WILBRAND'S KNEE OF THE PRIMATE OPTIC CHIASM IS AN ARTEFACT OF MONOCULAR ENUCLEATION*

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ABSTRACT

Purpose: The anterior chiasmal syndrome consists of a temporal hemianopia or complete visual field loss in one eye, plus a superior temporal hemianopia in the other eye. The superior temporal hemianopia in the other eye is thought to result from injury to Wilbrand's Knee of the optic chiasm. Wilbrand's Knee is a loop of decussating fibers which detours into the contralateral optic nerve before entering the optic tract. I studied the organization of fibers in the optic chiasm of monkeys and humans to verify the existence of Wilbrand's Knee and to elucidate further the pattern of visual field loss seen from lesions of the sellar region.

Methods: The primary optic pathway was labelled in monkeys by injection of [^{3}H] proline into one eye, followed by autoradiography. There were 8 intact Rhesus monkeys and 3 intact squirrel monkeys. In addition, the optic pathway was studied in the Rhesus monkey 6 months and 4 years after monocular enucleation. The optic chiasm was also examined using myelin stains in specimens obtained post-mortem from 3 patients. The patients had lost 1 eye 5 months, 2 years, and 28 years prior to their deaths. Finally, clinical observations were recorded in 3 patients with the anterior chiasmal syndrome.

Results: In normal Rhesus and squirrel monkeys, optic nerve fibers crossed the optic chiasm without entering the contralateral optic nerve. After short-term monocular enucleation, fibers from the normal optic nerve were drawn closer to the entry zone of the degenerating optic nerve, but Wilbrand's Knee was still absent. After long-term enucleation, a typical Wilbrand's Knee was induced to form. In the human, Wilbrand's Knee was absent 5 months after monocular enucleation, but emerged in the two cases involving long-term enucleation, in a fashion analogous to the monkey. The case reports describe 3 patients with variants of the anterior chiasmal syndrome from parasellar tumors.

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Conclusions: Wilbrand's Knee does not exist in the normal primate optic chiasm. It forms gradually over a period of years following monocular enucleation, presumably from shrinkage of the optic chiasm caused by atrophy of fibers from the enucleated eye. Therefore, the superior temporal hemianopia in the "other eye" seen in the anterior chiasmal syndrome cannot be due to compression of Wilbrand's Knee. I propose that it occurs from combined compression of the optic chiasm and one (or both) optic nerves.

INTRODUCTION

Isaac Newton was the first to propose that binocular vision results from a partial decussation of fibers at the optic chiasm.[1] In all mammals, the axons originating from ganglion cells in the nasal retina cross at the optic chiasm to enter the contralateral optic tract. As a result, the optic tract unites the temporal visual field of the contralateral eye and the nasal visual field of the ipsilateral eye. After a synapse in the lateral geniculate body, these inputs are conveyed to the visual cortex, where cells sensitive to retinal image disparity give rise to the perception of depth.[2]

The first modern diagram of fibers crossing in the optic chiasm was published in 1750 by John Taylor,[3] an itinerant strabismus surgeon (Fig 1). Although based entirely upon gross anatomic observation, it provided a fairly accurate depiction of the partial fiber decussation. John Taylor later gained notoriety as a charlatan for his habit of arriving in towns with great fanfare, and then departing quietly the next morning before the results of his surgery were known.[4,5] Although his conduct was deplorable, his work on the human optic chiasm was praiseworthy.

In the late 19th century, the development of myelin and fiber stains made it possible for investigators to use the microscope to trace the course of axons through the optic chiasm.[6] Specimens obtained postmortem from subjects with a history of monocular enucleation were particularly valuable, because loss of myelin caused a striking contrast to emerge between the staining intensity of fibers from the normal nerve and the atrophic nerve. In 1904, Hermann Wilbrand (1851-1935) described the anatomy of the human optic chiasm in Volume 3 of his monumental 10-volume handbook, *Die Neurologie des Auges,*[7] written with Alfred Saenger from 1899-1927. He reported 2 specimens: case NN sectioned coronally and case E sectioned horizontally. The interval in his subjects between loss of the eye and death was not specified, but it must have been considerable, judging from the severe optic nerve atrophy visible in his illustrations. In both cases, Wilbrand observed that crossing fibers took a detour of 1 to 2 mm backwards into the atrophic contralateral optic nerve before entering the optic tract. He called this errant loop of fibers the "knee" of the optic

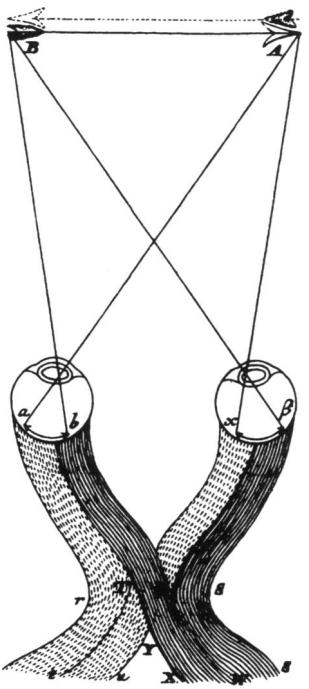

FIGURE 1
First depiction of the partial decussation of fibers in the human optic chiasm, published in 1750 by John Taylor,[3] an ophthalmic surgeon. The diagram was remarkably accurate, but erred by showing segregation of nasal and temporal fibers along the entire course of the optic nerve, and no intermingling of fibers in the optic tracts.

chiasm. It came to be known as "Wilbrand's knee," although it was also reported by Michel,[8] Kölliker,[9] Cramer,[10] Galemaerts,[11] Cajal,[12] and later researchers[13,14] who examined the optic chiasm after loss of 1 eye.

Perhaps the "knee" became identified so firmly with Wilbrand because he was the first to associate it with characteristic patterns of visual field loss produced by parasellar lesions. In 1915, Wilbrand repeated his description of case E in volume 6 of his handbook[15] (Fig 2). He stated that "lesions compressing the inferonasal aspect of the optic nerve just before the chiasm result in a temporal hemianopia from injury to crossing fibers" (Fig 3A). "A smaller temporal hemianopia appears in the other eye because of injury to the 'knee' fibers of the other nerve. If the lesion is large enough, complete blindness in 1 eye will be accompanied by a temporal hemianopia in the other eye" (Fig 3B).

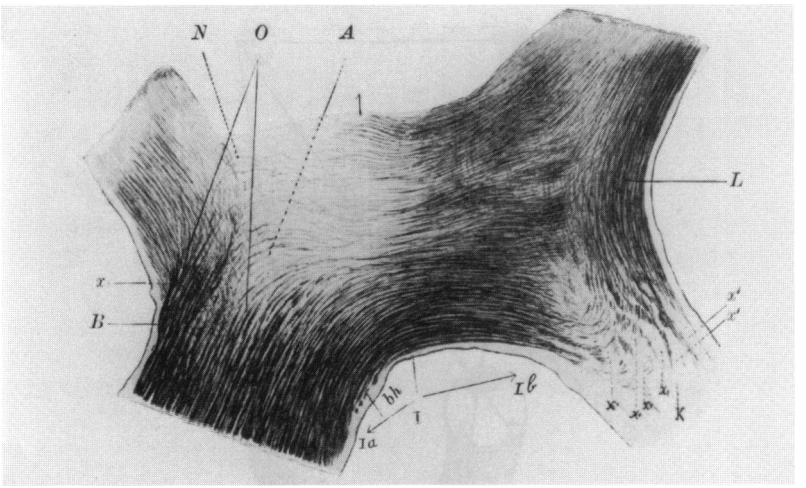

FIGURE 2

Case E of Hermann Wilbrand,[15] showing a loop of fibers (K) from the intact optic nerve (lower left) detouring into the atrophic optic nerve before proceeding to the contralateral optic tract (upper right). There was no scale marker, but judging from the dimensions of the optic chiasm, Wilbrand's knee extended 1 to 2 mm anterior to the junction of the optic nerves. This figure is upside down from the usual orientation of the optic chiasm.

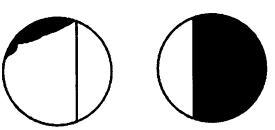

FIGURE 3A

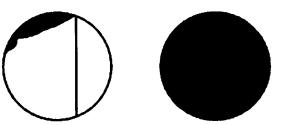

FIGURE 3B

A, Schematic diagram by Wilbrand[15] of the pattern of visual field loss produced by a lesion partially compressing the right optic nerve just before the optic chiasm. He attributed the small superior temporal field defect in the other eye to injury of its "knee" fibers. B, Schematic diagram by Wilbrand[15] of the pattern of visual field loss caused by complete interruption of the right optic nerve. By comparison with Fig 3A, Wilbrand was attempting to show that the degree of field loss in the affected nerve could vary, but a superior temporal field defect always occurred in the other eye from injury to "knee" fibers.

Wilbrand provided no clinical evidence to support his view that proximal lesions of one optic nerve can give rise to a superior temporal hemianopia in the other eye because of injury to "knee" fibers. Nonetheless, his anatomic explanation for the asymmetric pattern of visual field loss caused by prechiasmal lesions has become widely accepted. Wilbrand's

knee is reproduced in many standard textbooks[13,16-21] and provides a vivid example of the precision of clinico-anatomic correlation in neuro-ophthalmology.[22-24]

In 1926 Wilbrand published a review article about the organization of fibers in the human optic chiasm.[25] It contained his last, definitive version of the "knee" (Fig 4). He incorporated several changes in this rendition. First, the atrophic nerve containing the "knee" appeared normal in girth, in contrast with actual specimens (Fig 2). Second, the "knee" took a more generous excursion into the contralateral optic nerve. No scale marker was provided, but if one assumes an average chiasmal width of 13.3 mm,[26] the "knee" extended about 5 mm into the contralateral optic nerve. Previous drawings of anatomic specimens had shown fibers looping only 1 to 2 mm into the contralateral optic nerve (Fig 2). Third, his illustration showed fibers organized in an orderly, parallel fashion through the optic chiasm. In real specimens, fibers do not maintain such a tidy array.[27]

With his last revision (Fig 4), Wilbrand was attempting to convey an impression of the "knee" in the normal optic chiasm. However, the

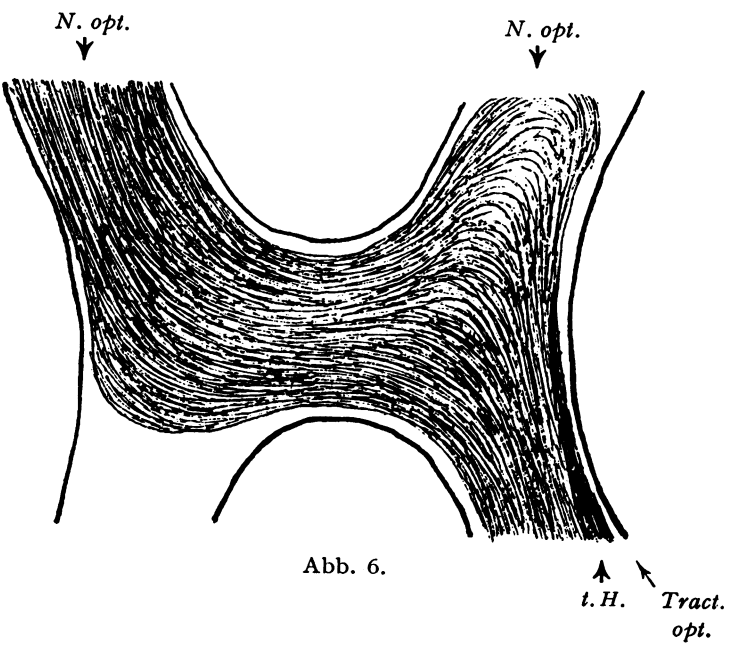

FIGURE 4

Final anatomic drawing by Wilbrand[25] of his "knee" showed little reduction in the girth of the atrophic nerve. The "knee" was also increased in size, so that it no longer fit entirely within the diagram. Fibers were shown passing through the optic chiasm in perfect order. None of these features was accurate.

anatomic methods available at the beginning of the century allowed him to visualize the "knee" only after loss of 1 eye.

I decided to label Wilbrand's knee in monkeys by injecting a radioactive tracer into 1 eye. Processing the optic chiasm for autoradiography allowed me to follow the course of fibers through the normal, intact optic chiasm. I found no evidence for Wilbrand's knee. However, it could be induced to form by enucleating 1 eye and waiting years for severe atrophic changes to occur. I also examined the optic chiasm obtained postmortem from patients at different times following monocular enucleation. These specimens provided indirect evidence that a similiar process accounts for the formation of Wilbrand's knee in humans.

In the final section of this report, I describe 3 patients with parasellar lesions. When I examined these patients initially, I interpreted their patterns of visual field loss in the context of Wilbrand's knee. My recent anatomic observations regarding Wilbrand's knee have altered my view. I present a simpler, alternative explanation for the pattern of visual field loss that develops from lesions originating at the anterior junction of the optic chiasm.

METHODS

Experiments were conducted in 10 Rhesus monkeys (*Macaca mulatta*) bred at the California Regional Primate Research Center. Each monkey received an injection of 2 to 4 mCi of L-[2,3,4,5-^{3}H]proline (Amersham), specific activity 99 to 106 Ci/mmole, into 1 eye. The label was dried under N_2 gas and reconstituted in 20 μL of normal saline. After anesthesia with ketamine HCl (10 mg/kg intramuscularly) and topical 4% tetracaine HCl, a 29-gauge needle attached to a U-100 0.3-mL insulin syringe (Becton-Dickinson) was used to inject the tracer into the middle of the vitreous. Following a survival time of 7 to 10 days, each animal was anesthetized with ketamine HCl (30 mg/kg intramuscularly) and given a lethal dose of sodium pentobarbital (250 mg/kg) into the peritoneal cavity.

A liter of 0.9% normal saline followed by a liter of 2% paraformaldehyde in 0.1 M phosphate buffer (pH 7.4) was perfused through the left ventricle. The optic nerves, optic chiasm, and optic tracts were dissected intact and placed in 2% paraformaldehyde for several days, followed by cryoprotection in 30% sucrose in 0.1 M phosphate buffer. Sections were cut at 30 μm with a freezing microtome in either the coronal or horizontal plane. Alternate sections were coated with emulsion (Kodak NTB2) for autoradiography or stained with the luxol fast blue,[28] Gallyas,[29] or Woelcke[28] methods to reveal the distribution of myelin. After 3 weeks the autoradiographs were developed (Kodak D-19) and analyzed under darkfield and lightfield illumination with a light microscope.

Four of the 10 Rhesus monkeys were normal animals.[30] Another 4 animals were deprived visually a few weeks after birth by suture of the right eyelids. This procedure was done in connection with unrelated experiments concerning amblyopia being conducted in my laboratory.[31] Early deprivation by eyelid suture has not been shown to affect the organization of fibers in the optic nerve or optic chiasm.[32] This conclusion is supported by the fact that similar results were obtained in the 4 normal monkeys and the 4 visually deprived monkeys. Therefore, the 4 deprived animals will be considered normal, intact monkeys for the purposes of this report.

The final 2 monkeys underwent enucleation of the right eye. Enucleation was performed using sterile technique under general anesthesia with ketamine (20 mg/kg intramuscularly) plus local anesthesia with retrobulbar lidocaine (2 mL of 1% solution with epinephrine, 1:100,000). Following surgery, buprenorphine (0.02 mg/kg intramuscularly) was given every 8 hours for 2 days to ensure analgesia. After a survival period of 6 months in the first animal, and 4 years in the second animal, [^{3}H]proline was injected into the remaining left eye. Ten days later the animals were perfused, and their tissues were processed as detailed above.

In addition, the primary optic pathway was labelled by [^{3}H]proline in 3 normal adult squirrel monkeys (*Saimiri sciureus*) from the California Regional Primate Research Center.[33] In each animal the tracer was injected into the right eye, as described for the Rhesus monkeys. Two specimens were cut horizontally, and 1 specimen was cut coronally.

I examined the optic nerves, optic chiasm, and optic tracts postmortem in 3 patients with a history of monocular enucleation. Information regarding each patient's clinical history is provided in the "Results" section. All specimens were fixed in 2% paraformaldehyde, sectioned horizontally at 30 μm, and processed for myelin using luxol fast blue, Woelcke, and Gallyas stains.

Finally, 3 patients were studied clinically after being referred for evaluation of monocular visual loss. In each patient I performed a complete neuro-ophthalmologic examination, including mapping of the visual fields with a Humphrey perimeter. The lesion reponsible for the visual loss was delineated by magnetic resonance imaging of the sellar region.

RESULTS

THE OPTIC CHIASM IN INTACT RHESUS MONKEYS

The optic nerve, optic chiasm, and optic tracts were labelled intensely by [^{3}H]proline in all animals. The heavy labelling occurred because of the large amount of [^{3}H]proline injected into the eye. The quantity we selected was actually intended for transneuronal labelling of striate cortex,

which requires about 10 times the amount of tracer used for labelling the primary optic pathway.[34] Parenthetically, we note that in every animal the cortical ocular dominance columns serving the injected eye were labelled completely in each hemisphere. This finding confirmed excellent uptake of the label by the entire retina. In the optic chiasm, the label appeared so intense that it could be seen easily under lightfield illumination. Darkfield illumination was also useful for analysis of the autoradiographs, especially to visualize unlabelled structures, like the optic nerve of the uninjected eye. However, darkfield illumination was so sensitive that light scattered from hotly labelled structures could be mistaken for actual label. For this reason, it was necessary to examine specimens under both lightfield and darkfield illumination to interpret accurately the pattern of autoradiographic labelling.

Figure 5 shows a representative section cut horizontally through the optic chiasm of a normal monkey after injection of [^{3}H]proline into the left eye. Fibers from the labelled nerve decussated by running directly across the optic chiasm into the contralateral optic tract. Wilbrand's knee was absent. As expected, the intensity of label was weaker in the optic tracts

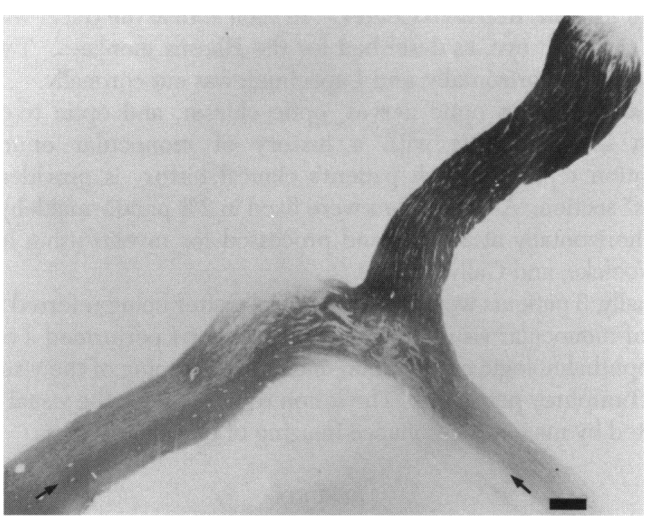

FIGURE 5A

Lightfield view of a horizontal section through the ventral portion of the optic chiasm after [^{3}H]proline injection into the left eye of a normal Rhesus monkey. Left is to reader's right, in this figure and in all subsequent figures. Note that crossing fibers from the left optic nerve do not enter the proximal right optic nerve. Along each optic tract, crossed fibers predominate medially, giving rise to a visible seam in the intensity of autoradiographic label (arrows). Bar = 1 mm, both panels same scale.

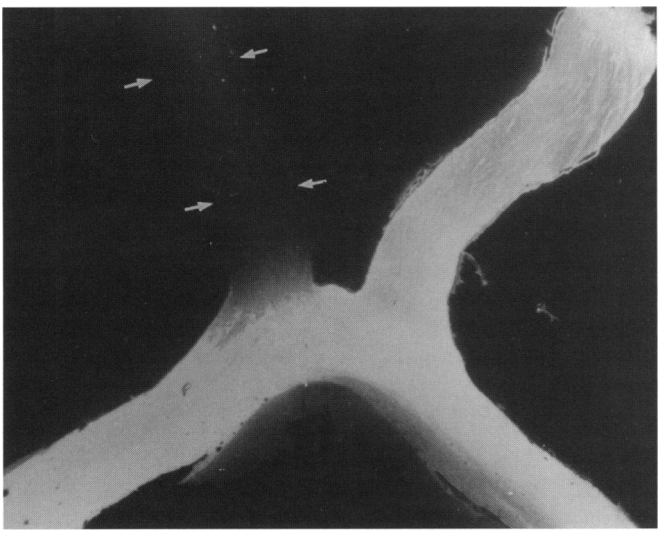

FIGURE 5B
Darkfield view of the same section, confirming absence of Wilbrand's knee, although glow emanating from the intense label in the optic chiasm casts some light upon the proximal right optic nerve. The unlabelled right optic nerve is seen faintly (arrows).

than in the left optic nerve, reflecting dilution of label by fibers from the unlabelled optic nerve. The right optic tract was labelled more intensely than the left optic tract, because the majority of the fibers in the optic nerve decussates, by a ratio of at least 53/47.[35] In the optic tract the integration of fibers serving each eye was incomplete. Crossed fibers predominated medially in the optic tract, whereas uncrossed fibers predominated laterally.

Figure 6 shows a horizontal section through the optic chiasm in another monkey after [^{3}H]proline injection into the left eye. At high power one can appreciate the interleaving of labelled and unlabelled fascicles, which Michel likened to the construction of a wickerwork basket.[36] No labelled fibers detoured into the optic nerve on the other side, confirming the result in the previous monkey. The optic chiasm was cut axially in 6 intact monkeys, yielding 45 to 60 serial sections in each animal. No section showed any evidence for Wilbrand's knee.

Figure 7 shows a series of coronal sections through the optic nerves and optic chiasm of an intact Rhesus monkey that received a [^{3}H]proline injection into the right eye. The most anterior section (Fig 7A,E), located 180 μm before the chiasm, contained no labelled fibers in the unlabelled optic nerve. The next section (Fig 7B,F) was cut right at the junction of

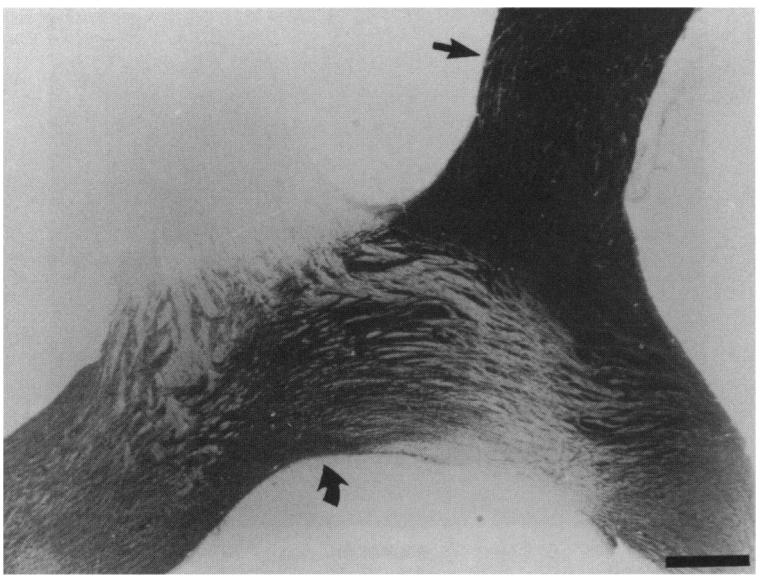

FIGURE 6
Axial section through the optic chiasm in another Rhesus monkey after [^{3}H]injection into the left eye showing dovetailing of labelled and unlabelled fasicles. No fibers from the labelled left optic nerve (arrow) enter the unlabelled right optic nerve. Note that posteriorly in the optic chiasm, crossed fibers predominate medially, giving rise to the so-called "posterior knee of Wilbrand" (curved arrow). Bar = 1 mm.

the two optic nerves. Again, no labelled fibers were seen in the unlabelled optic nerve. The next section (Fig 7C,G) passed through the optic chiasm 120 μm posterior to the fusion of the optic nerves. At this point, bundles of fibers were visible streaming across the chiasm from the labelled right side into the unlabelled left side. At 360 μm from the anterior pole of the optic chiasm (Fig 7D,H), the decussation was well under way. The optic chiasm was cut in the coronal plane in one other intact macaque. The same result was obtained: no labelled fibers entered the contralateral optic nerve.

THE OPTIC CHIASM IN INTACT SQUIRREL MONKEYS

Surprised by the absence of Wilbrand's knee in the Rhesus monkey, I decided to examine the optic chiasm in another species of primate. I chose the squirrel monkey, a small New World primate. Figure 8 shows an axial section through the middle of the chiasm after tracer injection into the right eye. The labelling closely resembled the pattern seen in the Rhesus monkey (compare with Fig 5). Wilbrand's knee was not present.

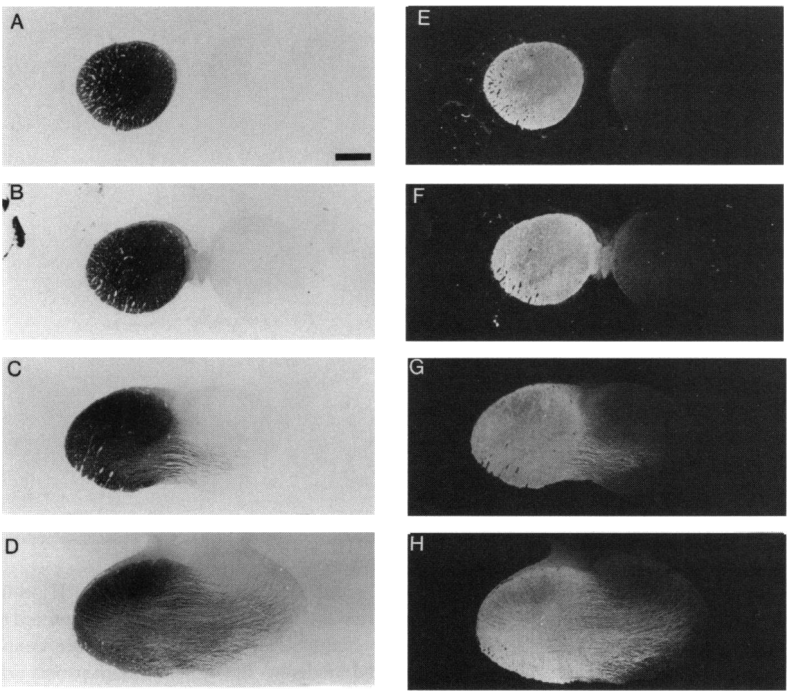

FIGURE 7

Matching lightfield and darkfield images of coronal sections through the optic nerves and optic chiasm of an intact Rhesus monkey after [^{3}H]proline injection into the right eye. At 180 μm (A,E) before the chiasm, no labelled fibers from the right optic nerve were present in the left optic nerve. Even as 2 nerves kissed (B,F), the left optic nerve remained devoid of fibers from the right optic nerve. The faint label seen in darkfield (F) along with the medial edge of the left optic nerve did not represent labelled fibers, but rather, an increased density of background grains caused by proximity to the strongly radioactive right optic nerve. At 120 μm after junction of the optic nerves (C,G), labelled fibers from the right optic nerve were seen coursing into the left half of the optic chiasm. At 360 μm from the anterior pole of the chiasm (D,H), much of the left chiasm was filled with labelled crossing fibers. Bar = 1 mm, all panels same scale.

In fact, labelled fibers from the right optic nerve assiduously avoided the anterior part of the optic chiasm on the left side.

THE OPTIC CHIASM IN THE MACAQUE AFTER SHORT-TERM ENUCLEATION

After failing to label Wilbrand's knee in normal animals, I hypothesized that enucleation of 1 eye might induce its formation. The right eye was removed under anesthesia in a juvenile Rhesus monkey. Six months later the left eye was injected with [^{3}H]proline. Autoradiographs through the optic chiasm showed no Wilbrand's knee, although labelled fibers were

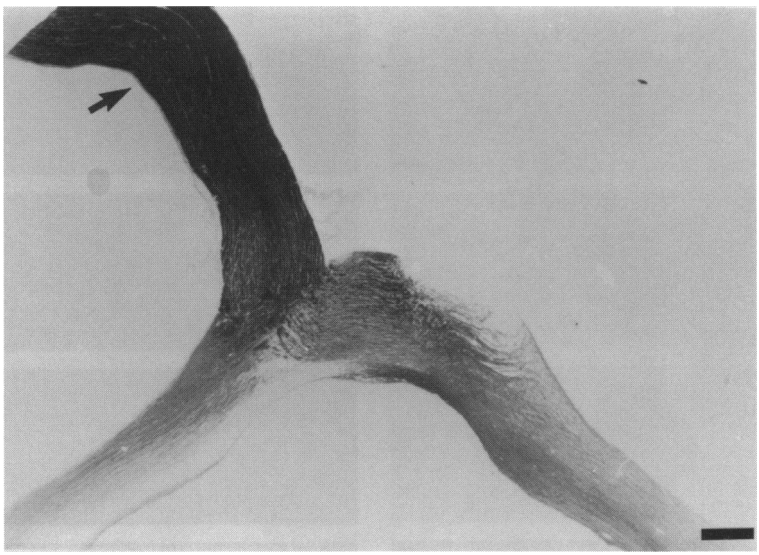

FIGURE 8A

Axial section through the optic chiasm in a normal squirrel monkey after [^{3}H]proline injection into the right eye. No labelled fibers from the right optic nerve (arrow) entered the left optic nerve. Just as in the macaque, the contralateral optic tract was more densely labelled, and crossing fibers tended to be located medially. Bar = 1 mm, both panels same scale.

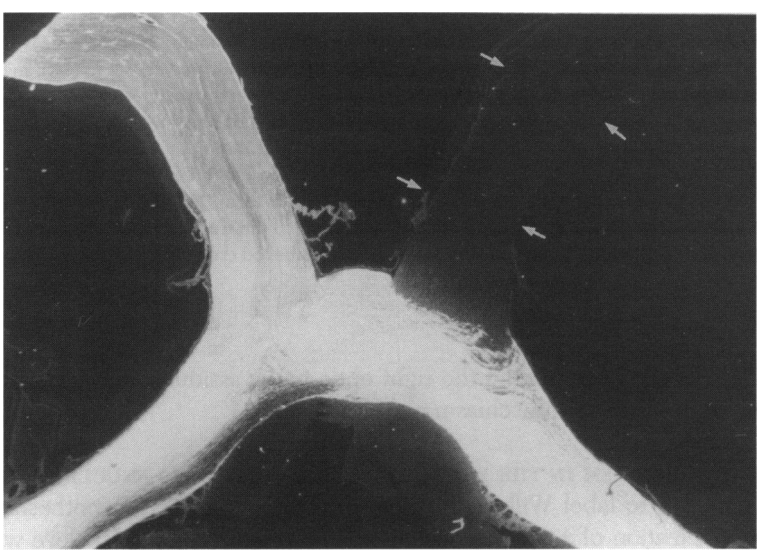

FIGURE 8B

Matching darkfield view, confirming absence of labelled fibers in the left optic nerve, which was only faintly visible (arrows).

drawn closer to the entry zone of the degenerating right optic nerve (Fig 9A). Myelin sections showed pallor of the right optic nerve, making it possible to distinguish between fibers of the normal eye and the enucleated eye (Fig 9B). The fiber arrangement of the optic chiasm seen with the myelin stain matched closely the pattern revealed by autoradiography.

The right optic nerve showed only a slight reduction in size, although it appeared pale in myelin preparations. The modest degree of shrinkage indicated that degeneration of the optic nerve requires much longer than 6 months to become complete.

THE OPTIC CHIASM IN THE MACAQUE AFTER LONG-TERM ENUCLEATION

In this monkey I waited 4 years after enucleation of the right eye before injecting [^{3}H]proline into the left eye. I theorized that Wilbrand's knee might develop if I allowed more time for advanced atrophy to ensue.

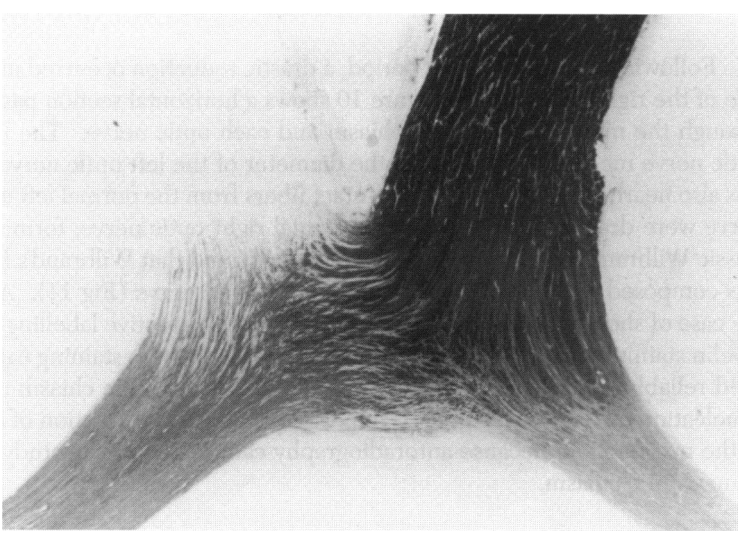

FIGURE 9A

Autoradiograph of the optic chiasm of a Rhesus monkey 6 months after enucleation of the right eye. The label from the left eye did not enter the right optic nerve, but it did draw closer to the entry site of the right optic nerve at the chiasm.

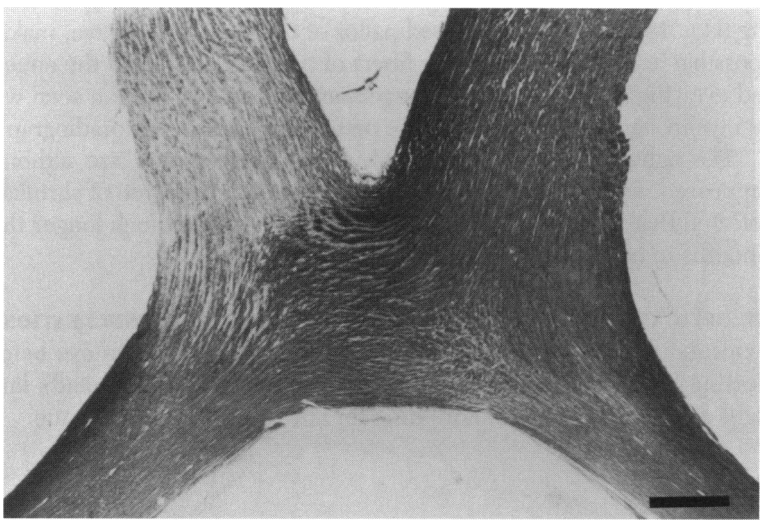

FIGURE 9B
Adjacent section processed with the Gallyas stain, showing loss of myelin in the right optic nerve, but not much reduction in size. Note the similarity between the pattern of fiber labelling by the myelin stain and the autoradiograph. Bar = 1mm, both panels to same scale.

Following a 4-year survival period, a drastic reduction occurred in the size of the right optic nerve. Figure 10 shows a horizontal section passing through the middle of the optic chiasm and each optic nerve. The right optic nerve measured only a third the diameter of the left optic nerve. It was also nearly depleted of myelin. Intact fibers from the normal left optic nerve were drawn 1.0 mm into the proximal right optic nerve, forming a classic Wilbrand's knee. Autoradiography confirmed that Wilbrand's knee was composed entirely of fibers from the left optic nerve (Fig 11). As in the case of short-term enucleation, the pattern of radioactive labelling and myelin staining was similar (Fig 11), indicating that myelin staining can be used reliably to chart the course of fibers through the optic chiasm after enucleation of 1 eye. This point is important for the interpretation of data in the next section, because autoradiography cannot be used to study the human optic chiasm.

ANATOMIC STUDIES OF THE HUMAN OPTIC CHIASM

The first patient (J.E.S.) was a 49-year-old man who developed pain and blindness in his left eye from a metastatic lung tumor. He died 5 months after the left eye was enucleated. Figure 12 shows an axial section through the optic chiasm. There was loss of myelin, but scarcely any reduction in

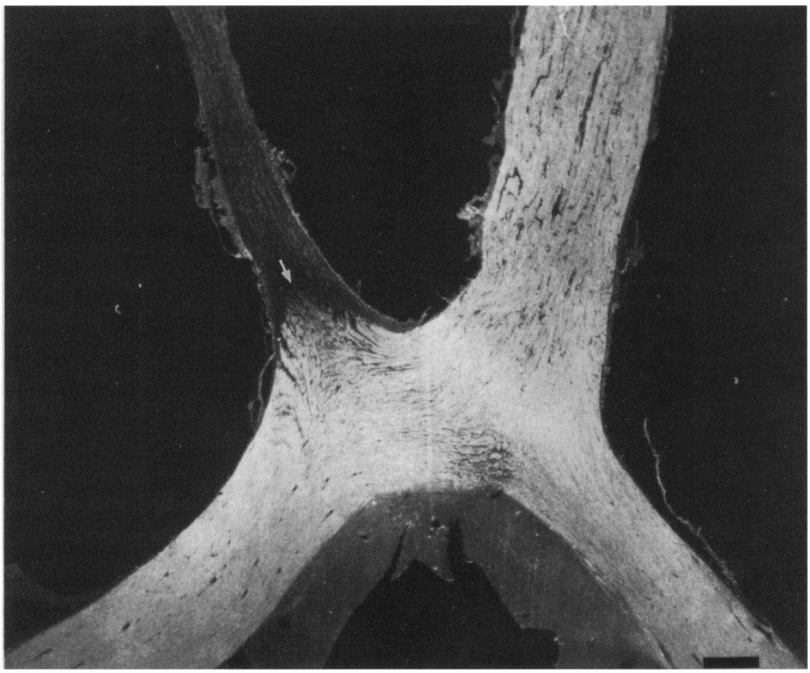

FIGURE 10

Distribution of myelin in the optic chiasm of a Rhesus monkey 4 years after enucleation of the right eye, revealed by illuminating a wet, unstained section with a darkfield technique that renders myelin bright.[37,38] The right optic nerve appeared nearly devoid of myelin and measured only 0.8 mm in diameter. By comparison, the left optic nerve was 2.4 mm in diameter (measurements were made along the top of the figure, where the nerves are truncated by the edge of the illustration). The section was cut through the middle of the nerves, chiasm, and tracts. Note that normal fibers from the left optic nerve entered the proximal right optic nerve (arrow), giving rise to Wilbrand's knee. Bar = 1 mm.

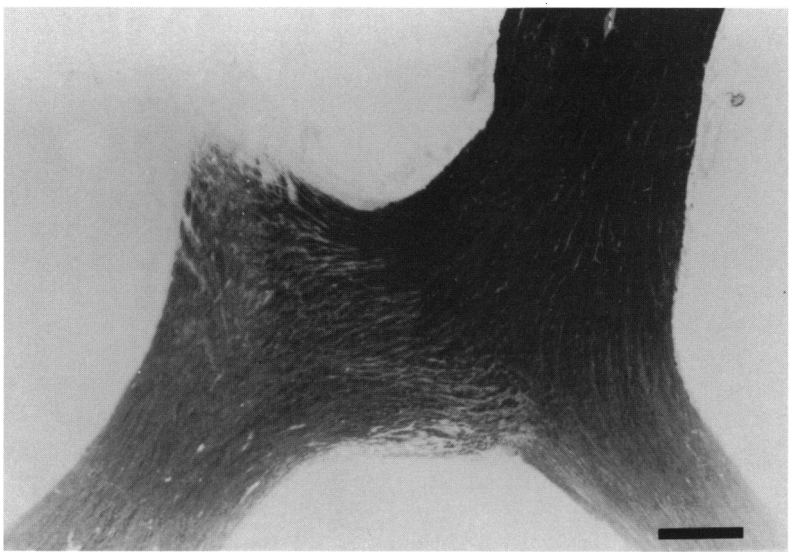

FIGURE 11A
Autoradiograph adjacent to Fig 10, showing labelled fibers from the left optic nerve creating Wilbrand's knee in the stump of the atrophic right optic nerve. Bar = 1 mm.

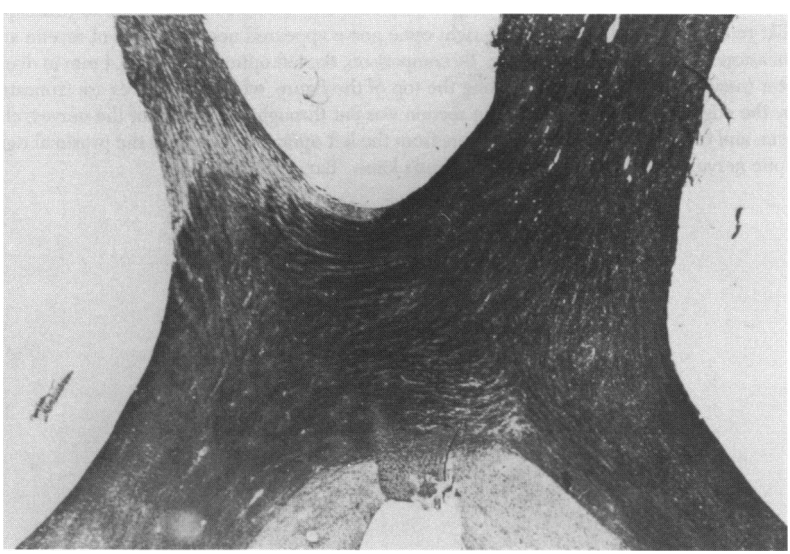

FIGURE 11B
Adjacent Gallyas section, showing Wilbrand's knee, revealed by loss of myelin staining in the right optic nerve. Note the good match between the myelin stain and the autoradiograph. Both panels to same scale.

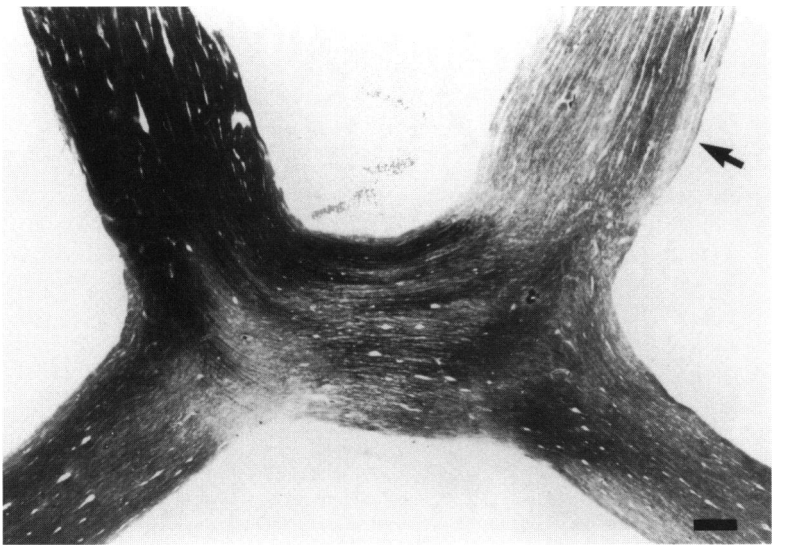

FIGURE 12

Patient J.E.S. died 5 months after loss of the left eye. A Woelcke stain showed loss of myelin in the left optic nerve (arrow), but no reduction in size. The optic chiasm was 12.0 mm wide. Wilbrand's knee was absent, but fibers from the right optic nerve were drawn closer to the proximal left optic nerve, an effect also seen in the macaque after a comparable survival period (see Fig 9). Bar = 1 mm.

the size of the left optic nerve. Wilbrand's knee was not present, but fibers from the intact eye did extend anteriorly into the left side of the chiasm, right up to the entry zone of the optic nerve. A similar effect was seen in the macaque 6 months after enucleation (compare with Fig 9).

The second patient (A.P.) was a 90-year-old woman whose right eye was enucleated because of a large choroidal melanoma. She died of systemic metastases 27 months later. There was more pronounced loss of myelin compared with the previous specimen, but still little shrinkage of the optic nerve (Fig 13). Fibers from the normal left optic nerve entered the proximal portion of the pale right optic nerve, giving rise to a small Wilbrand's knee.

The third patient (W.R.) was a 59-year-old man who died from a ruptured basilar artery aneurysm. His left eye had been enucleated 28 years previously because of a melanoma. Myelin stains showed pallor of the left optic nerve. It was reduced to less than half the normal diameter, except proximally, where fibers from the intact right optic nerve entered for a distance of 1 to 2 mm to give rise to Wilbrand's knee (Fig 14).

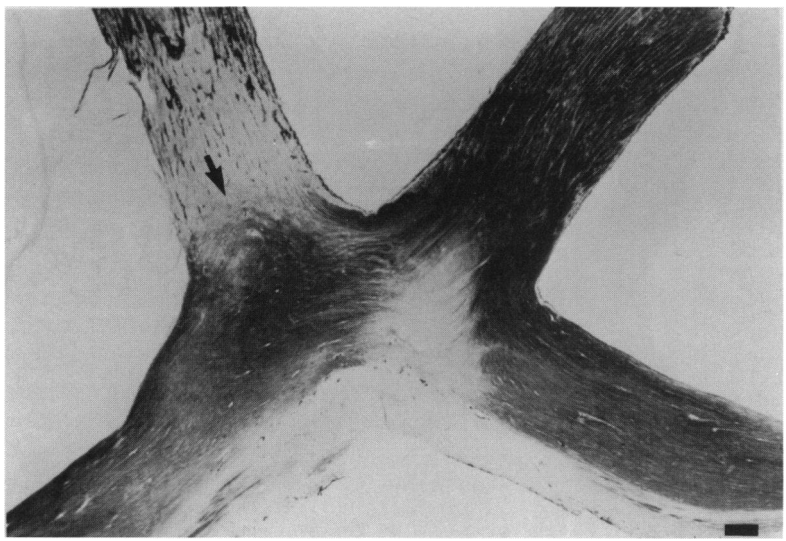

FIGURE 13

Patient A.P. died 27 months after loss of the right eye. The Woelcke stain revealed more pronounced atrophy of the affected nerve compared with the effect seen after only 5 months (see Fig 12). The optic chiasm was narrowed to 10.5 mm. A modest Wilbrand's knee had formed (arrow), extending anterior to the crotch of the chiasm, into the atrophic right optic nerve. Bar = 1 mm.

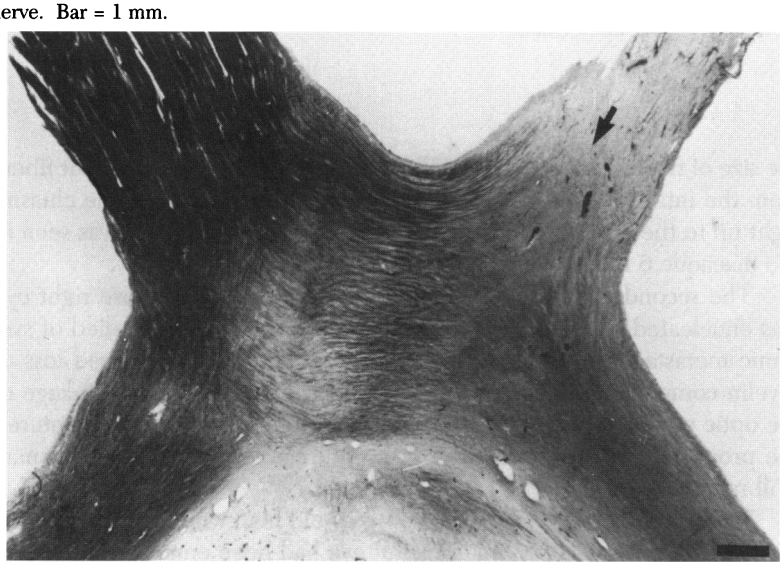

FIGURE 14

Patient W.R. died 28 years after enucleation of the left eye. The optic chiasm was reduced to a width of 9.25 mm. Compared with the previous two specimens involving relatively short-term enucleation, the optic nerve was severely shrunken, except near the chiasm, where fibers from the intact optic nerve entered about 1 mm to form a well-developed Wilbrand's knee (arrow). Woelcke stain. Bar = 1 mm.

CASE REPORTS OF PARASELLAR LESIONS

The next 3 patients were selected for description because their cases highlight issues regarding the anterior chiasmal syndrome that should be reconsidered in view of the preceding anatomic studies.

Case 1

Patient T.L.O. was a 30-year-old woman who experienced a decline in visual acuity to 20/400 in her left eye during the last trimester of pregnancy. Visual field examination disclosed a temporal hemianopia in the left eye and a hint of an upper temporal defect in the right eye (Fig 15). She was followed with a diagnosis of retrobulbar neuritis, until symptoms developed in her right eye. The visual acuity was still 20/20 in the right eye, but had fallen to hand motions in the left eye. Visual field examination showed a new temporal field defect in the right eye (Fig 16). I predicted a tumor at the anterior junction of the left optic nerve and chiasm, causing a left optic neuropathy and a temporal field defect in the right eye from injury to Wilbrand's knee. However, magnetic resonance imaging did not show a circumscribed lesion in this region (Fig 16). Instead, it revealed a large tumor, enveloping both optic nerves, flattening the optic chiasm, and extending posteriorly into the interpeduncular fossa.

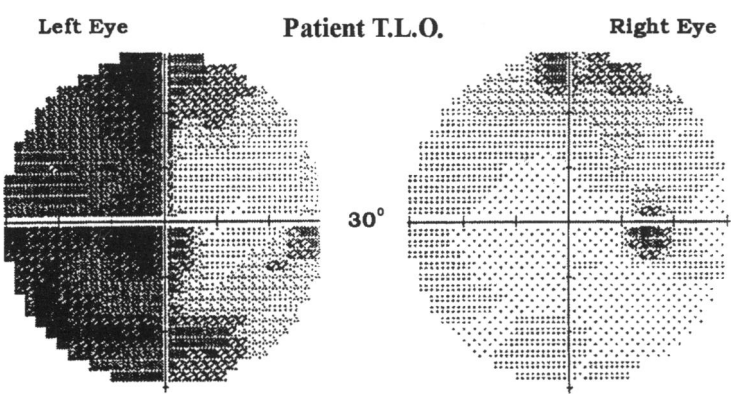

FIGURE 15

Patient T.L.O. lost vision in the left eye from presumed retrobulbar optic neuritis. Her 30-2 threshold visual fields performed with a Humphrey perimeter showed a temporal heminaopia in the left eye, with some involvement of the central field and the nasal field. The visual field of the right eye showed an early suggestion of an upper temporal defect. These fields correspond to the first pattern of visual field loss identified by Wilbrand (see Fig 3A).

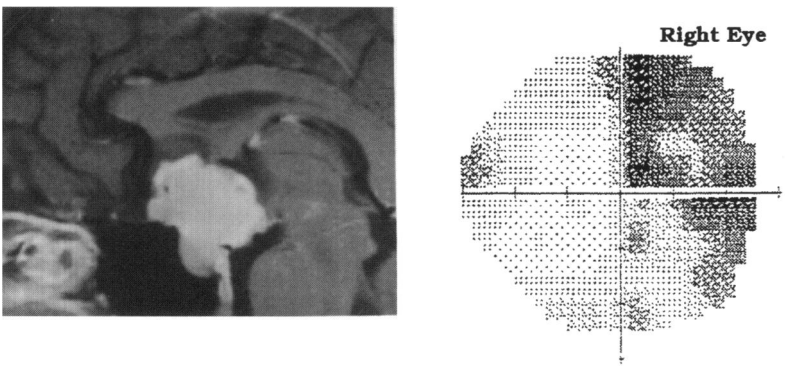

FIGURE 16

Left, Patient T.L.O. experienced progressive visual loss in the left eye, prompting a magnetic resonance imaging scan 3 years later. It showed a meningioma measuring 3.0 x 3.0 x 2.5 cm. The tumor filled the sellar region and crushed the optic chiasm, rendering it invisible. Right, Follow-up visual field examination showed complete field loss in the left eye (not illustrated) and progression of the temporal defect in the right eye. At this point, the visual fields resembled the second pattern identified by Wilbrand (see Fig 3B).

Case 2

Patient P.H.F. was an asymptomatic 58-year-old man noted to have cupping of the right optic disc on routine examination. Visual fields were performed searching for evidence of glaucoma (Fig 17). A junctional scotoma was found in the right eye; the field of the left eye was essentially normal. I expected to find a small lesion involving only the proximal right optic nerve. Instead, magnetic resonance imaging showed an large pituitary adenoma (Fig 18). In addition to compressing the right optic nerve, the tumor stretched and elevated the optic chiasm. Nonetheless, the visual field of the left eye was normal. This case was a reminder that a lesion causing a junctional scotoma is not necessarily small, nor confined to one optic nerve. It can be large and can compress the optic chiasm.

Case 3

Patient L.A. was a 37-year-old woman who developed blurred vision in the left eye. The visual acuity was 20/20 in the right eye and 20/70 in the left eye. There was a temporal hemianopia in the left eye and a smaller superior temporal defect in the right eye (Fig 19). Magnetic resonance showed a small meningioma of the tuberculum sellae compressing the left optic nerve (Fig 20). After its removal, the visual acuity and fields returned immediately to normal. This case served for years as the best example in my teaching files of Wilbrand's concept of the anterior chiasmal syndrome.

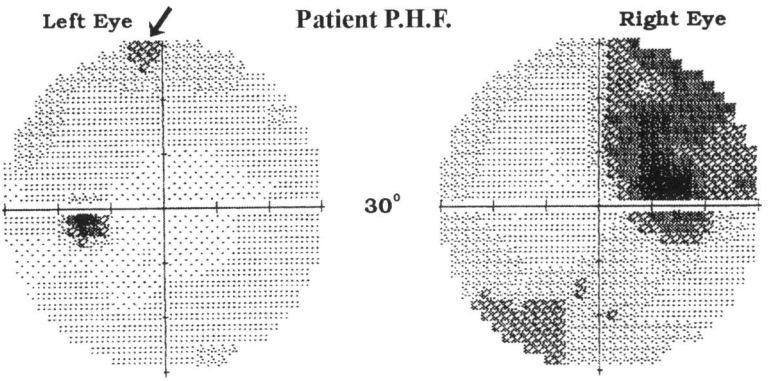

FIGURE 17

Patient P.H.F. had no visual symptoms. These 30-2 threshold visual field tests were obtained with a Humphrey perimeter because slight cupping of the right optic disc was noted upon routine examination. The visual fields show a classic junctional scotoma in the right eye. There was a single depressed point in the upper temporal field of the left eye (arrow), of uncertain significance. Classic teaching attributes this pattern of visual field loss to compression of only one optic nerve.

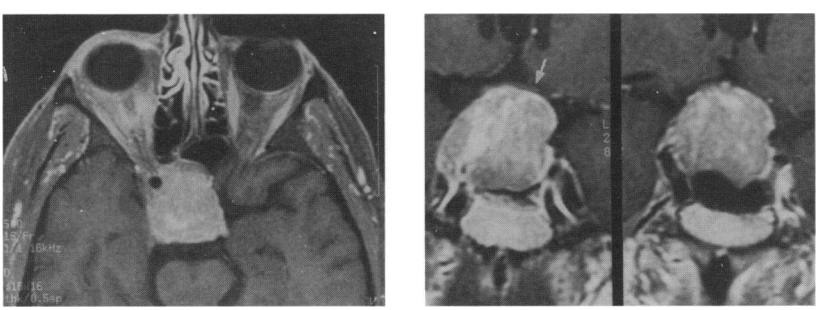

FIGURE 18

Left, Patient P.H.F. had 4.0 x 3.0 x 3.0-cm pituitary adenoma, which extended asymmetrically to the right side, causing the visual field defect shown above. Right, Two coronal views of the tumor at higher power, showing elevation and flattening of the optic chiasm (arrow). Although visual field examination suggested a prechiasmal locus for tumor, it proved to be a routine pituitary adenoma. The lesion compressed the optic chiasm, but visual field loss was confined essentially to the right eye.

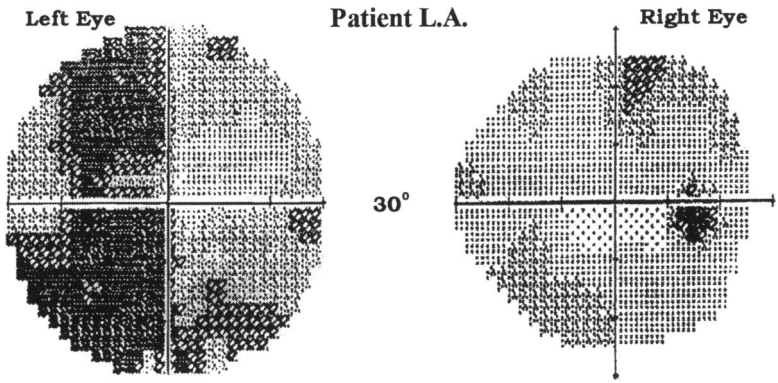

FIGURE 19
Patient L.A. had a temporal hemianopia in the left eye and a small superior temporal defect in the right eye. This is the classic pattern of visual field loss which Wilbrand associated with prechiasmal compression of one optic nerve (see Fig 3).

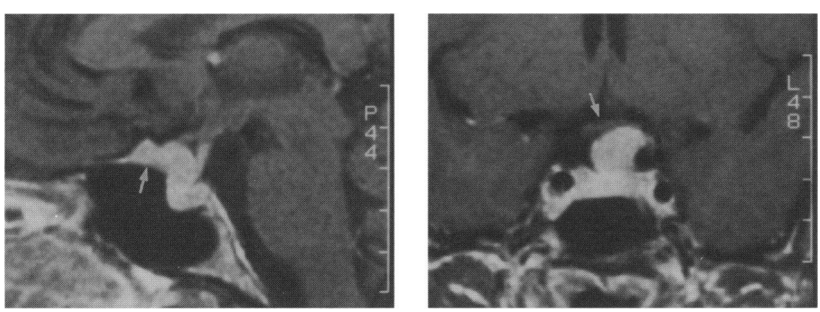

FIGURE 20
Left, Patient L.A. had a small tuberculum sellae meningioma (arrow), compressing the proximal left optic nerve, as seen in this sagittal magnetic resonance image. Right, Coronal view of the lesion, showing tilting of the optic chiasm (arrow). This early compression of the optic chiasm may explain the small superior temporal field defect in the right eye. Note that the previous patient (P.H.F.) had far more severe chiasmal compression, yet the visual field of his other (left) eye was less affected. The poor correlation between the degree of chiasmal compression and the size of visual field defects in these patients is a reminder that predicting the exact location and size of sellar tumors from analysis of the visual fields is a crude art.

The meningioma arose prechiasmally and caused a temporal field defect by compression of the left optic nerve. The "wedge" defect in the right eye could be explained by compression of Wilbrand's knee in the proximal left optic nerve. However, the tumor also compressed the left side of the optic chiasm, providing an alternative explanation for the temporal field defect in the right eye.

DISCUSSION

WILBRAND'S KNEE DOES NOT EXIST IN NORMAL SUBJECTS

I made intraocular injections of [^{3}H]proline in the monkey to label the fibers from one optic nerve by autoradiography. Wilbrand's knee was absent in all normal animals. Fibers decussating at the optic chiasm passed directly into the optic tract on the other side. They showed no tendency to detour into the other optic nerve before entering the optic tract. On the contrary, crossing fibers actually avoided coming near the entry zone of the other optic nerve in the anterior optic chiasm. These observations were made in serial sections through the optic nerves, chiasm, and tracts in 8 intact Rhesus monkeys and 3 intact squirrel monkeys. In each animal, a large injection of radioactive tracer was made into the eye, filling the fibers of the optic nerve intensely and completely. Effective labelling of all optic nerve fibers was confirmed by observing complete labelling of the ocular dominance columns in both striate cortices. Therefore, failure to detect Wilbrand's knee cannot be ascribed to weak or incomplete filling of the primary optic projection.

WILBRAND'S KNEE DEVELOPS AFTER MONOCULAR ENUCLEATION

In the monkey 6 months after enucleation, myelin staining was reduced but little physical shrinkage occurred in the optic nerve. Wilbrand's knee was absent, although crossing fibers from the intact nerve approached the entry zone of the degenerating nerve. Realizing that degeneration of the optic nerve might take years, rather than months, I repeated the experiment. By waiting 4 years, I was able to induce profound atrophy of the optic nerve and a typical example of Wilbrand's knee (Figs 10 and 11).

In the human, I demonstrated that Wilbrand's knee gradually emerges with progressively longer survival times following monocular enucleation. By analogy with my experiments in monkeys, I propose that Wilbrand's knee is absent in the normal human, but caused to form by monocular enucleation.

Loss of myelin allows one to differentiate between fibers of the intact eye and the missing eye by using simple histologic stains. Examination of such specimens led Wilbrand to his "knee." His mistake was to conclude that it represents a normal structure. He failed to consider seriously the

possibility that it might be an artefact induced by monocular enucleation. There is still no method available to distinguish between fibers of the left eye and the right eye in the normal human optic chiasm. Lipophilic carbocyanine dyes hold promise, but they do not diffuse far enough for this purpose.[39] Admittedly, I have no direct evidence that Wilbrand's knee is absent in the normal human optic chiasm. Until a suitable technique is developed, I am forced to rely upon indirect evidence to show that Wilbrand's knee is absent in normal humans. However, its absence in the normal monkey optic chiasm shifts the burden of proof to diehard defenders of Wilbrand's knee.

ORGANIZATION OF FIBERS IN THE OPTIC TRACT

In the monkey, the contralateral optic tract was more heavily labelled by [^{3}H]proline than the ipsilateral optic tract, because the majority of optic nerve fibers decussates (Figs 5 and 8). The exact ratio of crossed/uncrossed fibers is uncertain, but an estimate can be derived by measuring the territory occupied by each eye in striate cortex. In the normal macaque, 58% of layer IVc is occupied by the contralateral eye, and 42% by the ipsilateral eye.[40] A ratio of crossed/uncrossed fibers of 58/42 would be consistent with the relative density of autoradiographic label observed in the contralateral/ipsilateral optic tracts in our specimens. We also observed partial segregation of fibers from each eye in the optic tract, as reported previously by Reese and Cowey.[41,42] Ironically, this phenomenon was captured by John Taylor (Fig 1) in the first diagram of the primary optic pathway, although he exaggerated the degree of segregation. Partial segregation of left eye and right eye fibers undoubtedly explains the incongruity of field defects found in some patients with incomplete lesions of the optic tract.[43,44]

A MODEL FOR THE FORMATION OF WILBRAND'S KNEE

The following model is presented to suggest how Wilbrand's knee forms. It should be noted that after degeneration of one optic nerve, the other optic nerve remains normal in size. However, the optic chiasm shrinks, particularly in width. This shrinkage will shorten the path length of normal fibers from the intact eye that cross in the optic chiasm. It is unknown if axons passing through a structure undergoing a reduction in size have the capacity to shorten. If they are unable to take up the slack created by chiasmal atrophy, their extra length may herniate into the stump of the degenerating optic nerve on the other side, especially if this route offers relatively little resistance (Fig 21). This theory explains the gradual development of Wilbrand's knee, occurring in synchrony with degeneration of the optic nerve. It is remarkable that complete degeneration of the optic nerve takes so many years.

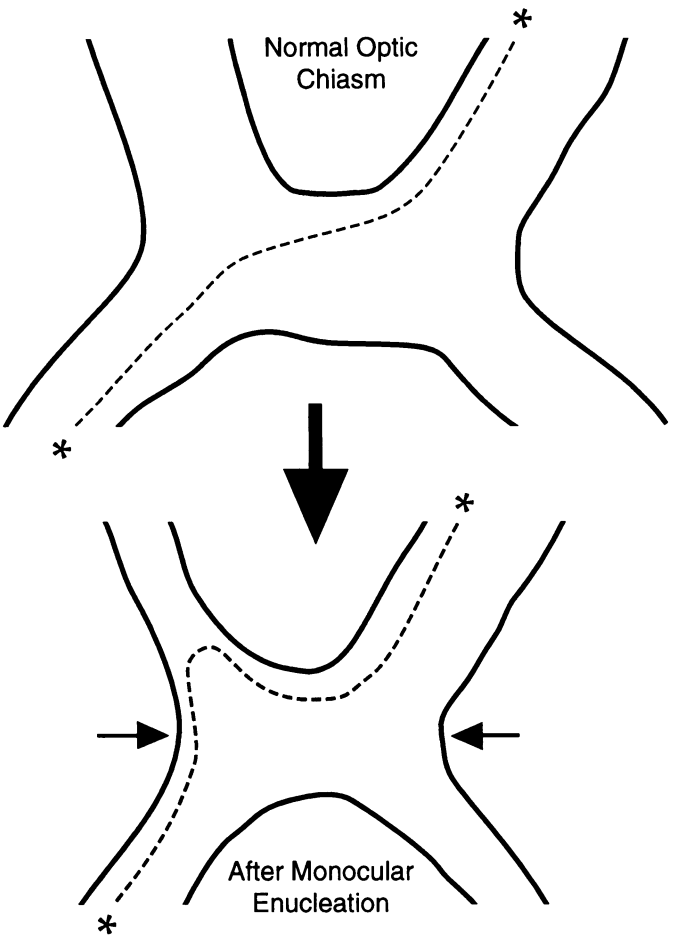

FIGURE 21
Schematic diagram suggesting how degeneration of one optic nerve might lead to formation of Wilbrand's knee in the primate optic chiasm. A single axon represents the path followed by decussating fibers. Years after loss of one eye, the optic chiasm is reduced substantially in width. This shrinkage shortens the length of path that fibers must follow as they cross the optic chiasm. The slack created by chiasmal atrophy may cause buckling of healthy fibers into the stump of the atrophic optic nerve. In this model, the length of a representative axon between the two points marked by the asterisks is identical before and after monocular enucleation.

THE ANTERIOR CHIASMAL SYNDROME

In a textbook catalogue of field defects, Wilbrand described a stereotypic pattern of visual field loss that has become known as the anterior chiasmal syndrome. It consists of a temporal hemianopia (Fig 3A) or global field

depression (Fig 3B) in 1 eye, accompanied by a superior temporal field defect in the other eye. Wilbrand ascribed the superior field defect in the other eye to compression of "knee" fibers. His idea was clever, but it was never supported by clinical evidence. Wilbrand's knee extends only about 1 to 2 mm into the contralateral optic nerve. A blunt lesion like a tumor would be unlikely to compress the proximal 2 mm of the optic nerve, without direct involvement of the optic chiasm. In a later figure, Wilbrand drew a 5-mm "knee," making such a phenomenon more plausible (Fig 4). However, this depiction of the "knee" was fanciful and misleading.

In 1929 Cushing and Eisenhardt[45] published a classic study of patients with optic atrophy from tuberculum sellae meningioma. Tangent screen visual fields in each patient were correlated with detailed anatomic drawings made intraoperatively. Many of the patients had typical visual fields of the anterior chiasmal syndrome. However, their surgical exploration revealed large tumors, involving the optic chiasm and at least 1 optic nerve. No patient had a lesion limited strictly to the tuberculum sellae, involving 1 optic nerve only. The study by Cushing and Eisenhardt provided no support for Wilbrand's scheme. Instead, it showed that the anterior chiasmal syndrome arises from combined compression of the optic nerve and chiasm.

I am not aware of any published cases with adequate documentation showing the anterior chiasmal syndrome from the mechanism suggested by Wilbrand, namely, compression confined to 1 optic nerve. For many years, I used the case of L.A., the third patient described in the "Results" section, to exemplify how injury to Wilbrand's knee causes the anterior chiasmal syndrome. However, I now realize that her superior temporal wedge defect in the other eye was due to early chiasmal compression, not to Wilbrand's knee.

Figure 22 explains how the visual field defects of the anterior chiasmal syndrome may arise from separate components produced by compression of the optic nerve and the optic chiasm. In this simulated example, the temporal hemianopia in the right eye from chiasmal compression is obscured by the larger field defect produced by nerve compression. The degree of chiasm versus nerve compression may vary from patient to patient, producing the gamut of field defects seen in the anterior chiasmal syndrome.

LIMITED LOCALIZING VALUE OF THE ANTERIOR CHIASMAL SYNDROME

The anterior chiasmal syndrome does not imply a small lesion localized to the junction of 1 optic nerve with the optic chiasm. It signifies only that the optic nerve and the optic chiasm are both involved. The lesion can be large (patient T.L.O.) or small (patient L.A.). It may have originated at the optic nerve/chiasm junction (eg, tuberculum sellae meningioma), but in

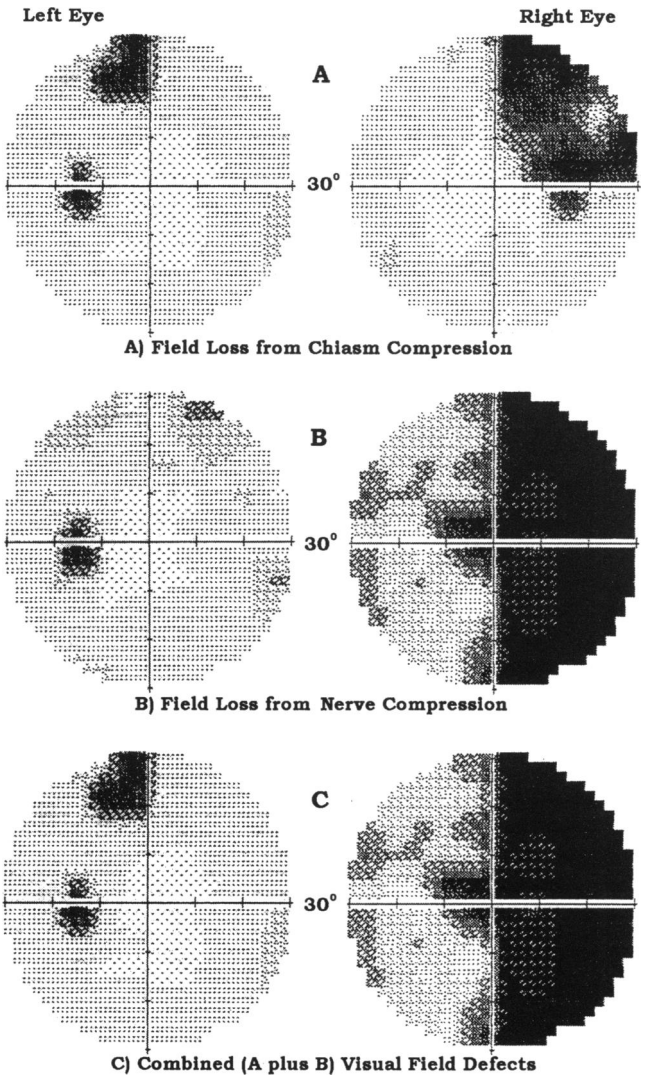

FIGURE 22

Visual fields simulated on a Humphrey perimeter to show how the visual field loss from (A) compression of the optic chiasm and (B) the optic nerve can be combined to explain (C) the anterior chiasmal syndrome. Depending upon the relative degree of optic nerve versus optic chiasm compression, a spectrum of visual field defects may be encountered. In this case, the temporal defect in the right eye from chiasmal compression is overshadowed by the temporal hemianopia from optic nerve compression. Although the pattern of visual field loss seen in the anterior chiasmal syndrome usually is attributed by clinicians to a small, prechiasmal lesion, in fact the majority of cases arises from large pituitary adenomas.

fact the majority of cases are caused by adenomas arising from the pituitary fossa. As Trobe and colleagues[46] were first to show, junctional patterns of visual field loss are extremely common with pituitary adenoma. They also stressed that most patients with visual symptoms report trouble in only 1 eye. In a sense, the term "anterior chiasmal syndrome" is a misnomer, because it occurs so often from a routine pituitary adenoma. However, it continues to be useful as shorthand for "an optic neuropathy or temporal hemianopia in 1 eye plus a superior temporal defect in the other eye produced by combined compression of the optic chiasm and 1 optic nerve."

A pure junctional scotoma was defined by Traquair[16] as a temporal field defect in 1 eye only. This pattern of visual field loss is rare. It is usually attributed to a circumscribed prechiasmal lesion impinging upon the medial aspect of 1 optic nerve. However, the case of P.H.F. (see "Results") shows that a junctional scotoma can arise from a large pituitary adenoma. In fact, most cases of junctional scotoma are caused by pituitary adenomas.[47] It is unclear whether the temporal hemianopia in such cases arises from compression of the optic nerve or the optic chiasm.

We still do not understand the curious vulnerability of crossed fibers to compression of the optic chiasm. Hedges[48] inflated balloons under the optic chiasm in fresh cadavers and showed that crossed fibers are stretched more than uncrossed fibers by expansion of a sellar mass. His mechanical hypothesis was criticized as simplistic,[49] but it may be right. Little is known about how tumor compression alters the fiber arrangement of the optic chiasm. There is no evidence that it induces formation of Wilbrand's knee. To the contrary, Wilbrand's knee appears to develop in response to shrinkage of the optic chiasm, rather than stretching (Fig 21). However, it would be helpful to learn more about how tumor compression disrupts the organization of fibers in the optic chiasm.[50]

Wilbrand's knee has served a useful purpose in the past by discouraging neurosurgeons from approaching the optic chiasm too closely when resecting unilateral optic nerve tumors. Such a practice is still wise. Tissue may be devitalized for several millimeters beyond a surgical incision. Moreover, Wilbrand's knee may develop in the optic chiasm of a patient with a unilateral optic nerve tumor like a glioma or a sheath meningioma, because of optic nerve degeneration.

In the past, neuro-ophthalmologists have overestimated their ability to localize precisely sellar lesions on the basis of visual field examination. Before the era of modern neuroimaging, complex rules were devised to pinpoint chiasmal lesions in order to guide the neurosurgeon to the best surgical approach. These rules were often unreliable, because they were based upon misconceptions regarding the arrangement of fibers and the degree of retinotopic order in the optic chiasm. In an elegant study,

Naito[51] has shown that the macaque optic chiasm contains only gross retinotopic order. For the physician in practice today, the main challenge is simply to recognize the telltale clue of a temporal hemianopia, and to realize that most patients with visual loss from a chiasmal lesion will be aware of symptoms in only 1 eye. This history may mislead the clinician, especially if the visual fields are not tested by formal perimetry. For the scientist, our work simplifies the task of explaining how fibers decide whether to cross in the optic chiasm. In the embryo the growth cones of navigating fibers are probably guided through the optic chiasm by chemotropic cues.[52-56] It will no longer be necessary for investigators to explain why ventral crossing fibers meander for several millimeters into the wrong optic nerve, before heading back in the right direction.

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