Eye Abnormalities and Skeletal Deformities in the Pierre Robin Syndrome: A Balanced Evaluation

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Eye abnormalities and the Pierre Robin syndrome have been associated in many reports. Most recently, a further connection has been drawn linking this condition with a progressive arthro-ophthalmopathy—the Stickler syndrome. (*24*) Early intensive eye examinations and bone and joint surveys have been urged as imperative for Pierre Robin patients. (*13, 21*) In an effort to assess the validity of these correlations and the necessity of these procedures we have reviewed our patient material and carried out a critical review of the literature.

Results

PATIENT REVIEW. For the purposes of this study the diagnosis of Pierre Robin syndrome was accepted if the patient exhibited micrognathia with or without a cleft of the palate, associated with symptoms of respiratory distress secondary to intermittent upper airway obstruction (glossoptosis).

The records of all patients with the diagnosis Pierre Robin syndrome (PR), cleft palate (CP), and cleft lip and palate (CL/CP) seen between 1952 and 1970 were reviewed. 436 cases were involved. Patients with severe cranial dysgenesis, named syndromes, and chromosome-linked syndromes were excluded. Of the remainder, 198 were CL/CP, 210 were CP, and 18 were PR. Of the PR cases all had cleft palates, none had a cleft lip: they constituted 9% of the CP population. No patient had significant joint anomalies and none developed a progressive arthropathy in the period of follow up which averaged 6 years.

The incidence of eye defects is shown in Table 1. While the percent incidence in PR is twice that of CP or CL/CP, very small numbers of patients and of defects are really involved. The abnormalities found are listed in Table 2. Microphthalmia was the most frequent and coloboma of the iris next in frequency. One case of retinal detachment was noted in a PR patient. (See Figure 1.)

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TABLE 1. Incidence of eye defects.

group	*total number of patients*	*patients with eye findings*	*percent of patients with eye findings*
CL/CP	198	9	5%
CP	210	11	5%
PR	18	2	11%

TABLE 2. Eye abnormalities found.

anomaly	*total number*	*CL/CP*	*CP*	*PR*
micropthalmia	6	4	1	1
coloboma-iris	4	0	3	1
esotropia	4	1	3	0
strabismus	3	1	2	0
epicanthal fold	3	1	2	0
coloboma-lid	2	1	1	0
coloboma-optic nerve	2	2	0	0
cataract	1	1	0	0
retinal detachment	1	0	0	1
lacrimal duct stenosis	1	0	1	0
ptosis	1	1	0	0

Literature Review

Pierre Robin Syndrome and Eye Abnormalities. Citations linking PR and eye deformities, reports correlating CP and eye defects, and series of PR cases were reviewed. The exclusions were the same as previously noted.

The criteria for accepting the PR diagnosis were as before: failure to find mention of respiratory distress and/or micrognathia left the diagnosis in doubt. The definition of a significant eye defect was a problem; it was difficult to accept "poor vision" as an eye anomaly worthy of mention. (*22*) The truly significant anomalies proved to be intraocular ones. The most frequently reported were myopia, cataract, glaucoma, and retinal degeneration-detachment.

Smith, et al, (*21*) were the first to link PR and such eye defects. Four of seven PR patients were found to have glaucoma, myopia, or retinal detachment. These same cases were included in a series of 39 PR patients of whom nine had major ocular lesions (*22*). It is not clear which of these nine had had a complete syndrome with respiratory distress. Ortlepp (*14*) reported a single individual with micrognathia, cleft palate, and glaucoma but without respiratory symptoms. The PR diagnosis is dubious in the cases recorded by Sacrez and the eye anomalies are not major ones (*17*).

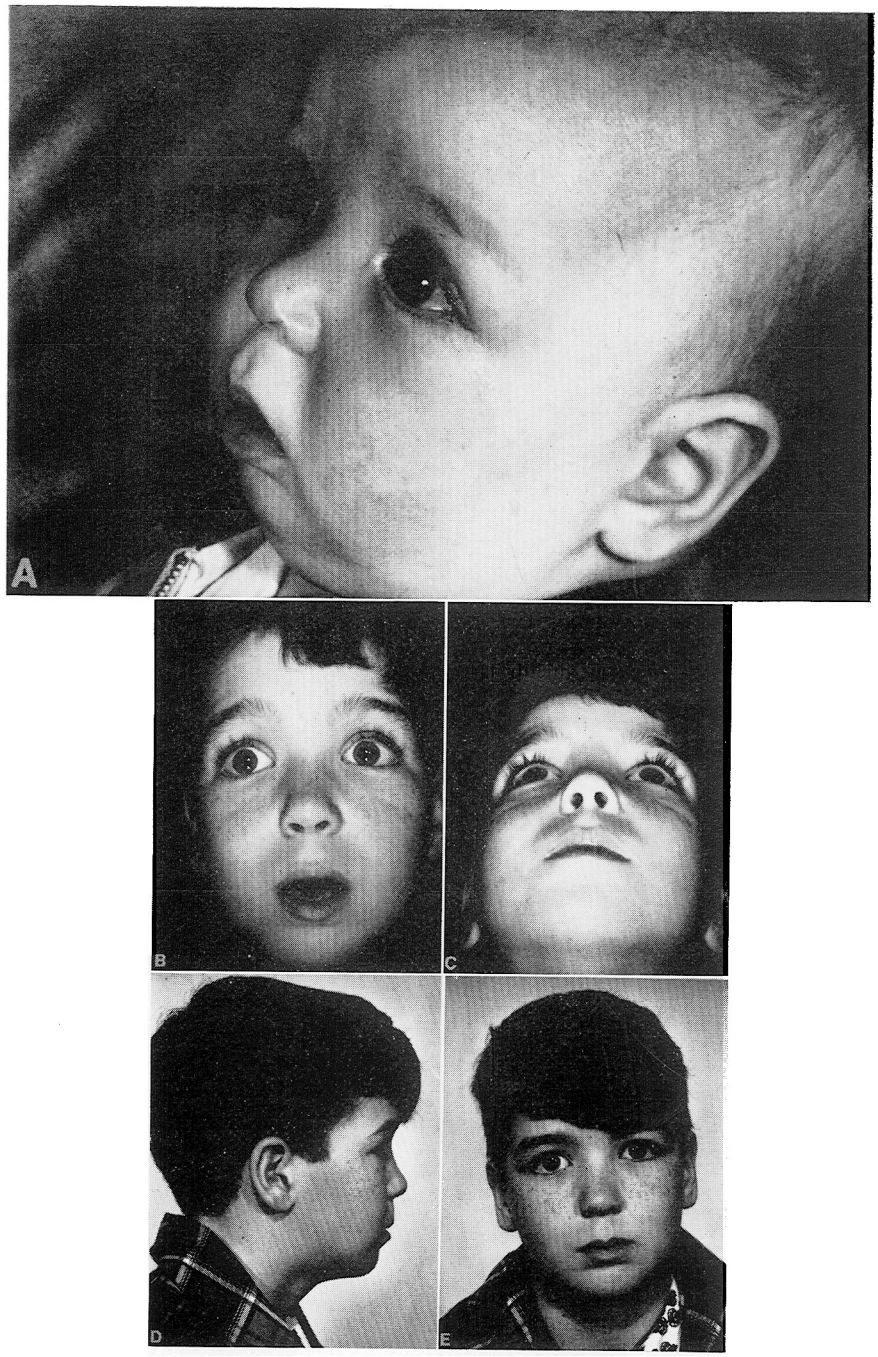

FIGURE 1. (A) Pierre Robin patient 1 year following Beverly Douglas operation and tracheostomy; now prior to closure of partial cleft palate. Eye examination normal. (B, C) Age 7 showing flat nasal bridge and malar eminences with mild epicanthal folds. Hearing at this time reduced bilaterally. (D, E) Age 10, prior to pharyngeal flap. Fundiscopic examination said to be negative. Spontaneous complete retinal detachment OD occurred 3 months later. Small breaks also found OS. Light coagulation partially successful. Now at age 13, patient is tall, thin, with normal hearing, without obvious joint defects, and playing basketball in spite of opthalmologic advice.

Myopia and retinal detachment were associated with severe micrognathia and cleft palate in Chivirot's case but respiratory difficulty was absent (*2*). The complete PR syndrome was present in Sauraux's single case associated with congenital glaucoma (*18*). A family history of both CP and cataract characterized Opitz's case of PR with myopia and retinal detachment (*12*). Perkins (*15*) reported four members in a pedigree involving CP, cataract and retinal detachment but made no mention of micrognathia or respiratory difficulty thus leaving the PR designation in doubt. Schumann (*20*) and Carroll (*1*) added single cases, the latter not specifying the eye anomaly involved. Monroe, (*11*) in a report of 65 PR patients listed 6 with eye findings of which two were significant. Whether these two actually had a complete PR syndrome is uncertain.

CP alone is strongly related to retinal degeneration-detachment in certain families. In general, the familial eye abnormality is the more penetrant of the two defects. Fogh-Anderson (*6*) reported one such case. Edmund reported two CP patients among eight members of a family all eight of whom had retinal detachment. Delaney (*4*) recorded six CP cases in 10 retinal detachment patients in a similar family. Stickler (*24*) studied a family in which five generations showed a progressive arthropathy as well as myopia and retinal detachment. Three members of this group also had CP. Retinal detachment and CP were associated in 11 cases in three pedigrees recounted by von Balen (*25*). Knoblock (*10*) added seven new cases of similar nature and re-reported one of Stickler's while emphasizing a particular facies shown by these patients and their multiple though nonspecific skeletal anomalies.

Table 3 summarizes these findings. While the total number of CP and PR cases is approximately the same, the majority of the CP cases occurred in family groups. In a majority of the PR cases the diagnosis must be con-

TABLE 3. Correlation of eye abnormalities with cleft palate and Pierre Robin Syndrome.

	cleft palate	*Pierre Robin**
number of cases recorded	31	29
number of families involved	14	21
familial history of cleft palate	23	9**
familial history of eye defect	31	9
eye anomaly		
retinal detachment	30	7
myopia	11	8
glaucoma	0†	5
cataract	2†	5
miscellaneous	0†	12

* Only 10 of the 29 PR cases had documented micrognathia and/or respiratory distress.

** 8 of the 9 PR patients with familial CP also had familial eye defects.

† Was not the primary defect.

sidered in doubt. In actuality, many of these may be simple CP cases. Familial history of both cleft palate and eye defect was stronger in the CP group. Of those PR patients with a familial cleft history however, nearly all also had a familial eye history. Retinal detachment and myopia were the most frequent specific eye abnormalities in both CP and PR. Congenital glaucoma was noted in the PR group although glaucoma sometimes developed in the natural history of the retinal detachment patients. The number of miscellaneous findings in the PR group may be a reflection of effort by the authors to find an eye abnormality in the PR patients.

Pierre Robin Syndrome and the Stickler Syndrome. Prominence has recently been given to patients said to have PR and specific skeletal deformities first reported by Stickler (*13*). That chondrodystrophic bone anomalies may occur in association with micrognathia and cleft palate had been recorded earlier (*26*). The cases studied by Stickler (*24*), however, were involved in a pedigree extending over 5 generations in a family essentially characterized by retinal degeneration and a progressive multiple joint arthropathy producing ultimate crippling. No one of the three CP members of this family had had respiratory difficulties in infancy and none were reported to have had micrognathia. The author did not claim these patients exhibited PR nor was this assertion made by Knobloch (*10*) when re-reporting one of them. It is difficult to understand how the concept arose that PR and SS are associated (*13*). While several authors, (*9, 12, 19*) claimed cases in which PR or CP, retinal degeneration, and bone abnormalities coexist it is clear that few of these deserve the PR diagnosis and not one of them has shown the progressive arthoropathy characteristic of SS. It is of interest that the most recently reported case (*19, 23*) whose PR designation is acceptable occurred in a family characterized by retinal detachment, cataract and myopia. Disparate bone changes, some suggestive of SS, some suggestive of spondyloepiphysial dysplasia, were described in 5 generations of this family but all were and had remained asymptomatic.

Discussion

Time and usage have pruned the initial fuzziness of Pierre Robin's description of the syndrome that immortalizes him (*16*). As appropriately used the eponym now retains real utility in calling attention to a life endangering clinical syndrome of respiratory distress associated with micrognathia and highly, although not absolutely associated with cleft palate. It seems clear from the reports of older series that the clinical picture of the syndrome can exist in the absence of cleft palate (*1*). The syndrome can also occur later in life in cases of severe micrognathia (*3*). Judged from our own series and those of others it would appear that approximately 10% of the patients with isolated cleft palate will have micrognathia and suffer respiratory distress (*7*). Micrognathia appears to be the essential anatomical feature and respiratory distress the essential symptom for the diagnosis

of PR (*8*). One cannot call every well infant with a small chin and cleft palate a case of PR or all possible meaning for the term is lost.

Appropriately defined, the syndrome is a valid clinical condition. The attempt to add occular and skeletal defects as additional features of PR stems from the quite different concept of PR as a disease entity. Neither our own experience nor a critical review of the literature substantiates this latter view. While it may be that the incidence of mscellaneous eye defects is somewhat greater in PR patients than in those with CP or CL/CP, the numbers are small and the differences are not profound. The serious intraocular defects found in occasional cases of PR are also found in CP. Indeed, the evidence for a linkage between CP and retinal degeneration-detachment seems very strong. It is certainly much stronger than any similar connection between PR and any one eye lesion. Further, many of the reported PR-eye defect cases were probably CP patients.

The relationship between PR and SS seems even more strained. The attribution of the connection to Stickler seems to represent a misreading of that author's report (*13, 24*). The special feature of SS is the progressive nature of its arthropathy. On the other hand, it may well prove true that skeletal anomalies occur as a part of the cleft palate-retinal degeneration-detachment syndrome. This is the group in which Knobloch's cases seem to belong (*10*). Many of the CP and PR cases reported with strong family histories of both these conditions and retinal defects probably represent this category. The older literature does not detail the facial appearance of these patients so that we cannot say if they share the facial characteristics noted by Knobloch. The PR case depicted here does share those features.

The incidence of cleft palate-retinal degeneration-detachment syndrome is low. The incidence of eye defects associated with PR, CP, and CP/CL is also low. The admonition to examine the eyes of the PR patient is equally true for the CP patient but the yield of significant intraoccular defects will be small. A family history is probably the surest guide to the liklihood of an intraocular eye deformity. The skeletal anomalies noted in all but Stickler's cases have been of mostly academic interest. The rationale for early intensive eye study and skeletal survey has not been borne out by clinical experience or critical literature review.

Summary

The Pierre Robin eponym calls attention to a valid and important clinical condition of respiratory distress with associated micrognathia often but not always associated with cleft palate. While the incidence of minor eye anomalies may be higher in Pierre Robin patients than in cleft palate or cleft lip/cleft palate patients, the evidence is not compelling. It is clear that serious intraocular anomalies such as retinal degeneration-detachment occur in both cleft palate and Pierre Robin patients. The evidence for a specific correlation between Pierre Robin syndrome and the Stickler syndrome seems completely lacking. There is, however, impressive evidence

for a syndrome consisting of cleft palate and retinal degeneration-detachment with associated multiple skeletal anomalies. The specific need for intensive eye examinations and skeletal surveys in PR patients without other stigmata has not been proven.

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References

1. Carroll, D. B., R. A. Peterson, E. W. Warton, and L. M. Birnbaum, Hereditary factors in the Pierre Robin Syndrome. *Brit. J. Plast. Surg., 24,* 43–47, 1971.
2. Chivirot, R., Zespól Pierre' a Robina ze zunianami ocznymi. *Klin. Oczna., 38,* 563–566, 1968.
3. Cosman, B., and G. F. Crikelair, Mandibular hypoplasia and the late development of glossopharyngeal airway obstruction. *Plas. reconstr. Surg., 50,* 573–579, 1972.
4. Delaney, W. V., W. Podedworny, and W. H. Havener, Inherited retinal detachment. *Arch. Ophthal., 69,* 44–50, 1963.
5. Edmund, J., Familial retinal detachment. *Acta Ophthalmologica, 39,* 644–654, 1961.
6. Fogh-Andersen, P., *Inheritance of Harelip and Cleft Palate,* N.Y.T. Nordisk Forlag, Amola Busch, Copenhagen, 1942.
7. Gunter, G. S., and A. R. Wakefield, Early management of the Pierre-Robin syndrome. *Cleft Palate J., 7,* 495–501, 1970.
8. Hoffman, S., S. Kahn, and M. Seitchik, Late problems in the management of the Pierre Robin syndrome. *Plast. reconstr. Surg., 35,* 504–511, 1965.
9. Holthusen, W., The Pierre Robin syndrome. Unusual associated developmental defects. *Ann. Radiol., 15,* 253–262, 1972.
10. Knobloch, W. H., and J. M., Layer, Clefting syndromes associated with retinal detachment. *Am. J. Opthal., 73,* 517–530, 1972.
11. Monroe, C. W., and K. Ogo, Treatment of micrognathia in the neonatal period. Report of 65 cases. *Plast. reconstr. Surg., 50,* 317–325, 1972.
12. Opitz, J. M., Familial anomalies in the Pierre Robin syndrome, *Birth Defects Original Article Series, 5,* 119, 1969.
13. Opitz, J. M., T. France, J. Herrmann, and J. W. Spranger, The Stickler Syndrome. *N. Eng. J. Med., 286,* 546, 1972.
14. Ortlepp, J., and H. P. Brandt, Hydrophthalmos bei Pierre-Robin-Syndrome. *Klin. Monat. Augenheilk., 148,* 46–49, 1966.
15. Perkins, T., Pierre Robin syndrome. *Tr. Ophthalmol. Soc. U.K., 90,* 179–180, 1970.
16. Randall, R., W. M. Krogman, and S. Jahina, Pierre Robin and the syndrome that bears his name. *Cleft Palate J., 2,* 237–245, 1956.
17. Sacrez, R., J. J. Francfort, J. M. Gigonnet, P. Beauvais, and G. Ball, A propos de la débilité intellectuelle et d'anomalies associeés a la triade symptomatique du syndrome de Pierre Robin. *Sem. d. Hop. d. Paris, 43,* 28–33, 1967.
18. Saraux, H., and P. Dhermy, Le glaucome du syndrome de P. Robin. *Arch. Ophthalmologie, 28,* 793–800, 1968.
19. Schreiner, R. L., W. H. McAlister, R. E. Marshall, and W. T. Schearer, Stickler syndrome in a pedigree of Pierre Robin Syndrome. *Am. J. Dis. Child., 126,* 86–90, 1973.
20. Schumann, M., and D. Schumann, Augenbeteiligung beim, Pierre-Robin-Syndrom. *Klin. Monat. Augenheilk., 158,* 554–600, 1971.
21. Smith, J. L., J. J. A. Cavanaugh, and F. C. Stowe, Ocular manifestations of Pierre Robin syndrome. *Arch. Ophth., 63,* 984–992, 1960.
22. Smith, J. L., and F. R. Stowe, The Pierre Robin syndrome (glossoptosis, micrognathia, cleft palate); a review of 39 cases with emphasis on associated ocular lesions. *Pediatrics, 27,* 128–133, 1961.

23. SPRANGER, J. W., and L. O. LANGE, Spondyloepiphyseal dysplasia congenita. *Radiology, 94,* 313–320, 1970.
24. STICKLER, G. B., P. G. BILAU, F. J., FARRELL, J. D. JONES, D. G. PUGH, A. G. STEINBERG, and L. E. WARD, Hereditary progressive arthro-opthalomathy. *Mayo Clin. Proc., 40,* 433–455, 1965.
25. VON BALEN, A. T. M., and E. L. F. FOLGER, Hereditary hyaloideoretinal degeneration and palatoschisis. *Arch. Ophthal. 83,* 152–162, 1970.
26. WEISSENBACHER, G., and E. ZWEYMÜLLER, Gleichzeitiges Vorkomen eines syndroms von Pierre Robin und einer fetalen chondrodysplasie. *Monat. Kindheil., 112,* 315–317, 1964.