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PODCAST TITLE

Developed by Maya Fields and Dr. Vicky Breakey for PedsCases.com

September 08, 2026

Introduction:

Welcome to PedsCases and thank you for listening to this podcast. Today's episode will cover an approach to pancytopenia in the pediatric population. My name is Maya Fields and I am a second year medical student at McMaster University in Hamilton, Ontario. This episode was created in collaboration with Dr. Vicky Breakey, a Pediatric Hematologist-Oncologist at McMaster University.

Learning Objectives

By the end of this podcast, the listener should be able to:

1. Define pancytopenia
2. Explain how clinical manifestations and investigations may point to a specific diagnosis
3. Understand how the presentation of pancytopenia can signal an underlying diagnosis of Acute Leukemia
4. Understand how the presentation of pancytopenia can be indicative of Aplastic Anemia

Clinical Case:

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Let's begin with a clinical case.

Robert, a previously healthy 6 year-old boy, presents to the emergency room with a two-week history of progressive fatigue, pallor, intermittent low-grade fever, and new onset bruising. His parents report decreased appetite, mild weight loss, and several episodes of epistaxis. On ROS, there is no history of recent infection, but he has complained of leg pain, especially at night, and has been less active. Physical exam reveals marked pallor, scattered petechiae, and ecchymoses on the lower extremities, mild hepatosplenomegaly, and non-tender cervical lymphadenopathy. No focal neurological deficits are present.

Initial lab investigations show Hb 78 g/L, WBC count 2.1 x 10^9/L, absolute neutrophil count 0.4 x 10^9/L, and platelets 32 x 10^9/L. The peripheral blood smear shows numerous atypical lymphocytes with reduced neutrophils and platelets.

Keep this patient in mind as we go through the rest of the podcast and we will return to this case throughout our discussion.

Defining Pancytopenia, its Clinica Presentation, and Investigations

Firstly, what is Pancytopenia? Pancytopenia is defined as a decrease in all 3 blood cell lines, those being erythrocytes (or Red Blood Cells), leukocytes (or White Blood Cells), and platelets (1). It is important to note that pancytopenia is not a disease itself, but rather a laboratory finding that may result from different etiologies. These etiologies can be infectious, hematological, oncological, or others. Determining the cause is important so that we can provide the correct treatment.

Let's break down how pancytopenia occurs. There are 3 main causes: we can have increased destruction of blood cells, meaning that something is breaking them down. We can also have impaired production of these cells, meaning something is stopping us from making them in the bone marrow to begin with. The final mechanism is a combination of both (1–3). For the purpose of this podcast, we will focus on impaired production. Impaired production is usually secondary to things like a nutritional deficiency (such as vitamin B12), bone marrow failure (such as aplastic anemia), infections, medications, or bone marrow infiltrating disorders (like malignancy) (1–3).

The clinical presentation for pancytopenia can be broad, but it can be helpful to think of the symptoms in relation to the blood line affected. For example, a decrease in erythrocytes leads to anemia, resulting in symptoms such as pallor, fatigue, dizziness, and decreased exercise tolerance (3). A decrease in platelets leads to thrombocytopenia, which causes symptoms such as bleeding (which may manifest as epistaxis or gum bleeding), bruising, and petechiae (3). Finally, a decrease in leukocytes or “leukopenia”, may be associated with symptoms such as fever, and increases the child’s susceptibility to infection, as there are less white cells available to mount an appropriate immune response (3). There are further presentations that may increase your suspicion of one etiology vs another, which we will discuss in the context of our two major differentials later-on.

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Pancytopenia is a laboratory finding, therefore, if you see symptoms of pancytopenia (as discussed above), it is essential to order a CBC to confirm the blood counts (4). Normal reference ranges for Hb and WBCs in children are age-dependent, however platelet ranges are the same throughout all ages.

If we look at Robert's bloodwork, everything is much lower than we would expect for a healthy 6 year-old. His hemoglobin is severely low, about half of what it should be. His WBC count is also very low, indicating a weak immune system. Specifically, his neutrophils, which are cells that fight bacterial infections, are almost absent. Finally, his platelet counts, which help with clotting and preventing bleeding, is also critically low. Taken together, all 3 major blood cell lines are reduced, and show pancytopenia. This raises concern for a serious underlying bone marrow problem. This is a good time to point out that although viral illness or infections can cause transient pancytopenia, generally, the counts would not drop this low, but rather the pancytopenia would be more mild to moderate and importantly, this would be transient, meaning that once the patient got over the illness, the counts would improve. Given the fact that our patient, Robert, has already been unwell for 2 weeks, there were no sick contacts, and the reduction in counts is quite severe across-the-board, this decreases our suspicion for viral illness. However, lab investigations should also include a work-up for common infectious agents that can affect blood cell production, such as hepatitis, CMV, Epstein-Barr Virus and Parvovirus B19. In children, pancytopenia is most commonly caused by transient viral bone marrow suppression, particularly from Epstein-Barr virus infection, Cytomegalovirus infection, Parvovirus B19 infection, influenza, and COVID-19. Less common but important infectious causes include bacterial sepsis, Typhoid fever, disseminated Tuberculosis, and travel-related infections such as Malaria and Visceral leishmaniasis. Severe or persistent pancytopenia, particularly when accompanied by hepatosplenomegaly or markedly elevated ferritin, should prompt evaluation for Hemophagocytic lymphohistiocytosis and underlying hematologic malignancy in addition to infectious causes.

Differential Diagnosis for Robert

Our first main differential for a child presenting with severe lab abnormalities of pancytopenia and symptoms would be Acute Leukemia. Leukemia is the most common malignancy of childhood, and there are two main types that present with pancytopenia: acute lymphoblastic leukemia (ALL) and acute myelogenous leukemia (AML) (5). ALL is the most common subtype, accounting for 80% of cases (5). The difference between ALL and AML is the cell of origin that is affected. In ALL, the cell of origin is in the lymphoid line, which includes lymphocytes, such as T and B cells- these are actually two different kinds of ALL, but we won't go into that much detail today. The AML cell of origin is in the myeloid line. This includes granulocytes, monocytes, erythrocytes, and megakaryocytes (5).

I want to call your attention back to the fact that ALL accounts for 80% of childhood leukemias, so that is the type of leukemia we will focus on. PedsCases has already published a note on ALL that you should check out for more details than we will discuss

here. We will continue to talk about ALL, but only in the context as an etiology for pancytopenia.

The clinical presentation of ALL is due to the clonal proliferation of leukemic blasts in the bone marrow, preventing normal production of RBCs, platelets, and neutrophils, thereby leading to pancytopenia due to impaired production (5). The degree of anemia, thrombocytopenia, and neutropenia can be variable, and as such, the symptoms can be variable as well (5). As we mentioned before, significant anemia can cause pallor, fatigue, dyspnea on exertion, headache, dizziness, and near syncope. Thrombocytopenia can cause bruising and petechiae, and sometimes bleeding. Fevers are common in patients with leukemia, however despite severe neutropenia, infection at the time of diagnosis is uncommon. Fever can be a symptom of the cancer itself (6). Another symptom that is present in our patient and would increase your clinical suspicion of ALL would be bone pain- this is because children with leukemia often have bone marrow that has been replaced with leukemic blasts, causing the bone marrow to expand and put pressure on the boney cortex (5). This can cause bone pain, limping, or a refusal to walk. Back pain can also occur. Additionally, leukemia can infiltrate organs outside the bone marrow, leading to lymphadenopathy, hepatosplenomegaly, and renal lesions. Thinking back to our case, Robert presented with bone pain and hepatosplenomegaly, as well as classic symptoms of pancytopenia. Taken with the fact that >1 cell line is affected, this increases our clinical suspicion for ALL.

We talked previously about how ordering a CBC and differential is important as a first step in investigations for Robert's presentation. The gold-standard in diagnosing ALL involves a bone marrow aspirate, which is a procedure where liquid marrow is withdrawn, usually from the posterior iliac crest, to obtain cellular material for diagnostic evaluation (5). You are essentially looking at the presence and percentage of lymphoblasts and providing a diagnostic assessment of them. A diagnosis of ALL requires >20% lymphoblasts in the marrow, but most commonly, the marrow is full of blasts, >90-95%. Morphology can also help distinguish ALL from other hematologic malignancies. Immunophenotyping using flow cytometry on the bone marrow aspirate can help differentiate ALL B-cell type from ALL T-cell type. If enough blasts are present, you could diagnose from a peripheral blood smear, but a bone marrow aspirate is considered gold-standard. Additional genetic testing on the blast cells provide important information on prognostication and guide treatment planning. In addition, all patients with acute leukemia require a lumbar puncture for CSF sampling to rule out CNS disease. If neurologic symptoms are present, then an MRI may be necessary. Finally, a thorough testicular physical exam should be performed in all male patients, as this can be a site for metastasis (5). For more information on treatment, check out the fantastic note already posted on ALL previously.

So to summarize our first major differential, for a child coming in with severe pancytopenia, with bone pain, hepatosplenomegaly and cervical lymphadenopathy, we should be highly suspicious for childhood leukemia, and specifically ALL (given that this accounts for 80% of cases). To confirm our suspicion, we should order a CBC + differential and a peripheral

blood smear. From there, a pediatric hematologist-oncologist should be consulted to further manage the patient, who will decide whether the patient requires a bone marrow aspirate, with further morphologic analysis and flow cytometry.

Let's move on to our second major differential diagnosis for pancytopenia in a child, aplastic anemia. Aplastic anemia is an acquired or congenital disorder characterized by pancytopenia with a hypocellular bone marrow due to decreased cell production (2). It is caused by failed hematopoiesis, either due to an acquired or congenital cause. Inherited causes are beyond the scope of this podcast. Acquired aplastic anemia is due to the autoimmune destruction of pluripotent hematopoietic stem cells by T cells. Essentially, there is unregulated lymphocyte activation, impaired regulatory T cells, and increased activity of IL-17 leading to autoimmune destruction of the hematopoietic stem cells in the bone marrow (the stem cells that can turn into any kind of blood cell), which is why the bone marrow is hypocellular (2).

The clinical manifestations of aplastic anemia are proportional to the level of cytopenias and include the common symptoms we discussed before, such as dyspnea on exertion, fatigue, easy bruising, epistaxis, bleeding gums, fever, and more. Some things that would differentiate aplastic anemia from ALL would be the absence of bone pain, hepatosplenomegaly, and lymphadenopathy.

Diagnostic criteria requires a marrow cellularity <25% OR <30% with residual hematopoietic cells and at least 2 of 3 peripheral cytopenias with neutrophils <0.5 x 10^9/L, platelets <20 x 10^9/L, and absolute reticulocyte count (immature RBCs) <60 x 10^9/L (7). In order to assess this, it is essential to order a CBC with differential, peripheral blood smear, bone marrow aspiration and biopsy, and genetic testing if you suspect genetic causes. The bone marrow aspirate and biopsy is necessary to demonstrate the hypocellularity (specifically, the core biopsy is needed to determine cellularity of the bone marrow), as well as rule out other causes, like ALL, because we would not expect to see any abnormal infiltrates in the marrow (9). There are other tests that can be ordered to rule out other differentials, but that is beyond the scope of this podcast. Finally, to treat aplastic anemia, it is important once again to consult with pediatric hematology-oncology so they can further manage this patient, but briefly, treatment consists of either immunosuppressive therapy or hematopoietic stem cell transplant, with the choice of treatment depending on the underlying cause (2).

To summarize our second major differential, for a child coming in with severe pancytopenia, we should consider the possibility of aplastic anemia. To confirm our suspicion, we should order a CBC + differential and a peripheral blood smear. From there, a pediatric hematologist-oncologist should be consulted to further manage the patient, who will decide

whether the patient requires a bone marrow aspirate and biopsy. Aplastic anemia is a life-threatening illness if not treated- patients are at risk for mortality because of bleeding or infection. However, if properly recognized and treated, survival rate is more than 90% (7,8).

Back to the Case

Let's end today's podcast by walking through our case one final time, with one last addition that we omitted originally as to not spoil our diagnosis.

Robert, a previously healthy 6 year-old boy, presents to the emergency room with a two-week history of progressive fatigue, pallor, intermittent low-grade fever, and new onset bruising.

This first phrase is pretty non-specific, but we are maybe thinking of some form of hematologic abnormality- we may be noting some anemic features, maybe some thrombocytopenia and leukopenia. But we would be keeping an open mind.

His parents report decreased appetite, mild weight loss, and several episodes of epistaxis. On ROS, there is no history of recent infection, but he has complained of leg pain, especially at night, and has been less active.

Now, alarm bells may be starting to go off- we have more symptoms to suggest pancytopenia, with the important point that there have been no sick contacts to explain the fever AND we have this complaint of leg pain. If it were just fever and leg pain, maybe we would be thinking something like Juvenile Idiopathic Arthritis, but taken together with the hematologic symptoms, we should be keeping a hematologic or oncologic differential in the back of our mind. It's also important to note that kids often have sick contacts, so the absence or presence of these contacts shouldn't make or break your differential.

Physical exam reveals marked pallor, scattered petechiae, and ecchymoses on the lower extremities, mild hepatosplenomegaly, and non-tender cervical lymphadenopathy. No focal neurological deficits are present.

This suggests some clinical signs of pancytopenia, specifically anemia and thrombocytopenia. The hepatosplenomegaly and non-tender cervical lymphadenopathy is

concerning- remember that lymph nodes in cancer are often enlarged, but not painful, unlike in infection, where they would be tender. The lack of neurological deficits is mentioned to decrease concern for CNS involvement, but does not rule this out.

Initial lab investigations show Hb 78 g/L (low), WBC count 2.1 x 10^9/L (low), absolute neutrophil count 0.4 x 10^9/L (low), and platelets 32 x 10^9/L (low). The peripheral blood smear shows numerous atypical lymphocytes with reduced mature neutrophils and platelets.

Robert had the additional work up we have discussed, which led to his definitive diagnosis. Bone marrow aspiration revealed >90% lymphoblasts, with immunophenotyping and cytogenetic analysis completed to classify the leukemia as B cell ALL, the most common type of leukemia in childhood.

It is important to note that acute leukemia does not always present with pancytopenia but may present with a normal white blood cell counts, with or without peripheral blast cells or with elevated white blood cell count due to circulating blasts in the peripheral blood. You can read more about ALL in the PedsCases infographic

Fortunately, the outcomes of B cell leukemia in children are very good, with upwards of 90% survival. Chemotherapy lasts just over two years and includes an upfront 7-8 months of more intense therapy that is given mainly in the outpatient setting. The latter part of the treatment, referred to as “maintenance” is mainly oral chemotherapy, with clinic visits only needed monthly.

We hope that this case can demonstrate how the presentation of pancytopenia can be variable and how various investigations can point you towards different etiologies.

<u>Summary:</u>

Revisiting some key points from our episode today, we covered the following information:

1. Pancytopenia is a reduction in blood cell counts across all three lines. Most commonly, we see childhood leukemia and aplastic anemia as the causes when the reduction is severe.
2. The differential is based on the clinical presentation. For example, leukemia may present with more B symptoms, lymphadenopathy, hepatosplenomegaly, and bone

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pain, while aplastic anemia is more likely to present with bleeding, in addition to classic pancytopenic features.

3. To diagnose pancytopenia, we need a CBC with differential. To identify its etiologies, we require further investigations, including a peripheral blood smear, bone marrow aspirate, and biopsy. The bone marrow aspirate is necessary to diagnose childhood leukemia, while a bone marrow biopsy is necessary to indicate the cellularity which is low in aplastic anemia.

Thank you for listening to today's episode on pancytopenia! We hope it was helpful for your learning and made you feel more comfortable with an approach to this presentation in pediatric patients. I also want to extend a special thank you to Dr. Breakey for her mentorship and guidance throughout the development of this PedsCases episode!

References

1. Chiravuri S, De Jesus O. Pancytopenia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Dec 23]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK563146/

2. Gnanaraj J, Parnes A, Francis CW, Go RS, Takemoto CM, Hashmi SK. Approach to pancytopenia: Diagnostic algorithm for clinical hematologists. Blood Rev. 2018 Sept 1;32(5):361–7.

3. Sharma R, Nalepa G. Evaluation and Management of Chronic Pancytopenia. Pediatr Rev. 2016 Mar 1;37(3):101–13.

4. Zubair AB, Razzaq MT, Hashmi AW, Ali SMY, Israr MM, Sadiq SM, et al. Clinical Characteristics and Etiological Spectrum of Pancytopenia in Pediatric Age Group: A Cross-Sectional Outlook From a Developing Country. Cureus. 14(8):e27842.

5. Kaplan JA. Leukemia in Children. Pediatr Rev. 2019 July 1;40(7):319–31.

6. Offenbacher R, Rybinski B, Joseph T, Rahmani N, Boucher T, Weiser DA. An 8-Year-Old Boy With Fever, Splenomegaly, and Pancytopenia. Pediatrics. 2020 July 1;146(1):e20192372.

7. Shimano KA, Narla A, Rose MJ, Gloude NJ, Allen SW, Bergstrom K, et al. Diagnostic work-up for severe aplastic anemia in children: Consensus of the North American Pediatric Aplastic Anemia Consortium. Am J Hematol. 2021;96(11):1491–504.

8. Yoshida N. Recent advances in the diagnosis and treatment of pediatric acquired aplastic anemia. Int J Hematol. 2024 Mar 1;119(3):240–7.

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9. Brodsky RA, Jones RJ. Aplastic anaemia. The Lancet. 2005 May 7;365(9471):1647–56.