The Fine Structure of the Retina. V. Abnormal Retinal Rods and their Morphogenesis. By KIYOTERU TOKUYASU* AND EICHI YAMADA. (*From the Department of Anatomy, School of Medicine, Kurume University, Kurume, Japan.*)‡

Electron microscope studies of vertebrate retinas (1–4) have established that the outer and inner segments of each rod are connected through the so called "connecting cilium" (2). Examination of a large number of sections of vertebrate retinas occasionally reveals however, abnormal rods whose outer and inner segments are in direct continuity. Morphogenetic studies of such abnormal rods can serve to check the earlier supposition concerning the capacity of the ciliary vesicles or tubules to induce the formation of rod sac precursors (5).

This brief note describes the results obtained to date from observations on adult mouse, rabbit, and human retinal rods, and on morphogenesis in kitten retinal rods. The procedures employed in preparing tissue samples were essentially those described in a previous paper (5).

In any given region of mouse or rabbit retina, abnormal rods are seen intermixed with much more numerous normal rods. An example is shown in Figs. 1 and 2. In these abnormal rods, the distal region (outer segment), where piles of rod sacs are contained, is directly connected with the proximal region (inner segment), in which mitochondria are observed, and often a row of rod sacs descends into the proximal region (Figs. 1 and 2).

Except for these abnormalities, the arrangement of rod sacs in the distal region appears as regular as in normal rods, and neither the width nor the length of the region differs much from that of normal rods (Fig. 1). In the section shown in Figs. 1 and 2, profiles of the basal body or ciliary tubules are not recognizable.

In man, abnormal rods are found seldom in the central region of the retina but with comparative frequency in the peripheral region. The human abnormal rod usually appears to have a short distal region (outer segment) (Figs. 3 and 4) in contrast to the long region of the mouse or rabbit. The width of this distal region is sometimes almost equal to that of the proximal region, that is, several times as wide as that of the normal outer segment (Fig. 4). In some abnormal rods the arrangement of rod sacs is as regular as in normal rods (Fig. 3); in others, however, rod sacs are divided into distinct groups with various orientations, and in some cases, arrays of rod sacs are even parallel to the plasma membrane of the rod (Fig. 4).

One or two centrioles can be seen in Figs. 3 and 4, but it is not clear in these sections whether all or any of them extend ciliary tubules.

In the abnormal primitive rod of the kitten, shown in Fig. 5, primitive rod sacs (*ps*) and ciliary vesicles (vc_1, vc_2) (cf. reference 5 for definitions of these terms) are found in the distal region of the rod, and mitochondria are accumulated in the proximal region. A centriole is present in the right upper corner of the proximal region. The profile of the primitive rod in this section is rather similar to that of the mature rod shown in Fig. 3. By following the serial sections in Figs. 6 and 7 one can see that there is another centriole that does extend ciliary tubules. This centriole may therefore be called the basal body.

The ciliary tubules extending from the basal body in Fig. 7 are continuous with those in Fig. 6 and also with the ciliary vesicles in Fig. 5. Since the ciliary tubules in Fig. 6, and ciliary vesicles in Fig. 5, are obviously within the cytoplasm of the rod, it appears that, once projected outside from the basal body, the primitive cilium reenters the cytoplasm of the rod. In other words, the ciliary tubules seem to be extended into the cytoplasm of the primitive inner segment through a short tubular connection which may be designated "ciliary tube" (refer to Text-fig. 1, II *A* and *B*).

Tubular structures are observed in abundance in a somewhat restricted portion of the distal region close to the distal plasma membrane and the rows of ciliary tubules and vesicles appear to be directed to this particular portion (Figs. 5 to 7).

With regard to the morphogenesis of the normal outer segment, earlier work led to the supposition that the ciliary tubules or vesicles extending into the primitive cilium might induce the formation of the tubular structures—the probable precursors of the rod sacs—at the distal plasma membrane of the cilium (5).

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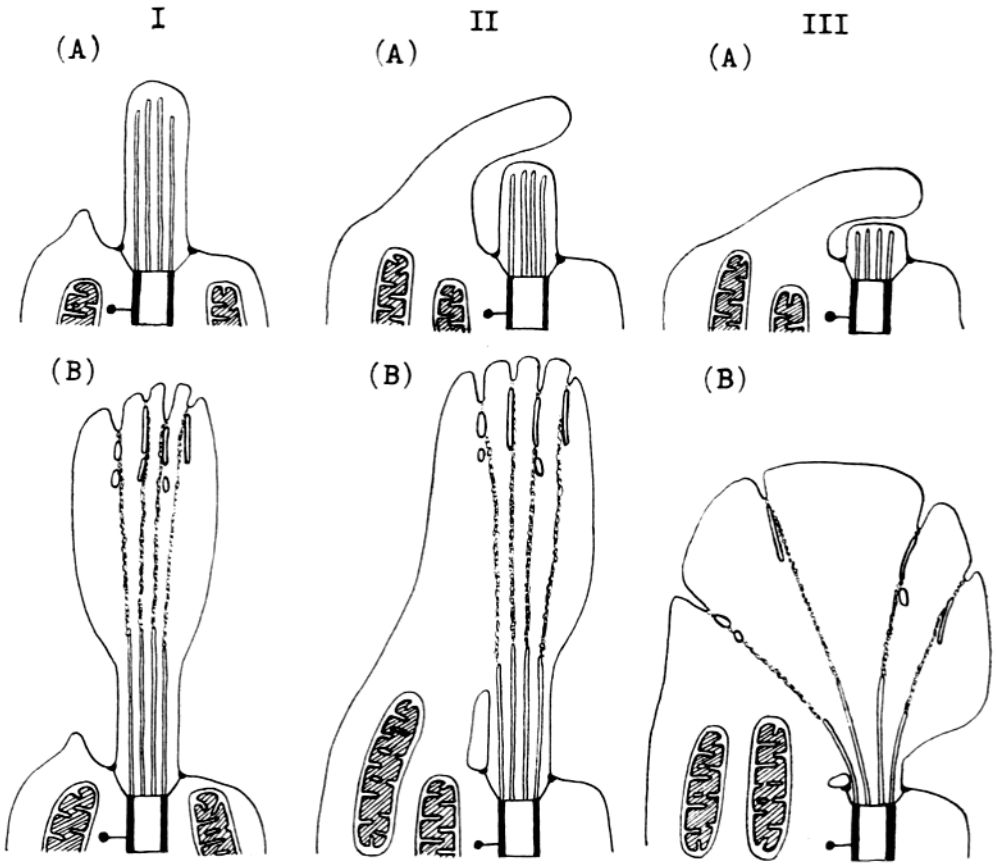

TEXT-FIG. 1. Schematic representation of probable morphogenetic sequence in normal and abnormal retina rods.

In the case of normal morphogenesis, the primitive cilium is extended out of the primitive inner segment (I *A*) and the distal region of the cilium becomes the primitive outer segment (I *B*).

In the morphogenesis of the abnormal rod, a part of the inner segment lies in the direction of the extension of the primitive cilium (II *A*). Thus, once extended outside, the ciliary tubules reenter the cytoplasm through the ciliary tube. The distal region of the inner segment is extended and becomes the abnormal primitive outer segment. The ciliary tubules or vesicles seem to induce the formation of the tubular structures at those regions of the distal plasma membrane where they establish contact (II *B*).

If the length of the ciliary tube were very short, the ciliary tubules could spread over a larger region in the cytoplasm (III *A*). It is assumed that extreme divergence of ciliary tubules and vesicles may lead to disordered morphogenesis (III *B*). See the text for more detail.

The present observation of an abnormal primitive rod suggests that the ciliary tubules or vesicles extending within the cytoplasm may be directed towards a somewhat restricted portion close to the distal plasma membrane where tubular structures are found in abundance. This finding implies that the ciliary tubules or vesicles may perform their inducting activity for the formation of the tubular structures even at the distal plasma membrane of the inner segment, and not necessarily in the primitive cilium. Except for the different site of formation, the tubular structures would appear to be formed in the same way as in the normal primitive cilium, and to be transformed similarly to primitive rod sacs and later to flattened mature rod sacs.

In the earlier report (5), the importance of the connections between each ciliary tubule and the corresponding dense band in the plasma membrane of the connecting cilium was discussed in relation to the direction of the corresponding rows of ciliary tubules and vesicles.

As described in the above observations, the ciliary filaments extend through the ciliary tube:

if the length of the ciliary tube were very short, the directions of ciliary tubules and vesicles might diverge sharply, thereby producing a disordered morphogenetic process (*cf.* Text-fig. 1, III *A* and *B*).

Whether or not there is a difference in photosensitivity between normal and abnormal rods is not known. A study of possible differences would help to clarify the function of the connecting cilium.

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EXPLANATION OF PLATE 100

FIG. 1. An abnormal retinal rod of the mouse. A row of piled rod sacs (*s*) descends into the region where mitochondria (*m*) are found. The outer and inner segments are directly connected with each other. × 6,000.

FIG. 2. An enlargement of a part of Fig. 1. Note that the pile of rod sacs (*s*) is as regular here as in the normal outer segment. In the cytoplasm, tubular structures (*ts*) are found in continuity with the rod sacs (*cf.* Fig. 21 in the previous paper (5)). × 10,000.

FIG. 3. An abnormal retinal rod found in the peripheral region of the human retina. Cross- and longitudinal profiles of centrioles (*c*) are recognizable in the central region of the figure. In this section, it is not definite whether or not either one of them extends ciliary tubules.

A projection (*p*) extending from the centriole of the cross-profile appears to be the cudgel-shaped (clavate) projection described in an earlier report (5). If so, this centriole might possibly be the basal body, since it extends such projections, while the other centriole does not—at least in the case of the normal rod.

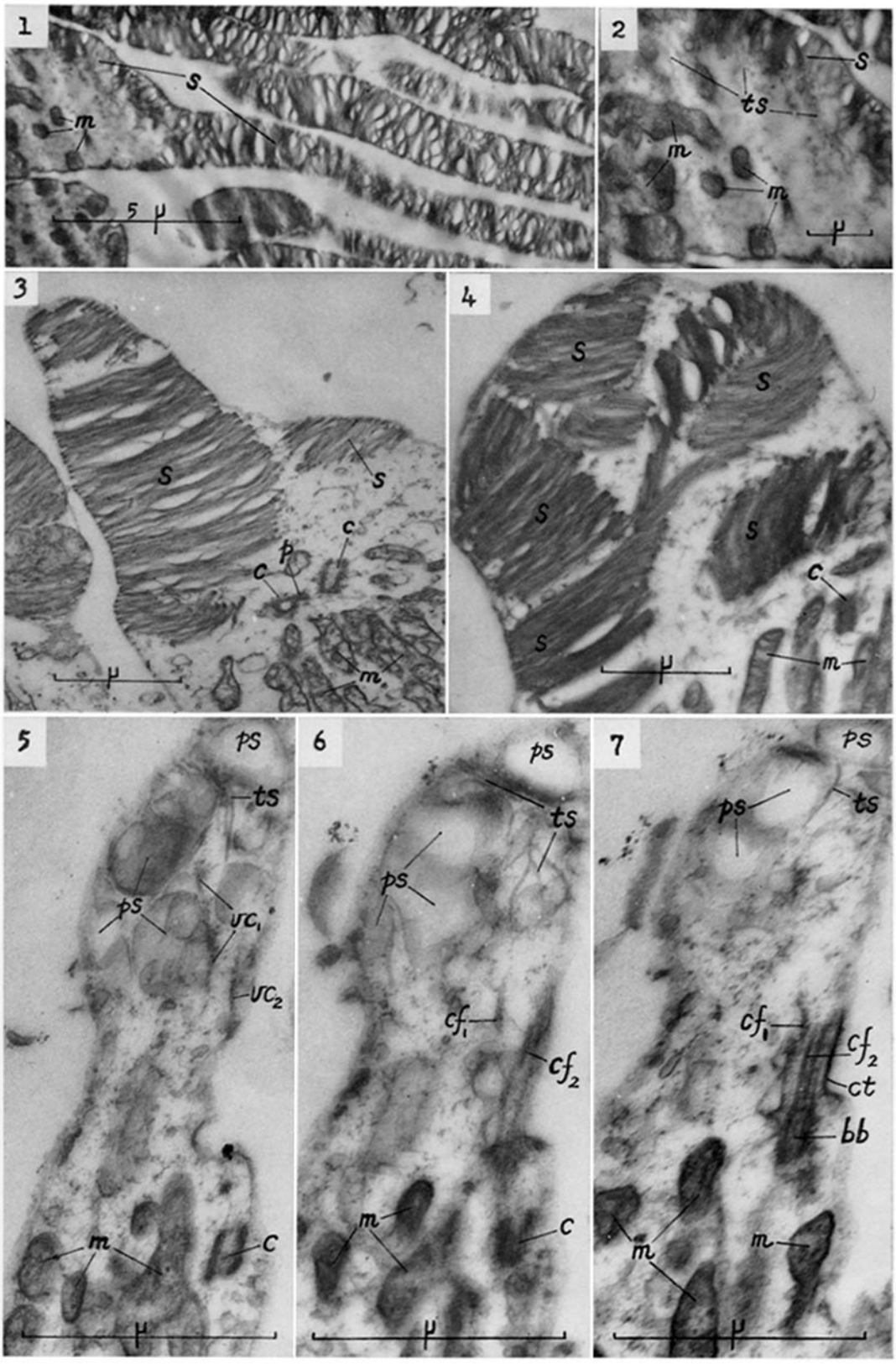
Note that the arrangement of rod sacs (*s*) is as regular here as in the normal outer segment. *m*, mitochondria. × 20,000.

FIG. 4. An abnormal retinal rod found in the peripheral region of the human retina. The distal region containing rod sacs (*s*) is several times as wide as the common outer segment, and the rod sacs are divided into many groups. The arrays of rod sacs in some of these groups are almost parallel to the plasma membrane. *c*, centriole and *m*, mitochondria. × 20,000.

FIG. 5. One of a group of three serial sections of an abnormal rod at an early stage of morphogenesis in the kitten retina. Figs. 6 and 7 show the other two serial sections.

Numerous primitive rod sacs (*ps*) are found in the distal region of the rod and tubular structures (*ts*) can be seen in abundance in a somewhat restricted region close to the distal plasma membrane. Note the profile of a centriole (*c*) in the lower right region of the rod. vc_1 and vc_2, rows of ciliary vesicles and *m*, mitochondria. × 40,000.

FIGS. 6 and 7. Serial sections following that in Fig. 5. These sections show another centriole besides the one noted in Fig. 5. This centriole extends ciliary tubules and is called the basal body (*bb*). The primitive cilium thus formed appears to have re-entered the cytoplasm, forming a bridge-like structure between the proximal and distal region of the rod. The structure is called "ciliary tube" (*ct*) here. Note that the profiles of ciliary tubules in Fig. 7 (cf_1 and cf_2) are each continuous with those in Fig. 6 (cf_1 and cf_2) and also to the rows of ciliary vesicles in Fig. 5 (vc_1 and vc_2). Note also that a cluster of tubular structures (*ts*) is found in a somewhat restricted region close to the distal plasma membrane and that the rows of ciliary vesicles appear to be directed to the particular region. *ps*, primitive rod sacs and *m*, mitochondria. Each, × 40,000.



(Tokuyasu and Yamada: Abnormal retinal rods)