Silicone oil with high specific gravity for intraocular use

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SUMMARY Silicone oil with a higher specific gravity than that of intraocular fluid or polydimethylsiloxane may have special indications in vitreoretinal surgery. Trifluorosiloxane is such a substance, and therefore its biological compatibility was investigated in rabbit eyes. It was found that this substance was clinically well tolerated within the observation time of up to 6 months, even if there was some neovascularisation from the inferior limbus. Histologically both an inflammatory response and tissue impregnation were more pronounced than with normal polydimethylsiloxane.

After the first introduction of silicone oil in the treatment of severe tractional retinal detachment by Cibis¹ this substance was thought to be a last resort for desperate cases with a doubtful outcome. However, since Scott² and later Zivojnovic et al.³ combined the injection of silicone oil with extensive vitrectomy this substance has gained widespread successful use as an intraocular tamponade in the microsurgical management of retinal detachment due to advanced proliferative vitreoretinopathy. While most of the oils now in use differ considerably in viscosity and chemical purity (Gabel et al., in press), all have a specific gravity less than that of the intraocular fluid. However, a tamponade of lower specific gravity may not be optimal for all cases, particularly for patients having inferior tears. We have therefore investigated the biological reaction to a silicone oil with a higher specific gravity than intraocular fluid. Such a substance was first mentioned by Watzke⁴ in 1967, but the suggestion was not followed up at the time. Now a silicone oil with high specific gravity has become available. It is produced in a special way to achieve a high level of chemical purity in terms of absence of low molecular components and catalyst residue. However, from a chemical point of view (Burkhardt, personal communication) it is more difficult to purify trifluorosiloxane than polydimethylsiloxane. It therefore seemed to us that careful studies of biological compatibility in animals were essential before its use in patients.

Material and methods

The only high specific gravity silicone oils available at present are fluorised silicone oils. For this study polytrifluoropropylmethylsiloxane (FS) was used. It first underwent a special treatment to eliminate low molecular components and catalysts as postulated for polydimethylsiloxane (PDMS) by our group.⁵ The absence of catalyst was proved by x-ray fluorescence analysis. Details of its chemical and physical properties are listed in Fig. 1.

A total of 21 eyes of chinchilla grey rabbits were prepared for silicone oil injection and extracapsular lenscetomy under ketamine-xylacina anaesthesia. The lenscetomy was performed to increase the total volume available for an injection of silicone oil as well as to obtain access for silicone oil to the anterior segment. The posterior capsule was left in place in three eyes, to confine silicone oil to the posterior segment. Four to eight weeks after lenscetomy pars plana vitrectomy with or without removal of the posterior lens capsule was performed on 17 eyes. A fluid gas exchange preceded the injection of silicone oil in 15 eyes. We employed two types of controls: two vitrectomised eyes received the normally used silicone oil of low specific gravity after removal of the posterior lens capsule, and four eyes were subjected only to lenscetomy, two of them with retention of the posterior lens capsule.

The clinical development was monitored by means of slit-lamp examination, ophthalmoscopy, and measurement of intraocular pressure. The animals in the two groups were killed after three and six weeks and after three and six months respectively and the
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CH$_3$ - Si - CH$_3$

CH$_3$ - Si - 0

CH$_3$

CH$_2$

CH$_2$

CH$_2$

CF$_3$

Fig. 1 Polytrifluoropropylmethylsiloxane. Viscosity (25°C) mPas, 5000. Average chain length approximately 50. Average molecular weight approximately 7800. Refractive index (25°C) 1.38. Density (25°C) g/cm$^3$ 1.29. Volatility 24 h 150°C ≤0.1%.

eyes prepared for histological examination by gross examination and light microscopy.

Results

Clinical Course
The postoperative clinical course (Table 1) in all eyes filled with silicone oil was quite similar. The intraocular inflammation, with mixed conjunctival congestion and Tyndall phenomenon in the anterior chamber, decreased during the first three weeks and continued to decrease in the following weeks. Two control eyes, one with low specific gravity oil and one without silicone oil, were lost during the first six weeks owing to increasing inflammation and accompanying intraocular pressure rise due to secondary glaucoma, which showed no evidence of being related to the silicone oil.

A silicone bubble reached the anterior chamber in all eyes in which the lens capsule had been removed. The bubble diameter in the anterior chamber was $\frac{1}{3}$ to $\frac{2}{3}$ of the corneal diameter and remained stable. The bubble was located at the inferior and superior limbus for high and low gravity silicone oil respectively (Figs. 2, 3). From about the fifth day after silicone oil injection all eyes showed varying degrees of central keratopathy, characterised by central opacification and thickening of the corneal stroma, but no staining with topical fluorescein (Fig. 4). However, this central keratopathy decreased in all eyes and was no longer present in any eye after six weeks. This type of central keratopathy was identical in the two eyes filled with PDMS; in contrast no keratopathy was observed in the two control eyes without any silicone oil.

![Fig. 2 Six weeks after injection of PDMS, silicone bubble in superior part of anterior chamber. Central opacification of cornea with stromal thickening.](http://bjo.bmj.com/)

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Clinical course of eyes under investigation</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Trifluorosiloxan</td>
</tr>
<tr>
<td></td>
<td>3 weeks</td>
</tr>
<tr>
<td>Posterior lens capsule</td>
<td>intact removed</td>
</tr>
<tr>
<td>Total number of eyes</td>
<td>4</td>
</tr>
<tr>
<td>Central keratopathy</td>
<td>4</td>
</tr>
<tr>
<td>Neovascularisation starting from the inferior limbus</td>
<td>—</td>
</tr>
<tr>
<td>Intraocular pressure</td>
<td>—</td>
</tr>
<tr>
<td></td>
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After six weeks two eyes began to develop clinically visible corneal neovascularisation from the inferior limbus. After three months five eyes showed this neovascularisation. Even after six months two out of three eyes having silicone oil in the anterior chamber displayed this type of neovascularisation (Fig. 5). Two eyes, one with the posterior lens capsule intact and the other with it removed, developed an increase of intraocular pressure which we could control by local application of betablockers. Two of the three eyes with intact posterior capsule showed no sequelae of the silicone oil in the anterior segment.

None of the 15 eyes showed any clinical signs of so-called emulsification or any side effects in the vitreous cavity, on the retina or on the disc.

HISTOPATHOLOGICAL RESULTS
Tissue responses, as detected by light microscopy, were observed at the corneal stroma and endothelium, on the iris surface and stroma, and to a minimal degree in the vitreous cavity. These tissue responses varied with the duration of the observation time and were much more pronounced in eyes filled with FS than in the control eyes filled with PDMS (Table 2).

The central corneal opacity noted clinically during the first six weeks of observation was unaccompanied by major histopathological changes except for possible mild stromal oedema.

Other corneal stromal changes were confined to the inferior cornea and were seen only in those eyes in which the lens capsule was defective and silicone oil had gained access to the anterior chamber of the eye. These eyes displayed a round cell infiltration and corneal stromal neovascularisation very early after silicone oil injection at the inferior cornea, where silicone oil was in contact with the endothelium. This corneal neovascularisation and round cell infiltration decreased in intensity after three months of observation. No corneal stromal thinning was observed in any of the eyes filled with silicone oil.

The corneal endothelium displayed a slightly increasing amount of cell loss during the observation period, confined mainly to the area of silicone oil contact and the area of limbal incision. Further, an increasing amount of endothelial silicone oil phagocytosis was seen the longer the observation period...
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went on. With the passage of time a moderate to marked retrocorneal fibrous tissue layer with phagocytosed silicone globules developed which was more pronounced at the superior border of the silicone oil bubble (Fig. 6).

The most prominent findings were observed at the iris. All eyes with FS displayed some oil droplets within the iris stroma. This reaction was observed also in eyes in which silicone had gained no access to the anterior chamber. Especially remarkable was the presence of a fibrous tissue layer on the anterior surface of the iris. It contained phagocytosed oil droplets similar to a foreign body reaction (Fig. 7a, b). This tissue response increased with time and appeared to be confined to the inferior iris leaflet, which was in contact with the heavy silicone oil. This tissue response was also observed in those cases where the lens capsule was left in place (Fig. 7c).

The vitreous, retina, and optic nerve displayed almost no tissue reaction even after six months. The only finding of any note was the presence of some macrophages on the retinal surface containing various amounts of clear spaces, presumably silicone droplets. No fibrocellular proliferation or tissue impregnation by silicone oil was observed.

When control eyes were filled with PDMS, with silicone oil at the superior part of the anterior chamber, they were observed for six weeks only. They showed less tissue response than those eyes filled with FS, which were examined after the same observation time, and displayed only minimal inflammatory reaction in the corneal stroma and no corneal neo-

### Table 2  Grading of tissue reaction of trifluorosiloxan and polydimethylsiloxan in control eyes as observed histopathologically

<table>
<thead>
<tr>
<th></th>
<th>Trifluorosiloxan</th>
<th>Polydimethylsiloxan</th>
<th>Control eyes</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>6 weeks</td>
<td>3 months</td>
<td>6 months</td>
</tr>
<tr>
<td>Lens capsule</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Defective</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corneal stroma, round cell infiltration of peripheral stroma</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Neovascularisation</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Corneal endothelium silicone phagocytosis</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Rarefactation of endothelial cell layer</td>
<td>+/+</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Retrocorneal fibrous tissue layer</td>
<td>-</td>
<td>+/+</td>
<td>++</td>
</tr>
<tr>
<td>Iris. silicone droplets in stroma</td>
<td>+/-</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Fibrocellular membrane on anterior iris surface: without oil droplets</td>
<td>+/-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with oil droplets</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Vitreous macrophages containing silicone droplets</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Retina and optic nerve tissue impregnation</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Fig. 6  Posterior corneal fibrous tissue layer with many interspersed and phagocytosed silicone globules. Cornea of rabbit eye filled with FS and having a silicone oil bubble within the anterior chamber. Follow-up three months.
vascularisation. No oil droplets were observed within the tissues. However, the anterior surface of the iris was also covered by a comparatively discrete inflammatory membrane.

Control eyes without any silicone oil displayed a mild amount of endothelial cell loss and various degrees of retrocorneal fibrous tissue located primarily in the superior part of the cornea close to the limbal incision site. Only a very mild round cell infiltration was observed at the limbus.

**Discussion**

**Chemical and Physical Properties of FS**
The molecule of FS is similar to that of PDMS, but with one methyl group replaced by a trifluorpropyl group in each dimethylsiloxane unit. This causes a higher molecular weight of the siloxane unit (MW=156) than that of PDMS (MW=74). However, the FS, with a viscosity of 5000 mPa s has an average chain length of only about 50 siloxane units and an average molecular weight of about 7800. In comparison PDMS with the same viscosity reaches a chain length of about 400 siloxane units and so a higher average molecular weight of about 30000. This may in part be responsible for the different tissue reaction observed and discussed later.

The main difference between FS and PDMS is the former's higher specific gravity, which is also higher than that of the intraocular fluid. This may offer some advantages in clinical use. Recently it has become clear that entirely filling the eye with silicone oil can lead to complications such as glaucoma and keratopathy. Incomplete filling, however, leads to some accumulation of fluid. In the case of low specific gravity oil this fluid accumulates under the tamponade, whereas the use of a high specific gravity material would lead to accumulation of fluid above. If the location of the intraocular fluid pocket coincides with the location of the retinal tear, an occlusion of the subretinal space is not accomplished, and this can lead to redetachment.

A second advantage is the greater technical ease of silicone oil injection and endodrainage in cases of giant retinal tears and selected cases of trauma, since

**Fig. 7a** Iris with increasing tissue impregnation from fluorosilicone oil globules. As early as six weeks after intraocular application of FS marked aggregation of silicone globules surrounded by macrophages are seen on the iris surface.

**Fig. 7b** After three months of observation smaller globules are present also within the iris stroma.

**Fig. 7c** After six months iris tissue is markedly invaded by FS globules although the lens capsule was intact in this eye.
heavy silicone oil sinks down to the posterior pole during an operation, so that it is unnecessary to make an endodrainage hole at the posterior pole.

The refractive index of FS is less than that of PDMS, which means that iatrogenic hyperopia after silicone oil filling is much less than that with PDMS. On the other hand the surface of the FS bubble is much more difficult to detect during the operation than that of PDMS.

**Tissue Reaction to FS**

Clinically a rather mild reaction to all types of silicone oil was observed. Whereas the transient central corneal stroma oedema was not confined to the area of contact between the silicone oil and the corneal endothelium, the more marked round cell infiltration and neovascularisation of the peripheral corneal stroma was confined to silicone-endothelial contact. The same was true for the iris tissue changes, such as tissue infiltration by FS droplets and silicone-containing fibrocellular membranes on the anterior iris surface.

Although these reactions are seen in the areas of direct contact between silicone and tissue layers, it is not quite clear whether they are merely mechanical or to some extent physicochemical in nature. The fact that after only six weeks the tissue reaction to FS was much more prominent than to PDMS points towards differences in reactions to various types of silicone oil. However, more comparative studies are needed to judge the significance of different reactions to various types of silicone oil.

Despite these differences in reactions in our experimental series, the extent of corneal changes observed in the rabbit eyes filled with FS was certainly less than that noted by Sternberg and associates. We saw no corneal stromal thinning in areas overlying the silicone oil bubble.

Histologically the most prominent pathological changes due to FS in our series were observed in the iris tissue. Whether this formation of fibrocellular membranes at the anterior iris surface, the phagocytosis of silicone oil droplets, and the marked tissue impregnation are of clinical importance is still unclear.

In contrast to the rather alarming reaction to silicone oil in the anterior chamber of the eye, the reaction within the vitreous cavity was minimal and very similar to what we have observed when using purified PDMS in human eyes. But in assessing changes in the anterior segment of the rabbit eyes one must take into consideration the fact that rabbits always have a much more pronounced reaction to any kind of ocular trauma than humans.

At present, in view of these findings, we consider the use of intraocular FS not to be justified until FS with better chemical and physical properties becomes available.

**References**


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