tive immunologists in further understanding the phylogeny of the vertebrate immune system.

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The Retina of the Newborn Human Infant

Abstract. *We have examined a pair of eyes from a normal, full-term infant who died at 8 days as a result of accidental injury. Eyes were obtained immediately after death, fixed, and sectioned for light microscopy. Results from both eyes were substantially the same. The macular region was still drastically immature at 1 week. Even though a foveal depression existed, all cell layers were still present across it. Furthermore, the inner nuclear layer was divided into two separate layers. The receptor layer was reduced to one or two cells thick; receptors had both inner and outer segments, but they were very short and stumpy. The region of immaturity covered about 5° of the retina. These findings suggest that the central region of a human infant's retina is probably not fully functional at birth.*

The visual capacities of infants are different from those of adults; behavioral and physiological studies have shown that an infant's visual capacity, particularly acuity, improves rapidly over the first few months of life (*1*). It is important to know the extent to which these differences between the capacities of infants and adults are accounted for by changes in retinal anatomy rather than by changes in higher centers. We now describe the state of the infant retina at birth and suggest that postnatal development of the retina may account for some of the improvement in visual capacity.

Little information is available about the human infant retina at birth. Standard sources (*2*) state that, at birth, the peripheral retina resembles that of the adult, but that the macular area is still immature; across the fovea, the outer nuclear layer is very thin, inner segments of receptors are broad, and outer segments are short and stumpy. It is only by the fourth month that the foveal cones are said to reach their full slender length and that the inner nuclear and ganglion cell layers move to the side to form the adult foveal depression. Most of these conclusions about foveal immaturity seem to be derived from work done early in this century; only drawings—not photographs—are presented, and the number of infants and the reasons for their deaths are unknown (*3*).

The development of the fovea has been more fully explored in macaque monkeys, who also show considerable increase in acuity after birth (*4*). In the monkey the fovea is still immature at birth (*5*), but the immaturity is not as drastic as suggested by the human data. It is often assumed today that the earlier work on humans overstated the degree of foveal immaturity at birth (*6*). We have undertaken to resolve this issue in order to facilitate the interpretation of measures of human infant visual function during development.

We have examined the retinas from several human infants at late prenatal and early postnatal ages. One especially important pair forms the basis of this report. The eyes were obtained from a normal, full-term male infant with no congenital anomalies who died at postnatal day 8 as a result of accidental burns. The eyes were removed 1 hour after death. One whole globe was fixed in Susa fixative containing picric acid, dehydrated in alcohol, embedded in low-viscosity nitrocellulose, serially sectioned at 10 μm, and stained with a modified Cason's stain (*7*). From this eye we have a complete set of regularly spaced sections across the entire eye, which allowed unambiguous identification of the macular region. The second eye was fixed in 2 percent paraformaldehyde and 2 percent glutaraldehyde in *p*H 7.4 phosphate buffer; it was then cut into identified areas and embedded in Epon. The block including the macula was serially sectioned at 2 μm, and sections were stained with azure II–methylene blue.

The macular region was still very immature, while more peripheral regions resembled those of the adult. Figure 1 (A to C) shows a series of photomicrographs taken at different positions along a single 10-μm horizontal section which included both the optic nerve head and the fovea. In the peripheral regions all retinal layers appear well-developed and mature (Fig. 1A).

In the nasal retina immediately adjacent to the fovea, major differences from the adult retina first appear. As the fovea is approached (right side of Fig. 1B), the inner nuclear layer begins to split into two distinct layers, the number of cells in the outer nuclear layer decreases, the layer becomes thinner, and the space between the external limiting membrane and the pigment epithelium decreases. At the fovea (Fig. 1C) there is a depression in the retina which is marked by a decrease in the thickness of all nuclear layers; however, both the ganglion cell and inner nuclear layers still extend across the fovea. The split in the inner nuclear layer extends to the edge of the fovea, possibly across the fovea, and is even more marked than in Fig. 1B. The outer nuclear layer is reduced to one or two cells thick, and there seems to be little space for inner and outer segments

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of receptors between the external limiting membrane and pigment epithelium. The foveal region shows some artifactual swelling, which is common in postmortem human retinas.

Figure 1D is a high-power photograph of a 2-μm Epon section through the fovea in the second eye. As in Fig. 1C, the outer nuclear layer is never more than two cells thick. Cone inner segments and outer segments are present, but all are very short and thick. Figure 1E is from the peripheral retina of the same eye. Both inner and outer segments of the cones (darkly stained nuclei) are longer than in the fovea and are more like those in the adult. Although only cones are seen in Fig. 1D, numerous, apparently well-developed rods are seen between the cones in Fig. 1E.

All major qualitative observations have been confirmed on eyes from other infants, but in these cases the eyes were obtained only some hours after death and the retinas are less well preserved.

The area of macular immaturity is about 1200 μm in diameter. The visual angle subtended by this area can be specified only tentatively, because it would depend on the exact diameter of the eye, the location of the nodal point in the eye, and the degree of tissue shrinkage in our sections. However, we conservatively estimate that this immature region subtends about 5° of visual angle.

Our findings are essentially the same as those stated early in the century by Bach and Seefelder (*3*). They gave no details about the infants, however, and the results for the newborn were published as an artist's drawing, which was presumably a composite from several infants. More recently Horsten and Winkelman (*8*) have published photographs of the periphery and of the "centre of retina in a full-term infant"; it is unclear if this refers to the fovea. Their photograph of the central retina does not show any marked foveal depression, all cell layers are present across the section in much the same fashion as in the periph-

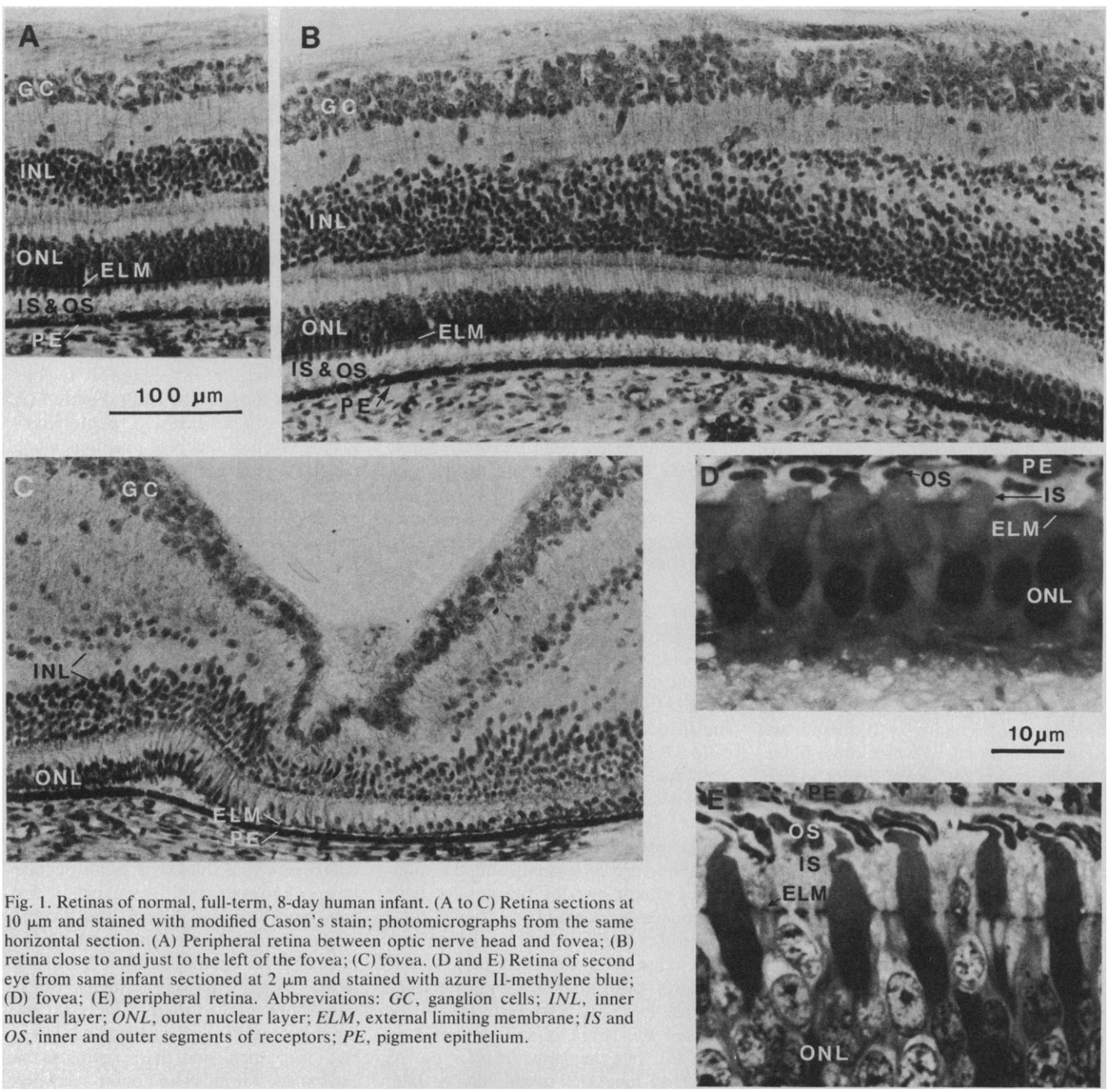

Fig. 1. Retinas of normal, full-term, 8-day human infant. (A to C) Retina sections at 10 μm and stained with modified Cason's stain; photomicrographs from the same horizontal section. (A) Peripheral retina between optic nerve head and fovea; (B) retina close to and just to the left of the fovea; (C) fovea. (D and E) Retina of second eye from same infant sectioned at 2 μm and stained with azure II-methylene blue; (D) fovea; (E) peripheral retina. Abbreviations: *GC*, ganglion cells; *INL*, inner nuclear layer; *ONL*, outer nuclear layer; *ELM*, external limiting membrane; *IS* and *OS*, inner and outer segments of receptors; *PE*, pigment epithelium.

ery, and none of the changes shown in Fig. 1 and by Bach and Seefelder (*3*) are apparent. Having examined full sets of horizontal sections through our sample of eyes, we suggest that Horsten and Winkelman's section was from the outer margin of the macular area. We therefore concur with Bach and Seefelder that the newborn infant's fovea is still very immature.

One notable feature in Fig. 1, B and C, is the prominent split in the inner nuclear layer near the fovea, at the vitread margin of a layer of larger and more densely stained cells. Bach and Seefelder (*3*) had described this split as the postnatal remnant of the "transient layer of Chievitz" between the amacrine cells ("inner horizontal cells") and the rest of the inner nuclear layer. Regardless of its nature, we find this split in the macular areas of all the human infant eyes we have examined, and it also can be seen near the fovea of the newborn macaque's retina (*5, 9*). The width of the split may depend on histological procedures; though present in all eyes from humans and monkeys, it is narrower in the eyes embedded in plastic.

The second major finding concerns the paucity of cones in the foveal region and their very immature appearance 8 days after birth (Fig. 1, C and D). Even though very young infants have considerable visual capacity (*1, 6*), we suggest that most of it is based on extrafoveal vision. This agrees with arguments from other considerations that vision in newborn infants is largely determined by peripheral regions of the retina (*10*). This could be the reason, for example, that color vision in young infants (*11*) shows some of the anomalies found in peripheral color vision in adults (*12*). When does the human fovea become adult in its morphology? Another eye from an 11-month-old female, which we have similarly processed, has slim, elongated foveal cones similar to those from adult eyes. We are attempting to obtain well-preserved retinas from intermediate ages to chart this maturation more precisely.

The peripheral retina of the newborn human infant is well developed, but the macular area is not; indeed, in the fovea the receptor layer is so poorly developed that it may barely be functional. This does not seem to be the case in the newborn macaque monkey (*5*); the macaque's fovea is immature at birth but its cones are far more mature than those of a newborn human. Even though the visual system of the macaque is often used as a model for the human system, our findings on the retinas of newborn human infants suggest that although newborn macaque monkeys may be models for somewhat older human infants, they may not be good models of newborn humans.

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Dietary Calcium in Human Hypertension

Abstract. *A pilot survey was made of the dietary calcium intake of normotensive and hypertensive individuals. Compared to 44 normotensive controls, 46 subjects with essential hypertension reported significantly less daily calcium ingestion (668 ± 55 milligrams compared to 886 ± 89 milligrams). The intake of other nutrients, including sodium and potassium, was very similar in the two groups. The hypertensives differed from the controls primarily in their consumption of nonfluid dairy products. The data suggest that inadequate calcium intake may be a previously unrecognized factor in the development of hypertension.*

Of the mineral elements in the human diet, sodium and potassium have received the greatest attention as being possible determinants in the pathogenesis of essential hypertension in humans (*1, 2*). Although the results of a number of dietary surveys have suggested a link between the dietary intake of these two cations and the development of hypertension, many other studies have shown no difference in the consumption of these two mineral elements among normotensive (NL) and hypertensive (HTN) individuals (*3, 4*). These seemingly disparate findings suggest that if sodium or potassium consumption in the diet influence blood pressure regulation, the effect may be mediated, in part, by other nutritional elements.

Calcium is an essential element in normal cellular physiology (*5*). Normal cardiovascular function is critically dependent on both extra- and intracellular calcium concentrations (*6*). Only recently, however, have abnormalities of extra- and intracellular calcium metabolism been identified in both human and experimental hypertension (*7–9*). Several of the reports (*7, 8*), as well as other studies (*10–12*), have suggested maintenance of an adequate or increased level of dietary calcium may protect the human or laboratory animal at risk. However, no studies appear to have been conducted on the dietary calcium intake of humans with essential hypertension. In this report we summarize our findings from a nutritional survey designed to compare calcium intake in humans with established hypertension with the intake reported in a normotensive population that was group matched for age, sex, and race. The data were also compared with nutritional data from the Health and Nutrition Examination Survey (HANES) of the National Center for Health Statistics (*13*).

The HTN population (diastolic blood pressure > 95 mmHg or mean arterial pressure > 105 mmHg) was composed of subjects recently identified as hypertensive in the Hypertension Clinic at the Oregon Health Sciences University (OHSU). The subjects were not receiv-

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