

skin of areas in direct contact with the ground. Clinical signs include red papules progressing to erythematous, thickened, alopecic areas of skin on the feet, sternum, ventral abdomen, posterior thighs, and tail. Diagnosis is based on history of contact with hookworm ova-containing feces, contaminated soil, or organic material. Treatment involves appropriate anthelmintic treatment of all dogs in the kennel or household, environmental decontamination, and symptomatic treatment.

Pelodera dermatitis occurs when larvae of *Pelodera strongyloides* invade the hair follicles of skin in contact with damp soil or decaying organic debris. Clinical signs include mild-to-intense pruritus with erythema, papules, and crusting of skin in contact

with the ground (feet, legs, ventral abdomen, and tail). Diagnosis may be made by finding the 600 to 650  $\mu\text{m}$  larvae on skin scrapings. Treatment involves removal of the contaminated bedding or soil and dipping the dog in a parasitic dip (e.g., 2% lime sulfur).

*Dracunculus insignis* is a parasite of dogs and wild carnivores. The intermediate host is a *Cyclops* ingested from contaminated water. The larvae develop in the host, and adults are located in subcutaneous tissues of the abdomen and limbs. A nodule forms at the site and fistulates. When the nodule contacts water, the female worm comes to the surface and releases large numbers of larvae. Surgical excision of the worms is the treatment of choice.

## CHAPTER • 18

### Edema

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#### INTRODUCTION

The well-being of cells and tissues depends not only on an intact circulation to deliver oxygen and nutrition but also on intercompartmental fluid homeostasis. Approximately 60% to 70% of lean body weight is water; of this value about two thirds is contained in the intracellular space and one third in the extracellular space. Most extracellular water (approximately 70%) is contained in the interstitium, a matrix of connective tissue and gel-like substrate that is the area between the vascular compartment and the cell membrane.

Under normal conditions, continuous water movement occurs across fluid spaces. Water is shifted from the vascular network into the interstitium; ultimately it crosses cell membranes to become incorporated in the intracellular cytoplasm or is returned back to the vascular network. Water return to the vascular space is controlled by transcompartmental pressure changes induced by the presence of large molecular weight proteins (colloids) in the vascular network. Because of a slight pressure difference between the hydrostatic force displacing water from the arterial-capillary network and the colloidal force promoting water return to the capillary-venous network, residual water remains in the interstitial compartment. This residual volume is drained back into the systemic circulation by lymphatic tributaries. Under normal conditions, no net transfer of water across tissue compartments occurs (Figure 18-1).

When this relationship is disturbed, increased water retention in the interstitial compartment often results. Abnormal collection of water in the interstitial space is defined as *edema*. Collection of water in body cavities (hydrothorax, hydropericardium, ascites) and generalized profound subcutaneous swelling (anasarca) are included in the edema category.

#### PATHOGENESIS

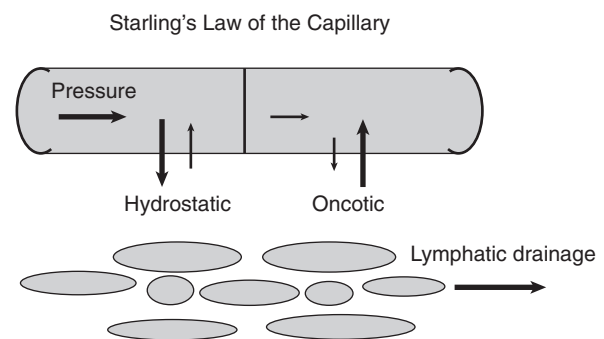
As previously noted, a defined physiologic relationship governs intercompartmental water balance. This relationship, known

as *Starling's law of the capillary*, represents two major factors in water distribution: hydrostatic and oncotic (osmotic) forces. The relationship between hydrostatic and oncotic forces have been extensively investigated and is described as the following mathematical relationship:

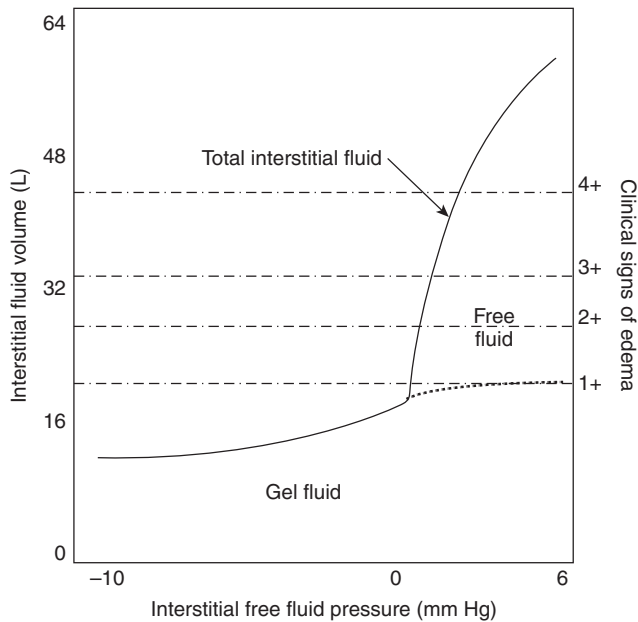
$$\text{Net filtration} = K_f[(P_{\text{cap}} - P_{\text{if}}) - (\pi_{\text{p}} - \pi_{\text{if}})]$$

where  $K_f$  represents net capillary wall permeability,  $P_{\text{cap}}$  represents hydrostatic pressure generated by the heart,  $P_{\text{if}}$  represents hydrostatic pressure generated by tissues,  $\pi_{\text{p}}$  represents oncotic forces in plasma, and  $\pi_{\text{if}}$  represents oncotic forces in tissues generated by protein and mucopolysaccharides (see Figure 18-1).

Under normal conditions, negative pressure is present in the interstitium. Negative pressure is maintained by the combination of oncotic forces and lymphatic drainage, with a combined drainage capacity that exceeds hydrostatically induced shift of water from the intravascular compartment. When factors associated with this relationship are changed, the outcome is often abnormal interstitial water retention creating a positive interstitial pressure. The conversion from



**Figure 18-1** Starling's law of the capillary.



**Figure 18-2** Effect of increasing interstitial fluid pressure on volumes of total interstitial fluid, gel fluid, and free fluid.

negative to positive interstitial pressure is believed to be a key factor in edema formation (Figure 18-2). Pathophysiologic changes commonly associated with edema formation include increased vascular permeability, decreased protein and

mucopolysaccharide concentration in the interstitial matrix, and reduced lymphatic drainage. Five categories of edema have been described based on changes in Starling’s law of the capillary: (1) increased hydrostatic pressure, (2) reduced osmotic pressure, (3) lymphatic obstruction, (4) sodium retention, and (5) inflammation. Specific clinical syndromes associated with each category are listed in Table 18-1.

**CLINICAL PRESENTATION AND DIAGNOSIS**

Edema is a secondary feature of many clinical presentations. Historical findings suggestive of edema include limb swelling, increase in abdominal girth, and postural related dyspnea. Physical findings include limb swelling in gravity-dependent regions, swelling of the ventral aspect of the mandible, prepuce, scrotum or mammary glands, periorbital swelling, increased breath sounds characterized by rales and rhonchi, and fluid presence in the abdomen or thorax. Superficial edema in subcutaneous tissue can be confirmed by applying digital pressure over the swollen area. Displacement of interstitial water leaves a finger-shaped depression that refills after a short time. This finger-shaped depression is called “pitting edema.”

Diagnostic procedures are focused on confirming edema presence and determining possible cause. Evaluation of the physiologic components of water balance (plasma protein concentration, erythrocyte mass, serum electrolyte levels, and system blood pressure) are important to determine which factor or factors associated with water balance are affected. Evaluation of underlying inflammation (white blood cell [WBC] count, differential, platelet count) is warranted in specific underlying causes.

**Table • 18-1**

**Causes of Edema**

CAUSE	CONTRIBUTING FACTOR	SPECIFIC CLINICAL SYNDROMES
Increased hydrostatic pressure	Impaired venous return	Congestive heart failure Constrictive pericarditis Ascites (cirrhosis) Venous obstruction or compression (thrombosis, external pressure, extremity inactivity)
	Small-caliber arteriolar dilation	Heat Neurohumoral dysregulation
Reduced plasma osmotic pressure	Hypoproteinemia	Protein-losing glomerulonephropathy (nephrotic syndrome) Cirrhosis (ascites) Malnutrition Protein-losing gastroenteropathy
		Lymphatic obstruction
Sodium retention	Excessive dietary intake with renal insufficiency Increased tubular sodium reabsorption	Renal hypoperfusion Increased renin-angiotensin-aldosterone secretion
Inflammation	Acute inflammation Chronic inflammation	
	Angiogenesis	

Modified from Mitchell RN, Cotran RS: Hemodynamic disorders, thrombosis, and shock. In Cotran RS et al, editors: *Robbins pathologic basis of disease*, ed 6, Philadelphia, 1999, WB Saunders.

Electrocardiographic and echocardiographic imaging is indicated in cases where edema may be associated with primary or secondary heart failure. Ultrasonographic imaging of the peritoneal space, thoracic space, and pericardial space is warranted if physical findings indicate cavity-based fluid collection.

Collection of edema fluid and fluid analysis may be helpful in determining the underlying disease process. The clinicopathologic features of edema fluid are typically a protein-poor transudate with a specific gravity less than 1.012 that has poor cellularity. In inflammation, increased protein content is noted; fluid is generally an exudate with a specific gravity greater than 1.020 and has the presence of inflammatory cell morphology (macrophages, degenerated white blood cells).

## TREATMENT

Treatment of life-threatening edema is an immediate goal irrespective of cause. Typically these presentations are associated with primary heart failure. Administration of parenteral furosemide or vasodilator drugs (or both) is considered the primary step for emergency management. The rationale for furosemide selection includes its known actions producing increased renal sodium excretion facilitating edema mobilization from interstitial sites, pulmonary and systemic vasodilation, and increased lymph flow in the thoracic duct. All of these responses positively affect transcompartmental water balance and reduce edema formation, especially in the lung. Vasodilators (hydralazine, nitrates) are used to reduce edema; they produce their primary actions through relaxation of systemic arterioles and venules promoting redistribution of central blood volume and reducing hydrostatic pressure. In fulminant cardiac failure, a sympathomimetic such as dobutamine

(1 to 5  $\mu\text{g}/\text{kg}/\text{min}$  constant rate infusion [CRI]) is started and titrated to achieve positive inotropic response. This will improve the Starling's relationship and help to mobilize edema.

Nonemergent edema management is achieved by using goal-directed therapeutic intervention to rebalance the Starling's relationship. Furosemide or other potent loop diuretics (bumetanide, spironolactone, triamterene, amiloride, and thiazide-class) may be used to promote edema mobilization by initiating physiologic responses previously noted for furosemide. Administration of plasma products (fresh plasma, fresh frozen plasma, and cryopoor plasma), hetastarch, or dextran 70 will increase intravascular oncotic pressure and favor water redistribution from the interstitial to intravascular compartment. These products are considered in cases demonstrating decreased oncotic pressure (hypoproteinemia), decreased osmotic balance (anemia), or increased endothelial permeability (inflammation). Decreasing osmotic forces by dietary modification to reduce sodium and chloride intake or through use of loop diuretics to increase sodium and chloride loss is an additional consideration in primary cardiac disease patients.

## PROGNOSIS

The prognosis for successful management of edema is based on the ability to treat and resolve the underlying clinical disorder. Edema secondary to inflammatory states, colloid imbalance, or primary cardiac disease is often successfully managed or resolved. Edema secondary to lymphatic pathology often requires long-term management to successfully correct.

# CHAPTER • 19

## Hepatocutaneous Syndrome

Catherine Outerbridge

**H**epatocutaneous syndrome (HS) is an uncommon skin disease associated with systemic metabolic disease. It has also been called *superficial necrolytic dermatitis* (SND), *metabolic epidermal necrosis*, *diabetic dermatopathy*, and *necrolytic migratory erythema* (NME). This disease was first described in a dog in 1968. The first English language reference comparing the disease to the human disease NME was in 1986, when the disease was described in four dogs with diabetes mellitus and was thus first called *diabetic dermatopathy*. The disease has been most commonly described in older dogs, although a histologically equivalent disease occurring in cats and the black rhinoceros has been reported. The etiopathogenesis of this disease is unclear, but it is likely multifactorial. Because different disease processes appear to cause similar histologic skin lesions, it might be more correct to refer to the skin disease as either *SND* or *metabolic epidermal necrosis*.

### COMPARATIVE ASPECTS WITH NECROLYTIC MIGRATORY ERYTHEMA AND THEORIES OF PATHOGENESIS

NME is a histologically similar disease that is seen in humans. Most often NME occurs in association with a glucagon-secreting tumor. Glucagonoma syndrome in humans is characterized by the skin lesions of NME, hyperglycemia resulting from carbohydrate intolerance or diabetes mellitus, weight loss, hypoaminoacidemia, and anemia. Humans with NME usually have a profound hypoaminoacidemia, presumed to result from the catabolic gluconeogenic effects of glucagon. However, NME has been diagnosed in some humans with normal plasma amino acid concentrations, and these have often been patients with nonglucagonoma-associated disease. Nonglucagonoma-associated NME has been reported in humans with celiac disease, chronic malabsorption, cirrhosis,