HEREDITARY ANCHYLOSIS OF THE PROXIMAL PHALANGEAL JOINTS (SYMPHALANGISM)

HARVEY CUSHING

Peter Bent Brigham Hospital, Boston, Massachusetts

[Received October 21, 1915]

INTRODUCTORY

Various types of developmental malformation of the hands and feet have been described under such terms as polydactylism, syndactylism, brachydactylism, ectrodactylism, macrodactylism, hyperphalangia and hypophalangia.[1]

Familial tendencies have been recognized in the case of some of these anomalous conditions, but the first definite record showing that one of them is a unit-character inherited in accordance with Mendelian laws was made in 1905 by WM. C. FARABEE. His recorded family were residents of Pennsylvania and in the affected members there occurred a shortening of the fingers and toes which possessed only one instead of two interphalangeal articulations (hypophalangia or brachydactylism). Subsequently DRINKWATER (1908) described an English family which had exhibited the same dominant character through seven generations. The affected persons in both FARABEE'S and DRINKWATER'S families, which were possibly related, possessed a notably shortened stature, so that probably more than one abnormal unit-character was concerned.

Still another type of familial malformation had been previously described by WALKER (1901) as a particular form of anchylosis involving more especially the midphalangeal joints. The number of his recorded cases was too small to justify any conclusions on a Mendelian basis, though the malformation, the degree of which varied considerably in the different individuals, had been transmitted through five generations. In one of the cases there was an actual loss of the terminal phalanges of the two postaxial (ulnar) fingers, but otherwise there were no abnormalities aside from the aforementioned anchylosis. This paper will present a

[1] Isolated examples are not uncommon. A brother and sister were recently admitted to the Brigham Hospital, for congenital cataract. Both of them had 12 toes and brachydactylous hands. Both were of very short stature. Their parents were first cousins and were unaware of a condition similar to that of their children in earlier generations.

much more complete family record of an inherited trait of similar nature which closely accords with Mendelian expectations. The malformation will be designated *symphalangism.*

In January of 1906 the writer was consulted by a patient with a cerebral glioma, who presented in addition to her specific malady an unusual condition of the fingers which could not be bent at the proximal interphalangeal joints. An uncle who accompanied her was similarly affected and her physician who was also present, had married her fifth cousin who likewise had what they all referred to as "straight fingers" in contradistinction to the normal which they termed "crooked fingers."

In no respect was there any indication of physical deterioration in the three members of the family that were interviewed. They were splendidly developed, vigorous people. The uncle was very tall, over six feet in height, and both of the women were large and fine looking. None of them regarded the malformation as in any sense a disability or as anything out of the ordinary deserving comment. They stated that in one instance a member of the family with presumably normal fingers had married an unrelated individual with normal fingers and there were "straight fingered" children among their offspring. Aside from this possible exception (to which we will return) it was recognized in the community that if the parents were both exempt, the children would be likewise.

THE INHERITED TRAIT

Judging from the hands of the three observed individuals, though the underlying condition is the same in each, the acquired appearances justify their description under three clinical types: 1, the type of hand shown by the distant cousin who had never been accustomed to rough manual work of any kind; 2, the type in which moderate manual labor had been indulged in, as was the case with the patient, a woman who had used her hands for domestic labor; and finally, 3, the type which has undergone some modification owing to hard manual labor, as exemplified by that of the uncle, a farmer, who was accustomed to driving a plow.

These three types are fairly well represented by the accompanying photographs. In figure 1 are shown the hands of the distant cousin (Gen. V, Fam. 3, Child 7). The photograph was taken to show the unusual degree of flexion acquired in the terminal phalangeal joints which serves in a measure to counteract the incapacitation of the deformity. The view shows at the same time the smooth column-like effect

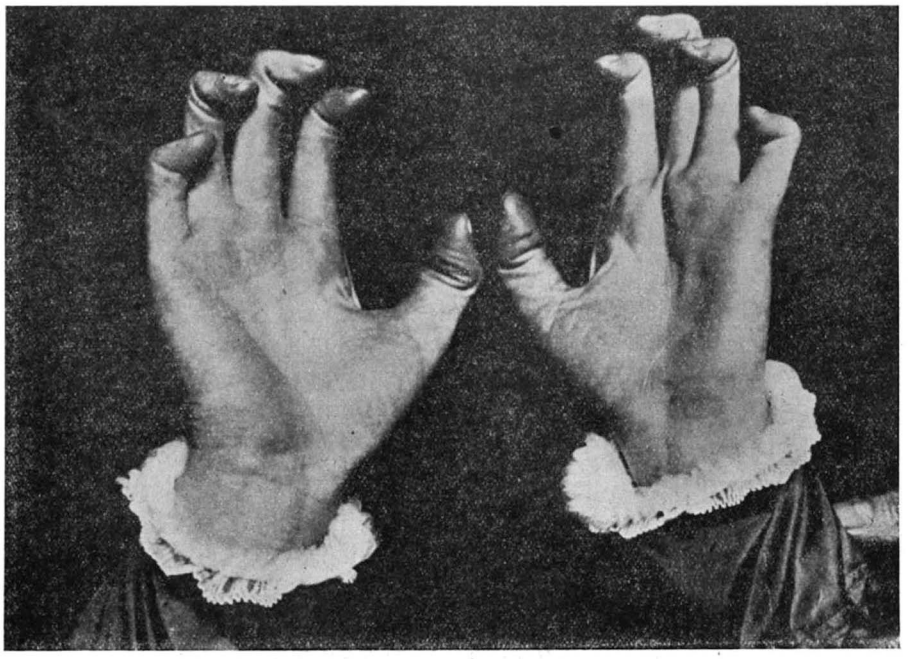


FIGURE 1.—The hands of the distant cousin unmodified by manual labor, showing the column-like fingers with their unusual capacity of over-flexion of the terminal phalanges. The proximal joint absent in all fingers.

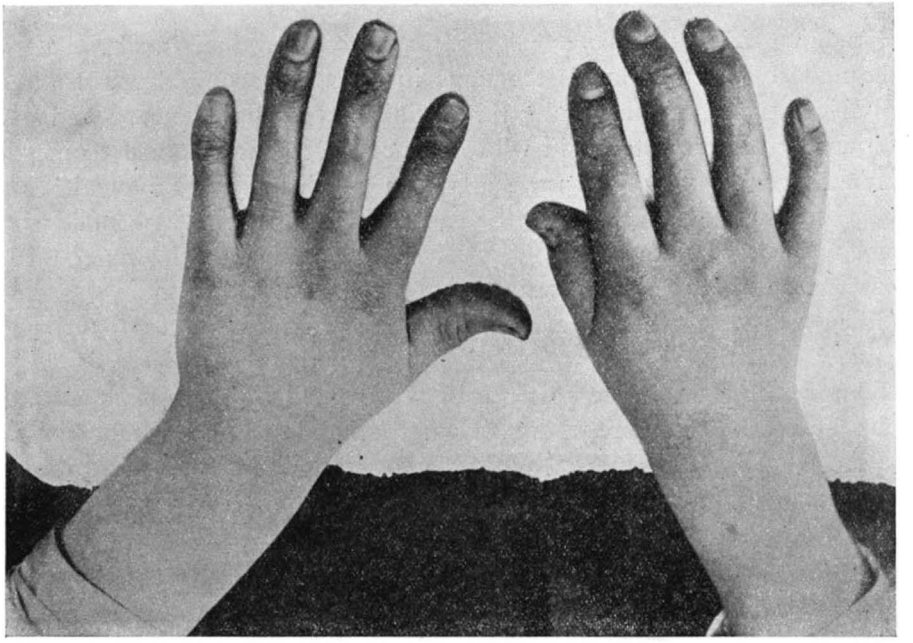


FIGURE 2.—Hands of the patient, the right modified by paralysis. No proximal interphalangeal joints present except in right index where it is slightly developed (cf. figure 7).

of the proximal two-thirds of the eight fingers with their smooth unwrinkled skin. In figure 2 are seen the hands of the patient (Gen. VI, Fam. 34, 5th Child), the right showing, at rest, slight flexion at the terminal phalanges owing to the coexistent paralysis. In the left hand it can be seen as in the above that there are no transverse cutaneous wrinkles of the proximal interphalangeal joints, the skin over the median portion of the fingers where they were thinner than normal being glossy and smooth like the skin characterizing certain neuropathic disturbances. There was a slight suggestion of flexion in the near joint of the right index finger to be explained by the X-ray findings. In figure 3 are

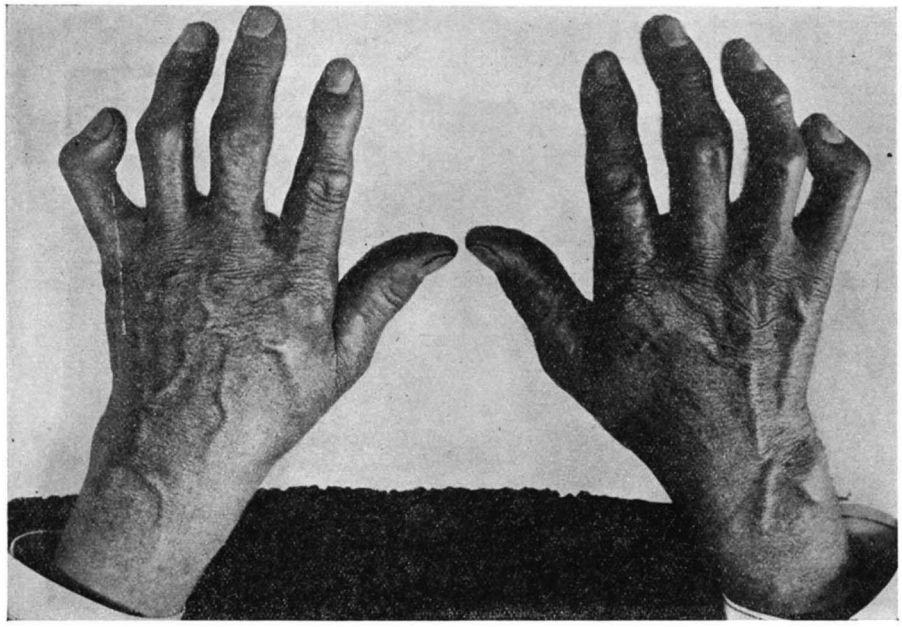


FIGURE 3.—The hands of the uncle as modified by hard manual labor. The indices possess a proximal interphalangeal joint but its development is imperfect in the other three fingers of each hand. (Cf. X-ray figure 9.)

shown the hands of the uncle, one of twins (Gen. V, Fam. 8, Child 7). At first glance they resemble somewhat the gnarled hands of an arthropathy but it can be seen that, except for the two indices, there is no cross wrinkling of the skin corresponding with the proximal phalangeal joints. In these two fingers slight movement was possible at these joints but in the other three the proximal joints were immovable, and though slightly bent the skin over them was smooth and unwrinkled, for no movement was present in them.

Though these "straight fingered" hands are very useful for all ordinary purposes, the succeeding three figures show how incapable these individuals are of effectively closing the hand into a fist. Figure 4 shows

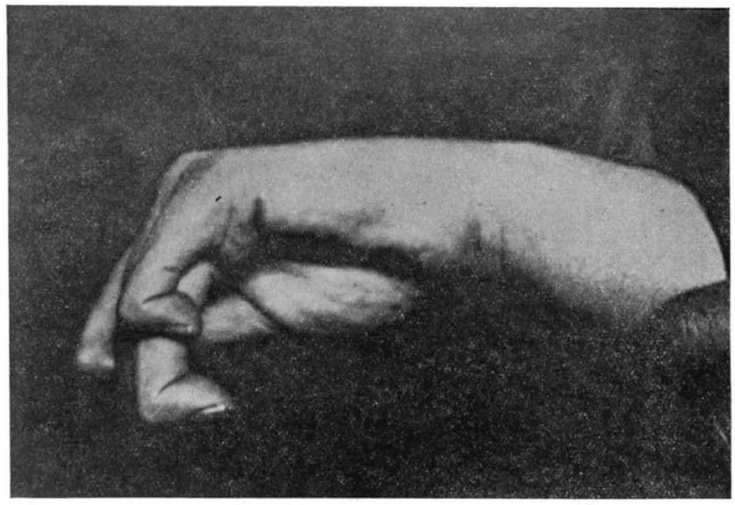


FIGURE 4.—Patient's left hand (cf. figure 2) with hand almost fully flexed.

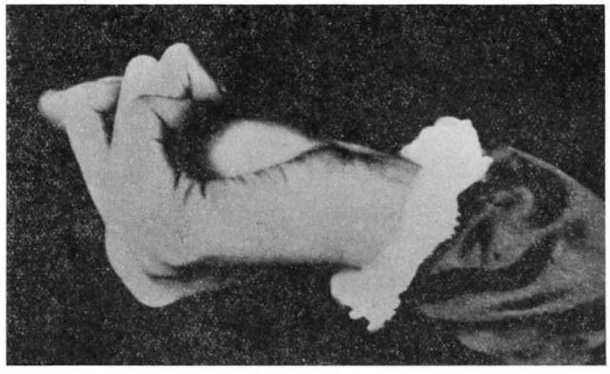


FIGURE 5.—Cousin's hand (cf. figure 1) in fist position.

the left (the intact) hand of the patient flexed to its full extent; figure 5 shows that of the cousin similarly closed; and figure 6 that of the uncle, which can be more completely closed owing to the slight permanent flexion, through toil, in the rigid joints.

PATHOLOGY OF THE LESION

The nature of the condition is disclosed by the radiogram (figure 7) of the patient's hands, which indicates a condition identical with,

or closely resembling, that which characterized WALKER'S family. It would appear that some sort of an anchylosing process had occurred

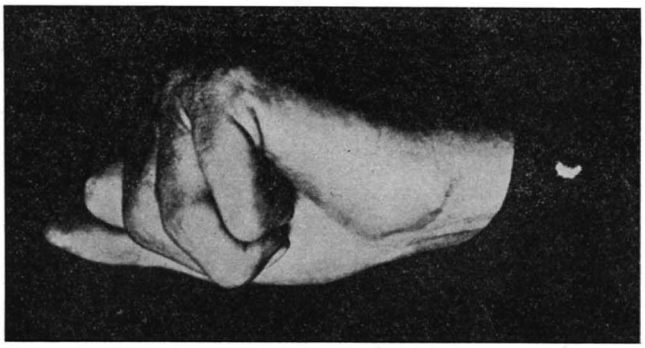


FIGURE 6.—Hand of the uncle (cf. figure 3) in fist position.

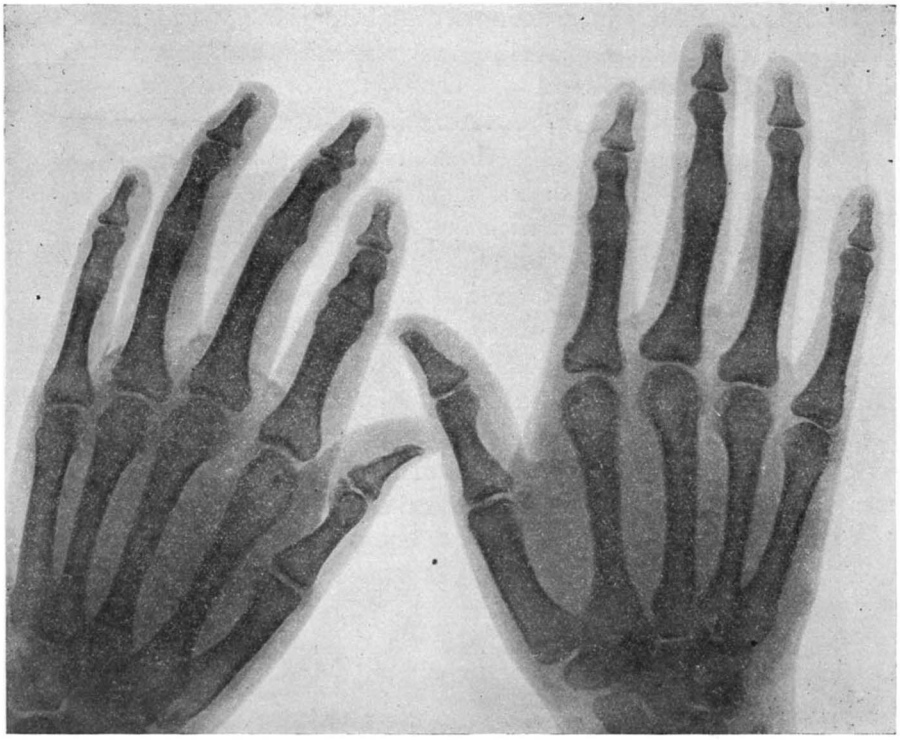
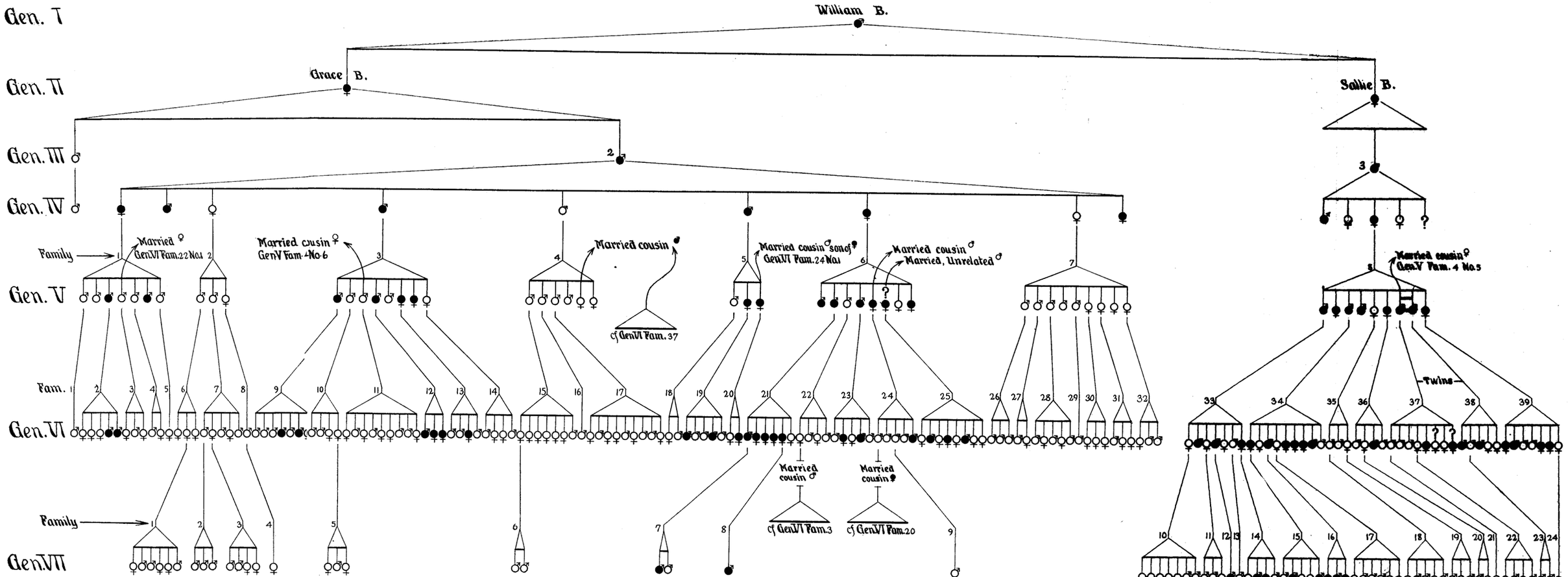


FIGURE 7.—Roentgenogram (reversed) of the patient's hands (Gen. VI, Fam. 34, No. 5), showing the anchylosis of all proximal interphalangeal joints with exception of right index.

through incomplete prenatal development of the joint, for though a trace of the joint is present with corresponding slight enlargements of the ends of the adjoining phalanges, it is largely masked by a fusion of the two bones. In the index finger of the right hand alone does a definite joint appear, though it was capable of very slight movement, and it may be added that, in hands of other members of the family from whom tracings and radiographic plates have been secured, the index finger tends to approximate the normal more often than any of the others. It is to be noted moreover that the middle phalanx of the right index finger is dwarfed, and this would suggest that possibly all of these manual deformations of congenital origin represent a very closely related condition. For it will be recalled that this dwarfing of the mid-phalangeal row was the main characteristic of DRINKWATER'S cases of minor brachydactyly and it appears also in some of the radiograms of WALKER'S family.

Just why the phalanges of the second row should suffer more than the others in most of these inherited malformations is difficult to understand, though doubtless it is associated in some way with the late appearance of the ossification centers in this phalangeal row. As shown by MALL (1906) and others, these are the last of the three rows of phalanges to ossify. Curiously enough, the terminal row of phalanges are the first to show centers of ossification, and apparently the centers are laid down serially from the first to the fifth finger, all of them having acquired a center of ossification by the 56th day. In the first or proximal row, the ossification centers for the index and middle finger only are present in the 58-day embryo, and not until the 64th day have centers appeared in this row for all the fingers. The second or middle row do not begin to ossify until the 75th day, when a center is present in the index finger, but the center for the fifth finger does not appear until the 83rd day. Hence it is possible that some inhibitory influence may be active at this prenatal period, which may account for these congenital anomalies, and it is conceivable that such an influence may be inherited. This would account not only for the dwarfing or non-development of the middle phalanges but also for the predominance of involvement of the postaxial (ulnar) fingers. This suggestion, however, though possibly explaining the underlying lesion characterizing brachydactyly, will not fully account for the condition with which we are dealing. For though a certain degree of brachydactylism does occasionally appear, the chief characteristic of symphalangism is a joint-lesion. Although we do not know what is the chronological succession of development for the interphalangeal


Gen. I
William B.
Gen. II
Grace B.
Sallie B.
Gen. III
2
3
Gen. IV
Family
Married ♀
Gen VI Fam. 22 No. 1
Married cousin ♀
Gen V Fam. 4 No. 6
Married cousin
cf Gen VI Fam. 37
Married cousin ♂ son of ♀
Gen VI Fam. 24 No. 1
Married cousin ♂
Married, Unrelated ♂
Married cousin ♀
Gen V Fam. 4 No. 5
Gen. V
Fam.
Twins
Gen. VI
Married cousin ♂
cf Gen VI Fam. 3
Married cousin ♀
cf Gen VI Fam. 20
Family
Gen VII

joints, it is quite probable that the articulations between the proximal and middle rows of phalanges are the last to be laid down, and that in these individuals an inhibitory influence checks their development at a stage a few days later than that which checks the formation of the ossification centers and produces brachydactyly.

The stages for an individual finger therefore would appear to be (1) a complete inhibition of growth of the middle phalanx (major brachydactyly), (2) a dwarfing of the middle phalanx (minor brachydactyly), with or without joint alteration, (3) a perfect development in length of the middle phalanx, but with an imperfect or absent proximal joint (symphalangism). Owing to the fact that the time of development does not exactly coincide in the several fingers, it might be possible in a single hand to find approximate examples of the three types of developmental inhibition.

It is apparent furthermore from the X-rays accompanying the papers by WALKER and DRINKWATER (minor brachydactyly), as well as from my own studies, that the postaxial side of the hand is chiefly affected, more especially the little finger. Thus in the phalangeal fusion typical of the family on which this paper is based, grades of involvement can be illustrated as follows:

(1) Fingers of normal length (cf. figure 1) but with bony anchylosis of the proximal joints of all four fingers (cf. patient's left hand, figure 7).

(2) Fingers of normal length anchylosed as above, except in the index finger which possesses an imperfect proximal inter-phalangeal joint, as was the case with the patient (cf. right hand figure 7) as well as (cf. figure 8) of one of her sisters (Gen. VI, Fam. 34, Child 6).

(3) Fingers of approximately normal length as in the case of the twin uncles (cf. hand of twin, Gen. V, Fam. 8, Child 8, figure 3), but which show a fairly well developed joint of the index, an imperfect joint of the middle, and bony fusion of the ring and little fingers, the latter evidently having an imperfectly developed middle phalanx; in fact all the middle phalanges are somewhat short (figure 9).

(4) Fingers of the hand of a supposedly unaffected daughter (Gen. VI, Fam. 37, Child 8) of one of the affected twins, in whom the X-ray shows an imperfect proximal inter-phalangeal joint and a dwarfed middle phalanx of the little finger alone (figure 10).

Hence the rule may be established for these conditions not only that *the middle row of phalanges and the proximal phalangeal joints suffer most severely,* but that *in lesser grades of the given malformation the nearer the preaxial (radial) side of the hand, the less outspoken is the lesion.* This however must be taken with certain reservations, so far as

the index finger is concerned, though it appears to be the rule for the three others.[2]

In many, if not in all, of the individuals in the family which is the subject of this report, the toes are likewise affected, and, as will be

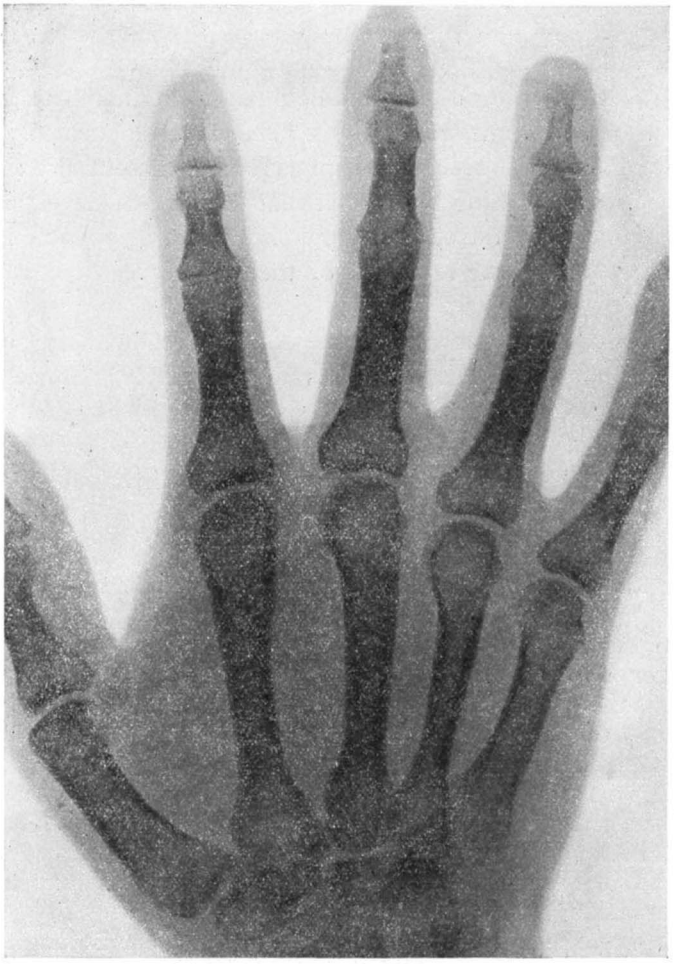


FIGURE 8.—Patient's sister: (Gen. VI, Fam. 34, Child 6) showing imperfect proximal interphalangeal joint of index finger without notable brachydactylous change of mid-phalanx. (Compare with right hand of figure 7.)

[2] One cannot resist the impression given by some of these radiograms, particularly by those of certain members of WALKER'S family, in whom the two terminal phalanges were actually missing from the fourth and fifth fingers (figure 11), that we may be dealing with a condition allied in some way with the elimination of the inner and outer digits in hoofed animals with five-toed ancestors.

seen, the involvement of the feet, in the case of the individual who presumably has normal hands and yet some of whose children have "stiff

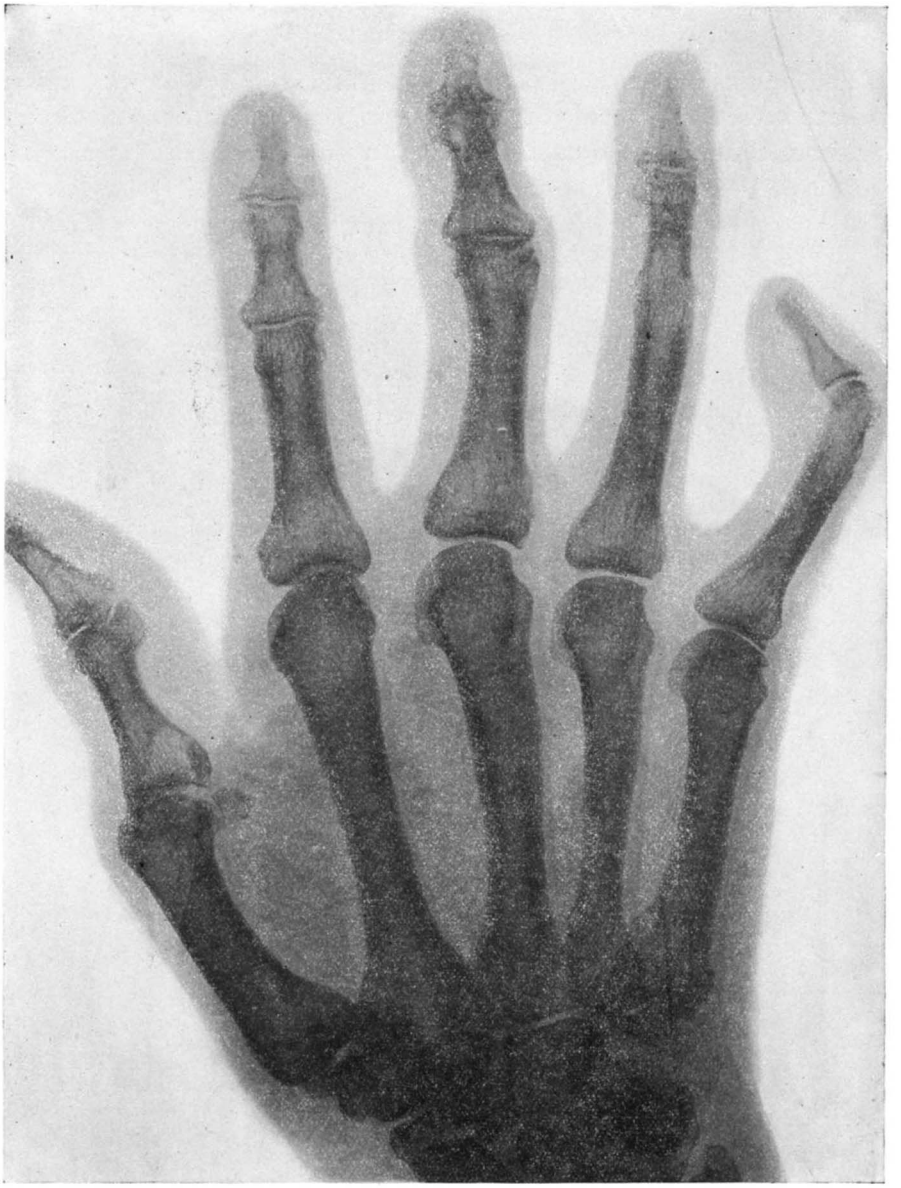


FIGURE 9.—Hand of one twin brother (Gen. V, Fam. 8, Child 7) showing tendency of preaxial fingers to escape from the anchylosing process. The nearer the postaxial (ulnar) side the more severe the involvement.

fingers," stamps her as presumably involved. I am informed that there have been instances of webbed toes and of supernumerary toes, as well as of anchylosed ones, but concerning this I have no exact information.

FAMILY RECORD

The original member of the family, William B., who was known to have been the possessor of "straight fingers," migrated to this country from Scotland in 1700 and settled in Virginia. He married, had

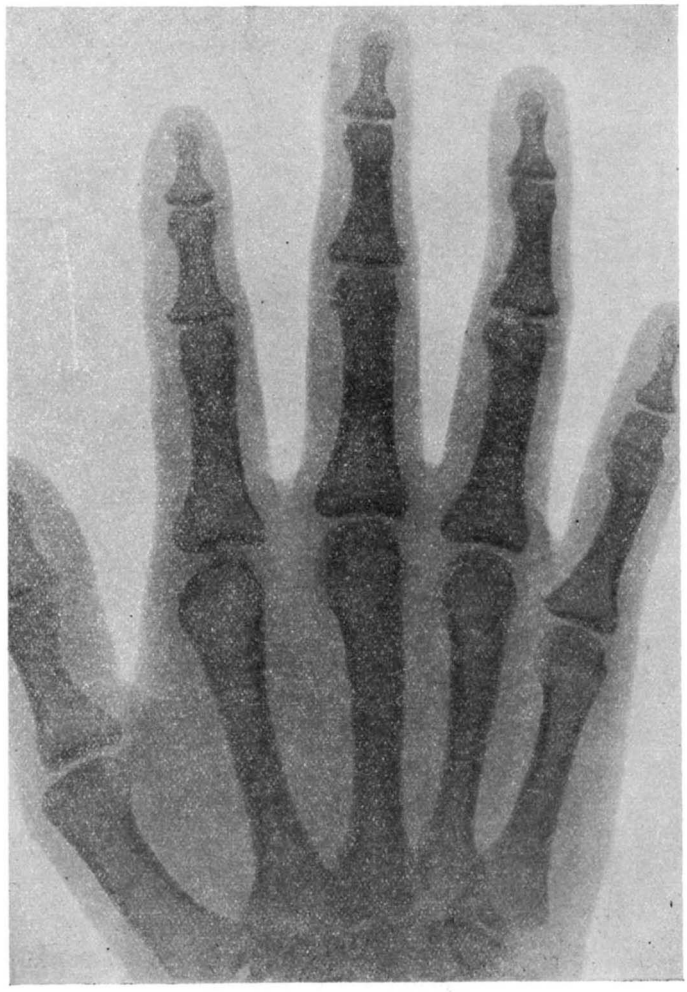


FIGURE 10.—Hand showing the mildest degree of involvement, confined to the most postaxial finger (Gen. VI, Fam. 37, Child 8).

a large family of children, some of them with "stiff fingers," and from this source have sprung the seven generations, most of whom still remain in the neighborhood country.[3]

The community in which these people live is situated in two valleys in Tazewell County, in the southwestern part of Virginia. One of these valleys is a curiously bowl-shaped depression surrounded by mountains on all sides except for a narrow pass, and it is here that many of the descendants of William B's daughter, Sallie B., reside. Other collaterals live in a much larger adjoining valley. There are some "straight fingered" descendants in every branch, and though intermarriages have occurred, they have been comparatively few (cf. chart).

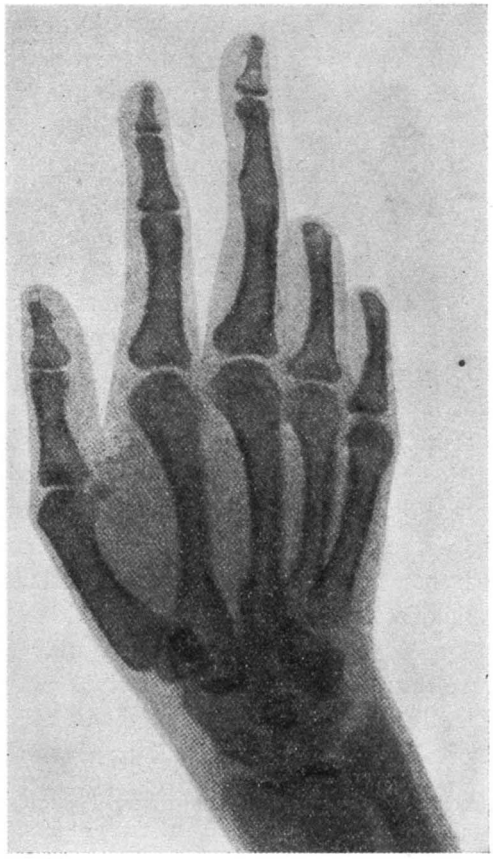


FIGURE 11.—An example of interphalangeal anchylosis with absence of the terminal phalanges of the two ulnar fingers. (From WALKER.)

[3] One of the twins (Gen. V, Fam. 8) of this American branch has had communication with a distant relative in Scotland who bears the same name as the founder of the American line and who shows the family trait.

So far as could be learned, these individuals were unrelated to the Maryland family reported by WALKER, though it is quite probable that offshoots of some earlier generation, of whom there is no record, may have migrated, for as can be seen by the chart, these people have been very prolific. William B. had several children, many of them affected, and our present record includes a line of descent from only two of them; indeed as far down as the fourth generation in the Sallie B. line, there were several children in one family whose offspring no attempt has been made to trace.[4]

The Sallie B. line of the chart which contains the tree of the patient's family was made out for me by the uncle and the details have been since corroborated from two other sources. The Grace B. line was secured by my friend, Dr. S. J. CROWE, who some years ago made a special visit to the community and secured the data on which it is based. This record has also been subsequently corrected and authenticated and further details have been added to it from time to time by my correspondent, a resident of the valley, to whose intelligent coöperation I am greatly indebted.

These two lines including the progenitor William B. comprise, all told, 313 individuals, and the following analysis may be made of them. In the *second generation,* the two recorded daughters from the large family of the original William B. were both "stiff fingered." In the *third generation,* there are only three recorded individuals, two with and one without the anomaly. In the *fourth generation,* there are fourteen individuals, eight recorded with and six without the anomaly, there being six affected and three free in the single fully recorded family.

In the *fifth generation,* the numbers increase sufficiently to be of some statistical value. Of the 53 individuals there are 18 unaffected children of 3 unaffected parents, whereas the 5 affected parents had 22 affected children and 13 unaffected children. This predominance of affected over unaffected is largely influenced by the one family (Gen. V, Fam. 8) in which there were 8 affected (2 of them twins) and but 1 unaffected child.[5] In the Grace B. line the 26 children of affected parents are about evenly divided, there being 14 affected and 12 unaffected children.

[4] My correspondent tells me that there are "stiff fingered" people, known descendants of William B., in Bland, Va., and another group of them in Princeton, West Virginia, who are presumably related.

[5] Particular inquiries have been made regarding the parents of this family and the supposedly unaffected daughter, owing to the suspicion that the parents might both have carried the trait and have been homozygous. But the father came from a distant community and was unrelated, and there can be no question but that the daughter is unaffected.

In the *sixth generation,* as the result of the recorded 39 marriages from the foregoing, there were 169 children, 79 (about 50 percent of them) being the unaffected offspring of 23 parents recorded as unaffected; whereas from the 16 affected parents there were 90 children, 40 of whom were affected and 50 unaffected.

In the *seventh generation,* as the result of 24 recorded marriages, there were 71 offspring, 55 unaffected of 18 unaffected parents, whereas from the 6 affected members of the previous generation who married, there were 10 affected and 6 unaffected children.

To analyze our data further, we can see that among the 312 descendants of William B. recorded in the chart there were 84 affected persons, a few more than the 25 percent of the total number which would be expected, did the affected and unaffected individuals mate with equal frequency and have an equal number of offspring. If however we exclude from this computation the incomplete families of the first few generations in which merely the affected individuals carrying "the lines" are given, we have 72 completed families in the four succeeding generations comprising 302 individuals, 78 of them being affected, namely 25.8 percent.

That there has been no discrimination in the mating of males or females whether affected or unaffected is apparent when we take a single generation such as Gen. V, in which all marriages likely to have fruition have presumably been made; for of the 53 individuals, there are 22 affected, 16 of whom (73 percent) have married and have families, whereas there are 31 unaffected, 23 of whom (74 percent) have married and have families. In the fourth and fifth generations an equal number, namely 8 affected and 8 unaffected individuals, have either not mated or have been without offspring.

It is obvious from the chart that there is no sex-limitation in the transmission of the trait, there being 17 affected male parents with affected offspring and 15 affected female parents with affected offspring.

To trace this matter further, in the 72 families of the later generations for which the records are complete, 44 of them were from the mating of unaffected parents with 152 children, all of course unaffected. On the other hand, in the 28 families with an affected parent there were 150 children, showing that the affected individuals have been proportionately more prolific than the unaffected. *Of the 150 children of affected parents in these 28 completed families, 78 of them, or 52 percent, carried the trait,* a figure which closely corresponds therefore with the normal Mendelian ratio for a single unit-character.

THE SUPPOSED EXCEPTION TO MENDEL'S LAW

In the sixth generation in the line of Grace B. there occurs what was regarded in the community as the single instance (Gen. VI, Fam. 25) of affected offspring (3 out of 8 in the family) from a presumably normal parent or at least from a parent with so slight a trait that it was not evident on casual observation of the hands. Suspicions were naturally aroused in regard to this family and unsuccessful efforts have been made to secure an X-ray photograph of the mother's hands. The suspicions, however, are in a measure confirmed by my correspondent who is a relative, and who writes that "she apparently has not stiff fingers, but she walks like the stiff fingered people whose toes or ankles are probably also stiff." On this basis she has been included (though questioned) with the affected individuals. Such a mild degree of involvement as is shown in figure 10 in the hand of a girl[6] (Gen. VI, Fam. 37, Child 8), who though originally tabulated as a suspect by Dr. CROWE was regarded as unaffected by my correspondent until the X-rays were taken, indicates how cautious one must be, without an examination, in accepting data concerning individuals who may pass for normal in the community. Still on this basis it is remarkable that local tradition records no other example of a suspected recession through the mating of presumed normals.

INTERMARRIAGES

It will be seen from the chart that there have been a few intermarriages though there is no recorded marriage of two affected individuals. In Generation V an unaffected son (Fam. 1, Child 4) of an affected mother married an unaffected relative of Generation VI (Fam. 22, Child 1) with three unaffected offspring. In the same generation another unaffected son (Fam. 3, Child 3) married an unaffected first cousin (Fam. 4, Child 6) who bore nine unaffected children. In Generation V also, an affected woman (Fam. 5, Child 3) married an unaffected relative of Generation VI (Fam. 24, Child 1) and has a family of two children, one of whom is affected. A third intermarriage in Generation V occurred between one of the affected twins (Fam. 8, Child 7) and an unaffected cousin (Fam. 4, Child 5) and among their eight children (Gen. VI, Fam. 37) five are free, only one, the fifth child, unmistakably carries the trait and she has only two fingers involved; another, the eighth child, is very mildly affected, with only one finger involved (figure 10), and a third is merely a suspect.

[6] Her elder sister (Child 6), also a suspect, has not been X-rayed.

MODIFICATION OF DOMINANCE

It is of interest that there is a local tradition which would signify that the dominance of the anomaly is becoming modified, for it is believed that the children of "stiff fingered" people are apt to have one less finger involved than their parents and I judge that the index finger, as has been indicated, is the first to escape, whereas the postaxial fingers tend longest to retain the anomaly. This tradition might be borne out by the line of Sallie B., for in the single recorded family of the fifth generation, though 8 out of the 9 children were affected, many of their offspring in the next generation are but mildly affected and this is particularly true of the children of the twins, who are, I may add, identical twins, even to the degree of the anomaly, as shown in the X-rays of their hands.

Opposed to this suggestion of fading dominance, however, is the following experience in the line of Grace B., for one of her grand-daughters (Gen. IV, Fam. 2, Child 7) who was only mildly affected, having merely the two postaxial fingers on each hand involved, had a family of eight children, five of whom had extensively involved hands, and a sixth was the suspect (Gen. V, Fam. 6, Child 6) whom we have discussed and whose family of eight contained three children with extensively involved hands.[7] It is probable therefore that *the trait may be transmitted in its most outspoken form by a parent who appears to be but slightly affected, but never through parents both of whom are unaffected.*

CONCLUSION

An abnormal character, designated symphalangism, which is transmissible by either sex, appears in seven generations as a bony anchylosis of the proximal interphalangeal joints of one or more fingers. In its milder degrees, the preaxial (radial) fingers are less likely to be involved than the postaxial. Both hands and feet of the affected individuals may be affected. The trait may be transmitted in its most outspoken form by a parent in whom it is inconspicuous, but never by unaffected parents.

Of 302 individuals in 72 completely recorded families, 25.8 percent of them were affected. Of the 150 children of the affected parents, 78 of them, or 52 percent, were affected. Hence the trait behaves as a

[7] Dr. W. E. CASTLE, who has been kind enough to look over this data, suggests that other inherited factors may affect the manifestation of the character without necessarily affecting its dominance, so that it may crop out in full force in later generations even if partially inhibited by these other factors in a particular case.

simple Mendelian dominant with an equal chance, among the offspring of affected individuals, that it will be or will not be inherited.[8]

LITERATURE CITED

FARABEE, WILLIAM C., 1905 Inheritance of digital malformations in man. Papers of the Peabody Museum of American Archaeology and Ethnology, Harvard University. **3**:69-77.

DRINKWATER, H., 1908 An account of a brachydactylous family. Proc. Roy. Soc. Edinburgh. **27**:35-57.

1911 Study of a brachydactylous family (minor brachydactyly) IV^e^ Conférence Internationale de Génétique. Pp. 549-562. Paris.

1912 Account of a family showing minor brachydactyly. Jour. Gen. **2**: 21-40.

1914 Minor brachydactyly no. 2. Jour. Gen. **3**: 217-220.

MALL, F. P., 1906. Ossification centers in human embryos less than one hundred days old. Amer. Jour. Anat. **5**: 433.

WALKER, G., 1901 Remarkable cases of hereditary anchyloses, or absence of various phalangeal joints with defects of the little and ring fingers. The Johns Hopkins Hospital Bulletin. **12**: 129-132.

[8] Since this article was submitted for publication, additional data have been received concerning 139 other individuals, including the West Virginia branch of the family, reaching into eight generations. Thus, all told, the tabulations comprise 452 individuals, though the percentages of affected and unaffected remain practically as computed from the two lines here presented. Moreover an X-ray photograph has been finally secured, unfortunately of the hand alone, of the suspect who was fully discussed, and it shows a brachydactylous median phalanx of the little finger of one hand.