GETTING THE MOST FROM YOUR PATIENT’S CBC
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The complete blood cell count (CBC) is an important diagnostic tool for specific diagnosis, as well as a component of a minimum data base. The CBC can be used to monitor response to therapy, gauge the severity of illness or as a first line of diagnosis. Interpretation of the CBC can be broken down into 3 sections: the erythron, the leukon and the thrombon. Each of these parameters can be interpreted individually; however integration of the data is important for the highest diagnostic yield.

Erythron
Interpretation of the erythron involves interpretation of the red blood cell count (RBC), packed cell volume (PCV), hemoglobin, mean cell volume (MCV), mean corpuscular hemoglobin concentration (MCHC) and mean corpuscular hemoglobin (MCH). The peripheral blood smear can provide additional information through examination of the red blood cell morphology. The PCV is measured as a percentage of packed cells in whole blood, spun in a microhematocrit tube. The hematocrit, however, is a calculation using MCV and RBC values from an automated hematology analyzer. The PCV is generally considered more reliable than the calculated hematocrit. The HCT and the hemoglobin should be in a 3:1 ratio. If it is not then a spun PCV should be performed.

Interpretation of the erythron should begin with the evaluation of the PCV and total protein. The PCV is a reflection of the circulating red blood cell mass. If the PCV is decreased, the animal is anemic, whereas an elevated PCV indicates polycythemia. Concurrent measurement of the total protein can assist in interpretation of the PCV. If the total protein is elevated, dehydration or inflammation should be considered. Dehydration may falsely mask anemia or may indicate the cause of polycythemia by falsely elevating the total red cell mass. A decreased total protein in an anemic patient could indicate blood loss as the etiology of anemia.

Anemia is a very common abnormality and accompanies a number of different disease processes. Characterization of the anemia as regenerative or non-regenerative can help to get to the underlying cause. The reticulocyte count is the best method available to determine whether an animal is responding to the anemia. Reticulocytes are immature red blood cells with increased RNA and organelles such as mitochondria and ribosomes. We can get an idea if a patient has circulating reticulocytes by evaluating a peripheral blood smear for polychromasia. This will reflect the reticulocyte count. Evaluation of the blood smear for polychromasia is a good tool for estimation of the regenerative/reticulocyte response; however, it may underestimate the actual reticulocyte response. Therefore staining the blood with New Methylene blue stain or
using an automated method for enumeration is recommended. Multiplying the percentage of aggregate reticulocytes by the RBC will give the absolute number of circulating reticulocytes. A normal dog can have up to 1% or 60,000 circulating reticulocytes. Healthy cats generally have less than 0.4% or up to 50,000 reticulocytes. The bone marrow takes 3-5 days to respond so acute blood loss may appear nonregenerative.

The red blood cell indices: MCV, MCH and MCHC are used to evaluate overall red cell size and hemoglobin concentration. The majority of anemias are normocytic, normochromic. In markedly regenerative anemias, macrocytic, hypochromic indices are observed (increased MCV, decreased MCHC), reflecting the increased size and decreased hemoglobin of the reticulocytes. This classification is consistent with regenerative anemia. The indices are considered a poorly sensitive indicator of regeneration. However, an elevated reticulocyte count is the best measure of regeneration. An elevated MCHC may indicate intravascular hemolysis if in vitro hemolysis and the presence of interfering substances are ruled out.

Hemorrhage or blood loss and hemolysis are often regenerative anemias, if the patient has a healthy bone marrow. Evaluation of other parameters such as total protein and total bilirubin can help to differentiate blood loss from hemolysis. Additionally, elevation of MCHC may be a common finding in patients with intravascular hemolysis.

Nonregenerative anemias are more common and are the result of decreased red blood cell production. They are generally normocytic, normochromic or microcytic hypochromic if the patient has a true iron deficiency. Many diseases can result in a nonregenerative anemia; the most common cause being anemia of chronic disease. This anemia is associated with inflammatory processes, chronic infections and disseminated neoplasia. Other causes of normocytic normochromic nonregenerative anemia include diseases which infiltrate the bone marrow such as myelofibrosis and myelophthisis, decreased erythropoietin levels as can be seen with chronic renal disease, and diseases or toxins which affect red cell maturation, including infectious etiologies such as FeLV, FIV and E. canis. Less common causes may include destruction in red blood cell precursors or reticulocytes, which can result in a nonregenerative response. Serial evaluation of the CBC for elevation of the PCV, or bone marrow aspiration, are important for appropriate interpretation.

Microcytic anemias are often associated with iron deficiency or iron unavailability. The red blood cells are small in these patients because the cells undergo an extra set of divisions in the marrow because they have less iron/hemoglobin available. The most common cause of iron deficiency anemia is chronic blood loss. Other diseases include
severe liver disease or liver failure and portosystemic shunts. Certain breed of dogs are normally microcytic; this include the Shiba Inu and Akita.

Elevation of the RBC, PCV and hemoglobin is termed polycythemia. The most common cause is relative or secondary to dehydration. However other causes include absolute increases in the red cell mass and those include hypoxia, fear, erythropoietin producing neoplasms or polycythemia vera. Absolute polycythemia is further characterized as secondary or primary. Secondary polycythemia is much more common. Patients with secondary polycythemia have elevated levels of erythropoietin due to tissue hypoxia or an ancillary source of erythropoietin such as a renal carcinoma. Primary polycythemia is uncommon and is classified as a myeloproliferative disease, polycythemia vera. These patients have a low normal to decreased erythropoietin level with normal arterial oxygen levels. Causes of secondary polycythemia need to be eliminated first, before a diagnosis of polycythemia vera can be made.

The final step to fully interpreting the erythron requires examination of the peripheral blood smear. Red blood cell inclusions including parasites, and size and shape of the red blood cell, can give important clues to the cause of an abnormality. Regenerative anemias may have polychromasia, macrocytes and nucleated red blood cells. With non-regenerative anemias the red blood cell morphology may be completely normal. Variation in cell shape (poikilocytosis) can also assist in diagnosis. Presence of schistocytes or red blood cell fragments may indicate disseminated intravascular coagulation. Spherocytes are red blood cells which have lost their discoid shape and consequently their central pallor and are commonly associated with immune-mediated hemolytic anemia. Oxidative damage to red blood cells may result in Heinz bodies, keratocytes or eccentrocytes.

The Leukon
Evaluation of the leukon involves interpretation of the white blood cell parameters, including the white blood cell count (WBC), differential count and white blood cell morphology. An elevated WBC is termed a leukocytosis while a decreased WBC is a leukopenia. A leukocytosis of >70,000 in the cat and >65,000 in the dog have been shown to have a poor prognosis. To characterize a leukocytosis, a differential count must be performed. A manual differential count is performed by counting 100-200 cells on the peripheral blood smear, giving a percentage of each cell type. An absolute count can be calculated by dividing the percentage by 100 and multiplying that value times the WBC. The absolute numbers, not the percentages, should be used to classify the leukon as inflammation, stress, excitement, hypersensitivity or neoplasia.
An inflammatory leukon is characterized by a leukocytosis or leukopenia with mature neutrophilia often with bands present, described as a left shift. If the number of bands is less than the neutrophils, this is described as a regenerative left shift. If the number of bands is greater than the neutrophils, this is termed a degenerative left shift and is a poor prognostic indicator. Additionally, the neutrophils should be evaluated for toxic changes. These include cytoplasmic basophilia, dohle bodies, azurophilic granules and foamy cytoplasm. In patients with leukopenia, identification of toxic changes within these cells can assist in differentiating leukopenia of inflammation from decreased production. Most inflammatory responses also have a concurrent stress response.

The stress leukon is mediated by glucocorticoid release. Characteristic changes include a mature neutrophilia, occasional hypersegmented neutrophils, lymphopenia, monocytosis (in the dog) and eosinopenia. Most sick animals will have a stress leukon; as mentioned above this may overlap with inflammation. In these instances, the lymphopenia is very helpful in identifying the stress component. Pure inflammation should not cause a lymphopenia. Additionally, patients with hyperadrenocorticism will generally have a stress leukon. Addisonian patients will often have an absence of a stress leukon.

Persistent antigenic stimulation or immune stimulation can occur with *Ehrlichia canis*, certain protozoal organisms and post-vaccination, and will result in a significant lymphocytosis. Occasionally the lymphocytosis can become severe enough it may be difficult to differentiate from chronic lymphocytic leukemia (CLL). The presence of reactive lymphocytes may help to differentiate CLL from immune stimulation as reactive lymphocytes are more commonly observed with immune stimulation. Additional testing (such as Ehrlichia serology) or history and physical exam findings are necessary to differentiate these two diseases.

Another cause of lymphocytosis is excitement. This leukon is the result of epinephrine release and is an immediate response. In addition to the lymphocytosis, the excited patient may have a mild elevation in PCV and a mild neutrophilia. These changes are transient and if a second sample is drawn under different conditions, the CBC may return to normal.

Eosinophilia is indicative of a number of different processes including allergic, parasitic and paraneoplastic syndromes. Depending on the level of the eosinophilia, eosinophilic leukemia and hypereosinophilic syndrome should also be considered. Neoplasms commonly associated with eosinophilia as a paraneoplastic response include T cell lymphoma and mast cell neoplasia.
A leukocytosis or leukopenia may be observed with neoplasia. Patients with leukemia often present with a marked leukocytosis, while in acute leukemia, immature cells or blasts may be observed. The acute leukemias include acute lymphoblastic leukemia, acute myeloid leukemia and erythroid leukemia. Additionally, circulating blasts may also be observed with stage V lymphoma and myelodysplastic diseases. Chronic leukemias can be more difficult to diagnose. These include chronic lymphocytic leukemia and chronic granulocytic leukemia. Often these neoplasms are diagnosed when no evidence of underlying inflammation or antigenic stimulation is identified in the presence of a marked leukocytosis. Absence of reactive lymphocytes and/or toxic changes in the neutrophils may assist with the diagnosis of chronic leukemia as these changes are more commonly associated with immune stimulation or inflammation.

The thrombon
Platelets are granular cytoplasmic fragments of megakaryocytic origin. Platelets function primarily in hemostasis. The platelet number, size and morphology are evaluated on the CBC. Platelet counts can be performed on an automated cell counter, manually via a hemacytometer or estimated from a peripheral blood smear. The blood smear should also be evaluated for platelet clumps as platelet clumps can falsely decrease the platelet count by all 3 methods. Platelet size can also affect the platelet count via automated method as the platelets may be counted with the red blood cells or may be too small to be detected. A platelet estimate from the blood smear may be beneficial in identifying any discrepancies between methods. Additionally, the platelet volume can be determined on automated counters as mean platelet volume (MPV).

In conclusion, the CBC is a beneficial diagnostic tool. Appropriate evaluation of all aspects of the CBC can lead to a specific diagnosis or assist in ruling out many diseases. To gain the full benefit of the CBC it must be used in conjunction with a good history and physical exam as well as additional components of the minimum data base including the chemistry panel and urinalysis.