Laboratory methods for the diagnosis of DIC in animals

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The objetive of this presentation is to give an overview of diagnostic aspects of disseminated intravascular coagulopathy (DIC) in animals. Depending on the prothrombotic trigger in relation to the underlying disease and phase of progress, different stages or severity degrees of DIC may occur: I. compensated activation of the haemostatic system, II. decompensated activation of the haemostatic system, III. "full-blown DIC". There is an indistinct borderline between an activated haemostatic system ("hypercoagulable state") and DIC.

In general, there are different possibilities for the diagnosis of DIC:

1. Screening tests / blood levels of haemostasis components: The diagnosis "DIC" can reliably be made if abnormal results of the screening tests of the haemostatic system (decreased platelet count, prolonged prothrombin time [PT], activated partial thromboplastin time [APTT], thrombin time) occur in patients in combination with an underlying disease which is frequently associated with DIC. Test results of the screening tests (PT, APTT and thrombin time) are normal in phase I of the syndrome and do not exclude an activation of the haemostatic system. If these tests are prolonged, coagulation is already markedly activated, causing a consumption of coagulation factors. Prolonged thrombin time indicates remarkable fibrinolysis, i.e. fibrin(ogen) degradation products (FDP) inhibition of fibrin polymerisation. Frequent measurements of PT, APTT and platelet count are helpful to monitor the course of DIC and therapy. A continuous decrease in platelet count in patients with acute DIC indicates thrombin induced intravascular platelet aggregation, whereas a stable platelet count suggests the end of thrombin generation. Global tests such as thrombelastography and resonance thrombography are valuable diagnostic tools for the DIC-hyperfibrinolysis complex where they give fast and summarized information on changes in the plasmatic and thrombocytic haemostatic potential and on additional influences by FDPs and anticoagulants used therapeutically.

   A decrease of activities of coagulation factors and inhibitors to values below 50 % indicates the presence of acute or high-grade DIC. Because its synthesis can be increased manyfold, a decreased fibrinogen plasma concentration is a rare finding in DIC patients, limited to cases with extreme hyperfibrinolyis. Antithrombin determination using synthetic substrate tests is a key test for the diagnosis and monitoring of therapy in DIC. In humans, antithrombin, protein C, plasminogen as well as plasmin-alpha$_2$-antiplasmin

(PAP) complexes and plasminogen activator inhibitor (PAI)-1 activity are related to the outcome of the patients.

2. Markers of coagulation activation: Increased blood levels of markers such as soluble fibrin, fibrinopeptide A (FPA), prothrombin fragment F_{1+2} (F_{1+2}) and thrombin-antithrombin (TAT) complex indicate the generation of thrombin and the effect of thrombin on coagulation factors. However, evaluation of these tests has been only very limited for animals and they are not immediately available in the routine laboratories. The determination of soluble fibrin is crucial for the diagnosis of DIC. A functional chromogenic test system is especially suited to determine soluble fibrin in the plasma of different animal species. Because blood coagulation can take place extravascularly (e.g. in peritonitis) increased FPA and F_{1+2} levels are not specific for the diagnosis of DIC. As soluble fibrin in plasma can only be generated intravascularly, it represents a specific test for the diagnosis of hypercoagulability. The results of all these tests depend significantly on optimal venous puncture.
3. Markers of fibrinolysis activation: Because an intravascular coagulation is almost always associated with a reactive hyperfibrinolysis, and primary hyperfibrino(geno)lysis occurs very seldom, markers of fibrinolysis are frequently used for the diagnosis of DIC. D-dimer tests are more sensitive and specific than FDP assays. Since fibrinogen and fibrin are also degraded extravascularly, an elevated FDP or D-dimer blood level does not prove intravascular fibrinolysis. In addition, FDP levels are influenced by liver and kidney function. Different commercially available FDP assays including D-dimer tests have been evaluated to detect FDPs in animal plasma. Because an extreme hyperfibrinolysis does not occur until circulating $alpha_2$-antiplasmin has been depleted, additional $alpha_2$-antiplasmin determination may be helpful. However, even in humans the determination of $alpha_2$-antiplasmin and PAP complexes, a valuable parameter of activation and inhibition of fibrinolyis, is not considered in routine diagnostic.

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