

Brachymesophalangia-5 without Cone-epiphysis Mid-5 in Down's Syndrome

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ABSTRACT Brachymesophalangia-5 proved to be far more frequent in 212 cases of Down's syndrome karyotype (i.e., 21%) than in 14,197 survey volunteers of European ancestry (1.4%). However, none of 28 juvenile Down's syndrome patients with brachymesophalangia-5 exhibited a cone-epiphysis on mid-5, as against the 47% that would be expected. Apparently the manifestation of brachymesophalangia-5 in the 47,G+ karyotype is not simply a dosage effect associated with trisomy of chromosome 21.

Down's syndrome or Down's anomaly, formerly called "Mongolism," includes brachymesophalangia-5 as a rather common characteristic (Holt, '43; Hall, '64; Penrose and Smith, '66). Except Roche ('61) and Greulich ('70), estimates of the frequency of this skeletal trait in Down's syndrome have not been seriously attempted. Previous workers, moreover, have not distinguished brachymesophalangia-5 from brachymesophalangia-5 with cone-epiphysis-5, in their radiographic studies of Down's syndrome cases, so that it is not clear which of the two skeletal variants is properly associated with this condition.

We have, therefore, investigated both brachymesophalangia-5 and the cone-epiphysis trait of mid-5 in 212 cases of Down's syndrome at the Plymouth State Home and Training School, Northville, Michigan. Postero-anterior hand-wrist radiographs of both left and right hands were employed in the investigation. Two hundred of the Down's syndrome cases were of the classical 47,G+ karyotype as shown by trisomy of a G group chromosome in the vast majority of leucocytes cultured. The remaining 12 Down's syndrome juveniles and adults included three D/G translocations, three G/G translocations, three 47/46 mosaics, one 48,XXX,G+ individual (i.e., 48 trisomy G, XXX)

and two karyotypically "normal" 46 chromosome Down's syndrome cases (cf. Gall, Garn, Harper and Stimson, '70).

For comparison, we turned to our own preliminary findings on 14,197 subjects of European ancestry, all of them participants in the 1968-1970 10-State Nutrition Survey of the U.S.A. (cf. Garn et al., '72). This provided the best possible sample, both in terms of size and analytic procedure. The question was how Down's syndrome patients and clinically-normal volunteers compared with respect to brachymesophalangia-5 and cone-epiphysis of mid-5.

As shown in table 1, brachymesophalangia-5 was exceptionally common in both Down's syndrome males and Down's syndrome females from infancy through adulthood. It was observed in approximately 21% of the institutionalized boys and girls and men and women. By contrast, less than 2% of the over 14,000 subadults and adults in the survey population exhibited the broad-short middle segment of the fifth digit or ray. Since three cases of brachymesophalangia-5 were "expected," using the population frequencies, while more than 40 were observed among the Down's syndrome patients, the resulting *p* value is astronomically low, and the difference significant at any conceivable level of confidence.

TABLE 1

The frequency of brachymesophalangia-5 in Down's syndrome patients and a national survey

Group	No.	Affected males		No.	Affected females	
		No.	Per cent		No.	Per cent
10-State Nutrition Survey	6456	76	1.2	7741	116	1.5
Down's syndrome patients ¹	123	24	19.5	89	21	23.6

¹ Compare with Greulich ('70), pp. 94-95, and Roche ('61), p. 389.

TABLE 2

Absence of cone-epiphysis in Down's syndrome juveniles with brachymesophalangia-5

Subjects with brachymesophalangia-5	With cone-epiphysis ¹		Without cone-epiphysis ¹	
	No.	Per cent	No.	Per cent
Affected normal juveniles	55	47	61	53
Affected Down's syndrome juveniles	0	0	28	100

¹ From the samples described in table 1. The epiphysis of mid-5 radiographically visible, but not united.

Now in clinically-normal juveniles, prior to epiphyseal union (but after the radiographic appearance of the epiphysis), brachymesophalangia-5 is often associated with cone-epiphysis of mid-5. This is shown separately for a subadult subseries of the Nutrition Survey subjects in table 2. In all, among 116 otherwise-normal juveniles with brachymesophalangia-5, selected for the present comparison, 47% also exhibited a cone-epiphysis on the middle segment of the fifth digit or ray. Among comparable Down's syndrome juveniles (prior to epiphyseal union of the proximal epiphysis of mid-5) none showed an unmistakable cone-epiphysis. To cite numbers, 28 of the Down's syndrome boys and girls exhibited the broad-short middle segment, 13.3 would be expected to show the combination of brachymesophalangia-5 and cone-epiphysis of mid-5, but none did in fact. If we compare the expected proportion (13.3:14.7) and the observed proportion (0:28), then the difference is highly significant, after correcting for continuity. In other words, brachymesophalangia-5 is extremely common in Down's syndrome ($p < 0.001$) yet strikingly unrelated to cone-epiphysis-5 ($p < 0.001$). The lack of association with cone-epiphysis-5 differentiates brachymesophalangia-5 in trisomy G from the com-

bination of brachymesophalangia-5 and cone-epiphysis-5 in apparently-normal individuals (cf. Garn et al., '72).

Brachymesophalangia-5 in Down's syndrome, is often associated with clinodactyly-5 (the bent little finger trait) as shown in figure 1. It is associated also with distal size reduction, as also depicted. There are other associations with length reduction of the phalanges and metacarpals that can be documented, from our measurements, and it is likely that brachymesophalangia-5 in Down's syndrome is the skeletal concomitant of reduced number of flexion creases in the fifth digit in Down's syndrome cases (cf. Penrose and Smith, '66, fig. 16).

The point here is that brachymesophalangia-5 is 15 times more frequent in Down's syndrome than in the apparently-normal population (accepting a 1.4% incidence in the normals and 21% in the "Mongols.") At the same time, brachymesophalangia-5 in Down's syndrome is remarkably independent from the cone-epiphysis of mid-5. By implication neither the prevalence nor the incidence of brachymesophalangia-5 in the 47,G+ and related karyotypes can be considered as a simple dosage effect, due to trisomy 21, but something with a different basis of development.



Fig. 1 Brachymesophalangia-5 shown in postero-anterior radiographs of four cases of the 47,G + (Down's) syndrome. As shown in the nine year old male and female in the examples on the left and in a 16 year old male and female (right) clinodactyly-5 — the bent little finger — and distal reductions are frequent concomitants of brachymesophalangia-5.

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