coincidentally or in relationship to the marrow infusions is not clear. Since then, the use of allogeneic bone marrow infusions has been well-nigh discarded for the induction of transplantation, chiefly because of the difficulties involved with suppression of the rejection phenomenon, as well as for the possibility of development of the graft-vs.-host reaction. Of the recovered cases referred to above, three patients have subsequently (as of June 1967) developed the characteristics features of PNH. Originally it occurred to us that this unusually high incidence of PNH might have some obscure relationship to the infused allogenic marrow, but since PNH may follow aplastic anemia *without* the mediation of introduced marrow, this idea did not appear very likely.

During a recent trip to the Far East where aplastic anemia appears to be unduly prevalent (perhaps because the use of chloramphenicol is relatively uninhibited), it was evident that the incidence of PNH was also unduly high. Thus, in Manila, the Philippines, Dr. Allen Caviles of the Philippines General Hospital informed me that he had observed 71 cases of aplastic anemia in three years, 53 of which had been subject to follow-up; one of these had developed PNH. In the same period, nine cases of PNH had also been observed, five of them having been previously diagnosed as aplastic anemia. Dr. Tien-tse Hwang in Taipei, Taiwan, reported that he had observed 10–14 new cases of aplastic anemia annually, as well as seven cases of PNH at the two hospitals where he worked, one of them the large National Defense Hospital. Among the first 10 cases of hypoplastic anemia he had seen in 1966, one of them subsequently developed PNH. From these several observations, the factor of coincidence for the two apparently disparate conditions of aplastic anemia and PNH seems unlikely.

Dacie and Gilpin [2] were the first to broach the possiblity that PNH and aplastic anemia might be related. This was subsequently further emphasized by Dacie [3, 4] and particularly in Lewis and Dacie's recent paper. Of 46 cases of aplastic anemia, seven had a positive Ham test for PNH and two actually developed clinical evidence of the disease. Conversely, of 60 patients with PNH, 15 showed aplastic anemia sometime during their course. In two such cases of PNH we observed, the acid hemolysis tests became negative when aplastic anemia developed. In the cases presenting first as pancytopenia-hypoplasia, then later developing hemoglobinuria, it has been customary to stress PNH as the real or fundamental condition and the previously apparent hypoplasia as simply a pre-PNH manifestation.

Names are important chiefly from the symbolic standpoint; they project images! They might be described as "bullets" profoundly affecting our response to a given set of circumstances. Thus, the term "PNH" invokes the concept of a peculiar form of hemolytic anemia in which hemoglobinemia (and hemoglobinuria) develop nocturnally. This puts the disease into the category of the various hemolytic anemias and the hemoglobinurias, which are characterized (among other features) by shortening of the red cell survival time, an active bone marrow with blood reticulocytosis, hemoglobinemia, and bilirubinemia. It has been shown that the shortened red cell survival in PNH is due to an intrinsic defect of the red cell.[5, 6] Such defects are almost always of genetic origin. However, in PNH there is every indication that the disorder is an acquired one. How then can aplastic anemia and PNH be related?

Pancytopenia in PNH has been noted since the early writings on this disease. Thus Crosby,[7] pointing to the usual leukopenia and thrombocytopenia—i.e., pancytopenia—suggested that all the bone marrow cells were involved in the disease. It is the red cell defect, however, that gives this condition its distinctive quality. Surely, the various factors in plasma which could be implicated in the actual hemolysis of the red cells (complement, "properdin," etc.) are of little importance as compared with the red cell defect. Actually, PNH may be thought of as an acquired defect of the erythron occurring in a previously healthy individual. Once having developed, this defect is apparently self-perpetuating and ecologically

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[3] Dacie, J. V.: Paroxysmal nocturnal hemoglobinuria. Proc. Roy. Soc. Med. 56: 587, 1963.

[4] Lewis, S. M., and Dacie, J. V.: The aplastic anemia—paroxysmal nocturnal haemoglobinuria syndrom. Brit. J. Haemat. 13: 236, 1967.

[5] Hellem, A. J., and Skaug, O. E.: Paroxysmal nocturnal hemoglobinuria. II. Permeability and phosphate turnover in the red blood cells. Scand. J. Clin. Lab. Invest. 7: 121, 1955.

[6] De Sandre, G., Ghiotto, G., and Mastella, G.: L'acetilcolinesterasi eritrocitaria. II. Rapporti con le malattie emolitiche. Acta Med. Patav. 16: 310, 1956.

[7] Crosby, W. H.: Paroxysmal nocturnal hemoglobinuria: Relation of clinical manifestations to underlying pathogenic mechanisms. Blood 8: 769, 1953.