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The Rubinstein-Taybi Syndrome: Familial and Dermatoglyphic Data

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Since Rubinstein and Taybi [1] described the syndrome which now bears their names, there have been over 100 cases reported in the literature. In 1968, Rubinstein [2] reviewed 114 cases which either had been published or had been reported to him directly. The main clinical features are mental retardation, broad thumbs and great toes, a characteristic facies, and a high arched palate. A number of other clinical features which are present in the patients in varying frequencies are listed in Rubinstein [2] and Padfield et al. [3]. Most of the published reports describe the clinical features of the cases in some detail together with a number of investigations carried out on the patients such as chromosomal analyses, various biochemical tests, and pregnancy and family histories. No common etiological factor has emerged for this syndrome.

Since 17 patients had already been diagnosed and studied clinically in this center and the series was larger than most others reported, it seemed worthwhile to study some parameters in their first-degree relatives. An attempt was made, therefore, to estimate the frequency of this syndrome among the sibs of our patients and, in addition, those of published patients. The means and distributions of parental ages for these families were compared with a control population.

The dermatoglyphics in the parents and sibs of the Rubinstein-Taybi patients were examined in the present study. Unusual dermatoglyphics have been reported in patients with the syndrome [3–5], but there have been no reports on the frequencies of dermatoglyphic patterns in relatives of the patients.

SUBJECTS AND METHODS

The relatives studied were those of the 17 patients described in Padfield et al. [3]. In addition, familial data from published cases were taken from the literature or from questionnaires returned to us by the authors. The birth date or age of the patient, the number, age, sex, and health status of the sibs, and the maternal and paternal ages at the birth of the patient were recorded for a total of 112 families. All of the above data were not available for each of the 112 families. The control for parental ages was obtained from the 1955 Canadian census. The year 1955 was chosen because it was the mean year of birth of the

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patients. For dermatoglyphic analyses, it was possible to print the palms of 22 parents and 41 sibs of our 17 patients.

RESULTS

Syndrome Frequency in Sibs

In the 112 families, two affected sibs (excluding the probands) and 241 normal sibs were found; that is, 0.82% of the sibs were affected. The frequency excludes the concordant monozygotic twins [6], since they would be considered as one individual genetically. The ratio is much less than would be expected for a Mendelian ratio (three nonaffected to one affected, or one nonaffected to one affected). On the other hand, the frequency of the syndrome in Ontario is estimated to be 1/300,000. This estimate is based on the observation that 1/300 of the institutionalized, mentally retarded population of Ontario was diagnosed as having the Rubinstein-Taybi syndrome [3] and 0.1% of the population is in such an institution [7]. The estimate is probably too low since it is based on the assumption that all cases are institutionalized which is not true for this syndrome.

Parental Ages

The mean age of mothers at the birth of the patient was 28.6 years ± 0.6 SE compared with 27.7 ± 0.01 years for the control. The mean paternal age was 31.9 ± 0.7 years compared with 31.4 ± 0.01 years in the control. Figure 1 shows that the normalized distributions of ages of the 86 mothers and 80 fathers whose ages were known at the birth of the patients with that of the ages of mothers and fathers of live births for Canada in 1955 (the mean year of birth for the patients) were essentially the same.

Dermatoglyphics

Table 1 shows the comparison of the dermatoglyphics in 63 relatives of 17 patients and a control consisting of 1,000 Canadian schoolchildren [3, 5]. The frequencies

TABLE 1

COMPARISONS OF FREQUENCIES OF DERMAL PATTERNS IN RELATIVES OF PATIENTS WITH RUBINSTEIN-TAYBI SYNDROME AND CONTROLS

		Percentage of Individuals with Pattern					Mean	
Sample	No. Individuals	Hypothenar	Thenar + Interdigital I	Interdigital II	Interdigital III	Fingertip Arches	atd Angle	Total Ridge Count
Parents	22	59.1	9.1	4.6	68.2*	3.3	44.9 ± 1.2	135.5 ± 8
Sibs	41	56.1*	4.9	2.4	43.9	7.6	45.1 ± 1.0	121.4 ± 7
Total	63	57.1**	6.4	3.2	52.4	5.9	45.0 ± 0.8	126.4 ± 5
Total	1,000	37.0	11.3	3.0	40.4	5.3	49.9	133.9 ± 2

NOTE.—Controls consist of 1,000 Canadian schoolchildren [3].
* Significantly greater than controls ($.05 > P > .01$).
** Significantly greater than controls ($P < .01$).

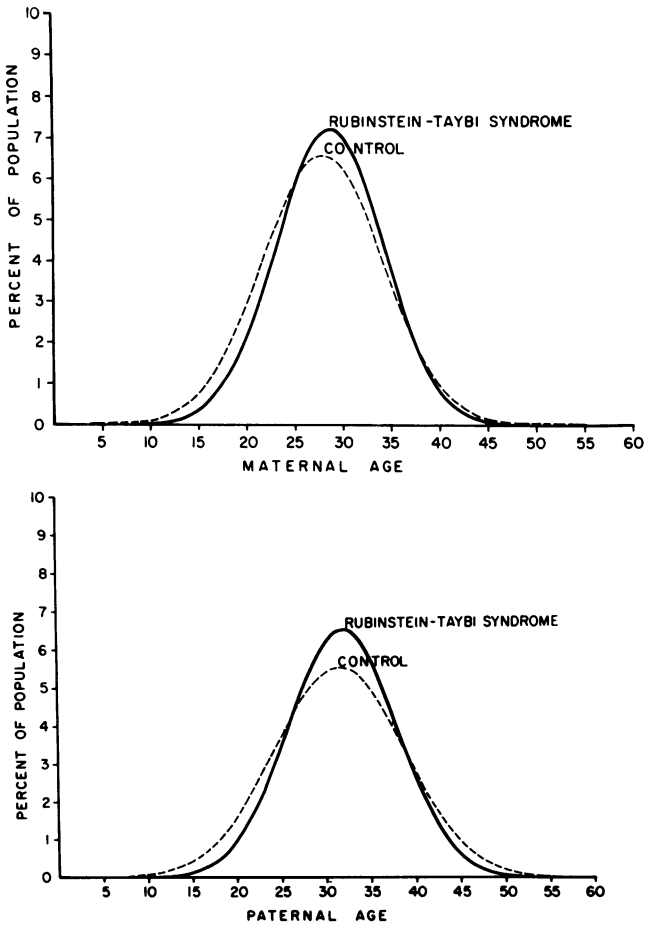

FIG. 1.—Normalized distributions of parental ages for mothers and fathers of Rubinstein-Taybi patients and of Canadian births for 1955.

of hypothenar patterns in the parents and sibs were similar to those found in the Rubinstein-Taybi patients [3–5] and occurred more frequently than in the controls. The χ^2 for 1 df was 9.4 ($P < .01$) when the frequencies of patterns in the hypothenar region for sibs and parents were combined and compared with the frequency in the controls. The frequency for the 22 parents alone was not significantly greater than in the controls, but the frequency for sibs was greater ($\chi^2 = 5.3$, 1 df, $.05 > P > .02$). There was also an increase of patterns in the third interdigital area of the palms of parents: 68% compared with 40% in controls ($\chi^2 = 5.8$, 1 df, $.02 > P > .01$). This was mainly a result of the high frequency (77%) in the 13 mothers. The atd angles were lower (not higher as in the patients) for parents and sibs, and the total ridge count was the same as in the controls. The frequencies of the other patterns characteristic of the Rubinstein-Taybi syndrome were not different from the controls (table 1).

DISCUSSION

The recurrence risk of about 1% in sibs makes it unlikely that the syndrome is determined by a single gene, although the hypothesis of a dominant lethal gene, as suggested by McKusick [8], cannot be completely ruled out. The frequency of the syndrome among sibs was substantially greater than in the general population, suggesting that the syndrome is at least familial. Although only one pair of monozygotic twins has been found, both members had the syndrome [6]. Therefore, the data suggest that the syndrome is determined genetically but not likely by a single gene.

The means and distributions of parental ages were found to be similar to that of a control population and in agreement with the findings of others [2]. Hypothenar patterns occurred more frequently in the parents, sibs, and patients than in the controls. This suggests that the patients' hypothenar patterns are familial and may or may not be associated with the syndrome. It was not possible to test whether there were more families whose members had hypothenar patterns among those families with a patient with the syndrome than among the families with no patient because the latter data were not available. However, some genetic control of the occurrence of hypothenar patterns has been suggested [9] and would seem a more likely reason for their familial occurrence than association with the Rubinstein-Taybi syndrome. The significance of a greater frequency of third-interdigital patterns, particularly in mothers of patients, is difficult to interpret.

The most strikingly unusual dermatoglyphic patterns which have been reported for the patients are those in the thenar and first-interdigital areas. Patterns in the thenar and first-interdigital areas did not, however, occur more frequently in the relatives of the patients and are more likely one of the features of the syndrome.

SUMMARY

Two sibs with the Rubinstein-Taybi syndrome were found among 243 sibs of patients with the syndrome. The sib risk of about 1% is substantially greater than the population risk of 0.0003% estimated for the syndrome in the province of Ontario. The means and distributions of parental ages were similar to those of controls.

The frequency of hypothenar patterns was greater in first-degree relatives than in controls and patients, suggesting that they may not be associated with the syndrome. The frequencies of thenar and first-interdigital patterns, however, were not increased in first-degree relatives over those in controls, which suggests that these patterns are probably features of the syndrome.

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