Properties of the blood such as blood coagulation, fibrinolysis, platelet functions etc are closely interrelated with blood flow and the condition of the vessel wall, and when, for some reason, the balance between them is disrupted, hemorrhagic or thrombotic tendencies arise. To diagnose hemorrhagic, thrombotic, and hemorrhagic-thrombotic tendencies respectively, we have devised the Hemorrhagogram, Thrombogram, and Hemorrhago-thrombogram, which combine the results of the tests performed on a particular blood sample and give us an overall view of them.

In the Hemorrhagogram, the tests on platelets and the vessel wall, namely platelet count, bleeding time, clot retraction, and capillary fragility, the tests on coagulation, namely clotting time, activated partial thromboplastin time (PTT), prothrombin time, and r and k values of thrombelastogram (TEG), and the tests on fibrinolysis, namely fibrinogen and euglobulin lysis time (ELT) are arranged with the normal range at the right of a scale which shows increasing hemorrhagic tendency towards the left. In thrombocytopenia, decrease in platelet count, prolongation of bleeding time, reduction of clot retraction, and increased capillary fragility can be seen. There are no abnormalities in coagulation and fibrinolysis.

In thrombasthenia, the platelet count is normal. The marked prolongation of bleeding time and the absence of clot retraction are characteristic.

Normal platelet count and markedly prolonged bleeding time are also observed in von Willebrand's disease. However, normal clot retraction and slightly increased PTT are observed.

In hemophilia, PTT, which indicates intrinsic coagulation, is markedly increased, while prothrombin time, which indicates extrinsic coagulation, is normal.

In cirrhosis of the liver, it frequently happens that hemorrhagic tendency is indicated throughout the three systems of tests: platelet count shows a tendency to decrease; in coagulation, PTT and prothrombin time are prolonged; and fibrinolysis also increases.

While hemorrhage and hemorrhagic tendency often run more or less parallel, it is frequently seen that thrombosis and thrombotic tendency do not necessarily do so. The earlier or progressive stages of thrombus formation, and the stages where the thrombus is organized and fixed often show completely different behaviour. Although diagnosis of thrombotic tendency is extremely important in prophylactic treatment of thrombosis, there are few tests appropriate for thrombotic tendency, and its diagnosis, unlike that of hemorrhagic tendency, is not well established. Five main factors, increased coagulation, decreased fibrinolysis, increased platelet function, slowing of blood flow, and defects of the vessel wall are involved in the occurrence of thrombotic tendency. We prepared the Thrombogram taking fibrinogen and heparin resistance as indicators for coagulation, platelet adhesiveness or platelet aggregation for platelets, plasma clot lysis time (PLT) and ELT for fibrinolysis, and blood viscosity and the TEG-ma value as overall indications. We then arranged these
Integrated Analysis of Hemorrhagic-Thrombotic Tendency

tests with normal range at the left of a scale which shows increasing thrombotic tendency towards the right.

If most of the test results lie to the right of normal, one should consider the thrombotic tendency to be strong. When the results offset each other, lying partly to the left of normal and partly to the right, a slight thrombotic tendency is indicated. Further, if most of the results lie to the left of the normal range, an anti-thrombotic condition is implied, and in these cases anti-coagulant or anti-thrombotic treatment is thought to be inappropriate. We have used this Thrombogram as a routine test in diagnosis of thrombotic tendency, and to date have performed tests on over a thousand cases. We investigated statistically the relationship between the tests and found some to be significantly correlated, and others not.

In analysis of hemorrhagic-thrombotic tendency where hemorrhagic tendency and thrombotic tendency are both present, we took a total of 15 tests, namely blood viscosity, platelet count, bleeding time, clot retraction, prothrombin consumption platelet factor-3 availability, platelet adhesive-ness, platelet aggregation, TEG-ma value, heparin resistance, prothrombin time, PTT, fibrinogen, PLT and ELT. I would like to emphasize that, because results can change in a short period of time, it is important to perform all of the tests on the same sample of blood. In the Hemorrhago-thrombogram, these tests are arranged with the normal range in the middle on a scale showing increasing hemorrhagic tendency in the upward direction, and increasing thrombotic tendency in the downward direction.

In thrombocythemia the occurrence of thrombi was unexpectedly low. In fact, sometimes hemorrhage occurred, in which case it was termed hemorrhagic thrombocythemia. Generally in this disease, decreased platelet adhesiveness is observed, along with increased prothrombin time and PTT, showing decreased coagulability. These phenomena are assumed to be involved in the occurrence of hemorrhage. The pattern of rupture called the "spintop phenomenon" is frequently observed in the TEG, and this is also thought to be due to decreased platelet adhesiveness.

On occasion, hemorrhage also develops in chronic myelocytic leukemia. In these cases the amount of fibrinogen and the TEG-ma value increase, and a decrease in platelet function, which is thought to be concerned in hemorrhage, is observed.

The TEG-ma value is closely related to the hematocrit value (Ht) of blood. When the Ht value is low, the clot becomes more elastic and the TEG-ma value is found to be high. In the patients suffering from chronic renal failure, before treatment by long-term hemodialysis, there is marked anemia and sometimes hemorrhagic tendency occurs in spite of the high TEG-ma value. Decreased platelet function, particularly decreased platelet factor-3 availability, due to the accumulation of guanidine derivatives has been cited as the cause. After hemodialysis a slight improvement in the decreased platelet factor-3 availability can be seen.

In thrombotic thrombocytopenic purpura (TTP), while a marked reduction in platelet count, prolongation of bleeding time and decreased platelet function are observed, prothrombin time, PTT and fibrinogen usually lie within the normal range, and increased fibrinolysis is also usually not detected. However, in the defibrination syndrome the decrease in fibrinogen is marked and frequently accompanied by prolonged prothrombin time and PTT and increased fibrinolysis. On occasion, only heparin resistance increases, showing traces of increased coagulation. Thrombelastogram of TTP differs in being somewhat rounded in the k-value region from that of defibrination syndrome.

In congenital cyanotic heart failure accompanied by marked polycythemia, hemorrhagic tendency is sometimes observed. Although platelet adhesiveness is increased, there is a tendency towards thrombocytopenia, prolonged bleeding time, decreased
TEG-ma value, increase prothrombin time and PTT. From these results this disease is thought to be a mild type of disseminated intravascular coagulation (DIC).

It is well known that the same kind of mild consumption coagulopathy also occurs in giant hemangioma. In a case of giant hemangioma of the liver accompanied by hemorrhagic tendency, test results showed decreased platelet adhesiveness and decreased TEG-ma value. There was some improvement on treatment.

Though the etiology of non-traumatic aseptic necrosis of the femoral head is still obscure, abnormality of platelets and coagulation have been reported in this disease. Our results have also indicated decreased platelet adhesiveness and aggregation, and since these are observed particularly in the earlier stages, the possibility of thrombus formation in the femoral head and secondary decrease of platelet aggregation is suggested.

On treatment with heparin, although decreased coagulability, as seen in the increased prothrombin time and PTT, and slightly increased fibrinolysis, as seen in the shortened PLT, were observed, the platelet aggregation was unexpectedly increased.

On testing blood samples taken immediately after and one hour after intravenous injection of 100,000 units of urokinase, together with the shortening of PLT and ELT, a slight decrease in platelet adhesiveness and aggregation was observed.

We have been testing the efficacy of platelet function inhibitory drugs, and would like to mention two of them here. Both bencyclane and melilotus-proxyphyl-line, brought about decrease in platelet adhesiveness and aggregation on intravenous injection.

In conclusion, these results confirm the need to make an overall judgement on the essential factors involved in hemorrhagic-thrombotic diseases. This kind of integrated analysis is thought to provide a useful indicator for the diagnosis and treatment of these diseases.