

1074 COMPARISON OF A NEW AUTOMATED AMIDOLYTIC ASSAY OF THROMBIN GENERATION WITH "PROTHROMBIN TIME" AND "THROMBOTEST".

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An automated method was developed for the determination of thrombin generation in citrated whole blood during activation by thromboplastin. The thrombin generated was allowed to split the chromogenic substrate Tos-Gly-Pro-Arg-pNA yielding p-Nitroaniline. The comparison with this method and "Prothrombin time" in 50 samples was significant ($r = 0,88$ $p < 0,001$) and also in 503 samples with "Thrombotest" ($r = 0,73$ $p < 0,001$). This assay may serve as a specific, precise and fast and cheaper alternative for "prothrombin time" and "Thrombotest" in large Thrombosis Services.

1075 A NEW BLEEDING MODEL: EFFECTS OF COMPOUNDS ON THE MECHANICALLY INDUCED BLEEDING LOSS OF SMALL SUBDERMAL VESSELS OF THE RAT

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Several models are described for the measurement of drug effects on bleeding. The haemostatic mechanism in large vessels is largely dissimilar from that in small vessels. Pharmacological bleeding models in which small vessels are used can be expected to be most relevant for the clinical situation, but these models have the disadvantage of a low reproducibility. Therefore, we developed a model in which reproducible bleeding is induced in small vessels. Male rats are anaesthetized with Nembutal®. The bleeding is induced by ripping off a flap of abdominal skin from the underlying tissue. The "wound" is covered with a gauze and blood loss is measured. Low doses of heparin (~350 IU/kg i.v.) which block the formation of fibrin do not affect the blood loss. However, higher doses of heparin (~700 and 1400 IU/kg i.v.) increase the blood loss significantly. Blood loss is also increased by treatment with anti-platelet serum. Acetylsalicylic acid, sulfapyrazone and Org 4122 in doses active in experimental arterial thrombosis, do not affect the blood loss. There is no agreement in literature about the effects of acetylsalicylic acid and sulfapyrazone in clinical bleeding time tests, but heparin, when given as i.v. bolus injections (7500-10000 IU) induces bleeding in quite a number of patients. Because our results are comparable to results obtained in humans and because of the good reproducibility, this test has advantages above other existing animal bleeding tests.

1076 COMPARISON OF ONE STAGE AND TWO STAGE FACTOR VIII ACTIVITY ASSAYS IN HEALTHY AND SICK SUBJECTS

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For the past several years, factor VIII assays have been performed on the same sample of plasma by the partial thromboplastin time method (PTT-VIII) and the thromboplastin generation time method (TGT-VIII) in a variety of clinical conditions. Mean (range) values for representative subject groups are given.

Group	% VIII-PTT	% VIII-TGT	Group	% VIII-PTT	% VIII-TGT
Normal adults	103(75-146)	102(80-140)	DLE-vasculitis	252(128-488)	201(130-290)
Term infants	120(70-200)	102(55-195)	Childhood nephrosis	181(100-220)	180(120-260)
Preterm infants	76(40-130)	55(38-90)	Oblig. carriers (VIII)	65 (39-106)	76 (40-130)
Sick preterms	55(40-80)	45(37-75)	von Willebrand's var.	61 (6-104)	14 (8-34)
Sickle cell dis.	236(90-600)	190(55-325)	Hemophilics-transfused	33 (6-118)	43 (17-140)

The methods compare well in inflammatory and metabolic diseases like diabetes and nephrosis. However, higher PTT-VIII values are seen in vasculitis, sickle cell disease, the hemolytic-uremic syndrome, thrombosis, and DIC. Lower values for VIII activity were seen by VIII-TGT in a group of vWd variant patients. Obligate carriers of hemophilia were best detected by the VIII-PTT. Lower than expected values for factor VIII were demonstrated in intensively transfused hemophiliacs by the VIII-PTT. These studies indicate that the level of factor VIII procoagulant activity is significantly different in many clinical situations depending upon the method of measurement.