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Acute tear of the retinal pigment epithelium

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Summary

The fluorescein angiographic findings immediately following a tear of the retinal pigment epithelium are presented and the mechanisms of fluid movement from the retina to the choroid are discussed. Our case represents a clinical correlate to recent experimental reports on fluid movement across the retinal pigment epithelium-Bruch's membrane complex.

Tears of the retinal pigment epithelium (RPE) are recently described sequelae of RPE detachments in the elderly [1–3]. Approximately 10% of eyes with RPE detachments secondary to age related macular degeneration are complicated by tears [4]. Tears may occur spontaneously or as a complication of laser photocoagulation [1]. Fluorescein angiography in eyes with RPE tears typically shows marked hyperfluorescence in the bed of the tear where the choriocapillaris is 'bare'. There is often hypofluorescence adjacent to the bed of the tear caused by the rolled edge of torn RPE. With time, remodelling and scar formation may obscure the cause of diminished vision [5]. Acutely, a tear of the RPE represents a defect in the blood-retinal barrier. The angiographic findings immediately following a tear of the RPE have not been reported previously. Herein we describe a patient who underwent fluorescein angiography within hours of developing a tear. This case represents a clinical correlate to recent experimental reports on fluid movement across the RPE-Bruch's membrane complex.

Case report

A 79 year old white male presented with a 2 week history of distortion of vision affecting the right eye. His visual acuity was 6/12 in the right and 6/9 in the left. In the right macula there was a serous detachment of the sensory retina inferior and nasal to the fovea (Fig. 1) but no haemorrhage or lipid. Fluorescein angiography confirmed the presence of choroidal neovascularization inferior and nasal to the fovea outside the foveal avascular zone in the right eye (Fig. 2a & b). The neovascularization was treated with Argon blue-green laser and confluent white photocoagulation was achieved throughout the area of neovascularization.

Two weeks after treatment his vision was 6/12 and fluorescein angiography showed leakage indicating the presence of residual neovascularization (Fig. 3a & b) and further Argon blue-green laser was applied. Seven days later the patient noticed a sudden drop in vision in the right eye and presented to the hospital within four hours. His vision was 6/24 in this eye and fundal examination revealed the presence of a retinal pigment epithelial tear (Fig. 4a). There was no haemorrhage or elevation of the sensory retina. Fluorescein angiography revealed intense fluorescence in the area of the bed of the tear but no leakage into the subretinal space (Fig. 4b & c). There was a small area of residual neovascularization. Over the following five days the retinal pigment epithelium rolled further revealing more of the bare Bruch's membrane and choroid (Fig. 5). Examination five months later showed atrophy of the choriocapillaris in the bed of the tear revealing large choroidal vessels (Fig.

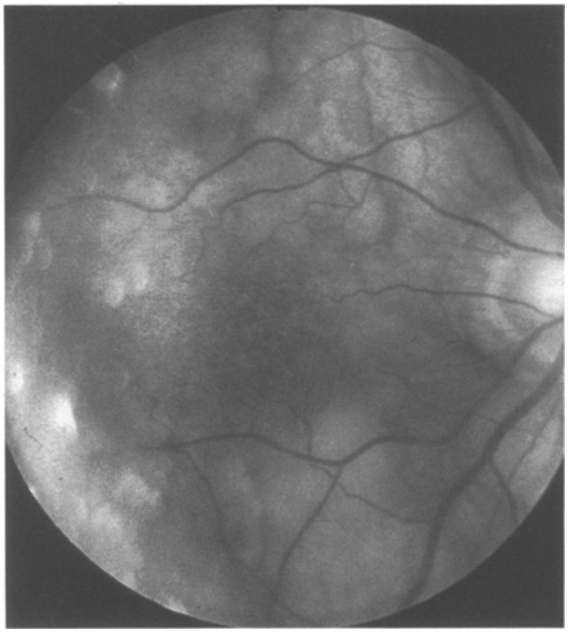


Fig. 1. Appearance of the right macula on presentation. The vision was 6/12 and there was a small serous detachment of the retina inferior and nasal to the fovea.

6a). The mound of torn retinal pigment epithelium remained hypofluorescent and there was no evidence of residual neovascularization at the original site but a large neovascular membrane on the bed of the tear (Fig. 6b).

Discussion

The tight junctions between adjoining RPE cells are an important component of the blood-retina barrier. This is demonstrated by studies in which peroxidase injected intravenously or intravitreally does not cross the zonulae occludens at the apical RPE cell junction [6, 7]. A tear of the RPE represents a breach in the normal barrier between the choriocapillaris and neurosensory retina, allowing free communication between these two compartments. Repair after tears of the RPE was recently described by Chuang and Bird [5]. They observed changes consistent with healing of the defect by a layer of RPE cells or fibrous tissue. This observation is in accordance with histologic evidence of

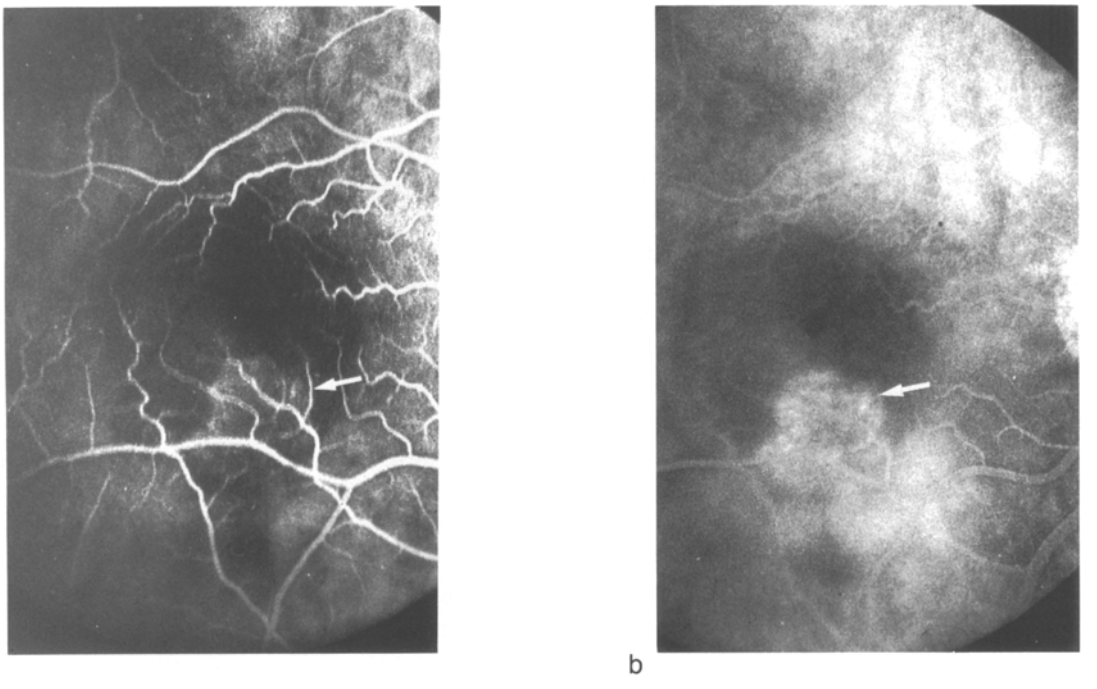


Fig. 2a & b. Early and late fluorescein angiograms reveal the presence of a subretinal neovascular membrane inferior and nasal to the fovea (arrow).

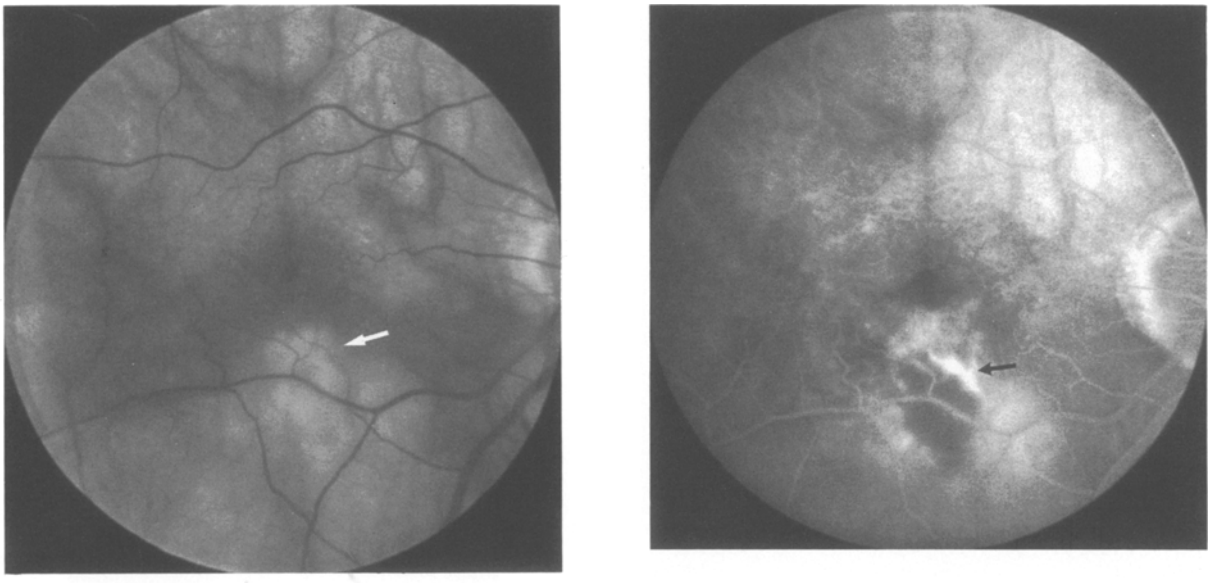
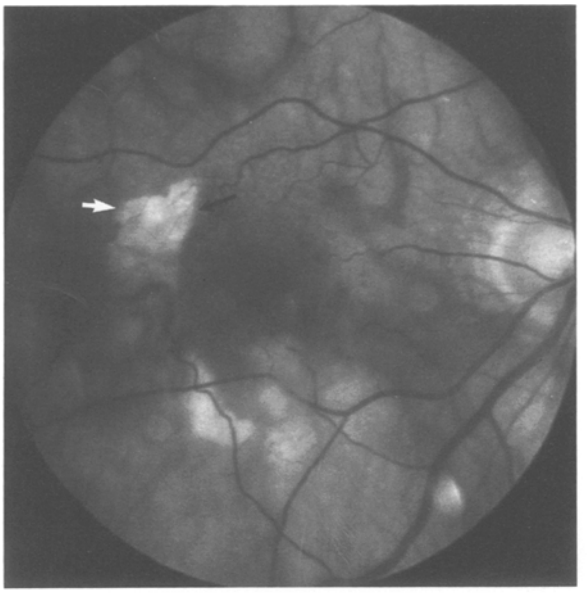


Fig. 3. a. Appearance of the right macula two weeks after treatment reveals the area of laser photocoagulation (arrow). b. Fluorescein angiography at 2 weeks reveals residual neovascularization (arrow).

RPE repair following experimental trauma [8–11]. Covering the defect does not necessarily reconstitute the blood-retina barrier since the repair tissue may not form competent tight junctions [10, 12].

As an integral part of the blood-retina barrier, the RPE regulates the flow of ions and fluid between the retina and the choroid [13]. Active transport mechanisms across the RPE have been demonstrated in experimental models [13–17]. RPE cell membranes contain metabolic pumps which regulate bidirectional ion transport and associated fluid movement. In experimental models various metabolic inhibitors influence ion and fluid movement across the RPE allowing manipulation of the rate of fluid resorption and the clearance of vitreous fluorescein [14–18]. Recently a clinical application of this ability was reported in the treatment of chronic macular oedema with acetazolamide [19].

A breakdown of the diffusion barrier occurs when there is a defect of the RPE. Electron-dense tracer substances such as peroxidase have been shown to diffuse freely from the vitreous space into the choroidal capillary network [6]. When injected intravenously peroxidase has been shown to diffuse through Bruch's membrane from the choroidal vessels although the concentration of peroxidase decreases to such an extent that it is no longer detected in the vitreous cavity [7]. Studies dealing with the barrier function of RPE have supported the theory that choroidal fluid might penetrate through a localized RPE defect and form a collection under the neurosensory retina and this has been accepted as the pathogenesis of central serous retinopathy [6, 20]. However, experimental evidence suggests that RPE alone is not responsible for fluid movement from the retina to choroid [17, 21] and it has been demonstrated that functional RPE is not necessary for maintaining choroidoretinal apposition [22]. Damage to the RPE by sodium iodate, a selective toxin, results in a substantial increase in the resorption rate of subretinal fluid experimentally [21]. It might be expected that such RPE damage would result in a loss of metabolic transport activity. The breakdown of the diffusion barrier would result in leakage of protein through the RPE and a loss of oncotic pressure. The resorption rate of subretinal fluid was only prolonged compared to a normal eye when the subretinal fluid consisted of serum. This implies that there is still an oncotic pressure difference between the subretinal space and the choroid and one explanation is that the



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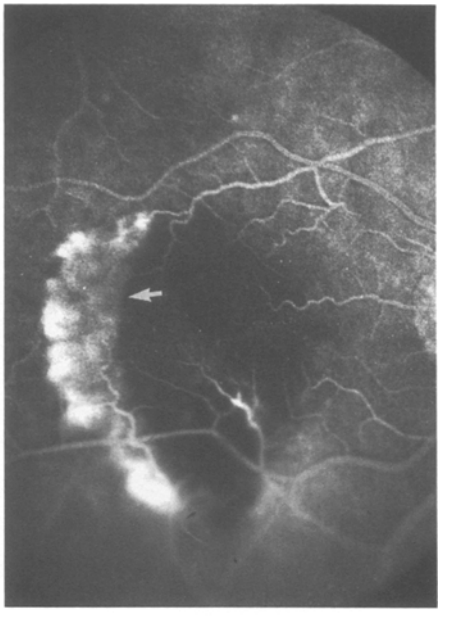

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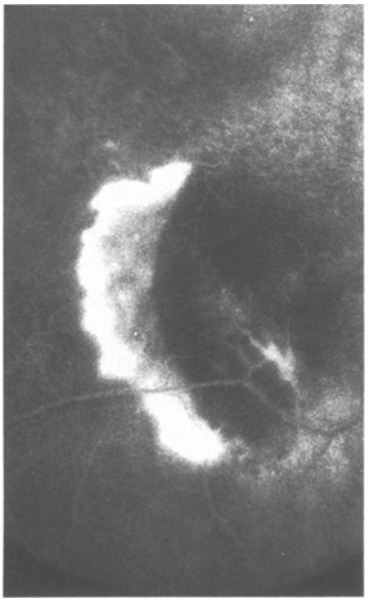

c

Fig. 4. a. A sharply outlined margin of the torn retinal pigment epithelium is seen (white arrows) together with a folded edge of torn RPE (black arrow). b. Early phase fluorescein angiogram shows hypofluorescence of the folded pigment epithelial edge (white arrow) and hyperfluorescence in the bed of the tear with a sharply defined margin of the tear. c. The late angiogram reveals more intense hyperfluorescence in the bed of the tear but no leakage into the subretinal space. Note the area of hyperfluorescence in the area of residual neovascularization.

protein concentration decreases as it diffuses from the choroid to the vitreous. This is supported by the peroxidase study discussed above [7]. These studies demonstrate that whereas interruption of the RPE results in free diffusion of substances in both a retinochoroidal and choroidoretinal direction, the net fluid movement remains in a retinochoroidal direction. A tear of the RPE might be a clinical counterpart to sodium iodate poisoning of the RPE, since both represent acute defects in the blood-retina barrier.

Based on experimental studies of fluid movements across Bruch's membrane, the fluorescein appearance of an acute RPE tear is not surprising. Fluorescein does not flood into the subretinal space in the absence of an intact RPE barrier since the direction of net fluid movement does not change. The intense hyperfluorescence seen on fluorescein angiography is explained by the absence of pigmented layer, not leakage into the subretinal space. However, fluorescein can slowly diffuse in a direction opposite to that of fluid movement, [12, 23] and this may account for the late and indistinct leakage sometimes observed. Our observations conform with Spitznas' hypothesis regarding another disorder of the RPE barrier - central serous retinopathy [23]. He maintains that a 'leak' in the

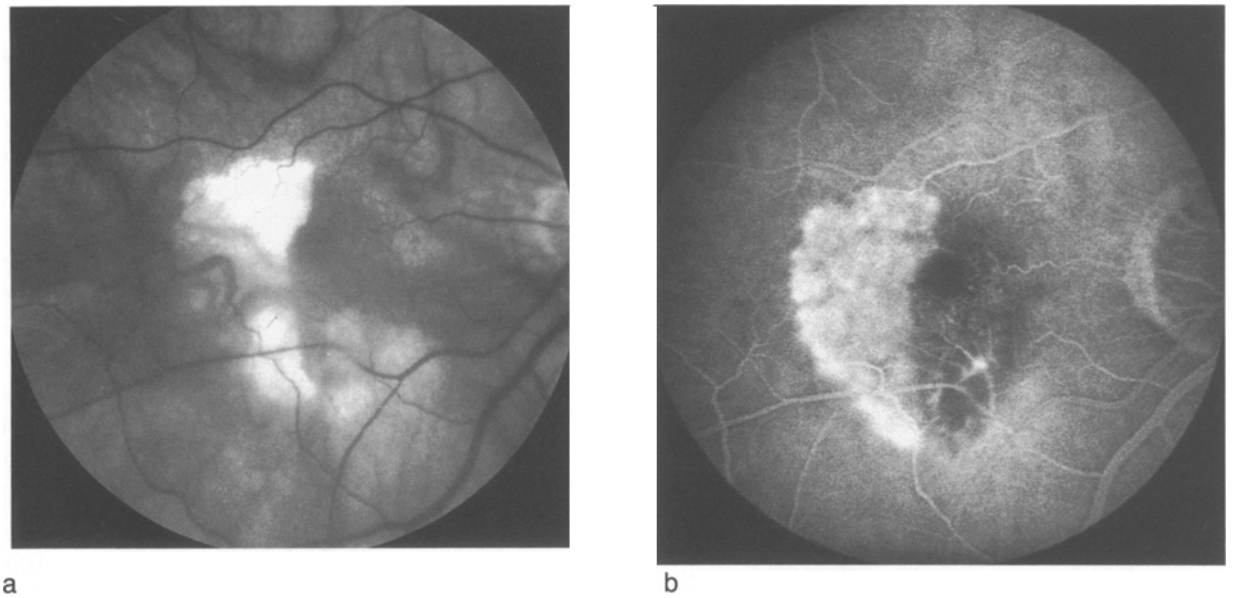

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Fig. 5. a. Five days after the acute event shows further rolling of the torn RPE revealing a larger bed of Bruch's membrane. b. Fluorescein angiography confirms the presence of residual neovascularization.

RPE would not result in passive fluid movement from the choroid to the retina.

The pathogenesis of RPE tears is uncertain. Gass proposed that continued leakage into the sub-RPE space from choroidal neovascularization causes increasing stress culminating in a tear [24]. Laser treatment may cause sudden contraction of fibrovascular tissue producing shearing forces able to rip the RPE [25]. However, choroidal neovascularization is not a constant feature of RPE detachments which tear [12]. Bird and co-workers suggest that hydrophobic lipid deposits in Bruch's mem-

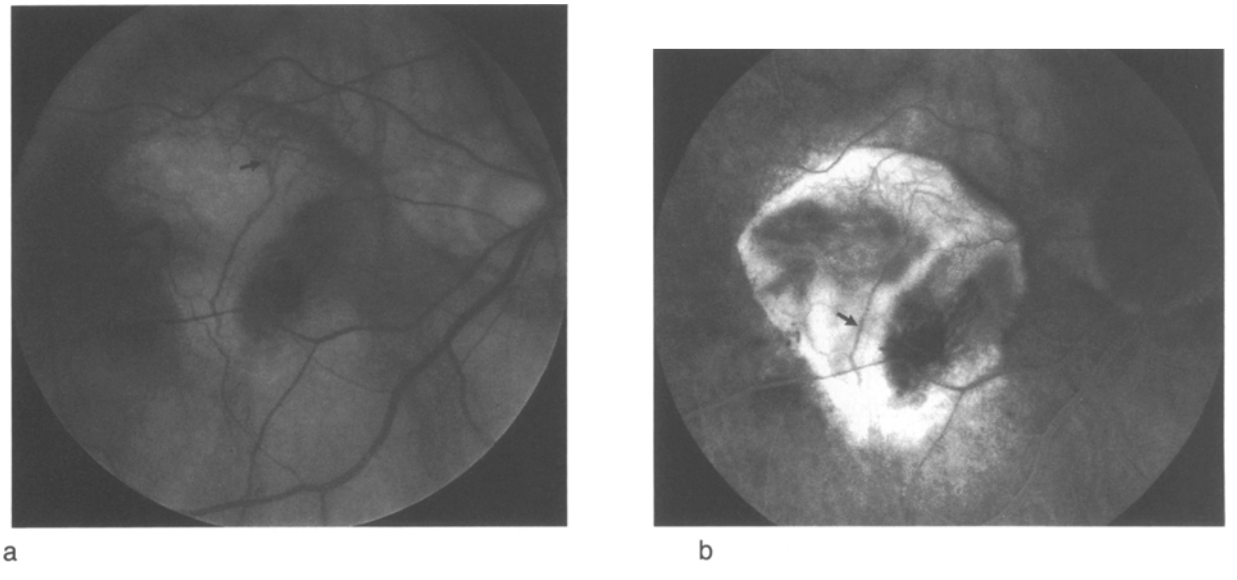

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Fig. 6a&b. Six months after the acute event there is atrophy of the choriocapillaris revealing large choroidal vessels. The mound of torn pigment epithelium remains hypofluorescent and there is a large neovascular membrane on the bed of the tear (arrow).

brane cause increased resistance to fluid movement towards the choroid [12, 26]. This may result in a progressively larger RPE detachment (Fig. 3b) which rips from mechanical stress either spontaneously or after laser treatment. It is possible that both models of RPE tears occur, and that avascular RPE detachments can be secondarily invaded by choroidal neovascularization [27]. The fluorescein characteristics of RPE tears are consistent with both hypotheses, since some show evidence of choroidal neovascularization and others do not.

Accumulation of dye in the subretinal space after a RPE tear is sometimes observed [12, 24, 25, 28]. Often fluid and dye accumulation is present initially but disappears after several weeks. Gass initially suggested that leakage of serous fluid from the choriocapillaris accounts for fluid in RPE detachments and this would therefore be the source of subretinal fluid in RPE tears [29]. Based on the experiments discussed above, it seems unlikely that the fluid comes from the choriocapillaris under the RPE tear, although fluorescein may diffuse into the subretinal fluid along a concentration gradient [12, 23].

Gass later suggested that leakage from neovascular membranes accounts for accumulation of fluid in the subretinal space after RPE tears [24]. In vascular RPE detachments which tear, the source of fluid and dye accumulation may be the choroidal neovascular membrane, since serous retinal detachment is a recognized feature of choroidal neovascularization [27]. There is a report of leakage accumulating after a rip in an area where an occult membrane was suspected [28]. Continued subretinal fluid accumulation might continue until a shift occurs in the equilibrium between neovascular leakage and the ability of the RPE to respond. Proliferating RPE cells can envelope neovascular membranes causing their involution and the resorption of subretinal fluid [30].

In avascular RPE tears, the fluid observed in the subretinal space may be the fluid which was previously trapped between the water-tight RPE and hydrophobic Bruch's. membrane. After the tear occurs a new route for fluid resorption is accessible via the neurosensory retina to an area of Bruch's membrane where fluid movement is unimpaired. This would also account for the appearance of subretinal fluid initially in some cases and its gradual disappearance. Another angiographic feature observed months after a tear of the RPE suggests late closure of the choriocapillaris in the bed of the tear [5]. This observation has basis according to experimental studies. The RPE has been shown to influence morphologic characteristics of the choriocapillaris [31]. Moreover, choriocapillaris atrophy has been induced by RPE destruction experimentally [32].

The interpretation of the angiographic findings is based on our current understanding of age-related changes which result in detachments and tears of the RPE. Ultimately, histologic and biochemical examination of eyes may prove helpful in characterizing the tissue changes and cellular alterations which influence ion and fluid movements in humans. This report is useful to the extent that it supplies clinical evidence which supports experimental data on fluid movement across Bruch's membrane.

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