tion of the structures in the anterior segment is well advanced at this time. The anterior chamber is formed and the cornea is covered by a two-layered epithelium and a normal endothelium overlying a thin Descemet’s membrane. The anatomical features of the lens are similar to those of the neonatal animal and the posterior mesodermal leaf of the iris has begun to extend forward over the surface of the lens. It is difficult to visualize that transient or prolonged hypoxia at midterm can have brought about the developmental disturbances seen in the anterior segment, as the separation of the lens vesicle from the cornea must have taken place earlier in the gestation period.

The circumscribed anterior cortical cataract observed in one eye was complicated by the adherence of a dense portion of the persistent pupillary membrane to the anterior pole of the lens, as is frequently seen in congenital anterior polar cataracts of man. The fetal nucleus was undisturbed, indicating that, as in the human eye, the error of development occurred later in fetal life. It is possible that the hypoxia experimentally induced at midterm delayed the involution or produced shrinkage of the pupillary membrane affecting the structure of the anterior pole of the lens.

No attempts can be made to discuss the mechanisms involved in the pathogenesis of the retinal abnormalities. The alteration of hemodynamics produced in the ocular vasculature by the intrauterine surgical procedures cannot be defined and the time course of the development of collateral circulation via the vertebral vessels is unknown. It is probable that the choroidal vasculature was not drastically injured by the experimental procedure. At full term, the undisturbed anatomy of the choroidal vessels correlated well with the over-all integrity of the outer layers of the retina. There remains then a wide area for speculation on the mechanisms responsible for the damage. In this preliminary report it can only be stated that deformities in eyes of infant monkeys subjected to surgical interference with the circulation at midterm resemble congenital anomalies of the human eye.

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Development of the rat retina

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Development of the rat retina during the first 2 weeks after birth was studied electron microscopically and electroretinographically to seek a correlation between development and the attainment of func-
Fig. 1. Epon embedded section of the newborn rat retina. The inner half of the retina has been differentiated to a degree that the nerve fiber (NF), ganglion (G), and inner plexiform (IP) layers are recognizable. The neuroblastic cells (Nbc) are tightly packed in the outer half of the retina. The outer limit of this layer is closely attached to the pigment epithelium (PE). Mitotic activity is seen only in this zone (arrow). (0.5 micron thick Toluidine blue stain, ×230.)

Fig. 2. The nerve fiber layer of the newborn rat retina. Newly formed axons contain microtubules and clusters of vesicles (arrow). Glia cell is seen occasionally in this layer. (×25,300.)
Fig. 3. The outer portion of the newborn rat retina. Apical ends of the elongated neuroblastic cells are firmly joined with each other at a row of junctional apparatus (arrow), and closely attached to the apical ends of the pigment cells. The pigment cell is forming the microvilli and is rich in melanosomes. One mitotic cell is showing in the center. (×7,700.)
tion. This paper is a summary of the previously reported findings.

At birth the rat retina was still in a premature state, about equivalent to that of the retina of the 4-month-old human embryo. Only the ganglion cells had differentiated to any degree and were distinguishable from other neuroblastic cells by their light staining round nuclei (Fig. 1). The nerve fiber and inner plexiform layers were also recognizable at this stage. The newly formed nerve fiber layer consisted of bundles of axons in which microtubules and clusters of vesicles were seen (Fig. 2). The inner plexiform layer was made of fine cell processes loosely packed without synaptic junctions. The outer half of the retina was occupied by tightly packed neuroblastic cells. These cells had relatively simple cytoplasm, in which ribosomes were the main microorganelle, and there was no intercellular space.

The apicolateral portions of the neuroblastic cells were tightly joined with each other by a conspicuous junctional apparatus, which was present from the earliest stage of development. The row of these junctions became the external limiting membrane. Many neuroblastic cells appeared to anchor the apical portions at this

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**Fig. 4.** Higher magnification of the apical portion of the neuroblastic cells of the newborn rat retina. The junctional apparatus is made of the chains of desmosomes. The cytoplasm contains the cluster of mitochondria (m), centrioles (c), microtubules (ntt), and peculiar electron dense granules (arrow). The pigment epithelium (PE) is forming microvilli (mo) by membrane infoldings and is closely attached to the neuroblastic cells. Several melanosomes (me) are seen in this area. (×32,200.)
Fig. 5. For legend see opposite page.

Fig. 6. For legend see opposite page.
zone and extend their cell bodies inward (Fig. 3). Mitotic activity was seen only in the neuroblastic cells situated at the junctional zone, and then only toward the end of the first postnatal week. The outer portion of the cell under mitosis often showed the junctional apparatus.

It appeared that the photoreceptor cells had been definitely fixed at the external limiting membrane in the early differentiating stage, and that these cells had elongated their bodies without actual alteration of their location. The inward movement of the nuclear position by the stretching of the cell was apparently interpreted as the migration of the neuroblastic cells. As the neuroblastic cells were compactly packed and were rich in desmosomes and tight junctions, the occurrence of free movement from one layer to another was unlikely. However, some daughter cells appeared to be pushed inward to form the bipolar cells.

The apical portions, or the outermost limits of the neuroblastic cells, were attached closely to the pigment epithelium. Although desmosomes between these cells, which were commonly seen in the earlier stage, had disappeared, the junction appeared to be quite tight. The pigment epithelium seemed to be well-developed and beginning to form microvilli by the infolding of the apical cell membrane (Fig. 4).

Photoreceptor segments were differentiated from the cells at the outermost zone, and the neuroblastic cells were divided into two layers during the first week of postnatal development. The progress of the differentiation of the retinal tissue during the period of 5 to 7 days after birth was extremely rapid.

Development of the photoreceptor

Differentiation of the photoreceptor segments began at the outermost portion of the neuroblastic cells. At the time of birth, a few mitochondria and a pair of prominent centrioles were seen in the apical cytoplasm, which was rapidly increasing its volume (Figs. 3 and 4).

Around the third day the cytoplasm with the accumulated mitochondria protruded beyond the external limiting membrane profoundly and gave the appearance of the ellipsoid. From one of the centrioles, which was situated near the cell membrane, the cilia extended toward the outside of the cell. The cell membrane always covered a little cytoplasm in which the cilia was extending (Fig. 5). Electron dense granules, often forming star-shaped aggregations, appeared around the centriole (Fig. 4). The other centrioles remained within the cytoplasm at nonspecific locations with no alteration of appearance. Some stayed near the fellow centriole.

On the fifth day the first lamellar outer segment membranes were found in the mi-
Fig. 9. Seven-day-old rat retina. In the axonal end of the developing photoreceptor cell electron dense granules aggregate to form the synaptic bar (arrow). Many vesicles are formed in this area. (×105,000.)

Fig. 10. Twelve-day-old rat retina. Well-developed synaptic organs are clearly seen in the inner plexiform layer. This rat shows small but definite electroretinographic response. (×100,800.)
nute cytoplasm around the cilia. This membrane formation site was closely embraced by the then well-developed microvilli of the pigment epithelium. The first lamellar membranes were found in a radial arrangement around the cilia, but soon became irregular in size and direction. The small thick membranes were often continuous to smooth endoplasmic reticulum or small vacuoles (Fig. 6). Formation of the lamellar by the direct infoldings of the cell membrane was not common in the developing rat retina.

During the first 7 to 10 days, newly formed lamellar membranes increased their length and number. Many were extremely long and arranged in parallel direction to the axis of the cells. Around the fourteenth day the majority of the outer segments were arranged in a fingerlike rod shape and formed a clear layer of the outer segment (Fig. 7). However, irregular lamellar membranes were still abundant in the microvilli of the pigment epithelium for another week. On the third week the appearance of the outer segment became that of the adult animals.

Development of the synapses

The tightly packed neuroblastic cells increased in number until the fifth day, when activity of the mitosis in the outermost layer lessened. The cells in the inner portion of the neuroblastic layer differentiated gradually into larger sizes with less dense nuclei. Early on the sixth day a few large lightly stained cells which were first seen in the innermost portion of the neuroblastic layer, formed a row in the inner one-third portion and suddenly developed cell processes in a horizontal direction (Fig. 8). These cells were the horizontal cells, and thus Chievitz's layer was formed. The cell processes of the horizontal cells branched out into fine ones and formed close contact with the extending axonal ends of the photoreceptor cells. Synaptic organs were formed at these places (Fig. 9). After meeting the horizontal cell processes, the cytoplasm of the axonal ends became large and developed numerous vesicles of various sizes. At approximately the same period, amorphous electron dense granules appeared in the matrix among the vesicles. This electron dense substance aggregated and finally became synaptic bars within a short time. At the end of the sixth
day completed synaptic organs were abundant in the outer plexiform layer.

Development of the inner synapses was found to be considerably slower than that of the outer ones. The loose cell processes in the inner plexiform layer began to form certain cellular junctions around the fifth day. However, the synaptic bars and vesicles were first seen on the eighth day. On the tenth day, the inner plexiform layer became more compact and the intercellular spaces were filled with Muller's cells. The synaptic organs became apparent and abundant on the twelfth day (Fig. 10).

The development of the lamellar membranes and the synaptic organs progressed equally at an extremely rapid speed. As the differentiation was so fast, marked differences were often observed between animals killed in an interval of 6 hours during the period of 4 to 7 days. On the eighth day, both the lamellar membranes and the outer synaptic organs were abundantly formed. However, the electroretinographic response was not recorded up to this developmental stage. After the rough completion of the development of the lamellar membrane and outer synaptic organs, inner synapses were formed. At this time the electroretinogram became positive. The earliest response was recorded in some animals on the eleventh day. The magnitude of the electroretinographic response increased markedly by the hour during the twelfth to fourteenth days; hence, the response was about the same as that of the normal adult rat (Fig. 11).

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A note on the development of the anterior chamber angle

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In 1955, a new concept of the development of the anterior chamber angle was presented. Taking issue with the thesis that development of the anterior chamber angle proceeded by a process of atrophy...