

Systemic granulomatous disease in a horse grazing pasture containing vetch (*Vicia* sp.)

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A 10-year-old quarterhorse gelding was presented to the California Veterinary Diagnostic Laboratory in early May for euthanasia and necropsy. Presenting clinical signs included weight loss; severe generalized dermatitis; dependent edema in the limbs, preputial sheath, and ventral abdomen; lymphadenomegaly of superficial and palpable lymph nodes;

and an elevated temperature (40 C), which began 5 weeks previously. The horse was unresponsive to trimethoprim and sulfadiazine, corticosteroids, and betadine baths given every other day starting 2 weeks prior to submission. Throughout the winter, this horse and 3 others were kept on pasture in the California Sierra foothills that contained a mixture of grasses and broadleaf plants, including *Vicia* sp. The only previous history of clinical disease in this horse was infection with *Streptococcus equi* 2 years previously.

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Gross examination revealed a thin horse with conjunctivitis and blepharitis and severe alopecia, crusting and scaling

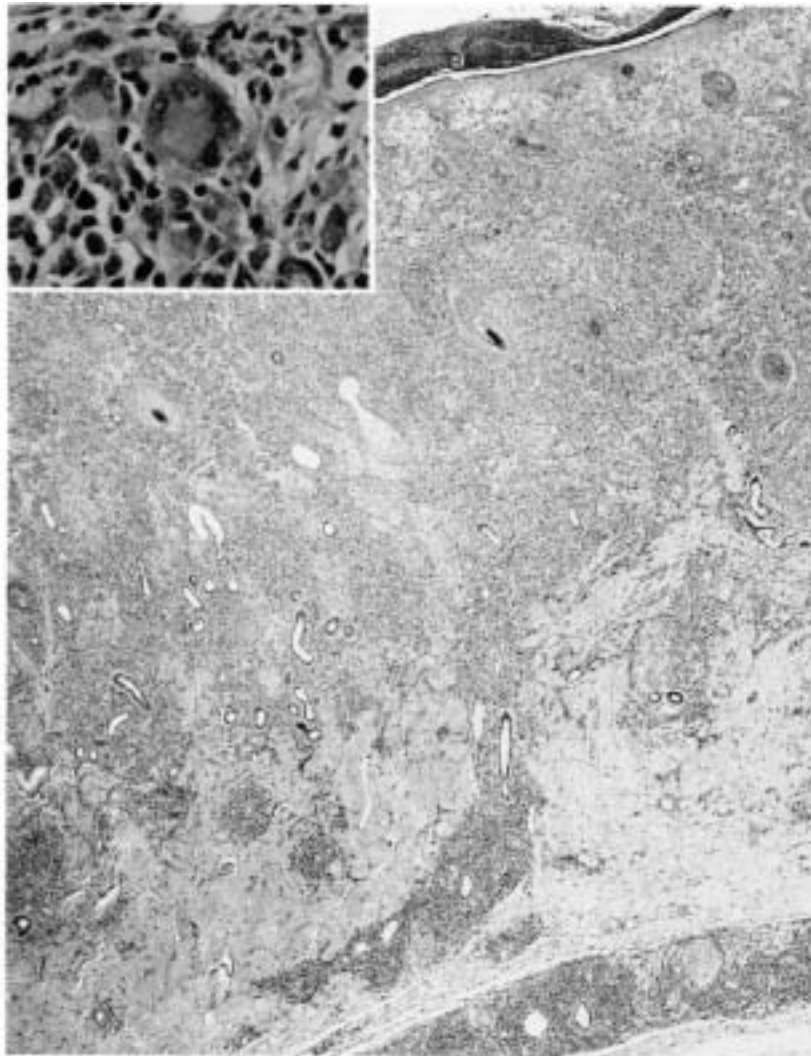


Figure 1. Photomicrograph of skin of a horse with systemic granulomatous disease. Diffuse granulomatous inflammatory cell infiltrates extend from the papillary dermis into the deep dermis. Multifocal perivascular infiltrates are seen in the subcutis. **Inset:** Infiltrate comprised of lymphocytes, plasma cells, macrophages and multinucleated giant cells. HE.

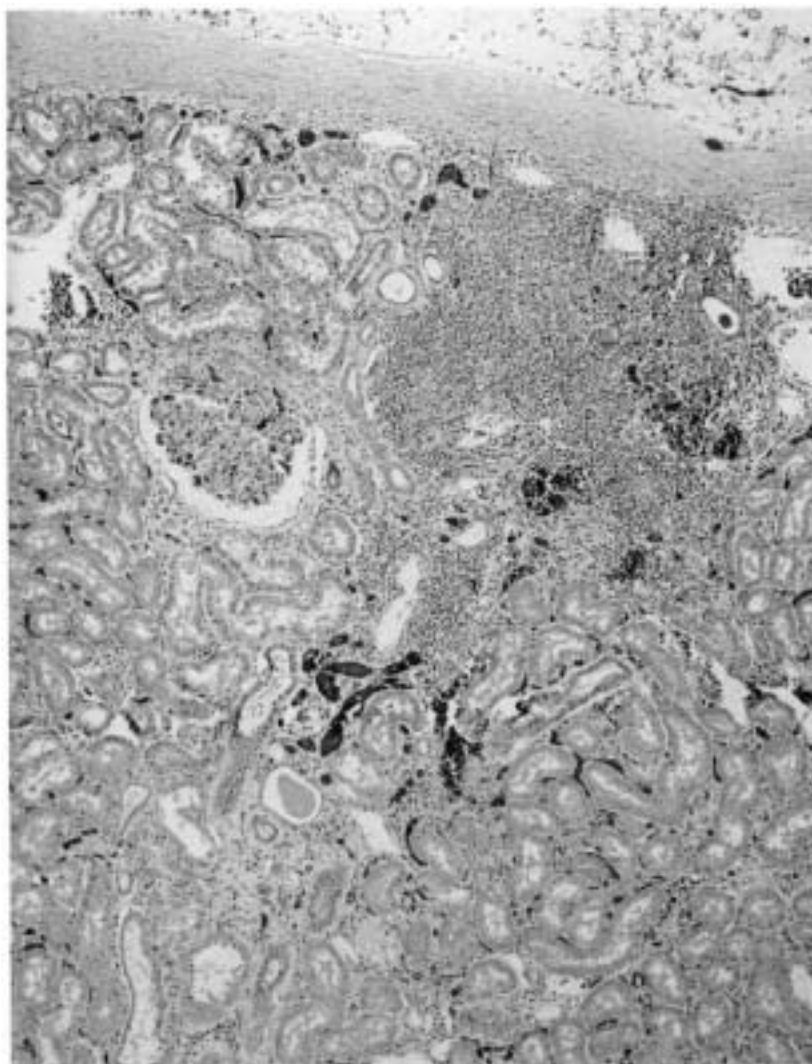


Figure 2. Photomicrograph of the kidney of a horse with systemic granulomatous disease. Note multifocal perivascular granulomatous inflammatory cell infiltrates located in the subcapsular region of the kidney extending into the superficial cortex. HE.

of the skin over most of the face (particularly prominent around the eyes, ears, and muzzle), sparing oral mucosa and mucocutaneous junctions. Seborrhea was severe on the withers, shoulders, back, and ventral abdomen. There were numerous, small subcutaneous nodules on the neck and shoulders. The axilla and preputial sheath were also alopecic and crusty with serous exudate. There were flat, annular lesions of various sizes on the perineum and thighs. Dependent edema of the legs, abdomen, and preputial sheath was pronounced. Superficial (retropharyngeal, superficial cervical, prescapular, inguinal) and internal (hepatic, mesenteric, renal, mediastinal) lymph nodes were enlarged and homogeneously white-tan with unrecognizable cortical or medullary architecture. Multiple 0.5-cm white firm nodules were distributed sparingly throughout the lungs. Small numbers of *Anoplocephala perfoliata* were identified in the digestive tract.

No aerobic pathogenic bacteria were isolated from liver and lung. *Trichophyton equinum* was isolated in small numbers from the skin. The agar gel immunodiffusion test for equine infectious anemia was negative. An organ pool of

lymph node, liver, spleen, brain, and lung was negative for viral cytopathic agents after 1 passage on rabbit kidney (RK₁₃) cells. Skin biopsies were placed in Michelle's medium, thin sectioned, and examined for deposition of IgG and complement using fluorescent antibody microscopy. IgG and complement deposition were not detected in the epidermis. A complete blood count revealed a normocytic, normochromic anemia (packed cell volume = 19.5%). Leukocyte parameters were within normal limits except for a mild monocytosis (1,860/ μ l). Plasma protein was normal (7.0 g/dl), and fibrinogen was increased (600 mg/dl).

Hematoxylin and eosin (HE)-stained sections of skin, liver, lung, spleen, kidney, lymph nodes, large intestine, small intestine, stomach, brain, heart, trigeminal ganglia, adrenal gland, and pancreas were examined histologically. In some sections of skin, dense, diffuse inflammatory cell infiltrates were seen throughout all regions of the dermis extending from the papillary dermis into the subcutis (Fig. 1). In other sections, the superficial dermis was only mildly affected, and the inflammatory cell infiltrate was primarily located around

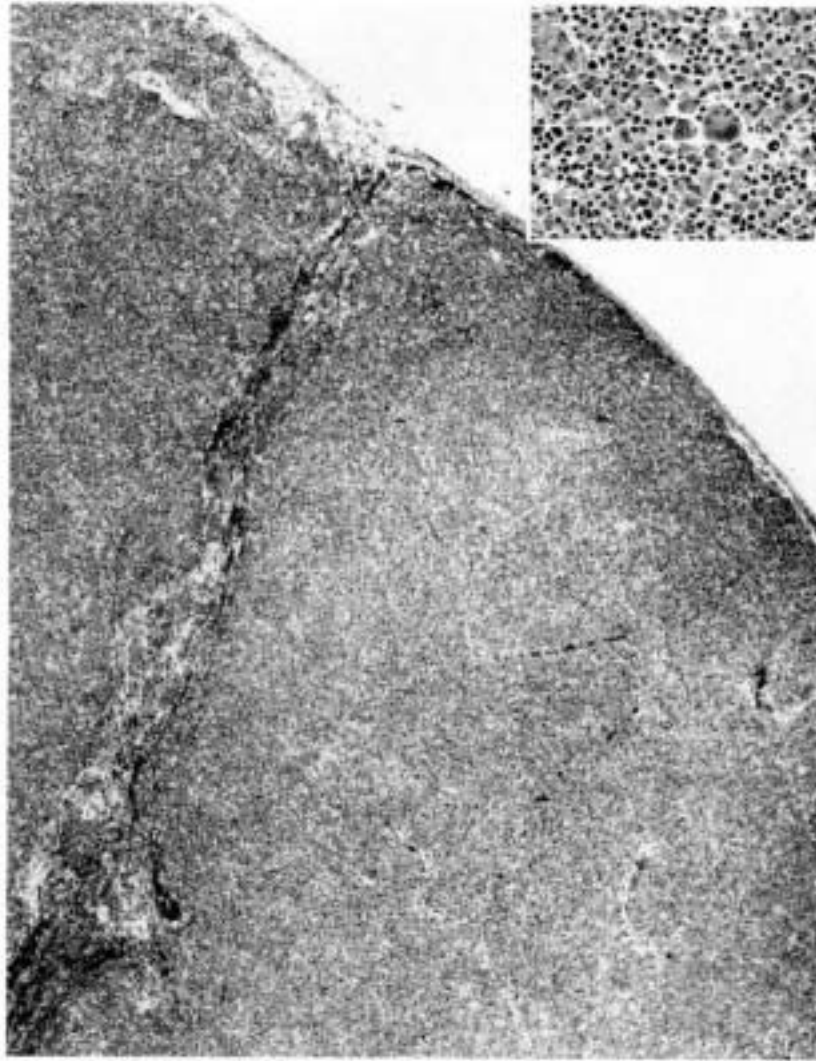


Figure 3. Photomicrograph of a lymph node of a horse with systemic granulomatous disease. Note effacement of the cortical-medullary architecture by diffuse sheets of inflammatory cells. **Inset:** Mixed mononuclear inflammatory cells with scattered multinucleated giant cells. HE.

vessels and nerves in the deep dermis and panniculus. These infiltrates were comprised of macrophages, many of which were epithelioid, along with plasma cells, lymphocytes, and scattered multinucleated giant cells. The epidermis had multifocal large subcorneal pustules, with associated superficial epidermal or intrapustular bacteria. There were multifocal epidermal ulcers with overlying necrotic serocellular crusts.

Plasma cells, lymphocytes, and macrophages were seen multifocally along the endocardial surface of the heart and infiltrated and separated myofibers in the adjacent myocardium. In the liver, there was a focally extensive region of necrosis surrounded by a dense cellular zone with numerous bile duct profiles and granulomatous inflammatory cells. Mixed mononuclear inflammatory cells, including epithelioid macrophages, were present in the portal regions of the liver. Multifocal perivascular infiltrates were located primarily in the subcapsular region of the kidney, extending into the superficial cortex (Fig. 2). Histopathology of the kidney also included a chronic, membranoproliferative glomerulonephritis. Representative samples of superficial and

internal lymph nodes had effacement of cortical and medullary architecture by diffuse sheets of mixed mononuclear inflammatory cells with scattered multinucleated giant cells (Fig. 3).

Brain and lung were also affected. Multifocal nonsuppurative infiltrates were present in the neuropil adjacent to the lateral ventricle of the brain. In the lungs, moderate, mixed mononuclear inflammatory cell infiltrates surrounded bronchioles and medium and large vessels. Fibrinoid necrosis and invasion of the vascular smooth muscle by similar infiltrates were evident in some arterioles, arteries, and veins (vasculitis) (Fig. 4). Gram's, periodic acid-Schiff, acid-fast, and Gomori's methenamine silver stains failed to reveal the presence of an etiologic agent within the granulomatous foci. Histopathologic lesions were compatible with equine systemic granulomatous disease.

Systemic granulomatous disease (SGD) in horses is characterized by generalized cutaneous crusting, scaling, and alopecia and multisystemic granulomatous inflammation.^{12,13} The cause is unknown. Rigorous diagnostic tests including

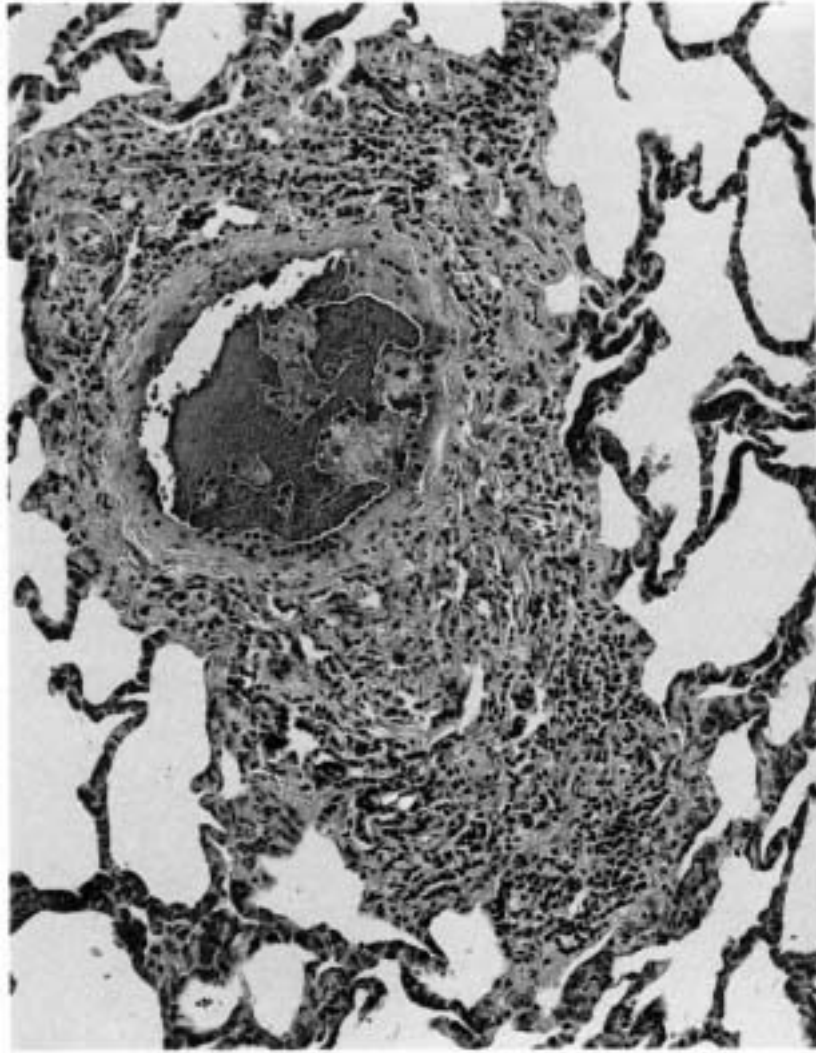


Figure 4. Photomicrograph of the lung of a horse with systemic granulomatous disease. Note large vessel with fibrinoid necrosis and invasion of the smooth muscle by mixed mononuclear inflammatory cells, which also surround the vessel and extend into the surrounding parenchyma. HE.

culture attempts for fungi, *Mycobacterium* sp., and aerobic and anaerobic organisms have thus far been unsuccessful in revealing a causative agent, as have special stains such as acid-fast, periodic acid-Schiff, Gomori's methenamine silver, and auramine O and transmission electron microscopic examination.¹³ Systemic granulomatous disease in horses has been likened to human sarcoidosis; this disease is referred to, in some texts, as equine sarcoidosis.¹² The cause of human sarcoidosis is also unknown, but the disease may result from a hypersensitivity reaction to a persistent antigen.¹⁴

An association of SGD in a horse and grazing on hairy vetch (*Vicia villosa*) was reported in 1983.¹ Diffuse granulomatous inflammation was reported in the heart, kidneys, lungs, dermis, lymph nodes, ileum, colon, skeletal muscle, and choroid. Those lesions and those in the horse in the present case are similar to lesions reported in naturally occurring^{3,5-7,9,10} and experimentally induced vetch toxicosis in cattle (Panciera RJ, et al.: 1989, Abstr Conf Res Workers Anim Dis #25). One manifestation of vetch toxicosis in cattle

is characterized by conjunctivitis, pruritis, and progressive exudative dermatitis. Between 50 and 100% of these animals develop progressive debilitation and die with multisystemic infiltrative granulomatous inflammation.^{8,9} Granulomatous infiltrates comprised of lymphocytes, plasma cells, macrophages, eosinophils, and multinucleated giant cells are most prevalent in the dermis, renal cortex, myocardium, and adrenal glands and less frequently in thyroid, spleen, lymph nodes, portal regions of the liver, and pancreas. Infiltrates are more intense around vessels, particularly in the dermis. Morbidity is usually low (6%) but has been reported as high as 68%.² Disease is usually associated with *Vicia villosa* Roth (hairy vetch), but disease induced by other varieties (*Vicia villosa/Vicia dasycarpa* hybrid and *Vicia dasycarpa*¹¹) have also been reported. The vetch identified in the pasture grazed by the horse in this case report was *Vicia benghelensis*, which is widespread in California and closely related to *Vicia dasycarpa*.

Vetch toxicosis in cattle has only recently been recognized

in the state of California, and only 2 cases have been reported,⁵ possibly because of lack of recognition of the disease. Vetch is not a major component of range and pasture land in the state of California but is abundant on disturbed soil from coastal areas to the Sierra foothills. It has been grown as a seed crop in northwestern California, and in other parts of California it has been used as a green-manure crop and for hay.⁴ In the 1950s and 1960s vetch was planted in the Sierra foothills of California by the Soil Conservation Service for soil erosion control. Vetch has become well established, and with increased awareness and recognition of the disease, reports may increase.

Systemic granulomatous disease in horses is most likely multifactorial. There may be multiple etiologies with a common pathogenesis. Consumption of vetch may be 1 etiology associated with SGD in horses, as it is in cattle. The organ distribution, the perivascular nature of the inflammatory infiltrate, and the components of the inflammatory infiltrate of both diseases are similar, except for the lack of a prominent eosinophilic component of the granulomatous inflammation seen in the horse in the present case. Eosinophils have been seen in some horses with SGD (L. W. Woods, personal observation). Many cases of SGD occur without known exposure to vetch pasture. Disease in cattle induced by vetch may be the result of a hypersensitivity to 1 or more plant constituents that are absorbed and combine with host constituents to stimulate the inflammatory response. These plant constituents or immunogens in vetch that induce disease may also be present in other forage or organisms.

References

1. Anderson CA, Divers TJ: 1983, Systemic granulomatous inflammation in a horse grazing hairy vetch. *J Am Vet Med Assoc* 183:569-570.
2. Burroughs GW, Neser JA, Kellerman TS, Van Niekerk FA: 1983,

- Suspected hybrid vetch (*Vicia villosa* crossed with *Vicia dasycarpa*) poisoning of cattle in the republic of South Africa. *J South Afr Vet Assoc* 54:75-79.
3. Cheeche PR, Shull LR: 1985, Proteins and amino acids. *In: Natural toxicants in feeds and poisonous plants*, pp. 271-273. Avi Publishing Co., Westport, CT.
4. Henson PR, Schotch HA: 1968, Vetch culture and uses. US Department of Agriculture, Farmers' Bull No. 1740, pp. 1-21. US Government Printing Office, Washington, DC.
5. Johnson BJ, Moore J, Woods LW: 1991, Systemic granulomatous disease in cattle associated with grazing hairy vetch (*Vicia villosa*). *Proc Annual Meet Am Assoc Vet Lab Diagn* 34: 23.
6. Kellerman TS, Coetzer JAW, Naude TW: 1988, Skin and adnexa. *In: Plant poisonings and mycotoxicosis of livestock in southern Africa*, pp. 219-220. Oxford University Press, Cape Town, South Africa.
7. Kerr LA, Edwards WC: 1982, Hairy vetch poisoning of cattle. *Vet Med Small Anim Clin* 77:257-258.
8. Odriozola E, Paloma E, Lopen T, et al.: 1991, An outbreak of *Vicia villosa* (hairy vetch) poisoning in grazing Aberdeen Angus bulls in Argentina. *Vet Hum Toxicol* 33:278-280.
9. Panciera RJ: 1978, Hairy vetch (*Vicia villosa* Roth) poisoning in cattle. *In: Effects of poisonous plants on livestock*, ed. Keeler RF, Van Kampen KR, James LF, pp. 555-563. Academic Press, New York, NY.
10. Panciera RJ, Johnson L, Osburn BI: 1966, A disease of cattle grazing hairy vetch pasture. *J Am Vet Med Assoc* 148:804-808.
11. Peet RL, Gardner JJ: 1986, Poisoning of cattle by hairy or wooly-pod vetch, *Vicia villosa* subspecies *dasycarpa*. *Aust Vet J* 63:381-382.
12. Scott D: 1988, Immunologic diseases. *In: Large animal dermatology*, pp. 326-328. W. B. Saunders Co., Philadelphia, PA.
13. Stannard AA: Generalized granulomatous disease. *In: Current therapy in equine medicine*, ed. Robinson NE, 2nd ed., pp. 645-646. W. B. Saunders Co., Philadelphia, PA.
14. Thomas PD, Hunninsshake GW: 1987, Current concepts of the pathogenesis of sarcoidosis. *Am Rev Respir Dis* 135:747-760.

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Systemic granulomatous disease in cattle in California associated with grazing hairy vetch (*Vicia villosa*)

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Hairy vetch (*Vicia villosa*) has been associated with a systemic granulomatous disease in cattle in Oklahoma and Texas for the past 25 years.^{2,4,5} Three cases of vetch-associated disease were observed on 2 different California farms over a period of 2 years. The first case was in a 5-year-old Angus cow that was on California coastal foothill pasture all winter and in May was found to be listless and had welts over various parts of the body, peeling of skin around the nares, and a fever of 41.1 C. The cow was treated with antibiotics and

cortisone. The skin lesions dried, but the cow was constantly rubbing and losing large amounts of hair. One week into the illness, the cow aborted a 4.5-month fetus, became much more lethargic, and died 2 weeks after the observed onset of clinical signs. The cow was submitted to the California Veterinary Diagnostic Laboratory System (CVDLS) at Davis for postmortem examination. Grossly, the skin was thickened with marked dry scaling and patchy alopecia over the ears, head, neck, tailhead, distal limbs, and udder. Thick, mucoid, greenish bilateral nasal discharge was present. The lungs failed to collapse and felt slightly rubbery with clear thickening of interlobular septa by edema. There was irregular pallor of the epicardium and pale streaking of the ventricular myocardium. The renal cortex had subtle pale mottling of the cut

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