Intellectual Development and the OFD Syndrome: a Review

AUBREY L. RUESS, PH.D.
SAMUEL PRUZANSKY, D.D.S.
EDWARD F. LIS, M.D.
Chicago, Illinois

The syndrome discussed in this report was first identified by Papillon-Leage and Psaume (*11, 12*) in 1954. In subsequent publications (*3, 6, 9, 10, 15*), additional cases were reported. Radiologic features of the syndrome (*1, 16*) and chromosomal abnormalities (*14*) have been identified. Because of the specific clinical anomalies of the mouth, face, hands, and feet, it has been labelled as the oral-facial-digital (OFD) syndrome (*15*).

A majority of the reports in the literature emphasize mental retardation as one of the distinguishing characteristics of the syndrome. There is no doubt that a substantial proportion of these patients show symptoms of mental retardation, but a significant proportion of them have average, or better, intellectual development. Thus, the condition is by no means incompatible with normal mentation.

The most basic and important reason, however, for calling attention to the problem resides in the fact that the long-term habilitative efforts may very well be vitiated in patients with this syndrome unless an enlightened and individualized approach is maintained concerning the potentiality of each patient. For the cleft palate child in general, it is also imperative to utilize the same standards in evaluating the various dimensions of personality in order to maximize the habilitative success.

Characteristic Symptoms

Malformations of the OFD syndrome in the oral cavity involve the palate, tongue, alveolar processes, and the gingival and buccal frena. Variable facial anomalies involve the orbits, nose, lip, and mandible. The digits have frequently associated mild deformities which include brachydactyly, clinodactyly, incomplete syndactyly, and atypical finger-size relationships.

Dr. Ruess is Assistant Professor of Psychology, College of Medicine, University of Illinois, and Psychology Program Administrator at the Division of Services for Crippled Children for the State of Illinois. Dr. Pruzansky is Professor of Dentistry in the College of Dentistry, University of Illinois, and Associate Director, Cleft Palate Center and Training Program. Dr. Lis is Director of the Division of Services for Crippled Children, Director of the Center for Handicapped Children and Cleft Palate Center at the Research and Educational Hospitals, Chicago, and Associate Professor of Pediatrics, College of Medicine, University of Illinois.

This research was supported by the U. S. Children's Bureau and by PHS Research Grant DE-01153, National Institute of Dental Research.

Speech impairments may be present, ranging from mild to severe. The speech deficits are variably related to the pathophysiology of the cleft palate, the degree of impairment of the other oral structures and, when present, the degree of mental deficiency. A more complete and detailed description is presented in the report by Ruess, Pruzansky, Lis, and Patau (*15*).

Radiographic analysis on five of the patients in our series has been discussed in detail by Schwarz and Fish (*16*) and by Aduss and Pruzansky (*1*). Characteristic abnormalities of the short tubular bones of the hands and/or feet are present. In some cases, the tubular bones show irregular, reticular areas of radiolucency extending through the entire shaft into the metaphyses. Cranial findings revealed distinct but not syndrome-specific features.

The syndrome is unique in that it occurs only in females and has been demonstrated to have a dominant mode of inheritance (*6, 15*). On the basis of analysis of the pedigrees of three families, it has been concluded beyond the probability of chance occurrence ($P = .03$) that the OFD syndrome is lethal in the male (*15*). The data reported by Doege and associates (*3*) also reveal the syndrome to be lethal for males and to have a dominant mode of inheritance. Patau and associates (*14*) have illustrated the nature of the genetic transmission that can be expected. However, Kushnick, Massa, and Baukema (*10*) have reported what they believe to be a case of the OFD syndrome in a male.

Number of Existing Cases and Incidence of Occurrence

The number of cases that has been identified to date is not known precisely because of the lack of specific case identification in published reports. Papillon-Leage and Psaume (*11, 12*) reported eight cases in their original study. Psaume (*13*) later identified six additional cases. Gorlin, Anderson, and Scott (*6*) described four cases, extending through three generations of one family. Three months later, Gorlin (*4*) reported the presence of twenty-eight apparently similar cases in the United States and England for which no data are available. Within the month following, Gorlin stated: "An additional two patients have been seen by us . . ." (*5*). Gorlin and Psaume's publication (*7*) in 1962 was an abstract presenting the incidence of anomalies in 22 patients with the syndrome. Whether these 22 include all, or part, of the OFD cases reported independently by Psaume and Gorlin previously is not known. Our earlier study (*15*) was made on twelve cases, and a report on a four-year-old girl was made by Kaplan and associates (*9*). More recently Doege and associates (*3*) reported the presence of fifteen females with this condition occurring in four generations of one family (*3*). Thus, a conservative estimate indicates that 46 cases have been studied by investigators familiar with the syndrome and that at least another 28 apparently exist for whom there is no available information.

On the basis of previous studies (*11, 12, 15*) where the size of the cleft palate population was known and from which OFD syndrome cases were identified, it has been concluded that the incidence of the syndrome can be tentatively established at eight to sixteen per thousand cleft lip and/or cleft palate cases. It is quite likely, however, that the incidence may be higher due to limited knowledge of the syndrome, *per se,* as well as to the fact that some cases are probably being seen primarily in cleft palate clinics (where the incidence of additional congenital anomalies is high) with a diagnosis of cleft palate with other congenital anomalies.

Incidence, Degree, and Etiology of Mental Deficiency

There is no doubt that mental deficiency occurs in a significantly higher proportion of persons with the OFD condition than in the general population so far as can be determined from the extant data. But there are indeed substantive questions in previous reports regarding the incidence, degree, qualitative variations, and etiologic factors of the mental deficiency associated with this syndrome. Papillon-Leage and Psaume (*11, 12*) reported one-half of their eight cases to be mentally defective. The degree of deficiency was not given, nor was information concerning the basis for their assertion presented.

Gorlin, Anderson, and Scott (*6*) indicated quite clearly that they considered three of their four cases to be mentally defective. Analysis of their report, however, raises significant questions in regard to the etiology, degree, efficacy of determination, and their classification of mental deficiency. In their series of patients, the grandmother (age 51 years) was classified as the most severely retarded. She had been committed to a state institution for the feebleminded in Minnesota in 1939 and was transferred to a state hospital in 1946. The reported intelligence quotient of the Lowe-Shimberg Mental Test was 85 (date of examination not given); she was also classified as manic-depressive. In view of currently existing intelligence-quotient criteria utilized in defining mental deficiency (*2, 8*) this woman would be classified as *dull-normal,* or *mild,* and it seems likely that many of her mental and behavioral limitations may have been due to a psychiatric condition. No measured intelligence was secured on the other three patients (the 27-year-old daughter and two granddaughters, aged two and six years) of whom the daughter and one granddaughter were judged to have 'oligophrenia'. The adjudged mentally defective granddaughter was two years of age. It is noted further that the family lived on a farm which suggests that environmental and cultural factors may also account for some degree of the alleged deficits. The entire line of reasoning from the facts given, however, is an apparent *non sequitur.*

We do not question the fact that the affected members of this family revealed behavioral and personality deficits. However, it is one matter to describe the apparent limitations of individuals from clinical and behavioral observations, but decidedly a more complex and difficult matter to establish on the basis of such scanty data, an antecedent-causal relation-

ship between a condition as involved and variable as the OFD syndrome and mental deficiency.

In less than a year after his original report, Gorlin published three brief communications, all relevant to the issue of mental deficiency in OFD patients. The following statements were made in order of their chronological appearance: "It appears that oligophrenia and 'granular skin' are *infrequent* components." (*4:* p. 1218, italics in the original), and 'Some patients have normal intelligence, but at least 40 per cent are subnormal.' (*5:* p. 150). His abstract, listing the incidence of specific symptoms for 22 patients, reveals that mental deficiency is considered to be a 'less commonly observed' characteristic and that eight of 16 patients are 'mentally retarded' (*7*). The mental status of the other six is not given.

The report by Kaplan and associates (*9*) described a four-year-old female. According to the case history, the child had marked speech and motor retardation. She walked only with support. Convulsions had been present since the age of two weeks despite the use of anticonvulsant medication. Our impression from a review of this report is that a central nervous system disorder is present in addition to the OFD symptoms.

Of the fifteen affected patients reported by Doege and associates (*3*), only eleven were examined. Six were given psychologic tests: one of the six was apparently found to be normal; and the other five were described as being retarded, having 'intelligence quotients falling within the mild to moderate range of retardation.' (*3:* p. 1075). Two others were reported to be mentally retarded on the basis of interviews by two physicians. Thus, moderate range of retardation' (*3:* p. 1075). Two others were reported to be retarded. One was apparently normal, and on the remaining seven there was apparently no information.

From the investigation of 12 OFD patients (*15*), some of whom have been followed periodically for developmental analysis and treatment for ten years to date, we have found a range of intellectual development from normal to severe mental deficiency. Four of the eight children in this series are categorically mentally defective. Significantly, these four children are apparently not retarded on any homogeneous basis. The youngest, age 13 months, has a diagnosis of hydranencephaly with severe retardation in all phases of development, functioning not above a two-month level in any respect. The second youngest, age 19 months, is developing overall at 50% of average for her age (Gesell Developmental Schedules and Vineland Social Maturity Scale); she has a communicating type of hydrocephalus with a large porencephalic cyst. An eight-year-old, who is in an educable, mentally handicapped class in the local public school system (Stanford Binet IQ 60, identical results obtained at six and eight years of age), also has severe speech impediments associated with considerable morphological deficiencies of the tongue and other oral structures. In addition, she shows chronic otitis media with a significant bilateral hearing loss, and there is evidence of an affective disturbance. The fourth child with mental deficiency is ten years of age (WISC IQ 64), and clinically she shows evidence

of minimal diffuse brain damage manifested by horizontal bilateral nystagmus, impaired visual perception (Raven Progressive Matrices) and visual-motor deficits (Bender Visual-Motor Gestalt Test), poorly developed body-image concept (Goodenough Test and confused left-right body orientation), and very slow school progress for her chronological age (functioning at a low second grade level). In addition, she lives in a culturally sub-marginal rural community, which may affect her intellectual development, also.

Four of the children show intellectual development within the average, or normal, range. Ages of the children and tests used to evaluate mentation are as follows: 22 months (Gesell Schedules and VSMS); 4 years (Merrill-Palmer Scale, Stanford-Binet, and VSMS); 4 years (Gesell Schedules, Stanford-Binet, and VSMS); 11 years (WISC, Goodenough, Bender Gestalt, and Raven Progressive Matrices). Also, we have secured developmental histories, evaluations of emotional maturation and stability, and speech evaluations. Speech impairments are present in all four ranging from very mild to moderately severe.

On the remaining four patients, the psychological data, although less extensive, do not indicate mental deficiency. Since intelligence testing could not be done because of situational factors, intellectual functioning was evaluated on the basis of clinical interview, speech and language functioning, educational history, and history and level of vocational competency. Two of the adults, ages 38 and 71 years, were mother and daughter. The mother, deceased in 1957, was evaluated on the basis of information secured from her daughter. The third adult, who was 36 years of age, was also the mother of the 11-year-old mentioned above. The fourth patient with the least extensive psychological evaluation was a 14-year-old who had been examined at Bethesda, Maryland, and normal intellectual development has been inferred on the basis of reported language ability, school grade placement, and social functioning.

Logical inferences concerning the mentation of these patients reveal that intellectual development may be quite variable in cases where the OFD syndrome is present. The etiological factors in the mentally defective individuals are apparently variable, also. Moreover, it is not a simple task to evaluate the effects of single factors in some patients, which alone may be essentially responsible for the mental deficiency. For other affected individuals the cumulative and compounding effects of multiple pathological elements make a clear evaluation of the cause-effect relationships exceedingly more difficult. On the basis of this study and previous reports, it is tentatively concluded that between one-third and one-half of patients with the OFD syndrome are mentally defective.

Comments

From the foregoing discussion of the available data on this syndrome, there are several variables that require clarification in regard to a defini-

tive diagnosis of mental deficiency in any given case. The somatic characteristics, since they are readily identifiable in nearly all cases, make the syndrome easily recognizable at an early age. It does not follow, however, that mental deficiency can be prognosticated in the majority of cases, as has been implied in previous reports, without longitudinal studies of all growth and developmental factors.

To be sure, in some cases there is unequivocal evidence of mental deficiency, but at the other end of the continuum there is also unequivocal evidence of normal intellectual functioning. In previous reports of the syndrome, including our own (*15*), it is noted that some of the patients were less than five years of age. Since a definitive diagnosis of mental deficiency below the age of five years is at best circumspect, except in cases where the antecedent-effect relationship is known to be invariable, it is necessary to consider the previous findings with caution so far as the efficacy in establishing parameters for the variable of intelligence is concerned.

For children having the cleft palate syndrome alone (without any other congenital anomalies) it is not uncommon to have the question of limited intelligence raised by parents, teachers, and others who interact with these children. When many of them are examined in regard to the alleged intellectual deficits, it is often found that the problem of retardation is not substantiated. One apparent reason for this false impression is the high incidence of impairments in the basic communication modalities, that is, speech and hearing problems, which may suggest limited intelligence in these patients. Since all reported OFD cases to date apparently have some degree of oral involvement and a lesser number have hearing impairments associated with chronic and recurrent otitis media, it is imperative that personality and mental studies be analyzed in relation to the cleft palate syndrome *and* the other OFD symptoms. It can be added, redundantly, that developmental, environmental, and situational factors should be analyzed, also, with extreme care.

Myriad professional and personal reasons undoubtedly reinforce the tendency of investigators to publish immediately any new facts or findings available to them. When published data emphasize only certain aspects of a phenomena that require refined multi-dimensional study, the issues cannot but regrettably become more confounded. The foregoing analysis seems to illustrate this problem clearly in regard to the OFD syndrome.

P. O. Box 6998
Chicago, Illinois 60680

References

1. Aduss, H., and Pruzansky, S., Postnatal craniofacial development in children with the oral-facial-digital syndrome. *Arch. oral Biol., 9,* 193–203, 1964.
2. *Diagnostic and Statistical Manual, Mental Disorders.* Washington, D. C.: American Psychiatric Association Hospital Service, 1952.
3. Doege, T. C., Thuline, H. C., Priest, J. H., Norby, D. E., and Bryant, J. S.,

Studies of a family with the oral-facial-digital syndrome. *New England J. Med., 271,* 1073–1080, 1964.
4. Gorlin, R. J., Letter to the editor. *New England J. Med., 264,* 1217, 1961.
5. Gorlin, R. J., Letter to the editor. *New England J. Med., 265,* 150, 1961.
6. Gorlin, R. J., Anderson, V. E., and Scott, C. R., Hypertrophied frenuli, oligophrenia, familial trembling and anomalies of the head. *New England J. Med., 264,* 486–489, 1961.
7. Gorlin, R. J., and Psaume, J., Oro-digito-facial dysostosis—an analysis of 22 cases of a new syndrome. *Internat. Assoc. dent. Res., 40,* 65, 1962.
8. Heber, R., A manual on terminology and classification in mental retardation. *Amer. J. ment. Def., 63,* 214–219, 1958–59.
9. Kaplan, H., Vaharu, T., Voorhess, M. L., and Gardner, L. I., Chromosomal analysis of a case of oro-facial-digital syndrome. *New England J. Med., 266,* 774–775, 1962.
10. Kushnick, T., Massa, T. P., and Baukema, R., orofaciodigital syndrome in a male. *J. Pediatrics, 63,* 1130–1134, 1963.
11. Papillon-Leage, (Mme.), and Psaume, J., Une malformation hereditaire de la muqueuse buccale: brides et freins anormaux. *Rev Stomatol., 52,* 209–227, 1954.
12. Papillon-Leage, (Mme.), and Psaume, J., Une nouvelle malformation hereditaire: dysmorphie des freins buccaux, huit observations. *Act. Odonto-Stomatol., 25,* 7–26, 1954.
13. Psaume, J., Personal communication with the author (SP), 1960.
14. Patau, K., Therman, E., Inhorn, S. L., Smith, D. W., and Ruess, A. L., Partial-trisomy syndromes II. An insertion as cause of the OFD syndrome in mother and daughter. *Chromosoma* (Berlin), *12,* 573–584, 1961.
15. Ruess, A. L., Pruzansky, S., Lis, E. F., and Patau, K., The oral-facial-digital syndrome: A multiple congenital condition of females with associated chromosomal abnormalities. *Pediatrics, 29,* 985–995, 1962.
16. Schwarz, E., and Fish, A., Roentgenographic features of anew congenital dysplasia. *Amer. J. Roentgen., 84,* 511–518, 1960.