

A Discussion of

Hemoglobinuria and Hematuria

R. L. Nelson

HEMOGLOBINURIA MAY BE DEFINED as the symptom of a pathological state in which the animal passes hemoglobin in the urine. In this condition the urine will be pink to brownish-red in color depending upon the amount of hemoglobin passed.

Hematuria is a symptom of that pathological condition in which the animal passes whole blood in the urine. The erythrocytes do not hemolyze and the urine will appear pink to brownish-red in color depending upon the amount of blood passed.

Neither hematuria or hemoglobinuria is a lesion but they are signs that lesions are present. Certain etiological factors are responsible for both hematuria and hemoglobinuria and it should be remembered that both of these conditions may occur simultaneously.

In general, it can be said that hemoglobinuria is due to a condition in the body which is pre-renal whereas hematuria is caused by a renal or post renal lesion.

The accompanying list of etiological factors gives an indication of the complexity of the problem of making a diagnosis on the basis of discovery of blood or blood hemoglobin in the urine. The factors listed are presented as the more important causes of hematuria and hemoglobinuria. It does not, of course, include all of the possible etiological agents which could

give rise to these symptoms. Some cases are of unknown causes.

Etiology of Hematuria and Hemoglobinuria

Bacteria and Viruses

- *Leptospira pomona of bovine
- *Corynebacterium renale
- *Clostridium hemolyticum
- *Bacillus anthracis
- *Staphylococcus sp.
- *Streptococcus sp.
- Proteus ammoniae
- Mycobacterium tuberculosis
- Erysipelothrix rhusiopathiae
- Tortor suis
- Pasturella multocida
- Clostridium perfringens

Physical Influences

- *Renal calculi
- Trauma
- Sulfonamide crystals
- Oxalate crystals
- Dystocia
- Infarction
- Embolism

Temperature Influences

- Severe burns
- Cold

Physiological

- *Myogenous toxins (Azoturia)
- *Heterologous blood transfusions
- *Post parturient hemoglobinuria
- Deficiency of blood platelets
- Right A-V insufficiency
- Local anaphylaxis
- Cystic ulcers
- Neoplasms of the bladder
- Prostatic cysts

Chemical Agents

- *Lead
- Arsenic
- Copper

The author is a member of the present junior class. This paper was prepared under the direction of Dr. F. K. Ramsey.

Mercury
Bismuth
Sulfur
Phosphorus

Dietary Deficiencies

Avitaminosis
Phosphorus

Miscellaneous

Trichlorethylene extracted soybean-oil-meal
Snake venom
Warfarin

Parasites

Protozoa

*Babesia sp.
Toxoplasma gondii??
Eimeria truncata??

Helminths

Dirofilaria immitis
Stephanurus dentatus
Dictophyma renale
Broad fish tapeworm?
Hookworms?
Ascarids?
Strongylus vulgaris
Capillaria plica

Plants

Sweet clover
Brachen fern
Rape
Mustard
Poisonous mushrooms
Fir tree sprouts and sawdust
Ergotized rye
Agave lecheguilla
Lupine
Black locust
Castor bean
Heliotrope
Quercus
Turnip
Beet pulp
Bryonia

Drugs

Cantharides
Sulfonamides
Carbolic acid
Potassium chlorate
Phenacetin
Antifebrin
Creolin
Napthaline
Turpentine
Phenol
Insulin
Phenophthalein
Purine

Pseudo-hematuria

Phenothiazine
Prontosil
*Idiopathic hemoglobinuria
?(Doubtful importance)
*(Important influences)

Since there are so many etiological agents, the practitioner should keep several of the more common causes foremost in his mind when attempting to make a diagnosis. The order of importance will

vary in the different areas of the country. The types of viral and bacterial diseases occurring frequently in the area, the type of vegetation and common nutritional deficiencies are all factors which will influence the order of importance of the etiological factors. For instance, the practitioner in the western and southwestern states would want to consider the poisonous plants as a common cause of the symptoms. Certain areas may have many cases of bloody urine or blood pigmented urine due to a particular species of parasite.

The most important factors causing the symptoms of hemoglobinurea and hematuria in the midwestern states can be listed as follows: (1) Leptospirosis pomona of bovine (2) Pyelonephritis (3) Anthrax (4) Bacillary hemoglobinuria (5) Urinary calculi (6) Streptococcus infections (7) Staphylococcus infections (8) Lead poisoning (9) Post parturient hemoglobinuria (10) idiopathic hemoglobinuria.

If the diagnosis does not indicate that the condition of hemoglobinuria or hematuria is caused by one of the above factors, then the other etiological factors should be considered more closely. The disease diagnosis will largely be made on the basis of the following: (1) The history of the condition or disease (2) Clinical symptoms (3) Palpation (4) Urine examination (5) Serological methods.

Since there may be a question in the practitioner's mind as to whether the animal has hematuria or hemoglobinuria it would be well to mention a few of the differences in the two symptoms. Either one may be present or both may occur at the same time. (1) Presence of blood clots in hematuria (2) Presence of whole erythrocytes in hematuria (3) Opacity of urine in hematuria while in hemoglobinuria there is a transparency which allows the reading of print through varying depths of urine (4) Settling of the erythrocytes with a relatively clear supernatant plasma in hematuria. A more stable solution characterizes the hemoglobinuria sample.

Hematuria

When the symptom of hematuria is observed then there are several important

etiological agents which should be considered first. Some of the more common conditions which exhibit the symptoms are: (1) Injuries of the kidney due to traumatism (2) Nephritis (inflammation) (3) Nephrosis (degenerative lesions in renal tubules) (4) Ureteritis (5) Pyelitis (6) Cystitis (7) Urethritis (8) Prostatitis (9) Generalized acute infections (toxins increase the permeability) (10) Accidental hematuria.

The last two conditions may require additional explanation. Generalized acute infections may cause hematuria by the liberation of toxins and thus resulting in an increased permeability of the glomerular filter. Accidental hematuria may be regarded as blood from the genital tract mixing with the urine and giving the false impression that the blood had its origin in the urinary tract.

Methods of attempting to reach a conclusion as to the location of the disorder giving rise to the hematuria will vary somewhat with the species of animal. In large animals rectal palpation would be of importance. The bladder would be palpated for the presence of calculi, tumors or other pathological changes in the wall. In thin animals the ureters could be palpated to detect any disturbances such as calculus or thickened wall.

It is not always possible but attempts should be made to palpate the kidney. Over-distention or constriction may be detected. Slight pressure should be applied to the kidney to check for pain; this may also be done externally on some species of animals. Rectal palpation may also be used in dogs to detect disorders of the prostate gland.

A careful examination of the urine may yield evidence indicating the specific location of the lesion. The condition of the blood in the urine, the type of epithelial cells present, and the type of sediment present are clinical signs which are used, especially by the small animal practitioner. A summary of the evidences indicating lesions of specific regions of the urinary system follows. It should be remembered that in a given situation all or none of these conditions may be met; they are presented as a clinical aid to diagnosis.

- I. Indications of urethral and vestibular lesions
 - A. Constant dripping of blood between periods of micturition (may be confused with hemorrhage from the genital tract)
 - B. Blood seen in the urine only at the beginning of urination
 - C. History of recent catheterization
- II. Indications of bladder damage
 - A. Most blood seen at the end of urination
 - B. Presence of large blood clots
 - C. Not a large amount of albumin present in relation to the amount of blood. Bacterial count may be high
 - D. Cellular content of the urine
 1. Presence of large epithelial cells irregular in size (a certain amount of squamous cells may be found in normal urine)
 2. Larger cuboidal to columnar cells indicates deeper damage to the bladder mucosa
 3. Presence of calculi
- III. Indications of ureter damage
 - A. Presence of long filaments
 - B. Presence of small, round globular-like cells (These cells are larger than those from the tubules but smaller than those from the pelvis of the kidney)
- IV. Indications of renal pelvis damage
 - A. If hemorrhage is rapid, may have a cast of the pelvis formed
 - B. Presence of pear shaped, lenticular to irregular cells which are smaller than bladder cells but larger than cells of the ureters.
- V. Indications of damage to the nephron unit and collecting units
 - A. Presence of very small clots
 - B. The more intimate mixture of blood with urine. Blood is more or less evenly distributed throughout urination
 - C. More fragmentation of the erythrocytes
 - D. Presence of casts which may be the entire epithelium of a tubule or a molded exudate. The presence of erythrocytes attached to the casts is good evidence that the lesions are of renal origin
 - E. Large amount of albumin in comparison to the amount of blood, with or without the presence of bacteria
 - F. Presence of very small cuboidal cells from the convoluted tubules, or very small columnar cells from the collecting ducts

Hematuria Associated with Pyelonephritis

The mechanism by which a common disease may result in hematuria can be illustrated by a brief account of pyelonephritis as it occurs in animals. Obviously, not all the diseases causing hematuria follow the same mechanism in regard to the manner by which the blood gains entrance into the urinary system; however, many of them follow a similar pattern.

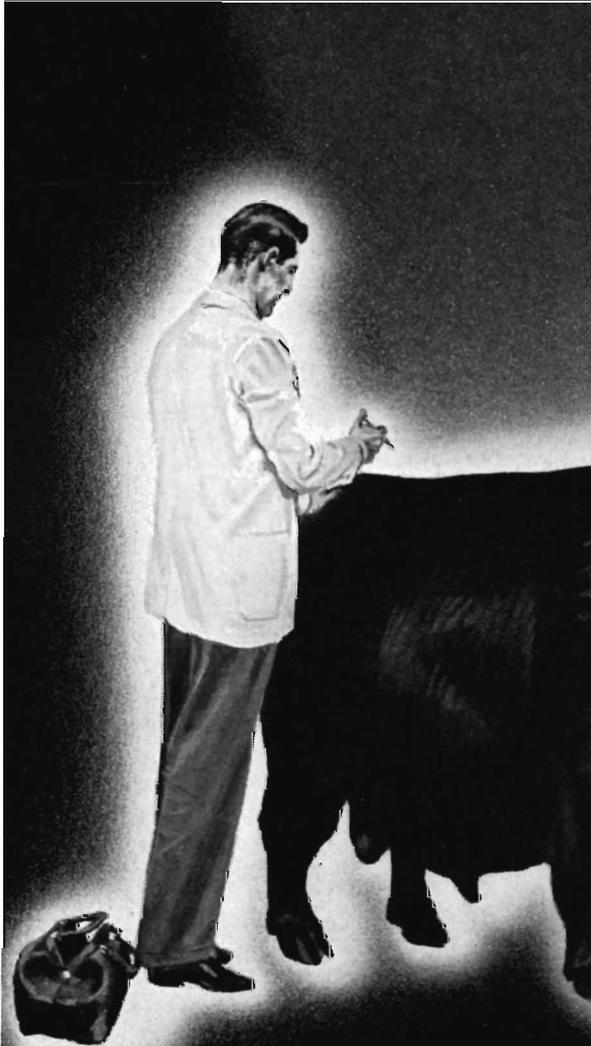
Pyelonephritis is a highly fatal, chronic

POLYOTIC*

Lederle Professional Line

- POLYOTIC* INTRAMUSCULAR:
100 mg.-500 mg.-1.0 Gm.-5.0 Gm.
- POLYOTIC INTRAVENOUS:
100 mg.-2.5 Gm.
- POLYOTIC OBLETS®: 4's-6 x 4's
- POLYOTIC CAPSULES: 50 mg., 25's-100's;
100 mg., 100's; 250 mg., 16's-100's
- POLYOTIC TABLETS: 50 mg., 25's-100's;
100 mg., 25's-100's; 250 mg., 16's-100's
- POLYOTIC MASTITIS OINTMENT: ¼ oz.
- POLYOTIC COMPOUND MASTITIS OINTMENT: ¼ oz.
- POLYOTIC OPHTHALMIC OINTMENT 1%:
6 x ¼ oz.
- POLYOTIC TOPICAL OINTMENT 3%: 1 oz.
- POLYOTIC SOLUBLE (Tinted) POWDER:
¼ lb.-½ lb.-1 lb.-5 lb.
- AVIANIZED® RABIES VACCINE. (Canine):
1 dose-5 x 1 dose-10 doses
- AVIANIZED RABIES VACCINE. (Cattle): 10 doses
- AVIANIZED CANINE DISTEMPER VACCINE:
1 dose-10 x 1 dose
- ANTI-CANINE DISTEMPER SERUM AND ANTI-INFECTIOUS
CANINE HEPATITIS SERUM: 20 cc. 100 cc.
- INFECTIOUS CANINE HEPATITIS VACCINE: 2 cc.-10 cc.
- BRUCELLA ABORTUS VACCINE: 1 dose-5 x 1 dose-
5 doses (25 cc.)
- FELINE DISTEMPER VACCINE: 1 immunization (2 vials
Vaccine, 2 vials Sterile Diluent, 2 cc.)
- ANTI-FELINE DISTEMPER SERUM: 50 cc.
- CARICIDE® Diethylcarbamazine TABLETS:
400 mg., 25's
- DIETHYLSTILBESTROL SOLUTION: 10 cc.-50 cc.
- LEPTOSPIRA CANICOLA-ICTEROHEMORRHAGIAE BACTERIN
Whole Culture Inactivated Vacuum-Dried.
Other products to be added.

*Trade-Mark



LEDERLE LABORATORIES DIVISION

Pearl River

AMERICAN *Cyanamid* COMPANY

New York

There must be a reason why 80%* of all practicing veterinarians dispense Vitamineral products!

**IN FACT,
THERE
ARE**

7

REASONS

* More than 8,000 licensed, graduate veterinarians endorse, recommend and dispense Vitamineral products.

1

Provide broader, more complete veterinary service by combining nutrition with medication.

2

Condition herds and flocks for the acceptance of serums and medicinals. Build up resistance against setbacks before treatment, speeding up recovery after treatment.

3

Eliminate chance of client purchasing useless and even harmful nostrums that interfere with health of herds or flocks.

4

Help to prevent, control or correct costly nutritional diseases that make medication doubly difficult.

5

Save clients' feed by supplying needed ingredients not found in ration.

6

Help clients make more money through faster, less costly growth, more potent reproduction among livestock and poultry.

7

Give veterinarian exclusive distribution of the only supplements that can meet these specifications:

- Finest quality calcium and phosphorus whose solubility is guaranteed by vitamins in sufficient potencies.
- Iodine.
- Six essential trace minerals.
- Antibiotics, where indicated.

**SOLD TO
VETERINARIANS
ONLY**

VITAMINERAL

**PRODUCTS COMPANY
PEORIA 3, ILLINOIS**

Dependable supplement feeds
since 1915

purulent inflammation of the bladder, ureters, and pelvis portion of the kidneys. It occurs chiefly in cows but has been found in horses, sheep, swine and dogs. The infectious agent responsible for pyelonephritis is *Corynebacterium renale*. The organism is spread by contact with infected animals via the urogenital tract.

Probably the most important diagnostic symptom of the disease is hematuria. This condition is caused by an increased permeability of the blood vessels and rupture of the capillary walls due to necrosis. The animal is restless due to the inflammation in the kidneys, ureters, and bladder and thus the swelling exerts pressure on the sensory nerve. There is a straining and frequent urination due to the large amount of urine formed. This increased amount of urine results in damages to the glomeruli and tubules and also because of irritation produced by the urine in the inflamed bladder. Severe anemia is produced as a result of loss of blood by way of the urinary tract. The circulatory and respiratory systems have an increased load placed upon them. This, coupled with the effect caused by toxic products from necrosis and suppuration, produce myocardial degeneration and final collapse of the heart with death by asphyxia. Death may be sudden if there is a rupture of the clots found in the ureters of bladder.

Hemoglobinuria Associated with Leptospirosis

One of the important diseases in which hemoglobin occurs in the urine is Leptospirosis and it can be used as an example to describe one mechanism by which a disease process can cause hemoglobinuria.

After the leptospira organism enters the respiratory tract it enters the blood stream and produces a septicemia and fever. Hemolysis of the erythrocytes is produced and this is thought to be caused by toxins which are liberated by the leptospira. The organism then localizes in the kidney where it produces interstitial nephritis. Reinhard has divided the disease into four stages: (1) incubation stage (2) septicemic period (3) hemolytic stage (4) interstitial-nephritis. The hemolytic period

may last for several weeks. This is the cause of the hemoglobinuria which may be an important symptom of the disease. Obviously, the hemoglobinuria may result in anoxemia which is responsible for many of the lesions observed in a case of leptospirosis. The urine varies in color from a light pink in the mild cases to a deep reddish-black in severely infected animals. In severe cases death may occur by the second day and is frequently attributed to massive erythrocyte destruction and the resulting fatal anoxemia.

Bibliography

- Boddie, G. F. Diagnostic methods in veterinary medicine.
Brooks and Alyea. Poisons.
Coffin, D. L. Manual of veterinary clinical pathology. 3rd edition.
Cotten. Toxicology text. Not bound.
Davison, F. R., Synopsis of materia medica, toxicology, and pharmacology.
Friedberger and Frohner. Veterinary pathology. 6th edition.
Gradivohl. Clinical laboratory methods and diagnosis. 3rd edition.
Hawk, Oser, and Summerson. Practical physiological chemistry.
Hemoglobinuria. Physiological reviews. 1942.
Kelanffe. Clinical urinalysis.
Lander, G. D. Veterinary toxicology.
Merchant, I. A. Veterinary bacteriology and virology.
Morgan and Hawkins. Veterinary helminthology.
Morgan and Hawkins. Veterinary protozoology.
Runnels, R. A. Animal pathology. 5th edition.
Stengel and Fox. Textbook of pathology. 6th edition.
Underhill. Toxicology.
U.S.D.A. Bulletin. Oak poisoning.
Van Brand, Theodor. Chemical physiology of endoparasitic animals.
1953 Reports on hematuria and hemoglobinuria.

Acknowledgements:

D. G. Erickson
G. S. Firkins
O. W. Nelson
W. J. Owen
J. H. Post
W. R. Richter
J. B. Doudna

*** Report**

(Continued from page 153)

an exotic disease to gain a foothold in this country with disastrous results to our entire cattle industry.

The following objectives were set up for future work on this problem. (1) To describe or classify each of these diseases