Vitreous haemorrhage in the diabetic eye

Hamish MA Towler

Vitreous haemorrhage is a serious sign indicating significant intraocular pathology in the diabetic eye and warranting prompt referral to an ophthalmologist for further assessment and management.

Vitreous haemorrhage most commonly occurs as a result of the separation of the posterior vitreous from the retina. This is a normal ageing event and occurs in the non-diabetic eye around the age of 60 years, but often develops earlier in diabetic and myopic eyes.

Vitreous separation can tear the retina leading to vitreous haemorrhage in the absence of diabetic retinopathy, and retinal tears or holes may then lead to retinal detachment. All eyes with vitreous haemorrhage must be examined by an ophthalmologist for retinal breaks or detachment within a day or two of onset. Ocular ultrasound is essential to assess retinal integrity when the retina cannot be seen.

In the presence of retinal neovascularization, posterior vitreous separation leads to vitreous haemorrhage through traction on the new vessels. Localized posterior vitreous separation at the macula may limit bleeding within the preretinal (subhyaloid) space where characteristically the red cells settle with a striking fluid level. YAG (yttrium-aluminium-garnet) laser disruption of the inferior posterior hyaloid face can assist drainage of blood into the inferior vitreous.

Intragel vitreous haemorrhage which does clear spontaneously is an indication for pars plana vitrectomy and laser photocoagulation. This procedure is easily undertaken under local anaesthesia as a day case, although general anaesthesia may be preferable if extensive retinal dissection is anticipated. Untreated neovascularization may progress rapidly behind non-clearing vitreous haemorrhage and devastate the retina. Early surgical intervention (within 3 months) is advisable; the Diabetic Retinopathy Vitrectomy Study (DRVS) research group (1985) showed early vitrectomy to be beneficial only in type 1 diabetes but this study predated the availability of endolaser photocoagulation and other significant surgical developments.

Vitreous haemorrhage may occur late after successful laser photocoagulation for proliferative retinopathy, as a result of avulsion of regressed neovascular vitreoretinal attachments. Enzyme-assisted vitreous separation may reduce the morbidity of spontaneous vitreous detachment in high risk eyes.

INTRODUCTION

The treatment of sight-threatening diabetic retinopathy has been firmly established by well-conducted clinical trials in the UK and the United States (Cheng, 1975; Diabetic Retinopathy Study Research Group, 1981; Early Treatment Diabetic Retinopathy Study Research Group, 1985; Diabetes Control and Complications Trial, 1995; UK Prospective Diabetes Study (UKPDS), 1998a,b). This has led to the introduction of screening programmes for the detection of early diabetic retinopathy, allowing early and effective treatment (Foulds et al, 1983; Rohan et al, 1989; Singer et al, 1992; Harding et al, 1995; Mason and Drummond, 1995; Javitt and Aiello, 1996).

The implementation and uptake of screening programmes has, however, been less comprehensive than desirable despite highly publicized initiatives such as the Saint Vincent declaration in Europe (Anonymous, 1990) and Diabetes 2000 in the USA. In England and Wales, the National Service Framework for Diabetes (www.diabetic-retinopathy.screening.nhs.uk) is establishing a comprehensive screening programme, with a target of 100% screening of diabetics in England by 2007.

Vitreous haemorrhage is a dramatic and often frightening event for the patient because of its association with a sudden and often profound painless loss of vision. Vitreous haemorrhage

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usually results from the mechanical separation of the vitreous gel from the retina which leads to bleeding within the vitreous gel or the intervening subhyaloid space between the retina and posterior vitreous face. This process of posterior vitreous separation (also known as posterior vitreous detachment) is a relatively normal ageing event which most commonly takes place in the non-diabetic eye around the age of 60–70 years.

Vitreous separation may take place at an earlier age in the diabetic eye as a result of the disturbance of the normal vitreo-retinal interface. This is initiated by the outgrowth of new vessels from the retina in response to retinal ischaemia, a process mediated by a number of cytokines of which vascular endothelial growth factor currently appears to be the most important. Treatment of retinal neovascularization by laser photocoagulation may accelerate the process of posterior vitreous separation and precipitate vitreous haemorrhage (Sebag et al, 1990). Even when retinal new vessels have regressed satisfactorily after laser treatment, vitreous haemorrhage can occur later as a result of vitreoretinal traction on the residual fibrovascular remnant when vitreous separation occurs.

In addition to causing bleeding from new vessels, vitreous traction on the retina can cause retinal tears and holes leading to retinal detachment which, if not identified, may result in serious visual loss. In the non-diabetic population, retinal tears caused by vitreous separation are the most common cause of vitreous haemorrhage, and this pathology must always be considered in the diabetic eye.

TYPES OF VITREOUS HAEMORRHAGE

Bleeding into the subhyaloid space between the retina and vitreous can have a striking appearance (*Figure 1*). Coagulation is not activated and the blood remains fluid, and the red cells may settle with a horizontal fluid level (*Figure 2*). Subhyaloid blood may remain confined to this compartment and reabsorb over a period of several months.

Bleeding into the vitreous gel (*Figure 3*) activates thrombosis and fibrinolysis which leads to a progressive changes in the vitreous gel structure, and often to a cycle of recurrent vitreous haemorrhage. Vitreous blood settles by gravity, and the stirring up of this blood by postural movements may give the impression of recurrent bleeds. The rate of clearance of vitreous haemorrhage is highly variable and unpredictable, varying from complete clearance over a few weeks to non-clearing haemorrhage persisting for several years.

EFFECTS OF VITREOUS HAEMORRHAGE

The main effects of vitreous haemorrhage are:

- Visual impairment
- Obscured visualization of the vitreoretinal interface and pathological processes

Figure 2. Spectacular premacular subhyaloid haemorrhage showing a horizontal level of settled red blood cells.

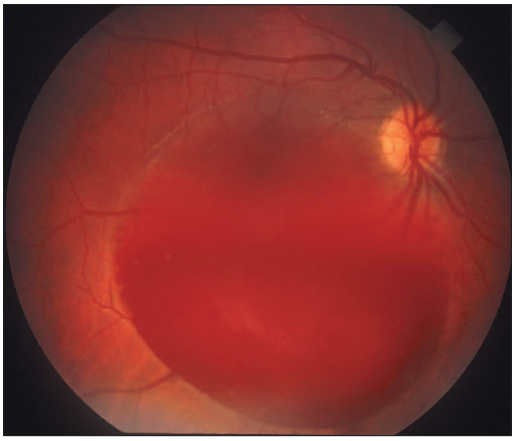


Figure 3. Intragel vitreous haemorrhage obscuring the macula. Some peripheral retina detail is visible and this haemorrhage is likely to clear within 3 months.

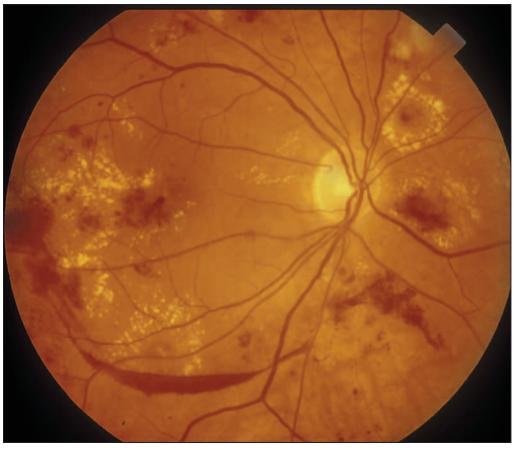
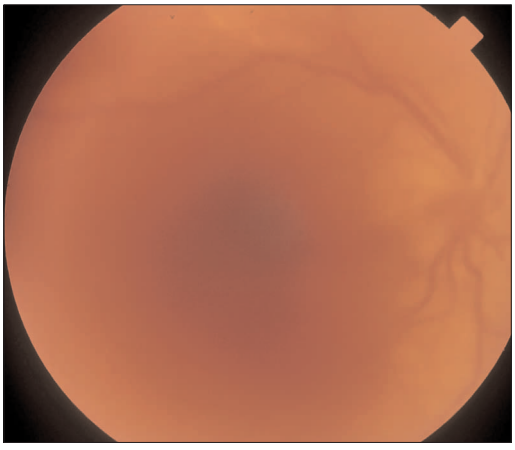


Figure 1. Severe non-proliferative diabetic retinopathy with crescent shaped inferior preretinal (subhyaloid) haemorrhage. This eye needs urgent panretinal laser photocoagulation.



- Prevention of laser photocoagulation
- Possible raised intraocular pressure.

ASSESSMENT OF VITREOUS HAEMORRHAGE

Visual acuity should be recorded in both eyes. The pupil reflexes should be recorded paying particular attention to any relative afferent pupil defect, the presence of which would suggest an underlying retinal detachment or major retinal vascular obstruction such as a central retinal vein occlusion. In diabetic eyes with significant retinopathy, the light reflexes may be sluggish as a result of autonomic neuropathy.

The pupils should be dilated with tropicamide 1% or cyclopentolate 1% drops. These can be augmented with phenylephrine 2.5% although the latter should used with care in patients with severe ischaemic heart disease or hypertension. Direct ophthalmoscopy may reveal an absent red reflex, but peripheral retinal visualization with this instrument is usually severely limited or impossible in the presence of significant vitreous haemorrhage.

Binocular indirect retinal examination by slit lamp biomicroscopy or the indirect ophthalmoscope may be possible through mild to moderate vitreous haemorrhage, and both methods afford a much better view of the peripheral retina where retinal tears most commonly develop.

If the retina cannot be seen, retinal integrity must be assessed by B-scan ultrasonography which may need to be repeated at intervals to exclude retinal detachment. Large retinal tears may occasionally be detected by ultrasonography, but flat retinal holes cannot reliably be excluded.

Patients with vitreous haemorrhage should be referred urgently to an ophthalmologist for assessment preferably within 48 hours and at most within 1 week.

NATURAL HISTORY OF VITREOUS HAEMORRHAGE

Approximately 25% of eyes with peripheral retinal new vessels will develop a vitreous haemorrhage within 5 years without laser photocoagulation (Turner et al, 1985). This risk is halved by panretinal photocoagulation (Diabetic Retinopathy Study (DRS), 1981). Moderate intragel vitreous haemorrhages (*Figure 3*) and those limited to the subhyaloid space are likely to clear spontaneously. Severe vitreous haemorrhage reducing visual acuity to 5/200 or less has a less than 50% chance of clearing spontaneously over 3 years (Ziemianski et al, 1980).

Premacular subhyaloid haemorrhage (*Figure 2*) can be treated by laser disruption of the posterior hyaloid membrane which allows the fluid preretinal blood to drain into the inferior vitreous and be absorbed (Ezra et al, 1996).

MANAGEMENT OF NON-CLEARING VITREOUS HAEMORRHAGE

Pars plana vitrectomy was first undertaken in 1970 by Robert Machemer for non-clearing diabetic vitreous haemorrhage of 5 years' duration, and resulted in restoration of visual acuity of 6/15 (Machemer et al, 1971).

The benefit and optimum timing of vitrectomy in severe diabetic vitreous haemorrhage (visual acuity of 5/200 or less) was established by the DRVS (1985, 1988) which clearly showed a benefit of early vitrectomy in type 1 diabetes but no early benefit in type 2 diabetes (*Table 1*).

These studies predated the use of endolaser photocoagulation which has helped to reduce the risk of total visual loss (no perception of light) in these eyes from 20% to around 5% mainly as a result of retinal detachment or neovascular glaucoma (Liggett et al, 1987). Other significant technical advances, including wide-field viewing systems, silicone oil and perfluorocarbon 'heavy liquids', intravitreal administration of fibrinolytic agents and steroids, have extended the surgical repertoire but vitrectomy still carries significant risks, particularly in eyes with extensive retinal neovascularization and membrane formation. These advances in vitreoretinal surgery have broadened the indications for vitrectomy to include:

- Non-clearing vitreous haemorrhage: type 1 >3 months; type 2 >6 months
- Threatened macular detachment
- Traction detachment of macula <6 months duration
- Severe fibrovascular proliferation
- Dense pre-macular haemorrhage
- Diabetic macular oedema and/or posterior hyaloidal traction
- Ghost cell glaucoma
- Iris neovascularization with opaque media.

TABLE 1.
Visual outcome results

Eye achieving 6/12 or better acuity	Early	Late
Type 1 diabetes	36%	12%
Type 2 diabetes	16%	18%
Eyes with no perception of light (NPL) vision at 2 years	25%	19%

From Diabetic Retinopathy Vitrectomy Study Research Group (1985)

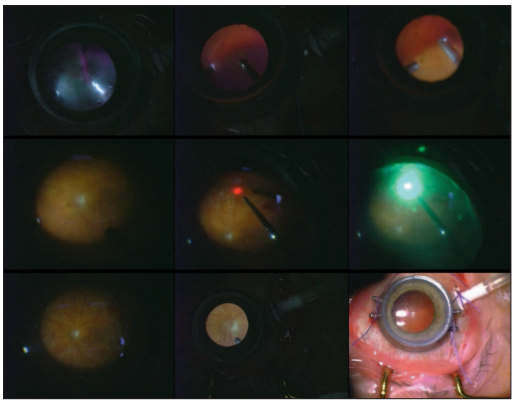


Figure 4. Composite of pars plana vitrectomy and laser surgery. A dense non-clearing haemorrhage (top left) is removed, panretinal laser applied, resulting in clear media with a good red reflex (bottom left).

Vitrectomy and endolaser photocoagulation (*Figure 4*) can be readily undertaken under local anaesthesia as a day case or a brief hospital admission in the majority of patients which is much less disruptive to their diabetes control. Where more extensive retinal surgery is anticipated or in younger type 1 diabetics, general anaesthesia may be preferred.

Vitreous haemorrhage may recur after vitrectomy, but usually within the first year. This may result from fibrovascular ingrowth at the scleral entry wounds, and may require further surgery (Liggett et al, 1987).

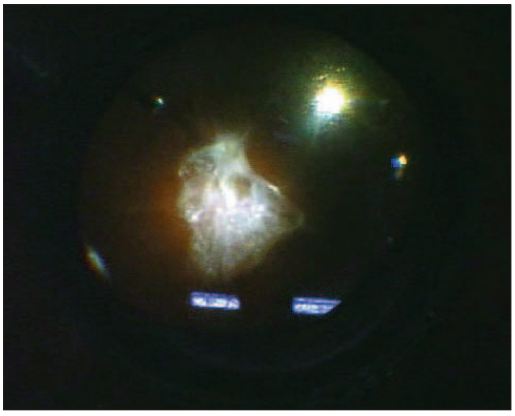


Figure 5. Intraoperative photograph showing an extensive fibrovascular membrane obscuring the entire macula and optic disc. This was successfully removed but visual acuity remained poor.

KEY POINTS

- Vitreous haemorrhage may be a sign of retinal detachment as a result of tearing of the retina.
- Patients with vitreous haemorrhage should be examined by an ophthalmologist within 48 hours.
- Vitreous haemorrhage may occur despite successful laser treatment for retinal neovascularization.
- Non-clearing vitreous haemorrhage can be removed by surgical vitrectomy under local anaesthesia as a day case in the majority of patients.
- Early vitrectomy should be considered for non-clearing vitreous haemorrhage in type 1 diabetics.
- Preretinal haemorrhage at the macula may be dispersed by laser disruption of the posterior hyaloid face without resorting to surgery.

The major factor determining the visual outcome of vitrectomy for vitreous haemorrhage is the extent of retinal neovascularization. Large neovascular membranes (*Figure 5*) are associated with more extensive retinal ischaemia, retinal fibrosis and distortion, and a higher risk of iatrogenic damage at the time of vitrectomy (DRVS, 1988).

PREVENTION OF VITREOUS HAEMORRHAGE

The key to the prevention of vitreous haemorrhage in diabetic eyes is the early identification and adequate treatment of proliferative diabetic retinopathy. The DRS (1981) showed that in eyes without high risk characteristics (less than one disc area of new vessels and without preretinal fibrosis or haemorrhage) the risk of serious visual loss was reduced to less than 10% with panretinal photocoagulation. In the presence of high-risk characteristics, treatment was still effective, the risk of severe visual loss being reduced from 44% to 20%.

Vitreous haemorrhage may still occur at a later date in well-treated eyes as a result of posterior vitreous separation. Eyes with localized areas of vitreoretinal attachment at sites of regressed new vessels have a better prognosis for good visual outcome after vitrectomy than eyes with extensive neovascularization (DRVS, 1985).

Enzyme-induced vitreous separation or 'pharmacological vitrectomy' is an attractive proposition which may reduce the risk of spontaneous vitreous haemorrhage. Autologous plasmin has been used to facilitate vitreous separation as an adjunct to surgical vitrectomy (Hikichi et al, 1999; Trese et al, 2000; Gandorfer et al, 2001; Williams et al, 2001). Further randomized studies are needed to assess the benefits of this technique. HM

Conflict of interest: none.

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