

THE PET HEALTH LIBRARY

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Anemia: Inadequate Red Blood Cells

Red blood cells are basically little microscopic bags of hemoglobin.

They have no nucleus and thus no DNA. They have no internal structures and thus no ability to perform complicated metabolism. Despite their simplicity, their function is crucial: they carry hemoglobin, the iron-containing complex protein that allows for oxygen transport to the tissues, as well as carbon dioxide transport to the lung for removal. Inadequate red blood cell quantity means inadequate hemoglobin, which means inadequate oxygen delivery. In the whole patient, this translates to lack of energy, poor appetite, and pallor - basically an important reduction in life quality.

There are three important ways in which the kidney patient loses red blood cells. The first way is bone marrow suppression. The second way is bleeding. The third way is called hemodilution. We will review all these and what can be done about them. Maintaining a stable red blood cell quantity keeps the patient energetic and spirited, and it is crucial to staying alive.

Bone Marrow Suppression

One of the functions of the kidney is the production of the hormone called erythropoietin (pronounced "urithro-po-eetin"). This hormone, often simply referred to as Epo, represents the command to the bone marrow to make more red blood cells. When the kidney is damaged, its ability to produce erythropoietin is compromised. Red cells are still produced but over time the red cell count drops.

Blood sample in a PCV tube being read against a chart

A simple measurement of red blood cell count is called the packed cell volume or PCV. The packed cell volume is an expression of the percentage of the blood's volume which is taken up by red blood cells. It can be measured using only a drop or two of blood and can be done while you wait in any veterinary office. The sample is spun in a machine called a centrifuge to separate the red cells, white cells, and serum. The blood tube is then read against a chart to get the packed cell volume. Hematocrit or HCT also measures the volume of blood as red blood cells but uses a measure of hemoglobin to determine it. Practically speaking, PCV and hematocrit measure the same thing.

	<i>Normal PCV</i>	<i>Normal HCT</i>
Dog	37 - 55%	43.3 - 59.3%
Cat	24 - 45%	29.3 - 49.8%

In renal patients, weakness becomes evident in dogs and cats when the packed cell volume drops below 20.

What Can we Do?

Thanks to genetic engineering, human erythropoietin is commercially available in an injectable form. This means that the hormone that the kidney has failed to make is replaced with injections. Injections are given three times a week at first but when the patient is more stable they can be backed off to twice or even once a week.

Pros

- The injections can easily be given at home.

- Treatment with erythropoietin injections is generally extremely effective as normal red blood cell counts are usually achieved within 4 weeks.

Cons

- An iron supplement must be given simultaneously so that the bone marrow will have the building blocks necessary to make red blood cells.
- Packed cell volume must be monitored weekly until the patient stabilizes so the patient will need frequent veterinary visits at least at first. If this monitoring is skipped, it is easy for the red cell count to become too high, thickening the blood and causing high blood pressure (which in turn creates more kidney damage in addition to other problems).
- Cost of treatment is reasonable for small pets such as cats and smaller dogs but could be prohibitive for even a medium-sized dog.
- Because the product used is a human origin protein, it can induce a cat or dog to generate antibodies against it. When the immune system is stimulated in this way, it not only attacks the human erythropoietin but also the patient's own erythropoietin, creating a severe anemia. If this happens, transfusions may be needed to manage the anemia. When the Epo injections stop, eventually the antibody production stops and the anemia resolves somewhat but Epo cannot be used in this patient again and periodic transfusions become the only means of managing anemia.

In a presentation by Dr. Sheri Ross at the 2006 meeting of the American College of Veterinary Internal Medicine, she noted that in one study of dogs and cats with naturally occurring kidney failure, two of three dogs treated with erythropoietin for greater than 90 days and five of seven cats treated for greater than 180 days developed refractory anemia that was attributed to anti-erythropoietin antibodies. A clinically significant immunologic reaction to erythropoietin has been reported to occur in 20-70% of treated veterinary patients. A more commonly published statistic is that antibody production is a problem in 30-40% of pets using human erythropoietin but this complication poses a sobering thought. It is important not to use this hormone at the first sign of anemia but wait until it is really and truly needed.

Is Darbepoetin better than Erythropoietin?

Darbepoetin is a synthetic hormone meant as an improvement over the natural hormone, erythropoietin. The synthetic version lasts longer and is less antigenic (less likely to create any erythropoietin antibodies). Cost is similar to erythropoietin and since most veterinarians have experience with erythropoietin, this is what tends to be prescribed. Furthermore, dosing for animals is still being worked out though there are some guidelines based on human conversions between darbepoetin and erythropoietin. It appears that the changes made in the amino acid sequence have made darbepoetin less likely to generate anti-erythropoietin antibodies but in a patient that is already having a problem with antibodies, darbepoetin is close enough to EPO to be inactivated as well.

Read more information on [erythropoietin](#).

Bleeding

The calcium-phosphorus imbalance that goes with renal disease is reviewed elsewhere in this center but the bottom line is that the excess blood phosphorus that results in renal insufficiency leads to demineralization of bone and mineral deposits in soft tissues. Mineralization is inflammatory and, when it occurs in the GI tract, it leads to bleeding, ulceration, and pain. The renal patient cannot afford appetite loss, nausea or further blood loss so treatment is needed while other efforts are made to control phosphorus levels.

Beyond the phosphorus level, another problem is a hormone called gastrin. Gastrin is a hormone involved in food digestion and is a stimulus for the stomach to release acid. Normally, when the need for gastrin has passed, the kidney removes it from the circulation but in the kidney patient gastrin is

not efficiently removed. The prolonged presence of gastrin also prolongs the stomach's secretion of acid, which can lead to ulceration.

How do we know there is Stomach/Intestinal Ulceration?

There are several clues in the lab work and in the patient's physical appearance that tell us that additional therapy is needed to control this kind of blood loss.

- Horrendous inflammation in the mouth (odor, bloody or purulent drool, sticky discharge on the lips and chin) includes ulceration. When ulceration in the mouth is this bad, we can assume similar erosion is occurring deeper in the tract.
- A blood urea nitrogen (BUN) level that is more elevated than the creatinine is a sign of GI bleeding. The BUN partly depends on dietary protein. Bleeding into the GI tract provides the intestine with blood to digest and the BUN rises further. Some laboratories include a BUN:creatinine ratio to highlight this phenomenon (a ratio greater than 20 suggests intestinal bleeding).
- Uncontrolled phosphorus in and of itself suggests mineralization in the GI tract.

What can we do?

Medications for nausea and appetite stimulation can be used. The most important treatment, of course, is going to be control of the phosphorus level. Other treatments include the following:

Antibiotics

When the mouth is purulent, there is probably secondary infection and antibiotics can help clear it. Antiseptic mouthwashes may also be of benefit.

Antacids

Reducing stomach acid helps reduce pain and bleeding when the GI lining is ulcerated (at least in the stomach). An assortment of antacids can be used to reduce acid.

Gastroprotection

Sucralfate is an oral medication that forms gentle webbing that is effectively a bandage over the ulcers, protecting them from further irritation.

Hemodilution

Pets coming to the vet's office in Stage IV or late Stage III kidney failure are often dehydrated. A typical scenario is a pet who had been drinking lots of water and eating fairly well suddenly stops eating and is listless. Possibly it is even noticeable that the pet has lost weight (though this is often erroneously attributed to age). The owner waits a day or two to see if the pet will start eating again and get better on his own and when that does not happen, the pet is brought to the vet. Once the diagnosis of kidney failure is made, fluid therapy will be recommended, possibly fairly aggressively to drive the toxin levels down quickly. At this point, the patient is usually dehydrated and whatever functioning kidney tissue is still working is not receiving adequate blood supply. Dehydration creates hemoconcentration and a falsely elevated hematocrit. Once the patient is rehydrated, the true hematocrit will be revealed and will most likely be substantially lower than it was on the initial tests. If the patient receives extra fluid beyond hydration, the hematocrit will be diluted and will be even lower.

This is not a big problem if the patient is not particularly anemic to begin with but if the patient is already low on red blood cells or if fluid therapy is aggressive, by the end of hospitalization or even in the middle of it, the patient may be feeling the effects of the low red cell count.

What can be Done?

One choice is to be less aggressive with the fluid therapy though this means a longer time to get to a livable toxin level. Another choice is the use of erythropoietin as above, possibly in addition to a less aggressive fluid administration rate. Using erythropoietin helps at least increases the red blood cell production to balance the dilution that comes with rehydrating the patient.

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