SYMPHALANGISM AND TARSAL COALITIONS: A HEREDITARY SYNDROME

A Report on Two Families

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Symphalangism was the term used by Harvey Cushing (1916) in his description of a family in which eighty-four persons among 313 examined exhibited a dominantly inherited ankylosis of the interphalangeal joints of the hand. There have been many other reports of families in which symphalangism occurs with no other associated skeletal abnormality (see bibliography). In fact, if Drinkwater's chronicle (1917) of the "Talbot fingers" in fourteen generations is accurate, symphalangism may have the longest pedigree of any human genetic anomaly known.

Another rare anomaly of the human skeletal system is fusion of the tarsal bones, commonly called tarsal coalition. Tarsal coalition has also been reported to be a hereditary phenomenon, though it is uncommon (see bibliography). There are many types and combinations of tarsal coalition. One of these, talo-navicular synostosis, was reviewed by Schreiber (1963), who found fewer than thirty cases in the world literature, though he suspected that it was more common than the sparse case reports indicated. He recorded five cases of talo-navicular coalition, three bilateral and two unilateral. No other associated skeletal abnormalities were described outside the feet, though three of the five patients reported in that series had the so-called ball-and-socket ankle joint—two on the affected side, one on the unfused side (Schreiber 1963).

It would be very unusual for these two rare skeletal anomalies, symphalangism and tarsal coalition, to occur in the same person by chance. The following are case reports of two families in which the hereditary syndrome of symphalangism and tarsal coalitions of the talo-navicular type are distributed in such a fashion as to suggest that the two defects are determined by a single gene. When this study was nearing completion, Elkington and Huntsman (1967) reported this combination in living members of Drinkwater's pedigree. Caffey (1967) has also recently added a case with both defects.

CASE REPORTS

Kindred 1—The proposita, III-9, is a twenty-six-year-old white barmaid who attended for pain in the right foot, worse on standing. On examination, bony prominences were noted projecting medially from both ankle regions. Tarsal movement was markedly decreased, with pain at the extremes. An incidental finding was absence of the proximal interphalangeal joints of the left fourth and fifth digits and right third, fourth and fifth digits of the hands. The patient stated that her daughter, her sister and perhaps her father shared this combination of deformities. She was uncertain about the state of the rest of her rather complex family line.

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Radiographs showed bilateral talo-navicular fusion and symphalangism (Figs. 1 and 2). She was treated by triple arthrodesis of the right foot, with relief of pain.

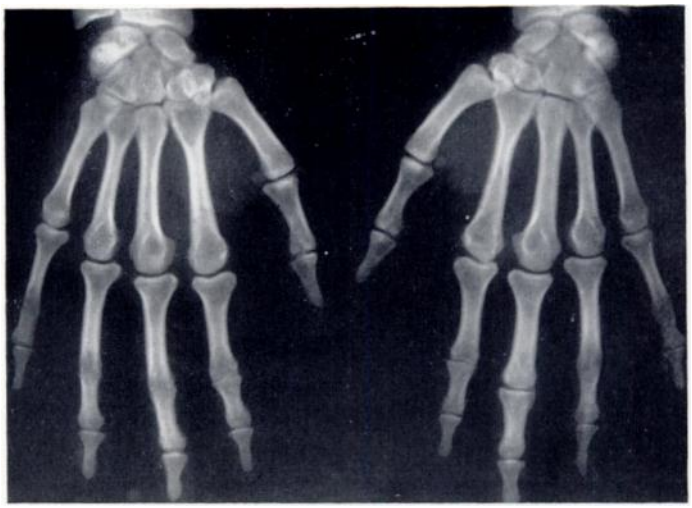

FIG. 1

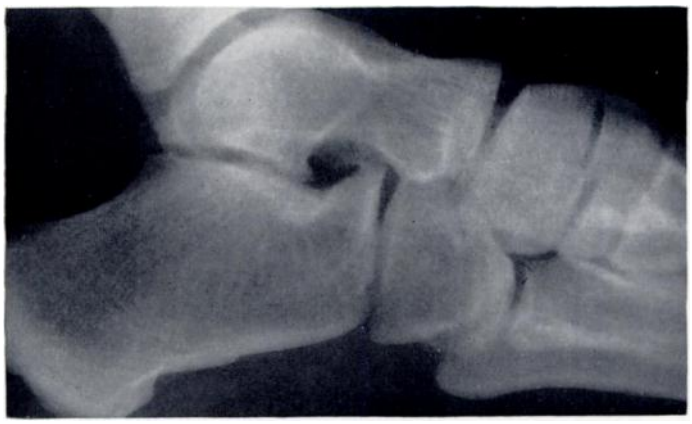

FIG. 2
Kindred 1. Hands and foot of III-9, the proposita, showing symphalangism and talo-navicular coalition.

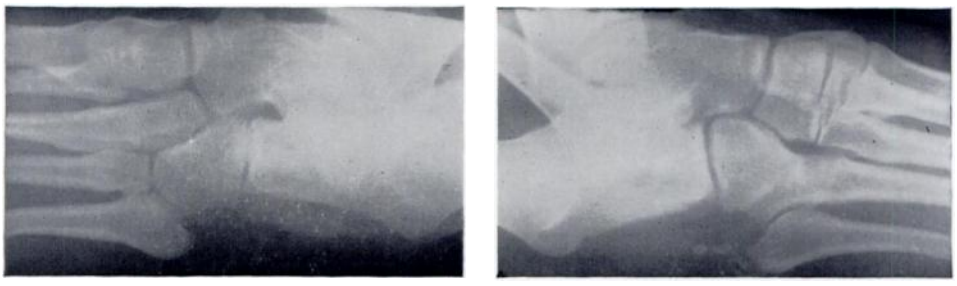

FIG. 3
Kindred 1. Feet of III-5, sister of the proposita, showing tarsal and tarso-metatarsal coalition.

There are three living children of the proposita, by two different mates with no reported malformations of the feet. The youngest, IV-8 (less than one year of age) and the eldest, IV-6 (six years), had no orthopaedic complaints, and radiographs of the hands and feet were

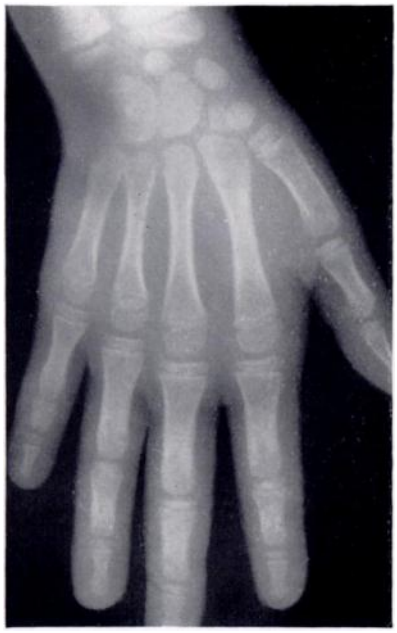

FIG. 4

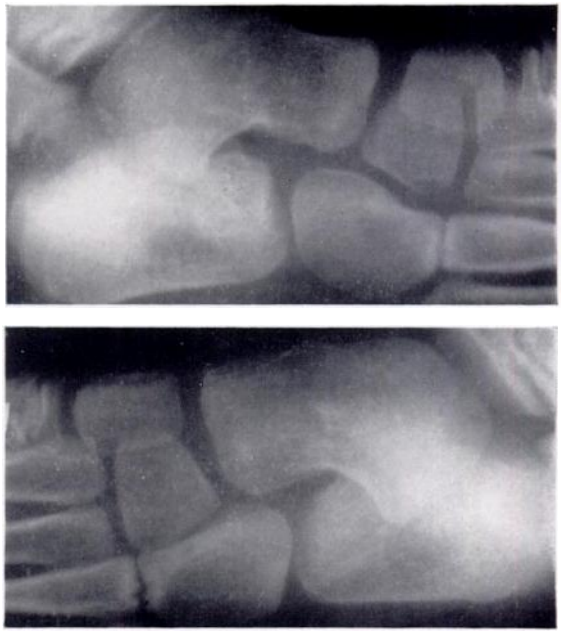

FIG. 5

Kindred 1. Right hand and feet of IV–2, daughter of III–5. Hand shows narrowing of joint space between the proximal and middle phalanges of the fifth digit and solid fusion of the hamate and triquetrum. There are multiple synostoses of the feet.

normal. The third child, IV–7, a four-year-old boy, had complained of foot pain since he began walking two years earlier. The only radiographic abnormality was delayed appearance of the centres of ossification for the navicular bones. A fourth child, IV–5, had died at birth.

The twenty-seven-year-old sister of the proposita, III–5, attended for lifelong foot pain, more severe recently on the right. Radiographs revealed bilateral talo-navicular coalition. On the left side there was also coalition of the lateral cuneiform and third metatarsal bones, and on the right there was coalition of the cuboid bone and fourth metatarsal and of the second and third cuneiform bones (Fig. 3). The hands showed symphalangism of the fourth and fifth digits on both sides. A double arthrodesis was performed on the right foot with relief of pain. The husband of this patient, III–6, had no complaints and was normal on examination.

IV–2, the six-year-old daughter of III–5, had no symptoms, but radiographic examination showed definite reduction of the joint space between the proximal and middle phalanges of each fifth digit, and the middle phalanx of each of these fingers was shorter than normal. This was thought to be an early stage in the development of symphalangism. There was

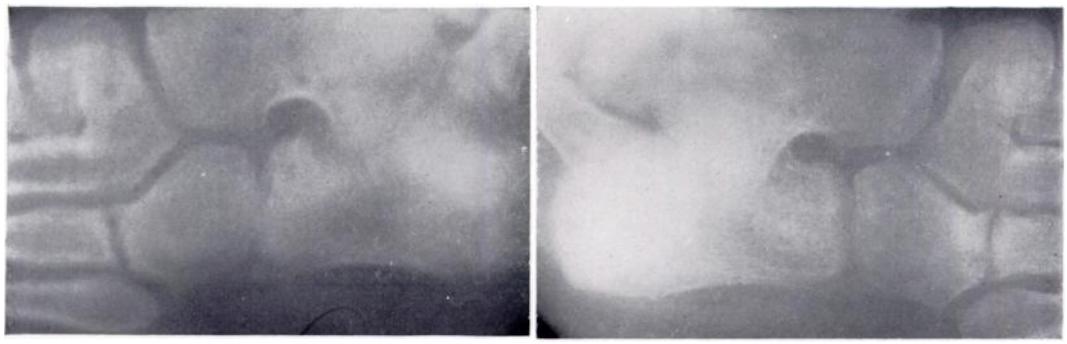

FIG. 6

Kindred 1. Feet of IV–3, second daughter of III–5, showing multiple tarsal coalitions.

solid fusion of the hamate and triquetrum in the right wrist. There was also bilateral talo-navicular coalition with fusion of the middle two cuneiforms and bilateral fusion of the fourth metatarsal to the cuboid (Figs. 4 and 5).

Another daughter (IV–3) aged five, was also free from symptoms. Radiographs showed symphalangism of the hands, bilateral talo-navicular coalition and other congenital fusions of the tarsals similar to, but not identical with, the other affected members of the family (Fig. 6). IV–4, the one-year-old daughter of III–5, showed no symphalangism upon

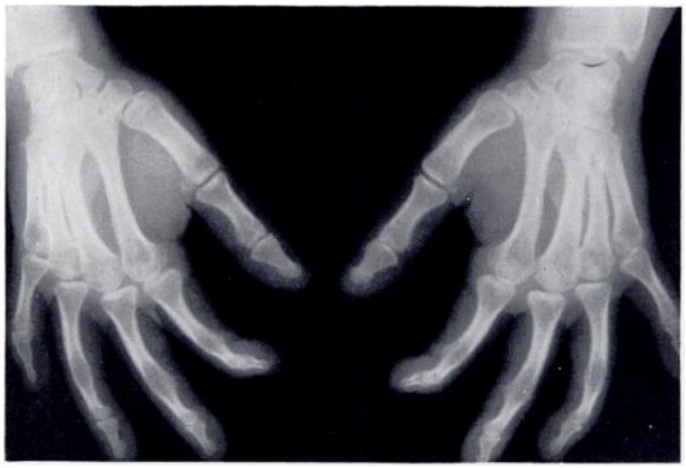

FIG. 7

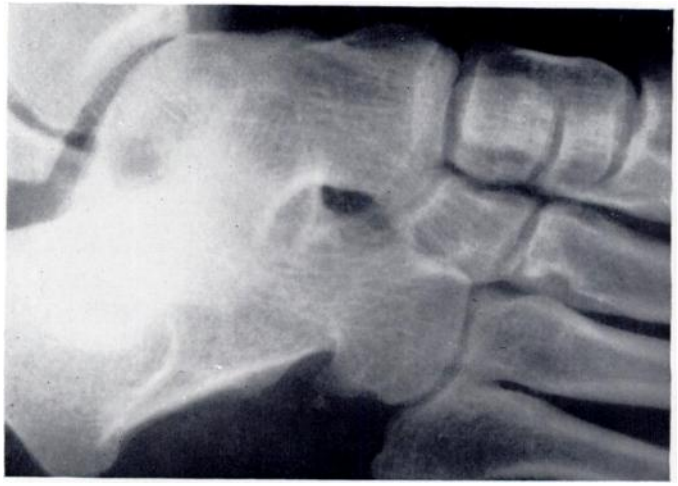

FIG. 8

Kindred 1. Hands and foot of III–11, sister of proposita, demonstrating symphalangism and talo-navicular and calcaneo-cuboid coalitions.

radiographic examination. The feet showed non-ossification of both tarsal naviculars and intermediate cuneiforms, possible normal findings at this age.

A twenty-five-year-old sister of the proposita, III–11, was unable to flex her fingers at the proximal interphalangeal joints. Radiographs showed fusion of the second, third and fourth digits at the proximal interphalangeal joints bilaterally, and fusion of the distal interphalangeal joints of the fifth digits (Fig. 7). Both feet showed talo-navicular coalition and solid fusion of each calcaneus to each cuboid (Fig. 8). In addition, in the left foot there was fusion of the second and third cuneiforms and the cuboid.

III–12, the divorced husband of III–11, was not known to have any orthopaedic complaints.

IV–9, the seven-year-old daughter of III–11, had symphalangism of the hands confirmed radiologically, and her feet showed bilateral talo-navicular and calcaneo-cuboid and talo-calcaneal coalition (Figs. 9 and 10). On the right there was fusion of the second and third cuneiforms and cuboid. On the left there was coalition of the second cuneiform and second metatarsal as well as third cuneiform and third metatarsal.

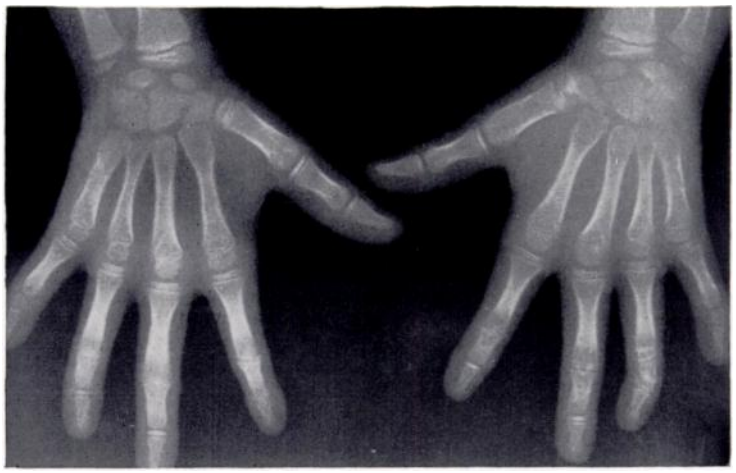

FIG. 9

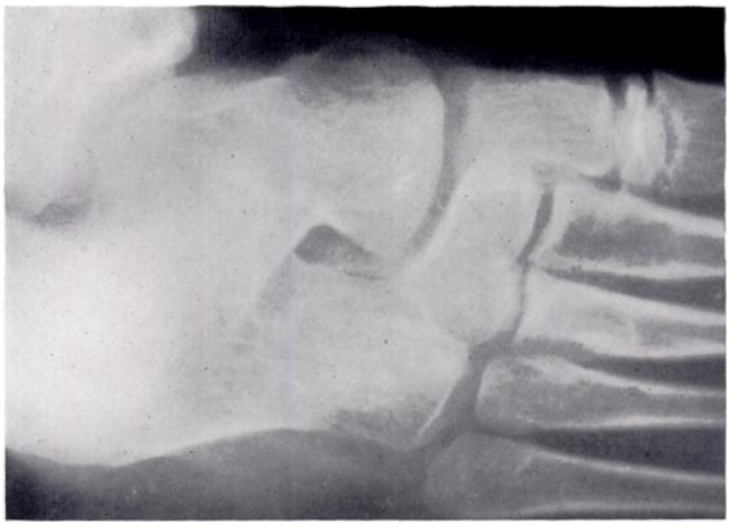

FIG. 10

Kindred 1. Hands and right foot of IV–9, daughter of III–11. The hands show symphalangism; the foot shows talo-navicular, calcaneo-cuboid and talo-calcaneal coalition, as well as synostoses in the cuneiforms.

IV–10, the one-year-old son of III–11, showed no abnormality radiographically.

The father of the proposita, II–9, was found in a tuberculosis sanatorium, admitted with the unconfirmed diagnoses of pulmonary neoplasm and tuberculosis. He revealed that he had shared skeletal abnormalities with his father and several half sisters, who had borne children similarly affected. Radiographs showed symphalangism in the hands; talo-navicular coalition, and coalition of the first, second and third cuneiforms and of the fourth metatarsal

with the cuboid (Fig. 11). He died from chronic lung disease while the investigation of this family was still in progress. Two fingers were obtained for study.

The decalcified sections (Fig. 12) showed tubular curved bone with no evidence of joint, capsule, or synovium. It was solid bone with no evidence of old or recent inflammation or

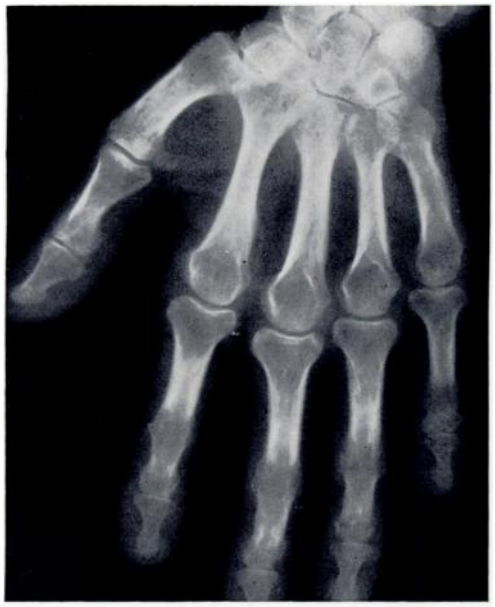

FIG. 11

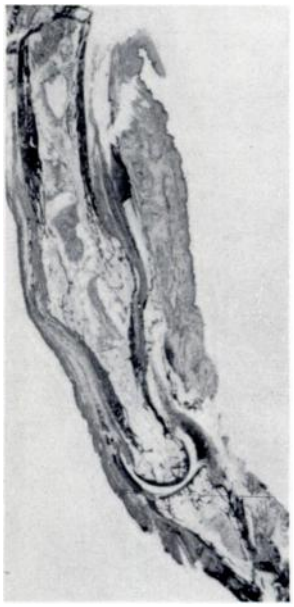

FIG. 12

Kindred 1. Figure 11—The left hand of II–9, father of the proposita, showing symphalangism. Figure 12—Section of a finger of II–9. The proximal interphalangeal joint is absent.

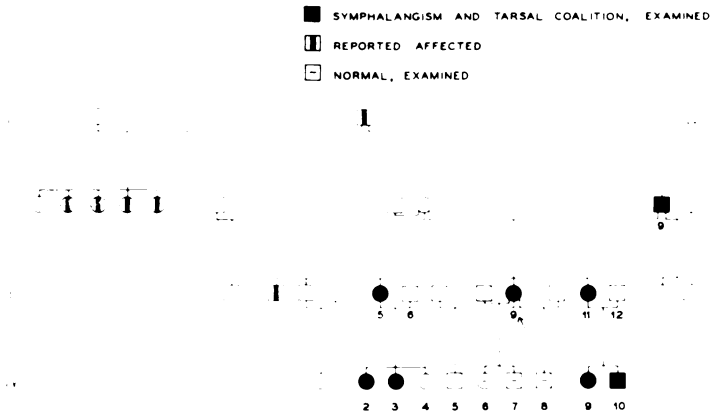

FIG. 13

Pedigree of kindred 1.

remodelling. The area of the absent joint resembled the centre of a long bone anywhere in the body. The pathologist reported that the proximal and middle phalanges appeared to have been formed as one bone.

In addition to the eight individuals examined and found to be affected with the syndrome who are described above, there are reported to be further affected members of the kindred as shown in the pedigree (Fig. 13).

Kindred 2—IV-8, the thirty-two-year-old white proposita of the second kindred, presented herself for treatment of rheumatoid arthritis. Before the onset of her arthritis she had had lifelong discomfort associated with her flat feet. Early in her life she was told she had " double ankles " because of a prominent bony swelling below each lateral malleolus, a condition that ran in her family along with " stiff fingers " (Fig. 14). She stated that she had had complete fixation of the proximal interphalangeal joints of her hands until the recent onset of her arthritis when pain and swelling of these joints in the index and middle fingers was accompanied

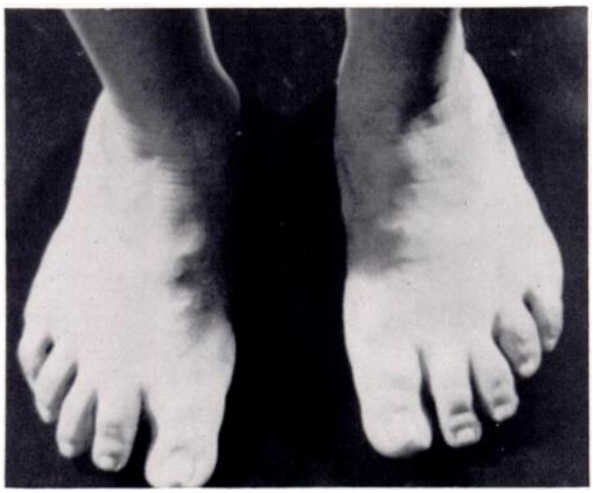

FIG. 14
Kindred 2. Photograph of the proposita's feet, showing " double ankles."

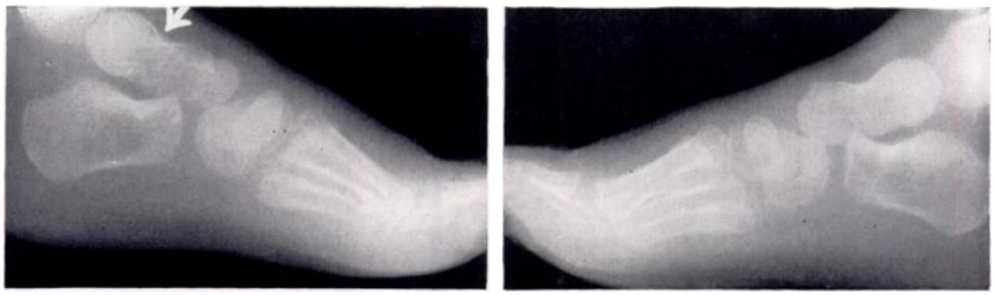

FIG. 15
Kindred 2. Feet of V-7, daughter of IV-8, the proposita. The arrow points to the notch which might signify the completion of talo-navicular fusion.

by passive movement for the first time in her life. Her rheumatoid arthritis was associated with subcutaneous nodules. She stated that she was the only member of her family afflicted with arthritis.

Radiographic examination of IV-8 showed bilateral ankylosis of the fourth and fifth proximal interphalangeal joints of the hands, with reduction of this joint space in the third digit. Both feet showed complete talo-navicular and middle and lateral cuneiform coalition (Fig. 14).

Radiographic examination of V-7, the two-year-old daughter of IV-8, showed reduction of the fifth proximal interphalangeal joints on both sides. Both feet showed talo-navicular coalition and fusion of cuboid and lateral cuneiform (Fig. 15).

IV–5, the thirty-eight-year-old single brother of the proposita, had symphalangism; radiographs showed solid fusion of the proximal interphalangeal joints of the second, third, fourth and fifth digits of both hands. Both feet showed complete fusion of talus and navicular, calcaneus and cuboid, middle cuneiform and second metatarsal (Figs. 16 and 17).

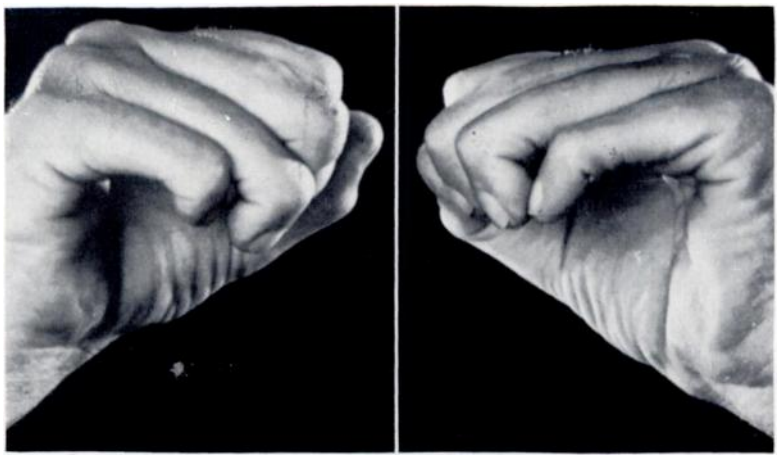

FIG. 16
Kindred 2. Photograph of IV–5, brother of the proposita, showing full extent of flexion of both fists.

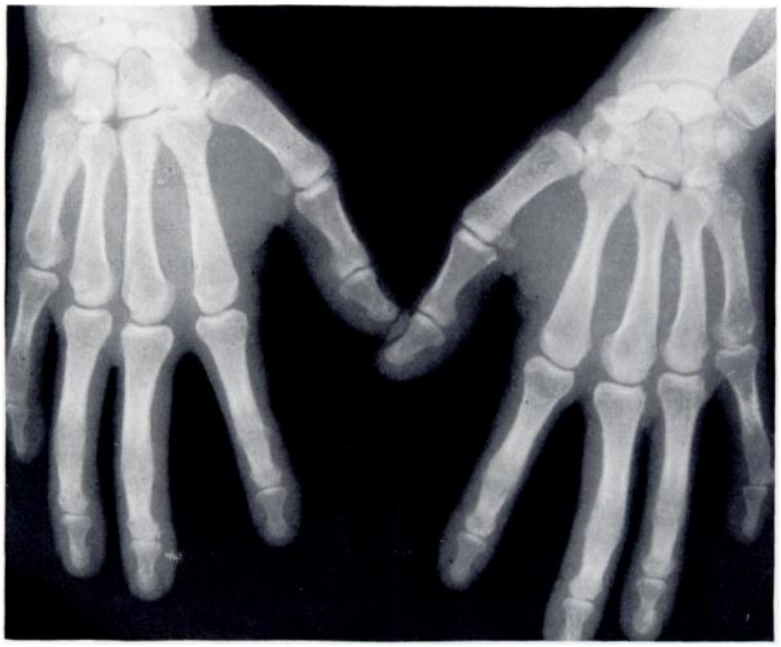

FIG. 17
Kindred 2. Radiographs of IV–5's hands showing symphalangism.

Family histories independently obtained from IV–5, IV–8 and IV–13 confirmed the presence of the trait in members of the preceding generations, as shown in Figure 18.

Linkage studies—In addition to the clinical, radiological and photographic examinations, the blood of each person in the kindreds studied was typed for study of genetic linkage. Typing

included the ABO, MNS, P, Rh, Kell, Duffy, Jk, Diego, Luther, Xg and Lewis systems of blood group antigens. The trait could not fully be linked with any blood groups tested in those affected.

DISCUSSION

In both kindreds the inheritance of this hand-and-foot syndrome follows the pattern of an autosomal dominant trait. This can also be seen in the pedigree of the second kindred in Figure 18. From these pedigrees, moreover, it appears that this dominant trait has a high degree of penetrance. To the best of our knowledge, these two kindreds are not related. Nor are they from regions or national origins that might lead us to suspect that they are related to any previously reported families with either symphalangism or tarsal coalition.

The trait as found in these families is always bilateral in hands and in feet, though the extent of the fusion may vary between the two sides of a given individual, as in the feet of IV–9 of the first kindred. It is interesting in this respect to compare Schreiber's (1963) observation about talo-navicular synostosis. He stated: " All of the cases recorded as familial were bilateral, although not all of the bilateral cases were shown to be familial." In addition to the talo-navicular synostosis, which is always present, other associated tarsal coalitions may be found. In several of these patients the tarsal coalitions extend to involve several of the metatarsals as well (IV–5 of kindred 2, and II–9, III–5, IV–2, IV–3 and IV–9 of kindred 1).

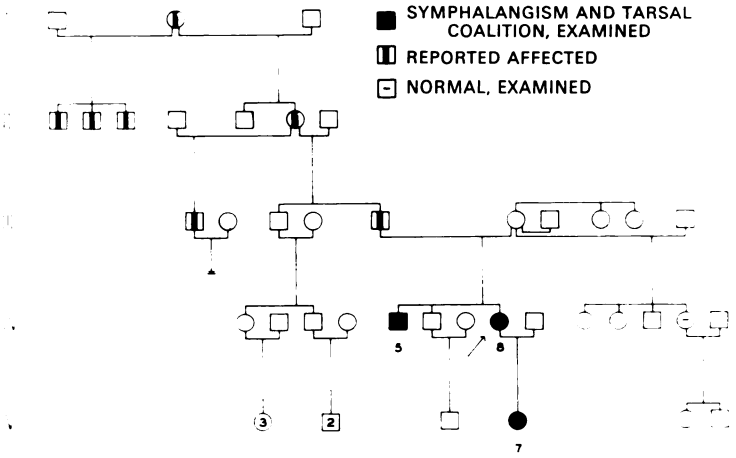

FIG. 18
Pedigree of kindred 2.

No other abnormalities have been detected by physical examination in any of these persons. Radiographic bone surveys of III–5 and III–9 of kindred 1 revealed no other skeletal anomalies. The so-called ball-and-socket ankle joint that was discovered in three cases of Schreiber's (1963) five reported cases of talo-navicular synostosis was absent in the members examined in these two families. In only one member of the families studied was there any anomaly of the carpal bones: IV–2 of the first kindred exhibited hamate-lunate fusion in the right wrist (Fig. 4). In none of the persons examined did symphalangism affect the toes.

None of the patients had associated muscular defects of the pectoral girdle, as was reported in the older literature in many cases of hereditary finger ankylosis (Stintzing 1889, Benario 1890, Silberstein 1906). The symphalangism and tarsal coalition syndrome was not part of the larger syndrome of multiple congenital articular rigidity, also called " arthrogryposis multiplex congenita," in which finger and tarsal ankylosis has been noted (Lewin 1925, Sheldon 1932, Comby 1933), but only a secondary arthropathy associated with aplasia of certain muscle groups.

It should be noted that only one patient (IV–8 of kindred 2) had arthritis, and that was only recently superimposed on her lifelong joint abnormalities. None of the other patients had had arthritis and there was no family history of rheumatic disease. Radiographically and histologically there was no evidence of inflammatory arthropathy that might have produced ankylosis; the congenital nature of the fusions also makes secondary ankylosis unlikely. It should be remarked that whatever disability is associated with the syndrome seems to come from the tarsal coalitions. The inability to make a fist does not bar these patients from manual labour, though persistent foot pain may interfere with their livelihood.

While these studies were in progress, Elkington and Huntsman (1967) examined five symphalangic members of the Talbot family and found " abnormalities of the tarsus " in each. They illustrated talo-navicular fusion but did not specify other tarsal fusions. They added: " No estimate of the frequency of tarsal abnormalities in earlier generations of the Talbot family is possible." If the hand and foot abnormalities were linked in the ancient Talbots as they are in the living Talbots and in the two families herewith reported, and if Drinkwater's assertion of the fourteen-generation descent of the first Earl of Shrewsbury's anomalies is correct, then perhaps this syndrome of symphalangism and tarsal coalition is the trait with the longest pedigree of any abnormality in man. At least this association brings to light half again as many talo-navicular coalitions as have been collectively reported.

The radiographs do not conclusively exclude the possibility that the tarsal abnormality arises from congenital absence of the navicular with expansion of the talus, rather than a coalition of talus and navicular. However, in some of the children, particularly V–7 of kindred 2, fusion is suggested by the occurrence of a notch at the plane where the two bones would be expected to fuse (Fig. 15).

SUMMARY

It has been known for well over a century that the corresponding ossification centres of the hand tend to appear before those of the foot (Mall 1906), although even now the range of variability remains poorly defined. Presumably a similar asynchrony also obtains for chondrification, although precise timing is more difficult here than for ossification. Accordingly, it is tempting with respect to this syndrome to relate fusions restricted to the phalanges of the hand and to the tarsal bones to the action of a gene which during a very limited period of development exerts an effect on those small bones of the hand and foot which are in a very specific stage of development. But since there are other inherited abnormalities of the skeleton, such as brachydactyly, where homologous bones are involved, it is clear that at the descriptive level gene action can either appear to be " stage-specific " or " homologue-specific." There are also mutations affecting the axial skeleton such as the type of polydactyly of the foot described by Neel and Rusk (1963) which appear to be neither " stage " nor " homologue " specific, involving only the foot. Finally then, there are syndromes, such as Lawrence-Moon-Biedl-Bardot, in which involvement of the hands and feet (polydactyly) is associated with such other apparently completely unrelated defects as retinitis pigmentosa and hypogonadism. While it is tempting to try to construct theoretical patterns and systems of developmental processes on the basis of results such as these, it is clear that the ultimate understanding of how genes can appear to act in so many ways almost certainly depends on the identification of a genetically controlled, qualitative or quantitative biochemical lesion. With the current parallel developments in biochemical and developmental genetics, new insights into these enigmas will surely be forthcoming in the relatively near future.

We wish to express our gratitude to Dr G. Brody for the studies of the necropsy material, Dr J. Holt for the radiological interpretations and Dr H. Gershowitz for the blood typing. We are also indebted to Dr A. Good for directing our attention to the proposita of the second kindred and Dr D. Rucknagel for assistance in obtaining the tissue for examination. The work was supported by NIH–1–PO1–GM–15419–02 National Institutes of Health, General Research Support 67, Medical Project 5.

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