absence of secondary aggregation. Either can be overcome by increased amounts of ristocetin. Gel-filtered and albumin-density gradient washed platelets have also been investigated. A similar but transient inhibition has also been observed in some normal subjects due to an unknown cause. These results are important when considering the diagnosis of von Willebrand's disease.

J. L. David and F. P. Herion (Institut de Médecine, Université de Liège, Belgique): **Response of Normal and Pathological Platelets to Heparin Added in Vitro and in Vivo. (83)**

Heparin one unit/ml added in vitro to normal citrated PRP increases the platelet aggregation induced by ADP or Adrenaline with regard to aggregation measured in citrated PRP without heparin. This phenomenon is accompanied by an increase of the release reaction of ^{14}C-5HT, ATP and ADP. In the same experimental conditions, pathological platelets ("aspirin-like syndrome") respond by an increased aggregation without release reaction. This effect of heparin on normal or pathological platelet aggregation is inhibited by ASA or by Dipyridamole. – In citrated PRP obtained from blood of heparinized normal subjects, platelet aggregation and release reaction of platelets are increased with regard to their response tested before heparinization. Addition of ASA or Dipyridamole in PRP inhibits the effects of heparinization. – In two subjects with a platelet disease and a mild bleeding tendency, heparinization in vivo does not lengthen the bleeding time but increases the aggregation without any release reaction. In vitro addition of ASA or Dipyridamole inhibits the increase of aggregation observed in absence of release reaction. – Besides their theoretical aspects concerning the mechanism of inhibition of platelet aggregation by ASA and Dipyridamole, these observations suggest the possible benefit of antiaggregant drugs for subjects treated by heparin.

J. M. Whaun, J. E. Dundas and H. Clarke (University of Calgary, Calgary, Alberta, Canada): **Daunomycin and Platelet Function. (84)**

Daunomycin, an antimetabolite antibiotic used in the treatment of acute leukemia, is highly cytotoxic to both normal and malignant cells. Thrombocytopenia occasionally noted with its use, has usually been attributed to its toxic effect on the bone marrow. Citrated platelet-rich plasma (PRP) from normal volunteers was tested in vitro in the aggregometer after addition of either aggregating agent, collagen, (0.083 mg/ml PRP), or varying concentrations of daunomycin, or both. Other aliquots were exposed to daunomycin or saline for 90 seconds before fixing in glutaraldehyde. The remainder, labelled with 0.5 μM 2-^{14}C-5-hydroxytryptamine binoxalate (^{14}C-5-HT), 27.5 c/mole for 15 minutes, was tested for ^{14}C-5-HT release before and after exposure (90 secs. 37° C) to collagen of final concentration 0.04 mg/ml.

At a concentration 0.001 mg/ml PRP, daunomycin was associated with decreased response of platelets to collagen with decreased ^{14}C-5-HT release. At 0.02–0.04 mg/ml daunomycin was associated with vacuole formation, loss of dense bodies as well as platelet lysis as well as liberation of newly absorbed ^{14}C-5-HT. Electron micrographs of platelets exposed to higher doses of daunomycin showed platelet swelling, vacuole formation, swollen mitochondria and granules and interruption of the trilaminar membrane.

G. J. Johnson and J. G. White (Veterans Administration Hospital and The University of Minnesota Medical School, Minneapolis, Minnesota, U.S.A.): **Platelet Dysfunction Induced by Parenteral Administration of Carbenicillin and Ticarcillin. (85)**

Carbenicillin treatment of humans has resulted in impaired platelet function occasionally accompanied by hemorrhage. Because of their therapeutic potential as anti-thrombotic agents, we have studied carbenicillin (CARB) and ticarcillin (α-carboxy-3-thienylmethyl penicillin) (TIC) effects on platelet function in the dog. Studies of platelet aggregation (AGG), adhesiveness (ADS), factor 3 availability (PF 3), bleeding time (BT), electron microscopy (EM), and serotonin (5HT) and adenine nucleotide (AN) content were performed sequentially in dogs given CARB or TIC. Progessive impairment of platelet