

THE WAGNER SYNDROME VERSUS HEREDITARY ARTHROOPHTHALMOPATHY*

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INTRODUCTION

IN 1938 WAGNER¹ DESCRIBED A SWISS FAMILY IN WHICH A DISORDER SHOWING VITREAL and retinal changes was inherited in an autosomal dominant manner. He coined the term "degeneratio hyaloideo-retinalis hereditaria." At the later suggestion of Alexander and Shea,² the eponym "Wagner disease" was applied to a series of patients who showed a vitreal degeneration in association with an increased incidence of retinal detachments. Since then, retinal surgeons have used the term Wagner disease for patients who develop retinal detachments that are presumably caused by vitreous traction due to an inherited abnormality of the vitreous. The original family report by Wagner¹ was followed up by Böhringer et al,³ and is being reexamined by Stoll.^{3a} The disease was classified by Ricci⁴ under the vitreoretinal degenerations.

Wagner¹ described 18 affected persons, ranging in age from 5 years to 42 years. After the later evaluation by Böhringer et al,³ the pedigree included 28 patients in five generations. None of the patients of Wagner's original family had had a retinal detachment, and none were observed in the later follow-ups. For statistical reasons, it seemed unlikely that these people suffered from the same disease that American retinologists refer to as Wagner disease. However, after reading the early publications on the Wagner syndrome, it was also unclear exactly why the patients lost vision.

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I therefore requested, and was kindly given permission to visit the eye department of the University of Zürich (Professor R. Witmer, Director), where patients of this family are still under follow-up.

CASE REPORTS

I examined six members of the original pedigree, one of whom had earlier been thought to be affected³ but on our reexamination proved to be normal. Thus, we were left with five patients whose years of birth ranged from 1923 to 1953. These five patients had been examined earlier by Wagner¹ and/or Böhringer et al³ (Fig 1). In addition, Prof Wagner provided us with one histologic slide from one eye of a patient from his original family.

CASE 1

This 29-year-old patient (Patient V/18 in Fig 1; V/16 in Ref 3) has worn glasses since age 12 or 13 years, with normalization of vision. At about age 20 she was diagnosed as having an exotropia. On ocular evaluation her visual acuity was: OD, 20/40 with $-4.25 + 0.75 \times 100$ and OS, 20/30 with $-3.25 + 0.25 \times 65$. She had a large positive angle kappa. Corneal diameters were 10 mm each. The keratometer readings were: OD, $45.0/47.5 \times 100$ and OS, $45.8/48.0 \times 65$. Intraocular pressures by applanation tonometry were 16 and 18 mm Hg in the right and left eyes, respectively. There were shallow anterior chambers, with grade 1 open angles. Slit lamp examination showed posterior cortical opacities that were compatible with the visual acuity. The vitreous was fluid, with occasional strands. The macula and optic disc had been dragged temporally in both eyes. The retinal vessels, especially the arterioles, were narrow. A few isolated round pigment spots were present, and also a vitreous condensation line overlying the equatorial retina. The vitreous membrane was partly fenestrated. The physical examination was unremarkable.

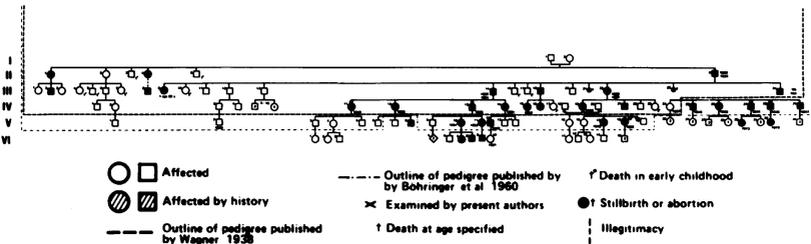


FIGURE 1

Pedigree of family originally described by Wagner¹ and further described by Böhringer et al.³

CASE 2

This 36-year-old patient (Patient IV/28 in Fig 1; IV/28 in Ref 3) was known to have visual problems since age 5 or 6 years. He has experienced a recent subjective decline in visual acuity. In 1982, his acuity was 20/30 OU with plano + 0.25 × 180 and -0.75 + 1.50 × 5. Intraocular tensions on applanation were 22 and 19 mm Hg, respectively. There was a large positive angle kappa. Stereo acuity was noted to be 50 seconds of arc. The corneal diameters were 10.5 mm each. On slit lamp examination and Goldmann three-mirror lens evaluation, he had an early posterior cortical cataract OU, vitreous liquefaction, and signs of early chorioretinal atrophy with dragging of the macula, OU.

CASE 3

This 38-year-old man (Patient IV/27 in Fig 1; IV/27 in Ref 3) was noted to be myopic in the first grade (RE, -5.00; L, -4.00). He developed painless, progressive loss of vision during the past 8 or 10 years and had a cataract extraction in the left eye in 1981 and in the right eye in 1982. The visual acuity OU was 20/20 with his contact lenses. On slit lamp examination the anterior vitreous face was visible, and there was a posterior vitreous detachment with almost totally liquefied vitreous. On Goldmann three-mirror lens evaluation he had a membranous strand of vitreous, with a posterior attachment that proceeded forward and inserted into the inferotemporal retina. This membrane was avascular. No circular membrane was present. His physical examination was normal.

CASE 4

This 59-year-old woman (Patient IV/11 in Fig 1; IV/11 in Ref 3) had worn glasses since before she started school, and she had never had normal night vision. In 1975 she had bilateral cataract extractions six months apart. Her electroretinogram (ERG) that year showed a reduced b wave and delayed implicit time. On ocular evaluation in 1982 her visual acuity was OD: 20/25 with +10.00 and OS: 20/30 with +10.25 + 0.25 × 60. Intraocular pressures on applanation were 15 and 14 mm Hg. Corneal diameters were 11.5 mm OU. Keratometer readings were: OD, 42.5/43.0 × 180 and OS, 42.5 sphere. On slit lamp examination she was bilaterally aphakic, with an optically empty vitreous cavity in both eyes. On fundus examination she had temporal pallor of the optic nerve, with striking chorioretinal atrophy involving the posterior pole but sparing the macular area. In the peripheral retina of both eyes she had large areas of vitreous condensation, and in the left eye this formed an almost total circular band (Fig 2 A and B). In both eyes, there were areas of sheathing of the retinal vessels and of lattice degeneration.

CASE 5

This 54-year-old man (Patient IV/13 in Fig 1; IV/13 in Ref 3) has had left strabismic amblyopia all his life. He has never had normal night vision, and he has had slowly progressive loss of vision in his right eye since age 35. The left lens was extracted in 1967, and the right lens in 1968. On ocular evaluation in 1982 his visual acuity

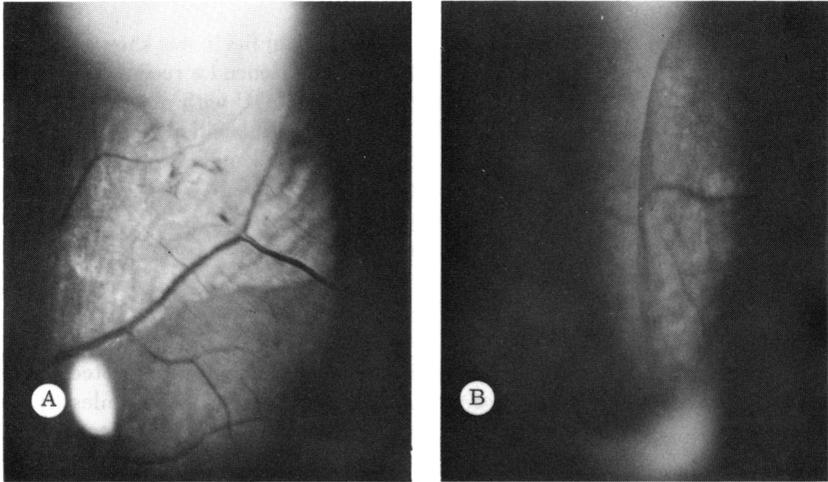


FIGURE 2

Fundus views of patient IV/11 (case 4) seen through Goldmann three-mirror lens. A: Area of transmission of normal appearing retina and B: area resembling retinitis pigmentosa.

was 20/40 in the right eye and counting fingers at 3 feet with a $+9.50 + 1.25 \times 40$ correction OD and balance lens OS. Corneal diameters were 10 mm OU. His intraocular tensions on applanation were 19 and 20 mm Hg. On slit lamp examination the patient was aphakic. In the right eye two parallel membranes could be seen in the vitreous cavity, and these probably corresponded to the anterior and posterior vitreous face. On fundus examination he had a pale optic nerve with constricted retinal vessels, and diffuse chorioretinal atrophy out to the midperiphery, with a slightly more normal macular area and far periphery. At the area of the equator there was vitreous condensation in a circular band (Fig 3 A and B). A visual field in 1982 showed a 5 degree central field to an I/4 test object with a residual peripheral field to a V/4 test object in the right eye, and similar but even more severe changes in the amblyopic left eye (Fig 4 A, B, and C). Dark adaptation studies performed at various times since 1965 showed an elevated final rod threshold with an earlier normal but later abnormal rod cone break (Fig 5 a, b, and c). In 1965 a dark adapted ERG showed b waves of 60 microvolts. In 1979 there were markedly reduced rod and cone responses with a delayed b wave implicit time (Courtesy Dr G. Niemeyer). The physical examination was unremarkable.

Prof Wagner kindly sent us a histologic preparation obtained from the eye of an additional family member (III/24 in Fig 1; III/24 in Ref 3). This patient had total bilateral lens dislocation. The lens dislocated into the vitreous cavity in the right eye, and on several occasions into the anterior chamber in the left eye. He developed secondary glaucoma in the left eye

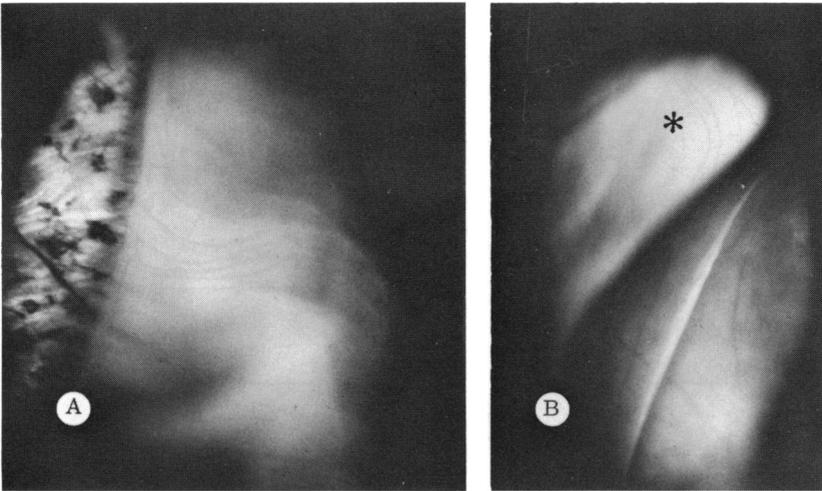


FIGURE 3

Fundus view of patient IV/13 (case 5) seen through the contact lens. A: Area of chorioretinal atrophy with pigment migration demarcated by the broad whitish membrane. B: Different area of same eye showing sharply delineated membrane, seen through sector iridectomy (asterisk marks the iris).

and purulent spontaneous perforation of a corneal ulcer led to enucleation. On histologic examination, there were several adhesions between the retina and choroid (Fig 6 A and B), the choroid itself showed large hemorrhagic detachments. The retina was thinned in all quadrants, and in part was reduced to a glial membrane. In other areas photoreceptor cells could be identified. There was perivascular pigment migration resembling retinitis pigmentosa (Fig 7 A and B).

Using data from the descriptions by Wagner,¹ Böhringer et al,³ and our own data, the following natural history can be summarized for this syndrome. Patients have mild night blindness in early childhood. At school age, a mild myopic prescription will normalize the visual acuity. The visual status remains stable until the age of 30 to 40 years, when the progressive developments of posterior cortical and posterior subcapsular cataracts greatly reduce the visual acuity. After cataract extraction, visual acuities of 20/20 were obtained in patients in the present generation. In previous generations, patients did not regain useful visual acuities after lens extractions. The causes of lack of recovery of vision after cataract surgery ranged from postoperative glaucoma to optic atrophy to chorioretinal degeneration, but the causes did not include retinal detachments. This slowly progressive chorioretinal degenerative disease leads to ring

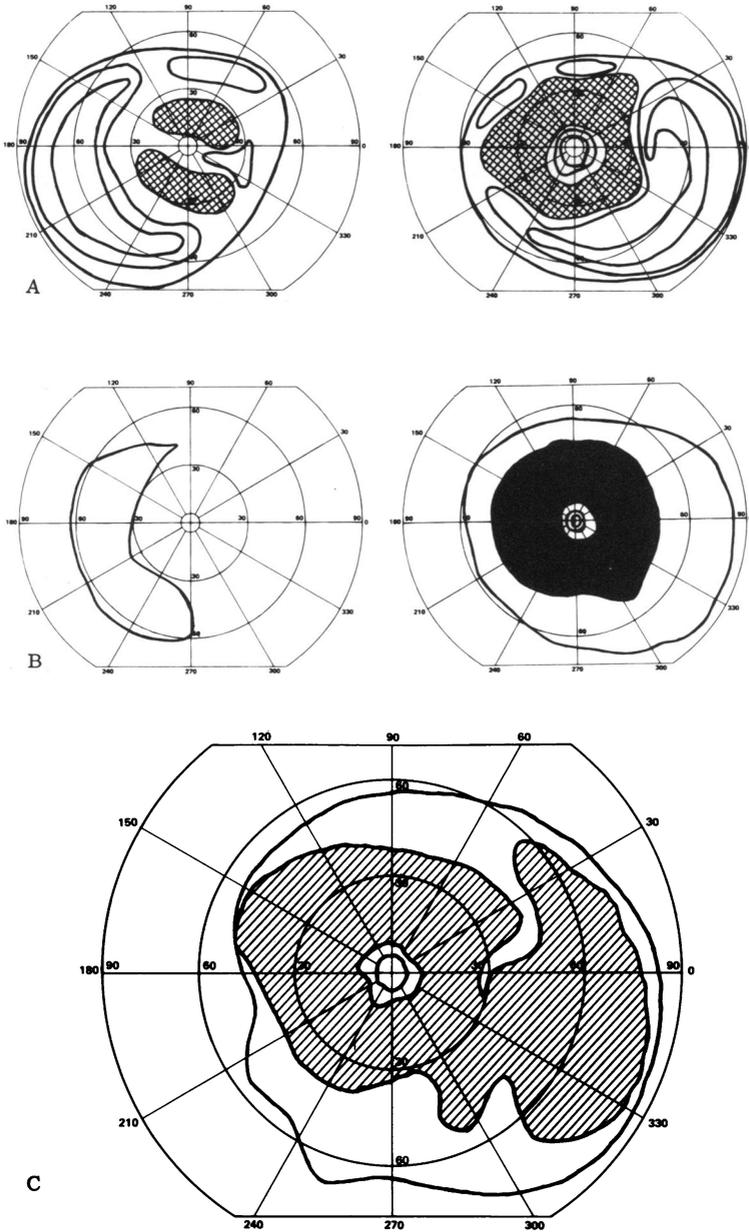


FIGURE 4

Progressive visual field loss during nine years in case 5. A: Left and right eye, respectively, in 1967. B: Left and right eye in 1976. C: Right eye in 1982.

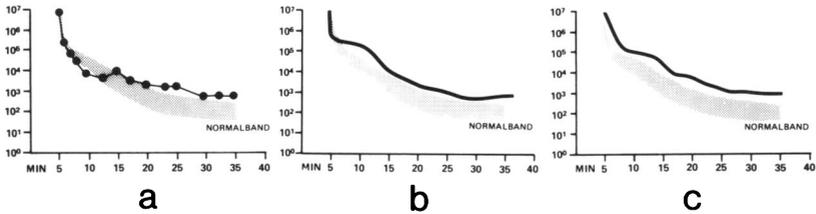


FIGURE 5

Dark adaptation rates in case 5 in a: 1965, b: 1967, and c: 1976, showing rod and cone involvement. Final rod threshold is only one log unit elevated, thus reflecting contribution of far peripheral retina to final level.

scotomata and presumably later loss of central visual acuity. Case 5 is now 54 years of age, and his visual field is constricted to a 5-degree field to a I/4 test object on the Goldmann perimeter, with residual peripheral islands (Fig 4). Considerable vitreal degeneration was a prominent feature in all patients with an optically empty vitreous cavity, in which isolated strands of vitreous were visible. Dense whitish membranous material was aggregated at the equator near the retina. At times, the demarcation was sharp, but it could be indistinct and progressively leading into normal retina. Dragging of the macula was noted in two patients, and a microcornea of 10.0 mm was seen in two members and assumed by the family members to be part of the ocular pathology. Dislocated lenses were reported in two patients by Wagner.¹ Thus, the disorder described by Wagner is characterized by progressive vitreoretinal degeneration with early myopia and a predominance of vitreal degeneration. The development of presenile cataracts requiring surgery at about age 40 years will temporarily reduce visual acuity, but normal acuities may be

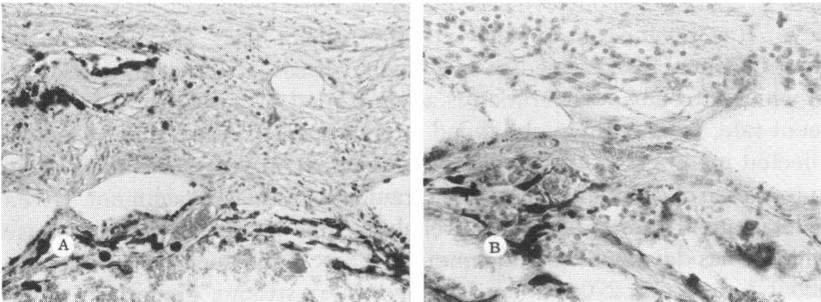


FIGURE 6

A: Chorioretinal adhesions with photoreceptor loss and pigment migration around a sclerosed vessel (H&E, $\times 200$). B: Chorioretinal adhesion at higher magnification (H&E, $\times 360$).

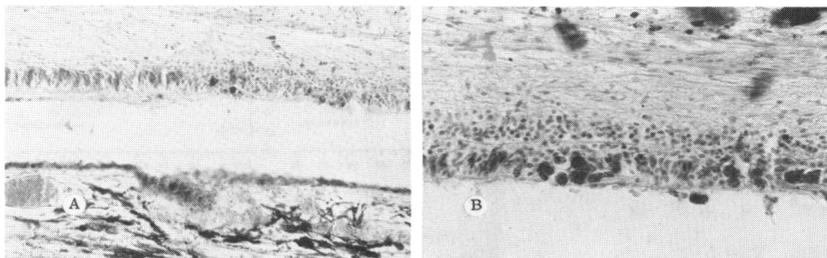


FIGURE 7

A: Area of transition between photoreceptor preservation and loss with preretinal pigment migration (H&E, $\times 150$). B: Shown at higher magnification (H&E, $\times 300$).

achieved after successful surgery, to be followed ultimately by visual loss to a level ranging from legal to total blindness as the result of a progressive chorioretinal atrophic process. This progressive chorioretinal atrophy, resembling retinitis pigmentosa, shows its first manifestation as night blindness in childhood.

Roentgenograms of the epiphyses of the spine, of the proximal femora, of the wrists and ankles were obtained on three patients. These roentgenograms were interpreted as normal. No patient had a cleft palate, cleft uvula, or a submucous cleft. There was no evidence of cardiovascular disease, premature arthritis or arthrosis, or of mid-facial hypoplasia. The patients considered themselves to be in excellent health except for their visual problems.

DISCUSSION

Five members of Wagner's original family were examined, and the histologic preparation of one eye was reviewed. What disease do these patients have? It is much easier to state what they do not have. They do not have what is commonly referred to as "Wagner disease,"²—that is, a disorder in which vitreous degeneration is accompanied by a 50% retinal detachment rate, frequently in childhood or adolescence. At present 28 known affected members in the family are older than 30 years, and there is no known case of spontaneous (or even traumatic) retinal detachment. Given a detachment rate of 50%, the probability that by chance none of these affected has developed a detachment is $0.5 \times E_{28}$ which is equivalent to about 1 chance in 270 million. However, very striking similarities to the entity of vitreoretinal degeneration with retinal detachments exist.² The vitreous degeneration looks virtually identical to, or actually more severe, in Wagner disease. There is an "optically empty" vitreous, with vitreous

veils that proceed off from a circular band at approximately the equator (Fig 2). There are perivascular pigment accumulations, sheathing, and areas of lattice degeneration (Fig 3). The retinal degenerative changes are much worse than those seen in vitreoretinal degeneration with retinal detachment. These changes are the predominant features in Wagner disease. Patients complain of having had night blindness since early childhood. They may have normal visual acuity, although one of these patients had an amblyopic eye with an esotropia. Dark adaptation rates (Fig 5 a, b, and c) and also final thresholds as measured by Wagner¹ showed a slowly progressive decline, with progressive involvement of rods and later of cones. At age 54, one patient has a remaining 5-degree central field with a residual peripheral field using the I/4 test object (Fig 4). His ERG showed greatly reduced responses. At this stage his chorioretinal changes cannot be differentiated from those seen in patients with typical retinitis pigmentosa, although the vitreous changes (as previously stated) are much more severe than those seen in retinitis pigmentosa.

What causes the vision loss in these patients? A typical case is that of AH, born in 1860. He was totally blind when he died at age 65. No attempt at lens extraction was done on this patient. Both of his sons had bilateral lens extractions and, by history, they never regained useful vision. Histologic observations on both eyes of both these patients are given by Manschot,⁵ who reports:

The sections clearly show that the circular equatorial line represents the site where a preretinal membrane—which centrally adheres to the retina and even covers the optic disc—bends away from the retina to the periphery of the vitreous cavity. The preretinal membrane contains holes; small free-floating membranes are branching off from it. The membrane ends free in the periphery of the vitreous space . . . the retina exhibits various types of retinal and chorioretinal atrophy. The greater part of the choroid is of normal structure.

Similar descriptions had been given earlier by Böhringer et al,³ based on the same histologic specimen. Thus, the progressive chorioretinal atrophy will lead to final blindness in patients with this syndrome.

The differential diagnosis is complex, but primarily the Stickler syndrome has to be considered in these patients (Table I).⁶⁻¹⁹ The patients in the family described herein have none of the extraocular complications seen in patients with classic vitreoretinal degeneration and retinal detachment. There is no known case of deafness—and all Swiss males are tested for their auditory status at the time of entry into the military

TABLE I: OCULAR FINDINGS IN HEREDITARY VITREORETINAL DISEASES

ENTITY	PREDOMINATING SYMPTOMATOLOGY	CORNEA	LENS	VITREOUS	MACULA
Wagner disease	Reduced night vision; visual loss due to progressive cataracts and later retinal degeneration	Microcornea	Dislocation occ.; posterior cortical & subcapsular changes ages 30 to 40	Vitreous membranes, veils; optically empty behind lens in many cases; preretinal avascular membranes	Normal until dragged macula (two cases)
Stickler syndrome	Retinal detachment 50% of cases	Normal	Occasionally dislocated, ²⁷ early cataracts (20 to 40)	Vitreous condensation; collapsed behind lens	Normal
Retinitis pigmentosa	Reduced night vision	Normal	Posterior subcapsular cataracts	Vitreous cells and degeneration	Cystoid macular degeneration
X-linked juvenile retinoschisis	Reduced central and peripheral vision	Normal	Normal	Vascularized preretinal vitreal veils	Radial striae and cystoid macular edema
Goldmann-Favre vitreoretinal degeneration	Peripheral retinoschisis with retinal vessels in veil, macular changes, poor night vision	Normal	Posterior subcapsular cataracts	Liquefaction with epiretinal membranes	Macular schisis

TABLE I: OCULAR FINDINGS IN HEREDITARY VITREORETINAL DISEASES (CONTINUED)

ENTITY	RETINAL PERIPHERY	PSYCHOPHYSICAL: ELECTROPHYSICAL TESTING	HISTOLOGIC FINDINGS	INHERITANCE	REFRACTIVE ERROR	AUTHORS
Wagner disease	Bone spicule pigments; perivascular pigment aggregation, radial vitreous condensations	Concentric constriction of visual field, dark adaptation rate mildly to markedly abnormal, reduced b-wave on ERG, abolished ERG	Epithelial gliotic membrane, leading to vitreous condensations; chorioretinal atrophic changes with pigment migration and chorioretinal adhesions	AD	Mild to moderate myopia, -8 D highest	Wagner ¹ Vogt ¹⁸
Stickler syndrome	Radial perivascular lattice, vitreous condensations in radial fashion	Reduced b-wave on ERG	No case observed yet	AD	Mild to high myopia	Stickler et al ^{16,17} Hirose et al ⁶ Hagler & Crosswell ¹² Delaney et al ¹⁰
Retinitis pigmentosa	Bone spicule pigmentation, constricted retinal vessels	Characteristic ERG & EOG abnormalities, visual field and dark adaptation changes	Photoreceptor loss with perivascular pigment migration and preretinal gliosis	AR, AD, X-linked	Mild to moderate myopia	
X-linked juvenile retinoschisis	Retinoschisis with perforated anterior retinal layers, pigmentary changes with perivascular sheathing	Normal dark adaptation, reduced b-wave, visual field defects	Nerve fiber layer splitting with retinal vessels contained in veil	X-linked		Kleinert ¹³ Mann & Macrae ¹⁴ Balian & Falls ⁷ Weve ¹⁹ Manschot ¹⁵

TABLE I: OCULAR FINDINGS IN HEREDITARY VITREORETINAL DISEASES (CONTINUED)

ENTITY	RETINAL PERIPHERY	PSYCHOPHYSICAL ELEC-TROPHYSICAL TESTING	HISTOLOGIC FINDINGS	INHERITANCE	REFRACTIVE ERROR	AUTHORS
Goldmann-Favre vitreoretinal degeneration	Retinal vessels in greyish peripheral retinal membrane with large holes, midperipheral retinal degeneration changes similar to RP	Reduced dark adaptation, ERG abolished at a young age	No case observed yet	AR	Myopia	Favre ¹¹ Ricci ⁴

service. With the exception of one young man, these patients were found fit to join the military service despite their visual problems, which apparently at that age were minor. There is no case of cleft hard or soft palate known in this family. No abnormalities of the head or soft palate, or a submucous cleft, were found in the patients I examined. Jansen²⁰ described similar vitreal findings in patients who apparently were systemically normal; and he described a high frequency of retinal detachments, which were difficult to cure. No detailed data on systemic evaluation of these patients are available; however, Dr Deutman (personal communication, 1982) told me that they are indeed physically normal. Many of the patients described in the United States and elsewhere with a diagnosis of vitreoretinal degeneration and retinal detachments have an unusual facial configuration, as described by Frandsen²¹ and others.²²⁻²⁶ These are clearly patients with extraocular manifestations of their disease; they have a distinct phenotype and should not be confused with Wagner's original patients, who were systemically normal. Vitreoretinal degeneration with retinal detachments occur in several types of bone dysplasia.²³ The vitreous pathology and the chorioretinal degeneration, without retinal detachment and without extraocular abnormalities, appear to be pathognomonic of Wagner disease (Fig 8).

For puristic reasons we should give the eponym of Wagner disease to the disorder he described, and we should reserve the term "vitreoretinal degeneration with retinal detachment" for application to a larger series of disorders, considering the fact that vitreoretinal degeneration as a complication is not specific to one single entity, but rather is seen in numerous disorders.

The question as to why the patients described by Wagner do not develop retinal detachments has not been solved, since preretinal glial proliferation is seen on histologic slides. Two patients seen by us had dragged maculae, but no retinal detachment was observed. However, I have never seen a patient with classical retinitis pigmentosa who had a retinal detachment. The chorioretinal adhesions that develop in the degenerative process in the patients described by Wagner, and in classical retinitis pigmentosa, may prevent detachments. The generalized connective tissue abnormality involving the vitreous in hereditary arthroophthalmopathy and related disorders may, in the absence of chorioretinal adhesions, lead to vitreous traction and retinal tears, as the blinding complication.^{2,8}

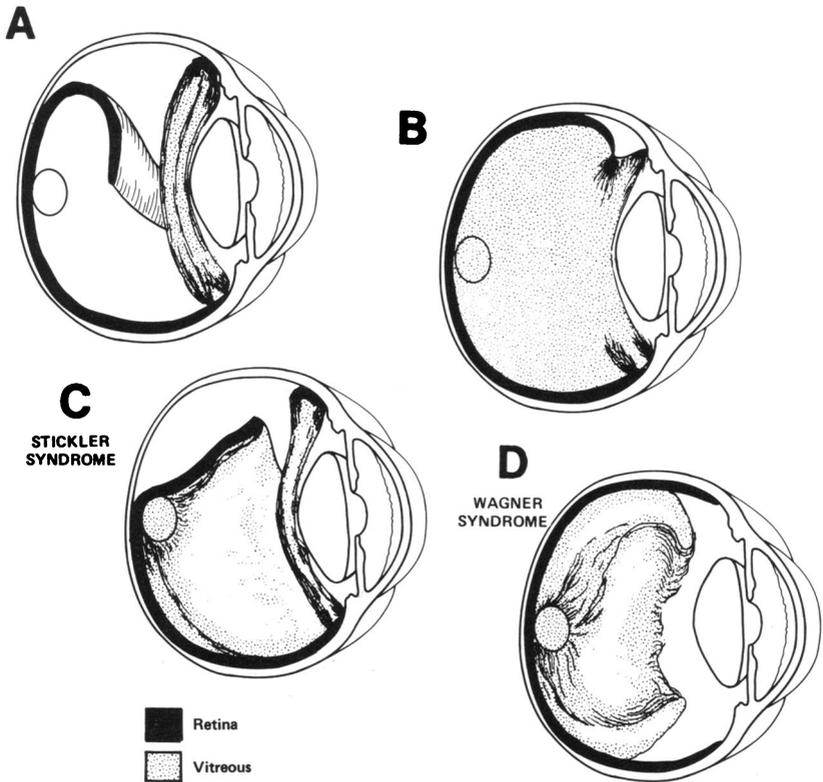


FIGURE 8

Relationship of vitreous to retina in A: retinal tear. B: Retinal dialysis. C: Stickler syndrome. D: Wagner disease.

REFERENCES

1. Wagner H: Ein bisher unbekanntes Erbleiden des Auges (Degeneratio hyaloideo-retinalis hereditaria), beobachtet im Kanton Zürich). *Klin Monatsbl Augenheilkd* 1938; 100:840-857.
2. Alexander RL, Shea M: Wagners disease. *Arch Ophthalmol* 1965; 74:310-318.
3. Böhringer HR, Dieterle P, Landolt E: Zur Klinik und Pathologie der Degeneratio hyaloideo-retinalis hereditaria (Wagner). *Ophthalmologica* 1960; 139:330-338.
- 3a. Stoll HU: Wagner's disease; the original pedigree revised (in preparation).
4. Ricci A: Clinique et transmission genetique des differentes formes de degenerescences vitreo-retiniennes. *Ophthalmologica* 1960; 139:338-343.
5. Manschot WA: Pathology of hereditary conditions related to retinal detachment. *Ophthalmologica* 1971; 162:223-234.
6. Hirose T, Lee KY, Schepens CL: Wagners hereditary vitreoretinal degeneration and retinal detachment. *Arch Ophthalmol* 1973; 89:176-185.
7. Balian JV, Falls HF: Congenital vascular veils in the vitreous—hereditary retinoschisis. *Arch Ophthalmol* 1960; 63:92-101.

8. Brown GC, Tasman WS: Vitrectomy and Wagners vitreoretinal degeneration. *Am J Ophthalmol* 1978; 86:485-488.
9. Cibis PA: *Vitreoretinal Pathology and Surgery in Retinal Detachment*. St Louis, CV Mosby Pub Co, 1965, pp 116-133.
10. Delaney WV Jr, Podedworny W, Havener WH: Inherited retinal detachment. *Arch Ophthalmol* 1963; 69:44-50.
11. Favre M: A propos de deux cas de degenerescence hyaloideoretinienne. *Ophthalmologica* 1958; 135:604-609.
12. Hagler WS, Crosswell HH Jr: Radial perivascular chorioretinal degeneration and retinal detachment. *Trans Am Acad Ophthalmol Otolaryngol* 1968; 72:203-216.
13. Kleinert H: Eine recessiv-geschlechtsgebundene Form der idiopathischen Netzhautspaltung bei nichtmyopen Jugendlichen. *Albrecht Von Graefes Arch Klin Exp Ophthalmol* 1953; 154:295-305.
14. Mann I, Macrae A: Congenital vascular veils in the vitreous. *Br J Ophthalmol* 1938; 22:1-10.
15. Manschot WA: Pathology of hereditary juvenile retinoschisis. *Arch Ophthalmol* 1972; 88:131-138.
16. Stickler GB, Belau PG, Farrell FJ, et al: Hereditary progressive arthro-ophthalmopathy. *Mayo Clin Proc* 1965; 40:433-455.
17. Stickler GB, Pugh DG: Hereditary progressive arthro-ophthalmopathy. II. Additional observations on vertebral abnormalities, a hearing defect, and a report of a similar case. *Mayo Clin Proc* 1967; 42:495-500.
18. Vogt A: *Textbook and Atlas of Slit Lamp Microscopy of the Living Eye*. Iris, Vitreous Body, Conjunctiva. Zürich, Schweizer Verlagshaus, 1941, vol 3, pp 1020-1022.
19. Weve H: Ablatio falciformis congenita (retinal fold). *Br J Ophthalmol* 1938; 22:456-470.
20. Jansen LMAA: Degeneratio hyaloideoretinalis hereditaria. *Ophthalmologica* 1962; 144:348-363.
21. Frandsen E: Hereditary hyaloideo-retinal degeneration (Wagner) in a Danish family. *Acta Ophthalmol* 1966; 44:223-232.
22. Knobloch WH: Inherited hyaloideoretinopathy and skeletal dysplasia. *Trans Am Ophthalmol Soc* 1976; 73:417-451.
23. Maumenee IH: Vitreoretinal degeneration as a sign of generalized connective tissue diseases. *Am J Ophthalmol* 1979; 88:432-449.
24. Opitz JM: Ocular anomalies in malformation syndromes. *Trans Am Acad Ophthalmol Otolaryngol* 1972; 76:1193-1202.
25. Opitz JM, France T, Hermann J, et al: The Stickler syndrome. (Letter) *N Engl J Med* 1972; 286:546.
26. Popkin JS, Polomeno RC: Sticklers syndrome (hereditary progressive arthro-ophthalmopathy). *Can Med Assoc J* 1974; 111:1071-1076.
27. Maumenee IH: Personal observation.

DISCUSSION

DR WILLIAM TASMAN. I would like to thank the Program Committee for allowing me to discuss Doctor Maumenee's paper on Wagner's Syndrome vs Hereditary Arthroophthalmopathy. Four years ago I co-authored an article having to do with Wagner's Vitreoretinal Degeneration. No sooner had it been published than I realized the condition we had described was Stickler's Syndrome rather than Wagner's. I mentioned this to my co-author and predicted that a letter to the editor would undoubtedly be forthcoming, a prediction which came true a week later. Since that time the difference between Wagner's Disease and Stickler's has become more apparent. However, there are some who feel that the two conditions are related and may represent different expressions of the same disorder.

Doctor Maumenee, by going back and reexamining some of the original Wagner's patients in light of our present day knowledge, has convinced me that this is certainly not the case.

In 1938 Wagner described what he referred to as hereditary hyaloideoretinal degeneration. His patients had a low degree of myopia and, as Doctor Maumenee has pointed out, no retinal detachments were reported in any of them. Anterior and posterior cortical lens opacities appeared in childhood. A decreased electroretinographic response and optic atrophy was also noted, but these findings were not emphasized.

By way of contrast, Stickler's Syndrome includes a high incidence of retinal detachment, arthropathy in 83% of cases, cleft palate in 28% of patients, micrognathia in 17% of patients and neurosensory deafness in 9% of patients. None of the five patients Doctor Maumenee was able to reexamine showed any of these changes.

Of particular interest, however, were patients in cases 1 and 2. Case 1 was myopic, had a positive angle kappa, corneal diameters of 10 mm, shallow anterior chambers, a fluid vitreous, a macula and disc dragged temporally, and a vitreous condensation line overlying the equatorial area which was partially fenestrated. Case 2 was myopic to a lesser degree than case 1, but also had a positive angle kappa and was described as demonstrating signs of early chorioretinal atrophy with dragging of the macula in each eye. This suggests that retrolental fibroplasia and familial exudative vitreoretinopathy should also be included in the differential diagnosis of Wagner's Disease. The patient in case 3 who is aphakic is described as having vitreous coming from the posterior aspect forward to insert into the lower temporal retina. Vitreous condensation was also noted in the retinal periphery of case 4 as was sheathing of the retinal vessels and lattice degeneration. The patient in case 5 had corneal diameters of 10 mm and chorioretinal atrophy out to the midperiphery. Chorioretinal atrophy when present caused night blindness similar to that seen in retinitis pigmentosa. All of these changes may appear in retrolental fibroplasia, and many appear in familial exudative retinopathy. Thus, these conditions enter the differential diagnosis.

None of the patients examined by Doctor Maumenee developed retinal detachment. In addition, the pathology slides supplied by Professor Wagner showed multiple adhesions between the retina and choroid possibly lessening the chance of retinal detachment. As Doctor Maumenee points out, retinal detachment is also rare in retinitis pigmentosa, again possibly due to marked chorioretinal adhesion. However, we have seen exudative retinal detachment in patients with retinitis pigmentosa on more than one occasion. Usually they are associated with abnormal telangiectatic retinal vessels.

In summary, the characteristic features of Wagner's Syndrome as described by Doctor Maumenee include vitreous degeneration with an optically empty vitreous cavity and vitreous veils which arise at the level of the equator. Perivascular pigmentation, sheathing, and areas of lattice are other features of the disorder. Patients also complain of night blindness from early childhood on, and there is

evidence that there is progressive decline in the dark adaptation rates showing a slowly progressive involvement of rods and cones later. Thus, we are indebted to Doctor Maumenee for helping to clarify the difference between Wagner's Syndrome and Stickler's Hereditary Arthroophthalmopathy. To my mind she has emphasized the true characteristics of Wagner's Syndrome and has made us aware of the fact that in many ways this is closer in symptomatology to retinitis pigmentosa than Hereditary Arthroophthalmopathy. Her description also makes us aware of retrolental fibroplasia and less likely familial exudative vitreoretinopathy in the differential diagnosis.

Finally, I am puzzled as to why this condition is not seen in other areas of the world. I have not seen a patient with true Wagner's Syndrome as described by Wagner in 1938 and now Doctor Maumenee in 1982. Perhaps the homogeneity of the Swiss population vs the heterogeneity of those living in the United States may offer a partial explanation.

DR IRENE H. MAUMENEE. I would like to thank Doctor Tasman for his in-depth discussion of my paper. I thank him for his suggestion of including familial exudative vitreoretinopathy into the differential diagnosis. I thought about this but did not do it for two reasons. I have not seen extensive vitreous abnormalities in patients with familial exudative vitreoretinopathy and patients with this latter diagnosis commonly have severe exudative signs with lipid storage around the macular region. The patients discussed here are certainly different in these two respects.

In 1937 Doctor Philip Lewis gave his first presentation to the American Ophthalmological Society. He was the last speaker on the last day of the meeting. I am here now in the same situation hoping that I will have as long and happy a relationship with this society as he has had over the years. I thank the Society for accepting me as a member