THE ORIGINS AND INSERTIONS OF THE EXTRAOCULAR MUSCLES: DEVELOPMENT, HISTOLOGIC FEATURES, AND CLINICAL SIGNIFICANCE*

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INTRODUCTION

THE TENDONS OF ORIGIN AND INSERTION OF THE EXrRAOCULAR MUSCLES SERVE TO attach these muscles to the bony orbit and to the sclera. By convention, the term "tendon" is used with extraocular muscles, where aponeurosis would be more correct: A tendon implies ^a rounded or oval cord, whereas an aponeurosis is broad, dense, flattened connective tissue that gives wide and extended purchase to the annulus of Zinn posteriorly and the sclera anteriorly. "Tendon" will be used in this dissertation, in keeping with presently accepted ophthalmic terminology.

Little research has been carried out with reference to the tendinous origins and insertions of the extraocular muscles. Previous investigations have been confined to gross measurements of the tendon's length, width, and site of insertion. 1-5

The purpose of this report is to describe the development and histologic features of the tendons of origin and insertion of the extraocular muscles. The evolution of tendons, from early in embryonic life through different stages of development to term, is examined, as is the source of the embryonic tissue from which tendons are derived. The unique manner of attachment of the tendon to the periosteum and sclera is described.

The detailed embryologic and histologic features of extraocular muscle tendons from early development to term are used to explain superior oblique tendon sheath syndrome and superior rectus muscle underaction associated with ptosis.

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PRESENT STUDY

MATERIALS AND METHODS

Sixty-four human eves from embryos and fetuses, ranging in size from 13.6 mm to term, were examined (Fig 1). Between 60 and 110 microscopic sections were examined, respectively, from each embryo and fetus. The normal development of the embryo/fetus was an essential prerequisite, so the conceptus of septic abortions was not accepted for investigation. If the mother had been exposed to teratogenic drugs during pregnancy, the embryo or fetus was excluded from the survey. Where salpingectomy was done (for ectopic pregnancy), the fallopian tubes were dissected with the aid of a dissecting microscope and the embryos retrieved. Usually these embryos were found within blood clots.

Age of Embruo/Fetus

The maternal history with reference to duration of pregnancy was found to be unreliable. A more satisfactory correlation was found between the clinical size of the uterus and the age of the embryo/fetus. Where possible, however, a correlation was attempted between the clinical age of the embryo/fetus and its crown-rump length. A micrometer gauge was

Crown-rump length (mm) and age (weeks) of embryos and fetuses examined.

used for measuring the length of the fetus up to 170 mm; thereafter, ^a centimeter metal rule was used. Development of the eye was correlated with development of other body organs. It was then possible to assess this interrelationship and therefore assign an age to the embryo/fetus. 6.7

Specimens were examined macroscopically with a dissecting microscope. Small specimens (< 80-mm crown-rump length) were fixed for at least 1 week and larger specimens $(> 80$ -mm crown-rump length) for at least 2 weeks.

All specimens were serially sectioned in conventional anatomic planes, either frontal (coronal) or transverse (horizontal). Stains used on the sections were hematoxylin-eosin, Masson trichrome, Mallory's phosphotungstic acid hematoxylin, Verhoeffs-van Gieson elastic, Bodian's silver nitrate, and Luxol fast blue. $8,9$

RESULTS

The tendon is best seen with the Masson trichrome and the Bodian silver stains. The latter demonstrates the reticulin argyrophilic fibrils in the tendon, while the Verhoeffs elastic stain demonstrates the collagenous elastic tissue.

Tendon Measurements of Rectus Muscles

The precise location of insertion of the rectus muscles in fetuses smaller than ³⁶ mm could not be measured because of the gelatinous nature of the tissue and the wide, elongated, ill-defined fusing of the rectus insertion to the sclera.

At 80 mm, tendon can be differentiated from muscle, but the precise line between the two structures cannot be accurately defined. Thick Tenon's fascia in this region causes difficulty in differentiating tendon from muscle. Because merging of tendon with sclera is imperceptible, the width of the tendon prior to ⁸⁰ mm is difficult to ascertain.

Measurement of tendon lengths with use of the microscope was considered inaccurate because of shrinkage resulting from preparation and fixation of the specimens.

Only in fetuses ¹⁶⁵ mm and larger can approximate tendon length be measured macroscopically with a caliper. In eight such specimens, the insertion site was determined where the tendon could be identified between a fine muscle hook (under the tendon) and forceps placed on the superficial surface of the developing tendon. The superficial and deep surfaces of the tendons were not dissected, so that the tissue was not disturbed or damaged for histologic examination (Table I).

490

CLINICAL INVESTIGATIONS

In the Department of Ophthalmology at the University of California, San Francisco, 46 patients who had had surgical treatment (bilateral medial rectus recession) for nonaccommodative congenital esotropia were assessed, with special reference to the sites of insertion of the medial rectus muscles from the limbus and the correlation between these sites of insertion and the degree of esotropia (Table II).

In addition) in the Department of Ophthalmology at the University of

Extraocular Muscles 491

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California, San Diego, and at Scripps Clinic, San Diego, 21 patients who had had surgical treatment (medial rectus recession and lateral rectus resection) for nonaccommodative congenital esotropia were evaluated to determine the site of insertion and the degree of esotropia was ascertained. The length and width of the tendons were measured (Table III). Special care was taken to identify abnormal adhesions, thickened tissue, or extramuscular slips at the insertion sites.

MORPHOGENESIS OF ORIGINS OF EXTRAOCULAR MUSCLES

Development of Annulus of Zinn

The tendons of the rectus muscles are first observed to be attached to the perichondrium at the apex of the orbit at ²⁶ mm (Fig 2).

The rectus muscles and their corresponding tendons mature, and the perichondrium at their sites of origin thickens in a ring-like configuration. As the cartilage at the apex of the orbit develops into bone (225 mm), the perichondrium becomes periosteum; this ring of thickened periosteum is called the annulus of Zinn, which is located over the optic foramen and the medial aspect of the superior orbital fissure.

The origin of the lateral rectus muscle has both superior and inferior heads that straddle the superior orbital fissure. These superior and inferior heads are first discernible in the 54-mm embryo.

At their origins, the superior and medial rectus muscles fuse with the dura of the optic nerve. The fusion of the medial rectus muscle to the anlage of the dura of the optic nerve is first observed in the 22-mm embryo (Fig 3). The superior rectus muscle is seen to merge with the dura of the optic nerve in the 70-mm fetus.

At term, the superior portion of the annulus (tendon of Lockwood) is attached to the body of the sphenoid bone, straddles the superior orbital fissure, and also attaches to a bony spur, the spina recti lateralis. The superior rectus muscle and the superior portions of the medial and lateral rectus muscles originate at the tendon of Lockwood. The inferior portion of the annulus (tendon of Zinn) is attached to the lesser wing of the sphenoid and to the infraoptic tubercle. The inferior rectus muscles and part of the medial and lateral recti arise from the tendon of Zinn.

The origin of the superior oblique muscle is continuous with the origin of the medial rectus muscle at the apex of orbit and is noted first in the 22-mm embryo. By term, with the development and enlargement of the orbit, the tendinous origin of the superior oblique muscle sequestrates from the annulus of Zinn and takes origin from the region of the frontoethmoidal suture immediately superior and medial to the origin of the medial rectus muscle.

492

	PATIENT AGE (MO)	TENDON MEASUREMENTS (mm)*						
PATIENT NO		MEDIAL RECTUS			LATERAL RECTUS			ESOTROPIA
		L	W	LIMB	L	W	LIMB	(DIOPTERS)
ı	6	$\overline{2}$	4.0	3.0	4.5	5.5	3.0	60
$\boldsymbol{2}$	7	$\mathbf{2}$	4.5	3.0	4.5	5.5	3.5	50
$\overline{3}$	7	2.5	4.5	3.5	4.5	5.0	3.0	50
$\boldsymbol{4}$	8	2.5	6.5	3.0	4.0	6.0	3.0	50
5	9	2.5	5.5	3.0	4.0	5.5	3.5	60
6	9	2.0	5.5	3.0	$5.5\,$	5.5	3.5	40
7	10	2.5	6.0	4.0	5.0	6.0	3.5	45
8	10	$2.5\,$	6.5	3.0	6.0	6.5	4.0	50
9	10	3.0	6.5	3.0	5.5	6.5	4.0	50
10	11	2.0	6.0	3.5	6.0	6.5	4.0	60
$\mathbf{11}$	11	2.5	7.0	3.5	6.5	7.0	4.0	50
12	12	2.0	6.5	4.0	6.5	6.0	4.5	60
13	12	2.0	8.0	4.5	6.5	6.5	3.5	50
14	12	2.5	8.0	5.0	7.0	7.5	5.5	40
15	12	3.0	8.0	5.0	6.0	6.5	4.5	40
16	15	3.0	8.0	5.0	6.0	7.0	5.5	50
17	18	3.0	8.5	5.0	7.0	6.5	5.5	45
18	18	2.5	8.5	5.0	7.5	7.5	6.0	40
19	18	3.0	8.5	5.5	8.0	8.0	5.5	55
20	24	3.5	9.0	5.5	8.5	8.5	6.5	60
21	24	3.5	9.0	5.5	8.5	8.5	6.5	60

TABLE III: CORRELATION BETWEEN SITE OF INSERTION OF MEDIAL RECTUS MUSCLES AND DEGREE OF ESOTROPIA IN ²¹ PATIENTS

*L, length; W, width; LIMB, site of insertion from limbus.

The origin of the inferior oblique muscle is attached to the periorbita adjacent to the bony opening of the nasolacrimal duct. This origin is muscular in the 38.2-mm embryo, becomes argyrophilic, and at term is attached to the perichondrium and later the periosteum via a tendon adjacent to the lacrimal fossa just posterior to the orbital margin.

The levator palpebrae superioris muscle, while playing no role in the movement of the eye, is embryologically and developmentally closely associated with the superior rectus muscle, and both muscles share a common epimysium.

Histologic Features in Development of Origins of Extraocular Muscles

The features of developing muscle⁸—early myoblast, myoblast, multinucleated myoblast, myotube (with longitudinal and cross-striations), and mature muscle cells—are not observed in developing tendons. At the proximal and distal ends of the extraocular muscles, mesenchymal cells contain minimal cytoplasm, become elongated, and are more compact than the cells of the muscle (36 mm).

Muscle endings are tapered, rounded, or split (Fig 4), with three forms

FIGURE 2 At annulus of Zinn (arrow), tendon (open arrow) fuses with cartilage (short arrow) at apex of orbit (2/72, 88.6 mm, Masson trichrome, \times 40).

EIGURE 3
Medical rectus muscle fuses with dura (*arrow*) of optic nerve (5/72, 70 mm, hematoxylin-eo-
sin, \times 9.0).

being found in any one muscle. Furthermore, in serial sections, what is interpreted as being tapered may in deeper sections be rounded or even split.

The distance between the muscle fibers and the tendon extending from the annulus of Zinn varies at different levels of section. The ends of muscle fibers in the center of the muscle are closer to the tendon of the annulus of Zinn than the more peripheral fibers.

Argyrophilic fibers form "caps" at the ends of muscle fibers where thickened fibers arise from the convex surface (Fig 5). These argyrophilic tissue caps are continuous with the endomysium that encases each muscle fiber. The argyrophilic cap and the loose connective tissue at the origin are first observed in the 36-mm embryo. In certain sections, muscle caps are derived from a thickening of the epimysium.

If the distance from the muscle fiber to the tendon of the annulus of Zinn is large, then the argyrophilic fibers thicken and these fibers become collagenous and lose the silver staining characteristics. If, however, the distance between the muscle and the tendon is short, these fibers may remain argyrophilic. Fine, argyrophilic fibril invaginations occur between the muscle fibers. These may be straight and slender, arrowhead, or spiral in shape. These projections are best observed in oblique sections of the musculotendinous junction. Occasional fibroblasts are seen within the dentate muscular extensions.

Myofibrils appear to end at the end of the muscle fibers and do not extend beyond it. The myofibrils with conical ends do not converge toward the center of the cone.

The cross-striations and subsarcolemmal nuclei extend as far as the end of the muscle fiber or end at a varying distance from it.

Internal nuclei, characteristic of embryonic muscle, are located between muscle fibers. In mature extraocular muscle, occasional internal nuclei are present at the origin, particularly if the muscle fibers are split.

If muscle is sectioned in the line of the long axis of the muscle, muscle fibers appear to be continuous rectilinearly with the tendon. Depending on the direction of the section, the angle with which the muscle meets the tendon is either acute or obtruse.

The mature tendon (165 mm) is composed of thick, closely packed parallel collagen bundles with distinct longitudinal striations that in crosssection appear as fine dots. The tendons are devoid of elastic fibers. Few fine capillaries are found in the epitenon.

General Disposition of Insertions of Extraocular Muscles

The tendinous insertions of the extraocular muscles are not identifiable before ⁸⁰ mm because of their gelatinous nature. Up to ⁵⁴ mm, the

Muscle fibers at sites of origin may be tapered (medical rectus, *arrow*), rounded (superior rectus, *double arrow*), or split (lateral rectus, *small arrow*) (82 mm, 36/72, Masson trichrome, \times 2.5).

EIGURE 5
 Argyrophilic fibers form "cap" at end of muscle fibers with thickened fibers arising from convex surface (*arrow***). Note annulus of Zinn (***open arrow***) (2/72, 88.6 mm, Bodian's silver nitrate,** \times **104).**

tendons are indistinguishable microscopically from the developing episclera and sclera; only after ¹⁶⁵ mm are they macroscopically identifiable as tendons and their sites of insertion can be measured with any accuracy (Table I). Up to 210 mm, the rectus muscle insertions are found to be equidistant from the limbus. At term, however, the insertions of the rectus muscles vary in shape and site of insertion. A continuous line joining the sites of insertion of the rectus muscles is called the spiral of Tillaux. 10

Histologic Features in Development of Insertions of Extraocular Muscles

The tendons of insertion and the muscular portion of the extraocular muscles develop simultaneously. For a more lucid comprehension of the development of the tendinous insertions, it is necessary to understand the morphogenesis of the corneoscleral area.

In 13.6- and 28.2-mm embryos, the corneal stroma and sclera merge imperceptibly and cannot be differentiated microscopically. From the 13.6- to the 22.0-mm stage of development, fibroblasts in the region of insertion of the recti muscles become elongated and closely packed together. The cytoplasm is pale and basophilic. Processes that extend from the cytoplasm in a stellate fashion are less basophilic staining. The nuclei are oval and contain fine chromatin and observable nucleoli. As these elongated cells mature, less and less cytoplasm is demonstrable, the nuclei become flattened and oval, and fibrocytes develop. Collagen fibrils, which develop between the fibroblasts and fibrocytes, become orientated in the long axis of the future tendon.

In the 26-mm specimen, at the anatomic site of the future limbus, there is a condensation of mesenchymal tissue that is orientated at right angles to the cornea and sclera. The adjacent scleral region is divided into two distinct areas, a superficial spongy area and a deep, more compact area. The spongy area is the location of the future episclera, while the more compact area is destined to become the sclera.

In the 36-mm embryo, sclera is distinguishable from the cornea. The characteristic corkscrew-like appearance of the immature collagen of the scleral fibers is different from that of the corneal stromal fibers, which are regularly disposed and orientated in the long axis of the cornea. In the 38.2-mm embryo, there is a condensation of mesenchymal tissue on both the outer and inner surfaces of the sclera. The outer mesenchymal cells mature to become fibroblasts which in turn form the tendon of the rectus muscle (Fig 6). The undulating tendon extends anteriorly and terminates at a dimple where the corneal epithelium merges with the conjunctival epithelium (Figs 7 and 8). The superficial and deep scleral condensations noted in the 38.2-mm embryo are more accentuated in the 54-mm em-

bryo. In the 78-mm embryo, the demarcation line between the corneal stroma and the sclera is more discernible and the distinct dimpling in the epithelium (vide supra) is less noticeable.

The merging of the tendon with the sclera differs slightly from that noted at the origin. Muscle fibers become attenuated and taper toward the tendon. Distinct argyrophilic caps are not observed at the insertional ends of the muscles. A distinct dividing line is not observed between the muscle and the tendon, but rather a gradual merging and blending of the two tissues occur.

While fine attenuated argyrophilic fibrils are present between the muscle fibers, distinct argyrophilic connecting tissue between muscle and aponeurosis (as observed at the origin) is not seen. Cross-striations may be present up to the end of the muscle fiber or terminate some distance from it.

Subsarcolemmal nuclei extend as far as the end of the muscle fiber, stopping short of the muscle end, and no internal nuclei are discernible.

The collagenous fibers of the tendon intertwine, interweave (Fig 9), and interlock with the scleral fibers. Superficial fibers extend more distally than do the deeper fibers, thus giving a wider and more extensive surface area of attachment.

Until late in development (210 mm), the tendinous insertions of the rectus muscles have wide attachments to the sclera. These areas of attachment extend from the equator of the eye to the limbus (Fig 10).

As the eve increases in size, there is posterior recession of the anterior attachment of the tendon and, concurrently, differential degeneration of the tissue between the tendon and the sclera. This degenerative process, which commences at the equator and extends anteriorly, is characterized by vacuolation, absence of nuclei, and less intense staining with hematoxylin-eosin and Masson trichrome.

In the full-term fetus the tendons are located between the adult site of insertion and the limbus. Mature (full-term) tendons of insertion of the rectus muscles and of the superior oblique muscle are made up of tendinous fascicles, hexagonal in cross section, and consisting of closely packed collagen fibers. These collagen fibers have been produced by fibroblastic tendon cells that remain closely attached. The fascicles are bound together by connective interfascicular tissue (endotenon), which is continuous with the perimysium of the muscle and the periosteum of the bone.

The closely packed collagen bundles are tightly bound together, lie parallel to one another, and show distinct longitudinal striations.

Applied to the collagen fibers are the tendon cells (fibroblasts) that produce them. These stellate-shaped fibroblasts occur in rows, are situ-

FIGURE 6 Fibroblasts form tendon (arrow) in developing sclera (7/72, 165 mm, hematoxylin-eosin, \times 40).

ated in spaces between the bundles, and contain oval nuclei with indistinct cytoplasm. The cells appear to be connected end-to-end, with extensions from the cells passing between the spaces of the tendon. The tendon is surrounded by either a synovial sheath or loose areolar tissue (paratenon).

After 18 months of age, the flat rectus muscles are attached to the sclera by way of sheets of fascia. With light microscopy, the precise site where the myofibrils lose their striations and become tendinous cannot be demonstrated, because not all sections-of each field are in the same optical plane. It is therefore difficult to show photographically that myofibrils follow directly into tendon fibrils. For this transition to be apparent, it is essential to have thin sections, to focus accurately, and to examine sections where there is no superimposition of the tendon fibrils over the muscle fibers.

Distal Tendon of Superior Oblique Muscle¹¹

The trochlea and tendon of the superior oblique muscle are derived from mesenchymal tissue located in the superomedial aspect of the orbit and are initially indistinguishable. In the 26-mm embryo, the trochlea be-

 $\begin{tabular}{l} \bf FIGURE~7 \\ \bf Medical\textbf{ rectus} tendon\textbf{ extends to limbus}\ (arrow)\ (19/72,\ 26.1\textbf{ mm},\textbf{ hematoxylin-eosin},\ \times \\ \textbf{15).} \end{tabular}$

FIGURE 8 Tendon of medial rectus muscle causing dimpling (arrow) of epithelium at limbus (19/72,
26.1 mm, hematoxylin-eosin, \times 120).

FIGURE 9 Collagenous fibers intertwine, interweave (arrow), and interlock with scleral fibers (36/73, 82.2 mm, Masson trichrome, \times 120).

FIGURE 10 Tendons of insertion of medial (short arrow) and lateral (long arrow) rectus muscles insert from limbus to equator of eye $(2/72, 88.6$ mm, hematoxylin-eosin, \times 12).

comes semilunar while the cells of the tendon are elongated and closely packed.

In the region of the trochlea, the mesenchymal cells become rounded (30-mm embryo) and their cytoplasmic processes are retracted. These chondroblasts lie in amorphous intercellular substance. Chondrocytes are noted in lacunae in the 83-mm embryo, and cell nests develop in the 210-mm fetus.

By the 26-mm stage of development, the mesenchymal cells in the region of the tendon become elongated and closely packed. The nuclei become ovoid and darkly basophilic staining. As the tendon traverses the trochlea, it is rounded and the cells are so closely packed that no intervening cytoplasm is present. Distal to the trochlea the tendon fans out. The cells in this location remain elongated and are not closely packed, and a distinct rim of cytoplasm is present. The tendon distal to the trochlea becomes a flattened aponeurosis that fuses and interdigitates with the scleral fibers.

Differential degeneration occurs between the developing tendon and the trochlea. In the 59.5-mm embryo, the mesenchymal cells in this region become vacuolated, their cell walls and nuclei break down, and spaces filled with lightly staining eosinophilic material are present. In the 83-mm embryo, numerous well-defined septae extend from the trochlea to the tendon (Figs 11 and 12). In the 210-mm fetus, these septae are less numerous and also are attenuated. Fine septae are located between the tendon and the trochlea in the term fetus; in the adult, septae are also present, but are fewer in number, between the capsule and the tendon just proximal and distal to the trochlea.

At term, the superior oblique muscle inserts as a flattened tendon into the superolateral and posterior aspect of the eye.

Insertion of Inferior Oblique Muscle

The distal end of the inferior oblique muscle is first observed in the 22-mm embryo. The insertion is muscular and fuses directly with the sclera. At the site of insertion, all the stages of muscle development (ie, myoblast, multinucleated myoblast, myotube, and mature muscle cell) are observed.⁸ No distinction can be made between muscle formation in the belly and muscle formation at the insertion of the inferior oblique muscle. No tendinous fibers are detected at the site of insertion of the muscle.

The muscle approaches the sclera tangentially. The superficial fibers extend beyond that of the deeper fibers, widening the area of insertion. The shapes of the ends of the muscle fibers are tapered, rounded, or split. Neither argyrophilic fibers nor argyrophilic caps are present at the ends of the muscle fibers. Cross-striations extend as far as the end of the muscle fibers to the scleral insertion.

At term, the inferior oblique muscle inserts via muscular fibers at the inferolateral and posterior aspect of the globe over the region of the macula.

Connective Tissue of Extraocular Muscles

Development of the connective tissue is inextricably associated with development of the extraocular muscles and their tendons. Up to 36 mm, the individual muscle cells are surrounded by mucopolysaccharide staining material and stellate mesenchymal cells. By 54 mm, argyrophilic fibrils are present between the muscle cells, to be replaced by fibroblasts at about the 80-mm stage of development. Mature connective tissue is present at about ¹²⁰ mm both within and surrounding the muscle.

The intramuscular connective tissue fibers (internal perimysium) are uniformly distributed and consist of fine argyrophilic and elastin fibers. There is minimal mucopolysaccharide staining material in the intramuscular connective tissue by 225 mm. This tissue merges with the capsule or sheath (external perimysium or epimysium) of the extraocular muscles.

FIGURE 11 Mesenchymal remnants: trabeculae (long arrow) between superior oblique tendon and trochlea (short arrow) (33/73, 59.5 mm, Masson trichrome, \times 15).

FIGURE 12 Fine trabeculae (*arrow*) are present between superior oblique tendon (Te) and trochlea (Tr) $(33/73, 59.5 \text{ mm}, \text{Masson trichrome}, \times 650).$

Tenon's capsule (fascia bulbi) is composed of fine connective tissue that encompasses the eye. Anteriorly it extends from the limbus, where it fuses with the conjunctiva and sclera. Posteriorly it fuses with the dura of the optic nerve and merges with the connective tissue of the orbital fat. Tenon's capsule is penetrated posteriorly by the rectus muscles in relation to the equator of the eye. These muscles are surrounded by an extension of the capsule. Falciform fascial folds extend from each rectus muscle to the adjacent Tenon's capsule and also attach to the sclera. These fine attachments between the muscles and the sclera are termed "footplates."

The anterior two thirds of the rectus muscles are surrounded by relatively thick sheaths, which become continuous at the intermuscular septum. From the sites where the medial and lateral rectus muscles pierce Tenon's capsule, thickened parts of their capsules form check ligaments by attaching to the tubercle of the Zygomatic bone (lateral rectus muscle) and to the lacrimal crest (medial rectus muscle). ¹²

DISCUSSION

MESENCHYMAL/MESECTODERMAL ORIGIN OF TENDONS OF EXTRAOCULAR MUSCLES Some investigators 13,14 maintain that only vascular endothelium and the extraocular muscles are derived from mesenchymal tissue and that the remaining connective tissue of the eye arises from neural crest tissue. Mesectoderm is therefore a more accurate term for the cellular origin of the connective tissue of the eye other than the endothelium and the extraocular muscles.^{13,14}

On the basis of the present investigation, it is not possible to determine whether the tendons of origin and insertion of the extraocular muscles are derived from mesenchymal tissue or from mesectodermal tissue.

The close continuity of the muscle fiber ends with the connective tissue of the tendons favors a derivation from mesenchymal tissue similar to that of the extraocular muscles. Other features indicating the close embryologic relationship between extraocular muscle and tendon development are the interdigitations of the tendon fibers with those of the extraocular muscle, the presence of muscle nuclei between adjacent tendon fibers, and the observation that the endomysium, perimysium, and epimysium of the extraocular muscles converge, fuse, and thicken to become modified as tendons.

DERIVATION OF EXTRAOCULAR MUSCLES AND TENDONS FROM SUPERIOR AND INFERIOR MESENCHYMAL COMPLEXES

Previous investigations¹⁵⁻²² have suggested that extraocular muscles and their tendons arise from muscle plates, which surround the head cavities, and that these muscle primordia migrate forward into the orbits. It is contended that groups of these muscles "grow" toward their ultimate destination. 19-22 If the migratory theory were correct, then the anlage of the extraocular muscles would first be observed at the posterior aspect of the orbit and later on in development be recognizable anteriorly. In this investigation, the tendons of origin and insertion, as well as the belly of the extraocular muscles, were found to develop at the same time. The previous misconception concerning the origin of the extraocular muscles and their tendons most likely arose because histologic sections were examined individually rather than serially in embryos and fetuses.⁸

The extraocular muscles and their tendons appear to be derived from a superior and an inferior mesenchymal complex (Fig 13). This theory is supported by the following findings.

1. Superior mesenchymal complex (Figs 14 and 15).8 The superior oblique, superior rectus, and levator palpebrae superioris muscles and their tendons are derived from the superior complex. This is evidenced by the insertions of these muscles in a familiar lamellar fashion at the level of the eye anteriorly, and furthermore, their lateral limits coincide. These tendons of insertion are surrounded by ^a common epimysium early on in development. This is particularly well seen up to the 54-mm embryo. The close developmental relationship of the levator palpebrae superioris and superior rectus muscles is observed in the clinical condition of congenital ptosis, where there may be associated underaction of the superior rectus muscle.

The origin of the superior oblique muscle is in close proximity and abuts against that of the superior rectus and levator palpebrae superioris muscles. In addition, distinct extensions of condensed mesenchymal tissue, which arise from the epimysium surrounding the superior rectus and levator palpebrae superioris muscles, extend to attach to the trochlea of the superior oblique muscle. Finally, in favor of a superior mesenchymal complex is the similar motor nerve supply (ie, the superior branch of the oculomotor nerve to the superior rectus and levator palpebrae superioris muscles).

2. Inferior mesenchymal complex (Figs 14 and 15).⁸ The inferior rectus muscle and tendon and the inferior oblique muscle develop from the inferior mesenchymal complex. The inferior oblique muscle sequestrates from the inferior rectus muscle at the 80-mm stage of development but retains distinct attachments to the inferior rectus muscle. The respective

FIGURE 14

Tendons at apex of orbit. Levator palpebrae superioris (LPS), superior rectus (SR), superior oblique (SO), part of lateral rectus (LR), and part of medial rectus (MR) tendons arise from superior mesenchymal complex; inferior rectus (IR), part of medial rectus (MR), and part of lateral rectus (LR) tendons arise from inferior mesenchymal complex.

FIGURE 15

Tendons at anterior aspect of orbit at level of their insertions. Levator palpebrae superioris (LPS), superior rectus (SR), superior oblique (SO), part of lateral rectus (LR), and part of medial rectus (MR) tendons arise from superior mesenchymal complex. Inferior rectus (IR), part of medial rectus (MR), part of lateral rectus (LR) tendons, and muscular insertion of inferior oblique (10) muscle arise from inferior mesenchymal complex.

epimysia fuse at the site of crossing.

3. Lateral rectus muscle and tendon. The origin of the lateral rectus muscle straddles the superior orbital fissure. The superior limb of origin is derived from the superior mesenchymal complex and has a continuous origin with the superior rectus muscle. The inferior limb arises from the inferior complex, and its tendon of origin is continuous with that of the inferior complex.

4. Medial rectus muscle and tendon. The origin of the medial rectus muscle is continuous with that of the inferior rectus muscle (inferior complex) and the superior rectus muscle (superior complex).

The origins of the lateral and medial rectus muscles from the superior and inferior mesodermal complexes do not detract from the basic concept concerning the derivation of the extraocular muscles. These horizontally acting muscles arise from the boundary zone and thus have a dual origin from both complexes. Furthermore, the lateral rectus muscle has a bifid origin because of the development of the superior orbital fissure.

VARIABILITY OF INSERTIONS OF RECTUS MUSCLES

The accepted length and width of the tendons of the rectus muscles and the sites of insertion of these muscles from the limbus vary with different investigators (Table IV). These measurements appear to have been based on investigations done between $1884¹$ and $1913⁵$ and sometimes have been based either on tissues fixed in preservative or on the extraocular muscles of cadaveric eyes. Furthermore, these investigations do not describe the precise methods of measurement or the anatomic definition of the insertions of these muscles.

Weiss³ described measurements of the sites of insertion of the rectus muscle tendons in infants but did not describe the precise method of measurement or the technique of assessing the size of the eye and the age of the fetus and infant. Mühlendyck²⁹ assessed the progressive growth of the eye and rectus muscles based on measurements of the adult³⁰ and the $\sin \theta$ ³¹ eve. Both Volkmann³⁰ and Schneller³¹ were imprecise and vague as to their methodology of measuring the sites of insertion and the size of the eyes.

In this investigation, no distinct dividing line was found between the muscle and the tendon; the fibrous tissue of the tendon extends into the muscle, while muscle cells can be found between the tendon fibers exending even to the insertion. This dovetailing results in a tenon-andmortise blending of two different tissues, which while adding to its strength, makes measurement of the length of the tendons of the rectus muscles difficult and imprecise (Fig 16).

Up to 165 mm, the anterior borders of the tendon are ill-defined because the tendon imperceptibly merges with scleral tissue. Furthermore, the thickened Tenon's fascia and check ligaments mask the tendons' margins. For these reasons, the lengths and widths of the tendinous insertions cannot be accurately measured up to ¹⁶⁵ mm (Table I).

In the 67 patients with esotropia (Tables II and III), no abnormal adhesions between the tendons of the medial and lateral recti and the sclera were noted. No thickening of Tenon's capsule in relation to the tendons and no unusual muscular slips were observed.

TRANSMISSION OF FORCE OF CONTRACTING MYOFIBRILS TO TENDON

The manner by which the force of contracting myofibrils is transmitted to tendon in skeletal muscle has been disputed. $32,33$

Goss³⁴ maintained that the myofibrils were attached to the inner surface of the sarcolemma at the end of the muscle fiber, while Carr, 35 Butcher, 36 and Speidel 37 contended that myofibrils were continuous with the tendon fibrils. Schultze³⁸ suggested that there were perforations in

the sarcolemma at the end of the muscle and that the myofibrils joined the tendon fibers through these perforations. Muir³⁹ found that the collagen of the tendon invaginated the sarcolemma of the muscle.

Barer⁴⁰ did not detect any connection between muscle fibers and the sarcolemma by electron microscopy and believed that the sarcolemma was not continuous with the tendon fibrils and that the transmission of the contractile force from the myofibrils to the sarcolemma was by frictional force between these two elements.

Long⁴¹ maintained that in the rat tail there was no continuity between the tendon and the muscle fiber. The muscle fiber was contained within the sarcolemmal envelope to which the muscle fibers were attached. Reticular fibers extended from this envelope to attach to the tendon. However, there was no substantial evidence that either the muscle substance or the contractile elements of the muscle were continuous with the sarcolemma.

Porter⁴² investigated with use of the electron microscope the junction between the muscle cell and the tendon in the cordal myotome of amblyostoma larvae. The muscle fiber was encased in a plasma membrane, which in turn was surrounded by sarcolemma. The latter was made up of an inner nonfibrous layer and an outer fibrous membrane. The fibrous membrane of each muscle fiber, which fused to form the tendon, was very slender, did not have the periodicity of collagen, and was not continuous with the myofibrils or other intracellular fibers. Some myofibrils ended short of the muscle cell.

Mair and Tome⁴³ noted at the myotendinous junction that fine filaments connected the collagen of the tendon with the basement membrane of the muscle. The muscle interdigitated with the collagen fibers, and the plasma membrane was thickened at the myotendinous junction. In teased preparations of muscle, individual muscle fibers were observed to pass from one tendon to another (intratendinous), to end at one extremity, or to do both, within the muscle fasciculus (intrafascicular). The intratendinous muscle fibers had a rounded or cone-shaped termination, while the intrafascicular muscle fibers ended in a thread-like extremity.

In dealing with the morphology and the transmission of force of contracting myofibrils to the tendon, these previous investigators $32-43$ have only examined individual histologic and electron microscopic specimens of the myotendinous junction. It is concluded from this investigation that for a more accurate understanding, serial sections of this area are necessary as well as different histologic staining methods, particularly hematoxylin-eosin, Masson trichrome, Verhoeffs-Van Gieson elastic, and Bodian silver nitrate stains.

FIGURE 16

Interlocking of muscular and tendinous fibers of lateral, superior, and medial (arrow) rectus muscles at apex of orbit. Inset, Tenon-and-mortise joint showing tendon (T) and muscle (m) (10/72, 83 mm, Masson trichrome, \times 150).

'L, length; W, width; LIMB, site of insertion from limbus.

In the present investigation, it is observed that if the muscle and tendon are sectioned in the line of their long axes, then the muscle fibers appear to be continuous rectilinearly with the tendon.

Prior to 80 mm, the argyrophilic tisue, which forms ^a cap at the end of the muscle fibers, is located between them and the tendon. With maturation (fetus about 120 mm), the argyrophilic tissue becomes collagenous and then fibrous tisue. The force of contracting myofibrils is transmitted to the tendon by way of these fibrous tissue caps at the origin and insertion of the extraocular muscles (except for the muscular insertion of the inferior oblique muscle). Where the distance from the muscle fiber to the tendon is large, the fibrous tissue thickens and forms projections, to which the muscle fibers attach and via which their contracting force is transmitted to the tendon.

CLINICAL SIGNIFICANCE OF DEVELOPMENT OF TENDONS OF ORIGIN OF EXTRAOCULAR MUSCLES

The interdigitation of the tendinous and muscular fibers is first observed in the 36-mm embryo, when there are cap-like argyrophilic fibers present at the distal end of the individual muscle cells (Fig 5). As the fetus matures to ¹²⁰ mm these argyrophilic fibrils become interdigitating fibrous tisue (Fig 16).

While early on in development argyrophilic fibrils can be differentiated from the perichondrium at the apex of the orbit, as the cartilage matures to become bone (210 mm), so the periosteum thickens at the annulus of Zinn and the tendons of origin merge at this site with the periosteum. Their sites of purchase, while anatomically being localized, are in effect more extensive because the annulus of Zinn is continuous with the periosteum at the apex of the orbit. A further added site of purchase for the annulus of Zinn is at the bifid origin of the lateral rectus muscle. The tenon-and-mortise-like origin (Fig 16) of the extraocular muscles at the apex of the orbit is unique in its strength and, in addition, allows for mobility in all directions of extreme gaze.

These strong origins prevent avulsion of the muscles at the orbital apex when significant traction is applied during strabismus and retinal surgery. Furthermore, laceration of the extraocular muscles at their origins is extremely rare following significant trauma to the orbit that may be severe enough to result in avulsion of the optic nerve or even in severe fractures of the orbit.

A characteristic feature of thyroid myopathy is lymphocytic and mucopolysaccharide infiltration of the extraocular muscles, particularly the medial and inferior rectus muscles.⁴⁴⁻⁴⁶ This infiltrative process involves

the muscles and not the tendons. Because of the interdigitating peculiarities of the muscular and tendinous fibers at the origin of the rectus muscles, and further because of the presence of individual muscle cells between the tendons, this infiltrative process extends right up to the annulus of Zinn. Thus, in thyroid myopathy with thickening of the muscles, compression of the optic nerve may occur at the orbital apex. 44-50

A further feature of clinical importance with reference to the origins of the extraocular muscles is the attachment of the medial and superior rectus muscles to the dura of the optic nerve (Figs 3 and 17). This is observed as early as 68.5 mm. The clinical significance of this observation is that with optic neuritis, pain occurs with ocular movements, particularly when the superior and medial rectus muscles contract on the inflamed dura of the optic nerve.

CLINICAL SIGNIFICANCE OF DEVELOPMENT OF TENDONS OF INSERTION OF RECTUS AND SUPERIOR OBLIQUE MUSCLES

The tendinous insertions of the extraocular muscles develop by a process of organization and maturation of mesodermal tissue and also by a process of degenerative differentiation of this tissue. Clinical conditions that illus-

FIGURE 17 Medical rectus muscle fuses (arrow) with dura of optic nerve (20/72, 68.5 mm, hematoxylineosin, \times 30).

trate these processes are the superior oblique tendon sheath syndrome, ptosis associated with underaction of the superior rectus muscle, and the varying locations of the sites of insertion of the medial and lateral rectus muscles during different phases of maturation.

Superior Oblique Tendon Sheath Syndrome (Brown's Syndrome)51

Different theories have been postulated for the cause of the superior oblique tendon sheath syndrome (Brown's syndrome) (Table V).

In this investigation, 11,57 in the embryo up to 22 mm, the cellular structure of the trochlea and the superior oblique tendon were indistinguishable. With further development and maturation, the tendon and trochlea became discernible as separate structures (78 mm). Well-defined trabeculae extend from the trochlea to the tendon, and these persist up to the 225-mm fetus (Figs 11 and 12). Thereafter, selective degeneration occurs within these trabeculae and eventually only fine remnants or "adhesions" remain. At term, these trabeculae are noted for a short distance on either side of the trochlea between the superior oblique tendon and its sheath. These fine trabeculae between the tendon and the trochlea persist into adulthood and most likely act as tethering strands to control and limit the excursions of the tendon in the trochlea.

Persistence of thickened embryologic anlage of these trabeculae could account for the superior oblique tendon sheath syndrome.^{11,57}

Ptosis and Superior Rectus Muscle Underaction⁵⁸

The association of ptosis and superior rectus muscle underaction has been described by Anderson and Baumgartner⁵⁹ and Burke⁶⁰ and has been observed in 25% of patients with unilateral ptosis and in 62.5% of patients with bilateral ptosis.⁵⁸

During embryologic development both the superior rectus and levator palpebrae superioris muscles evolve from the superior mesenchymal complex, where minimal mesenchymal tissue separates the two muscles⁵⁸ (Fig 18). Throughout embryologic and fetal development, these two muscles have ^a common epimysium, which is rather thick and well demarcated early on in development (70 mm) but gradually thins out with maturation (225 mm).

Clinical observations have defined the presence of thickened and dense fibrous tissue, which is often found between the superior rectus and levator palpebrae superioris muscles and their respective tendons during the dissection for surgical repair of congenital ptosis. 59,60 Based on investigation of the development of the superior rectus and levator palpebrae superioris muscles and the clinical observation, in some cases of ptosis, of thickened fibrous tissue between the two muscles, it is suggested that in

FIGURE 18

Early on in development, superior rectus (SR) and levator palpebrae superioris (LPS) muscles and tendons share common epimysium and epitenon, and abundant mesenchymal tissue lies between these two tendons. SO, superior oblique tendon (68/74, 210 mm, hematoxylin-eosin, \times 50).

ptosis and associated underaction of the superior rectus muscle, separation of the two muscles is inadequate and fibrous tissue persists with incomplete atrophy of the intervening mesenchymal tissue.

Role of Insertion of Medial Rectus Muscle in Congenital Esotropia

A wide variety of theories exist concerning the cause of concomitant strabismus. These theories are broadly divided into sensorimotor and anatomic or mechanical.

Sensorimotor theories include abnormalities of the fusional mechanism, 61 abnormal reflex responses, 62 defective optomotor reflexes, $63, 64$ and aversion to bifoveal stimulation.⁶⁵ Donders⁶⁶ emphasized the role of accommodation and refraction in concomitant strabismus, while Snellen⁶⁷ maintained that nonaccommodative heterotropia was paralytic in origin. Parinaud⁶⁸ suggested that the mechanism lay in the vergence system.

Mechanical or muscular theories $69-73$ include abnormalities in the structure, length, size, and elasticity, anomalies of insertion, and structural abnormalities of the orbit. Scobee⁷⁰ noted thickening and posterior extension of the check ligaments as well as extra muscle slips and footplates, which he suggested prevented muscular relaxation. Nordlow $69,71$ concluded that at the onset of esotropia, mechanical factors are present that produce the strabismus. Goldstein⁷³ found that the medial rectus muscle insertion was closer to the limbus in esotropia than in autopsy eyes.

The present investigation includes an embryologic evaluation of the insertions of the rectus muscles and their detailed histologic features. Furthermore, the sites of insertion from the limbus of the rectus muscles were measured in eight fetuses (Table I). Finally, the sites of insertion from the limbus of the medial and lateral recti were ascertained at different ages (6 months to 3 years) in patients with congenital esotropia.

Embryologic Development of Tendinous Insertions of Rectus Muscles

The tendons of the rectus muscles are first observed as undulating (Fig 9) compressed mesenchymal tissue that passes between the developing episclera and the sclera (38.2 mm). These tendons terminate at a dimple (Fig 8) in the epithelium at the developing limbus where the cornea, with its regularly arranged fibers, abuts against the tortuous scleral fibers. It is unlikely that the dimpling effect is due to contraction of the rectus muscles, as longitudinal striations are not observed in the developing muscle at this early stage of development.⁸ The distinct dimpling effect of the epithelium is most likely due to differential accelerated growth of the cornea relative to the slow growth of the sclera and rectus muscles. As the corneal diameter enlarges and the tendon recedes posteriorly, the dimpling of the corneal epithelium becomes less overt (78 mm).

During the development of tendons of the rectus muscles, differential degeneration occurs between the tendons and the episclera superficially and between the tendon and the underlying sclera (Fig 10). The superficial selective degenerative process occurs in an anteroposterior direction, while the deep degenerative process occurs in a posteroanterior direction (Fig 19). At the same time, the anterior segment of the eye, particularly the cornea, enlarges. By these well-orchestrated processes of selective degeneration and ocular growth, the insertions of the medial rectus muscles are located at their accepted adult sites of insertion.

Up to the 210-mm stage of development, the tendinous insertions of the rectus muscles are equidistant from the limbus. Only about at term do these distances vary, accounting for the formation of the spiral of Tillaux.10 The latter is a line joining the sites of insertion of the rectus muscles, which are not equidistant from the limbus.

Measurement of Tendinous Insertions of Rectus Muscles in Fetuses

In the eight fetuses examined (Table I), which ranged in size from 165 mm to term, it was observed that the tendons are (macroscopically) not

Diagrammatic representation of development of rectus muscle insertions. A: Posterior recession of anterior attachment from limbus. B: Differential degeneration of tissue between developing tendon from sclera.

precisely discernible. Therefore, the measurement of tendon lengths and breadths is only approximate. Furthermore, the sites of insertion prior to ¹⁶⁵ mm are indistinct, as the tendons fuse imperceptibly with the sclera. In the 165-mm fetus, the insertion is approximately ³ mm from the limbus. From ²¹⁰ mm until term, the distance of the tendon insertion from the limbus varies from approximately ³ to 3.5 mm (Table I).

Measurenent of Tendinous Insertions of Medial Rectus Muscles in Esotropia

Two series of congenital esotropia were assessed. In one, both medial recti were recessed (Table II), and in the other, a recession of the medial rectus muscle and a resection of the lateral rectus muscle were performed (Table III). In both series, the medial and lateral recti insertions gradually receded from the limbus with maturation and only attained their adult locations between 18 months and 2 years of age.

It therefore behooves the strabismologist during corrective surgery to measure the amount of recession or resection from the limbus rather than from the insertion site, particularly in patients under 18 months of age.

In this investigation, no correlation was observed between the site of insertion of the medial rectus muscle and the degree of esotropia (Tables II and III). In addition, no abnormal adhesions between the tendons of the medial and lateral recti and the underlying sclera were noted. Tenon's

522

capsule was not thickened at these tendons, and aberrant muscular slips from these respective muscles were not observed.

SUMMARY AND CONCLUSIONS

The tendinous origins and insertions of the extraocular muscles were studied embryologically by macroscopic and microscopic methods. It is concluded from this investigation that these tendons of origin and insertion arise from mesenchymal tissue similar to that of their respective muscles. These tendon-muscle groups have developed from superior and inferior mesenchymal complexes.

The origins of the extraocular muscles are attached to the periorbita by an interlocking of the tendinous and muscular fibers, which allows for mobility of the extraocular muscles in all extreme directions of gaze and also results in a strong mechanical mooring for these muscles. Avulsion at the origins of the extraocular muscles following severe traction or trauma is rare. The additional origin of the superior and medial rectus muscles to the dura of the optic nerve explains the pain that may occur on movement of the eye in optic neuritis. Optic nerve compression and thyroid myopathy is explained by mucopolysaccharide and inflammatory cell infiltration of the muscular interdigitations that extend up to the site of origin of the rectus muscles.

Findings of this investigation suggest that the association of ptosis and superior rectus muscle underaction may be due to a persistence of fibrous tissue that has endured from embryologic development between the superior rectus and levator palpebrae superioris muscles. Superior oblique tendon sheath syndrome is explained by embryologic strands remaining between the tendon of the superior oblique muscle and the trochlea.

The insertions of the rectus muscles extend from the equator of the eye to the limbus early on in development. By processes of differential degeneration between the sclera and the rectus tendon, posterior recession of the tendon from the limbus, and contemporaneous growth of the anterior segment of the eye, these tendons reach their adult location only between the ages of 18 months and 2 years. In strabismus surgery, measurements for muscle adjustments should be assessed from the limbus rather than from the sites of insertion of these tendons.

In the series of patients with esotropia, no mechanical abnormalities were noted in relationship to the insertions of the medial or lateral recti muscles. Furthermore, no correlation was found between the site of insertion of the medial rectus muscle and the degree of esotropia.

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REFERENCES

- 1. Fuchs E: Beitrage zur normalen Anatomie des Augenapfels. Albrecht Von Graefes Arch Klin Exp Ophthalmol 1884; 30(4):1-60.
- 2. Merkel H: Handbuch der Topographischen Anatomie, ed 2. Brauschweig, F Vieweg & Sohn, 1885-1890, vol 1, pp 291-293.
- 3. Weiss L: Uber das Verhalten des M. rectus externus und rectus internus bei wachsen der Divergenz der Orbita. Arch Augenheilkd 1894; 29:298-323.
- 4. Whitnall SE: The Anatomy of the Human Orbit. London, Oxford Medical Publications, 1904.
- 5. Hesser C: Der Bindegewebsapparat und die glatte Muskulatur der Orbita beim Menschen im normalen Zustande. Anatomische Heft 1913; 49:1-302.
- 6. Arey LB: Developmental Anatomy. Philadelphia, WB Saunders, 1942, pp 129-133.
- 7. Tuchmann-du Plessis H, David G, Haegel P: Embryogenesis Illustrated Human Embryology. London, Chapman & Hall, 1972, pp 88-91.
- 8. Sevel D: A reappraisal of the origin of human extraocular muscles. Ophthalmology 1981; 88:1330-1338.
9. — : Developme
- 9. : Development of the nerves of the extraocular muscles, in RD Reinecke (ed): Strabismus II. New York, Grune & Stratton, 1984, pp 645-657.
- 10. Tillaux P: Traite d'Anatomie Topographique. Paris, Asselin et Houzeau, 1890.
- 11. Sevel D: Brown's syndome: A possible etiology explained embryologically. Ophthalmology 1981; 18:26-31.
- 12. Eggers HM: Functional anatomy of the extraocular muscles, in F Jakobiec (ed): Ocular Anatomy, Embryology and Teratology. Philadelphia, Harper & Row, 1982, pp 783-791.
- 13. Ozanics V, Jakobiec FA: Prenatal development of the eye and its adnexa, in F Jakobiec (ed): Ocular Anatomy, Embryology and Teratology. Philadelphia, Harper & Row, 1982, pp 11-96.
- 14. Le Lievre C, Le Douarin N: Mesenchymal derivatives in the neural crest: Analysis of chimaeric quail and chick embryos. J Embryol Exp Morphol 1975; 34:125-154.
- 15. Gilbert PW: The origin and development of the human extrinsic ocular muscle. Contrib Embryol Carnegie Inst 1957; 36:59-78.
- 16. Iwasaki T: Studies on the initial growth of the extraocular muscles of Japanese. Acta Soc Ophthalmol Jpn 1958; 62:2584-2607.
- 17. Adams RD, Denny-Brown D, Pearson CM: Embryology and histology of skeletal muscle, in Diseases of Muscle. New York, Harper & Bros, 1962, pp 3-15.
- 18. Fink WH: The development of the extrinsic muscles of the eye. Am J Ophthalmol 1953; 36:10-23.
- 19. Gilbert PW: The origin and development of the head cavities in the human embryo. J *Morphol* 1952; 90:149-187.
20. — The premandibul
- ---: The premandibular head cavities in the opossum, didelphys virginiana. J Morphol 1954; 95:47-75.
- 21. Marshall AM: On the head cavities and associated nerves in Elasmobranchs. Q ^J Microbiol Sci 1881; 21:72-97.
- 22. Hewer EE: The development of muscle in the human foetus. J Anat 1928; 62:72-78.
- 23. Parks MM: Ocular Motility and Strabismus. New York, Harper & Row, 1975, ^p 4.
- 24. Harley DR: Strabismus, in RD Harley (ed): Pediatric Ophthalmology. Philadelphia, WB Saunders, 1983, ^p 209.
- 25. von Noorden G: von Noorden-Maumenee's Atlas of Strabismus. St Louis, CV Mosby, 1977, p 13.
- 26. Helveston EM: Atlas of Strabismus Surgery. St Louis, CV Mosby, 1977, pp 15-16.
- 27. Warwick R: Eugene Wolff's Anatomy of the Eye and Orbit. Philadelphia, WB Saunders, 1976, pp 254-267.
- 28. Moses RA: Adler's Physiology of the Eye. Clinical Application. St Louis, CV Mosby, 1975, pp 86-94.
- 29. Mühlendyck H: Wachstum und Länge der äusseren Augenmuskeln. Ber Dtsch Ophthalmol Ges 1978; 75:449-452.
- 30. Volkmann AW: Zur mechanik der Augenmuskeln. Ber Verh Konige Sachs Ges Wsch 1869; 20:28-69.
- 31. Schneller H: Anatomish-physiologische Untersuchungen uber die Augenmuskeln Neugeborener. Albrecht Von Graefes Arch Klin Exp Ophthalmol 1899; 41:178-226.
- 32. Henneman E, Olsen CB: Relations between structure and function in the design of skeletal muscles. J Neurophysiol 1965; 28:581-598.
- 33. Peace DC, Baker RF: The fine structure of the mammalian skeletal muscle. Am J Anat 1949; 84:175-195.
- 34. Goss CM: The attachment of the skeletal muscle fibers. Am ^J Anat 1944; 74:259-289.
- 35. Carr RW: Muscle—tendon attachment in the striated muscle of fetal pig. Am J Anat 1931; 49:1-42.
- 36. Butcher EO: The development of striated muscle and tendon from the caudal myotomes in the albino rat, and the significance of myotomic cell arrangement. Am J Anat 1933; 53:177-189.
- 37. Speidel CC: Studies of living muscle: Histological charges in single fibers of striated muscle during contraction and clotting. Am ^J Anat 1939; 65:471-529.
- 38. Schultze 0: Ueber den direkten Zusammenhang von Muskel fibrillen und Sehnenfibrillen. Arch Mikr Anat 1912; 79:307-331.
- 39. Muir AR: Observations on the attachment of myofibrils to the sarcolemma at the muscle-tendon junction, in JD Boyd, FR Johnson, SD Lever (eds): Electron Microscopy in Anatomy. New York, Academic Press, 1961.
- 40. Barer R: The structure of the striated muscle fiber. Biol Rev 1948; 23:159-200.
- 41. Long ME: Development of the muscle-tendon attachment in the rat. Am ^J Anat 1947; 81:159-198.
- 42. Porter KP: The myo-tendon junction in larval forms of Amblystoma punctatum. Anat Rec 1954; 118:342-368.
- 43. Mair WGP, Tome FMS: Normal striated muscle, in Atlas of the Ultrastructure of Diseases Human Muscle. New York, Longman (Churchill Livingstone), 1972, pp 1-11.
- 44. Trobe JD, Glaser JS, Laflamme P: Dysthyroid optic neuropathy: Clinical profile and rationale for management. Arch Ophthalmol 1978; 96:1199-1209.
- 45. Trobe JD: Optic nerve involvement in dysthyroidism. Ophthalmology 1981; 88:488-492.
- 46. Trokel SL, Jakobiec FA: Correlation of CT scanning and pathologic features of ophthalmic Graves' disease. Ophthalmology 1981; 88:553-564.
- 47. Hay ID: Clinical presentations of Graves' ophthalmopathy, in CA Gorman, RR Waller, JA Dyer (eds): The Eye and Orbit in Thyroid Disease. New York, Raven Press, 1984, pp 129-142.
- 48. Kennerdel JS, Rosenbaum AE, El-Hoshy M: Apical optic nerve compression of dysthyroid optic neuropathy on computed tomography. Arch Ophthalmol 1981; 99:807-809.
- 49. Naffziger HC: Pathologic changes in the orbit in progressive exophthalmos: With

special reference to alterations in the extraocular muscles and the optic disks. Arch Ophthalmol 1933; 91:1-6.

- 50. Sevel D: Extraocular muscles: Their development and peculiarities, in CA Gorman, RR Waller, JA Dyer (eds): The Eye and Orbit in Thyroid Disease. New York, Raven Press, 1984, pp 33-42.
- 51. Brown HW: Congenital structural muscle anomalies, in JH Allen (ed): Strabismus Ophthalmic Symposium. St Louis, CV Mosby, 1950, p 205.
- 52. Stein HJ, Papst W: Electromyographische Untersuchungen zur Pathogenese und Therapie des musculus obliquus-superior-sehnenscheidensyndroms (Brownsyndrome). Ber Dtsch Ophthalmol Ges 1968; 69:618-624.
- 53. Sanford-Smith JH: Intermittent superior oblique tendon sheath syndrome. Br J Ophthalmol 1969; 53:412-414.
- 54. Crawford JS: True Brown syndrome: Surgical treatment. Am Orthopt J 1977; 27:15-20.
- 55. Reinecke RD: Superior oblique surgery. Am Orthopt ^J 1974; 24:23-26.
- 56. Parks MM, Brown M: Superior oblique tendon sheath syndrome of Brown. Am ^J Ophthalmol 1975; 79:82-86.
- 57. Sevel D: The trochlea: A study of the anatomy and physiology. Ophthalmology 1982; 89: 132-133.
- 58. Ptosis and underaction of the superior rectus muscle. Ophthalmology 1983; 91: 1080-1085.
- 59. Anderson RL, Baumgartner SA: Strabismus in ptosis. Arch Ophthalmol 1980; 98-1062-1067.
- 60. Burke RN: Congenital ptosis: A classification of 200 cases. Arch Ophthalmol 1949; 41:188-197.
- 61. Worth C: Squint, Its Causes, Pathology and Treatment. London, Bailliere, Tindall & Cox, 1929.
- 62. Chavasse FB: Worth's Squint or the Binocular Reflexes and the Treatment of Strabismus. New York, P. Blakiston, 1939.
- 63. Keiner GBJ: New Viewpoints on the Origin of Squint. The Hague, Martinus Nijoff, 1951.
- 64. Zeeman WPC: Conservative treatment of strabismus. Doc Ophthalmol 1954; 7/8:527-533.
- 65. Bielchowsky A: Lectures on Motor Anomalies. Hanover, NH, Dartmouth College Publications, 1943.
- 66. Donders FC: On the Anomalies of Accommodation and Refraction of the Eye, WD Moore (trans). London, The New Sydenham Society, 1864.
- 67. Snellen H: Die Ursache des Strabismus Convergens Concomitans. Arch Ophthalmol 1913; 84:433-458.
- 68. Parinaud H: Le strabisme et son traitement. Paris, Gaston Doir & Cie, 1899, p 88.
- 69. Nordlow W: Age distribution at the onset of esotropia. Br ^J Ophthalmol 1953; 37:593-624.
- 70. Scobee RG: Anatomic factors in the etiology of heterotropia. Am ^J Ophthalmol 1948; 31:781-795.
- 71. Nordlow W: Uber den Entstehungsmechanismus und die Fruhoperation des Einwartsschielens. Acta Ophthalmol 1945; 23:97-123.
- 72. Duke-Elder S, Wybar K: Ocular motility and strabismus, in System of Ophthalmology. London, Henry Kimpton, 1973, vol 6, pp 238-239.
- 73. Golstein JH: Strabismus and insertion of horizontal rectus muscles. Am ^J Ophthalmol 1969; 68:695-698.