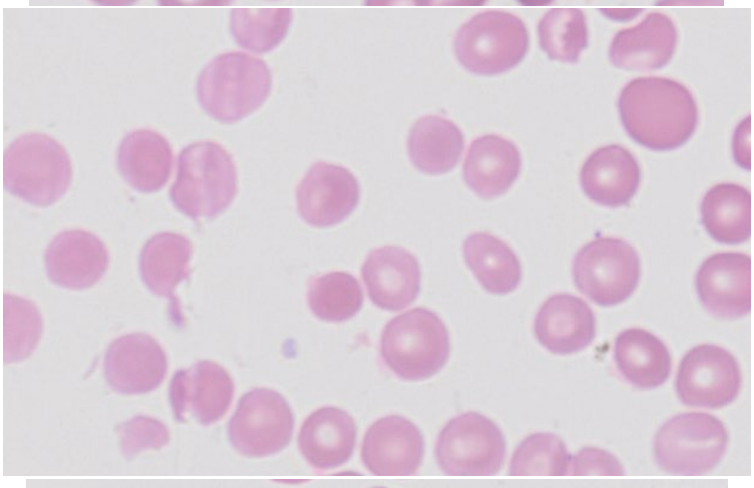
The morphologic findings confirm the reported CBC data, which demonstrate mild normocytic anemia and thrombocytopenia. RBCs demonstrate significant variation in size, ranging from spherocytes to large polychromatophilic forms, as well as forms infected with irregularly shaped mature Plasmodium ring forms, trophozoites, and gametocytes. Infected RBCs are frequently larger than background uninfected RBCs. Platelets show normal granularity and size. Leukocytes, including neutrophils, monocytes, and lymphocytes, are morphologically unremarkable.

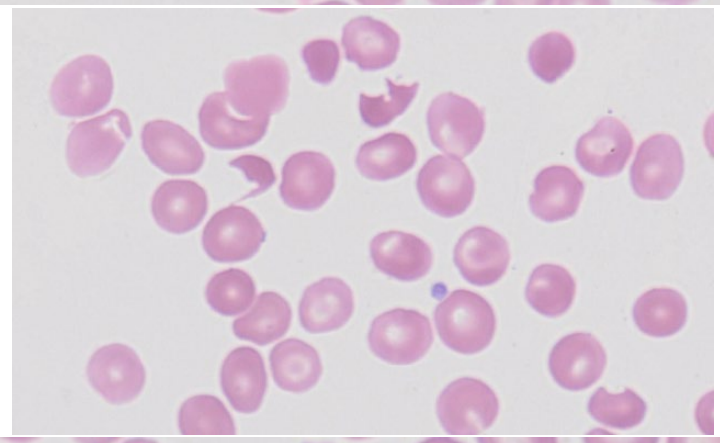
We really try to bring the abnormal findings to the forefront, which is why they are important for both patients and for PT surveys like this.

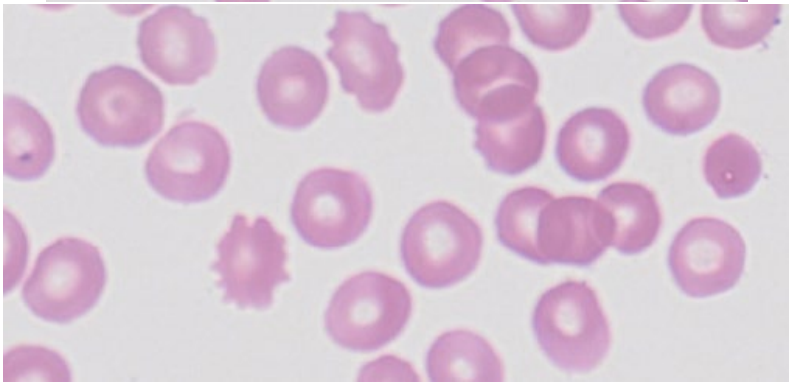
One more to go….almost there!!!

Can you name some red cell morphology features seen in these images? Keep in mind to note anything significant.









There were MANY RBC morphology answers we could have given for this sample. We did give good and acceptable answers. However, the #1 answer amongst all participants was RBC fragments at 65% of participants. This means we probably should have forgone something like macrocytes AND polychromasia so we could include an important finding like RBC fragments. It is especially important because this patient's platelet count was only 21! The physicians MUST be aware of RBC fragments or schistocytes when the platelet count is low so they can be on the lookout for DIC or spleen problems or liver problems (possibly others but those are the big ones).

We did a good job of noting the target cells in the sample because they were very prominent as well as noting the anisocytosis present. If you notice, there are also a few spherocytes present here as well, which means if there is room we should probably notate those as well. You can also notice the presence of burr cells in the images.

Again, we did a good job. We just want to make sure the serious or meaningful morphology gets noted both on our patients and in these surveys. I have no doubt all of this would have been marked on a real patient, but these educations are opportunities to make sure we are all on the same page and seeing what we need to see. Thank you all for your time and dedication.