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April 8, 1971

Dr. Victor McKusick
The Moore Clinic
Johns Hopkins Hospital
Baltimore, Maryland 21205

Dear Victor:

In regard to possible presentations at the Fourth Conference on the Clinical Delineation of Birth Defects, several presentations might be of interest.

1. The association of pulmonary valvular stenosis and neurofibromatosis. We have also seen one person with aortic valvular stenosis and neurofibromatosis, and are currently attempting to get other members of this family studied. One uncle said to be affected with at least the cafe-au-lait spots of neurofibromatosis is evidently being considered for heart surgery in the Army.
2. We have recently seen a child with a coarctation of the aorta and atrial and ventricular septal defects, and multiple vertebral and rib anomalies, similar to the changes seen in the basal cell nevus syndrome but more severe than usual. This child had a sib who died of the hypoplastic left heart syndrome, who on a retrospective examination of a chest film showed vertebral and rib anomalies also. These children are maternal second cousins of the three children with the basal cell nevus syndrome whom I presented at the Third Conference. The Sprick children had skeletal anomalies, jaw cysts and basal cell nevi in one of the children. Their mother had basal cell nevi but no evidence of skeletal anomalies. The grandfather of the children, who is the great-uncle of our recent patients, also showed no evidence of skeletal anomalies. The father of the current family with skeletal anomalies and heart disease shows no evidence of either skeletal anomalies, basal cell nevi, or heart disease. His father is, unfortunately, deceased. I was asked to see the living child as she was going off to surgery, and had made the suggestion that basal cell nevus syndrome was one of the possibilities to be considered regarding the skeletal anomalies, and only later discovered the family relationship. The question, obviously, arises as to whether this is a manifestation, again previously unrecognized, of basal cell nevus syndrome. One would not expect to find patients with basal cell nevus syndrome and the heart abnormalities since it would be expected that affected children would die early in infancy.

No instance of congenital heart disease is mentioned in Bob Gorlin's review, and he tells me he has seen none himself. I thought it might be useful to present the findings on these two children and their relationship to the family with basal cell nevus syndrome, and ask those in attendance whether they have noted infant mortality from congenital heart disease in families with patients with basal cell nevus syndrome. A letter to perhaps the New England Journal, asking for family histories of patients with basal cell nevus syndrome regarding congenital heart disease, might turn up additional cases. Similarly, a request for cases of association of congenital heart disease with neurofibromatosis might be useful in preparing the final paper for the Conference. The interesting aspect of both of these situations is the possibility that, as in the multiple lentiginos syndrome, there may perhaps be a predisposition to congenital heart disease in some patients with dominantly inherited skin abnormalities. The last statement, obviously, may be an overly large jump from the previous data.

3. We have also seen a fascinating family in which a Mormon couple have had two children with total anomalous pulmonary venous drainage. The brother of the mother of these children has subsequently had a child who also has total anomalous pulmonary venous drainage. We have studied the mother of the first two children mentioned, including cardiac catheterization, and find no evidence of shunting in her. I do not yet have complete data on the brother and his child. We do know, however, that for at least six generations back, the brother and his Finnish wife, are not related.

We have also seen a number of patients with the Holt-Oram syndrome, showing various divergent manifestations of that disorder, as you are aware. We have also seen patients with Noonan's syndrome. As far as presentations are concerned, I think it would be more useful to present some or all of the first three entities mentioned above. These could be exceedingly brief and presented one after the other.

You may recall that I asked concerning autopsies on patients with Sanfilippo's syndrome. Our subsequent metabolic studies on the surviving sib in this family show that the patient probably has a new mucopolysaccharidosis, rather than Sanfilippo's syndrome. This is a patient of Arthur Prensky's, who in addition to x-ray changes of mucopolysaccharidosis and severe neurological problems and retardation, shows chondroitin sulfate C in large excess, along with heparitin sulfate. We are in the process of further laboratory studies to confirm this impression.

I am looking forward to the Conference.

Sincerely,



Robert L. Kaufman, M.D.
Division of Medical Genetics