LIBRO PARA LA FORMACIÓN DE LOS RESIDENTES EN OFTALMOLOGÍA

RETINA

6. Desprendimiento de retina

# 6.6 Intraocular tamponades

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## OBJECTIVES

To promote an understanding of the role of surgical adjuvants in vitreoretinal surgery, including heavy liquids, expandable gases, and silicone oil.

## DEFINITION

Intraocular tamponades work solely by virtue of their physical properties such as specific gravity, buoyancy, and interfacial tension. They are classified as medical devices.

## HISTORY

The idea of «filling the eye» following retinal detachment surgery goes almost back to the times of inception of retinal detachment surgery itself as pioneered by Jules Gonin in its first ever case series published in the early 20$^{th}$ century (1). Rosengren, a Swedish ophthalmologist first described injecting air into the vitreous cavity during retinal detachment surgery (2). Silicone oil was injected into the eye by Cibis even before vitrectomy (3) which encountered many complications at first. Intraocular gases were used in the treatment of retinal detachment since the early 1970's (4,5). After the advent of modern vitrectomy, silicone oil made a comeback (6) and has since been subject to continuous improvement and diversification. Modern intraoperative tools, such as perfluorocarbon liquids have been further additions to the vitreoretinal surgeon's armamentarium (7).

## MECHANISM OF ACTION

Understanding the exact mechanism through which intraocular tamponades work providing tamponade to the retina is necessarily linked to the understanding of the process from retinal detachment to its subsequent reattachment. A retinal detachment is maintained, because there is communication between the subretinal space and the vitreous cavity usually through one or multiple retinal breaks. The success of retinal detachment surgery relies on two principles: identifying all retinal breaks through careful examination and sealing these breaks through retinopexy. The main role of tamponades in the treatment of retinal detachments is to provide tamponade to the retina for enough time for the retinopexy to form a watertight seal around the retinal breaks thus cutting off the communication of fluid and allowing the retinal pigment epithelium (RPE) - pump to evacuate all fluid from the subretinal space therefore keeping the retina attached.

## INDICATIONS AND RATIONALE

Although in use primarily in the treatment of retinal detachment usually following vitrectomy, tamponade indications extend into their use for displacement such as in pneumatic retinopexy (8) and in the displacement of subretinal haemorrhage (9). Since liquids are incompressible, tamponades such as silicone oil have also been used extensively in ocular trauma surgery and to stabilise choroidal haemorrhage.

Since tamponades work only by physical interaction, we aim to explain how the main forces involved such as specific gravity of the tamponade, its buoyancy, and its interfacial tension act together to provide tamponade to the retina.

It is a commonly held belief that a tamponades' mode of action is by exerting pressure onto the retina around the retinal breaks, but does this belief really stand up to scrutiny?

The actual hydrostatic pressure exerted on the retinal surface by any given tamponade can be calculated: p = h x s x g, whereby where h is the height of the column of water, s is the specific gravity and g stands for gravitational acceleration. (10). The highest pressure acts on the retina at its lowest point of the vitreous cavity because at this point it bears the pressure of the tallest column of liquid. All other points only need to bear less pressure. For a water-filled eye of about 2.2 cm in diameter the pressure is calculated at: 2.2 cm (assumed diameter of an average vitreous cavity) x 1 g/cm$^3$ x 980 cm/s$^2$ = 2.156 dynes/cm$^2$ representing 1.62 mmHg. It turns out that even for perfluorophenanthrene whose specific gravity at 2.03 g/cm$^3$ is about twice that of water, the resulting pressure on the retina at its highest point is only 3.28 mmHg. After subtracting the pressure of the water column (1.62 mmHg), the actual increase in pressure on the retina caused by perfluorophenanthrene results in only an additional increase of 1:66 mmHg. In contrast, for an eye filled with silicone oil the buoyancy would cause pressure on the retina at its highest point. We proceed to calculation in analogy to the above: 2.2 cm x (1-0.97g/cm$^3$) x 980 cm/s2 = 64 dynes/cm$^2$ which in turn translates to 0.05 mmHg for silicone oil. This means that the pressure exerted at the highest point would be 0.05 mmHg above the intraocular pressure which is practically negligible and lies well within the diurnal variation of normal intraocular pressure (IOP). It is therefore established that there is indeed no significant force which «pressures» the retina back into place and that one must look elsewhere to understand the way in which tamponades effect retinal reattachment. None of the tamponades available are miscible with water, therefore forming an interface with it. Since the effectiveness of a tamponade agent is derived directly from its physical properties, one must explore it from the point of view of its specific gravity and interfacial tensions. Given that it is difficult to achieve a complete fill of the eye, tamponade agents cannot be expected to achieve total retinal reattachment by acting simply as space fillers. The success of retinal detachment repair using tamponade agents relies on their ability to act as a splint to close retinal breaks by occluding them and preventing communication of aqueous into the subretinal space.

*Learning point:* The practical significance of understanding tamponade effectiveness, not as the result of some strong force, but as intraocular current interruption via retinal break occlusion lies in the realisation that for successful retinal reattachment to occur, no choice of tamponade can substitute what remains paramount strategy for any vitreoretinal surgeon: to always search and identify all retinal breaks and relieve all vitreous traction first.

## TAMPONADE EFFICIENCY

The difference in interfacial tension and specific gravity when compared to intraocular aqueous as well as retina will determine the shape of the tamponade bubble, hence enhancing or diminishing a tamponade's efficiency. Contact angle measurements have proven to be a good indicator of the arc of retinal contact of a given tamponade thus describing tamponade efficiency (12). When searching for an ideal tamponade one is looking for a substance which maximises specific gravity and interfacial tension differences between the tamponade, aqueous and retina. Air/gas for example have a very low specific gravity compared to aqueous and the difference in interfacial tension is equally large. This leads to gas having a flat-bottom bubble which happens to make it a very efficient tamponade (fig. 1a).

Such an efficient tamponade is one in which most of its volume goes into making contact with the retina and least of its volume is dedicated to forming the interfacial meniscus (13). Parver and Lincoff demonstrated earlier that about a 50% gas fill equated to covering about 50% of the retinal circumference (14). For silicone oil for example the difference in specific gravity to water is small (0.97g/cm$^3$ vs. 1). The same applies to the difference in interfacial tension. This means that a silicone bubble inside the eye is round-shaped, so much more of its volume is dedicated to forming the meniscus with

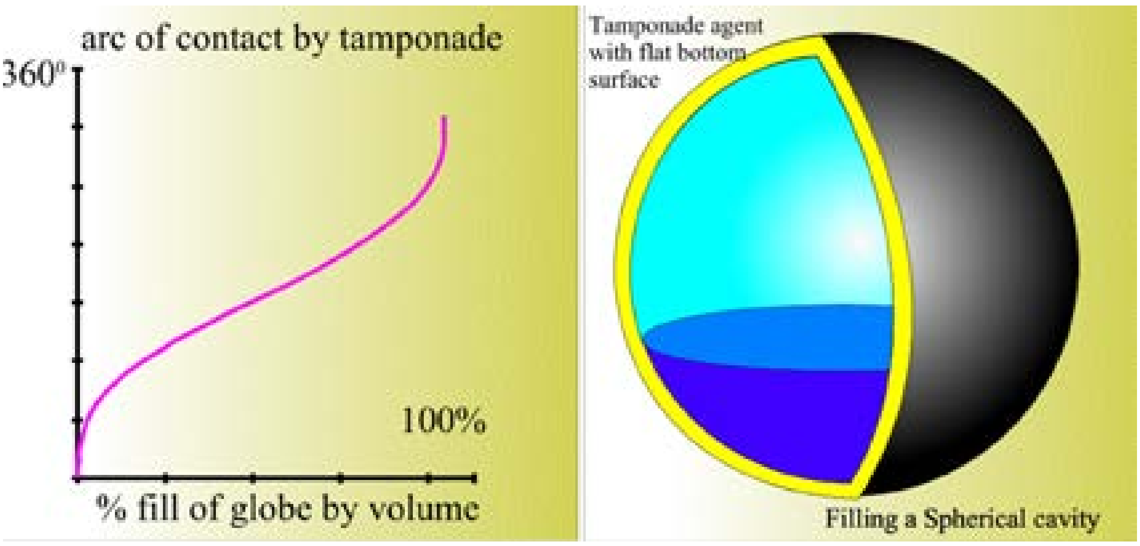


**Figura 1a:** Gas = Efficient Tamponade: Most of the tamponade volume goes toward providing retinal contact and the least volume goes toward forming the interfacial meniscus.

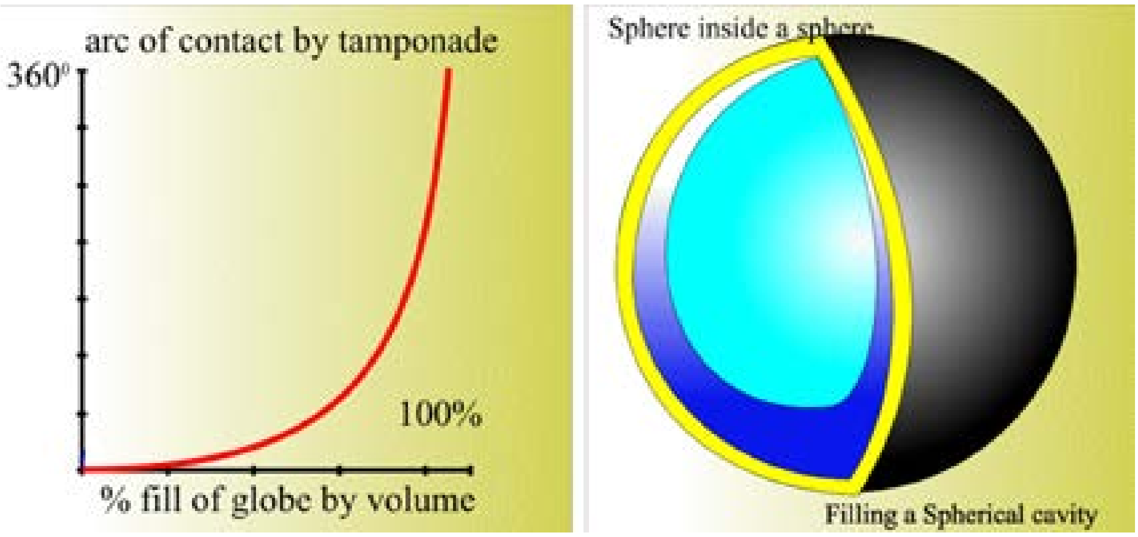


**Figura 1b:** Oil = Inefficient Tamponade: it requires a 85% oil fill to have 50% retinal tamponade«. Fawcett IM, Williams RL, Wong D. Contact angles of substances used for internal tamponade in retinal detachment surgery. Graefes Arch Clin Exp Ophthalmol 1994; 232: 438-44.

the aqueous phase leaving much less to provide contact and therefore tamponade to the retina. Contrary to gas, silicone oil is an inefficient tamponade (fig. 1b).

Fawcett showed that even a slight oil underfill of 85% of the vitreous cavity already led to a loss of 50% of the retinal tamponade (12). This means that good retinal contact is only achieved at nearly total oil fill. Tamponade efficiency has been systematically measured by our group using a model eye chamber which had been surface-modified to mimic the surface properties of the retina. Owing directly to their physical properties, an efficient tamponade like gas was able to fill an eye cavity almost completely, including recesses around scleral buckles or encircling bands making them well-suited for combined surgery, whereas a silicone oil/heavy silicone oil bubble only touched the tip of an indentation of a simulated buckle/encircling band, actually drawing aqueous around the most sensitive areas around the buckle where the retinal breaks actually lie, thus reducing the tamponade efficiency of the internal tamponade part of combined buckle and oil surgery as well as leading to a relative oil underfill (15) (fig. 2).

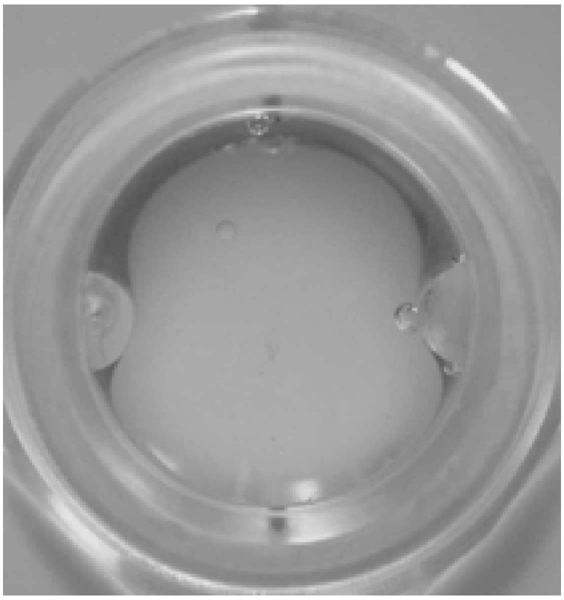

**Figura 2:** Model Eye Chamber: The presence of a buckle/encircling band reduces the oil's tamponade efficiency even further as the silicone oil bubble barely touches the apex of the indent and aqueous is even drawn to the area around the buckle where the retinal tears are.

*Learning point:* Being able to correctly understand tamponade efficiency and interactions may assist in surgical decision making: Firstly, in the case of silicone oil, the surgeon may only achieve significant tamponade effect at almost complete oil fill, adding emphasis to all techniques aimed at removing every residue of vitreous or subretinal fluid from the vitreous cavity before silicone oil injection to achieve maximum retinal contact. Secondly, given silicone oil's poor tamponade efficiency, as far as combining scleral indentation surgery with vitrectomy/gas may represent a synergetic approach maximising the benefits of both surgeries, in the case of a combination with silicone oil, the presence of a buckle or encircling band may diminish the overall efficacy of the oil tamponade.

## INTRAOCULAR GASES

Since air injection only lasted intraocularly for a very short time, Norton experimented with several gases which offered longer-acting tamponade owing to one novel physical property: these gases were expansile at certain concentrations. Lincoff investigated a family of perfluorocarbon gases in the treatment of retinal detachments (16). Further advances especially in combination with vitrectomy by Machemer (17) demonstrated gas tamponade effectiveness in the treatment of giant retinal tears and even proliferative vitreoretinopathy. The first of the family of such inert, non-toxic gases was sulfurhexafluoride ($SF_6$) which was soon joined by several other perfluorocarbon gases ($C_nF_{2n+2}$, $_{n=1-4}$). Owing to their highest interfacial tension difference to aqueous of all known intraocular tamponades (over 70 dynes/cm), the gas bubble is able to bridge the gap created by a retinal break therefore blocking the passage of fluid into the subretinal space as well as that of potentially proliferating cells, creating «compartmentalisation» (18). Since they are lighter than water, one can harness their buoyancy to direct a force vector towards the retinal break, hence the benefit of postoperative posturing of the head. The main protagonists in use today are $SF_6$, $C_2F_6$ and $C_3F_8$. If used pure, in a first phase, these gases are expanding, owing to a much higher solubility of mainly nitrogen ($N_2$), but also $O_2$, $CO_2$ and water vapour from the surrounding tissues *inward* into the gas bubble than gas diffusion *outward* from the gas bubble. They do so to varying degrees with $SF_6$ doubling, $C_2F_6$ tripling and $C_3F_8$ quadrupling in volume. The most rapid rate of expansion happens in the first 6-8 hours which is most critical for a possible rise in intraocular pressure. A second, plateau phase is reached when maximal expansion occurs between 24-48 hours for $SF_6$ and 72-96 hours for $C_3F_8$; at this time the rate of nitrogen diffusing into the gas bubble is equal to the diffusion of the gas into the surrounding tissue. Finally, during a third phase, the intraocular gas concentrations do not change any longer and the bubble diminishes according to first-order decay (19). This also has direct consequences for the longevity of the intraocular gas bubble ranging from 10-14 days for $SF_6$, 30-35 days for $C_2F_6$ to 55-65 days for $C_3F_8$. Nowadays, these gases are mainly injected as a mixture with air at certain inflexion points, specific concentrations at which these gases are considered non-expansile. For $SF_6$ these are 18-20%, for $C_2F_6$ around 16% and for $C_3F_8$ 12-14% (20). Failure to accurately calculate and deliver intraocular gas at these specific concentrations represent one of the greatest risks in modern vitreoretinal surgical risk management. The other vital consideration in the postoperative management of vitreoretinal patients with intraocular gas is the potential for a subsequent administration of inhalation-based general anaesthesia with nitrous oxide. Nitrous oxide is 34 times more soluble than nitrogen and quickly penetrates an air-filled eye. Worse, in a $SF_6$-filled eye, the diffusion rate for nitrous oxide into the eye is 117 times higher than the diffusion of $SF_6$ out of the eye, causing a rapid intraocular gas expansion and pressure rise with subsequent central artery occlusion and potentially catastrophic, permanent vision loss. All efforts must be undertaken to inform the patient of such risks and mitigation strategies, such as wrist bands may be implemented. Lastly, rapid decompression of the surrounding atmospheric pressure such as experienced during air travel or even rapid ascent into mountainous territory by car pose a separate, significant risk to the patient in the postoperative period and must be avoided for as long as gas persists in the patient's eye. Although the outflow facilities in the patients' eye may compensate for such an IOP rise (21), such outflow varies between patients and is often additionally impaired by the surgery, so it cannot be relied upon from a patient safety perspective.

*Learning point:* Careful patient information from consent to postoperative counselling as to the effects of intraocular gas must be part of any vitreoretinal patient care pathway.

## SILICONE OIL

It remains a basic requirement for any intraocular tamponade that it has to stay in situ for long enough for chorioretinal adhesion to develop. However, even as gas tamponade seems ideally suited to our tamponade needs, it eventually recedes and may expose the retina to late re-detachments due to the occurrence of proliferative vitreoretinopathy PVR, which often needs several weeks or months to play out, hence the need for a long-term tamponade agent. Even though first experiences by Cibis of injecting liquid silicone oil without vitrectomy resulted in successful treatment of some complex cases, increasing reports of complications related to long-term intraocular silicone oil cast a shadow over its use, especially in the United States. It was up to European surgeons Scott (22) and Leaver (23) in England as well as Zivojnovic (24) in the Netherlands to integrate silicone oil from an adjunct to membrane dissection into a tamponade agent in modern vitrectomy. The sentinel Silcone Oil Study (25) looked at the safety and efficacy of silicone oil vs. long-acting gas for complex PVR-retinal detachments. Among the main findings were that for severe PVR cases, silicone oil was superior to $SF_6$ and, in some subgroups to $C_3F_8$. Its indications have since expanded greatly to a wide range of complex conditions such as proliferative diabetic retinopathy with unrelieved traction, giant retinal tears, non-closed macular holes, infectious retinitis, endophthalmitis, ocular trauma and paediatric retinal detachment. On the other hand, otherwise less severe ocular conditions may also require silicone oil tamponade such as imminent air travel, living at high altitudes or a mentally or physically impaired patient's inability to postoperatively posture. Given this wide variety of indications, silicone oil has physical constraints that need further investigation: Viscosity: Silicone oil consists of long molecular chains of polydimethylsiloxane. Early inflammatory complications may have been caused by impurities i.e., short molecular chains in the silicone oil. One way of improving silicone oil quality has been to remove such short, low viscosity chain length molecules, so that most molecules had a similar chain length. Such oils were labelled «ultrapurified» and invariably increased the shear viscosity of the oil. Another physical phenomenon related to silicone oil is emulsification: It occurs when shear forces are exerted at the interface between two immiscible liquids. If the shear stress becomes large enough, small pull-out oil ligaments will fracture. Larger bubbles may coalesce back into the bulk oil, but ever smaller oil bubbles will become permanently separated, as they are stabilised by their surface tension with intraocular polar proteins acting as emulsifiers (fig. 3).

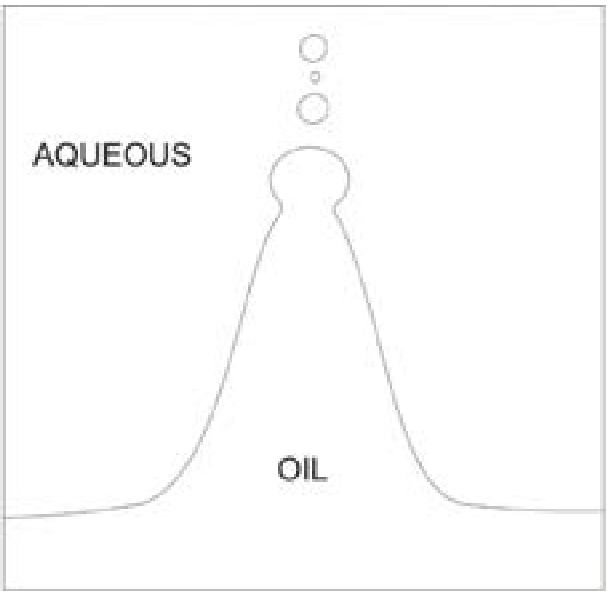

**Figura 3:** Emulsification: Shear forces at the interface of two immiscible liquids lead to the breakout of small droplets. Larger bubbles may coalesce back into the bulk oil, but ever smaller oil bubbles will become permanently separated, as they are stabilised by their surface tension with intraocular polar proteins acting as emulsifiers.

This process is compounded by the shear force of every eye movement and leads to the break-up into ever smaller droplets (fig. 4a).

This happens to a such a degree that quantitatively, most of the emulsified droplets break up into ever smaller droplets. It has been reported that a particular small size of between 1-30µm of otherwise inert foreign bodies may trigger a strong macrophage-led inflammatory response and such droplet inclusions have been documented in histological specimens of the trabecular meshwork a possible cause of secondary glaucoma (fig. 4b).

The classic way of trying to reduce emulsification has been to increase the oil's shear viscosity from around 1000 mPas to 5000 mPas. However, modern vitrectomy has led to ever smaller gauge 23G, 25G and 27G vitrectomy, making the latter all but incompatible with the use of such higher-viscosity silicone oil, due to reduced flow. Recently, to address this trend, further improvements in silicone oil design have led to the development of novel, molecularly designed silicone oils which have aimed to address both shortcomings: faster flow and reduced emulsification. The addition of high molecular weight additives (as high as 1.2M chain length) to 1000 mPas silicone (base) oil have managed to alter standard silicone oil's behaviour from a Newtonian to a more poly-

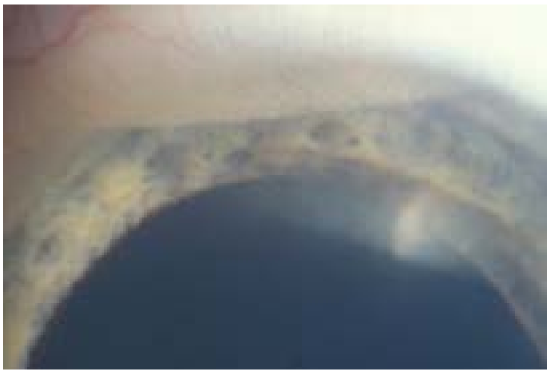

**Figura 4a:** Visible oil emulsification droplets in the angle.

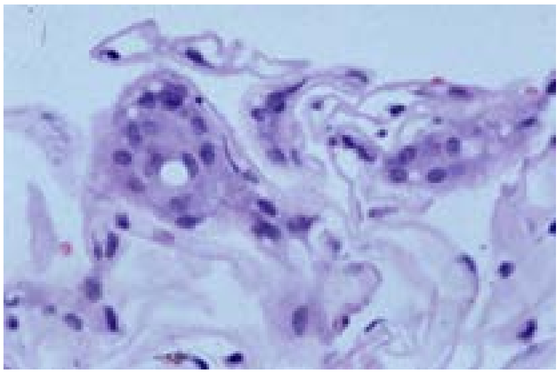

**Figura 4b:** * Vacuole of emulsified silicone oil droplets visible in the trabecular meshwork cell.

mer-like non-Newtonian substance (26). The effect is a lowered shear viscosity under stress of injection allowing up to a third faster injection times through the same gauge or injection of oil through smaller gauges (27). By altering its extensional viscosity though a reduced tendency for emulsification could be demonstrated (28). Clinically, in terms of emulsification, the such a modified 2000 mPas silicone oil consisting of 5% high molecular weight additive was proven non-inferior to conventional 5000 mPas oil (29) and another 5000 mPas-equivalent silicone oil employing the same principle consisting of 10% high molecular weight additive and aiming to maximise emulsification resistance showed a marked reduction in emulsification compared to a conventional 5000 mPas silicone oil (30). With ever-increasing number of patients eligible, the management of silicone oil-related complications have become relevant factors in the daily practice of vitreoretinal specialists and general ophthalmologists alike. Most surgeons therefore aim to remove silicone oil from patients within a few months. Despite this, there are still patients in real-life practice who, for various reasons, end up having to live with long-term silicone oil tamponade (31). There is a clear clinical need for novel silicone oils with improved physical properties to address these issues.

*Learning point:* Silicone oil remains the only approved long-term intraocular tamponade. It is effective and widely used to treat retinal detachments complicated by PVR.

## HEAVY LIQUIDS

Initially intended as substitute for blood due to their large oxygen-binding capacity, perfluorocarbon liquids are colourless and odourless substances that have proved very helpful as intraoperative tools for vitreoretinal surgery. Chang pioneered their use in humans (32). The most widely used are perfluoro-n-octane and perhydrophenanthrene. Owing to their physical properties such as high density, they allow for the smooth reattachment of the macula without retinal folds, they can evacuate subretinal fluid by displacing it back through the break therefore obviating the need for a posterior retinotomy. Due to their low viscosity, they are easy to handle, inject and remove. They are seen as a «third hand» for the surgeon. As their specific gravity is that much higher than that of water or oil for that matter, these substances have excellent tamponade efficiency, allowing for the flattening of the retina in cases of giant retinal tear and PVR (33). Conceived purely as intraoperative tools, there is controversy though about their use as longer-term tamponade for up to 2 weeks. Further indications are in the management of dislocated crystalline lenses, suprachoroidal haemorrhages or even in the displacement of submacular haemorrhages. Given their very low viscosity, they have a high propensity to break up and emulsify, causing extensive ocular inflammation. Their main complication though is migration or surgical displacement into the subretinal space usually through iatrogenic manipulation. Once in the subretinal space they may lead to retinal atrophy and should ideally be removed as soon as possible. Several challenging techniques are described to achieve this goal, from using a very fine needle to aspirate the bubbles (34) to the use of Laplace's Law in aiding their extrusion (35).

*Learning point:* Perfluorocarbon liquids are a welcome addition to the vitreoretinal surgeons' armamentarium. They have a proven track record of improving surgical outcomes in PVR detachments as well as in giant retinal tears. For the time being they are to be regarded as intraoperative tools, their role as tamponades remains under consideration.

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## PREGUNTA TIPO TEST

(pulse en la flecha para comprobar las respuestas)

**1. Which statement about ocular tamponades is TRUE:**

a) C3F8 gas in a concentration of 23% is non-expansile and is therefore used routinely in retinal detachment surgery.

b) SF6 gas in a concentration of 14% is expansile and may therefore lead to a very high postoperative intraocular pressure rise 6 to 8 hours after vitreoretinal surgery.

c) During pneumatic retinopexy a 0.1 ml bubble of pure SF6 gas doubles in volume in the vitreous cavity after injection.

d) A patient requiring emergency surgery can have nitrous gas-induced general anaesthetic, because he only had air tamponade 2 days prior to intervention and not C3F8 gas.

e) C2F6 gas in a concentration of 23% is non-expansile and thererfore used routinely in retinal detachment surgery.

**2. Which of these statements is TRUE? How does the choice of intraocular tamponade help to reattach the retina?**

a) Silicone oil is indicated and often used in complex cases of PVR-retinal detachment, because it exerts more pressure on the retina than intraocular gas.

b) Intraocular gas needs to fill the eye completely for it to be an effective tamponade agent.

c) A vitreoretinal surgeon should aim for a 85% silicone oil fill in order to offer tamponade to about 85% of the retinal circumference.

d) Silicone oil is superior to intraocular gas as an intraocular tamponade, because of its higher specific gravity.

e) Owing to its high interfacial tension, intraocular gas manages to exclude the aqueous phase from a retinal break and is therefore preventing communication of liquid between the vitreous cavity and the subretinal space.