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Iron and iron deficiency in animals

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Introduction

Iron concentrations are measured to determine the body's iron reserves. Serum or plasma iron, on the other hand, is not a strong indicator of bodily iron storage. Because iron is continually turned over (often enters and exits cells) during normal metabolism, blood iron concentrations change rapidly, and inflammatory cytokines and a protein called hepcidin have a considerable influence. Rather, the assessment of hepatic iron storage is the "gold standard" for body iron stores (which is rarely done in living animals as it is a quite invasive procedure to get a 1 g liver biopsy to measure hepatic iron). Subjective examination of bone marrow iron (with a Prussian blue stain detects hemosiderin within macrophages) can be used as a surrogate for liver iron, but this is also done infrequently for iron deficiency anemia diagnosis. Iron levels in serum or plasma do not measure "free" iron (which is a strong free radical that would cause significant tissue damage if truly "free") or iron in hemoglobin in RBCs. Rather, the iron linked to apotransferrin, the iron transport protein in blood, is being measured. In fact, we use low pH conditions to liberate iron from transferrin and analyze it in serum or plasma.

Etiology

Iron deficiency is particularly common in newborn animals whose only supply of iron is the milk of their mothers. Milk is a poor supplier of iron. Iron deposits in the newborn's liver are insufficient to support normal hemopoietic function for more than 2-3 weeks especially piglets.

Epidemiology

Iron deficiency is uncommon in farm animals, with the exception of the very young who are confined to a milk diet. Anemia caused by a lack of iron is called iron deficiency anemia. Three reasons exist for iron deficiency in nursing piglets:

1) They don't have access to soil.
2) Rapid growth and their absolute size is increasing.
3) Milk is an iron-deficient food.

Clinical illness commonly appears in piglets between the ages of 3 and 6 weeks. *Trichuris suis* and *Ascaris*

suum infections in pigs are made worse by iron shortage. Nursing lambs who are housed and do not have access to soil do get iron deficiency anemia within the first 7-10 days of life. Subclinical anemia and iron deficiency can develop as a result of continued blood loss due to bleeding in any animal. Sucking lice-infested cattle might suffer from acute and possibly deadly anemia. The chronic form is characterized by a non-regenerative anemia with subnormal levels of serum iron, and treatment with iron is necessary for an optimal response. Pale-colored veal is generated by feeding calves an all-liquid milk replacer diet with a low iron content. The goal of veal calf management is to tread the fine line between maximal white meat production and a degree of anemia that does not interfere with maximum production. Newborn calves and kids can also develop subclinical iron deficiency anemia. Calcium carbonate in the food of weaning and finishing pigs can create a conditioned iron deficiency and moderate anemia, but not in adult pigs. Manganese could have a similar antagonistic effect.

Pathogenesis

Hemoglobin contains more than half of the iron in the body of an animal. Myoglobin and certain enzymes that play a role in oxygen use include a little quantity of it. Hemoglobin levels in newborn piglets range from 90 to 110 g/L.

⬇

All pigs experience a physiological drop to 40-50 g/dL, with the lowest levels occurring around the 8th-10th day of life.

⬇

Iron levels in the liver at birth are particularly low in this species, and supplemental feeding of the sow during pregnancy has no effect.

⬇

Iron-dextran formulations injected intramuscularly into sows during late pregnancy raise hemoglobin levels in piglets during the first few weeks of life, but not enough to avoid anemia.

⬇

Piglets who have access to iron begin to restore to normal hemoglobin levels around the 10th day of life, whereas pigs who do not have access to iron continue to lose hemoglobin.

⬇

The quickly with which piglets grow in early postnatal life is one of the main causes in their high frequency of anemia.

⬇

Piglets often attain four to five times their birth weight after three weeks and fifteen times their birth weight after eight weeks.

⬇

During the first few weeks of life, the daily iron need is around 15 mg.

⬇

At around 2 weeks of age, iron-deficient piglets appear to be more prone to diarrhea than piglets who have received iron.

⬇

In iron-deficient piglets, there is a significant reduction in acid and chloride output, as well as atrophic gastritis occurs.

In iron-deficient piglets, villous atrophy of the small intestine and alterations in the gastrointestinal flora occur, which may contribute to the increased susceptibility to diarrhea. Lymphocytic function is hindered in iron-deficient piglets, resulting in a decrease in circulating B-lymphocyte counts and immunocompetence.

Clinical findings

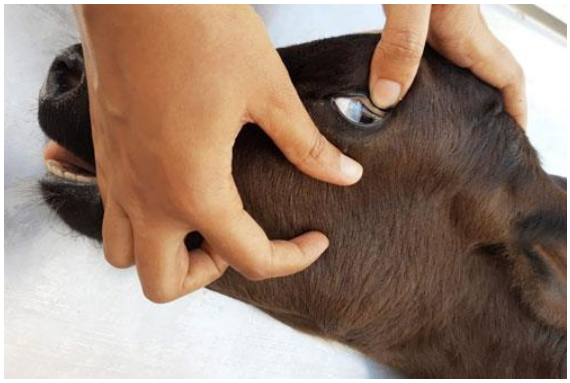
- Iron deficiency anemia in piglets is most common at 3 weeks of age, but it can occur up to 10 weeks of age. Pigs that are affected may be in good health. Although slight diarrhea may develop, the color of the feces is usually normal.
- Exercise causes dyspnea, tiredness, and a significant increase in the amplitude of the heart's peak beat. The mucosae and skin are both pale.
- Edema of the head and forequarters may be present, giving the animal a puffed-up appearance.
- The majority of deaths happen suddenly. The litters of sows suffering from iron deficiency anemia have a high rate of stillbirths.

Clinical pathology

During the first 10 days of life, normal piglets' hemoglobin levels drop to around 8 g/L, and in some cases as low as 4-5 g/L. During the third week, iron-deficient pigs' blood iron

Clinical significance

- Some common causes for a low amount of iron in blood include –
  - ✓ Iron deficiency anemia
  - ✓ Blood loss
  - ✓ Long-standing infections or diseases
  - ✓ Last trimester of pregnancy



- Some common causes for too much iron in blood include –
  - ✓ Conditions that cause RBCs destruction e.g. hemolytic anemia
  - ✓ Iron or lead poisoning
  - ✓ Iron overload e.g. hemochromatosis
  - ✓ Many blood transfusions
  - ✓ Liver damage

Reference values

Normal range of serum iron in different animal species is as follow -

Species	Iron (µmol/L)	References
Dog	5.9 – 26.3	Weeks *et al*. (1988)
Cat	5.9 – 24.2	Andrews *et al*. (1994)
Horse	9.0 – 35.4	Smith *et al*. (1986a)
Cattle	7.0 – 27.7	Kolb (1963) , Smith (1997)
Pig	9.8 – 33.5	Kolb (1963), Smith *et al*. (1984a)

Interpretation

Decreased concentrations (hypoferremia)

- ✓ Transient fluctuation & sequestration as a result of inflammatory cytokines are the most common causes of low iron (which inhibit iron absorption and prevent iron

release from macrophages through upregulating hepcidin).

- ✓ True iron deficiency (due to decreased intake/absorption or external blood loss) is a less prevalent cause of low serum or plasma iron concentrations than the other two.
- ➢ *Artifact* - EDTA or another chelating anticoagulant has been shown to contaminate the sample.
- ➢ *Physiologic* - Some young animals, such as kittens between the ages of two and four weeks, may have low iron levels.
- ➢ *Iatrogenic* - Dexamethasone injections have been demonstrated to reduce iron levels in cattle (by up to half) - the mechanism behind this is unknown.
- ➢ **Pathophysiologic** -
  - *Decreased absorption or intake*: Acidosis, hepcidin, copper deficiency (an important cofactor of hephaestin, which facilitates release of iron from intestinal cells), zinc excess (inhibits copper uptake), inadequate dietary supply (e.g. milk is deficient in iron) and intestinal disease all reduce absorption in the duodenum.
  - *Sequestration*: Inflammatory or chronic illness situations cause iron to be sequestered inside cells (usually iron storage cells like macrophages or hepatocytes). The most prevalent cause of low iron concentrations in both anemic and non-anemic animals is inflammatory cytokine-mediated sequestration, which does not result in microcytic hypochromic red blood cells (like true iron deficiency).
    - Trauma
    - Inflammation
    - Portosystemic shunts
    - Cancer
  - Loss: Because red blood cells (hemoglobin) store a large portion of the body's iron, continuous external hemorrhage will result in iron deficiency after macrophage stockpiles are depleted. In adult animals, bleeding into the gastrointestinal tract is the most prevalent cause of iron deficiency anemia. GI neoplasia, intestinal parasites (e.g. hookworms, whipworms), and vascular ectasia or angiodysplasia (a condition associated with dilation of large intestinal mucosal blood vessels, which causes chronic intestinal hemorrhage in dogs) are all common causes of iron deficiency anemia in older small animals. Infestation with *Haemonchus contortus* is a prevalent cause of iron deficiency in camelids.

Increased concentrations (hyperferremia)

- ➢ *Artifact* - Potentially hemolysis
- ➢ *Iatrogenic* - Corticosteroid administration may increase iron in dogs and horses (up to 2x).
- ➢ *Pathophysiologic* –
  - Release from intracellular stores
  - Increased red blood cell turnover
  - Decreased erythropoiesis
  - Iron overload

Necropsy findings

- Pallor, watery blood, and moderate anasarca are all visible on the carcass.
- The heart is dilated all of the time. The heart dimensions of highly anemic neonatal pigs show constant dilation & hypertrophy.
- In all cases, the liver is enlarged & mottled tan-yellow in appearance.
- The erythroid line's maturation is asynchronous & there are no hemosiderin reserves, according to a histological investigation of the bone marrow.

Diagnosis

Based on signalment, clinical symptoms,clinical pathology, necropsy findings & estimation of serum iron levels.

Differential diagnosis

- Copper deficiency - should not be overlooked especially if the response to administered iron is poor.
- Isoimmunization hemolytic anemia - differentiated by the presence of jaundice & hemoglobinuria and the disease occurs in much younger pigs.
- Eperythrozoonosis - occurs in pigs of all ages & the protozoan parasites can be detected in the erythrocytes.

Treatment

- Organic iron preparations such as iron-dextran, iron-sorbitol-citric acid complex, iron saccharate, or gluconate are typically used in parenteral treatment.
- The weekly dosing rate is 0.5-1 g elemental iron per injection.
- Vitamin B_{12} (cyanocobalamin) is frequently given in a single injection at a dose rate of 5000 ug/week.
- Oral iron sulfate or gluconate treatment at a dose rate of 2--4 g daily for 2 weeks is just as effective and significantly less expensive.

Control

Dietary supplementation

- ✓ Iron deficiency anemia in piglets can be successfully avoided by feeding sows a diet supplemented with 2000 mg iron/kg DM of diet.

Oral dosing

- ✓ A daily dose of 4 mL of 1.8 percent ferrous sulfate solution is sufficient.
- ✓ Iron pyrophosphate (300 mg/d for 7 days) can also be used.
- ✓ A single iron-dextran or iron-galactan oral therapy has been advised. Because reduced iron does not irritate the gastrointestinal mucosa, it can be given in large amounts. Anemia can be prevented with a single dose of 0.5-1 g given once a week.
- ✓ Painting a solution of ferrous sulfate on the udder of the sow has also been suggested (450 g ferrous sulfate, 75 g copper sulfate, 450 g sugar, 2 L water - applied daily).

Intramuscular injection of iron preparations

- ✓ Appropriate preparations must be utilized, and piglets are normally injected intramuscularly (IM) only once, between the 3rd and 7th day of life.
- ✓ The most prevalent ingredients are iron-dextran, fumarate, and glutamate.
- ✓ Multiple injections boost hemoglobin levels, but they don't seem to help in weight gain.
- ✓ A new formulation (Heptomer) includes 200 mg/mL iron, allowing for a single injection of the entire dose.
- ✓ Piglets fed iron-dextran compounds parenterally suffer from acute poisoning and quick death if the sows were lacking in vitamin E and selenium during pregnancy.
- ✓ When piglets are deficient in selenium, a combination of sodium selenite and iron-dextran is administered at 3 days of life and is superior to treatment with iron alone.
- ✓ Iron deficiency anemia in housed lambs can be avoided by injecting 300 mg iron dextran intramuscularly at 24 hours of age.
- ✓ The most cost-effective technique of giving iron to adult cattle and horses with iron deficiency anemia is to give ferrous sulfate orally at a dose of 2-4 g daily for two weeks.

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