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Genetical studies on the skeleton of the mouse

XXXI. THE MUSCULAR ANATOMY OF SYNDACTYLISM AND OLIGOSYNDACTYLISM

BY K. M. KADAM

Medical Research Council Experimental Genetics Research Unit, University College London, and Department of Zoology, Central College, Bangalore, India

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INTRODUCTION

Compared with the many osteological studies of inherited anomalies which have been published, little attention has been paid to the changes in muscular anatomy which inevitably must accompany such skeletal anomalies. The present paper deals with the genes for syndactylism (*sm/sm*) and for Oligosyndactylism (*Os*/+) in the mouse whose skeletal anatomy and development have been described in earlier papers of this series (Grüneberg, 1956, 1960, 1961). Whereas in the case of *sm/sm* the changes in muscles and tendons are comparatively simple and easily explained as consequences of the skeletal anomalies, the situation encountered in *Os*/+ is complex and suggests that the interpretation based on the skeleton alone may have been an oversimplification. It thus appears that studies of this kind may be of value for a fuller understanding of the mechanisms of morphological gene effects.

RESULTS

In *sm/sm* mice, as already described by Grüneberg (1956, 1960), the third and fourth digits always undergo various degrees of fusion in their osseous and soft parts. The second digit is also involved, though to a lesser extent. Consequently, the musculature also shows deviations from the normal condition. As there is no published account of the muscles of the normal mouse, the description of the rat by Greene (1935) was followed as a basis for comparison. However, it was found that, although the description of the rat corresponds broadly with the condition found in the mouse, there were a considerable number of important differences which might be usefully recorded in this paper.

The fore-limb of the normal mouse

M. Extensor digitorum communis (Fig. 1). This muscle gives rise to five tendons, one for each of the digits 2 to 5 with the exception of the third digit which has an additional one. The tendons insert at the base of the second phalanx and do not extend up to the base of the distal phalanx as described by Greene for the rat. Instead, there is a ligament extending from the base of the distal phalanx to the distal interphalangeal joint. Greene mentions that in the rat there are four tendons inserting into the distal phalanx of digits 2 to 5.

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M. Extensor indicis proprius (Fig. 1). Greene states that the tendon of this muscle divides into two slips which insert at the base of the distal phalanx of the second and third digits. In the mouse, the muscle gives rise to a single tendon which inserts at the base of the middle phalanx of the second digit.

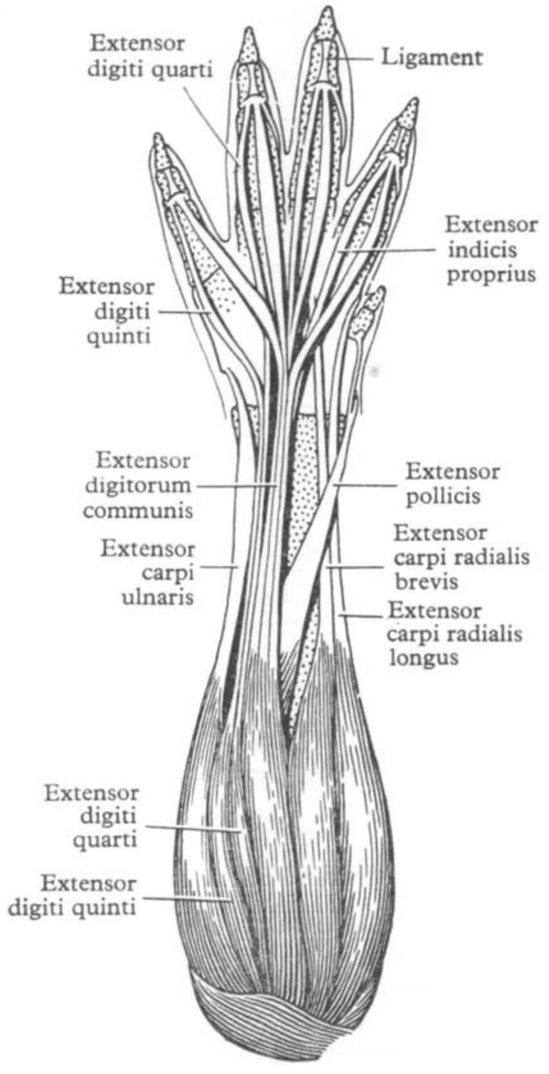

Fig. 1. Extensor muscles of the left forearm and manus of a normal mouse. All drawings are semidiagrammatic and camera lucida drawings.

M. Extensor digiti quarti (Fig. 1). While Greene describes that this muscle also has two tendons inserting at the base of the distal phalanx of the fourth digit, her figure (Fig. 87) shows only one tendon. In the mouse, the single tendon of this muscle inserts at the base of the second phalanx of the fourth digit.

M. Extensor digiti quinti (Fig. 1). The insertion of this muscle is on the base of the second phalanx of the fifth digit.

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M. Extensor pollicis (Fig. 1). In place of the extensor pollicis longus and extensor pollicis brevis muscles of the rat, there is a single large muscle in the mouse. The broad tendon of this muscle inserts on the base of the first metacarpal and sends off a small slip to the base of the proximal phalanx of the pollex.

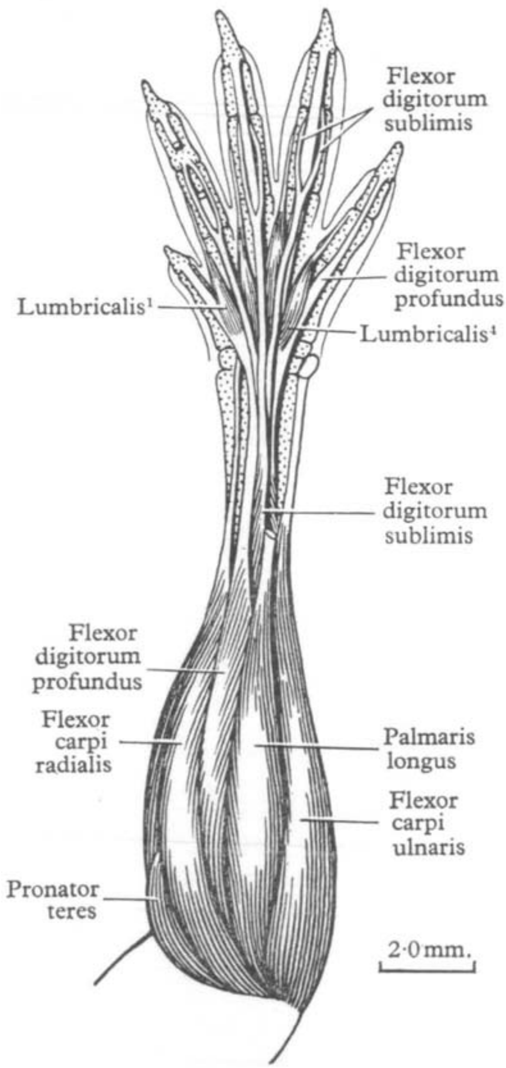

Fig. 2. Flexor muscles of the left forearm and manus of a normal mouse. In all the flexor surface views muscles of the deep layer are omitted.

M. Flexor digitorum sublimis (Fig. 2). There are only three stout tendons of this muscle to the digits 2, 3 and 4; there is no tendon to the fifth digit unlike in the rat.

M. Flexor digitorum profundus (Fig. 2). The four tendons of this muscle unite to form a tendinous plate in the middle of the palm. From this plate a tendon is

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given off to each of the five digits. According to Greene there is no tendon to the pollex in the rat.

MM. Lumbricales (Fig. 2). The four muscles which take their origin from the tendinous plate of the flexor digitorum profundus run on the preaxial side of the digits 2 to 5. Their tendons, except that of the fourth lumbricalis, cross over to the extensor surface and, along with the tendons of the interossei muscles, join the extensor ligaments at the base of the middle phalanx of the corresponding digits. The tendon of the fourth lumbricalis is inserted at the distal end of the proximal phalanx of the fifth digit.

The hind-limb of the normal mouse

In addition to the discrepancies noted by Carter (1951) in the description of the hind-limb of the normal mouse by Hovelacque (1920), some more differences observed in my dissections will be recorded below.

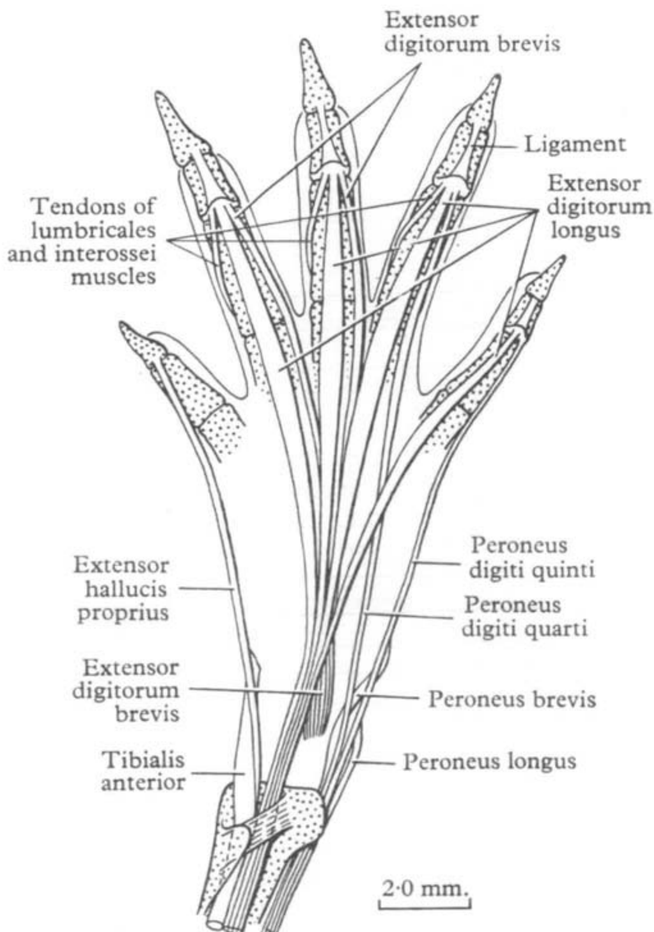

Fig. 3. Extensor muscles of the right hind-foot of a normal mouse.

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M. Peroneus digiti quarti and m. peroneus digiti quinti (Figs. 3, 5). The origin of these muscles is as described by Carter, but the insertion of the tendons, which has not been mentioned by him, differs from the description of the rat by Greene. In the mouse, the tendons insert at the base of the second phalanx of digits 4 and 5.

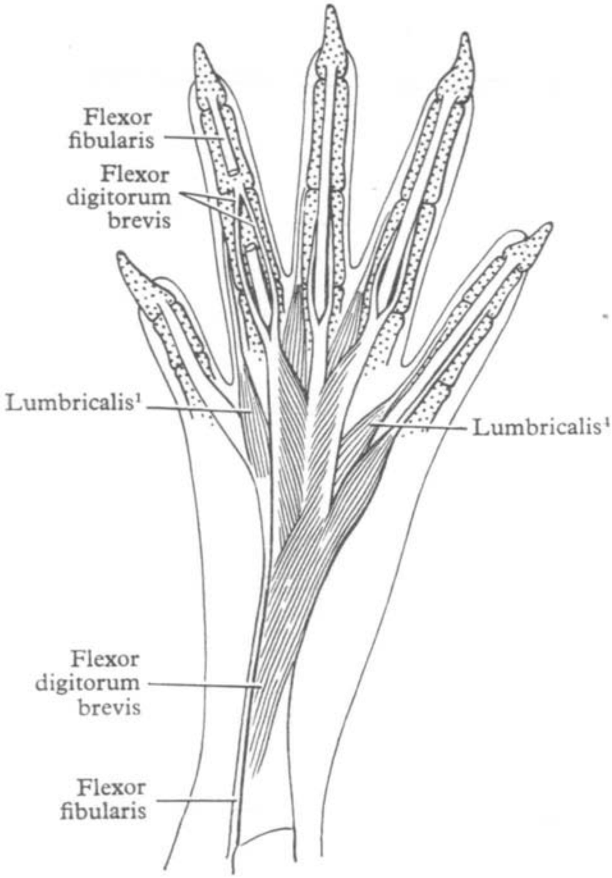

Fig. 4. Flexor muscles of the right hind-foot of a normal mouse.

M. Extensor digitorum longus (Figs. 3, 5). The four tendons of this muscle insert at the base of the middle phalanx of digits 2 to 5 and not on the proximal phalanges as mentioned by Hovelacque nor on the base of the third phalanges as mentioned by Greene for the rat.

M. Flexor digitorum brevis (Fig. 4). Greene states that this muscle has three muscular lobes with their tendons passing to the second, third and fourth digits. In addition to these three, in the mouse a large muscular belly separates itself from the main muscle and gives off a tendon which runs along the fibular side of the long flexor tendon of the fifth digit. This fourth tendon of the flexor digitorum brevis inserts at the base of the middle phalanx of the fifth digit.

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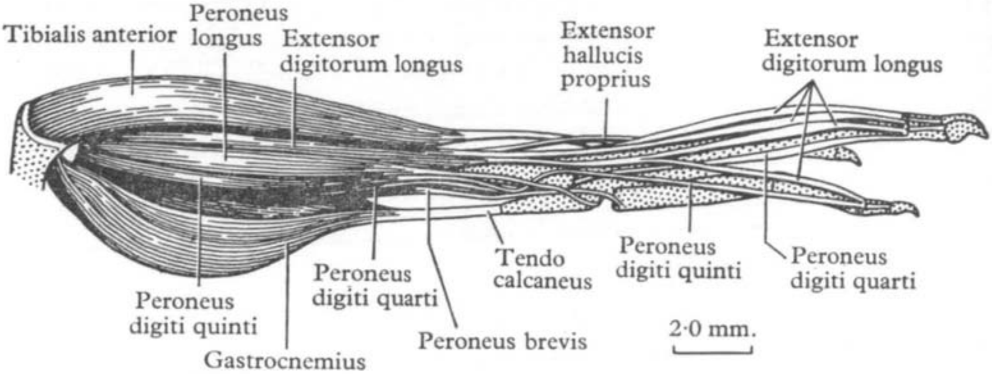

Fig. 5. Lateral muscles of the right lower leg and foot of an *sm/sm* mouse.

Syndactylism

The anomalies of *sm/sm* limbs may be now considered. The limbs of six adult mice were studied under the dissection binocular microscope. The fore-limbs are slightly affected. The muscles that exhibit the effects of syndactylism are the extensor digitorum communis, the flexor digitorum sublimis, the flexor digitorum profundus and the lumbricales. In the fore-limbs where the digits are joined by soft tissues only the musculature is normal. When there is a great degree of fusion of the osseous elements of the phalanges, which is less common in the fore-feet, the muscles show a proportional degree of variation. The muscles as such are less affected than their tendons. Thus, the tendons of the extensor digitorum communis, flexor digitorum sublimis and flexor digitorum profundus tend to fuse and insert together. The fusion of the tendons proceeds from the metacarpal region towards the distal ends of the digits. In a mouse where there was a complete fusion of digits 3 and 4, the muscular bellies of the corresponding tendons of the flexor digitorum sublimis and the extensor digitorum communis were fused from their origin to the point of insertion.

The lumbricalis of the fourth digit is either greatly reduced or totally absent when there is a fusion of digits 3 and 4 involving also the fusion of the tendons of flexor digitorum profundus from which it arises.

The situation is similar in the hind-feet except that there is a greater degree of fusion and variation. The second digit is involved more frequently.

The tendons of the extensor digitorum longus remain separate up to the metatarsophalangeal joint of the syndactylous digit or a little beyond and further distally fuse to form a broad flat tendon which inserts at the base of the second phalanx of the fused digits. Though the second digit is also closely involved in some feet, the long and short extensor tendons remain distinct (Fig. 6). The tendon of the extensor digitorum brevis to the third digit always inserts at the metatarso-phalangeal joint of the third and fourth digits. When there is no fusion of the hard parts, the tendon extends normally up to the base of the second phalanx.

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The flexor tendons (Fig. 7) are more affected than the extensor ones. The slips of the tendons of the flexor digitorum brevis through which the long flexor tendons pass become variously fused with one another. Generally, the tendons to the third and fourth digits fuse and divide into two or three slips; the lateral one follows the normal course and inserts at the base of the second phalanx of the fourth digit; the other slips either fuse with the tendon of the second digit or pass beneath the long flexor tendon and insert at the base of the second phalanx of the second

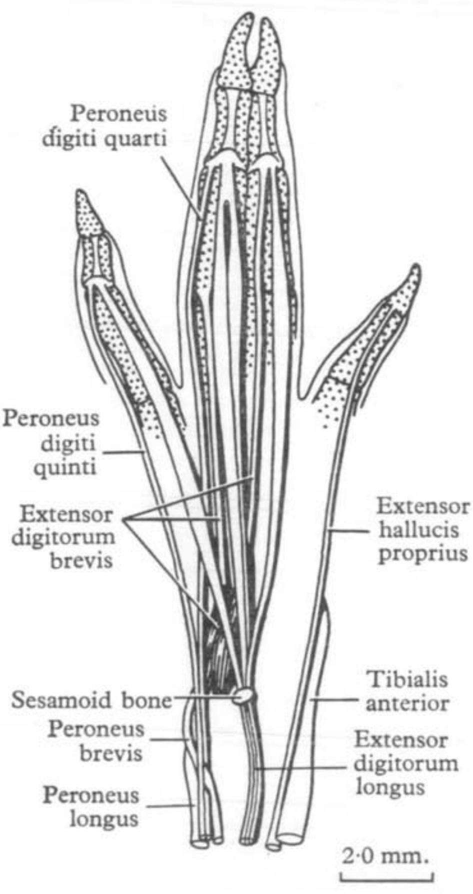

Fig. 6. Extensor muscles of the left hind-foot of an *sm/sm* mouse.

or third digits. The tendons of the flexor fibularis of the third and fourth digits fuse to form a stout tendon which bifurcates before inserting at the distal end of the syndactylous digit. The long flexor tendon of the second digit has always a separate origin and inserts normally; but during its course it becomes fused to a greater or lesser extent with the tendons of the digits 3 and 4.

The lateral muscular belly of the flexor digitorum brevis to the fifth digit shows certain deviations. In two cases out of the twelve examined the muscle was smaller in size and its muscle fibres were inserted on the lateral border of the long flexor

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tendon of the fifth digit. In one case, the entire muscular portion had its origin on the long flexor tendon appearing as if its origin had been transferred from the flexor digitorum brevis to the flexor fibularis.

The lumbricales (Fig. 7) are greatly affected by the fusion of the long flexor tendons of the digits 3 and 4. As the lumbricales take their origin from in between the bases of the ventral surface of the long flexor tendons and run between them,

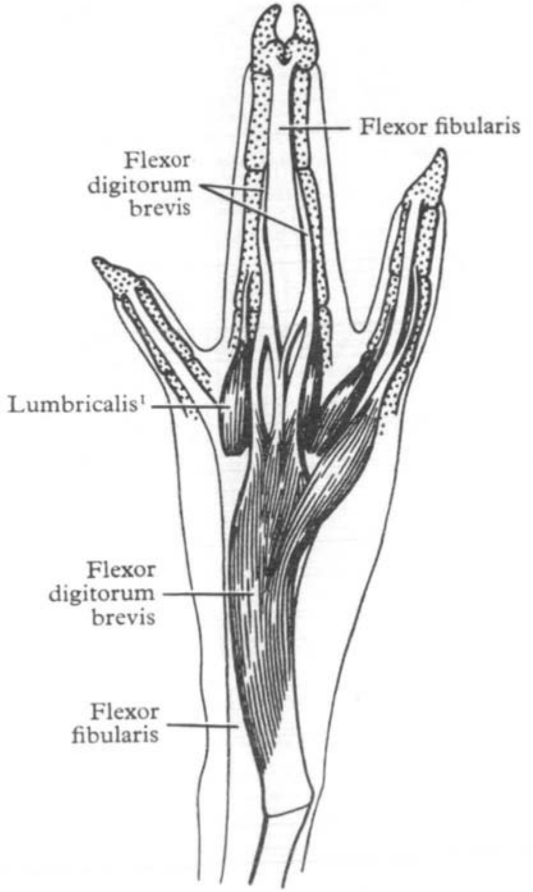

Fig. 7. Flexor muscles of the left hind-foot of an *sm/sm* mouse.

the fusion or the close proximity of the tendons to digits 2, 3 and 4 has resulted in the dislocation of their origin. The first and the fourth lumbricales are not affected. The second and especially the third lumbricalis has changed its origin from the ventral surface to the dorsal surface of the fused long flexor tendon. The insertion is always disturbed and the tendons do not reach the extensor surface but end up on one of the proximal or middle phalanges or sometimes on the tendon of the flexor digitorum brevis.

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Oligosyndactylism

The dissection of the fore-limbs and hind-limbs of six *Os*/+ mice has revealed certain unexpected and complicated anomalies which, unlike those in *sm*/*sm* mice, cannot be entirely correlated with the skeletal abnormalities.

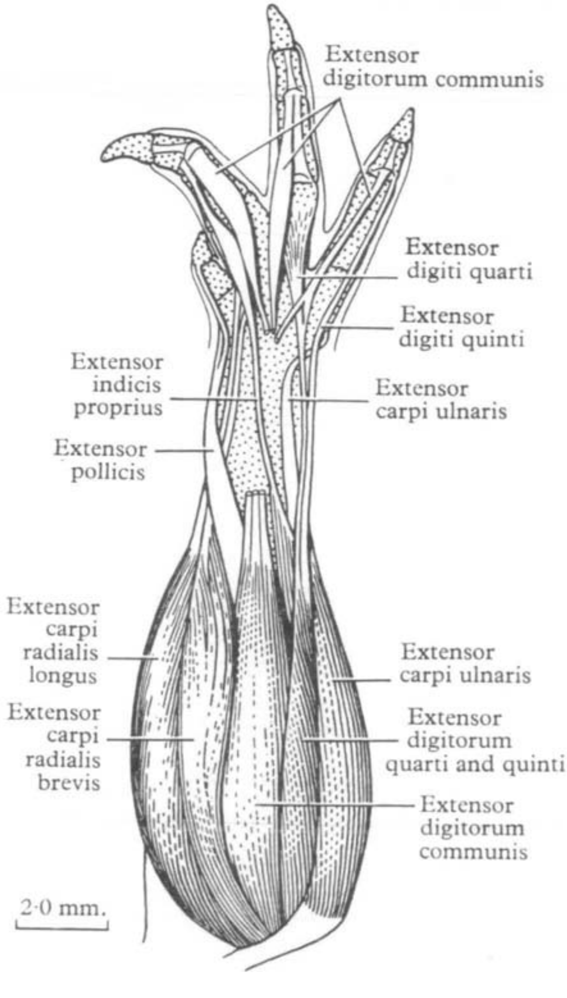

Fig. 8. Extensor muscles of the right forearm and manus of an *Os*/+ mouse.

The muscles of the fore-limb which are affected are the extensor indicis proprius, the extensor digitorum communis, the extensor digiti quarti, the extensor digiti quinti, the flexor digitorum profundus, the flexor digitorum sublimis and the lumbricales.

The extensor digitorum communis (Fig. 8) divides into three tendons instead of the normal five. The muscular portions as well as the tendons of the second and third digits have fused to form one unit. The single tendon thus formed inserts

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by a broad surface on the base of the second phalanx of the fused digit. In those feet where the fusion of the digits 2 and 3 is not great, the tendons are separate at the insertion but their origin is fused.

The tendon of the extensor indicis proprius acquires a broad insertion and occasionally sends a small slip to the pollex.

The muscular bellies of the extensor digiti quarti and extensor digiti quinti tend to fuse into a single muscle (Fig. 8) while their tendons always remain separate. More often the tendon of the fourth digit is greatly reduced in size and it flattens

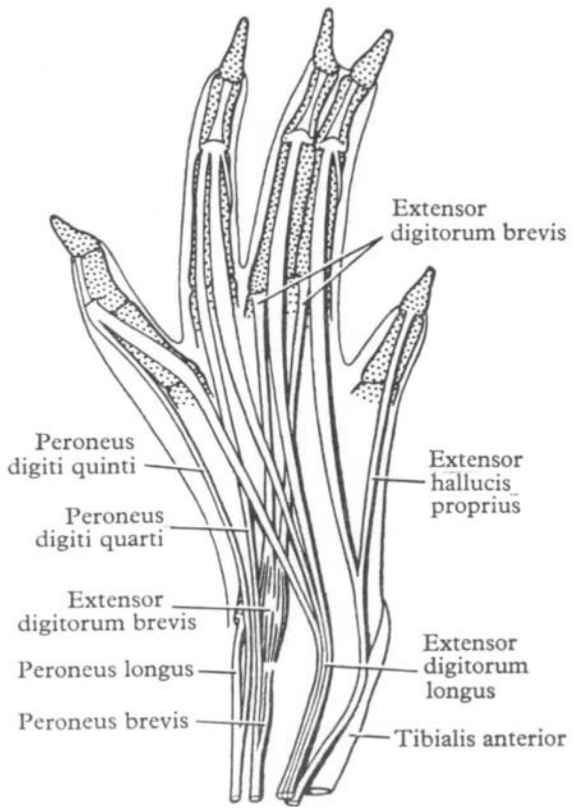

Fig. 9. Extensor muscles of the left hind-foot of an *Os*/+ mouse.

out in the mid-metacarpal level partly fusing with the extensor digitorum communis tendon of the fifth digit and partly inserting on the metacarpal bone. The more distal part of the tendon thus becomes separated.

The flexor digitorum sublimis divides into two tendons; one to the fourth digit being normal and the other to the fused second and third digits being stouter indicating the fusion of the two tendons. The preaxial and postaxial slips of the tendon of the fused digits are also so completely fused that there is no indication of their double nature. The deep flexor tendons are similarly fused into a single tendon but the tendon generally betrays its dual character at the distal end of the digit.

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Of the four lumbricales only the third and fourth are normal. The first and the second which are associated with the second and third digits undergo reduction and may be completely lost.

The situation is more complex in the hind-limb and most of the muscles are involved.

The extensor digitorum longus (Fig. 9) has lost one of its normal tendons irrespective of whether there are four separate digits other than the hallux or not.

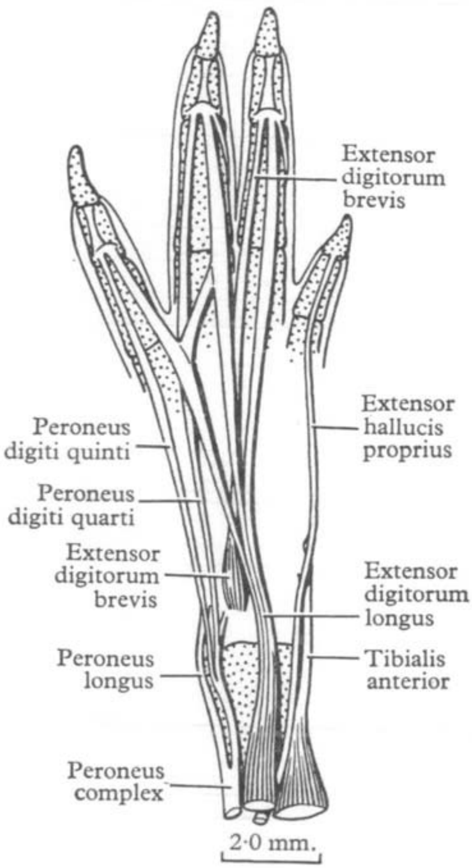

Fig. 10. Extensor muscles of the left hind-foot of an *Os*/+ mouse.

In the feet where the second and third digits are discernible, the extensor digitorum longus tendon of the second digit dissociates itself from the extensor digitorum longus muscle and unites with the tendon of the extensor hallucis proprius. In others where there are only four digits (Figs. 10, 11) the tendon going to the digit next to the hallux (which corresponds to digit 3 (Grüneberg, 1956)) originates from the extensor digitorum longus muscle. The extensor tendon to the fifth digit is deflected towards the fourth digit at the metatarsal joint by a strong tendinous band.

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The tendon of the extensor hallucis proprius tends to fuse with the tendon of the tibialis anterior. In such specimens the extensor hallucis proprius muscle is also fused indistinguishably with the tibialis anterior muscle and the tendon of the tibialis anterior (Fig. 11). Where the extensor hallucis proprius muscle is distinct with its own tendon, the extensor tendon of the second digit unites with it. In one specimen illustrated in Fig. 12, however, the tendon of the extensor hallucis

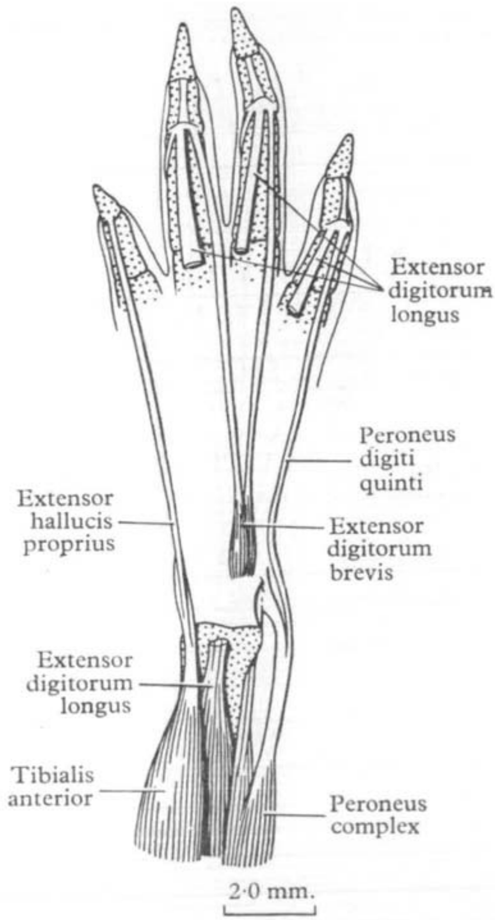

Fig. 11. Extensor muscles of the right hind-foot of an *Os*/+ mouse.

proprius runs to the second digit and inserts at the base of the second phalanx. The true extensor hallucis proprius tendon inserting on the distal phalanx of the hallux originates as a branch of the tendon of the tibialis anterior. An interesting intermediate condition was noticed in one of the hind-feet where the tendinous branch of the tibialis anterior to the hallux had fused with the tendon from the extensor hallucis proprius muscle to the second digit.

The extensor digitorum brevis in the normal mouse gives rise to two tendons which insert at the base of the second phalanx of the second and third digits. Due

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to the reduction or fusion of these two digits in *Os*/+ hind-feet, the tendons and the muscle show variation. The tendons may arise from a common base (Fig. 13) or separately (Figs. 9, 11) and insert together (Fig. 13) or separately (Figs. 9, 11) at the metatarsophalangeal joint. In some cases the postaxial tendon is absent as in Fig. 10 or greatly reduced and may be united with the tendon of the peroneus digiti quarti or replace it as in Fig. 11.

The greatest amount of variation is seen in the peroneal group of muscles. The four muscles often undergo fusion with each other and thus give rise to one (Figs. 10, 11) or two (Figs. 9, 13) compound muscles which have been called here the 'peroneus complex'. The tendons of the four muscles remain more or less distinct in their distal parts. The peroneus longus is always distinct and its tendon has acquired a new insertion on the base of the fifth metatarsal and on a new ligament which extends from the base of the fifth metatarsal to the lower surface of the talocalcaneum. In the normal condition, the tendon of the peroneus longus traverses the flexor surface and inserts on the base of the first metatarsal and the first cuneiform. The tendon of the peroneus brevis is generally reduced and has lost is normal insertion on the base of the fifth metatarsal. In the abnormal condition the tendon sometimes fuses with the lateral malleolus or becomes

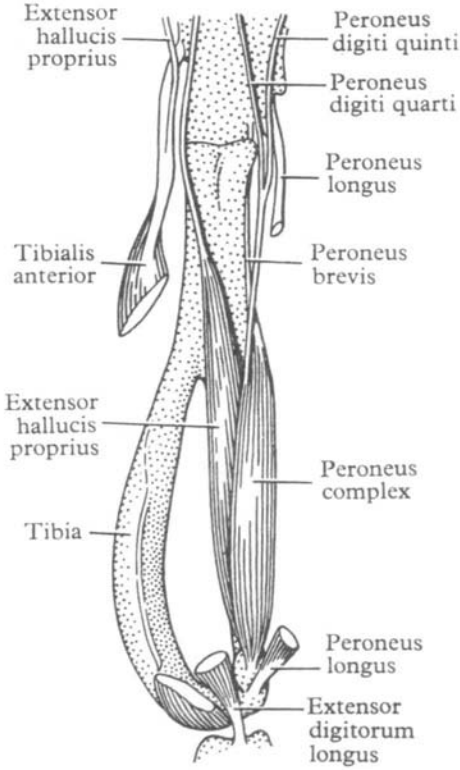

Fig. 12. Dissection to show the variation of the m. extensor hallucis proprius and the peroneus muscles of the right lower leg of an *Os*/+ mouse.

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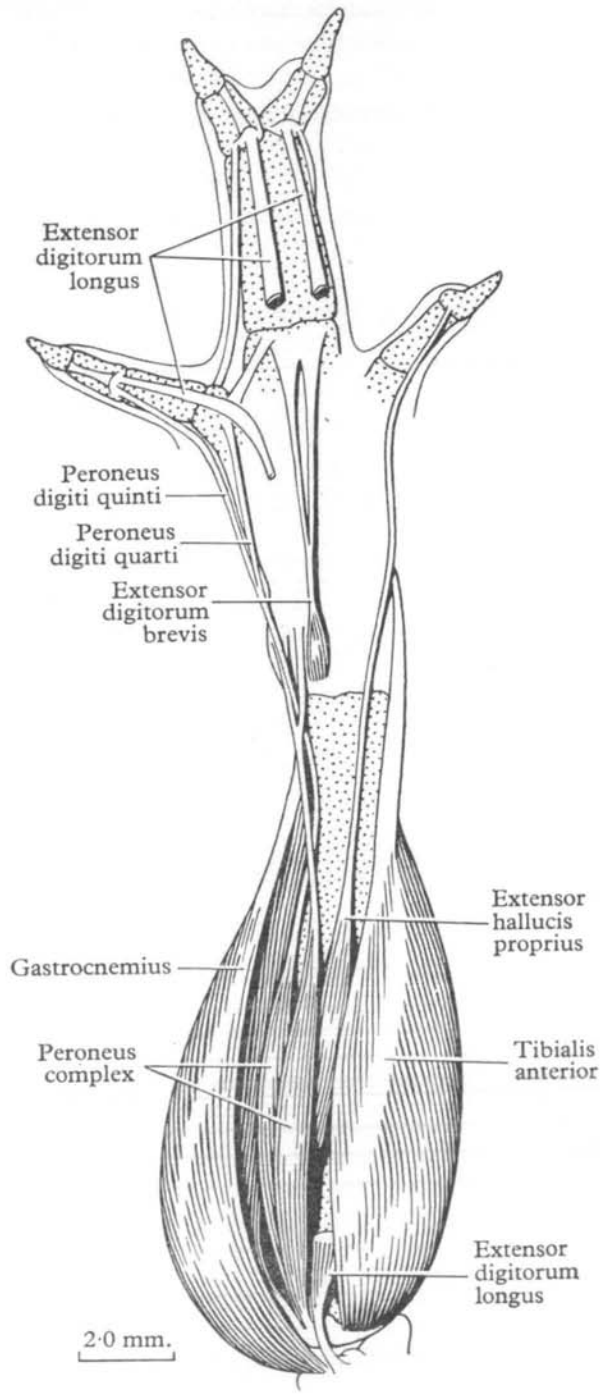

Fig. 13. Extensor muscles of the left lower leg and foot of an *Os*/+ mouse.

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aponeurotic and inserts on the fascia covering the dorsal surface of the talocalcaneum. The tendon of the peroneus digiti quarti is, in some cases, greatly thinned out in the mid-metatarsal level or completely lost as illustrated in Fig. 11. Only the proximal part of the tendon is present and inserts on the lateral malleolus. In one case illustrated in Fig. 13, the tendon branched off from the peroneus digiti quinti and thinned out at the distal part of the fifth metatarsal. The distal part of the tendon was noticed to extend from the inner surface of the fifth metatarsophalangeal joint to the base of the second phalanx of the syndactylous digit.

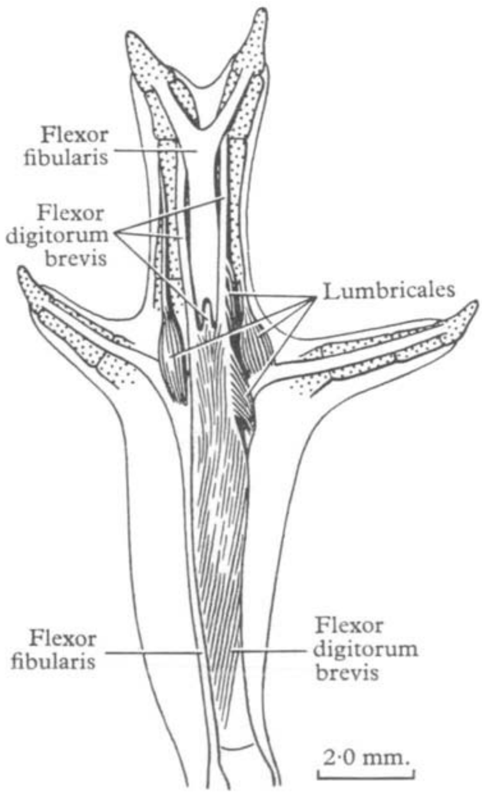

Fig. 14. Flexor muscles of the left hind-foot of an *Os*/+ mouse.

The flexor digitorum brevis, as in *sm*/*sm* hind-feet, tends to give rise to fused tendons to the fused digits. However, one distinguishing feature of the *Os*/+ hind-feet is the great reduction of the muscular belly of the flexor digitorum brevis to the fifth digit. In some feet, as in the one illustrated in Fig. 14, this muscular portion is entirely absent. The lateral border of the tendon is held to the long flexor tendon by a group of muscle fibres which probably represents the proximal lumbricalis. The distal lumbricales show variation as regards their origin and insertion. The tendons generally insert directly on the middle or

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proximal phalanges. The lumbricales of the third and fourth digits more often originate on the dorsal surface of the fused tendon of the flexor fibularis and insert on the slips of the flexor digitorum brevis tendons. The latter tendons sometimes do not divide into preaxial and postaxial slips as the normal ones do. On the other hand, they proceed one on either side of the fused long flexor tendon and insert at the base of the second phalanx.

The flexor fibularis gives rise to four tendons instead of five. The second tendon is a composite one and in the feet where the second and third digits are distinguishable the tendon separates into two at the base of the distal phalanx. In the four-toed feet there is not the slightest indication of a composite nature. In such feet the lumbricales and other structures are correspondingly reduced in numbers.

One of the important characters of the *Os*/+ feet is the absence of the quadratus plantae. This thin muscle was uniformly absent in all the hind-feet examined.

DISCUSSION

Genetically determined anomalies of the muscles in higher animals are either systemic or localized. Examples of systemic anomalies are the lethal muscle contractures in cattle, sheep and pigs (for references see Hadorn, 1961) and the muscular dystrophy of the mouse (Michelson, Russell & Harman, 1955). Some of the localized muscular defects (such as peroneal atrophy, absence of the m. palmaris longus, dislocation of the digital extensor tendons and others in man as listed by Gates (1946)) are isolated entities. Other anomalies and variants of muscles occur in association with skeletal defects. Examples are the muscular variants associated with polydactylism in the cat (Danforth, 1947); muscular anomalies in the scapular region associated with absence of an osseous acromion in undulated (*un*/*un*) in the mouse (Grüneberg, 1954); a shift in the point of origin of the longus colli muscle associated with the changes in the atlas in Danforth's short-tail (*Sd*/+; Grüneberg, 1953); and the extensive muscular anomalies associated with hemimelia tibiae (Carter, 1951). In some, at least, of this latter group, the muscular anomalies seem to be the direct consequences of the skeletal anomalies with which they coexist. The same is probably true for the muscular anomalies of *sm*/*sm* described in this paper. The situation is much less clear in *Os*/+ where some of the muscular anomalies show no very obvious relation to the skeletal changes; this is particularly so in the hind-limbs where the most striking muscular anomalies are present on the postaxial side of the limb while the main digital anomalies are localized preaxially. Danforth (1947), studying polydactylism in the cat, suggested that all the anatomical changes observed later in life might be attributable to an excess of tissue on the preaxial side of the limb buds, and Grüneberg (1961) was inclined to adopt the same principle in the case of *Os*/+ where there is a demonstrable deficiency of material on the preaxial side. Whether this deficiency of material on the preaxial side can bring about the entire complicated muscular anomalies on the postaxial side is, I believe, still an open

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question. More recently, on the basis of other facts, Grüneberg (1962) has also come to doubt whether a simple deficiency of preaxial material can adequately explain the whole *Os*/+ syndrome.

The causal relationships between the various muscular anomalies in *Os*/+ are at present obscure. Valid hypotheses may emerge when a series of similar mutants can be compared with each other.

The unusual insertions of some of the muscles in *Os*/+ hind-feet contravene the well-founded concepts of homologies and render dubious their value for the identification of the structures concerned. For instance, in the four-toed hind-foot illustrated in Fig. 11, the two middle digits are the original third and fourth toes since it is known that it is the second digit which is lost in Oligosyndactylism (Grüneberg, 1956). Consequently the short extensor tendon of the extensor digitorum brevis should have disappeared along with the second digit. On the other hand, both the tendons of the extensor digitorum brevis are present, and if their insertions are any criterion at all, the middle two digits would have to be regarded as the second and third toes. Another instance is shown in Fig. 12 where the extensor hallucis proprius muscle has its own independent tendon inserting on the digit next to the hallux instead of inserting on the hallux itself. The tendon to the hallux originates from the tendon of the tibialis anterior. In another foot the extensor hallucis proprius muscle gave rise to a tendon which divided into two; one of them inserted on the hallux and at the same time united with the tendon of the tibialis anterior by means of a tendinous slip; the other tendon inserted on the second digit. A bifid tendon of the extensor hallucis proprius (longus) is present in the polydactylous cat (Danforth, 1947) and its existence is understandable as the foot is hexadactyl.

Attention may also be drawn to the unusual insertion of the peroneus longus at the base of the fifth metatarsal in spite of the existence of its normal site of insertion, viz., the base of the first metatarsal.

It is thus clear that in the case of an anomaly like *Os*/+ the application of the usual criteria of homology may lead to erroneus conclusions. Whether the same may also occasionally happen when comparing different species is, of course, a different question.

SUMMARY

1. Changes in muscles and tendons in *sm*/*sm* are confined to hands and feet. They are closely correlated with the changes in the osseous skeleton.

2. In *Os*/+, muscular changes are much more complex and not confined to hands and feet, but include the muscles of the forearms and of the lower legs. Some of the muscular changes, especially on the postaxial side, are not correlated with the changes in the osseous skeleton.

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