EDUCATIONAL COMMENTARY – IMPACT OF HEMOLYSIS ON HEMATOLOGY TESTING

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Learning Objectives

On completion of this exercise, the participant should be able to

- recognize complete blood cell count abnormalities that may indicate interference due to hemolysis;
- take appropriate action to correct for interferences or initiate re-collection;
- describe the pattern of laboratory findings associated with each of the major subtypes of hemolysis encountered in the laboratory (artifactual, intravascular, and extravascular);
- correlate hemolysis and blood film findings to define the likely diagnostic reason(s) for the abnormalities;
- recognize cases in which sample hemolysis may be physiologic and re-collection may therefore not be indicated;
- systematically evaluate additional causes of high mean corpuscular hemoglobin concentration; and
- correct or add a disclaimer to results with high mean corpuscular hemoglobin concentration as appropriate.

Introduction

Hemolyzed samples are a problem frequently encountered in the clinical laboratory, with potential effects on test quality, turnaround time, and patient discomfort due to re-collections. Hemolysis is the most common reason for specimen rejection, accounting for approximately 25% of re-collections. Although attention to pre-analytic variables including careful phlebotomy and appropriate sample handling can minimize hemolysis, occasional hemolyzed samples will unavoidably reach the laboratory. Having a documented system to detect significant hemolysis and follow up appropriately is essential to ensure test quality.

Compliance considerations also reinforce the need for established policies. The College of American Pathologists (CAP), for instance, requires the following:

- Complete blood cell counts (CBCs) be checked for “significant in-vitro hemolysis and possible interfering lipemia before reporting results” (HEM.22200).
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- There must be an “appropriate plan of action” when analytic interferences are present (COM.40500).³
- There must be written criteria for handling of suboptimal specimens, and rejection of unacceptable specimens (COM.06300).³

Hemolysis: What Is a Significant Level?

Plasma containing 0.02 g/dL of hemoglobin (HGB) can be recognized as faintly pink; at the level of 0.10 g/dL, plasma is generally clearly red (see Figure 1 for illustration).⁴ If bilirubin levels are elevated to 20 mg/dL, hemolysis may be masked up to a level of 0.20 g/dL; this combination of abnormalities is particularly common in neonatal CBC collections.⁵

![Figure 1. Appearance of plasma at various hemoglobin concentrations. Photograph courtesy of the author.](image)

Tube diameter significantly influences the ability to visually detect hemolysis, icterus, and lipemia.⁶ Because of this, spinning down capillary tubes to rule out hemolysis/lipemia should be avoided, unless this is necessary owing to low sample volume. Centrifuging an aliquot of blood in a test tube is optimal for detection of hemolysis, icterus, and lipemia.

It takes a very small amount of red blood cell (RBC) lysis to result in visible plasma HGB. Unlike potassium and lactate dehydrogenase (LDH) levels, the CBC results will show trivial changes with
minimal levels of hemolysis (≤ 0.05 g/dL HGB). As shown in Table 1 below (using % lysis to extrapolate % drop in hematocrit [HCT]), with mild hemolysis at the level of 0.05 g/dL, the HCT will drop by approximately 0.2, which is well within the range of analytic variation. Another thing to note is that to elevate a mean corpuscular hemoglobin concentration (MCHC) from 34.0 to 36.0, severe hemolysis (>0.7 g/dL free HGB) is generally required, which suggests that most cases of mild to moderate hemolysis are not routinely detected by MCHC monitoring and will be reported without detection unless the hemolysis is noted during other testing.

Table 1. Theoretical effect of hemolysis on hematocrit and MCHC at two different hemoglobin levels (calculated by author).

<table>
<thead>
<tr>
<th>Plasma Color</th>
<th>Patient Hemoglobin, g/dL</th>
<th>Free Hemoglobin, g/dL</th>
<th>Lysis, %</th>
<th>Patient Hematocrit, %</th>
<th>Patient MCHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yellow</td>
<td>14.0</td>
<td>0.00</td>
<td>0.0</td>
<td>41.2</td>
<td>34.0</td>
</tr>
<tr>
<td>Orange</td>
<td>14.0</td>
<td>0.05</td>
<td>0.4</td>
<td>41.0</td>
<td>34.1</td>
</tr>
<tr>
<td>Red</td>
<td>14.0</td>
<td>0.15</td>
<td>1.1</td>
<td>40.7</td>
<td>34.4</td>
</tr>
<tr>
<td>Very dark red</td>
<td>14.0</td>
<td>0.78</td>
<td>5.6</td>
<td>38.9</td>
<td>36.0</td>
</tr>
<tr>
<td>Yellow</td>
<td>7.0</td>
<td>0.00</td>
<td>0.0</td>
<td>20.6</td>
<td>34.0</td>
</tr>
<tr>
<td>Orange</td>
<td>7.0</td>
<td>0.05</td>
<td>0.8</td>
<td>20.4</td>
<td>34.1</td>
</tr>
<tr>
<td>Red</td>
<td>7.0</td>
<td>0.15</td>
<td>2.2</td>
<td>20.1</td>
<td>34.4</td>
</tr>
<tr>
<td>Very dark red</td>
<td>7.0</td>
<td>0.78</td>
<td>10.6</td>
<td>18.4</td>
<td>36.0</td>
</tr>
</tbody>
</table>

What is not captured in the table above is the influence a difficult phlebotomy could have on the specimen. If collection is difficult, the specimen could be nonrepresentative, especially if diluted from line contamination. Also, effects on white blood cell (WBC) and platelet (PLT) counts due to problems with collection or handling are not predictable. For these reasons, investigation of samples with more than slight hemolysis may be warranted for possible re-collection.

A working approach is to spin down the sample and, if the plasma is more orange than red, report the CBC with a disclaimer such as “CBC results may be affected by slight hemolysis.” If the plasma is more red than orange (moderate/marked hemolysis), the sample should be re-collected unless the HGB concentration is very low. In that case, the slide should be examined for evidence of acute hemolytic anemia (spherocytes and/or schistocytes with elevated polychromasia and/or nucleated RBCs [NRBCs]). If present, the hemolysis may be intravascular, and re-collection may not improve the sample quality. In such cases, it is best to report the CBC with a comment (see example in Case 2 below as an example of misguided re-collection of a hemolyzed sample).
Effect of Hemolysis on CBC Results

Hemolysis results in decreased RBC count and HCT values due to RBC lysis. Hematology instruments typically lyse the sample before measuring HGB, PLT count, WBC count, and WBC differential cell count, so those values are usually unaffected by hemolysis. However, if the hemolysis occurred due to pre-analytic variables (for example, from freezing or drawing from a line), all results are potentially unreliable.

Because hematology samples are not centrifuged before testing, hemolysis is typically detected by one of three routes.

1. Other testing (chemistry, serology) was also ordered.
   - Hemolysis was noted visually in the serum/plasma after centrifugation; or
   - Hemolysis was flagged on a chemistry analyzer due to a high “hemolysis index,” or in the evaluation of a dubiously high LDH and/or potassium level.

   In such cases, all specimens from that re-collection are suspect and should be investigated.

2. The CBC was run, and an unexplained high MCHC was obtained.
   - Because MCHC is calculated using the formula (HGB ×100)/HCT, a spuriously low HCT divided into an accurate HGB will result in a spuriously high MCHC. The normal range for MCHC will vary depending on the analyzer and must be determined for each laboratory; however, typical levels triggering review range from greater than 36.0% to greater than 37.0%. Mean corpuscular hemoglobin concentration values at 37.0% are close to the solubility value for HGB, and further increases may lead to crystallization. The MCHC serves as a very useful index for detecting interferences, and although no hematology analyzers report hemolysis index, almost all report MCHC.

   - NOTE: The temptation (often suggested by instrument vendors) is to set the MCHC review level high to minimize cases requiring review; however, doing so will result in missing significant abnormalities, including hyperlipidemia and icterus, warm and cold agglutinins, hereditary spherocytosis with true hyperchromic RBCs, and hemolyzed samples. Hereditary spherocytosis is the most common inherited RBC defect leading to hemolysis, and missing the diagnosis can have serious consequences for the patient. A conservative and empirical approach is to review cases that are above the upper MCHC reference range determined from a local normal study using a 3-SD range for the MCHC. Because the 3-SD range includes 99.7% of normal samples, 0.15% or 1 to 2 cases in 1000 normal results would be expected to fall above that range. The laboratory’s review level can then be adjusted upward if an excessive number of false-positive sample reviews (high MCHCs without an identified reason) occur relative to the number of true abnormal results encountered.

3. The CBC was run and histogram abnormalities occur, triggering an instrument flag (e.g., RBC fragments, RBC abnormal scattergram).
In practice, these flags are rarely seen with most analyzers and are insufficient as the sole screen for hemolysis. When encountered, slide review for true RBC fragmentation (schistocytes) and plasma inspection for hemolysis are appropriate.

Algorithmic Approach to Evaluating High MCHCs

When evaluating for hemolysis, other interferences may be noted and require further investigation. Procedures must be customized for each laboratory to reflect the medical need, instruments available for backup testing, and other practical considerations. A number of approaches have been reported in the literature.9-12 A sample field-tested protocol is detailed below for reference.

- If RBC is low and mean corpuscular volume (MCV) is high, consider a warm or cold agglutinin.13-16
  - Prepare a slide to look for microscopic agglutination. See Figure 2 for illustration.
  - Warm the specimen at 37°C for 20 minutes, then mix and rerun immediately. If the MCV and MCHC drop and RBC increases, a cold agglutinin is suggested. If slide review supports a cold agglutinin (visible agglutination without marked polychromasia or anemia), report the warmed results with a comment (e.g., "Results corrected for cold agglutinin by warming").

- If the slide shows agglutination that is not reversible on warming, the automated RBC, HCT, and indices will be unreliable. If possible, perform a spun micro HCT and calculate the corrected MCHC. Report with a comment (e.g., "Unable to determine RBC, MCV, and MCH due to RBC agglutination that is not reversible at 37°C"). If a spun HCT is not available, HGB should be the only RBC parameter reported, with a comment such as the following issued:

![Figure 2. Cold agglutination. Note rounded cluster of RBCs (unlike rouleaux, which are linear) and absence of regenerative changes (polychromasia and/or NRBCs) in the background, which would suggest a warm agglutinin. Photomicrograph courtesy of the author.](image-url)
“Unable to determine RBC parameters other than HGB due to an agglutinin that corrects incompletely with warming.”

There are three reasons for failure of agglutination to completely correct after warming. In order of frequency:

- A strongly reacting cold agglutinin with high thermal amplitude. These patients do not have in vivo hemolysis, and the RBC morphology will be normal without severe anemia and without a striking increase in polychromasia or the reticulocyte count. Once the sample is cooled to room temperature, however, the RBCs will show only partial disaggregation after warming, and the high MCHC will persist when the warm sample is retested.

- A warm agglutinin, suggesting autoimmune hemolytic anemia. These patients have autoantibodies that result in RBC clearance by splenic macrophages. The findings on the blood film include spherocytes, increased polychromasia (≥2+), and/or increased NRBCs (≥1/100 WBC). If detected as a new finding, pathologist review is recommended so that a diagnostic comment can be added to the report.

- Cryoglobulins (antibodies precipitated by the cold) are a rare cause of plasma turbidity in samples that have been refrigerated. Such samples may have a high MCHC that normalizes after warming. In such cases, amorphous globules of protein may be noticeable on the Wright-stained slide made before sample warming (Figure 3), and the centrifuged plasma will show turbidity due to protein that will pellet on the bottom of the tube with centrifugation (unlike turbidity due to lipids) (Figure 4). Although the finding of cryoglobulins is nonspecific, it can indicate an important underlying condition (infection, autoimmune disease, or lymphoproliferative disorders), so it should be reported if detected.

**Figure 3.** Cryoglobulin on Wright-stained slide. Globular protein, often adherent to WBC. Image provided by the author.

**Figure 4.** Centrifuged sample after refrigeration. Abbreviation: “sl.” indicates slightly hemolyzed. Image provided by the author.
• If the MCHC is elevated and agglutination is not detected, centrifuge an aliquot of sample (enough to yield 300 µL of plasma). Inspect for lipemia, icterus, or hemolysis.17- 21
  o If grossly hemolyzed (more red than orange), verify on the slide the absence of many spherocytes and marked polychromasia indicating possible intravascular hemolysis, which will not be improved by re-collection.
    ▪ If these findings are absent, artifactual hemolysis is suggested, and the specimen should be re-collected.
    ▪ If the patient has features of intravascular hemolysis (RBC spherocytosis and/or fragmentation, increased NRBCs and/or polychromasia and marked anemia), re-collection will not improve specimen quality. The automated HGB will correctly reflect total blood HGB, and the automated HCT will be correct (assuming the absence of visible agglutination). The MCH and MCHC will be incorrect, however, because the HGB measurement will include plasma free as well as intracellular HGB. In this case, report HGB, HCT, and MCV but not MCH and MCHC, and include a comment in the report (e.g., "Unable to determine MCH and MCHC due to apparent free HGB in patient plasma which may be seen in acute hemolytic anemias. If artifactual hemolysis is suspected, re-collection is recommended.").
  o If lipemia or icterus is noted in the plasma, the HGB result must be corrected for the interference, and the MCH to MCHC ratio recalculated. Red blood cells, HCT, and MCV values are not affected by lipemia or icterus. There are two common methods for this correction:
    ▪ Plasma blank: Transfer lipemic/icteric plasma into a separate tube, mix well, and run through the automated hematology analyzer to obtain a plasma HGB value. Obtain a corrected HGB using the following formula:
      \[
      \text{Corrected HGB} = \text{Original HGB} - \left[ \frac{\text{Plasma HGB} \times (1.00 - \text{Original HCT})}{100} \right]
      \]
      The advantage of the plasma blank is that it produces a highly accurate correction. The disadvantage is that it requires manual computation.
    ▪ Plasma replacement: With a micropipette, remove the majority of the plasma sample from the centrifuged specimen, and replace it with an equal volume of saline. Mix and rerun the sample.
      The advantage of the plasma replacement procedure is that the HGB value obtained from the manipulated sample can be reported without computation. The disadvantage is that the pipetting steps and inability to remove all lipemia both introduce error to the reported HGB value.
In either case, results should be reported with a comment (e.g., “Results corrected for gross lipemia,” or “Results corrected for grossly icteric plasma”).

NOTE: If a sample is hemolyzed, or is both lipemic and hemolyzed, no HGB correction can be performed because with either method above, the free HGB will be excluded in the final HGB result. This will result in an overcorrection of the HGB, MCH, and MCHC. If the hemolysis is not sufficient to warrant re-collection, report the CBC including RBC/HCT/MCV, but do not report HGB/MCH/MCHC and include a comment in the report (e.g., “Unable to determine HGB/MCH/MCHC due to gross lipemia [or icterus] and hemolysis”).

- If uniform spherocytosis is noted on the slide without marked anemia and marked polychromasia, hereditary spherocytosis (Figure 5) may be causing the high MCHC (typically in the range of 37%-38%). In this disorder, the high MCHC is reflecting true hyperchromia and is a legitimate and reportable result. If this is a new finding, review by a pathologist to generate a diagnostic comment is recommended. High MCHCs have also been reported with homozygous HGB S (Hgb S) and Hgb C disease in sickle cell crisis, which will be readily detected on slide review.

- Rare patients will have lysis-resistant RBCs. This is most frequently associated with hemoglobinopathies (Hgb S or Hgb C). Resistance to lysis has also been observed in RBC osmotic fragility studies with thalassemia, postsplenectomy, iron deficiency, polycythemia vera, and in conditions with target cells such as liver disease. Lytic conditions in most analyzers are aggressive enough to be immune to interference in those conditions. In practice, lysis-resistant RBCs tend to interfere more with impedance WBC counts than with HGB measurements. If other causes for the high MCHC have been ruled out, examination of the slide for sickle cells or target cells to suggest hemoglobinopathy may be warranted.

- Unexplained high MCHCs are encountered occasionally. If repeated cases are encountered over a short period of time, an instrument problem should be considered. Because MCHC is calculated from three parameters (HGB, MCV, and RBC), small calibration errors can compound in the calculation, resulting in a shift in normal patient values. This property of MCHC has been exploited by many instrument vendors, who calculate the weighted “moving average” (XB) of patient MCHCs (usually in batches of 20 samples) over time as a sensitive
metric to detect calibration or fluidic problems. In theory, a series of iron-deficient patients with true low MCHCs may drop the moving average for MCHC; however, a shift of MCHC to the high side is almost always an instrument issue. Reviewing instrument quality control, doing patient comparisons with different instruments, and consulting with instrument technical services, if necessary, may be useful in resolving such problems.

Case Presentation 1

A lavender tube was received in the hematology department with a CBC order on a 95-year-old woman. Automated results obtained were as follows: WBC = 7.5; RBC = 4.15; HGB = 14.2; HCT = 36.9; MCV = 89.0; MCHC = 38.5; and PLT = 220. The specimen was warmed at 37°C and rerun after incubation, without normalization of the MCHC. The Wright-stained blood film was examined, and the RBCs showed no morphologic abnormalities. A fraction of the sample was centrifuged and showed marked hemolysis. The phlebotomist was called, who reported that the collection had been difficult due to small veins and a large hematoma on the arm and that the tubes had filled very slowly through a small needle. The normal HGB level with visible plasma hemolysis, in combination with this history, was consistent with artifactual hemolysis. A re-collection was requested, and the MCHC normalized on the fresh sample.

Causes of Artifactual Hemolysis

Many reasons for artifactual sample hemolysis have been reported. These can be minimized by careful adherence to the Clinical and Laboratory Standards Institute (CLSI) guidelines for blood sample collection. Some possible causes of artifactual hemolysis are as follows:

- Phlebotomy technique variables (exposure of blood to alcohol; vigorous aspiration via syringe; drawing through a hematoma; probing for a vein; a loose needle on a syringe, resulting in frothing of the blood; pressing a plunger to force blood into a tube, resulting in high shear stress)
- Phlebotomy from vascular assist devices, especially if air leaks occur during collection
- Drawing blood from intravenous or central lines
- Puncture sites other than antecubital fossa have an increased incidence of hemolysis.
- Emergency department collections have increased incidence of hemolysis.
- Heel-stick or finger-stick collections, especially with “milking” (strong, repetitive squeezing) of the extremity
- Using excessively small needles. Use of a 23-gauge or smaller needle increases the chance of hemolysis. It is sometimes necessary to use 25-gauge needles with small veins in premature infants and other neonates.
- Prolonged tourniquet application
- Underfilling tubes
- Excessive specimen shaking
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- Repeated or prolonged centrifugation
- Some pneumatic tube systems (high impact; poorly cushioned)
- Exposure of the sample to temperature extremes (freezing; heat)

**A Note on Intravascular vs. Extravascular Hemolysis**

Hemolytic anemias have a number of laboratory features in common:

- Anemia (may be mild with chronic, compensated anemias)
- Evidence of a bone marrow regenerative response
  - Elevated reticulocyte count
  - Polychromasia and basophilic stippling noted on Wright-stained blood films
  - Elevated RBC distribution width, reflecting anisocytosis due to polychromasia with or without schistocytes
  - Circulating nucleated RBCs in moderate or severe cases
  - Erythroid hyperplasia in bone marrow
- Evidence of RBC destruction
  - ↑ Indirect bilirubin
  - ↑ Lactate dehydrogenase
  - ↓ Haptoglobin: very sensitive, but as an acute-phase reactant, it is increased by infection, malignant neoplasms, pregnancy, and steroid therapy

NOTE: Documenting RBC destruction is important in diagnosing hemolytic anemia. Findings of RBC regeneration without RBC destruction could indicate a myeloproliferative disorder such as polycythemia vera or appropriate bone marrow response to acute blood loss.

- Increased bone marrow iron levels and increased blood ferritin levels (reflecting increased bone marrow iron stores). The body increases iron absorption with chronic anemias to compensate for possible iron deficiency. This can be a problem in patients with chronic (for instance, inherited) hemolytic anemias, because persistent high levels of iron absorption can result in iron overload, leading to liver failure, heart failure, and endocrine disorders.

NOTE: Ferritin is an imperfect measure of bone marrow iron, because it is an acute-phase reactant protein, which can result in a misleading elevation in healthy patients, or a false-normal result in patients with early iron deficiency.

Hemolytic anemias can be sub-classified based on the mechanism of hemolysis into intravascular and extravascular categories (see Figure 6).
Intravascular hemolysis occurs when RBCs are damaged acutely in circulation, with release of cell contents directly into circulation. This can have dramatic clinical consequences, because cell enzymes can induce inflammatory reactions including fever/chills, hypotensive shock, tachycardia, and dyspnea.

Causes of intravascular hemolysis include the following:

- Microangiopathic hemolytic anemias: Thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, disseminated intravascular coagulation
- Infectious agents: malaria, Babesia, Bartonella bacilliformis, clostridial sepsis
- Paroxysmal nocturnal hemoglobinuria: Complement-mediated direct hemolysis
- Isoimmune hemolytic anemias: Transfusion reaction, hemolytic disease of the newborn
- Mechanical damage due to damaged or prosthetic heart valves or prolonged walking (march hemoglobinuria)
• Thermal, chemical, or venom-induced RBC injury

The most common RBC abnormality seen in the above conditions are schistocytes, most dramatically in the microangiopathic hemolytic anemias (Figure 7).

![Figure 7. Twenty-five-year-old woman with thrombotic thrombocytic purpura.](image)

Extravascular hemolysis occurs when RBCs are removed by macrophages in the reticuloendothelial system (primarily the spleen, but also liver and bone marrow). The classic example of this occurs in autoimmune hemolytic anemia, where RBCs are coated with antibody. Splenic macrophages detect the bound antibody and phagocytize and digest the RBCs; this is done without leakage of RBC enzymes into circulation, so inflammatory responses (e.g., fever and chills) are usually minimal. Many RBCs escape with only partial loss of cytoplasmic membrane, and those cells lose their central pallor and are visible as spherocytes in the peripheral blood. Patients with chronic extravascular hemolysis typically develop splenomegaly, which can be substantial. Clinical symptoms with extravascular hemolysis disorders are generally milder and more stable than those seen with intravascular hemolysis, although cases of acute hemolytic crisis can occur and may be dramatic.

Causes of extravascular hemolysis include the following:

• Autoimmune hemolytic anemia: DAT positive
  With severe cases, free HGB may circulate and the case may resemble intravascular hemolysis because the capacity of the macrophage system to process damaged RBCs is exceeded

• Most hemoglobinopathies and thalassemias
The most common RBC abnormality seen in the above conditions are spherocytes, although target cells and sickle cells may be seen in hemoglobinopathies and bite cells with Heinz body hemolytic anemias. See Figure 8 for examples.

<table>
<thead>
<tr>
<th>Hereditary spherocytosis</th>
<th>Hereditary elliptocytosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalassemia (microcytosis, teardrop cells, basophilic stippling)</td>
<td>Target cells (e.g., hemoglobinopathies, liver disease, postsplenectomy)</td>
</tr>
<tr>
<td>Sickle cell disease (Hgb SS)</td>
<td>G6PD deficiency (bite cells)</td>
</tr>
</tbody>
</table>

Figure 8. Examples of RBC abnormalities. Photomicrographs courtesy of the author.
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A full review of hemolytic anemia classification is beyond the scope of this discussion. For a more comprehensive overview, review of key hematology references is recommended.⁷,²⁵,²⁶

Case Presentation 2

A 47-year-old student experienced acute fatigue and fever after her kickboxing class and went to her physician, who noted jaundice, pallor, and splenomegaly. He referred her to the local hospital emergency department, where an EDTA tube was collected and sent to the hematology lab for a CBC. The following automated results were obtained: WBC = 4.8; RBC = 1.27; HGB = 5.5; HCT = 14.7; MCV = 115.8; MCHC = 37.5; PLT = 340; reticulocyte % = 28.9. The specimen was centrifuged to investigate the high MCHC, and hemolysis was noted. The hematology laboratory initiated a re-collection. After two more rounds of phlebotomy yielding the same findings, the emergency department physician called to say that he thought the patient had intravascular hemolysis, and to request that the cycle of re-collections be discontinued.

Belated examination of the blood film (Figure 9) showed variable spherocytosis (not uniform, as seen in hereditary spherocytosis) with increased polychromasia and NRBCs. Some RBC agglutination was also noted, which explained the high MCV; the agglutination did not normalize after warming, suggesting a warm agglutinin. Results of other studies included the following: DAT positive for anti-IgG; DAT negative for anti-C3d; bilirubin, 18.9 mg/dL (reference range, 0.1-1.2); LDH, 2325 U/L (reference range, 89-192); haptoglobin, <9 mg/dL (reference range, 30-200); antinuclear antibody negative; rheumatoid arthritis negative; vitamin B₁₂ and folate concentrations normal.

Diagnosis: Autoimmune hemolytic anemia in acute hemolytic crisis, with increased levels of free plasma HGB.

Takeaway lesson: Hemolysis in an apparently anemic sample should have a blood film examination performed for findings consistent with in vivo hemolysis, before the specimen is rejected (see the discussion of high MCHC above for reporting of such cases).
Figure 9. Autoimmune hemolytic anemia. Clockwise from top left: elevated spherocytes, polychromasia, autoagglutination, and NRBCs. This case also had Howell-Jolly and Pappenheimer bodies without previous splenectomy, indicating possible autosplenectomy. Photomicrographs courtesy of the author.

References


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