

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Wagenfeld L, Zeitz O, Richard G. Visual loss after povidone-iodine pleurodesis. *N Engl J Med* 2007;357:1264-5.

**First patient: male, 27 years**

The patient was sent to a thorax surgery department with a lying thorax drainage due to a recurrent spontaneous pneumothorax, which recurred even after operation. No concomitant systemic or eye disease was known. During thoracoscopic surgery parts of the pleura were dissected and PVP-iodine instillation was performed for disinfection and to cause pleurodesis. One day after the operation he developed undefined disturbances in vision and aching of the eyes. His lids were swollen and hyperemic. One day later he developed central scotoma and visual acuity dropped to perception of hand movements for both eyes. Four days after the first symptoms, and 2 days after the first disturbance of vision, the patient was presented to the University Eye Clinic Hamburg. Visual acuity was perception of hand movements. The anterior segment showed no irregularity. The fundus showed small granular pigment changes between the optic disc and the macula. We performed a fluorescein and indocyanine green angiography, and found multiple defects of the pigment epithelium surrounding the optic disc, configured in lobular manner, most likely subsequent to the confluence of the short posterior ciliary arteries. The pattern-VEP (visual evoked potential) did not generate any potentials, and the flash-VEP generated flat but reproducible potentials. After a period of 2 months the vision had recovered to 20/25 on both eyes with a persisting para-central scotoma.

**Second patient: male, 38 years**

Like the first patient, this man was also operated because of spontaneous pneumothorax; some bullae and the apex of segment 6 had been dissected. In addition to the pneumothorax, he suffered from Crohn's disease and a cholinesterase deficiency. During the operation the anesthetist had to replace the tracheal tube

after dislocation of the tubus. A PVP-iodine pleurodesis was performed at the end of the operation. On the following day, the patient reported foggy vision, and his lids were red and swollen. Seven days after the initial drop in the central vision, the patient underwent a fluorescein and indocyaninegreen angiography. The findings were almost the same as those for the first patient. The anterior segment and fundus were almost regular. Visual acuity was limited to perception of hand movements for both eyes. Until the last examination in our clinic approximately 2 months after onset of symptoms the vision did not recover to more than 20/400 on both eyes.

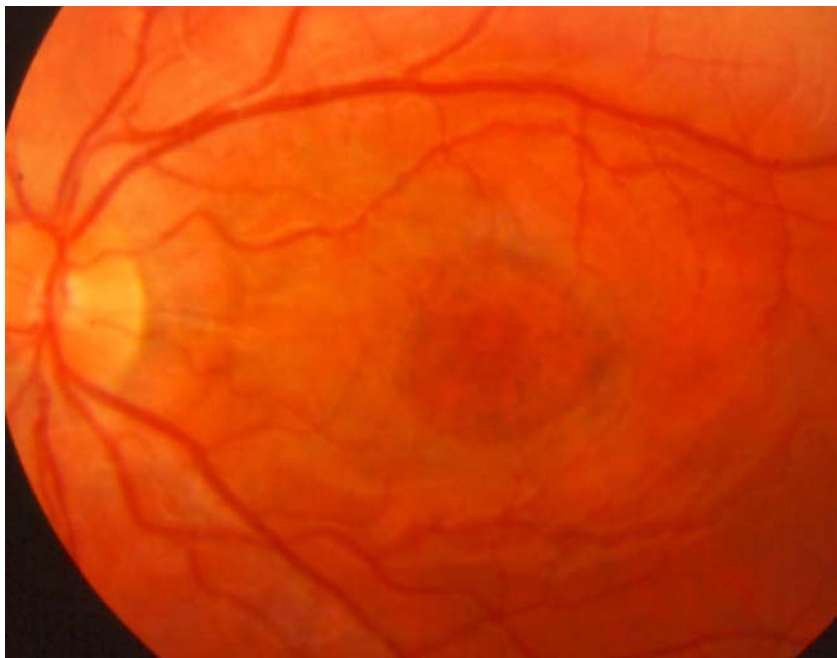
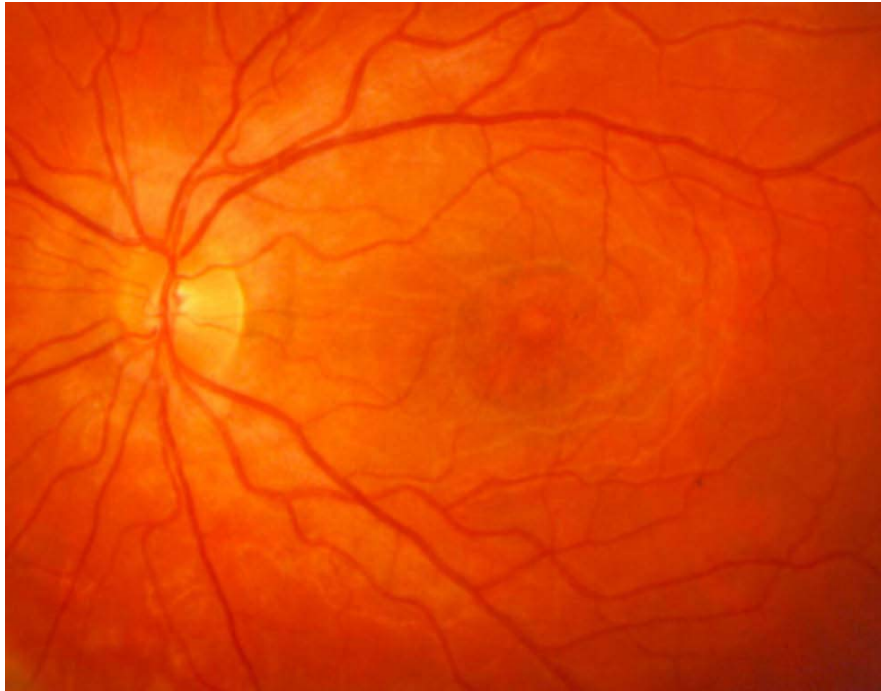
### **Third patient: female, 16 years**

This girl was operated because of persistent pneumothorax. A partial pleurectomy and apex resection was performed. At the end of the operation 200 ml 10% PVP-iodine were instilled. Two days after the operation, she complained about flickering vision. This patient was sent immediately to our clinic; the visual acuity was 20/800 for the right eye and counting fingers on the left eye, the anterior segment was normal, the fundus showed only very delicate changes in terms of consolidated reflexes, and fluorescein angiography revealed a hyperfluorescence that had the same configuration as in the other two cases but was more homogenous. As a hemodynamic disruption within the ciliary arteries was presumed to be responsible for the vision loss, we performed a Color Doppler Imaging (CDI). This examination did not show a definite alteration, and all measured velocities were comparable to the results from a healthy control population that have been published previously. We tried a high-dose corticosteroid treatment. One day later, the visual acuity had recovered to 20/25 and 20/20, but the patient had only a very small central visual field. Testing of the visual field showed bilateral defects corresponding to the pigment epithelium changes. Pattern-VEP showed reduced amplitudes, flash VEP was

normal. Photopic and scotopic electroretinogram (ERG) were normal, but the Pattern-ERG showed a reduced central peak in both eyes. During the first week after the onset of the symptoms the patient developed pigment epithelium changes, as seen for the other two cases, and showed the same angiographic findings. Some weeks later the findings were more pronounced, and stayed nearly stable over a period of 2 months. The visual acuity stabilized at 20/25 and 20/20, but a paracentral ringscotoma persisted.

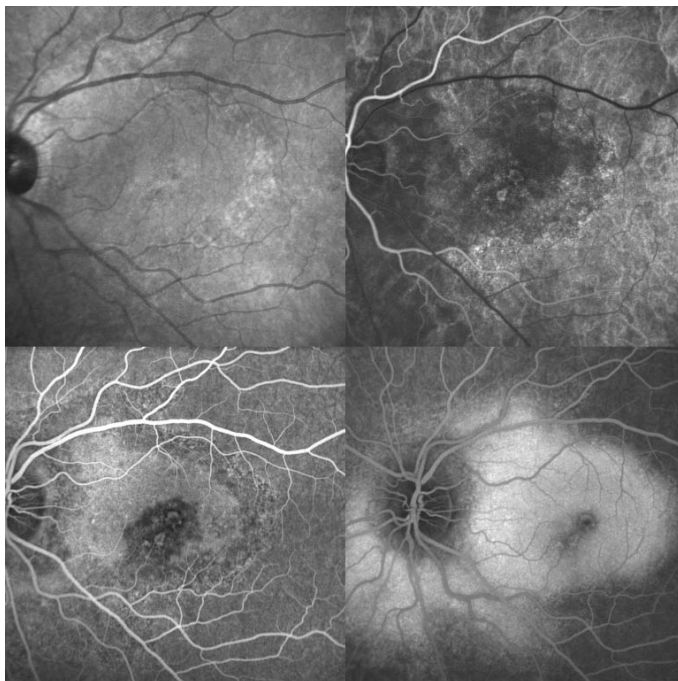
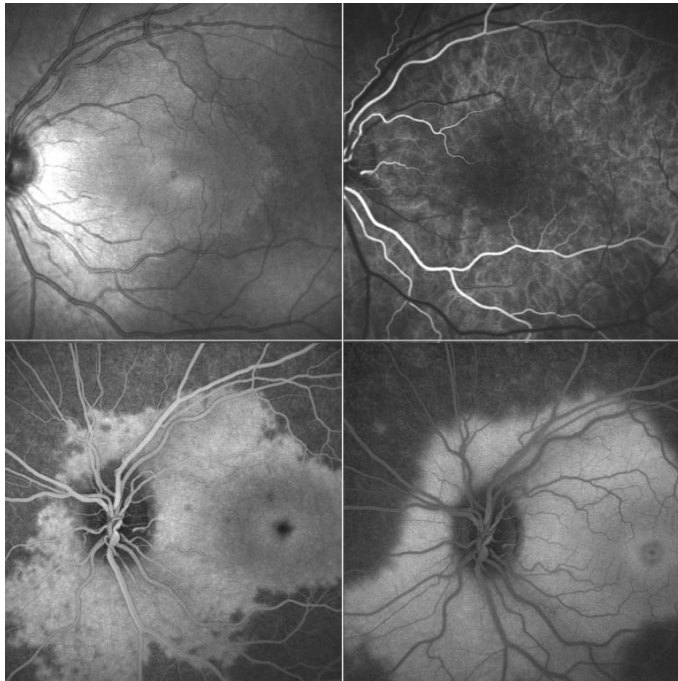
*Fundus photographs: WebFig1 and 2:*

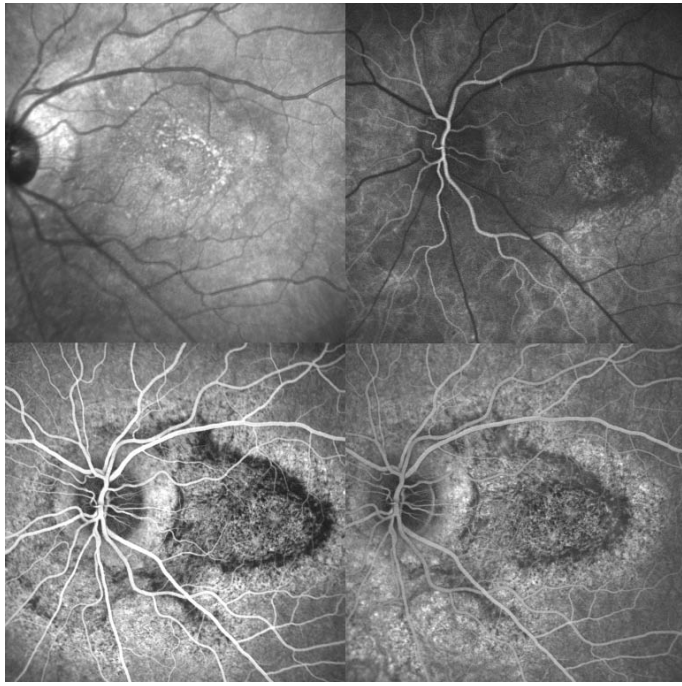
These pictures show the color fundus photographs of the left eye of patient three at days 4 and 14 after onset of symptoms. The development of stippled RPE changes and atrophy over a period of two weeks can be seen.



*Angiograms: WebFig3-5:*

All angiograms were taken from the left eye of patient three. These three angiograms show a redfree photograph of the fundus (upper left), an early phase (upper right), an arteriovenous phase (lower left) and a late phase (lower right). While the first angiogram shows a diffuse hyperfluorescence, the patient develops stippled RPE changes and atrophy over a period of two weeks. Iodate as an oxidant leads to increased oxidative stress at the RPE. This is further enhanced by reduced scavenging capacity of the RPE due to the interaction of iodate with melanin. This free radical burst has apparently the potential to induce RPE damage.

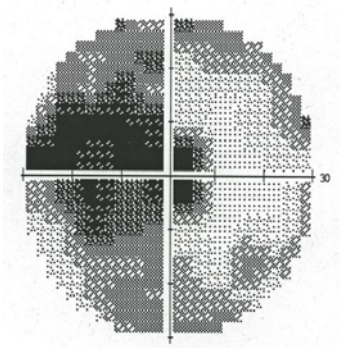




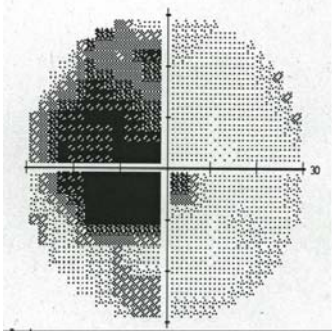
*Visual fields:*

These visual fields were taken from the left eye of patient three. Visual field defects corresponding to the RPE defects can be seen. While the visual acuity recovers in this patient, the visual field still reveals a central skotoma after two weeks.

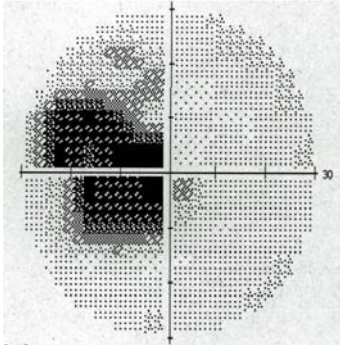
**Visual field of the left eye, one day after onset, patient 3.**



**Visual field of the left eye, four days after onset, patient 3.**



**Visual field of the left eye, eight days after onset, patient 3.**



**Table 1:**

Summary of the clinical findings of all three patients at initial presentation. Not all examinations were possible at this visit due to the general reduced condition of the patients shortly post-op.

	<b>first patient</b>	<b>second patient</b>	<b>third patient</b>
<b>Visual acuity</b>	R/L Perceptions of Handmovements	R/L Perception of Handmovements	R 20/800 L Counting fingers
<b>Anterior Segment</b>	R/L no pathology	R/L no pathology	R/L no pathology
<b>Fundus</b>	Small granular pigment changes between optic disc and fovea, otherwise normal	Small granular pigment changes between optic disc and fovea, otherwise normal	Small granular pigment changes between optic disc and fovea, otherwise normal
<b>Angiography</b>	Lobular shaped hyperfluorescence, alterations of backgroundfluorescence, no leakage Changes develop to a dry ARMD like picture after 2-3 weeks	Lobular shaped hyperfluorescence, alterations of backgroundfluorescence, no leakage Changes develop to a dry ARMD like picture after 2-3 weeks	Lobular shaped hyperfluorescence, alterations of backgroundfluorescence, no leakage Changes develop to a dry ARMD like picture after 2-3 weeks
<b>Pupil movements</b>	normal	R: afferent defect	normal
<b>Pattern-VEP Flash-VEP</b>	R/L no Signal L>R flat, but reproducible	-	R/L normal implicit time, flat amplitudes R/L normal
<b>photopic ERG Skotopic ERG</b>	normal photias L normal potentials R Examination not possible	-	R normal L no examination R normal potentials L no examination
<b>Pattern ERG</b>	-	-	R/L reduced amplitudes for a and b waves
<b>CDI</b>			within normal values
<b>Vision in last examination</b>	R 20/25 L 20/25	R 20/400 L 20/400	R 20/25 L 20/20