

PedsCases Podcast Scripts

This is a text version of a podcast from PedsCases.com on the “Approach to Pediatric Anemia and Pallor.” These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedcases.com/podcasts.

Approach to Pediatric Anemia (Part 1)

Developed by Chris Novak and Dr. Karen Forbes for PedsCases.com.
June 11, 2015.

Intro

Chris: Hi everyone, my name is Chris Novak. I’m a medical student at the University of Alberta. I’m joined today by Dr. Karen Forbes, a pediatric hospitalist and Associate Professor of Pediatrics at the University of Alberta. She is also the director of the Pediatric Clerkship. Welcome Dr. Forbes and thank you for joining me:

Dr. Forbes: Thanks, I’m happy to be here.

Chris: This two-part series is designed to give an approach to diagnosis and management of anemia in children. In the first podcast of this series we will:

- 1) Review the differential diagnosis of anemia based on pathologic process
- 2) Review the clinical presentation of anemia on history and physical exam

In the second podcast of this series we will discuss:

- 1) Ordering the appropriate investigations to identify a cause of anemia in children
- 2) Approach to the underlying etiology of anemia based on interpretation of the CBC
- 3) An introduction to management, with a particular focus on the most common cause of anemia in children, iron deficiency.

We will start with a clinical case.

Clinical Case – You are a 3rd year medical student doing a rotation in an outpatient pediatric office. Today you are seeing Sam, an 18-month-old male of Southeast Asian descent coming in for his extended well child check. You ask mom if she’s had any concerns since her last visit and she shares that Sam is previously healthy and seems to be doing well. On further probing, mom states that she has noticed that in the past few months he has seemed irritable, sluggish and tires more easily than some of his peers at daycare.

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What disease processes could cause these symptoms? What questions do you want to ask, and how will you come to a diagnosis? We will return to Sam's case as we go through the podcast.

Anemia is a common presentation that affects an estimated 20% of children at one point in their childhood. Anemia has a broad differential ranging from benign problems to serious medical conditions, which may require urgent management. It is important to have a solid approach to this common problem.

Definitions

Chris: Let's start with the basics. Dr. Forbes what is the definition of anemia?

Dr. Forbes: First, we need to remember that anemia is not a diagnosis, but a lab finding that warrants investigation. It is defined as a decrease in the number of red blood cells or the amount of hemoglobin in the blood and more specifically as a hemoglobin level of less than the 5th percentile for age. This is important to remember because hemoglobin varies by age and there is not an absolute "cut off" value that defines anemia. The result of reduced hemoglobin is a decreased ability for the blood to carry oxygen to tissues.

Etiology

Chris: Anemia has a broad differential so it's important to think of a number of possible causes when approaching a patient. How do you organize your thoughts when thinking about the differential diagnosis for anemia?

Dr. Forbes: It is helpful to think of anemia according to the underlying pathologic process that is occurring, which can be broken down into 3 broad categories: Production, Destruction and Loss. We'll go through each one.

Production problems are caused by inadequate production of red blood cells. First let's briefly review some physiology. Red blood cells are produced from progenitor cells in the bone marrow via the process of hematopoiesis. Hematopoiesis is stimulated by the hormone erythropoietin or EPO, which is produced in the kidneys. When bone marrow cells receive the signal from EPO they start to produce new RBCs and require essential building blocks, which include iron, folate and vitamin B12. A problem in any step of the production process can lead to anemia.

- A patient cannot produce sufficient red blood cells if they do not have the required building blocks. You can see anemia with deficiencies in iron, folate and vitamin B12. Iron deficiency is certainly a common cause of anemia in children.
- The bone marrow can be damaged or suppressed by toxins, medications, certain infections, chronic inflammation, or radiation. Malignancies like leukemia or lymphoma can infiltrate the bone marrow space and interfere with hematopoiesis.

- In renal disease, damaged kidneys may not produce enough EPO to stimulate the bone marrow. Without EPO, anemia results.

The next category to consider is “Destruction.” Even if the body is able to produce sufficient red blood cells, it will not be able to keep up if the RBCs are destroyed at an increased rate. The destruction of red blood cells is called hemolysis. Hemolysis can be caused by a number of factors, and it is helpful to think from the outside in. Factors that are external to the cells include mechanical valves, or issues in the blood vessels that can cause mechanical trauma and lead to shearing of cells. We see this in processes such as disseminated intravascular coagulopathy (DIC) or hemolytic uremic syndrome (HUS). Moving inwards, antibodies reacting on the cell membrane can lead to an autoimmune hemolysis. This can be seen in an acute transfusion reactions, hemolytic diseases of the newborn including ABO incompatibility or Rh disease, or in a number of autoimmune processes where the patient’s immune system is fooled into attacking its own red cells. Factors that are internal to the cells include RBCs membrane abnormalities which can make cells prone to lysis by making them too round, too long or just too strangely shaped to pass through small blood vessels. These conditions include hereditary elliptocytosis where the cells are shaped like ellipses and spherocytosis where the cells are shaped like spheres. Next, abnormalities in the proteins and enzymes inside the cell can cause increased destruction of cells. This is seen in sickle cell anemia, thalassemias, and various enzyme deficiencies.

The last, and simplest, major category to consider is “Loss.” Simply put, if someone is losing blood or bleeding faster than new cells are being produced, the net result will be a loss and subsequent anemia. Blood loss can be major or minor, and can be acute or chronic with ongoing loss. Any hemorrhage can cause anemia. This bleeding can occur from trauma, surgery, GI bleeding as seen in inflammatory bowel disease or peptic ulcer disease, or in post-menarchal females, heavy menstrual losses. Bleeding disorders can lead to frequent hemorrhages, which accumulate into an anemia.

Chris: Ok, to review, the 3 pathologic causes of anemia are “Production,” “Destruction” and “Loss.” Reduced production of RBCs can be due to inadequate building blocks or ineffective production machinery in the bone marrow. Destruction of cells can be caused by a variety of factors that can be thought of using an outside-in approach. Finally, loss of cells due to hemorrhage can cause anemia. We will keep these 3 processes in mind as we move on to conducting a history, physical and investigations.

History

Chris: Now let’s review important questions to ask on the history. Dr. Forbes, how do you structure your history in a patient with suspected anemia?

Dr. Forbes: In all patients, you want to conduct a full medical history including history of presenting illness, past medical and surgical history, medications, allergies and family history. If you suspect anemia you should ask questions around symptoms that may be present in anemia, followed by questions that might lead you to a more specific etiology.

You can structure your history around the 3 pathologic processes of Production, Destruction and Loss to ensure that you are not missing key features.

Chris: Ok, what are some of the common symptoms children with anemia present with?

Dr. Forbes: First, many patients with anemia, especially if mild, will be asymptomatic. Symptoms are more likely to occur when there is an abrupt decrease in hemoglobin or in cases where anemia is more severe, although this may still be subtle if it has developed over time. Some symptoms are common to all types of anemia. These are lethargy, tachycardia and pallor. Without enough oxygen being delivered to the tissues, children become tired and weak and may lose interest in normal activities. The heart has to work harder to meet demands, and the heart rate increases. Pallor appears because fewer red blood cells are present to give you a pink complexion. A parent may not note pallor on history, as it may develop slowly over time, but you are more likely to note it on your physical exam when you see the child for the first time. It is also important to note that the body is very good at adapting to anemia over time, so if the anemia is chronic, the child may have few or no symptoms. In contrast, an acute anemia such as one caused by a major blood loss will cause much more significant symptoms.

Chris: Once you have assessed if a child's anemia is symptomatic, how do you approach finding a cause on your history?

Dr. Forbes: Let's start with Production problems. You can think about these problems in three broad categories of nutrition, chronic disease, and bone marrow suppression.

The most common causes of anemia are related to deficiencies in the building blocks for red blood cells, so it is important to take a detailed dietary history.

- I would want to know if the child is eating iron containing foods, and specifically what and how much. You need to get details about what they drink, including what kind and how much milk, as well as juice. Many toddlers who are so called "picky" eaters consume large quantities of milk, which fills them up and limits their appetite for taking in other more nutrient rich foods. In young toddlers, getting information about how the baby was fed in the first year of life is also helpful, with respect to breast milk versus iron supplemented formula, timing of introduction of solids, as well as timing of transition from breast milk or formula to milk. This is important because a full term infant has enough iron stores for about the first 6 months, after which they require iron in their diet.
- Additionally, children with iron deficiency may present with pica, a strangely increased desire to eat non-food items such as clay, dirt, or ice.

The next major group of production problems has to do chronic disease and inflammation.

- Here we want to explore if the child has any chronic medical conditions that could induce an anemia. These can include inflammatory bowel disease, rheumatologic disease, chronic kidney disease, chronic infections or malignancies. Some of these conditions are associated with a family history. The anemia may be one of the first features presenting from a condition, and they may not yet have developed other symptoms of the underlying disease, so it is important to keep your mind open to the possibility of a chronic disease. Another clue in this regard would be the child's growth pattern, as this may also be affected early in chronic disease before other more obvious symptoms.

The last group of production problems involves bone marrow suppression.

- I would want to ask if the child is taking any medications, or has had any exposure to toxins like lead or radiation therapy, which may cause bone marrow suppression.
- When you consider malignant processes, I would want to ask if the child has any constitutional or "B" symptoms, which include fever, weight loss or night sweats.
- It is also important when considering bone marrow causes of anemia to ask about other cell lines, like the production of platelets and leukocytes. I would ask if the child has been prone to bruising and bleeding, or if the child has had frequent or severe infections. A history suggestive of multiple cell line involvement is much more alarming than an isolated anemia.

Dr. Forbes: Next we can talk about destruction processes or hemolysis. Hemolysis leads to increased serum bilirubin and can cause jaundice, scleral icterus and dark urine. We would want to ask about these symptoms when thinking about hemolytic disease, but then focus your questions around recent acute illness, travel history and family history.

Acute illness such as from serious bacterial infections or sepsis can lead to severe hemolytic processes such as DIC or HUS. Some acute viral infections such as with EBV can also cause hemolysis.

- I would want to ask if the child has been recently ill with any infectious symptoms such as respiratory symptoms, rashes, vomiting, or diarrhea.
- Urine output would be important to ask about if you are considering HUS.
- A history of recent transfusions might help you consider the possibility of a hemolytic transfusion reaction.

On travel History I would want to ask about travel history to malaria endemic areas, as malaria can cause a hemolytic anemia.

Family History of anemia or jaundice can be very helpful. Several causes of hemolysis such as sickle cell Disease and thalassemias run in families and are associated with certain ethnic groups. Sickle cell Disease has a large array of other features beyond anemia, but is beyond the scope of this podcast.

Dr. Forbes: Finally, we will discuss blood loss. Blood loss may be overt and obvious, or more chronic and occult.

With overt blood loss:

- I would ask if the child has had any obvious blood loss or trauma, and if there has been any blood in stool, or black, tarry, melena stools.
- In a post-menarchal girl you should also take a menstrual history to consider menstrual losses.

Occult blood loss can be more subtle to identify.

- I would ask about mucosal bleeding such as bleeding from the gums or epistaxis, which may represent repeated small bleeds.
- In a hospitalized child, consider iatrogenic blood loss from repeated blood draws.
- Family history again can be very helpful in this category, to identify the possibility of an inherited bleeding disorder. History of family members who have required transfusions or who have had severe bleeding with procedures can be clues to this.

Chris: Ok, that's a lot to keep straight, let's review that, by returning to our clinical case.

You start to collect a history from Sam's mother. Sam has a number of the vague general symptoms of anemia including fatigue, irritability and decreased exercise tolerance. These symptoms started gradually over the last 3 months and his mom hasn't noticed if he has become more pale than usual. You then ask questions around each of the three pathologic causes of anemia. Starting with Production, you take a nutrition history. Sam has always been a picky eater. His favourite foods are pasta, rice and some fruits. He drinks four-to-five eight-ounce bottles of homogenized milk per day, and some juice. He sometimes drinks from a cup but mom still gives his milk and most of his fluids through a bottle. He has no known chronic diseases, exposure to radiation and is not taking any medications. He has not lost any weight or had any B symptoms, and if anything has increased his weight percentiles on the growth curve. You find that in the last few months he has had an increasing number of bruises on his arms and shins, and has had a number of upper respiratory tract infections. Next you ask around Destruction problems. Mom has not noticed any jaundice, or dark urine. He has not had any recent diarrheal illness, no travel outside of Canada and while you make note of his Southeast Asian heritage, he has no family history of anemia or transfusions. Finally when asking about losses, Sam has not had any significant overt bleeds, or blood in stools, with the only suggestion of bleeding being the bruises that mom had mentioned earlier.

Physical Exam

Chris: Now let's move on to the physical exam. Dr. Forbes, what signs on a physical exam would support a diagnosis of anemia?

Dr. Forbes: Always start with vital signs. In particular, pay attention to heart rate for tachycardia. Next, measure and plot your growth parameters and plot previous measurements so you can assess the child's growth. Afterwards, you should conduct a full physical exam, however there are some specific features that can lead you towards a diagnosis.

Pallor is a physical sign that is suggestive of anemia. Pallor is observed in areas where capillary beds are readily visible such as the palms, nail beds and conjunctiva, and can be seen regardless of skin colour. Check the rims of the eyes, the fingernails and the palms and soles. If areas that should be pink are not, then the child has pallor. Different studies have evaluated the physical sign of pallor as a diagnostic tool for anemia and have found that pallor, particularly around the conjunctival rim, is a very specific sign for anemia, but it is not very sensitive. This means that in a child with pallor, you should have a strong suspicion of anemia. However, many children with significant anemia may not appear pale.

Your physical exam should then search for specific signs that could be associated with production, destruction or loss. For production problems, you should perform a full lymph node exam and an abdominal exam for hepatosplenomegaly. Lymphadenopathy or splenomegaly may suggest a malignant cause. Petechiae and bruising may suggest other cell lines are involved. For destruction problems, you should inspect for signs of jaundice or scleral icterus. Hemolysis causes the release of bilirubin from ruptured red blood cells and leads to jaundice. For problems of blood loss, look for mucosal bleeding.

Chronic anemia is often well compensated and may have few clinical findings. Severe chronic anemia, however, may exhibit signs of a high cardiac output state including tachycardia, active precordium and a murmur, and in extreme cases, a gallop rhythm. A flow murmur may be present in less severe anemia without signs of overt heart failure.

Chris: Excellent. Now let's return to our clinical case by reviewing the physical exam.

Starting with vital signs you see that Sam has a pulse of 130 beats per minute, which is on the high end of normal for his age. Other vital signs are normal. On general inspection Sam appears well and has been playing with a toy during the history. He does not appear jaundiced, and you cannot appreciate any pallor on his palms, soles, or conjunctival rim. He does have a few bruises on bony prominences, including his shins, elbows and a small bruise on his forehead but no petechiae. On the head and neck exam, you cannot palpate any lymph nodes and his tonsils are not enlarged. In auscultation of the heart he has a slight mid-systolic ejection murmur at the pulmonic area rated 2/6. He has no hepatosplenomegaly and the rest of his exam is normal.

This concludes part 1 of our podcast. We have reviewed the differential for anemia in children guided by the 3 pathologic processes of production destruction and loss. We have also discussed key points to look for on a history and physical in a child with

suspected anemia. Be sure to check out part 2 of this series for an approach to investigation and management of anemia and the conclusion of our clinical case.

Thanks for listening!

Approach to Pediatric Anemia (Part 2)

Chris: Hi everyone, and welcome back to the second part of our two part series of podcasts on anemia and pallor in children. My name is Chris Novak, a medical student at the University of Alberta. I'm joined today by Dr. Karen Forbes, a pediatric hospitalist and Associate Professor of Pediatrics at the University of Alberta. She is also the director of the Pediatric Clerkship. In our last podcast we discussed the differential diagnosis of anemia in children, focused around the 3 pathologic processes of Production, Destruction and Loss. We discussed how to structure a history for a child with signs of anemia or pallor, and reviewed relevant signs on the physical exam.

In the second podcast of this series we will discuss:

- 1) Ordering the appropriate investigations to identify a cause of anemia in children
- 2) Approach to the underlying etiology of anemia based on interpretation of the CBC
- 3) An introduction to the management, with a particular focus on the most common cause of anemia in children, iron deficiency.

Throughout the podcast we have been going through a clinical case of Sam, an 18 month-old male. Let's return to the case.

You have completed the history and physical exam, and it is now time to present your findings to your preceptor, focusing on pertinent positives and negatives. Sam is a previously well 18-month old male of Southeast Asian Descent. He is presenting today for a well child visit, but you were able to elicit a 3-month history of fatigue, irritability and decreased exercise tolerance. He is a picky eater, with excess intake of milk and juice, with little intake of iron-rich foods. He has not been recently acutely ill. He has no history of radiation exposure, medications or chronic disease, and no family history of blood disorders. He has developed a number of bruises on bony prominences in the last few months, and has had a number of URIs in the past 6 months. He has no features on history suggestive of a hemolytic process such as jaundice or dark urine. He has had no obvious blood loss or bleeding. On exam, he is mildly tachycardic, with a 2/6 systolic ejection murmur at the Left Upper Sternal Border. He has no noted pallor, jaundice, lymphadenopathy or hepatosplenomegaly.

Dr. Forbes: Good summary. This patient certainly has a clinical picture suggestive of anemia. He has a history suggestive of iron deficiency. I wouldn't be too concerned about his history of bruises on bony prominences or his URIs. At 18 months of age children are walking and falling and this type of bruising is common. For a child in

daycare, frequent infections are very common. However, I do think this case would warrant investigation, so let's move on to the work-up for a child with anemia.

Investigations and Diagnostic Approach

Chris: With such a broad differential for anemia, the list of possible investigations is vast. However, it is best to start simple and then expand from there. Dr. Forbes, how do you approach ordering investigations for a child with suspected anemia?

Dr. Forbes: Always start with a CBC. Understanding a diagnosis of anemia requires an understanding of some basic indices on a Complete Blood Count or CBC, so we will spend some time discussing the CBC in more detail.

Anemia is defined as a hemoglobin level or hematocrit that is less than the 5th percentile for age. Hemoglobin is reported on a CBC as HGB and is measured by the concentration of hemoglobin in whole blood in g/L. The hematocrit, or HCT, is the fractional volume of hemoglobin in a whole blood sample expressed as a percentage. For American listeners, please note that we will be referring to SI units used in Canada, in contrast to the measurement units used in the United States.

Once you know how many red blood cells you have, there are further indices, which tell you more about the size of the cells and the concentration of hemoglobin in each cell. The first one to look at is the Mean Corpuscular Volume or MCV, which is a measure of the average volume of a red blood cell. Red blood cells that are of a normal volume are described as normocytic. Smaller red cells are described as microcytic, while bigger red cells are described as macrocytic, represented by lower or higher numbers respectively.

The mean corpuscular hemoglobin concentration (MCHC) is a measure of the average concentration of hemoglobin in each red blood cell. The Red cell distribution width or RDW is a measure of the variation of red blood cell sizes within a sample. A high RDW indicates that there is a wide variability in sizes among red cells within the sample. I kind of think about it like your confidence interval for your red blood cells. You use all of these different indices when interpreting a CBC.

Normal ranges vary significantly with age, particularly in infancy so it is important to ensure that you are using age and sex adjusted normal values. A link to the reference ranges used in Alberta is included in the supplementary materials on PedsCases.com (<http://www.dynalifedx.com/Portals/0/pdf/Lab%20procedure%20or%20protocol/Pediatric%20CBC%20reference%20values.pdf>). There are some general trends to remember about how hemoglobin changes with age. First, at birth hemoglobin is quite high, as a result of the relatively low oxygen state in utero. This higher hemoglobin that is present in the first days-weeks of life gradually declines as fetal hemoglobin, or HbF is replaced with adult-type hemoglobin, or HbA. Remember that HbF has a shorter life span than HbA. This results in a normal decline in hemoglobin, or what is called the physiologic nadir, around 2 months of age. After this, hemoglobin steadily increases until about age

12 where ranges approximate adult values. For the MCV, remember that newborns have big red blood cells, and they decrease in size as a child ages.

When interpreting a CBC, first look and see if anemia is present based on the HGB. Next, look at the MCV to see if the cells are small, normal, or large. Different types of anemia will present with cells of different sizes. You should also look at white blood cell and platelet numbers to assess if this is an isolated anemia, or is suggestive of a more concerning pancytopenia. Using these different indices, combined with your history and physical you will be able to point yourself towards a more specific etiology.

Children most commonly present with microcytic anemia. These disorders result in production of abnormally small red blood cells. Iron deficiency is the most common cause of microcytic anemia, but it is important to consider other options in your differential. The differential for microcytic anemia may be commonly remembered by the acronym “I See The Little Cells”:

- I – Iron Deficiency Anemia
- S – Sideroblastic anemias
- T – Thalassemias
- L – Lead toxicity
- C – Anemia of Chronic Disease

Hemoglobinopathies or disorders of abnormal hemoglobin can also cause microcytic anemia with the exception of sickle cell anemia. Anemia of chronic disease may cause microcytic or normocytic anemia. A microcytic anemia with an elevated RDW strongly suggests iron deficiency anemia.

Normocytic Anemias have normal sized red blood cells, but you just don't have enough of them. The differential for normocytic anemia includes problems of bone marrow suppression, red blood cell destruction and loss. To differentiate the etiology of normocytic anemia you will likely need additional lab testing. It is important to go back to your history to explore the possibility of chronic disease.

Macrocytic anemias are rare and the least common type of anemia seen, and result in the production of abnormally large red blood cells. It's important to remember that newborn, and especially preterm infants have larger red blood cells than normal, but this is part of normal development, and they will decrease in size with time. Always remember to use age-adjusted values. Pathologic causes of macrocytic anemia include:

- B12 and folate deficiency most commonly, but also
- Some medications
- Hypothyroidism
- Some hereditary conditions
- And other bone marrow disorders

Chris: Ok, so let's review that approach to the CBC. You can make the laboratory diagnosis of anemia based on a decreased HGB or HCT. Once you've diagnosed anemia, you can use the MCV to focus your differential into microcytic, normocytic and macrocytic causes based on whether the red cells are small, normal or large. Dr. Forbes, once we have a CBC, what further tests might be useful?

Dr. Forbes: The ordering of further tests should be based on your history and physical leading you to suspect a specific cause of anemia. Do not just take a shotgun approach and order a test for every possible cause of anemia. While there are many possible tests you could order, here are a few important ones to consider.

A peripheral blood smear is a valuable tool in working any hematologic process. The smear involves visualizing a sample of blood by microscopy. This can tell you what the cell looks like, and a number of abnormal morphologies, which can point towards a diagnosis. While specific interpretation of the peripheral smear is beyond the scope of this podcast, a smear is indicated when you suspect malignancy, a hemoglobinopathy or hemolysis.

Next we will consider the reticulocyte count. When the bone marrow is under stress and is actively producing new red blood cells, immature red blood cells called reticulocytes are released into the circulation. Note that the retics are young red blood cells and are bigger in size than mature RBCs; they may be represented by an increased RDW for example, after initiation of treatment for iron deficiency. An appropriate response to anemia would be to ramp up RBC production and as a result you would see increased reticulocytes. If the reticulocytes are low or normal, this would be an inappropriate response, as the bone marrow is not responding. Based on the reticulocyte count we can categorize the anemia as:

- Retics Appropriately Increased - This indicates that the bone marrow working hard to produce more RBCs. This means that the anemia is either due to a "Destruction" process or blood "Loss" as discussed previously.
- Retics Inappropriately Low or Normal - This indicates that the bone marrow is not responding appropriately and is depressed or inactive. This usually indicates a "Production" problem.

You should suspect a hemolytic anemia if you have a suggestive history, observe jaundice on physical exam, or have an appropriately elevated reticulocyte count with no obvious causes of blood loss. The workup for hemolysis includes a Coombs test, total bilirubin, haptoglobin, LDH and peripheral smear.

A hemoglobin electrophoresis is required to diagnose a hemoglobinopathy and is one of many other tests could be ordered to identify a specific etiology. However, a stepwise approach is always best and if you start with the basics, you should be well on your way to making a diagnosis.

Chris: What about iron studies?

Dr. Forbes: In all honesty, iron studies are seldom helpful or add more to what you know based on history and your CBC indices. Ferritin represents iron stores, but is also an acute phase reactant, which means it is often elevated in the context of an infection or inflammation, which is often when we see children and note the anemia on blood work. Iron, saturation index and TIBC (total iron binding capacity) can confirm iron deficiency, but again you usually already suspect iron deficiency based on anemia in the context of a low MCV and high RDW. Where iron studies can be helpful is when a patient's anemia is seemingly not responsive to iron therapy, or if there is concern that iron deficiency is contributing in a patient who has another reason for anemia, such as in thalassemia.

Chris: All right, let's apply what we just learned to our clinical case.

You review the case with your preceptor and they agree it would be appropriate to order a CBC to assess Sam for anemia. That afternoon, the results appear on your electronic medical records. Sam has a Hgb of 65 g/L, which confirms a diagnosis of anemia. The MCV is 65, which would classify this anemia as microcytic. The RDW is elevated, and his WBCs and Platelets are in the normal range. You recall from your history that Sam has a diet low in iron, with a high intake of milk and juice. You review with your preceptor and they agree that the most likely diagnosis would be iron deficiency anemia. Given the ethnic background of this patient, you would also want to keep in mind the possibility of thalassemia.

Management

Chris: Now let's discuss management of anemia. Anemia has a huge differential, and the management for each different disease process is quite different. A detailed discussion of all of the different types of anemia is beyond the scope of this podcast, but we would like to discuss two points: Iron Deficiency Anemia and Indications for Transfusion.

Dr. Forbes: Iron Deficiency is the most common cause of anemia in children. Iron is one of the critical building blocks for hemoglobin and without it you cannot produce sufficient red blood cells. Without enough iron to fill up the red blood cells, they present as small, shrunken or microcytic. Risk factors for iron deficiency include a low SES, prematurity or low birth weight. At birth children have adequate iron stores and they are able to live exclusively on breast milk or formula without developing iron deficiency. Beyond 6 months, these stores start to run out and iron-containing foods need to be introduced into the diet. Iron-rich foods include meat, eggs, lentils and fortified infant cereals. A diet that is low in iron rich foods will lead to iron deficiency. Often these children are described as "picky" eaters and drink excessive amounts of milk, which fills them up and contributes to a lack of appetite for iron containing solids.

In a child with a microcytic anemia, assess the clinical picture. If the child is clinically stable, less than 2 years of age, has risk factors or a dietary history in keeping with iron

deficiency, and another cause does not seem more likely, you can empirically treat with oral iron supplementation. A recommended dose would be 4 to 6 mg/kg/day of elemental iron. How closely you follow up will depend on the severity of the anemia. If it is relatively mild, you can follow-up after about one month of treatment. If the hemoglobin has increased >10 g/L, this confirms the diagnosis of iron deficiency anemia. You would expect to see reticulocytosis peak about 3 to 5 days after starting therapy, and would manifest by increase in the retics and also an increase in the RDW. In my experience, hemoglobin often increases and can return to normal fairly quickly, however you still need to continue iron supplementation for at least 3 months to ensure you replenish iron stores.

In older children, or children without a history consistent with iron deficiency, or children who fail to respond to empiric oral iron, a more thorough diagnostic work-up would be indicated to help elucidate the cause of the anemia. This would likely include a peripheral blood smear, iron studies and potentially other tests such as hemoglobin electrophoresis or fecal occult blood testing as appropriate. In those children, therapy will be determined based on the underlying cause.

Chris: In a patient with anemia, what is the cutoff for transfusion?

Dr. Forbes: That is a great question. There is no single hemoglobin cutoff value that would necessitate transfusion. Rather, we need to take into consideration the context of the anemia, in particular whether the process is acute or chronic, as well as the underlying process causing the anemia. For example, a patient who has acute blood loss and is symptomatic certainly is likely to require transfusion. However, if the process is chronic, the body can compensate very well even in more significant anemia, so there is not the same urgency to transfuse. This is where consideration of the underlying cause is important. If it is a production problem due to iron deficiency, for example, simply providing the substrate that is required to stimulate production is the safest way to manage the anemia. Conversely, in a situation where there is ongoing destruction such as in a hemolytic anemia, transfusion may be required to maintain hemoglobin levels until the hemolytic process ceases.

Chris: So to summarize, the decision to transfuse will be based on acuity of the development of anemia as well as the underlying process.

Chris: Now let's conclude our clinical case. You discuss Sam's case with your preceptor. You decide that the most likely cause of his anemia is iron deficiency, but also consider thalassemia in your differential. You plan for a trial of oral iron therapy and nutritional management with close follow up. You call Sam back to your office, and inform his mother of the most likely diagnosis. You counsel Sam's mother that she should limit his intake of milk to 2 cups per day and should restrict juice. You recommend they focus on giving Sam iron-rich foods every day, including meat, eggs, lentils and iron-fortified cereals. You prescribe iron supplementation with oral iron at 6 mg/kg/day of elemental iron for the next three months. One month later they return with a repeat CBC, and his anemia has improved dramatically. Sam's mother reports

success in dietary changes and is happy that Sam's energy levels have improved and he is back to full play.

Key Points

Before we leave, we wanted to leave you with the following key take home points:

- 1) Anemia is a lab finding and not a specific diagnosis.
- 2) History and physical should target a search for the underlying process, which may be a production problem, a destruction problem, or due to blood loss.
- 3) Interpretation of CBC based on the MCV can help you focus in on an underlying cause of anemia.
- 4) Iron deficiency is the most common cause of anemia in childhood and, if history and lab findings are in keeping with this, patients can be treated empirically with oral iron and close follow up.

That concludes our presentation. Thanks for listening to PedsCases podcasts!

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