SKIN NECROSIS COMPLICATING ORAL ANTICOAGULANT THERAPY. H.J.Krzywanek. Department of Angiology, Medical Center, University Frankfurt a.M., Germany.

Since the first report in 1943 far more than 100 cases of skin necrosis as a complication of oral anticoagulant therapy have been reported, mainly in European countries. Breast, thigh, legs and abdomen are the predominant sites of the lesions, obese women are most frequently affected. 10 cases which we observed over the last ten years are presented and the etiology is discussed. The common feature of our patients is a history of fever, probably caused by a bacterial or viral infection, treated with a variety of antibiotics. A complicating or preexisting thrombosis or thrombophlebitis of the leg leads to the initiation of oral anticoagulant therapy. Regularly on the 4th (3.-5.) day of anticoagulant treatment the skin necrosis develops within hours. We suggest that the administration of antibiotics and perhaps also the infectious process are predisposing factors. The high loading dose at the beginning of coumarin treatment and an abnormal sensitivity of the patient seem to be other important etiologic factors for coumarin necrosis. These points are substantiated by the facts that skin necrosis occurs only in the first days after the start of oral anticoagulant therapy, and by one of our patients who developed another skin necrosis when coumarin therapy was repeated several years later. Oral anticoagulant therapy should not be initiated when antibiotics must be given at the same time. In case anticoagulant treatment is necessary during antibiotic therapy we propose the administration of heparin instead of using coumarin derivatives.

THE EFFECTS OF DIFFERENT ROUTES OF ADMINISTRATION AND INJECTION SCHEDULES OF THROMBOPOIETIN ON PLATELET PRODUCTION IN ASSAY MICE. T.P. McDonald. University of Tennessee Memorial Research Center, Center for the Health Sciences, Knoxville, Tennessee, U.S.A.

Mice have been used in several studies for the assay of a thrombocytopoiesis-stimulating factor (TSF or thrombopoietin). Little information however, is available on the optimum assay time or injection schedule. Therefore, the present work compares the % ^{35}S incorporation into platelets of mice in rebound-thrombocytosis after subcutaneous (sc) and intraperitoneal (ip) injections of TSF-rich preparations with different injection schedules. For production of thrombocytopenia, mice were given a single ip injection of rabbit anti-mouse platelet serum 5 days before injection of TSF-rich test materials. TSF administered sc or ip resulted in almost identical % ^{35}S incorporation values. Various doses of TSF injected sc 4 times over a 2 day period to thrombocytotic mice gave a linear dose-response. Also, this injection schedule gave the greatest response to the same total dose of TSF when compared to other injection schedules. Single injections of TSF did not give as great a response as did multiple injections using the same total dose. Results of this work indicate that for maximum % ^{35}S incorporation values, TSF-rich materials should be administered in multiple injections to mice, either sc or ip, over a period of approximately 2 days.

TIME AND TEMPERATURE DEPENDENT CHANGES OF PLATELET AGGREGATION. K.Breddin, H.J.Krzywanek. Department of Angiology, Medical Center, University, Frankfurt/M., Germany.

ADP-, collagen and epinephrine-induced aggregation change markedly if citrate blood or PRP are kept at different incubation temperatures or/and if the time interval between blood sampling and testing varies. With a growing time interval the response of PRP to ADP, collagen or epinephrine increases. Desaggregation after ADP-aggregation decreases with time. If PRP is incubated at 40°C or 10°C aggregation is increased in comparison with room temperature. At 37°C aggregation is markedly inhibited. This inhibitory effect is almost fully reversible several hours after blood sampling. Corresponding results were obtained with PAT III, measuring spontaneous aggregation tendency. Morphologic platelet changes show some correlation with the time and temperature dependent changes of the aggregation pattern. In clinical studies the time interval between blood sampling and testing and the incubation temperature of PRP should be strictly controlled. If enhanced platelet aggregation is to be studied the time interval between venepuncture and performance of the test should be 30 - 60 min for ADP- or collagen-induced aggregation and between 90 and 360 min for PAT III. PRP should always be kept at 20 - 25°C.