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QUALITATIVE DEFECT IN THE FACTOR VIII/VON WILLEBRAND FACTOR PROTEIN (FVIII/VWF) IN A FAMILY WITH HEREDITARY HEMORRHAGIC TELANGIECTASIA (HHT). C. Conlon, R. Weinger, J. Moake, C. Rudy. Medical Service, Boston VA Medical Center, Boston University School of Medicine, Boston, MA., USA.

A 63 year old man with HHT has a lifelong history of recurrent epistaxis and a 6 year history of gastrointestinal bleeding which required frequent transfusions. He had a normal prothrombin time, activated partial thromboplastin time, thrombin time, template bleeding time, platelet count and platelet aggregation studies. Factor VIII-coagulant activity, factor VIII-VWF and factor VIII-VWF related antigen levels were elevated. On two-dimensional crossed immunoelectrophoresis (2D-CIE) his plasma FVIII-VWF antigen had abnormal, anodal mobility on repeated testing of different plasma samples. Patient platelet-rich plasma (PRP) did not agglutinate in response to ristocetin concentrations lower than required to agglutinate normal PRP, as is the case in type IIB von Willebrand's disease. However, binding of patient plasma FVIII-VWF antigen to normal formalin-fixed platelets occurred at lower ristocetin concentrations than required to induce binding of normal plasma FVIII-VWF antigen. Similar clinical and laboratory features were present in his 61 year-old clinically affected sister, but not in his unaffected brother. Because of the abnormal 2D-CIE, 10 units of normal cryoprecipitate were infused. Fifteen minutes later, 2D-CIE of patient plasma FVIII-VWF antigen was normal; by 8 hours mobility was abnormally rapid again. During the next weeks, his RBC transfusion requirement was not affected by infusions of cryoprecipitate (6 units) three times weekly, or by daily ε-aminocaproic acid (24 grams). Because glucocorticoids suppress endothelial cell synthesis of the anti-aggregation substance, PGI_2, he was given a trial of daily prednisone (20 mg.). Concurrently, his RBC transfusion requirement decreased by ~75%. HHT (with abnormal endothelial cell proliferation) in this family is associated with a qualitative defect of plasma FVIII/VWF protein and, possibly, with prednisone-responsive excessive local production of PGI_2.

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ORAL BLEEDING IN HEMOPHILIA: A 21 YEAR COMPOSITE. A. Sonis, W.A. Andes, B. Smith, Louisiana State University School of Dentistry, Tulane Medical School, Ochsner Foundation Hospital, Children's Hospital of New Orleans,New Orleans,Louisiana, U.S.A.

The charts of 132 patients with proven factor VIII deficiency were analyzed for severity of disease, mean age, mean age at diagnosis, and number of patients diagnosed following a bleeding episode, In addition, the frequency of bleeding episodes requiring factor infusion was determined for a single calendar year. Infusions for dental care (i.e. restorations, extractions) were excluded from the study. Severe and moderate hemophiliacs comprised 71% of the patient's studied. Their mean age was 27 years and their mean age when a bleeding disorder was suspected was under 1 month. Mild hemophiliacs comprised 27% of the patients studied. Their mean age was 27 years and their mean age when a bleeding disorder was suspected was 8 months. Persistent oral bleeding resulted in the diagnosis of hemophilia in 9% of the patients. None of these patients were severe hemophiliacs. The group diagnosed as a result of persistent oral bleeding was comprised of 11 mild and 1 moderate hemophiliacs. This constituted 29% of all the mild hemophiliacs and 2% of all the moderate hemophiliacs. The average annual frequency of bleeding episodes per patient requiring factor was as follows: severe-24 infusions of which were for oral bleeds, moderate-21 infusion of which were for oral bleeds, mild-16 infusions for which were for oral bleeds. The anatomical distribution of oral bleeds requiring infusion revealed the lips most frequently involved (48.5%) followed by the tongue (35.3%), buccal mucosa (15.4%), gingiva and palate (0.9%). The results of this study suggest that mild hemophiliacs are diagnosed at a later age than moderate and severe hemophiliacs, and that 29% of mild hemophiliacs are diagnosed as the direct result of an oral bleed. In view of these findings, a persistent oral bleed should alert the physician or dentist to a possible bleeding disorder.

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A MULTIDISCIPLINARY APPROACH TO HEMOPHILIA AT A NEW REGIONAL CENTER: HOW EFFECTIVE IS IT? W.A. Andes, W.B. Smith, K. Wulff, K. Ohene-Frempong, A. Sonis, O. Edmunds. The Louisiana Comprehensive Hemophilia Care Center, New Orleans, LA, USA

This study reports data on 74 patients initially evaluated for bleeding disorders at a one year-old hemophilia center. These patients represent a majority of 100 patients currently using any replacement therapy in the state's hemophilia program. Thirty-five percent of the patients were self-referred, 45% professional-referred, and 20% came to the center through advice from the state NHF Chapter. Diagnoses established were factor VIII deficiency (65%), Christmas disease (19%), von Willebrand's disease (10%), factor XI deficiency (1 patient), and severe carrier status for factor VIII (6%). Factor VIII inhibitors were found in 7 patients. Several patients did not know their deficient factor, most did not know their inhibitor status, and only 2 patients knew that they had inhibitors. Approximately 50% of the patients were receiving adequate replacement therapy prior to being seen. Care in 5 patients has not improved after their center visit (1 died, 1 is retarded, 2 resist advice or therapy in a rural area, and 1 generally rejects therapy for bleeding for her severe von Willebrand's disease). Home therapy was available to 32% of patients when initially seen, and 21% more went on home therapy later. A startling number of patients (20% of all) required replacement therapy for untreated bleeds which began within 12 hours prior to a center visit, although 86% of the patients travelled by auto to the visit. Data on 68 patients suggests that they spend an average of $6,500 per year on factor concentrate. Since the immediate family averaged 5.3 persons and the mean income was only $12,500, the burden of the disease was great. Although at least 30% of patients are receiving improved care since their initial center visit, several patients do not yet avail themselves of resources available in this region. Only long-term, even relentless efforts will correct some less than optimal aspects of therapy and such efforts are being made.

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COMBINED FACTOR VIII AND PLASMA EXCHANGE THERAPY IN THE MANAGEMENT OF PATIENTS WITH FACTOR VIII INHIBITORS. **R.T.Wensley, R.F.Stevens and A.M.Burn. University Department of Clinical Haematology, Manchester Royal Infirmary, England.**

Five patients with Haemophilia A and Factor VIII inhibitors and three patients with spontaneous Factor VIII inhibitors presented with severe or life-threatening haemorrhage. All, except one, received intermittent high dose human Factor VIII therapy combined with one or more plasma exchanges. The exception was a patient with spontaneous Factor VIII inhibitors who was plasma-exchanged without receiving Factor VIII. The five Haemophilia A patients showed a uniformly good clinical response to treatment with complete resolution of their bleeding episodes. Their inhibitors were reduced to a level approaching zero and adequate plasma Factor VIII levels were achieved. In contrast, the three patients with spontaneous Factor VIII inhibitors failed to show any clinical response to therapy. They had measurable plasma Factor VIII levels before the Factor VIII therapy, but the administered Factor VIII produced no additional increment. Their inhibitor levels were only minimally altered by therapy. Studies of the inhibitors from the haemophiliacs showed complete Factor VIII neutralisation in incubation mixtures, but inhibitor plasmas from the spontaneous cases failed to completely neutralise the admixed Factor VIII. It is postulated that in haemophiliacs with antibodies, replacement therapy is associated with the formation of stable immune complexes which remain in the intravascular space and are removed at subsequent plasma exchange. These complexes do not show coagulant or anticoagulant activity. However, in non-haemophiliacs with acquired Factor VIII inhibitors, weaker association of Factor VIII and antibody in the immune complexes may account for the measurable plasma Factor VIII activity, and also enable the dissociated antibody to diffuse out of the intravascular space and hence be unavailable for removal by plasma exchange.