OCULAR FINDINGS IN THE HERMANSKY-PUDLAK SYNDROME*

BY *Natalio J. Izquierdo,* MD (BY INVITATION),
William Townsend, MD AND
Irene E. Maumenee Hussels, MD

ABSTRACT

Background: The Hermansky-Pudlak syndrome (HPS) is defined by the autosomal recessively inherited triad of tyrosinase-positive oculocutaneous albinism, bleeding diathesis and accumulation of ceroid in tissues. Late complications include: interstitial pulmonary fibrosis; inflammatory bowel disease; and renal failure.

Patients and Methods: We undertook a non-concurrent prospective study of 55 Puerto Rican patients with HPS (age range 1 to 54 yrs; mean = 19.7 yrs). These patients had a comprehensive ocular examination and a systemic evaluation for HPS.

Results: Visual acuities ranged from 20/50 to 5/200. All patients had nystagmus. Forty-three patients had strabismus; esotropia was found in 24 patients; exotropia in 18 patients; and one patient had hypertropia. Posterior embryotoxon occurred in 15 patients and Axenfeld anomaly in 4 patients. Iris pigmentation varied from minimal to almost completely normal. Three patients had cataract formation. The retina was typically albinotic with macular hypoplasia. All patients had cutaneous albinism, bleeding diathesis and various systemic manifestations as part of HPS.

Conclusion: Ocular findings in HPS include reduced visual acuity, congenital nystagmus, strabismus and cataract. Diagnosis of the syndrome ought to be made preoperatively to help minimize the potential complications associated with bleeding diathesis at the time of extraocular muscle and intraocular surgery in patients with HPS.

* From the Department of Ophthalmology, Medical Sciences Campus, University of Puerto Rico, San Juan (Dr. Izquierdo and Dr. Townsend), and the Wilmer Ophthalmological Institute, The Johns Hopkins Medical Institutions, Baltimore (Dr. Maumenee Hussels). Supported in part by the Laura Kriebel and the Walter Edel Funds of the Johns Hopkins Center for Hereditary Eye Diseases.

INTRODUCTION

The Hermansky-Pudlak syndrome (HPS) consists of the autosomal recessively inherited triad of tyrosinase-positive oculocutaneous albinism (ty-pos OCA), bleeding diathesis, and deposition of a ceroidlike material.[1] Patients with HPS have variable deficiencies of cutaneous pigmentation.[2,3] The bleeding diathesis in patients with the syndrome is related to deficiency of dense bodies in platelets and abnormal platelet aggregation.[3-7] Patients with HPS also have a multisystem deposition of a ceroidlike material in peripheral tissues including lungs, gastrointestinal epithelium, renal tubular epithelium, and cardiac muscle. This leads to development of interstitial pulmonary fibrosis,[8-10] granulomatous colitis,[11] renal failure,[12] and cardiomyopathy.[12] Ocular manifestations in patients with HPS have been outlined in previous studies.[13-15] We expand on the ocular findings and report the surgical complications observed among 55 patients with HPS.

PATIENTS AND METHODS

We undertook a nonconcurrent prospective study of 55 patients with HPS. These patients had had a comprehensive ocular examination by one of the authors during the previous 4 years. All patients in this study were Puerto Ricans with ty-pos OCA. The diagnosis of HPS was confirmed at the University of Minnesota or the Puerto Rico Medical Center by demonstration of deficiency of platelet dense bodies.

A history of visual function, photosensitivity, and previous surgery was obtained. Best-corrected visual acuity for each eye was measured with Snellen and/or Early Treatment Diabetic Retinopathy Study (ETDRS) charts. A +5.00 spherical lens was used for occlusion of the contralateral eye. Amblyopia was defined as a difference of two or more lines of best-corrected visual acuity on the Snellen chart. Motility evaluation included assessment of nystagmus, versions, and muscle balance for distance and near.

The anterior segment was examined for anomalies such as prominence of Schwalbe's line, iris processes, iris transillumination, and lens opacities. Gonioscopy was done using the Zeiss or Sussman gonioscopy lens. Transillumination defects were compared with standard photographs described by Summers and coworkers[14]: grade 0, normal iris pigmentation; grade I, punctate transillumination defects located in the periphery of the iris; grade II, reduced iris pigment with punctate iris transillumination in variable locations; grade III, minimal pigment often clumped on the collarette expressed as almost complete iris transillumination; and grade IV, no iris pigmentation leading to full iris transillumination. Intraocular pressures were measured with a Goldmann or Perkins applanation tonometer.

Pupils were dilated using tropicamide 0.5% or cyclopentolate hydrochloride 1% drops. Retinal evaluation included indirect ophthalmoscopy

and slit-lamp examination with a 60-diopter lens. Foveal hypoplasia was defined as absence of the foveal depression and reflex. Macular transparency was graded according to the description of Summers and coworkers[14]: grade I, choroidal vessels easily visible in the transparent macular area; grade II, choroidal vessels visible in macula but somewhat indistinct owing to translucent-appearing retinal pigment epithelium (RPE); and grade III, choroidal vessels not visible in macula owing to opaque appearance of the RPE.

RESULTS

Fifty-five Puerto Rican patients with HPS were evaluated. Ages ranged from 1 to 54 years (average, 19.7). There were 25 male and 30 female patients. There were three sib pairs in the 52 pedigrees examined. All patients had white skin with varying numbers of freckles.

All patients had photosensitivity. Subjective photosensitivity varied from minimal to severe. Six patients had minimal, 28 patients had moderate, and 21 patients had severe photosensitivity.

Best-corrected visual acuities in the better eye ranged from 20/50 to 5/200. The visual acuities were equal in both eyes in 26 patients (Snellen or ETDRS charts). Thirty-nine of 55 patients had a difference of one or more lines. Five patients had amblyopia, defined as a difference of two or more lines between the two eyes. None of the patients had received occlusion therapy. Thirty-four of 55 patients had best corrected visual acuities equal to or less than 20/200. Refractive errors in diopters of spherical equivalent ranged from -10.00 sph to +6.50 sph (average, +0.02) and from -9.00 sph to +6.50 sph (average, +0.05) in the right and left eye, respectively. Twenty-five patients had compound with the rule astigmatism. One patient had compound against the rule astigmatism. Three patients used a telescopic binocular visual aid. This improved their visual acuity to 20/30 as measured on the Snellen chart.

Forty-three patients had strabismus (Fig 1). Eighteen patients (32.7%) had exotropia (range, 7 to 50 prism diopters; average, 18.4Δ); 24 patients had esotropia (42.7%) range, 10 to 50 prism diopters; average, 18.4Δ); and one patient had hypertropia (1.8%). No strabismus could be detected in 12 patients (21.8%) with use of the prism cover test. Two patients had had previous stabismus surgery. One of the patients described profuse serosanguinous exudation in the first 24 hours postoperatively. Four patients had spontaneous head posture, and all patients had horizontal nystagmus.

Slit-lamp examination showed posterior embryotoxon in 15 patients. Small strands of iris were adherent to the corneal periphery in 4 patients. Iris transillumination findings are depicted in Fig 2. Ten patients had almost completely normal iris pigmentation (grade I), with only scattered peripheral transillumination defects. Twenty-one patients had irregularly located transillumination defects (grade II). Twenty-three patients had mini-

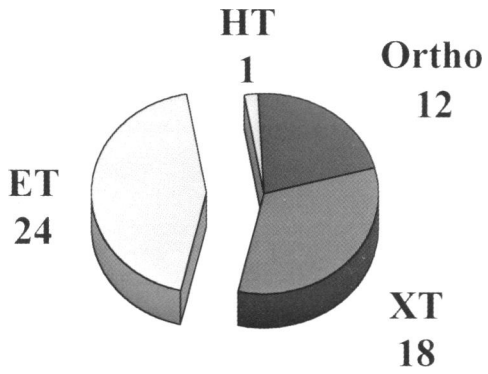

FIGURE 1
Number of patients per type of strabismus: 24 patients had esotropia (ET), one patient had hypertropia (HT), no strabismus could be detected in 12 patients (ortho), and 18 patients had exotropia (XT).

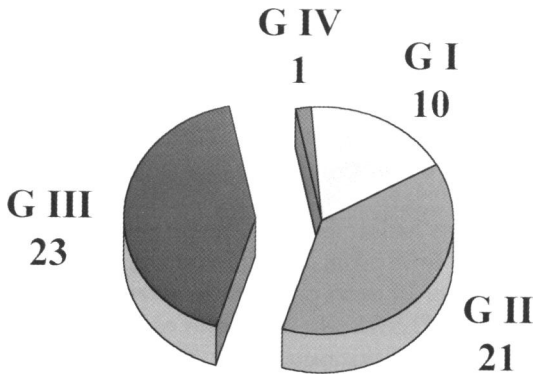

FIGURE 2
Number of patients per iris transillumination grading: 10 patients had grade I (punctate transillumination defects located in periphery of iris); 21 patients had grade II (reduced iris pigment with punctate iris transillumination in variable locations); 23 patients had grade III (minimal pigment often clumped on collarette leading to almost complete iris transillumination); and one patient had grade IV (no iris pigmentation leading to full iris transillumination).

mal pigmentation (grade III) at the collarette. One patient had total iris transillumination (grade IV). Eight of 23 (34.8%) patients with markedly reduced iris pigmentation (grade III) reported severe photosensitivity. Four of the 10 patients (40%) with grade I iris pigmentation reported severe photosensitivity.

Three patients had cataract formation. One patient had previously undergone bilateral extracapsular cataract extraction. She had sustained intraoperative bleeding. This patient had pseudophakia in the right eye and aphakia on the left. The second patient had bilateral total cataracts. The latter underwent phacoemulsification through the clear cornea with intraocular lens implantation by one of the authors. Neither of these two patients had used systemic steroids. One patient had bilateral mild posterior subcapsular cataracts and reported use of systemic steroid therapy.

Two patients had bilateral intraocular pressures above 21 mm Hg.

The optic nerve heads were pale in all patients, but their contours and cups were normal. All eyes showed complete lack of foveal development. The macular appearance in these patients is depicted in Fig 3. Eleven patients (20%) showed a grade I transparent macula; 34 patients (61.8%) had a grade II translucent macula; and 10 patients (18.2%) showed a grade III

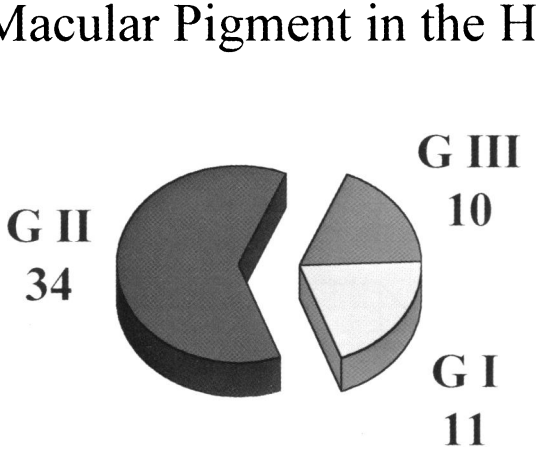

FIGURE 3

Number of patients per macular transparency grading: 11 patients had grade I (choroidal vessels easily visible in transparent macula); 34 patients had grade II (choroidal vessels visible in macula but somewhat indistinct due to translucent-appearing retinal pigment epithelium; and 10 patients had grade III (choroidal vessels not visible in macula due to opaque appearance of retinal pigment epithelium.

opaque macula.

As depicted in Fig 4, 1 of 11 patients (9.1%) with a transparent (grade I) macula had visual acuities better than or equal to 20/160 in their better eye. Eight of 34 patients (23.5%) with translucent (grade II) macula had visual acuities better than or equal to 20/160 in their better eye. Four of 10 patients (40%) with an opaque (grade III) macula had visual acuities better than or equal to 20/160 in their better eye.

Six patients had symptomatic pulmonary fibrosis. Two patients had granulomatous colitis, and 12 patients had gastrointestinal symptoms. Frequent bruising occurred in 22 patients.

DISCUSSION

Ocular findings in patients with HPS vary. In our series, best corrected visual acuities ranged from 20/50 to 5/200 in the better eye. Thirty-four of the 55 patients (61.8%) examined were legally blind with a visual acuity equal to or less than 20/200 in their better eye. One of our patients had a best corrected visual acuity of 20/50. Five patients had amblyopia. Therefore, due to large phenotypic variability, visual acuity cannot be predictable in children with HPS.

In our series, refractive errors varied. Twenty-five patients had compound astigmatism with the rule, the most common type of astigmatism found in patients with the syndrome. Three patients used a telescopic aid, which markedly improved their visual acuities. Low-vision aids facilitated mainstream education in patients with HPS.

Subjective photosensitivity varied. Forty-nine patients complained of

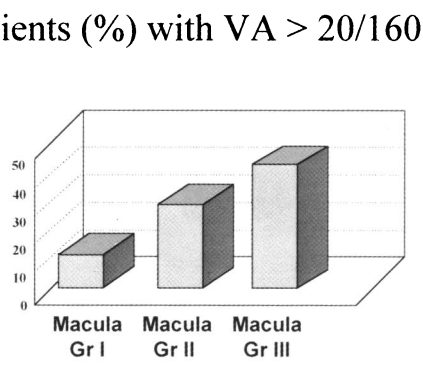

FIGURE 4

Percent of patients with visual acuities equal to or better than 20/160 in their better eye: 9.1% of patients with transparent macula (grade I); 23.5% of patients with macular translucency (grade II); and 40% of patients with opaque macula (grade III).

moderate to severe light sensitivity.

Strabismus is a common finding in all forms of albinism. In our study, esotropia was the most frequent (43.7%) type of strabismus (Fig 1). Eighteen patients (32.7%) had exotropia, and one patient had a left hypertropia (1.8%). No strabismus was found in 11 patients (21.8%). Two patients with HPS had a history of previous strabismus surgery. One of the patients reported profuse serosanguinous exudation following strabismus surgery. All patients had horizontal nystagmus.

Previous studies reported anterior segment abnormalities in patients with OCA. In our series, 15 patients had posterior embryotoxon and 4 patients had iris processes adherent to anterior Schwalbe's line. It has been suggested that the association is not coincidental.[14,16] Two patients had elevated intraocular pressures. Further studies are needed to assess the prevalence of glaucoma in patients with ty-pos OCA.

Iris pigmentation varies in patients with HPS. In our study, patients most commonly had minimal iris pigmentation located around the pupillary area (23 patients) (Fig 2). Only one patient (aged 25 years) had complete iris transillumination (no pigment on iris). We found no correlation between the degree of photosensitivity and iris pigmentation. In our series, older patients had more pigmented irides than younger patients. It has been suggested that ocular pigment increases with age. Long-term evaluation of patients with HPS will help to answer this question.

In our study, cataractous lens changes had occurred in three patients. Only one patient reported use of systemic steroids for the presumptive diagnosis of systemic lupus erythematosus. The second patient had mature cataracts at age 25 years. The third patient's age was 52 years at the time of cataract surgery. Systemic steroids are commonly used for the treatment of pulmonary fibrosis in patients with HPS, and therefore systemic steroids may lead to an increase in the observed frequency of lens opacities in patients with the syndrome.

Retinal hypopigmentation characterizes patients with OCA. The retinal periphery is albinotic and the fovea is always hypoplastic in patients with OCA. Macular transparency varies in patients with HPS. In our series, the patients had most commonly a translucent appearance of the RPE (61.8%) with visibility of choroidal vessels in the macular area (Fig 3). This result is compatible with the previous findings of Summers and coworkers.[14] Macular transparency occurred in 20% of patients. Macular vessels were not visible in 18.2% of the patients owing to pigmentation of the retinal pigment epithelium. In our series, a total of 13 patients had best corrected vision equal to or better than 20/160 in their better eye. Of these, 1 of 11 patients (9.1%) had a transparent macula (grade I); 8 of 34 (23.5%) had macular translucency (grade II); and 4 of 10 (40.0%) had an opaque macula (grade III). Increased macular pigmentation correlated with better visual acuities (Fig 4).

Frequent bruising and bleeding after surgical procedures occur as part of the bleeding diathesis found in patients with HPS. In our study, 22 patients complained of frequent bruising. Bleeding is the leading cause of mortality in patients with HPS. Platelet function should be evaluated prior to surgery in all patients with ty-pos OCA to rule out HPS. A preoperative hematology consultation is advisable for all patients with HPS. Preoperative use of desmopressin,[17] platelet transfusion, or cryoprecipitate infusion[18] should be considered for prolonged bleeding time. Platelet concentrate should be available in case bleeding occurs during or after surgery.

In our series one patient had a history of intraoperative bleeding during an extracapsular cataract extraction. Another patient had an uncomplicated phacoemulsification with intraocular lens implantation through clear cornea. Intraoperative irrigation with refrigerated balanced salt solution and epinephrine may have helped prevent intraocular hemorrhage. However, this patient had bleeding associated with subconjunctival injection of antibiotics. A third patient complained of bleeding during the first 24 hours following extraocular muscle surgery.

We do not recommend retrobulbar blocks for patients with HPS. If subconjunctival, peribulbar, and/or retrobulbar injections are needed, the patient requires close monitoring postoperatively to detect orbital hemorrhage. Aspirin and indomethacin are contraindicated in patients with HPS, since they exacerbate the platelet abnormality.

In our series, 6 patients had symptomatic pulmonary interstitial fibrosis, 2 had granulomatous colitis, and 12 had gastrointestinal problems. Interstitial pulmonary fibrosis[8-10] and chronic inflammatory bowel disease[11] have been previously reported in patients with HPS. Pulmonary fibrosis is the major cause of morbidity in patients with HPS.[12] Pulmonary consultation is advisable in patients who need endotracheal anesthesia.

Patients with HPS have cutaneous hypopigmentation.[19] Hair and skin pigmentation augment as patients grow older. Skin coloring varies between patients. In our series, patients had white skin with freckles. Hair color varied from light blonde to light brown and was darker in male patients. HPS is most prevalent in Puerto Rico and southern Holland.[3] However, 7 million Puerto Ricans and their progeny live in the continental United States. HPS is an autosomal recessively inherited disease, and some pedigrees show pseudodominance[12] owing to consanguinous marriages in a population with a high gene frequency.

Genetic linkage analysis of HPS to the tyrosinase gene was done in a Puerto Rican family with HPS at the Genetic Laboratories of the Johns Hopkins Center for Hereditary Eye Diseases. Results using the LIPED program[20] showed a LOD score of -2.033. It is unlikely that the mutation in this family occurred within the tyrosinase gene (Izquierdo NJ, Zhu DP, and Maumenee IH. Unpublished data). Further studies are needed to assign the gene responsible for HPS.

We were unable to perform visual evoked potentials and fluorescein angiography. Previous studies showed abnormal decussation of the optic tracts in patients with OCA.[14,21,22]

The diagnosis of oculocutaneous albinism is easily established by ophthalmologists. However, HPS needs to be considered in the differential diagnosis of patients with ty-pos OCA, based on patients' history of bleeding, with or without a history of systemic manifestations due to deposition of ceroidlike material in peripheral tissues. Puerto Rican or Dutch ancestry should alert physicians to the possibility of HPS. Preoperative diagnosis of the syndrome will help minimize the potential complications resulting from bleeding diathesis and pulmonary fibrosis at the time of extraocular muscle and intraocular surgery in patients with HPS.

REFERENCES

1. Hermansky F, Pudlak P: Albinism associated with hemorrhagic diathesis and unusual pigmented reticular cells in the bone marrow: Report of two cases with histochemical studies. *Blood* 1959; 14:162-169.
2. Palmer DJ, Miller MT, Rao S: Hermansky-Pudlak oculocutaneous albinism: Clinical and genetic observations of six patients. *Ophthalmic Paediatr Genet* 1983; 3:147-156.
3. Witkop CJ, Almodóvar C, Piñeiro B, Nuñez M: Hermansky-Pudlak syndrome (HPS): An epidemiologic study. *Ophthalmic Paediatr Genet* 1990; 11(3):245-250.
4. White JG, Edson JR, Desnick SJ, et al: Studies of platelets in a variant of the Hermansky-Pudlak syndrome. *Am J Pathol* 1971; 63(2):319-329.
5. Witkop Cj, Krumwiede M, Sedano H, et al: Reliability of absent platelet dense bodies as a diagnostic criterion for Hermansky-Pudlak sydrome. *Am J Hematol* 1987; 26:305- 311.
6. Gerrard JM, Lint D, Sims PJ, et al: Identification of a platelet dense granule membrane protein that is deficient in a patient with Hermansky-Pudlak sydrome. *Blood* 1991;77(1):101-112.
7. White JG, Witkop CJ: Effects of normal and aspirin platelets on defective secondary aggregation in the Hermansky-Pudlak syndrome: A test for storage pool deficient platelets. *Am J Pathol* 1972; 68:57-66.
8. Garay SM, Gardella JE, Fazzini EP, et al: Hermansky-Pudlak syndrome: Pulmonary manifestations of a ceroid storage disease. *Am J Med* 1979; 66:737-747.
9. Hoste P, Willems J, Devriendt J, et al: Familial diffuse interstitial pulmonary fibrosis associated with oculocutaneous albinism: Report of two cases with a family study. *Scand J Resp Dis* 1979; 60:128-134.
10. White D, Walker GJ, Cooper JA, et al: Hermansky-Pudlak syndrome and interstitial lung disease: Report of a case with lavage findings. *Am Rev Respir Dis* 1984; 130:138-141.
11. Schinella RA, Greco MA, Cobert BL, et al: Hermansky-Pudlak syndrome with granulomatous colitis. *Ann Intern Med* 1980; 92:20-23.
12. Witkop CJ, Nuñez M, Rao GH, et al: Albinism and Hermansky-Pudlak syndrome in Puerto Rico. *Bol Assoc Med PR* 1990; 82(8):333-339.
13. Simon JW, Adams RJ, Calhoun JH, et al: Ophthalmic manifestations of the Hermansky-Pudlak syndrome (oculocutaneous albinism and hemorrhagic diathesis). *Am J Ophthalmol* 1982; 93:71-77.
14. Summers CG, Knobloch WH, Witkop CJ, et al: Hermansky-Pudlak syndrome: Ophthalmic findings. *Ophthalmology* 1988; 95(4):545-554.
15. Suzuki T, Ohga H, Katayama T, et al: A girl with Hermansky-Pudlak syndrome. *Acta Ophthalmol* 1991; 69:256-260.
16. Larkin DFP, O'Donoghue HN: Developmental glaucoma in oculocutaneous albinism. *Ophthalmic Paediatr Genet* 1988; 9(1):1-4.
17. Wijermans PW, van Dorp DB: Hermansky-Pudlak syndrome: Correction of bleeding time

by 1-desamino-8D-arginine vasopressin. *Am J Hematol* 1989; 30:154-157.
18. Gerritsen SW, Akkerman JW, Sixma JJ: Correction of the bleeding time in patients with storage pool deficiency by infusion of cryoprecipitate. *Br J Haematol* 1978; 40:153-160.
19. Frenk E, Lattion F: The melanin pigmentary disorder in a family with Hermansky-Pudlak syndrome. *J Invest Dermatol* 1982; 78:141-143.
20. Ott J: Estimation of the recombination fraction in human pedigrees: Efficient computation of the likelihood for human linkage studies. *Am J Hum Genet* 1974; 26:588-597.
21. Creel D, O'Donnell FE, Witkop CJ: Visual system anomalies in human ocular albinos. *Science* 1978; 20:931-933.
22. Coleman J, Sydnor CF, Wolbarsht ML, et al: Abnormal visual pathways in human albinos studied with visually evoked potentials. *Exp Neurol* 1979; 65:667-679.

DISCUSSION

DR. J BRONWYN BATEMAN. It is a pleasure to discuss this study presented by Dr Izquierdo and Doctors Townsend and Maumenee Hussels. I congratulate the authors on a fine study of a most interesting genetic syndrome. Hermansky-Pudlak is a curious disease with multisystem manifestations; it is one of a small group of autosomal recessive albinism syndromes, and the gene defect affects lungs, kidney, gastrointestinal tract, and heart. The ophthalmologic manifestations include the pigment epithelium and, presumably, the central visual pathways. Since not all organ systems are diseased, the normal function of this gene will be of great interest.

This study has been very well done and is most informative. The authors have demonstrated considerable phenotypic variability among Puerto Ricans with Hermansky-Pudlak syndrome. The correlation of the macular appearance with the visual acuity is most interesting and may prove to be useful prognostically. Because the study population is large, the authors may wish to apply statistical analyses to confirm their findings and perhaps identify other factors that predict for acuity. Additionally, because pigmentation increases with age in this disease, I would be curious to know if iris and/or macular pigmentation correlates with increasing age.

The relatively high prevalence is curious. Either heterozygotes for the Hermansky-Pudlak syndrome have had a competitive reproductive advantage in Puerto Rico or the high prevalence reflects a founder effect. One could postulate a resistance to disease in the heterozygote, as occurred in Africa with sickle disease and malaria. However because Puerto Rico is an island, assuming a founder effect may be more logical. If we make this assumption, we expect that most, if not all, of the affected individuals from Puerto Rico have a common ancestor. Thus most, if not all, have the same Hermansky-Pudlak mutation, and we would not anticipate significant phenotypic variability. Since the authors have confirmed wide clinical variability, we can only speculate on the mechanism. Perhaps other environmental factors or genes influence the phenotype.

I wish to congratulate the authors on a fine study and thank them for the opportunity to read their manuscript.

DR. MARILYN MILLER. Thank you. I enjoyed this paper very much. We have had a number of cases of Hermansky-Pudlak syndrome in our clinic in Chicago. I learned something from one sad situation in which a family with two little affected children who didn't speak English too well were being accused of child abuse because their children always were black and blue. Now when I see a child with oculocutaneous albinism my first question is do they bruise easily? It is important to help protect these families in an era of looking for child abuse.

DR. EDWARD L RAAB. This was a very informative and enjoyable paper. I have one question for the authors. I would like to know whether the authors consider strabismus in this syndrome to be an element of the expression of the syndrome, or merely derivative of the fact that it involves a sensory anomaly. I ask this because it is a source of confusion. I frequently have occasion to be consulted by pediatricians and geneticists who are troubled by the fact that they are confronting a syndrome in which strabismus is described, and it is not present in a given patient; therefore they worry about accepting what is an otherwise obvious constellation of findings. I also receive other consultation requests in which strabismus is present, but there is not enough else to support a particular genetic diagnosis. I think here the strabismus is not an expression of the gene, but merely a consequence of the sensory anomaly.

DR. IRENE MAUMENEE HUSSELS. I would like to thank the discussants, especially Dr. Bateman, for having taken the time to discuss this paper. She was recently appointed chairman of Ophthalmology in Denver and I know she has many constraints on her time. She is the first among the fifty or so fellows who trained with me who have become a chairperson and I would like to offer her my congratulations.

I presume there is a founder effect in this community and that a single mutation caused the disease in Puerto Rico. We are basing our work on this hypothesis and are hoping to find the gene assignment through linkage analysis.

One can see a large variation of pigmentation in Puerto Rican citizens. Many genes are involved in pigmentation and I presume that an overlay of secondary genes or epistasis creates this wide variability in pigmentation in patients with the Hermansky-Pudlak syndrome.

We do not have a long follow-up of these patients and can only presume that an increase in pigmentation occurs with advancing age. We certainly see this in other types of tyrosinase-positive albinism. We expect this to be the case in this condition. With time a statistical analysis may become possible to clarify the question as to whether an increase in pigmentation correlates with improved visual acuity.

This condition has world wide distribution but often remains unrecog-

nized. I am truly touched by the unfortunate family accused of child abuse because of the bruising so typical of this condition as pointed out by Dr. Miller. We wanted to give this paper to draw attention to it.

In answer to Dr. Raab, the nystagmus in albinism is presumably secondary to the sensory anomalies. Again I would like to thank the discussants.