EXTRACORPOREAL THERAPIES. NEW OPPORTUNITIES

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Extracorporeal therapies in small animal medicine have evolved a long way since the first experimental hemodialysis on a dog was performed by John Abel in 1914. Perfection of the technique for human treatments and development of animal-specific treatment protocols in more recent years have helped to transition from an empirical therapy to a standard of care for small animals with renal failure. Most of the treatments on dogs and cats have been performed worldwide for the therapy of acute kidney injury (AKI), reflecting its use as a bridge to recovery rather than a long-term therapy for chronic end-stage kidney disease. Progresses in equipment, material, drugs and techniques have opened the door to dogs and cats with a wide range of weights and ages. Dogs and cats under 2 kg now can be hemodialyzed routinely and safely with the available equipment.

Initially dialytic therapies were based purely on the principle of diffusive clearance with passive solute transfer from the blood compartment to the dialysate across the dialysis membrane, down a concentration gradient. Molecular size cutoff with available membranes was in the range of 1000 Da, sufficient for the removal of the main small molecular weight uremic solutes. Over time however, refinements in the technique were aimed at the removal of larger molecular weight solutes, the so-called middle molecules held responsible for some of the residual syndrome of uremia despite "adequate" dialysis of CKD patients. In the acute setting, many inflammatory mediators fall in the same molecular size range and their removal may play a significant role to help control the cytokine storm associated with severe disturbances of the inflammatory balance. Filters used modified synthetic membranes and treatments were based increasingly on convection (active fluid and solute removal through the membrane) rather than on pure diffusion. Diffusive therapies are called hemodialysis (HD), convective therapies hemofiltration (HF), and combined diffusive-convective therapies hemodiafiltration (HDF).

Newer developments also targeted removal of specific toxins, especially highly protein-bound toxins. For this, protein-binding is competing with adsorption to a sorbent filled in a column and the blood flows over this sorbent instead of through a membrane filter. This procedure, hemoperfusion (HP), can be used for removal of exogenous or endogenous protein-bound drugs (e.g., some NSAIDs, fluoroquinolones) and toxins (e.g., some mycotoxins). Modifications of the procedure use a circulating suspension of activated charcoal that is continuously regenerated to increase efficiency for the use in liver failure for example. Specific binding of endogenous or exogenous toxins to albumin can be displaced by adding albumin to the dialysate in standard hemodialysis. This technique (single-pass albumin dialysis, SPAD) was used successfully in severely hyperbilirubinemic animals and it significantly reduced the bilirubin concentration to less toxic levels.

Another development of extracorporeal blood purification techniques includes the whole group of apheretic techniques with which a specific blood component can be removed: plasma (plasmapheresis) or blood cell components (cytapheresis for erythrocytes, leukocytes, platelets, or stem cells). Plasma separation can be achieved by centrifugation or by filtration using membranes with large pores retaining only cellular blood components. When removed plasma is replaced by fresh plasma from healthy donors, we speak of therapeutic plasma exchange (TPE) and its main indications include immune diseases (targeting the reduction of immunoglobulins), toxicities (targeting highly protein-bound solutes), hyperviscosity syndromes (targeting the excess of abnormal serum proteins), and severe systemic disorders such as sepsis (targeting a restauration of a more physiological cytokine balance). Both centrifugal and membrane TPE have been used successfully in dogs for these indications. Many variations of these TPE techniques have been developed recently to target more specifically pathological plasma components without having to replace the whole plasma. They include among others Coupled Plasma Filtration Adsorption (CPFA) where plasma separated from the circulating blood is treated with a specific sorbent to remove specific cytokines, bilirubin or other blood component. In Cascade filtration or Double Filtration PlasmaPheresis (DFPP), the filtered plasma is sent through a second filter with differing pore size characteristics allowing targeted removal of a solutes with a narrower molecular size range.

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Another generation of blood purification techniques include extracorporeal membrane oxygenation (ECMO) and membrane CO2 removal for support of the patients with respiratory failure. Whereas ECMO requires very high blood flow rates, significant amounts of CO2 can be removed at flow rates achieved with standard dialysis platforms and this therapy is currently available on some machines developed primarily for continuous renal replacement therapies.

In summary, extracorporeal blood purification techniques offer many new opportunities in the therapy of small animals and they are no longer restricted to the treatment of renal failure. Their expansion in the field of immune diseases and of respiratory support are just some examples.