Wagner Vitreoretinal Degeneration

Follow-up of the Original Pedigree

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Purpose: Wagner disease belongs to a heterogeneous group of hereditary vitreoretinal degenerations. The authors have observed complications of this disorder that have not been reported before and therefore re-examined Wagner's original pedigree to further delineate the spectrum of the associated findings and its prognosis.

Methods: Sixty members of the family agreed to be examined. All had complete clinical eye examinations, 40 had dark adaptation studies as well as single-flash and Ganzfeld rod and cone electroretinography. Fluorescein angiograms were performed in selected patients.

Results: Twenty-eight family members were affected. The most consistent finding was an empty vitreous cavity with avascular strands or veils. Chorioretinal atrophy and cataract increased with the patients' age and had occurred in all patients older than 45 years of age. Four patients had a history of a rhegmatogenous retinal detachment in one eye at a median age of 20 years. The authors observed peripheral tractional retinal detachments in 55% of eyes among patients older than 45 years. Glaucoma was present in ten eyes (18%), four of which showed neovascular glaucoma. Of all patients, 63% showed elevated rod and cone thresholds on dark adaptation, and 87% showed subnormal b-wave amplitudes of the rod- and of the cone system on the electroretinography.

Conclusions: Clinical expressivity of Wagner disease varies from unaffected carriers to bilateral blindness. Rhegmatogenous retinal detachment is observed infrequently, whereas peripheral traction retinal detachment, chorioretinal atrophy, and cataracts are present in most of the elderly affected individuals. Progression of the chorioretinal pathology is paralleled by electrophysiologic abnormalities.

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Hans Wagner,[1] in 1938, described an inherited vitreoretinal disease in a Swiss family. Features of this disease included autosomal dominant inheritance, vitreous pathology characterized by a mostly empty vitreous cavity with avascular membranes, strands and veils, lattice degeneration of the retina, chorioretinal atrophy with loss of the retinal pigment epithelium, complicated cataracts, and mild myopia. The disease could be evident in early childhood and showed a progressive clinical course.

Since Wagner's original description, many studies have been published on this and related entities, two of which update the findings in Wagner's original pedigree.[2,3] Although retinal detachment was not reported in this family, the eponym "Wagner disease" often has been applied to familial vitreoretinal degenerations associated with rhegmatogenous retinal detachment.[3,4] It is, however, well recognized that other related entities, such as those described by Jansen[5] in 1962 and Stickler et al[6] in 1965, can be differentiated based on ophthalmic as well as systemic findings.[4,7] Erosive vitreoretinopathy, just recently described by Brown et al,[8] is another clinical entity that seems to be very similar to Wagner disease. Meanwhile,

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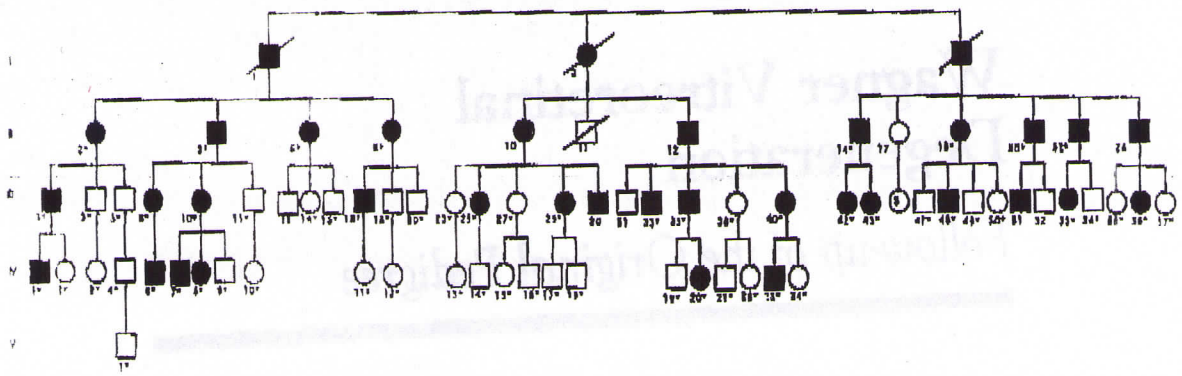


Figure 1. Pedigree of the family. Star = the individual has been examined; circles = females; squares = males; solid symbols = affected patients; a slash through a symbol = the individual is deceased.

molecular genetic defects of the procollagen II locus have been linked to Stickler syndrome, thus providing further insight in the understanding of these conditions.[9–11] A new genetic study disclosed that erosive vitreoretinopathy and Wagner disease are allelic disorders, which are distinct from *COL2A1*-associated Stickler syndrome.[12]

In the last few years, we have observed complications of Wagner disease that have not been described previously. There is considerable overlap in typical ophthalmic findings of the above-mentioned entities. We have, therefore, conducted a new follow-up study of Wagner's original pedigree to update our understanding of the clinical course and the prognosis of this disease. In the current study, we report the clinical and electrophysiologic features of this condition.

Patients and Methods

The patients studied belong to a single, large pedigree. Of the 75 members of the pedigree who we were able to trace, 60 agreed to be examined at the Department of Ophthalmology of the University Hospital of Zurich. All individuals (120 eyes) received a complete clinical eye examination. In consideration of the wide, clinical spectrum of Wagner disease, we had to define minimal findings among patients at genetic risk who were suggestive of a gene carrier. A patient supposedly was affected by the disease if he/she had fibrillary condensations or avascular strands in an otherwise empty vitreous cavity or if he/she, regardless of ophthalmic findings, had a clearly affected offspring. Selected patients who showed significant retina pathology and clear media had fluorescein angiograms (n = 7) and fundus photographs (n = 24). Forty members of the pedigree had dark-adaptation studies and electroretinography (ERG). Dark adaptation was done with the Goldmann-Weekers dark adaptometer.

Electroretinography testing was performed by single-flash Ganzfeld stimulation of the rod and cone system, using matched-band filters as developed by Berson et al[13] and Gouras.[14] The mean amplitudes and peak times of b-waves of our laboratory and their standard deviations in a control group have been published by Hatt and Niemeyer[15] and by Knobel and Niemeyer.[16]

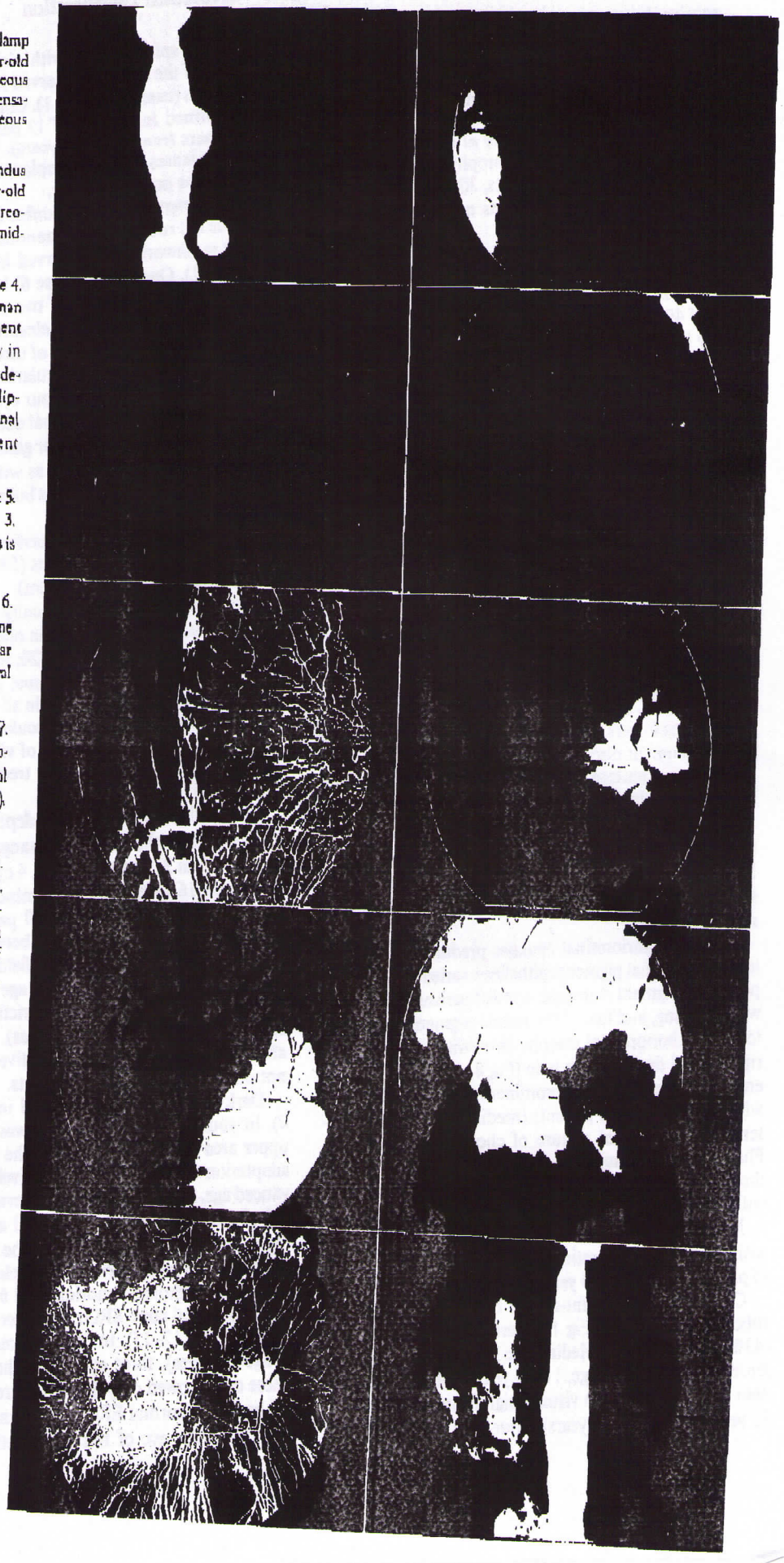
Results

Of 60 patients examined, 28 were identified to be affected by the disease based on our criteria of Wagner disease. None of the remaining 32 patients showed suggestive findings of the disease, such as midperipheral chorioretinal atrophy, cataracts, or retinal detachments. The age range of all patients was 11 to 70 years (median, 40 years). The average age of affected patients was 34 years, and the average age of unaffected individuals was 25 years.

Inheritance was autosomal dominant as demonstrated by the family pedigree (Fig 1). More than three consecutive generations were affected. No consanguineous marriage could be documented.

Because of the clinical definition of the disease used in this study, characteristic vitreous pathology such as "empty" vitreous cavity with fibrillary condensations or circumferentially oriented avascular strands and veils (originating from midperipheral vitreoretinal adhesions and extending to the peripheral vitreous, thus simulating peripheral vitreous detachment) was present in all except two patients (both of whom had to be gene carriers because of their affected offspring—cases III.10 and III.40; Fig 1). Fibrillary condensations seem to reflect early degenerative changes of the vitreous (present in 10 of 24 eyes of patients younger than 30 years of age; Fig 2), whereas avascular strands and veils were observed among elder patients (present in 28 of 32 eyes of patients older than 30 years of age; Fig 3). None of our patients showed posterior vitreous detachment. Synchysis scintillans was noted in four eyes of two patients (50 and 53 years of age, respectively), one of whom also had a history of recurrent bilateral vitreous hemorrhage.

Rhegmatogenous retinal detachment had previously occurred in four eyes of four patients (cases II.14, III.16, IV.6, and IV.7; Fig 1) at an average age of 20 years. In three eyes, the retinal detachment was due to flap tears and/or atrophic holes; they could be reattached by con-



Top left, Figure 2. Slit-lamp photograph of an 11-year-old boy shows early vitreous changes (fibrillary condensations). Most of the vitreous appeared "empty."

Top right, Figure 3. Fundus photograph of a 44-year-old affected man shows vitreoretinal adhesion in the midperipheral retina nasally.

Second row left, Figure 4. In this 67-year-old woman traction retinal detachment is seen inferotemporally in the left eye with early deposition of intraretinal lipids. Sheathing of retinal vessels as well as pigment clumping are noted.

Second row right, Figure 5. Same eye as in Figure 3. Sheathing of retinal vessels is seen inferotemporally

Third row left, Figure 6. Mid-phase angiogram of same eye as Figure 3. An avascular retina is seen in the temporal periphery

Third row right, Figure 7. A 22-year-old man with abnormal distribution of central retinal vessels (situs inversus). Visual acuity was 20/20.

Fourth row left, Figure 8. Same eye as in Figure 3. Marked chorioretinal atrophy with pigment migration into the retina and sparing of the macular area are seen. Visual acuity was 20/25.

Fourth row right, Figure 9. A 65-year-old man with advanced chorioretinal atrophy, mimicking choroideremia. Visual acuity was counting fingers

Bottom left, Figure 10. Fluorescein angiogram of same eye as in Figure 3 in early venous phase. There is extensive atrophy of choriocapillaris, sparing only the macular area.

Bottom right, Figure 11. In this 41-year-old woman, there is a visually significant posterior subcapsular cataract. Visual acuity was 20/40.

ventional scleral buckling procedures. In one eye (case II.14), surgery in 1962 was unsuccessful, with consecutive amaurosis and complicated cataract; the configuration of this retinal detachment could not be evaluated retrospectively.

Two eyes (4%) had a history of retinal breaks without detachment. In both cases, prophylactic treatment had been performed. Of 20 patients, 30 eyes (54%) had lattice retinal degeneration, which was not treated prophylactically in any of the eyes.

Peripheral tractional retinal detachment was observed in 12 eyes of ten patients (cases II.2, II.3, II.6, II.8, II.19, II.20, II.22, III.29, III.33, and III.43; Fig 1) at an average age of 49 years (Fig 4). The detachment progressed centrally in four eyes of two patients (cases II 19 and II.22) with a Coats-like exudative retinopathy and massive Synchysis scintillans. Traction retinal detachment seemed to be due to organization and contraction of midperipheral and peripheral vitreoretinal adhesions. Fibrovascular proliferation was not observed, although the peripheral retina appeared to be poorly vascularized in these patients, and extensive perivascular sheathing or obliteration was noted (Figs 4 and 5). Unfortunately, fluorescein angiography in the retinal periphery could be performed only in selected patients (Fig 6) because of poor pupillary dilation and/or cataract in these eyes. A pars plana vitrectomy with silicone oil tamponade was performed in one eye (case II.22) for traction retinal detachment, which involved the entire posterior pole of the retina. The retina was reattached, and vision improved from light perception to counting fingers. Two eyes with complete traction retinal detachment disclosed phthisis bulbi.

Abnormal pattern of the central retinal vessels ("situs inversus" or "dragged vessels") was noted in 30 eyes (54%) of 15 patients (Fig 7). Only a few of these patients had evidence of peripheral retinal traction that might account for dragging of retinal vessels. Macular pucker was observed in two eyes, whereas cystoid macular edema was seen in one eye.

Atrophic chorioretinal changes predominantly at the level of the retinal pigment epithelium varied from isolated peripheral pigment clumping, a radial perivascular pattern with thinning, and loss of the retinal pigment epithelium to severe chorioretinal atrophy involving the retinal periphery and the posterior pole (Fig 8). Advanced degenerative changes were more prominent in the older patients, with six eyes of three patients (median age, 62 years) resembling the clinical picture of choroideremia (Fig 9). Fluorescein angiography in these patients showed loss of the choriocapillaris and the retinal pigment epithelium with preservation of only larger choroidal vessels (Fig 10).

Marked optic atrophy was noted only in older patients with advanced chorioretinal atrophy—6 eyes of 20 eyes of patients older than 45 years had marked optic atrophy.

Cataracts (mainly point-shaped opacities and posterior subcapsular cataracts, Fig 11) were observed in 24 eyes (43%) of 14 patients. Median age of patients with clear lenses was 22 years (range, 11–45 years), whereas the median age of patients with visually significant opacities was 32 years (range, 21–53 years). Four eyes of two patients showed spherophakia with visible zonula fibers; sublux-ation of the lens was observed in both eyes of one of these patients (case III.16; Fig 1). Cataract extraction had to be performed in 21 eyes of 12 patients at a median age of 38 years (range, 33–43 years). Posterior chamber intraocular lenses had been implanted in six eyes without any problems postoperatively.

Dysgenetic anterior chamber angles with high insertion of the iris root and membranous structures at the trabecular meshwork were observed in 20 eyes of ten patients (Table 1). One patient (case 6) had congenital glaucoma in both eyes. Four eyes of two patients (median age, 46 years) had a chronic angle-closure glaucoma after IC-cataract extraction. Four eyes of three patients (median age, 48 years) had iris neovascularization with neovascular glaucoma. Three of these four eyes were aphakic and all had peripheral traction retinal detachment. Three eyes of two patients with neovascular glaucoma were treated with a filtering procedure as well as with several cyclodestructive cryoapplications. Phthisis bulbi later developed in two eyes.

Refraction (Table 2) was performed in 34 phakic eyes (in 20 patients). Eighteen eyes (53%) were myopic up to 6 diopters (spherical equivalent).

Visual acuity (Table 3) usually was normal in young patients and severely affected in older patients. Seven eyes (13%) had visual acuity of 20/20; the median age of these patients was 25 years. The visual gain after cataract extraction was progressively lost in all eyes due to increasing chorioretinal atrophy, neovascular glaucoma, or optic atrophy. In one eye, the cause of visual loss was a retinal detachment that could not be treated successfully (case II.14; Fig 1).

Visual fields were affected, depending on lens transparency and chorioretinal changes. Among patients younger than 31 years (20 eyes), 4 eyes (20%) had normal fields and 16 (80%) had only minor field defects (mild concentric constriction or small paracentral scotomas). Among five individuals (9 eyes) between 45 and 60 years of age, none had normal visual fields; four of six eyes in patients older than 60 years of age disclosed a marked field loss (severe concentric constriction, large paracentral scotomas, or ring-shaped scotomas). Orofacial or skeletal abnormalities suggesting connective tissue disease were not observed in any of the patients.

Dark adaptation was recorded in 24 patients (Table 4). In young patients, it usually was normal, but in the upper area (lower sensitivity) of the normal band. Dark adaptation tended to be progressively pathologic in advanced age. Patients who had an elevated final rod threshold of more than one log unit had a subjective form of night blindness. In these patients, the amount of final rod threshold elevation corresponded clearly with the morphology of pathologic chorioretinal findings.

The rod and cone ERGs were recorded in 27 patients (53 eyes; Figs 12–15). In patients younger than 30 years of age (24 eyes), three eyes (13%) had a normal ERG. These eyes showed only little chorioretinal atrophy. One eye had a subnormal ERG after retinal detachment surgery (the other eye of this same patient had a normal

Table 1. Prevalence of Various Features of Wagner Disease

Features	Age (yrs) <30 No. of Eyes (%)	30–45 No. of Eyes (%)	46–60 No. of Eyes (%)	>60 No. of Eyes (%)	Total No. of Eyes (%)
No. of eyes	24	12	12	8	56
Anterior chambers angle					
Dysgenesis	14 (58)	0 (0)	2 (17)	4 (50)	20 (36)
Narrow	2 (8)	2 (17)	4 (33)	2 (25)	10 (18)
Iris neovascularization	0 (0)	0 (0)	4 (33)	0 (0)	4 (7)
Cataracts	14 (58)	8 (67)	2 (17)	0 (0)	24 (43)
Aphakia/pseudophakia	0 (0)	3 (25)	10 (83)	8 (100)	21 (38)
Fibrillary vitreous	10 (42)	0 (0)	0 (0)	0 (0)	10 (18)
Vitreous strands	14 (58)	8 (67)	12 (100)	8 (100)	42 (75)
Synschisis nivea	0 (0)	0 (0)	4 (33)	0 (0)	4 (7)
Chorioretinal atrophy	20 (83)	8 (67)	12 (100)	8 (100)	48 (86)
Lattice degeneration	16 (67)	6 (50)	8 (67)	0 (0)	30 (54)
Status post rhegmatogenous RD	2 (8)	1 (8)	1 (8)	0 (0)	4 (7)
Tractional RD	2 (8)	1 (8)	6 (50)	5 (63)	14 (25)
Lipid retinopathy	0 (0)	0 (0)	4 (33)	4 (50)	8 (14)
Foveal ectopy	10 (42)	6 (50)	2 (17)	2 (25)	20 (36)
Macular pucker	2 (8)	0 (0)	0 (0)	0 (0)	2 (4)
CME	1 (4)	0 (0)	0 (0)	0 (0)	1 (2)
Situs inversus	4 (17)	0 (0)	4 (33)	0 (0)	8 (14)
Optic atrophy	0 (0)	0 (0)	4 (33)	2 (25)	6 (11)

RD = retinal detachment; CME = cystoid macular edema

ERG). The remaining 20 eyes of patients younger than 30 years of age had a pathologic ERG corresponding to their more severe chorioretinal pathology: b-wave amplitudes of the rod system usually were better preserved than those of the cone system; b-wave amplitudes of rod and cone system were reduced similarly in five eyes (21%).

In patients between 30 and 45 years of age (12 eyes), four eyes (33%) had a normal ERG. In the remaining eight eyes with subnormal ERGs, rod ERGs usually were better preserved than those of the cone system. In two eyes, b-wave amplitudes were reduced equally in the rod and in the cone system.

In patients older than 46 years (17 eyes), none of the eyes had a normal ERG. B-wave amplitudes of the cone system usually were better preserved than those of the rod system; b-wave amplitudes were reduced equally in the rod and in the cone system in at least five eyes (29%). Interestingly, with progression of disease, there is a greater reduction of the rod response than that of the cone response.

In all the eyes with subnormal b-wave amplitudes, implicit time of cone b-wave amplitudes were prolonged more than 2 standard deviations (Fig 14).

Five affected patients have been followed at our clinic for extended periods of time, with an average follow-up of 10 years (range, 1–20 years). "Wagner-associated" findings always were bilateral, and the clinical course clearly was progressive.

Table 2. Refractive Error in 34 Eyes*

	No. of Eyes (%)
Myopia, ≤6.0 D	18 (53)
Myopia, >6.0 D	11 (32)
Emmetropia	4 (12)
Hyperopia	1 (3)
Total	34
Astigmatism, >1.0 D	24 (71)

D = diopter.

* 21 aphakic/pseudophakic eyes were not included, and refraction was unknown in 1 eye with dense cataract.

Discussion

Wagner disease belongs to a group of hereditary vitreoretinal degenerations that share some common features.

Table 3. Visual Acuity at Last Examination

Age (yrs)	No. of Eyes	Visual Acuity (%) >20/40	20/50–20/100	20/200–CF	HM, NLP
<30	24	19 (79)	2 (8)	3 (13)	0
31–45	12	9 (75)	2 (17)	1 (8)	0
46–60	12	5 (42)	2 (17)	0	5 (42)
>60	8	4 (50)	2 (25)	2 (25)	0

CF = counting fingers; HM = hand motions; NLP = no light perception.

Table 4. Dark Adaptation in 24 Patients at Last Examination*

Age (yrs)	No. of Patients	Normal Results No. of Patients (%)	Elevation of FRT <1 Log U No. (%)	Elevation of FRT >1 Log U No. (%)
<30	11	7 (64)	3 (27)	1 (9)
30–45	6	2 (33)	1 (17)	3 (50)
46–60	3	0	2 (67)	1 (33)
>60	4	0	2 (50)	2 (50)

*Dark adaptation was not done in 4 patients.
FRT = final rod threshold

Distinction between these various syndromes can be difficult in isolated cases and is based on the prevalence and expression of one or several of these features. The diagnosis of Wagner disease in a given pedigree has to be based on clinical findings because previously the underlying genetic defect is not known. "Empty vitreous" with fibrillary condensations or avascular strands and veils seems to be the hallmark of the disease and can be observed in nearly all gene carriers. In this study, patients were supposed to be affected by the disease, if either the characteristic vitreous findings were present or if their offsprings clearly showed Wagner disease. Among 60 members of the original pedigree who were examined for this study, 26 showed the characteristic vitreous pathology, whereas only 2 had to be identified because of their affected offsprings. None of the remaining 32 family members showed chorioretinal degenerative changes, early cataracts, or retinal detachments that also might suggest Wagner disease. We, therefore, believe that our definition of being affected was sensitive enough to include most patients at genetic risk.

Expressivity of Wagner disease is age dependent, and a progressive clinical course is well known in these patients.[1–3] The earliest findings usually are related to vitreous degeneration with fibrillary condensations in an otherwise empty vitreous. This could be observed in a patient as young as 7 years of age (case IV.1; Fig 1). Visual acuity as well as lens and chorioretinal findings usually are normal up to approximately 30 years of age. Progres-

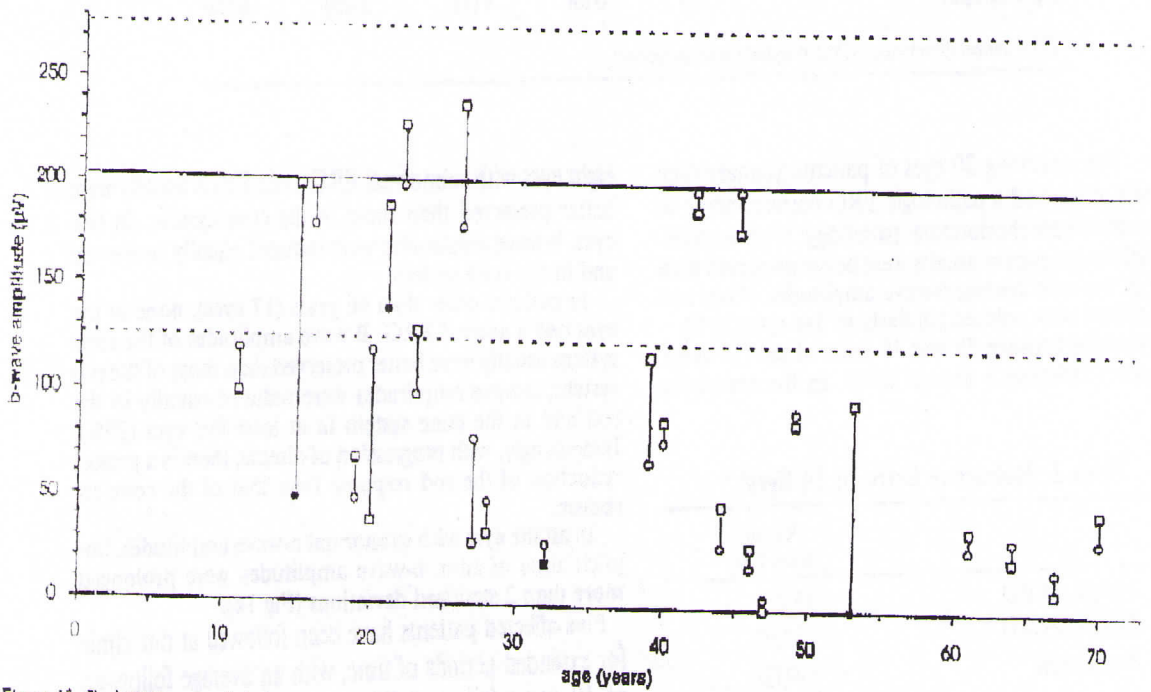


Figure 12. Rod ERGs, recorded after 20 minutes of dark adaptation, using a short wavelengths filter in the Ganzfeld and the number 8 setting of the built in Grass flash generator. Only a few patients have normal b-wave amplitudes, whereas the vast majority have subnormal to extinguished rod b-waves. Open circles = right eye; open squares = left eye; closed circles/squares = status post retinal detachment surgery; horizontal line = mean amplitude of control group; horizontal dashed lines = 95% confidence interval.

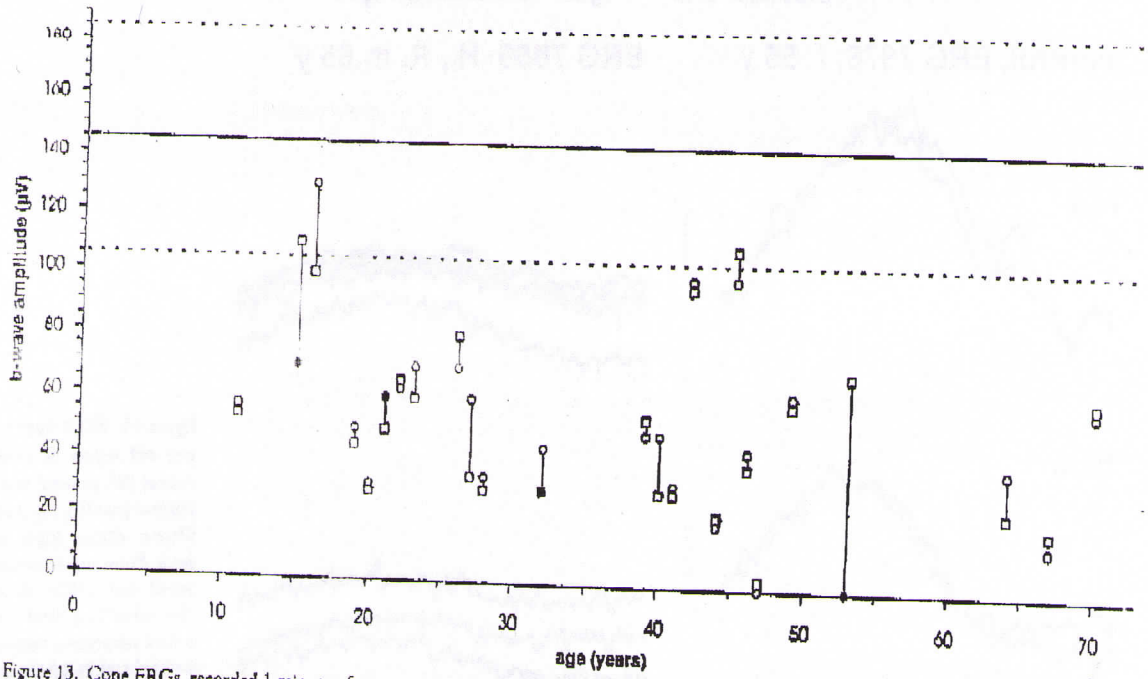


Figure 13. Cone ERGs, recorded 1 minute after onset of light adaptation, using a long wavelengths stimulus. Only three eyes have normal b-wave amplitudes. The younger patients have subnormal, although better preserved, b-waves than the older patients. Open circles = right eye; open squares = left eye; closed circles/squares = status post retinal detachment surgery; horizontal line = mean amplitude of control group; horizontal dashed lines = 95% confidence interval.

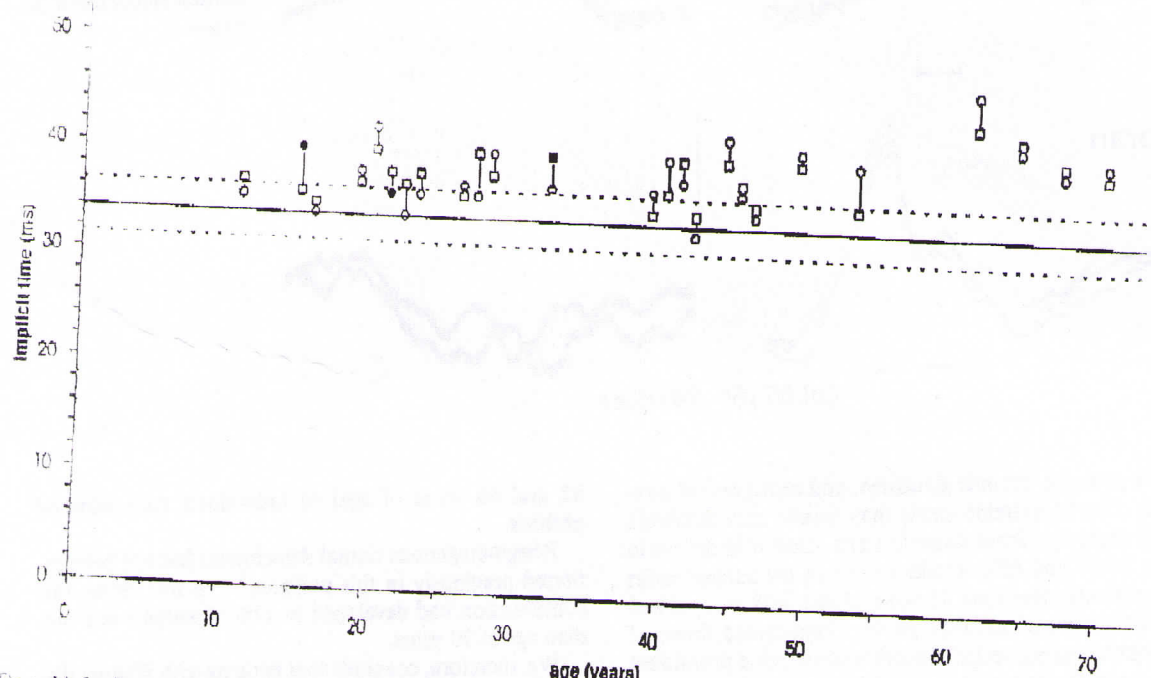


Figure 14. Implicit times of cone b-waves, recorded 1 minute after onset of light adaptation. The cone ERGs from only 14 eyes revealed a normal time course, the remaining cone b-waves had a clearly prolonged implicit time. open circles = right eye; open squares = left eye, closed circles/squares = status post retinal detachment surgery. horizontal line = mean amplitude of control group; horizontal dashed lines = 95% confidence interval.

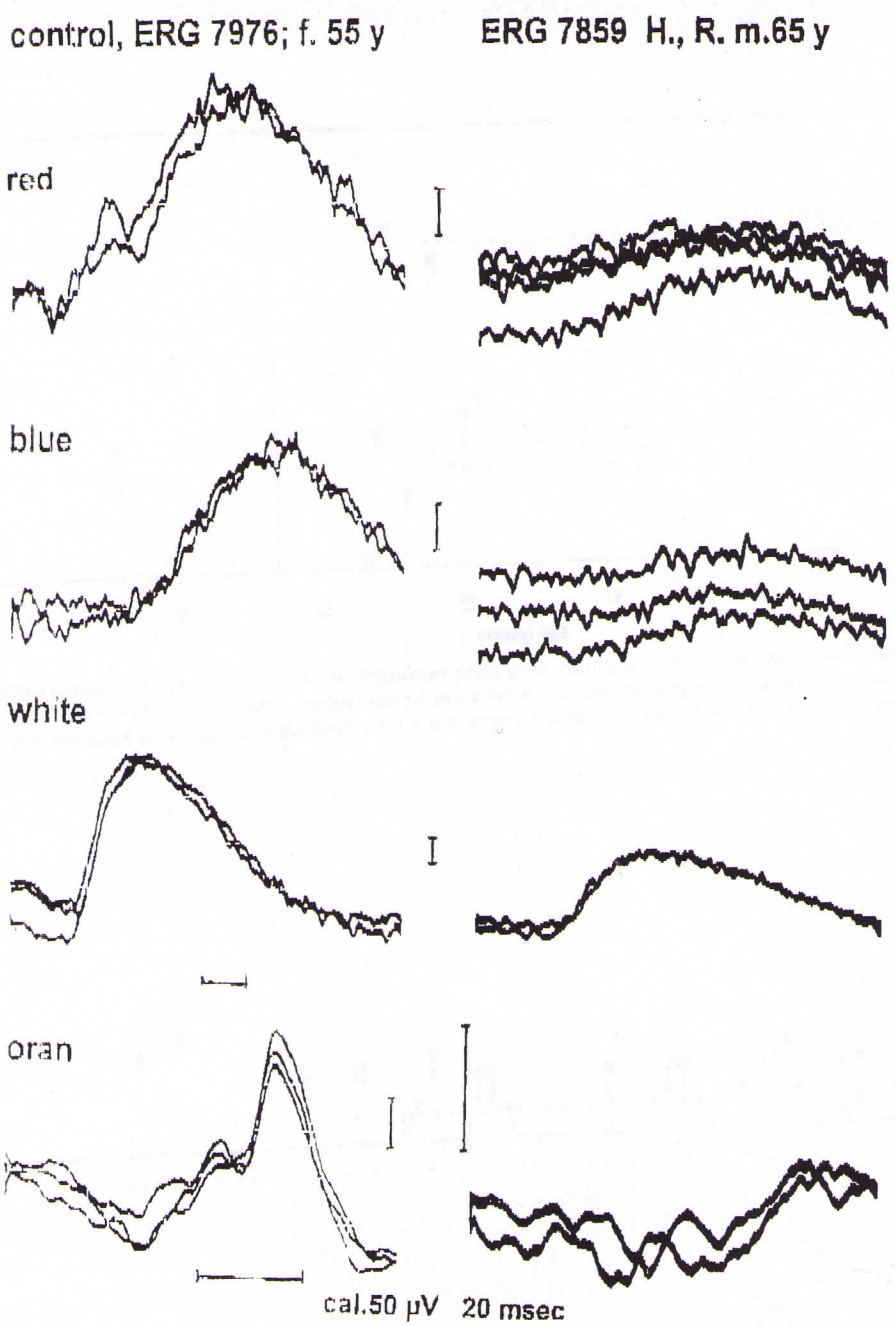


Figure 15. ERGs from a 55 year old female as normal control (left column) and of a patient (case IL3, Fig 1) with Wagner disease (right column). From top to bottom, typical rod ERGs elicited with red or blue band filters in dark adaptation, response to a bright white light in dark adaptation, and in the lowermost row, a typical cone ERG elicited with a long wavelengths (orange) band filter in light adaptation. The patient's ERGs are all markedly reduced in amplitude, the cone ERG shows reduced oscillatory potentials and an increased implicit time of the b-wave.

sive cataracts, chronic glaucoma, and chorioretinal atrophy that (in extreme cases) may mimic choroideremia will cause significant visual loss and visual field defects in the fourth and fifth decades of life. In the current series of patients older than 45 years of age, 60% of eyes had visual acuity of less than 20/40. Complicated forms of rhegmatogenous retinal detachment are not a prominent cause of severe visual loss in Wagner disease, although they frequently are observed in other vitreoretinal syndromes.[5,6,8,17-20] However, even among patients of similar age, we observed a considerably variable expressivity, ranging from basically unaffected carriers (2 patients of 42 and 45 years of age) to individuals with bilateral phthisis.

Rhegmatogenous retinal detachment has not been reported previously in this pedigree.[1-3] In our series, this complication had developed in 14% of patients at a median age of 20 years.

We, therefore, conclude that patients with Wagner disease do have an increased risk of rhegmatogenous retinal detachment, although this feature is not as prominent as in other hereditary vitreoretinal degenerations as described by Jansen,[5] Stickler et al,[6] or Brown et al.[8] Vitreoretinal pathology of rhegmatogenous retinal detachment ob-

served in this series was similar to idiopathic findings and could be managed by routine scleral buckling procedures in three of four patients. This, again, is unlike those complicated retinal detachments that are observed in other related vitreoretinal syndromes.[5,6,8,17–20] We agree with the hypothesis of Maumenee et al[3] that older patients with Wagner disease are, despite vitreoretinal traction and extensive lattice degeneration, protected from this complication because of progressive chorioretinal atrophy and scarring.

Peripheral traction retinal detachment in Wagner disease has not been reported previously. However, it seems to be a common late complication of this disease and, in the current series, was observed in 25% of all eyes and in 55% of eyes among patients older than 45 years of age. In all of these patients, sheathing or obliteration of peripheral retinal vessels was present, whereas preretinal neovascularization was not observed. We speculate that contraction of the peripheral vitreoretinal adhesions, possibly caused by migration and proliferation of retinal glial cells in the presence of lattice degeneration, is responsible for this finding. Peripheral traction retinal detachment was complicated further by Coats-like exudative retinopathy in four eyes of two patients, and by iris neovascularization in four eyes of three patients.

Congenital glaucoma (1 patient), chronic angle-closure glaucoma (2 patients), and neovascular glaucoma (3 patients) all were observed in patients in the current series. Among previously published studies on Wagner disease, only Frandsen[17] had reported on three patients with congenital glaucoma. Of the four eyes that showed neovascular glaucoma, all disclosed peripheral traction retinal detachment, whereas three also were aphakic. Ischemia of the peripheral retina may be the underlying pathogenetic mechanism in this patients as demonstrated in selected fluorescein angiograms.

Cataract extraction was performed in 21 eyes, representing 38% of all eyes or 90% of eyes among patients older than 45 years of age. No postoperative complications were noted in eyes treated with extracapsular cataract extraction and posterior chamber lens implantation (n = 6), whereas iris neovascularization was observed in 20% of patients (n = 15) after intracapsular cataract extraction. We suggest that cataract extraction in patients with Wagner disease should be done with extracapsular techniques preserving a barrier between the anterior and posterior chambers that may protect from neovascular glaucoma.

In testing dark adaptation, we found an elevated rod threshold already in young patients. Böehringer et al[2] and Maumenee et al[3] found similar impairment of dark adaptation in this pedigree. Dark adaptation is a good parameter for assessing the subjective severity of Wagner disease.

In the ERG, rod and cone b-wave amplitudes can be within the normal range mainly in young patients with only mild chorioretinal atrophy. B-wave amplitudes were subnormal and implicit time was prolonged, however, in patients with more severe chorioretinal pathology. It becomes apparent from comparing the patient's b-wave amplitudes with the normal ranges in Figures 12 and 13 that the cone system is overall equally or more affected than the rod system. Because the ophthalmoscopic changes described and illustrated above resemble at least in part those of retinitis pigmentosa. A comparison of the ERG abnormalities in these heredodegenerative diseases shows the changes in b-wave amplitude and the prolongation in the cone b-wave's implicit times in Wagner disease match closest the progressive cone–rod degeneration variety of retinitis pigmentosa. Thus, we cannot document ERG abnormalities pathognomonic for Wagner disease. However, the changes in the ERG appear to indicate accurately extent and progression of the chorioretinal damage. It seems that photoreceptor dysfunction is more severe in advanced-stage Wagner disease than previously described[2,3,18] and also more severe than in the clinically very similar erosive vitreoretinopathy.[8] In our series, three eyes had a nonrecordable ERG, whereas this was not reported in erosive vitreoretinopathy.[8]

The question of whether Wagner disease represents a unique vitreoretinal pathology or whether it has to be regarded as part of the spectrum of familial vitreoretinal degenerations associated with retinal detachment will have to await further molecular genetic studies. From the clinical point of view, Wagner disease shares most typical ophthalmic findings with Jansen[5] and Stickler syndrome[6] as well as with erosive vitreoretinopathy.[8] However, rhegmatogenous retinal detachment is less prominent in Wagner disease than in those entities. Characteristic systemic findings and a mutation of the procollagen II gene, however, differentiate Stickler from Wagner syndromes and erosive vitreoretinopathy.[8,12] The latter two, however, seem to be closely related and have been demonstrated to be allelic disorders.[12] Late traction retinal detachment with exudative retinopathy as well as iris neovascularization in patients with Wagner disease probably represent unspecific end-stage complications and do not imply a relation to other vitreoretinal dystrophies such as Criswick syndrome[21,22] or autosomal dominant neovascular inflammatory vitreoretinopathy.[23]

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