

DWARFISM IN THE AMISH

I. The Ellis-van Creveld Syndrome

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Elsewhere (1) the group characteristics which make the Amish useful for genetic studies have been reviewed. Dwarfism was selected for initial study because "achondroplastic dwarfism" was noted by one of us (D.E.K.) to be unusually frequent in the Amish and because dwarfism is a trait for which essentially complete ascertainment could be expected (2).

METHODS

By multiple methods of ascertainment an attempt was made to identify all cases of dwarfism in the Old Order Amish. Correspondence with acquaintances in many Amish communities, inquiries to over 500 physicians practicing in Amish areas and information from Amish dwarfs and their families about other Amish dwarfs were the main approaches.

Because classical achondroplasia is a dominant, whereas both parents of the multiple cases in Amish sibships were said to be normal, and because of inbreeding of the Amish, it was suspected before the study was initiated that some recessive form of dwarfism, such as the Morquio syndrome (3), the Ellis-van Creveld syndrome, or diastrophic dwarfism (4) was involved rather than true achondroplasia. The additional information was obtained that some of the "achondroplastic dwarfs" have polydactyly. That the Ellis-van Creveld syndrome is the basis for at least some cases of dwarfism was, therefore, suspected and was confirmed by examination of several dwarfs early in the study. Thereafter, polydactyly was included in the inquiries to lay and medical contacts.

Since neonatal or infant death is frequent in cases of the Ellis-van Creveld syndrome, inquiry was made concerning the presence of polydactyly and short extremities in cases of early death. In the vital records of the states of Pennsylvania, Ohio and Indiana, chondrodystrophy and polydactyly were sought in birth certificates and death certificates. In Pennsylvania, where space for recording of congenital malformations has been provided on the birth certificate since 1948, several cases subsequently established as the Ellis-van Creveld syndrome were discovered in this way. As part of a general search for genetic disease, the death certificates were examined for infant deaths over a 10-year period (1953-1963) as known to the undertaker who handles most of the Amish funerals in Lancaster County. This procedure also uncovered several previously unknown cases of the Ellis-van Creveld syndrome (EvC). The death certificates of infant deaths occurring in close relatives of established cases of the Ellis-van Creveld syndrome were also

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screened. Death certificates are available in Pennsylvania back to 1906. Although no new cases were identified, some cases were called to our attention by the school nurses.

The records of the following institutions were surveyed: Lancaster General Hospital, St. Joseph's Hospital (Lancaster), Lancaster Osteopathic Hospital, Cleft Palate Clinic (Lancaster), Lancaster County Society for Crippled Children, State Hospital for Crippled Children (Elizabethtown, Lancaster County), Ephrata (Pa.) Community Hospital, Children's Hospital of Philadelphia, St. Christopher's Hospital (Philadelphia), Shriner's Hospital (Philadelphia), Children's Hospital, Columbus, Ohio.

All living cases were examined and special studies, especially radiologic, cardiologic and dental, were performed in selected instances. Skeletal X-rays were examined in nine patients and, in several, serial studies were available. All available medical records were accumulated in deceased cases and the parents or other close relatives were visited. Many possible cases were excluded by this process. Only cases of indubitable EvC are so indicated in this study. Since another type of dwarfism is frequent in the Amish, the existence of polydactyly was an especially valuable diagnostic feature in deceased cases.

Genealogic information was collected for all established cases.

RESULTS

Types of dwarfism. One patient with the Turner syndrome was referred as a dwarf (5). In another family four sibs were found to have a condition with some features, including dwarfism and mental retardation, suggesting Mongolism but with normal chromosomes. In several instances dwarfism was interpreted as polygenic in origin, because body proportions were normal and short stature occurred also in close relatives, without any clear Mendelian pattern of inheritance.

Two types of dwarfism occur in the Amish with unusually high frequency. One type, the Ellis-van Creveld syndrome, is the subject of the discussion that follows. The second type, a newly recognized disorder which we shall call cartilage-hair hypoplasia (CHH), will be the subject of a later presentation (6).

Clinical features of the Ellis-van Creveld syndrome. Although few more than 40 cases of EvC have been reported (7), its cardinal and consistent features are well established: short-limbed, disproportionate dwarfism (Figs. 1, 3, 6, 8, 9), polydactyly (Figs. 2, 4, 5, 6) and dysplasia of fingernails (Figs. 6, 8, 9). The shortening of the extremities is most striking distally, in contrast to classical achondroplasia, which shows more striking shortening in the proximal part of the limbs. The affected adults are usually not able to make a tight fist (Fig. 6D); the reason is that the proximal phalanges are relatively long compared with the other phalanges (Fig. 6E). A consistent feature is fusion of the hamate and capitate bones of the wrist (Figs. 5B, 6E, 8C, 9D). Another consistent skeletal feature is a defect of the lateral aspect of the proximal part of the tibia (Fig. 2C) resulting in "knock-knees" (Figs. 8D, 9E).

The presence of dysplastic nails suggested a synonym for this condition,



FIG. 1. Ellis-van Creveld syndrome in 19-year-old Amish girl. The stumps of amputated extra fingers, the dysplastic fingernails, and the peculiar foreshortened and sunken upper lip are evident. The patient is 42 $\frac{3}{4}$ inches tall. See also Figure 11F.

chondroectodermal dysplasia. The upper lip is short (Figs. 1, 9B) and bound down, with absence of the usual groove between it and the mandibular alveolar ridge. The teeth are poor.

On the basis of reported cases, congenital heart disease has been said to occur in as many as 60 per cent of affected persons (8). Single atrium (Fig. 7), or large atrial septal defect, has been the most frequent malformation (9). Because of the cardiac involvement in the syndrome, it has been cogently proposed (10) that the disorder should be termed *mesoectodermal dysplasia*. However, rather than introduce terminologic confusion it seems best to retain the eponyms until understanding of the disease permits a designation based on the nature of the basic defect.

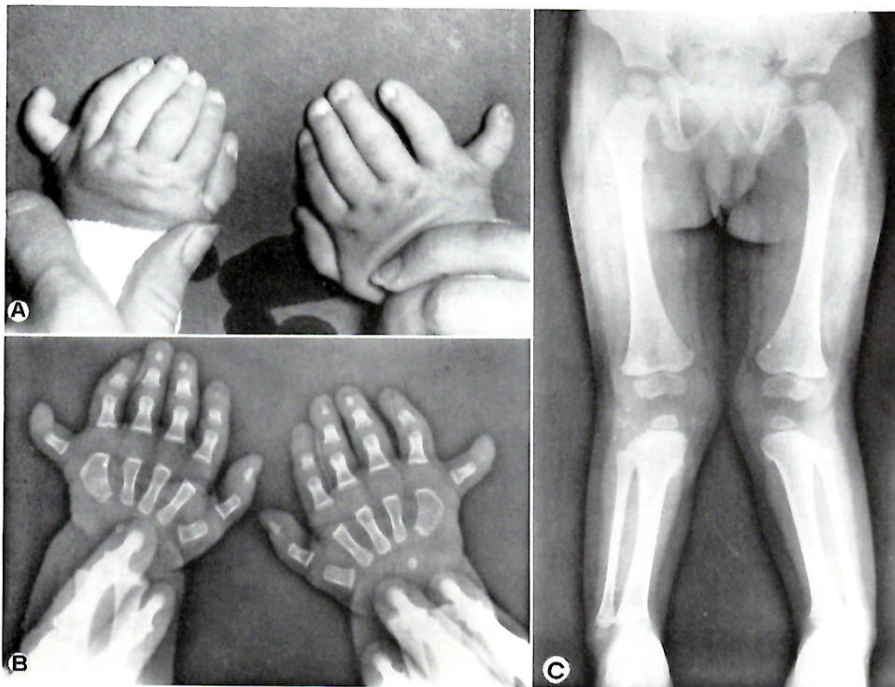


FIG. 2. A, B. Hands at six months in an Amish boy with Ellis-van Creveld syndrome. The characteristic polydactyly is shown. The fingernails are essentially normal, however. C. At 30 months of age, in the same child, X-ray shows erosive changes in the lateral aspects of the proximal part of the tibia producing "knock-knees." The greater sciatic notch is small and peaked, similar to that seen in cases of classic achondroplasia.

The following clinical aspects of the Amish patients are noteworthy:

1) *Polydactyly* in the hands is a consistent feature but occurs in the feet in only a minority of cases (cf. Figs. 8E, 9G). One patient had six digits removed from all four extremities. The third and fourth toes were partially fused and by X-ray an abortive toe was demonstrated between them (Fig. 9G). Thus, the patient had had seven toes on one foot. (Ellis and Andrews (7) state that eight of 40 reported cases had pedal polydactyly, with which the experience of this series would agree.)

The extra finger is post-axial or post-minimal, i.e., lateral to the normal fifth finger, and is reasonably well formed and functional. Higher numbers of fingers than six were not observed or recalled by our informants. By the time of this survey, however, the extra fingers had been amputated in all except three of the patients (Fig. 2 shows one of these). In some of these patients the extra fingers were removed by ligature in infancy. This method is not to be recommended, however, because it is rather barbarous

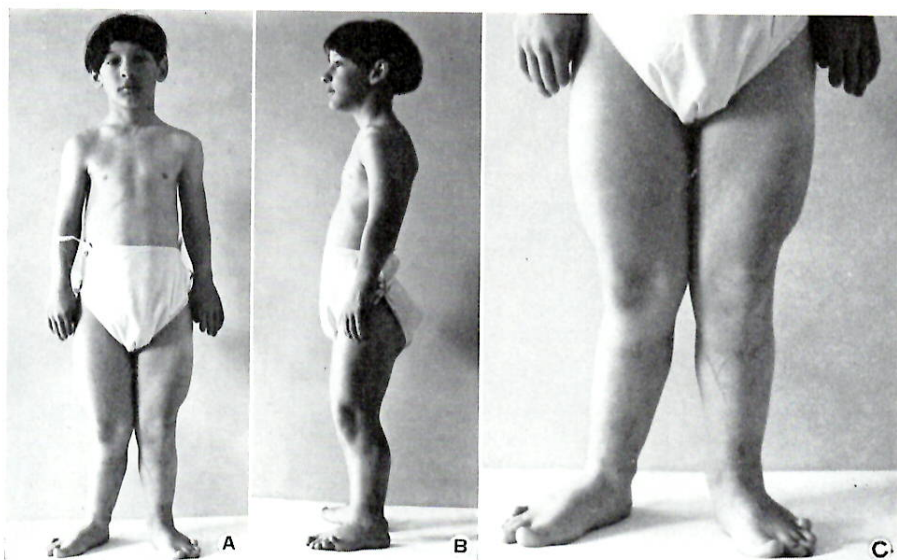


FIG. 3. A-C. Twelve-year-old Amish boy with EvC. Height 43 inches. Note the overlap of the fourth toe by the fifth. The extra fingers were amputated at six months of age.



FIG. 4. Polydactyly in Amish girl, age four months, with other features of Ellis-van Creveld syndrome.

in view of the relatively large size of the digit, and because the result is poor. Figures 1 and 9 show the unsatisfactory results of the ligature technique.

It has been suggested (7) that the skeleton of an infant with seven fingers bilaterally, reported by Kerckring in 1670 (Fig. 10), was a case of EvC. A feature atypical of EvC was the presence of eight and nine toes on the

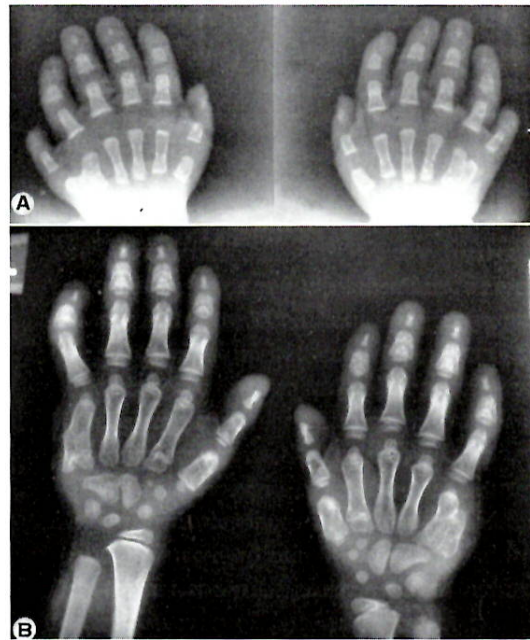


FIG. 5. A. Polydactyly in six-month-old Amish girl with Ellis-van Creveld syndrome. Amputation of the extra fingers was performed at this time. B. The X-ray appearance of the hands in the same patient at the age of $5\frac{1}{4}$ years. In the wrists, the hamate and capitate bones are fused on one side only.

right and left feet, respectively. More than six fingers on a hand in the Ellis-van Creveld syndrome have been described in a few instances (7). Kerckring's case was rather more similar to that reported by Meitner (11), and it is doubtful that either had EvC.

Overlapping of the fourth toe by the fifth was frequent (Fig. 3).

2) *The lip defect* (Fig. 9B) was usually referred to as partial harelip. Surgical repair was performed in one case (sibship 6). The upper lip is abnormally short and is bound down by multiple frenula. Because of these multiple stringy attachments "lip-tie" is an appropriately descriptive term. The superior gingivo-labial groove may be entirely missing. The upper lip is also sunken because of the hypoplasia of the anterior maxilla described below.

3) In most patients *teeth* were already erupted at birth or appeared in the first month or two. In one patient six teeth were erupted at birth. Most of the Lancaster County Amish have poor teeth; however, dentures are probably required unusually early in the EvC patients. Premature exfoliation as well as premature eruption of teeth is characteristic of EvC.

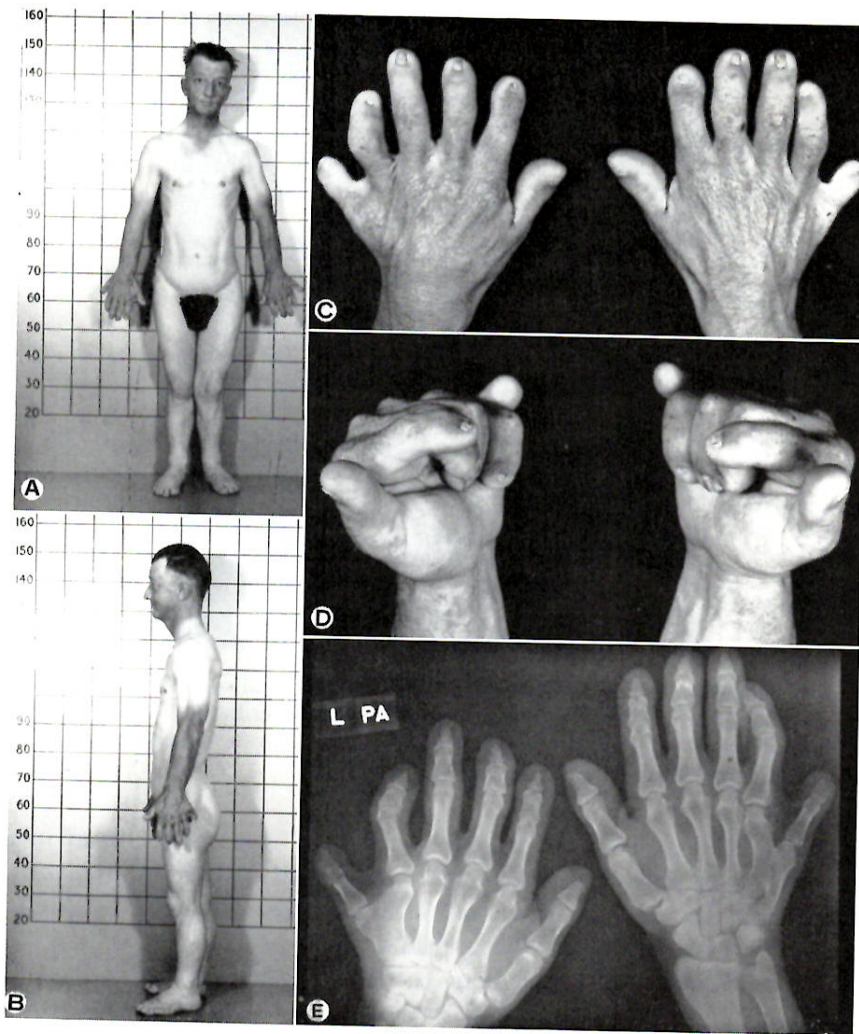


FIG. 6. A, B. A non-Amish man, now 44 years old, with Ellis-van Creveld syndrome. The findings are strikingly similar to those in the 58-year-old Amish man in this study, except that the extra fingers have been amputated in the Amish patient. The Amish man would not permit photographs. C. In the hands note the polydactyly, brachydactyly and dysplastic fingernails. D. The patient cannot make a tight fist. The reason is shown in E. The proximal phalanges are long relative to the middle and distal phalanges. Note the partial fusion of the hamate and capitate bones of the wrist, seen at an earlier stage in the patient in Figure 5. F. Mild epispadias is shown. In one Amish child (sibship 6) with EvC it was sufficiently marked to cause troublesome deviation of the urinary stream.

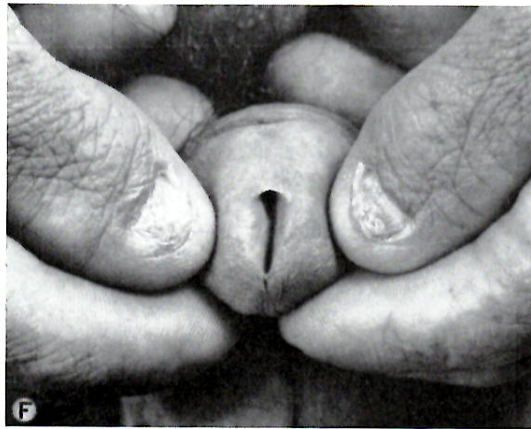


FIG. 6.

Deficiency of teeth (Fig. 11), mainly incisors, inferior and superior, was found in five patients in whom complete dental studies were done. In all of these cases precocious eruption and exfoliation had occurred. It is likely that permanent tooth buds were also lost early or never formed. Fusion of teeth was present in at least one case (Fig. 11F). This feature was illustrated also by Ellis and Andrew (7). Bodenhoff and Gorlin (37) commented on the fact that EvC is one of the few conditions in which teeth are present at birth.

4) Mild *epispadias* was noted in several males with EvC (Fig. 6F). See Metrakos and Fraser (12) for similar cases. *Hypospadias* has also been reported (13) and vaginal atresia with *hydrocolpos* was present in one published case (14). (Hydrometrocolpos was observed in two female infants in each of two Amish sibships (38). Since all four parents trace their ancestry to a single ancestral couple, it is proposed that the form of hydrometrocolpos in these cases is inherited as a simple recessive. None of the stigmata of EvC was present in these cases and it is unlikely that a connection between the two conditions exists in the Amish.)

5) *The adult height* of affected persons ranged from 42¾ to 60½ inches. The latter measurement was found in the 58-year-old man described below.

6) *Birth weight* was often normal in those cases without serious cardiac defect, but in all the chondrodystrophy was usually recognized at birth by reduced length of the limbs. *Length at birth* and height at all ages was under the third percentile in most.

7) The estimate of 60 per cent for the incidence of *cardiac malformation* based on cases in the literature may be an exaggeration. The cases

at two days of congestive heart failure. Essentially complete absence of both the interventricular and the interatrial septum was found. The aorta was hypoplastic and the pulmonary artery larger than normal. (In their second case, Smith and Hand (15) also found total lack of the cardiac septa, as well as transposition of the great vessels.)

9) A defect in the mechanics of *respiration* was suspected as the cause of neonatal death in a number of cases. Malformation of the thoracic cage, lungs and bronchial tree seems to be involved. Moore (16) has provided documentation for the occurrence of bronchial collapse, with resulting tension lobar emphysema, due to absence of bronchial cartilage. Smith and Hand (15), among others, have described chest deformity. In most patients the chest is impressively long and narrow.

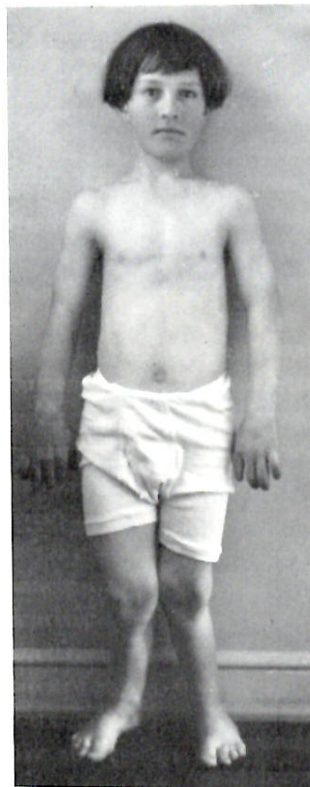


FIG. 8. Ellis-van Creveld syndrome in 14-year-old Amish boy. A. The height is 48 inches. Note the genu valgum. B. Note the dysplastic fingernails and brachydactyly. The extra fingers were neatly amputated at an early age. C. X-ray findings in the hands. The hamate and capitate bones are fused bilaterally. D. Changes at the knee resulting in genu valgum are shown. E. Although no polydactyly is present in the feet, the bones are obviously misshapen and short. (See also Fig. 11E.)



FIG. 8.

10) *Mental retardation* was described in one of the cases reported by Metrakos and Fraser (12). The patient had microcephaly and congenital cataract, both features not observed in other cases. Some other reported cases have had mental retardation. The extensive experience with EvC in the Amish suggests that mental defect is not an integral part of the syndrome. Among offspring of consanguineous marriages it is possible for more than one recessively inherited disorder to occur in a given individual. Caution must, therefore, be exercised in the interpretation of these less frequently occurring features.

11) The *hair* was not affected to any impressive degree in the patients of this series. Sparse hair was described by Ellis and van Creveld (17) in their original report, and by several writers since that time.

Prognosis. Three members of the present series were born during the twelve-month period of the study. Of the 52 cases, 30 died under six months of age. EvC was the cause of stillbirth in at least three cases and of death under two weeks of age in at least 20 of the 52 cases.

Seventeen patients were living at the time of study. Particularly note-

worthy were the nine adult patients in this series: male born 1906, female born 1934, female born 1938, male and female born 1941, two females born 1944, female born 1945, and female born in 1876, died in 1918. One of these, a 58-year-old man, is married, has seven children and is self-supporting through employment as a carpenter. A second male has recently married a non-Amish girl and is also self-supporting. None of the affected females has married. The last adult mentioned above (sibship 30) was recognized all her life as having congenital heart disease and died at 42 years of age of "cardiac dropsy."

Frequency and distribution. Fifty-two definitely affected persons distributed in 30 sibships have been identified. Of the 52, 25 are male. All the affected sibships except one reside in Lancaster County, Pennsylvania. The exception is an Amish family living in Mifflin County, which is located slightly east of the center of Pennsylvania. This family has relevant genealogic connections with the Lancaster County Amish. No EvC has been found in the Amish of Ohio, Indiana or elsewhere. On the other hand, the CHH syndrome (6), the second type of dwarfism frequent in the Amish, has a wide geographic distribution in this group.

The frequency of EvC in Lancaster County is about two per 1000 living persons: 16 cases now live in Lancaster County and the Amish group there is estimated at about 8000 (18). Thirty-five deceased cases are known. The frequency of EvC in all live births may be five or more per 1000. The latter estimate is insecure because a proper figure for the denominator is not available. The frequency of heterozygous carriers of the EvC gene is probably about 13 per cent in the Lancaster County Amish.

How relatively frequently the Ellis-van Creveld syndrome occurs in this group is indicated by the fact that two affected Amish children from families previously unknown to each other were, by chance, hospitalized simultaneously in the same room for amputation of supernumerary digits. Furthermore, as many cases of EvC have been identified in the Lancaster County Amish as have been reported in the entire medical literature (7).

The earliest born case of EvC on which we have unequivocal information was born in 1876 (sibship 30). Short-limbed infants with polydactyly may have been born previously in this kindred. Family traditions suggest earlier cases; it is recalled, for example, that a woman with children born between 1863 and 1887 expressed the concern she had during her child-bearing years that her offspring might be affected. (On p. 320 see discussion of an equivocal case born in 1863.)

Genetics. In Figure 12, the 30 affected sibships are represented. Further children will undoubtedly be added to several of the sibships. Both parents were unaffected in all instances except one. In the case of sibship No. 22

the father is affected; the mother is unaffected but is a relative of the father (Fig. 14). Recessive inheritance is suggested by this distribution of cases in an inbred group.

Consanguinity of the parents was reported in 10 of 31 affected sibships reviewed by Dayer (19). Because of parental consanguinity recessive inheritance of EvC was suspected in the original report (17) and was supported (12) by observation of multiple affected sibs with normal parents.

The segregation analysis shown in Table I assumes complete ascertainment of affected persons and makes use of the classic Lenz-Hogben, or *a priori*, method of correction for the ascertainment bias which is created

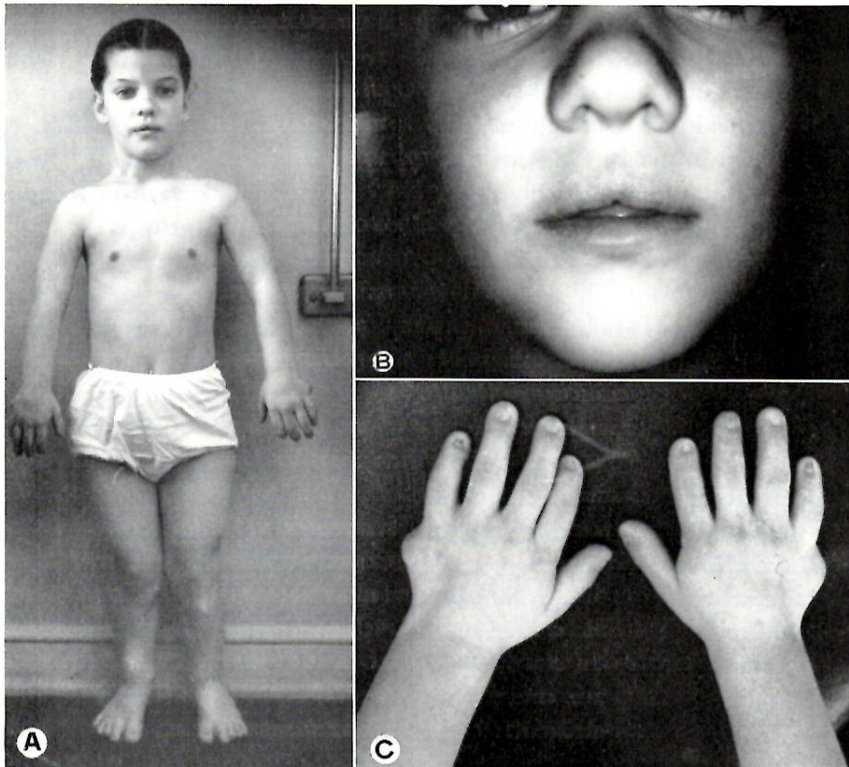


FIG. 9. 11-year-old Amish girl with Ellis-van Creveld syndrome. A. Height is 44½ inches. B. "Partial harelip" is shown. C. The nails of the third and fourth fingers are essentially normal. The amputation of the extra fingers was performed soon after birth by tying a thread tightly around each. The crude result is obvious. D. Typical changes are shown, including fusion of the hamate and capitate. E. Changes at the knees responsible for genu valgum are shown. F. The toenails are dysplastic. On the right the third and fourth toes are partially fused. G. The X-ray demonstrates an abortive extra toe between the third and fourth. (See also Fig. 11D.)

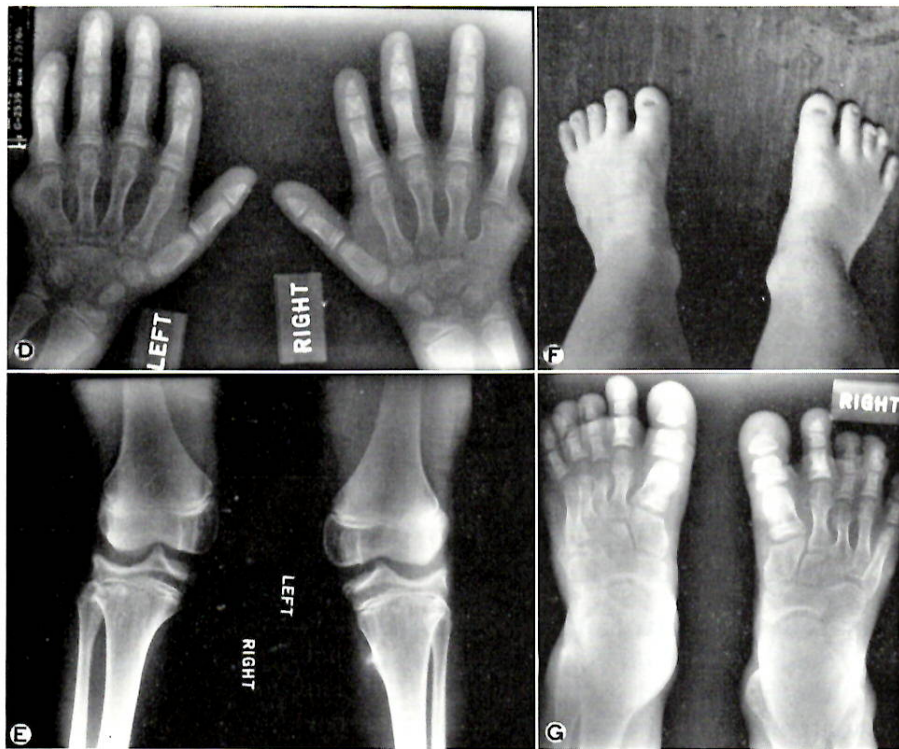


FIG. 9.

when the heterozygous parents can be identified only by the occurrence of at least one affected child among their progeny. The number of affected observed agrees closely with the number expected on the basis of the recessive hypothesis. (Twenty-seven, rather than 30, sibships appear in the analysis, because in two (No's. 18 and 26) only the proband was affected and in one (No. 22) one parent was affected.)

The genealogic interrelations of these 30 sibships are highly complex, as is indicated by the pedigree chart which is shown in the fold-out and which demonstrates only the first 26 sibships. As demonstrated elsewhere (1), about half of the Amish families in Lancaster County carry the name Stoltzfus (or Stoltzfoos), King, or Fisher. Most of these are descendants of three persons: Nikolas Stoltzfus, Samuel King and Christian Fisher. As will be seen below, the single individual in sibship 26 is a special case. Of the 58 parents of the other 29 affected sibships, 57 trace their lineage back to Christian Fisher (1757-1838), who by each of two unrelated wives, had many affected descendants (20). Fifty-six of the 58 parents can be

TABLE I
The Ellis-Van Creveld Syndrome

Sibship Size	Number of Sibships	Number Affected		Variance
		Observed	Expected	
2	2	2	2.2856	0.244
3	3	6	3.8919	0.789
4	6	7	8.7768	2.520
6	4	6	7.2992	3.104
7	3	9	6.0588	2.910
8	4	7	8.8900	4.688
9	1	4	2.4328	1.380
10	1	2	2.6490	1.592
11	1	2	2.8710	1.805
12	1	2	3.0980	2.020
14	1	1	3.5630	2.446
Totals	27	48	51.8161	23.498

S.D. = ± 4.847

traced back to Nikolas Stoltzfus, who immigrated in 1766. On the other hand, the lineage of *all* 58 parents can be traced to Samuel King and his wife, who immigrated in 1744.

In only one of the 52 cases is the diagnosis of EvC considered insecure; the infant, born in 1863, lived only two months (sibship 26). This infant can be traced to Samuel King through the mother and not through the putative father, but non-paternity is a possibility. The *Fisher Family History*, which is known, however, to contain numerous inaccuracies of dates, states as follows: "_____, Ronks, \times 1, Pa.; b. Feb. 24, 1838; d. Jan. 23, 1893; m. _____, 1864; b. Nov. 28, 1842; d. Dec. 3, 1931; occ. farmer; church, Old Order Amish. Children: Lydia, b. Dec. 22, 1863; d. Feb. 22, 1864; Isaac L., b. Jan. 22, 1865; Betsy; Christian L.; Jacob L.; Katie; Fannie; Sarah; Mary; Aaron L.; Rebecca; Samuel L." The information in the family is equivocal as to whether Lydia had EvC. All the children except the first survived to adulthood, were unaffected, and left descendants. (At least four of these had descendants with EvC.) Note that the first child was born before the putative parents were married and may also have died before their marriage. Thus, the paternity of Lydia is in question. This case is listed as an only child in sibship 26 of Figure 12, and in the large pedigree (see fold-out) the father is indicated as unknown.

Not only are all parents traced back only to Samuel King (with the qualifications given for sibship 26), but also the pedigree charts (see Fig. 13 for an example) suggest that the parents of affected persons can

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Tab. VIII

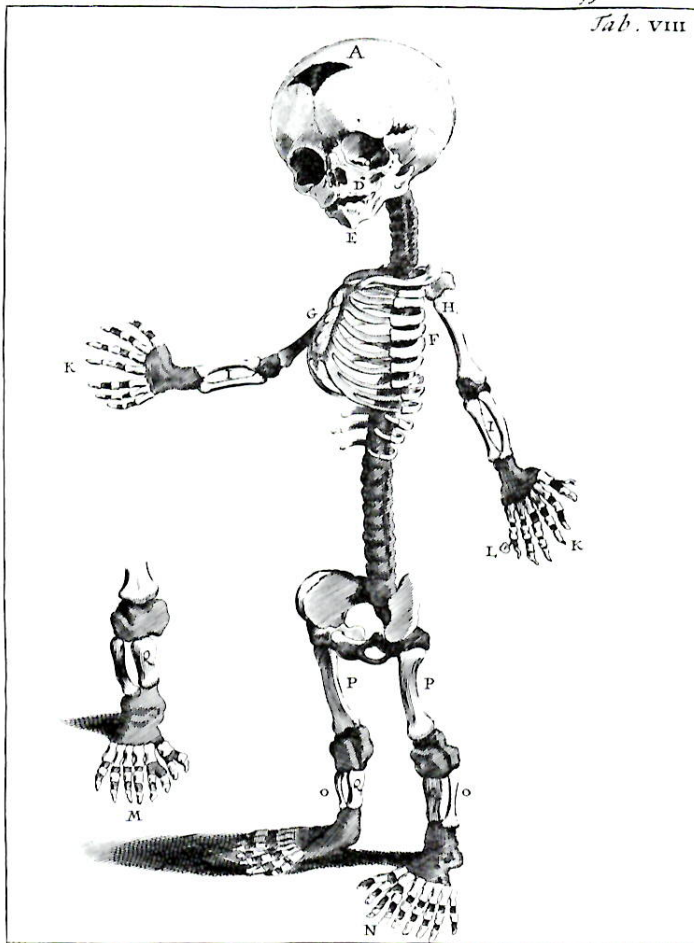


FIG. 10. In 1670 Kerckring described a polydactylous dwarf who, as suggested by Ellis and van Creveld (1940), might have had the form of chondrodystrophy which bears their name. (Theodor Kerckring: *Spicilegium anatomicum*, etc., Amsterdam, 1670.) The infant had been thrown into the river at birth. The hands had seven digits and the right and left feet eight and nine, respectively. The bones of extremities and the ribs were short. The head was large. (Jonathan Hutchinson called attention to this case in his *Archives of Surgery* (1893).)

trace their ancestry to Samuel King through more paths than they can to the other two. The existence of more paths connecting Samuel King with the heterozygous parents provided greater opportunity for the gene for EvC to pass to these persons.

Thus, the evidence suggests that Samuel King (or his wife) carried the

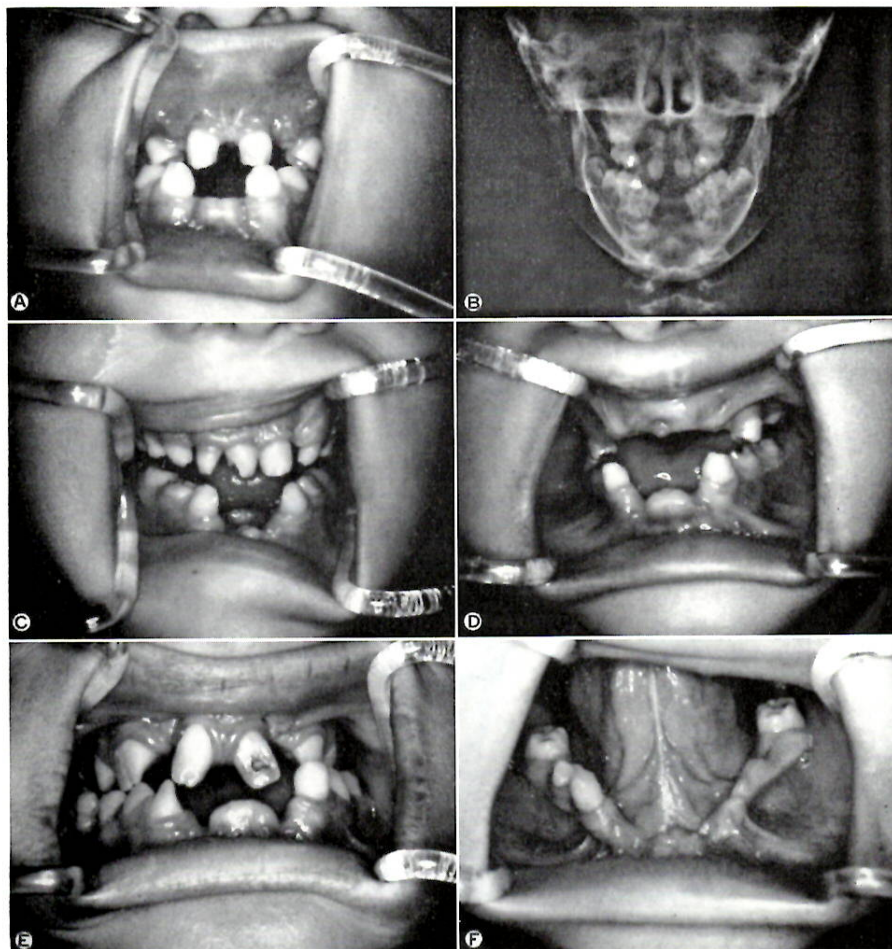


FIG. 11. The teeth in Amish cases of the Ellis-van Creveld syndrome. A. Absent upper and lower incisors in five-year-old boy. B. X-ray findings in same case. No tooth buds for the upper lateral incisors and none for any lower incisor are demonstrable. C. Absent upper and lower incisors in another five-year-old boy. D. Absent upper and lower incisors in an 11-year-old girl. E. Absent upper and lower incisors in a 14-year-old boy. Note the double tooth due to fusion of an upper right incisor with the canine. See reference 7 for a similar case. F. Many absent teeth in 19-year-old woman.

gene for the Ellis-van Creveld syndrome. The matter cannot, however, be considered as completely settled because Christian Fisher belongs to one generation more recent than that of Samuel King and information on the descendants of Christian Fisher's sibs is incomplete. Christian Fisher's father, who was probably the immigrant and who was also named Christian

THE ELLIS-VAN CREVELD SYNDROME

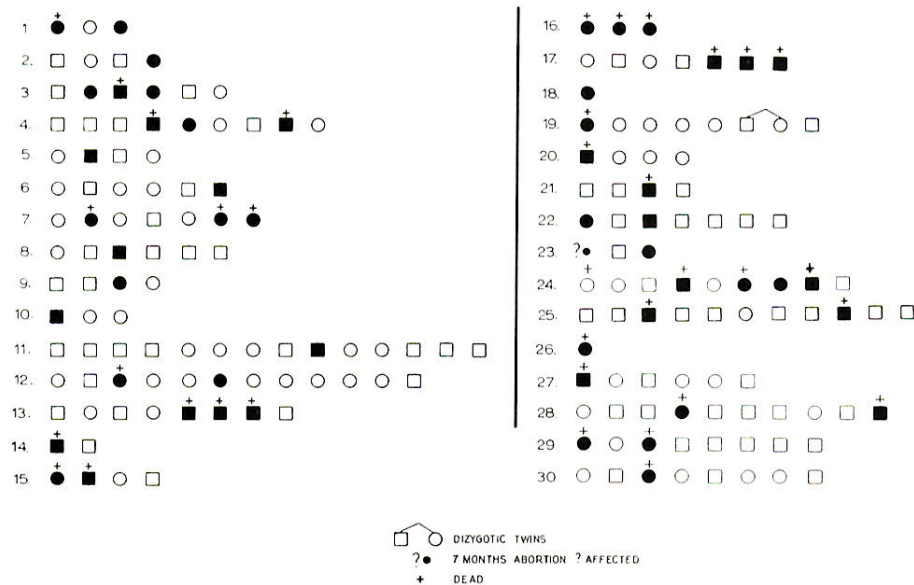


FIG. 12. The distribution of affected persons in the 30 affected sibships. In all except No. 22 both parents are unaffected. See Appendix. Several deceased unaffected persons are not indicated as dead. The next to last member of sibship 25 is female, not male.

Fisher, may, for example, have imported the gene—or his wife may have done so. That more than one of the ancestors imported the gene which has been observed in the 30 sibships described here is considered unlikely.

The earliest definite case of EvC occurred among the great-great-grandchildren of Samuel King, in a person born in 1876 (sibship 30). An earlier possible case was that of an infant born in 1863 (sibship 26). According to traditions of the community, cases of EvC had occurred even earlier than 1860.

Shown in Figure 14 is the pedigree of the family in which the father and two children are affected. It is presumed that the mother is heterozygous. As mentioned earlier, the father in this case is 58 years old and generally well. His two affected children, age 26 and 23 years, are relatively healthy and no cases of EvC died young in either sibship. The skeletal features are typical, although the father is the tallest in the series, 60½ inches. No cardiac abnormality is detectable. The three oldest cases in the series are this father and his two children. Whether genetic modifiers in this branch of the kindred may produce a milder form of the disease is a matter solely for speculation.

The four unaffected offspring of the affected male shown in Figure 14 must be heterozygotes. Two of them are married to relatives who are also

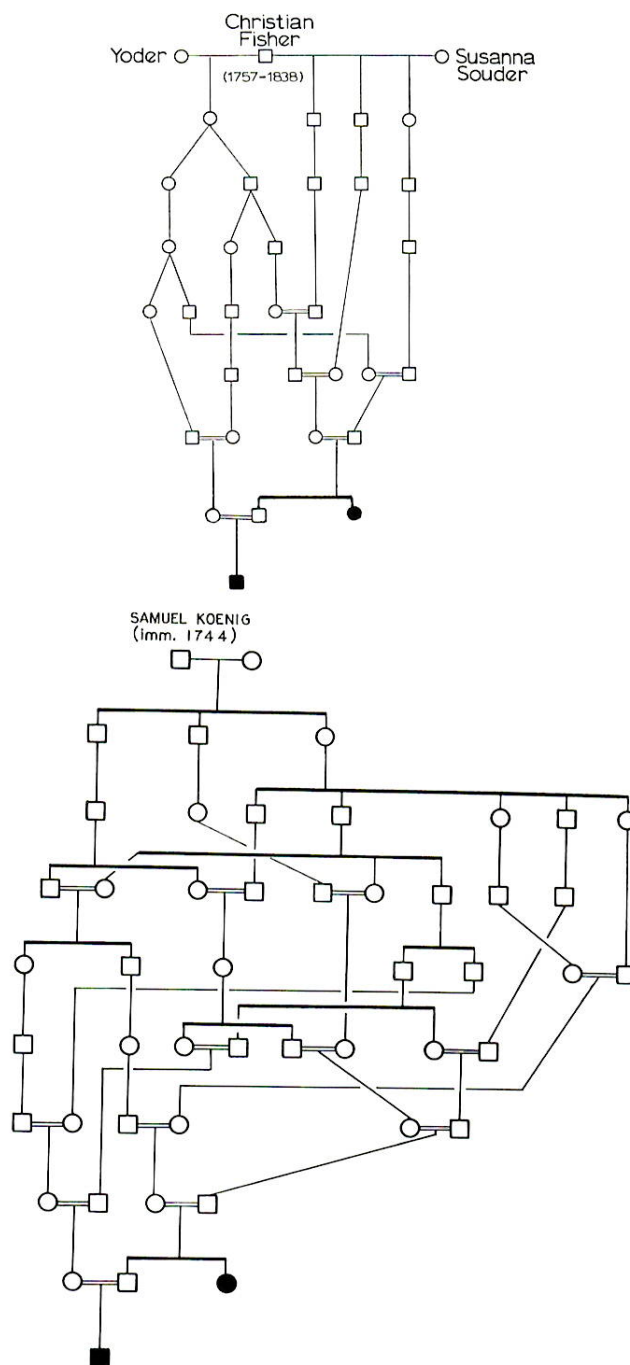


FIG. 13. The descent of two affected sibships from Christian Fisher (A) and Samuel King (B) is shown.

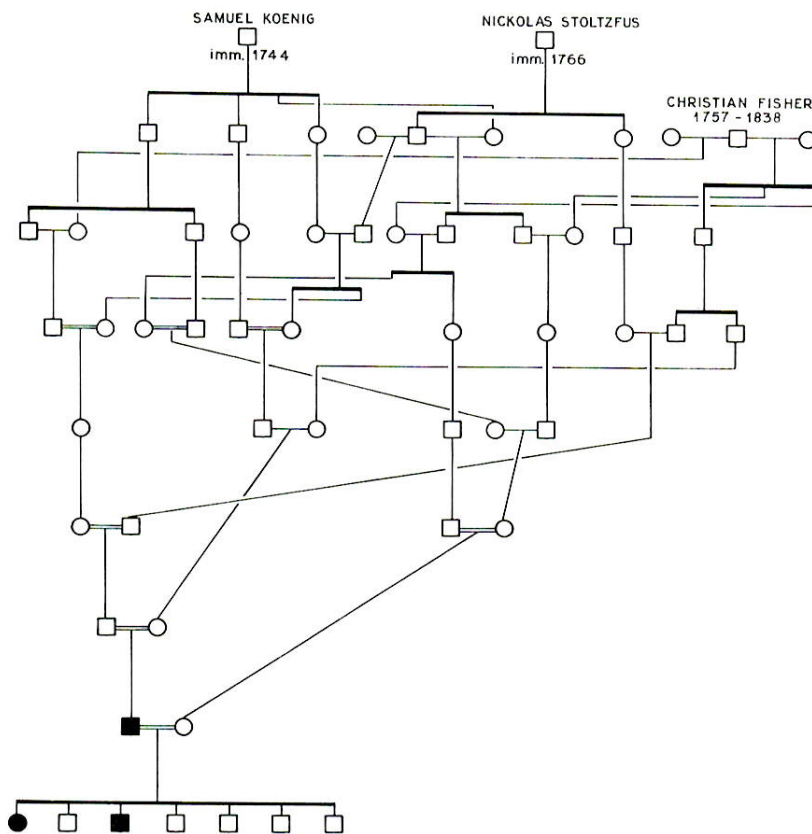


FIG. 14. The descent of two affected sibships (affected father and affected children) from Christian Fisher, Samuel King and Nikolaus Stoltzfus is shown here in a single pedigree chart.

descendants of both Christian Fisher and Samuel King. The risk of affected children is probably appreciable. The affected son has recently married an unrelated non-Amish woman.

Although no special studies, such as X-rays of the skeleton, were performed, no peculiarity was noted in the parents of the EvC cases that might be a heterozygous effect of the gene.

DISCUSSION

In this series the occurrence of polydactyly of the hands was invariable and was the most consistent clinical feature. To be sure, we relied on polydactyly for confirmation of the diagnosis in many cases. However, there is no reason to think that EvC occurs without polydactyly. For example, in no family ascertained through a case of polydactyly was there a case with features of EvC exclusive of polydactyly.

Polydactyly occurs as a part of other genetic disorders, e.g., the Laurence-Moon-Bardet-Biedl syndrome (21) and trisomy 13-15 (22), and as an isolated genetic defect (23, 24, 25). Although frequently used as a "text-book" example of simple Mendelian inheritance, simple polydactyly often fits better a polygenic model of inheritance (26). In those instances where simple Mendelian dominant inheritance seems defensible (24, 25) the nature of the polydactyly has been different from that in EvC. In the survey for cases of EvC, several families with simple polydactyly were discovered, and the frequency of simple polydactyly may be greater in the Amish than in the non-Amish white population. However, the clinical characteristics of the simple polydactyly were quite different from EvC, in addition to the fact that the other syndromal features of EvC were lacking. In the cases of simple polydactyly the feet were as often affected as the hands, and sometimes only the feet showed the change. The extent of development of the extra finger was variable; often it was merely a post-minimal tag and rarely was it a fully developed and functional extra finger. In some cases the type of polydactyly was quite different from that of EvC, being combined, for example, with syndactyly. For these reasons it seems unlikely that isolated polydactyly is a manifestation of the heterozygous state, although this possibility cannot be rejected out of hand inasmuch as at least five reports have described polydactyly in close relatives of cases of EvC: In Weyers' case 1 (27) the father had rudimentary sixth fingers; the father and mother were related. Polydactyly was described in the antecedents or collateral relatives of the patients reported by Weller (28), Midulla (29), and Zunin (30). Debré and colleagues (31) observed a sibship of 13 children of whom two had the full-blown syndrome, one had simple polydactyly, one had congenital heart disease, one had club foot, four had dental anomalies and four were normal. The parents were first cousins.

The features differentiating EvC from true, or classic, achondroplasia are sufficiently obvious not to require lengthy discussion. The skull, spine, and pelvis in EvC do not show the changes typical of achondroplasia; these characteristic changes will be reviewed (6) in connection with a discussion of cartilage-hair hypoplasia which resembles achondroplasia more closely. As mentioned earlier, the shortening of the limbs is greatest proximally in achondroplasia, distally in EvC.

The pre-Revolutionary immigrants from whom the present-day Lancaster County Amish descended almost certainly numbered no more than 200 persons. The number of persons from the first settlement in Berks County who founded the Lancaster County group was even smaller. Only one of these persons was, in all probability, a carrier of the EvC gene. The

frequency of the gene was, then, as low as one in 400 in the founding group and almost certainly not greater than one in 50. The present gene frequency of about one in 14 requires explanation.

Three related but distinct factors might be involved either alone or in some combination. One is the founder principle, which is defined as follows by Mayr (32), who introduced the concept: "This term designates the establishment of a new population by a few original founders (in an extreme case, by a single fertilized female) which carry only a small fraction of the total genetic variation of the parental population." The Ellis-van Creveld gene is ordinarily very rare. If the frequency of the gene in the founding group was one in 50, then the founder principle was involved to some extent in the presently high frequency. The "founder" in this specific case was Samuel King or his wife.

A second factor is *differential fertility*. If for any reason whatever the persons carrying the EvC gene had more children on the average than did those without the EvC gene, then the presently high frequency would be explained.

A third factor is *random genetic drift* (33, 34). In a small population, even if fertility of all persons is identical, segregation may by chance alone differ appreciably from the ideal 50-50 and drift toward higher or lower gene frequencies can take place in a few generations. It is difficult to evaluate the separate contributions of the last two factors.

The limitation of EvC to Lancaster County is consistent with historical evidence on differences in origin of these Amish and those of Ohio and Indiana and also with the relative isolation of the eastern Amish from the western Amish which obtained until quite recently (35). It is noteworthy that the surname King, borne by the "founder" who is thought to have imported the EvC gene, is not found in a single instance in the Holmes County (O.) Amish community (39), whereas it accounts for 12-14 per cent of Lancaster County Amish families. The Lancaster County and Holmes County Amish constitute separate and distinct demes, this being the term introduced by Murdock (40) for endogamous local communities, or consanguineal kin groups.

At least four cases of EvC have been reported from Switzerland (19, 36). The wide distribution of races represented by the reports of cases indicates that although the gene is, in general, rare, the normal allele must have undergone mutation on many separate occasions. The review by Dayer (19) indicates that the disorder has been reported in Jewish, English, Dutch, Turkish, Italian, French, Tunisian-Algerian, and French-Canadian persons. Smith and Hand (15) reported the condition in the American Negro; three of seven non-Amish sibships with the Ellis-van Creveld syndrome

studied at the Johns Hopkins Hospital are Negro. Thus, EvC is by no means limited to the Amish but is more frequent in this group than in any other population of comparable size yet studied. Furthermore, it is limited to one subgroup of Amish.

Since few persons with the EvC syndrome have children, the gene must be selected against severely in the homozygote. However, the gene has by chance achieved relatively high frequency in Lancaster County Amish, and endogamy maintains a continuing appearance of homozygotes. Elimination of all homozygotes reduces gene frequency only very slowly.

No clue to the nature of the basic defect in EvC is available. The fact that inheritance is recessive suggests that an enzyme defect may lie at the root of this syndrome of malformations. The enzyme fault, if such it is, must have its effects early in embryogenesis to result in cardiac malformation and polydactyly but may continue to have its effects in the bones and fingernails until after completion of growth and perhaps throughout life.

SUMMARY AND CONCLUSIONS

The most frequent variety of dwarfism in the Amish of Lancaster County, Pa., is the Ellis-van Creveld syndrome. Fifty-two cases distributed in 30 sibships have been identified. The frequency is about two per 1000 living persons and five or more per 1000 births. The frequency of the EvC gene may be as high as .07, in this group; as many as 13 per cent of Lancaster County Amish may be heterozygous carriers of the gene.

Although cardiac malformation is an important part of the syndrome, the proportion of cases showing this feature may have been exaggerated somewhat. Disorder in the mechanics of respiration is probably another important cause of neonatal death. The Ellis-van Creveld syndrome is a cause of stillbirth and over a third of the cases die before two weeks of age.

In the group of 52 cases of the Ellis-van Creveld syndrome nine affected adults (19 years old and older) were observed. The oldest is age 58 years. Furthermore, an affected male married to a relative has seven children, of whom two are affected.

No case of the Ellis-van Creveld syndrome has been discovered in the Amish of Ohio, Indiana, or other areas. Furthermore, all 60 parents of Ellis-van Creveld cases can probably be traced back to one Samuel King and his wife, who immigrated in 1744. The factors responsible for the unprecedentedly high frequency of the Ellis-van Creveld gene in Lancaster County Amish have been discussed.

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SAMPLE NO. 1

I

II

III

IV

V

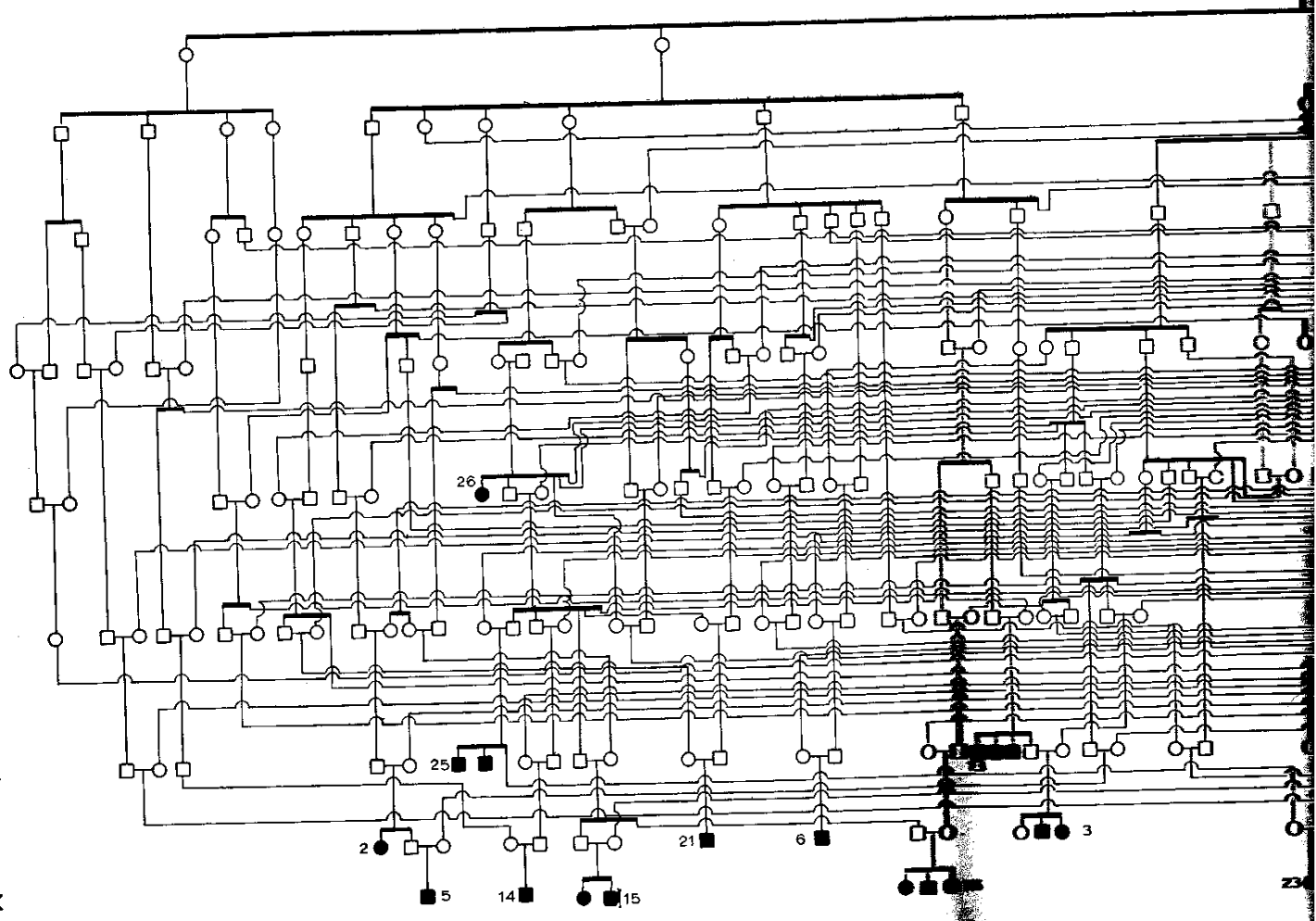
VI

VII

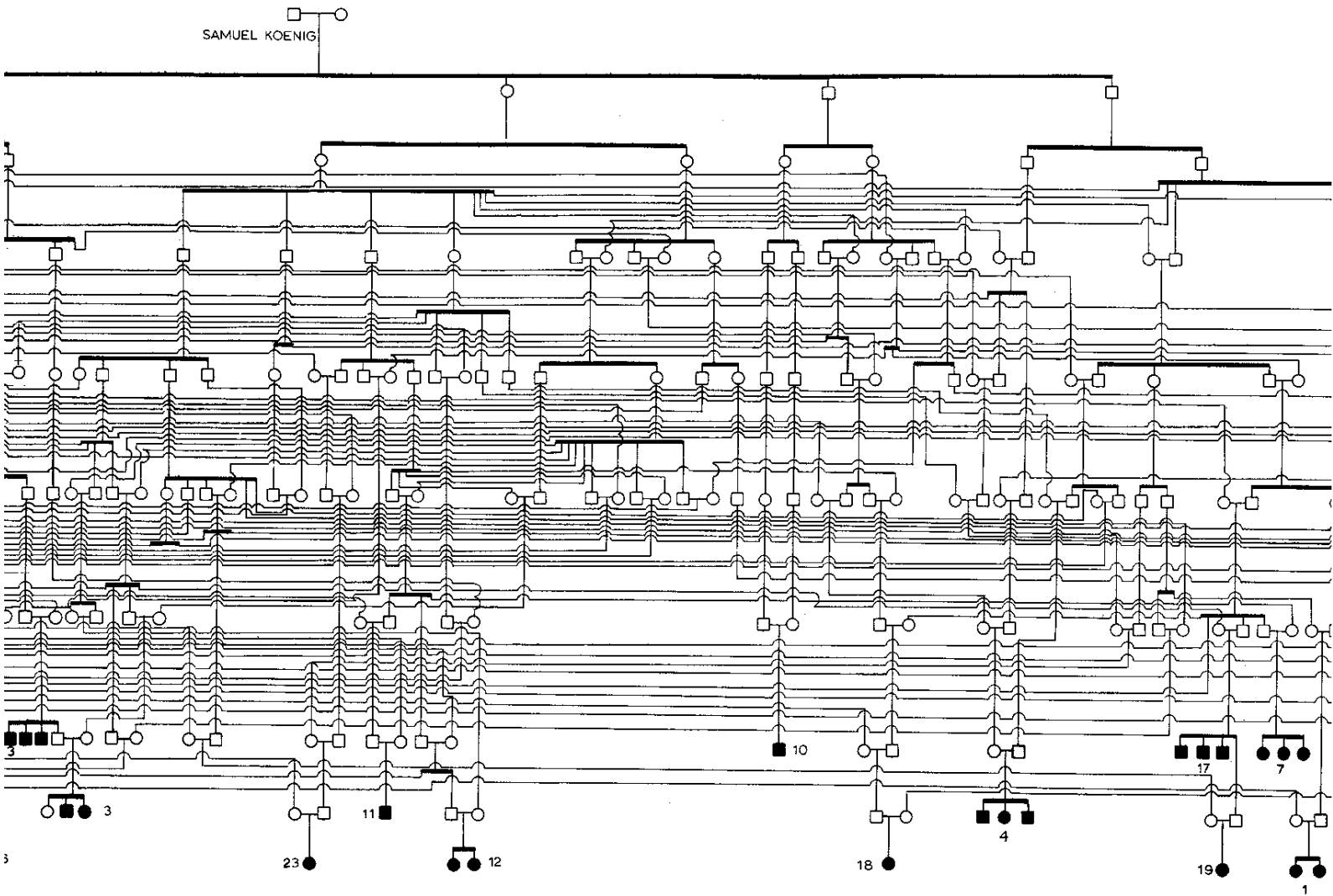
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IX

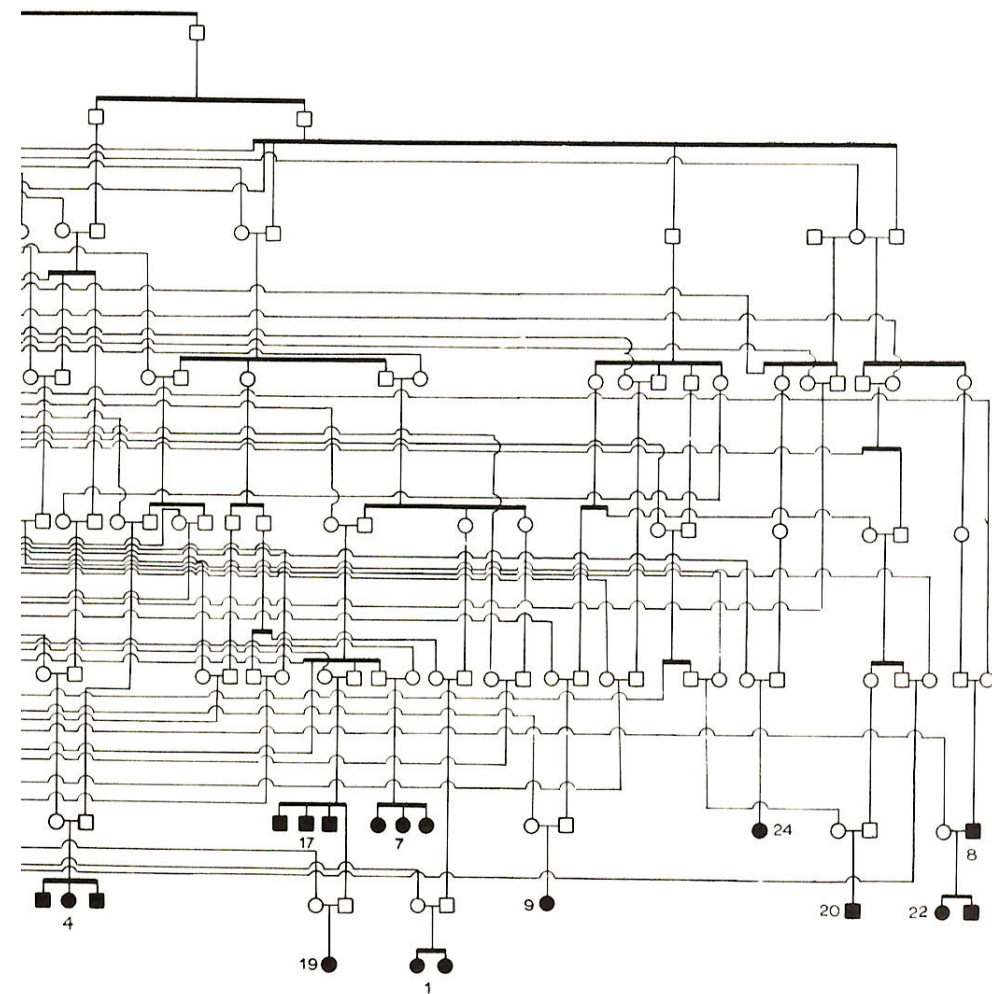
X



SAMUEL KOENIG



The descent of both parents and his wife is demonstrated. It is also uncertain that this is numbered in the same way as not indicated in this diagram



The descent of both parents of Ellis-van Creveld cases from Samuel King and his wife is demonstrated. The paternity of affected person 26 is in question but it is also uncertain that this infant was in part affected. The affected sibships are numbered in the same way as in Figure 12. One affected member of sibship 3 is not indicated in this diagram.

APPENDIX

The frequency of EvC as determined in this study is so unusually high and such a large proportion of the cases had died before the study was performed that it is deemed essential to outline briefly the features of each sibship, and to indicate the mode of ascertainment and the basis for diagnosis in each case.

In many instances the sibship was ascertained through several means. The several modes of ascertainment (by which we mean both finding out about the sibship and confirmation of the diagnosis) are as follows: physician (P), undertaker (U), congenital malformation section of birth certificate (BC), hospital index (H), Amish informants including parents and/or sibs in most cases (A), death certificate (DC), Fisher genealogy (F), school nurse (N). The symbol given first indicates the first ascertainment. In the case of all living affected persons, the diagnosis has been confirmed by examination. In deceased cases, all available diagnostic information has been assembled and is presented here. Isolated clinical features of particular interest are presented in some instances.

The numbering of sibships is the same as that in Figure 12 and in the fold-out. M or F, male or female, in bold letters indicates "affected with the Ellis-van Creveld syndrome." Brackets indicate "deceased." Asterisk at the end indicates "sibship complete or probably complete." (?) means "questionably affected dead case." MF means "dizygotic twins." (A) means "abortion." Numbers preceded by F indicate the family number in the Fisher genealogy (20).

Sibship 1: (F) F F. Ascertainment: P, BC, H, A, N. Proband: M. S. Z., third daughter of C. Z. (F 235), born Oct. 30, 1958, at Lancaster General Hospital. At birth 6 lbs., 2 oz., 46 cm. long. Diagnosis of achondroplasia with polydactyly made immediately at birth; "cleavage in upper and lower gums" noted (birth certificate 198340). Polydactyly corrected at 6 mos. Height Aug. 10, 1963: 86 cm. Feb. 5, 1964: Ht. 35¾ in.; wt. 28½ lbs. First and second toes widely separated. Fifth toe overlaps the fourth. Hair somewhat thin. Heart sounds normal. See Figure 5. The first child of this family, born Aug. 26, 1954, lived less than a day, had deformed chest and extra fingers. Death certificate 67302-54: "Multiple congenital malformations."

Sibship 2: M F M F.* Ascertainment: P, A. Proband: M. S., fourth child of G. S. (F 166), female born June 1, 1944. (For affected nephew, see sibship 5.) Three teeth present at birth fell out soon after. Heart ailment detected at age four years when she had "congestion on the chest." Digitalis was taken intermittently for several years. No murmur heard in 1963. The stumps of the extra fingers are prominent as is usual when they have been removed by ligature. See Figure 1. Aug. 12, 1963: Height 42¾ in. Markedly sunken upper lip and markedly hypoplastic anterior maxilla. See Figure 11F.

Sibship 3: M F (M) F M F.* Ascertainment: P, H, A. Probands: S. G. and R. G., daughters of C. G. (F 1059), born Dec. 22, 1941 and Aug. 31, 1944, respectively. (For affected sibs of the father, see sibship 13.) S. G. has small extra postminimal toe on the left. R. G. requires hearing aid for deafness thought to be due to otitis media. Both have sunken upper lip, poor teeth, dysplastic fingernails, short distal extremities and relatively long proximal phalanges. R. G. is one of the taller affected females. In 1942 S. G. (Lanc. Gen. Hosp. A 69685) was hospitalized for amputation of extra fingers in the same room at the Lancaster General Hospital and at the same time as D. F. (sibship 22); the two families had not previously been acquainted. Their hospital unit numbers are only 3 digits apart. Another affected child is clear: Infant male born Oct. 10, 1943, lived four hours. Death certificate (90121-43): "Premature birth, achondroplasia." Mother confirms presence of polydactyly.

Sibship 4: M M M (M) F F M (M) F*. Ascertainment: P, H, A, DC. Probands: 1. L. K., dau. of A. B. K. (F 563), born Dec. 15, 1952. Polydactyly and harelip diagnosed at birth but chondrodystrophy not recognized. Aug., 1963: height 44 in. In addition to corrected hand polydactyly, extra toes had been removed from both feet. Fused third and fourth toes on the right persisted. Feb. 5, 1964: Height 44½ in., weight 51½ lbs. Prominent systolic murmur. See Figures 9, 11D. The stumps of the extra fingers are prominent, as is the case when the fingers are removed by ligature. 2. R. K. (Lanc. Gen. Hosp. B29085), born June 18, 1951, died Nov. 11, 1951. Supernumerary fingers and absence of maxillary alveolar cleft noted in hospital record. A small amount of "loose tissue" was removed from the mouth on the fifth day of life and diagnosed "? toothbud" by the pathologist. X-rays at 11 days of age showed considerable cardiac enlargement. 3. E. K., born May 8, 1958, lived two days. Autopsy (the only one in this series) showed "mild harelip," polydactyly, "marked degree of absence of the interventricular and interatrial septum," hypoplastic aorta, and abnormally large pulmonary artery. The left atrium was described as hypoplastic.

Sibship 5: F M M F. Ascertainment: P, A. Proband: A. S., son of A. S. (F 166) and M. S. (F 15), born May, 1958. See sibship 2 for affected paternal aunt. Aug., 1963: Ht. 35½ in. Prominent systolic murmur. Obviously bright.

Sibship 6: F M F F M M. Ascertainment: P, H, A, N. Proband: E. S., Jr., son of E. S. (F 965), born June, 1958. "Partial harelip," achondroplasia and epispadias diagnosed at birth. Operation to free-up and lengthen upper lip. Polydactyly uncorrected. At birth: ht. 19½ in., wt. 7 lbs. 13 oz. Height on birthdays: two yrs., 28½ in.; three yrs., 32 in.; four yrs., 33 in.; five yrs., 35 in. Wears glasses for high grade myopia.

Sibship 7: F (F) F (M) F (F) (F)*. Ascertainment: A. Learned about this sibship from sister-in-law of the father; see sibship 17 for affected children of this woman. Father, I. L. K. (F 238). Mother, B. E. S., died Dec., 1963. Father confirmed following information: 1) R. S. K. (second child), b. Jan. 14, 1919, d. Feb. 7, 1919. Typical features including polydactyly and dwarfism. 2) K. D. K. (sixth child), b. June 18, 1926, d. Aug. 20, 1926. Also typical features. Died of "ether pneumonia" in connection with surgery for extra fingers. 3) L. S. K. (seventh child), b. Aug. 20, 1927, d. June 1, 1928. Typical features. Cause of death said to be whooping cough. A respiratory complication of EvC may have been the true cause or may have contributed. The father states that J. S. K. (fourth child) was not dwarfed and had no polydactyly; in fact, there were only four fingers on one hand. He died from "congestion of lungs" after illness of one and one-half day's duration.

Sibship 8: F M M M (M) (M)*. Ascertainment: P, A. Proband: C. B. F. (F 2301), born 1906. Married at age 29 years. Skilled carpenter doing cabinet work and building truck bodies. Limp from "bad right knee." Extra fingers amputated at age nine years; otherwise hands very similar to those in Figure 6. Complete artificial dentures at age 45 years. In 1963: ht. 60½ in., wt. 127½ lbs. Father of this sibship M. F. living at age 90 years. The following information is given on deceased children: 1) E. F. (fifth child), b. May 28, 1910, d. Feb. 16, 1928, contracted pneumonia after measles at age 16 and thereafter suffered from chronic suppurative lung disease until death at age 18 years. Death certificate (14586-28): Lobar pneumonia. 2) M. F. (sixth child), born Oct. 7, 1912, d. Feb. 17, 1913. This baby was short and chunky but apparently had no extra fingers. However, teeth were said to have been present at birth. Probably mentally retarded. Death certificate (16487-13): "patency of foramen ovale."

Sibship 9: M M F F*. Ascertainment: A. E. E., dau. of J. E. (2641), born Aug. 27, 1945. Typical features including short, sunken upper lip and bad teeth. Extra digits removed at 14 months. Gets tight in her chest with colds.

Sibship 10: M F F (A). Ascertainment: A, BC. Proband: D. H. S., son of S. S. (F 1977), b. Jan. 19, 1958. Was said to be four weeks postmature. (Other children born late. Last pregnancy ended in miscarriage.) Birth certificate (12392-58): "Extra fingers, bilateral." Extra fingers removed at Geisinger Medical Center, Danville, Pa., at age of six months. X-rays of genu valgum at same time (see Fig. 2). As infant often choked and turned blue in feeding. Single tooth present at birth, but fell out with "proud flesh" after several months. Ht. 31 in. at second birthday. Oct., 1963: Only upper incisors. Other teeth poorly formed and badly deranged. Nails underdeveloped. Short upper lip. Heart apparently normal. Marked genu valgum with obvious tibial deformity bilaterally.

Sibship 11: M (M) M M F F F M M F F M M M.* Ascertainment: H, A. Proband: E. S. S., b. Feb. 19, 1949 (F 526). Sept., 1963: Works hard with horses on farm. Ht., 3 ft. 8 in. Dystrophic nails. Polydactyly corrected surgically Feb., 1955. Double tooth (Fig. 11E). Pigeon breast. Short, low-pitched, early diastolic murmur heard at left sternal border (? tricuspid flow murmur). Genu valgum, bilateral. See Figure 8.

Sibship 12: F M (F) F F F F F F F M. Ascertainment: P, BC, H, DC. Proband: A. S., dau. and sixth child of J. L. S. (F 1124), born Oct., 1955. X-rays of hand taken at Lancaster Osteopathic Hospital in Feb., 1956, when amputation of extra fingers performed. Sept., 1963: ht. 42¾ in. Birth certificate noted polydactylism. See Figure 4. Mary S., third child of family, born Sept. 27, 1949, died 10 days later. Birth certificate (160016-49): "Congenital chondrodysplasia, bilateral polydactylism, three adventitious teeth." Death certificate (87743-49): "uremia, polycystic kidney (congenital), polydactylism, chondrodystrophy, adventitious teeth."

Sibship 13: M F M F (M) (M) (M) M.* Ascertainment: A, DC. This is the sibship of the father of sibship 3. Children of J. G. and S. F. (F 2458). Information from the father of sibship 3, from his mother and from the death certificates (see below). The occurrence of polydactyly in the three indicated as affected is absolutely certain in the minds of the Amish informants. 1. Henry F. (fifth child), b. Dec. 5, 1924, d. Dec. 6, 1924. Death certificate (113996-24): "Cretinoid development, large abdomen, narrow chest, two teeth, paddle-like hands." 2. John F. G. (sixth child), b. Apr. 21, 1931, d. May 5, 1931. Death certificate (53268-31): "deformities at birth of the body structures." 3. Samuel F. G. (seventh child), b. June 21, 1933, d. same day. Death certificate (55339-33): "polydactylism, contracted chest and over-sized head with hare-lip."

Sibship 14: (M) M: Ascertainment: H, BC, DC. Proband: M. F., son of J. B. F. (2619) and R. S. (F 2634), born Aug. 18, 1960, died May 6, 1962. Dwarfism and polydactyly were recognized from birth; birth certificate (146370): "6 fingers on each hand; achondroplastic dwarf?" Dwarfism and polydactyly were recognized from birth; diagnosis of congenital heart disease made on the basis of cyanosis and dyspnea (Lancaster General Hospital). No autopsy. Death certificate (47960-62): "Congestive heart failure. Congenital heart disease. Pneumonia. Achondroplastic dwarf."

Sibship 15: (F) (M) F M. Ascertainment: A, H, DC. Children of J. F. (F 1092). 1. S. S. F. (first child), b. March 8, 1952, d. May 31, 1952. At Lancaster General Hosp. was described as having respiratory distress due to abnormal rib cage. Death certificate (52794-52): "Congenital lungs and heart. Achondroplastic dwarf." 2. Stillborn male child, b. July 19, 1953. Mother describes polydactyly. Death certificate (F2326-53): "Transverse lie. Fetal anomaly."

Sibship 16: (F) (F) (F). Ascertainment: A, U, BC, DC. Children of A. F. (F 1089), bros. of J. F. (see sibship 15). In all three children, dwarfism and polydactyly was present. 1. Susan G. F., born 1960, died Feb. 1, 1961 (ae. 10 mos.). Death certificate (15311-61): "Pneumonia. Congenital heart with enlarged heart. Malformed with extra fingers."

2. Emma G. F., born March 15, 1962, died March 18, 1962. Death certificate (26846-62): "Congenital heart failure. Enlarged heart." 3. Stillborn female, b. Feb. 7, 1964. Death certificate (F 498-64): "Congenital anomalies."

Sibship 17: F M F M (M) (M) (M)*. Ascertainment: P, A, DC. Information on affected status from mother. Children of A. L. K. (F 260). 1. Amos S., b. Sept. 9, 1935, d. Sept. 16, 1935. Death certificate (79521-35): "child cretin at birth and unable to nurse." 2. Daniel K., b. Sept. 20, 1936, d. Dec. 11, 1936. Death certificate (111622-36): "Patency of foramen ovale. Acute bronchitis." 3. Aaron S., b. Oct. 12, 1943, d. Dec. 22, 1944. Death certificate (106258-44): "Bilateral lobar pneumonia. Achondroplastic dwarfism with hypothyroidism and polydactylism."

Sibship 18: F. Ascertainment: P, A, H. Proband: M. K. L., only child of B. S. L. (F 242) and L. S. K. (F 756), b. Sept. 29, 1963. Typical features. X-rays from Ephrata Community Hospital show typical hand changes. At birth: 19 in., 6 lbs., 15½ oz. Heart sounds normal. Upper incisor present at birth fell out a few weeks later. Upper alveolar groove absent. No extra toes.

Sibship 19: (F) F F F F MF M. Ascertainment: P, BC, DC. Proband: First child of B. S. K. (F 262), female infant, born and died Feb. 13, 1948. Lived five hours. Bilateral hand polydactyly; feet normal. Wt. 5 lbs. Information from physician who did delivery. Death certificate (12631): "Atelectasis. Polydactylism, right and left hands." The parents were married Nov. 28, 1946.

Sibship 20: (M) F (F) F. Ascertainment: BC, DC, A, H, P. Proband: First child of E. K. B. (F 744) and S. K. (F 961), born and died March 25, 1959. Death certificate (24832-59): "Prematurity. Polydactylism of hands. Cleft palate. Achondroplasia." The diagnosis of cleft palate is probably in error; partial cleft lip may have been intended. The third child was born and died at Lancaster Osteopathic Hospital, July 5, 1961. Lived about three hrs. No stigmata of EvC. Death certificate (065211-61): "Respiratory insufficiency. Prematurity. Possible neg. Rh factor."

Sibship 21: M M (M) M. Ascertainment: BS, DC, P, A, J. B. B., third child and son of E. K. B. (F 2471), born Sept. 14, 1957, died Sept. 15, 1957. Birth certificate (175390): "Multiple abnormalities." Death certificate (81264-57): "Congenital heart disease. Supernumerary fingers and toes. Outward flare of ribs."

Sibship 22: F M M M M M M*. Ascertainment: H, A, P. Probands: children of C. F., the proband in sibship 8 (F 2844). 1. S. E. F., b. Mar. 11, 1938. about 57 inches tall. Surgery for bilateral genu valgum. 2. D. M. F., b. Nov. 6, 1941. Married Canadian Mennonite girl, June, 1964. About 5 ft. tall like father. Was hospitalized (Lanc. Gen. Hosp. A69682) at six mos. for amputation of extra fingers at same time as S. G. (sibship 3). At birth described as having dislocated hips and "hypertrophy of hard palate" (Lancaster General Hosp.). Six teeth erupted. Dwarfism not noted. Had surgery for bilateral genu valgum. In 1949 X-rays (Lanc. Gen. Hosp.) revealed, among many changes "exostosis on the inner side of the left tibia near its upper end." See Figure 3. The fourth sib, born 1943, necessarily a heterozygote, has recently married M. Z. (F 45), who may also be heterozygous because her brother P. Z. S. has an affected child (sibship 23). The oldest son is married to a woman with only remote affected relatives.

Sibship 23: (A?) M F. Ascertainment: A, P, N. Proband: R. F. S., dau. of P. Z. S. (F 45) and A. F. (F 1225), b. Apr. 18, 1964. Examined May 11, 1964: Partial hare-lip; feet said to be dislocated; seems intelligent, since already notices parents; two teeth present at birth; extra fingers being removed by ligature. They are gangrenous. Baby very un-

comfortable from barbarous treatment. Judging from the similar treatment of cases in sibships 2 and 4, the results are not satisfactory, furthermore.

Sibship 24: (F?) F M (M) F (F) F (M) M*. Ascertainment: A. Proband: A. B., seventh child of J. L. B. (F 1337-information incomplete), b. Dec. 25, 1930. When seen in June, 1964, poor fingernails and scars of amputated extra fingers, bilaterally, were evident. She is comparable in height to R. G. of sibship 3, i.e., is taller than many. Other deaths: 1. Mary, first child, b. Aug. 24, 1915, d. Mar. 14, 1916. Death certificate (26393): "Pneumonia." 2. John S., fourth child, born and died Nov. 22, 1923. Death certificate (111275): "Malformation of chest, arms, legs, feet, hands and head—almost a monstrosity." 3. Katie M., sixth child, born Apr. 22, 1927, died May 8, 1927. Death certificate (48228): "malformation of heart—blue—weak circulation." 4. Infant son, eighth child, b. and d. July 3, 1933. Death certificate (63695): "Monstrosity, stillborn, normal delivery."

Sibship 25: M M (M) M M F M M (M) F M*. Ascertainment: A, DC. Probands: children of Bishop A. M. F. (F 1225). 1. Third child, stillborn male, b. Mar. 5, 1934. Lived about 30 min. Death certificate (29588-34): "Premature. Atelectasis. Dwarf. Faulty development." 2. A. E. F., ninth child, male, b. Mar. 17, 1945, d. Mar. 19, 1945. Death certificate (24151-45): "congenital deformity. Atelectasis." The mother states that polydactyly was present in both infants. See sibship 23 for affected child of normal member of this sibship.

Sibship 26: (F) . . . *. This sibship was ascertained exclusively through Amish informants. No public records were kept at the time of birth and death. Lydia, first child of S. F. (F 2440), b. Dec. 22, 1863, d. Feb. 22, 1864. Information from several sources including a brother suggests that dwarfism and polydactyly were present, but there is not complete certainty or unanimity in the matter. Eleven subsequent children were unaffected although at least four had affected descendants. The Fisher genealogy, which is notably accurate and honest, states that whereas Lydia was born Dec. 22, 1863, her putative parents were married in 1864. The putative father is the only parent who does not trace his ancestry back to Samuel King and wife, one of whom is thought to have carried the EvC gene. Of the 52 cases this is the only one in which the evidence for presence of EvC is insecure.

Sibship 27: (M) (F) M F (F) (M). Ascertainment: DC, A. Proband: Daniel S., first child of J. H. B. (F 2711), b. Dec. 23, 1954, d. Dec. 29, 1954. Death certificate (102646-54): "Respiratory and cardiac failure. Congenital heart. Multiple congenital anomalies." Three children have died at 18 months or less of an identical degenerative encephalopathy, of which the exact nature has not been determined.

Sibship 28: F M M (F) M M M F M (M)*. Ascertainment: DC, P. Probands: children of A. B. S. (F 1100). 1. Mary F., fourth child, June 18, 1940, d. Nov. 21, 1940. Birth record (77361) says nothing about malformation. Death certificate (102647-40): "Bronchopneumonia. Dwarfism. Poor resistance to infection." 2. Daniel F., tenth child, b. July 31, 1952, d. Aug. 1, 1952, lived only six hrs. Death certificate (61791-52): "Congenital deformity, heart, lungs, skeletal. Polydactylism. Achondroplastic dwarf." Physician reported narrow chest and "almost no lung action" as impressive features.

Sibship 29: (F) F (F) M M (M) M M*. Ascertainment: DC, A. Probands: children of J. F. L. (F 2359). 1. Elizabeth, first child, born Feb. 19, 1915, d. Apr. 11, 1915. Death certificate (33314-15): "Pneumonia." Parents state extra fingers were present. 2. Katie, third child, b. Dec. 3, 1917, d. Feb. 1, 1918. Death certificate (18044-18): "Patency of foramen ovale." Parents state extra fingers were present. 3. John, sixth child, b. Dec. 13, 1921, d. Feb. 19, 1922. Death certificate (20064-22): "Patency of foramen ovale. Con-

vulsions due to meningitis." Parents state no extra fingers and no deformity; death due to a "cold which went to his head." The first and second cases are considered quite certain also because the Amish woman who assisted as practical nurse at the delivery recalls extra fingers.

Sibship 30: F (M) (F) F M F F M*. Ascertainment: F, A. (Through the Fisher book it was learned that the proband was a dwarf and the sister R. S., F3313, confirmed this fact and provided the information below.) Proband: Susan Yost (F 1623), dau. of Eli Yost and Lydia Petersheim, b. Nov. 6, 1876, d. Apr. 10, 1918. Information from sister: ht. about 4 ft.; polydactyly present and never corrected; fingernails dysplastic; trunk long, limbs short; cardiac ailment present all her life; death due to "cardiac dropsy." However, death certificate (38982-18) lists cause of death as "pulmonary tuberculosis."

Addendum in proof: Recently another sibship with three affected children has come to attention.

Sibship 31: M (F) F F F (M) F M M (M)*. Ascertainment: DC, A. Affected (F 2709): 1) Nancy H. B., b. July 12, 1919, d. Dec. 8, 1919. DC (118520): Lobar pneumonia. 2) Moses H. B., b. Dec. 3, 1928, d. Nov. 25, 1929. DC (111642): Influenza; [illegible]. 3) David H. B., b. Oct. 5, 1936, d. Dec. 27, 1936. DC (114463): Bronchial pneumonia; dwarfism; malnutrition. The father states that polydactyly and other stigmata of EvC were present in all three.