**Respiratory complications in ICU: what can go wrong?**

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Respiratory complications are a common occurrence in ICU patients. They could be directly related to the disease (e.g. blunt trauma, aspiration pneumonia), but could also be secondary to our treatment (e.g. fluid overload, transfusion related ALI..). They are often associated with bad prognosis and should be treated aggressively.

This lecture will review diagnosis, treatment of the most common respiratory complications encountered in ICU.

1. **Fluid overload**

Fluid overload (FO) should always be a considered a risk of IV fluid therapy, but obviously some patients are at much greater risk than others. The highest risk for FO occurs in patients with heart disease or kidney disease that reduce the patient's capacity to compensate for increased fluid intake. For example, dogs and cats with occult heart disease are more likely to develop FO; and cats in particular seem at highest risk.

1. Clinical signs

Animals receiving intravenous fluids should be monitored closely. Body weight should be monitored daily (or more often if indicated), and a physical examination should be performed at least twice daily to assess the animal’s mental status, skin turgor, heart rate and pulse quality, mucous membrane color, capillary refill time, extremity temperature, and respiratory rate and effort. Serial lung auscultation should be performed to monitor for increased breath sounds, crackles, or wheezes. Clinical signs in animals receiving too much fluid include weight gain, serous nasal discharge, chemosis, jugular venous distention, and interstitial pitting edema1. In the early stages of pulmonary edema, an increase in the respiratory rate will occur, followed by inspiratory crackles, wheezes, and dyspnea due to pulmonary edema or pleural effusion. Abdominal distension can be seen in case of abdominal effusion. It is therefore of utmost importance to monitor the respiratory rate and effort of all patients receiving fluid therapy. The development of gallop sound or heart murmur during hospitalization were identified as good indicators of FO in one study2. In dogs, critically ill dogs are at higher risk to develop FO than stable patient3. In cats and dogs, length of hospitalization and hospitalization-related costs are significantly increased in cats with FO, highlighting the importance of monitoring and treatment of FO.

1. Treatment

This is important to carefully monitor fluid administration in at risk patients. For this purpose, physical examination, FAST and urine output are good help. T-FAST will show increase B-lines or presence of pleural effusion. AFAST will detect abdominal effusion. Urine output can be compared with fluid administered to help guide fluid therapy and prevent the administration of too much or too little fluid.

Treatment of fluid overload often requires discontinuation (or at least severely limiting) IV fluid therapy, administration of a diuretic such as furosemide if not contraindicated and thoracocentesis in case of pleural effusion. It is recommended to start with low doses of furosemide and increase the dose as necessary until adequate urine output is achieved. In anuric states (e.g., acute kidney injury) higher doses can be used initially. Additionally, dialysis can be used in patients with anuric AKI to manage fluid overload.

1. **Aspiration pneumonia**

Aspiration pneumonia refers to pulmonary inflammation and infection secondary to aspiration of oropharyngeal secretions, gastric contents, or other materials (e.g., barium). It seems to be more frequent in dogs than in cats. Aspiration pneumonia is a serious and potentially life-threatening inflammatory lung process. Pathologic damage to the lungs results from insults to the alveolar capillary membranes, and loss of surface area for gas exchange leads to ventilation-perfusion mismatch and hypoxemia4. Gastric acid aspiration directly causes alterations in surfactant function that result in loss of surface tension and atelectasis. Subsequent bronchoconstriction increases airway resistance and the effort required for breathing.

Prognosis is usually good but is variable and dependent of the underlying disease.

1. Risk factors

Several risk factors are well known and well documented, particularly in dogs. Many of these risk factors are present in the ICU patients, contributing to its common occurrence. Risk factors for aspiration pneumonia include esophageal disease, gastrointestinal disease (especially those that result in delayed gastric emptying, vomiting or regurgitation), an altered level of consciousness (including sedative/anesthetic drug related), laryngeal disease, and forced administration of drugs or food. Certain breeds, as brachycephalic dogs, are at higher risk for aspiration pneumonia due to their anatomical conformation or because of predisposition to disease leading to aspiration pneumonia.

Inadvertent placement of a nasoenteric tube in the airway and subsequent delivery of water or food material into the lungs could be a source of aspiration pneumonia. This complication could be easily avoided by careful verification of good nasoenteric placement by thoracic radiographs before use of the tube. Nasogastric tube allows an easier control of the adequate placement compared with nasoesophageal.

1. Clinical signs and diagnosis

Clinical signs of aspiration pneumonia can be variable and nonspecific, making a definitive diagnosis difficult. However, the history of a patient with aspiration pneumonia will commonly include at least one present predisposing risk factor or witnessed aspiration event4. Common clinical signs include lethargy, cough, tachypnea or respiratory distress and occasionally nasal discharge. Other signs may reflect the primary underlying disease, such as regurgitation if megaesophagus or noisy breathing (stridor) if laryngeal paralysis is present. A study by Kogan et al. determined that less than 50% of dogs with aspiration pneumonia had fever, tachycardia or tachypnea (i.e., evidence of the systemic inflammatory response syndrome). Cough was reported in 57%, while increased respiratory effort was noted in 55%5. The majority of dogs (68%) did have abnormal lung sounds but clearly these are nonspecific.

Diagnosis approach is based on clinical signs, thoracic radiographs. On radiographs, previously unreported interstitial-to-alveolar infiltrates independent lung lobes is the standard diagnosis of aspiration pneumonia in the clinical setting. The most common sites for aspiration pneumonia are the most gravity dependent: the right middle lung lobe, followed by right cranial lung lobe, and left cranial caudal lobe. Note that the positioning of the patient during aspiration events dictates the location of pulmonary infiltrates. So, in critically ill patient, or after general anesthesia, it is not surprising to have lesion in caudal lobes.

Other diagnosis finding could be hypoxemia (PaO2<60 mmHg), leukocytosis, signs of inflammation on the broncho-alveolar lavage, but are not specific from aspiration pneumonia.

1. Treatment

Treatment for aspiration pneumonia centers on administration of IV fluids, oxygen therapy, antibiotics and other supportive care as chest physiotherapy techniques and nebulization. Caution should be taken in patients with known risk factors and predisposing underlying diseases should be treated aggressively.

Broad-spectrum parenteral antimicrobials are the mainstay of treatment for dogs with aspiration pneumonia. Although initially treatment will always be empirical, subsequent therapy should ideally be based upon culture and sensitivity testing (particularly in dogs at risk of MDR infections). The Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious

Diseases believes that either no treatment or parenteral administration of a beta lactam antimicrobial like ampicillin, ampicillin-sulbactam, or the first-generation cephalosporin cefazolin might be sufficient in patients with no signs of sepsis. If clinical findings in dogs or cats with pneumonia suggest the existence of sepsis (eg, injected mucous membranes, hypoglycemia), the Working Group recommends concurrent parenteral administration of either enrofloxacin or marbofloxacin (available in injectable form in some countries) combined with a drug with Gram-positive and anaerobic spectra until bacterial culture and antimicrobial susceptibility testing results return. The Working Group states that common options for Gram-positive and anaerobic bacteria include ampicillin or clindamycin administered parenterally6.

Chest physiotherapy techniques could be of great help to improve mucus expectoration, and nebulized medications such as hypertonic sodium chloride (…%) (mucolytic action, increased muco-ciliary function, anti-inflammatory), antibiotic when infectious disease is suspected (e.g.: Gentamicin), and heparin (specially in case of ARDS and ALI induced by smoke inhalation) could be added to the therapeutic plan. Physiotherapy and nebulization techniques will be described in this lecture.

1. **Pulmonary complication of trauma**

While blunt trauma can affect any and all organ systems, lung injury presents one of the most common, and life-threatening aspects of these cases. Pulmonary injuries require immediate recognition and treatment, as aggressive fluid therapy can make some of these injuries worse. It is important to assume some degree of thoracic and pulmonary injury in all trauma patients. In one study, thoracic injuries were present in 72% of the dogs presented for severe blunt trauma8. Pulmonary contusions, pneumothorax, and fractured ribs were most commonly observed. As these complications are frequent, T-FAST (at admission and during hospitalization) and thorax radiographs (if clinically stable) should be done in all traumatized patients.

Initial stabilization of respiratory distress traumatized patient should include analgesia, oxygen therapy, thoracentesis if necessary and fluid therapy.

Tranexamic acid, an anti-fibrinolytic drug (10 mg/kg IV q8h), should be used at admission of all traumatized patient, and continued until absence of signs of bleeding.

1. Pulmonary transfusion related complication

These adverse effects can occur despite appropriate prescreening of donors, blood collection techniques and pre-transfusion compatibility testing.

Complications of transfusions can be divided into immunologic and non-immunologic reactions and are summarized in Table 1.

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| **Immunologic reactions** | **Non-immunologic reactions** |
| Type I hypersensitivity allergic reactions | Transfusion-associated circulatory overload (TACO) |
| Immune-mediated hemolysis | Hypothermia |
| Febrile non-hemolytic reactions | Coagulopathy |
| Transfusion related acute lung injury (TRALI) | Hypophosphatemia |
|  | Citrate toxicity, Hypocalcemia |
|  | Infectious disease transmission |
|  | Sepsis |

**Immunologic reactions** include hemolytic, allergic, hyperthermia, transfusion related lung injury (TRALI) and thrombocytopenia. In one study9, fever was the most common complication, followed by hemolysis. Age of stored RBC products was associated with increased risk of transfusion-related hemolysis, but not with fever. TRALI is a rare complication of transfusion in dogs. The overall incidence in one population of patients that received transfusions was reported at 3.7%10.

**Non-immunologic complications** typically arise from physical properties of the blood components or through transmissible diseases. A transfusion induced intravascular volume overload (TACO) may occur, resulting in a cardiogenic pulmonary edema.

Avoiding transfusion related complications is important to minimize risk to the recipient. Having standardized protocols for collection, processing, handling, administration, and monitoring of blood product transfusions is essential to minimize complications. Pre-screening of donors for infectious disease, appropriate blood typing and crossmatching as well as having a dedicated method for administration and monitoring is key to identification of early complications

1. **Pulmonary Thromboembolism and hemorrhages**

Pulmonary thromboembolism (PTE) refers to obstruction of blood flow in the pulmonary vasculature from a thrombus formed in the systemic venous system or right heart. Causes of PTE are as for any thromboembolic disease; so essentially abnormalities in Virchow's triad. Remember Virchow's triad includes abnormalities of blood flow (turbulence or stasis), endothelial damage, and hypercoagulability. The key with PTE is to look for the underlying disease (if not immediately apparent). PTE is a common respiratory complication in ICU patients as multiple concurrent risk factors are often present.Diseases known to predispose to hypercoagulability include neoplasia, cardiac disease, heartworm disease, protein losing enteropathy (PLE), protein losing nephropathy (PLN), hyperadrenocorticism, exogenous corticosteroid administration, indwelling IV catheters, immune mediated hemolytic anemia (IMHA), disseminated intravascular coagulation and sepsis. Theoretically any systemic inflammatory state can result in a systemic procoagulant state and predispose to PTE.Diagnosis of PTE can be challenging. One of the first things to clue you in is often that the degree of respiratory distress is out of proportion with changes on thoracic radiographs. If you are lucky thoracic radiographs may be helpful (e.g., focal hypolucency, vessel truncation etc.), however, they may be normal. Significant PTE results in pulmonary hypertension, and thus there may also be evidence of main pulmonary artery and/or right heart enlargement on thoracic radiographs. In some cases, the PTE may be visualized via echocardiography. Advanced imaging (such as CT angiography or much less commonly a V/Q scan with nuclear scintigraphy) is usually required to confirm the diagnosis.Treatment involves oxygen supplementation and treating the underlying disease. We uncommonly use thrombolytic therapies (e.g., T-PA), but do generally start anticoagulants (unfractionated or low molecular weight heparin), and/or anti-platelet drugs (e.g., Clopidogrel: 18.75 mg/cat once a day or 1 mg/kg once a day in dogs) to reduce the risk of further thrombus formation.

In the author’s practice, the non-related trauma pulmonary hemorrhages occur most frequently in Leptospirosis dogs. Leptospirosis pulmonary hemorrhage syndrome (LPHS) is a frequent manifestation of Leptospira infection in dogs and is associated with a high morbidity and mortality. Dogs with LPHS develop multi-focal intra-alveolar hemorrhage, which can be rapidly progressive and lead to massive hemoptysis and respiratory failure. LPHS is associated with mortality rates of up to 70%. Intra-alveolar hemorrhage can be detected even in dogs without overt respiratory signs.

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