INTRODUCTION

Perftoran was developed in the Institute of Theoretical and Experimental Biophysics of the Russian Academy of Sciences, and was registered in Russia in February 1996 (later in Ukraine and Kazakhstan) as an oxygen-carrying blood substitute manufactured by the Scientific Productive Company Perftoran (Ivanitsky, 2001). Perftoran is an emulsion of 10 volume percent of perfluorochemicals (PFCs), the main two being perfluorodecaline (PFD) and perfluoro-N-4-(methylcyclohexyl)-piperidine (PFMCAP) in the ratio 7:3 (Maevsky et al., 2003). The intravascular retention half-time for Perftoran is 9 hours in rats and about 20 hours in rabbits. The half-times for removing PFD and PFMCAP from the organism are about 2 and 13 weeks, respectively. PFC emulsion is stabilized by the 4 percent polyoxyethylene-polyoxypropylene copolymer Proxanol P268, and contains a physiologically acceptable saline solution (Table 26.1). Perftoran is packed in 100-, 200- and 400-ml bottles, and can be stored for 3 years at −4°C−−18°C, and for 2 weeks at 4°C.

Table 26.1 Composition of Perftoran® (from the Scientific-Productive Company 'Perftoran', Russia)

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfluorodecalin and its co-products</td>
<td>7.0 ml</td>
</tr>
<tr>
<td>Perfluoro-N-(4-methylcyclohexyl)-piperidine and its co-products</td>
<td>3.0 ml</td>
</tr>
<tr>
<td>Proxanol P268</td>
<td>4.0 g</td>
</tr>
<tr>
<td>NaCl</td>
<td>0.6 g</td>
</tr>
<tr>
<td>KCl</td>
<td>0.039 g</td>
</tr>
<tr>
<td>MgCl₂</td>
<td>0.019 g</td>
</tr>
<tr>
<td>NaH₂PO₄</td>
<td>0.065 g</td>
</tr>
<tr>
<td>Glucose</td>
<td>0.2 g</td>
</tr>
<tr>
<td>H₂O</td>
<td>100 ml</td>
</tr>
<tr>
<td>[F⁻]</td>
<td>10 μM</td>
</tr>
<tr>
<td>Osmotic pressure</td>
<td>300 mOsm</td>
</tr>
<tr>
<td>pH</td>
<td>7.3</td>
</tr>
<tr>
<td>Viscosity</td>
<td>2.3 cPs</td>
</tr>
<tr>
<td>Average particle size</td>
<td>60 nm</td>
</tr>
</tbody>
</table>

HISTORY AND COMPOSITION OF PERFTORAN

In the Soviet Union, the development of PFC-based oxygen carriers for blood replacement...
was initiated by Zoya Chaplygina and Grigory Rosenberg in the early 1970s. At that time the chemical school of the academician Knunyants provided a foundation for the manufacture of PFCs for military and civilian needs. The first PFC emulsions were developed independently by Irina Kuznetsova (Leningrad), Natalia Konovalova (Krupavna) and Dmitry Sidlyarov (Moscow). In 1979, Professor Felix Baloyartshev, together with the academician Knunyants and a corresponding member Ivanitsky, began to advance the multipurpose scientific studies of biomedical applications of PFCs. It was the starting point for the creation of Perftoran. In 1980, the efforts of different specialists of biomedical and technological institutes and enterprises were consolidated within the All-Union Scientific-Industrial Programme. An original PFC composition for Perftoran, including PFD and PFMC, was suggested by Kirill Makarov and Lev Gervitz at the Institute of Elemental Organic Compounds.

Some Perftoran properties resemble those of Fluosol-DA, but we would like to note some differences between the two. As described in the Green Cross Technical Information (1978), the stem emulsion in Fluosol-DA contains PFD and perfluorotripropylene (PFTPA), which are emulsified with Pluronic F68 and yolk phospholipids. However, the emulsion of PFD and PFMC in Perftoran is stabilized only by Proxanol P268. Pluronic F68 and Proxanol P268 are both copolymers, but it seems that Proxanol P268 is less toxic and more biocompatible than Pluronic F68. Moreover, the whole composition of Fluosol-DA includes an oncotic agent, 3 per cent hydroxyethylstarch, which can destroy the adsorption layer of emulsion particles. Perftoran does not contain any oncotic agents.

Regarding storage, the ready-for-use Perftoran is packed in a single bottle, while Fluosol-DA is presented as three separate solutions that must be mixed prior to use. Both the stem emulsion of Fluosol-DA and the whole Perftoran composition can be kept in a frozen state, but once Fluosol-DA has been thawed and mixed it can only be used for infusion for up to 8 hours, whereas defrosted Perftoran can be used for about 2 weeks.

As for side effects, the technology that was accepted in 1996 provided for a narrow distribution of emulsion particles with an average size of 0.05–0.07 μm, whereas the average particle size in Fluosol-DA is 0.12 μm. Owing to the smaller particle size (reduced from 0.12 to 0.07 μm in Perftoran), the frequency of side reactions with Perftoran has decreased from 8–10 per cent to 2–4 per cent (Vorobyev and Ivanitsky, 1997). It is evident from the above mentioned differences that Perftoran is a more user-friendly drug than Fluosol-DA.

**PRECLINICAL STUDIES**

Preclinical experimental studies have shown that Perftoran is harmless and non-toxic for mice, rats, rabbits and dogs. The intraperitoneal median lethal dose (LD₅₀) is 239 ml/kg for adult mice and 183 ml/kg for young mice; the intravenous LD₅₀ exceeds 140 ml/kg for rats (Rybalkin et al., 2002). We did not observe any toxic symptoms, changes in body weight or food consumption, or significant shifts in hematological and biochemical parameters in the blood of rats for more than 6 months following intravenous administration of Perftoran (20 and 50 ml/kg). Repeated intravenous Perftoran infusions into rabbits, of 50 ml/kg each day for 3 consecutive days, were followed by a transient increase in the concentration of urine, bilirubin and cholesterol, as well as transaminase activities in the blood 24 hours after the last infusion. However, later and for 6 months these parameters returned to a normal level. Weight indexes of liver and spleen grew in proportion to the dose of Perftoran and normalized within the period of the PFC’s retention time. Our composition of PFD with PFMC enables complete elimination of toxicity in rabbits, which is an attribute of emulsions containing PFD (Skilias et al., 1993). Owing to its low lipophilicity PFMC has a rather long half-time of retention in organs (90 days), and this led us to carry out thorough safety testing. Complete elimination of PFCs from organs was not followed by any side effects in tissue morphology or cell ultrastructure in the liver, spleen, lungs, bone marrow, kidneys and other organs (Vasiliev and Golubev, 1984). Perftoran and its components do not have any mutagenic or carcinogenic activity. Moreover, some of the malignant neoplasms among spontaneous tumors occurred 1.5 times less often in the group undergoing repeated Perftoran administrations than in the control group of intact animals. After 11 successive intraperitoneal Perftoran infusions (a total dose of 275 ml/kg) into pregnant rats during the first stage of pregnancy, symptoms of teratogenicity were found. Perftoran does not induce hypotensive reactions either in rats or in dogs, in contrast to Fluosol (Faithfull and Cain,
Figure 26.1 Comparison of Perftoran® and salt solution influences on the mean arterial blood pressure (MAP) in rats SHR-SP (the mean weight of the rats is 290 g). Arrow 1 – infusions of Perftoran or salt solution (the same salt content as in Perftoran) in doses of 7.5 ml into femoral vein through the preliminary inserted catheter; arrow 2 – taking 2 ml blood for examination of thrombocoagulation parameters; arrow 3 – taking 5 ml blood. MAP was measured with the electromanometer connected with a polyethylene catheter which was inserted into the femoral artery the day before the experimental procedure. Analogue signals of 512 cPs were sent from the electromanometer to the computer. #, comparison with the control level (P < 0.05); *, comparison with control or salt solution (P < 0.05). (From Tuhovskaya et al., 2004.)

Furthermore, Perftoran infusion of 7.5 ml/kg before moderate blood loss maintains the mean arterial pressure (MAP) in rats better than salt solution (Figure 26.1). After massive blood replacement with Perftoran, the hematopoiesis in rats was activated in the usual way.

Because of the low PFC concentration and small oxygen capacity of Perftoran (6.9 ml/dl of oxygen at PO₂ 760 mmHg), we estimated the oxygen-carrying efficiency of Perftoran by the function of rat liver mitochondria (RLM) after massive blood replacement in rats. The animals' survival was almost identical: 19 out of 20 with Perftoran, and 18 out of 20 with albumin-salt solution. However, their quality of life was different; the respiratory and phosphorylation activities of RLM were completely destroyed after isovolemic replacement with protein-salt solution, while with Perftoran (supplemented by 3% albumin) RLM retained the enhancement of phosphorylation and the respiratory rate as with autologous blood (Figure 26.2).

Onishenko et al. (1990) demonstrated better oxygen delivery by Perftoran, estimating the survival of kidney grafts isolated after hemorrhagic shock induced by an acute blood loss (35 ml/kg). The arterial blood pressure decreased from 150/70 to 50/30 mmHg, and the kidney blood flow dropped from 2000 ± 120 ml/min per kg to 800 ± 60 ml/min per kg. One hour later, the

Figure 26.2 Diagrams of polarographic registration of respiratory rate of rat liver mitochondria (RLM) during oxidation of 5 mM potassium succinate (succ.) and phosphorylation of 150 μM ADP. Each curve is a mean value of six measurements (s.e.m. <10% of mean value). RLM were isolated in 6 h after blood replacement by scavenged autologous blood, protein-salt solution or by Perftoran (Hb content decreased from 16.0 ± 1.4 to 5.0 ± 0.6 g/dl in both groups). Incubation medium for RLM: 250 mM sucrose, 10 mM KCl, 10 mM Tris-HCl (pH 7.4), 3 mM KH₂PO₄, 3 mM MgCl₂, (RLM protein 2–3 mg/ml), t 26°C. After blood replacement by protein-salt solution or by Perftoran, animals were kept at PO₂ of 550–600 mmHg. (Based on data from Maevsky et al., 1999.)
bleeding dogs were treated with infusions of dextran 60 or Perfortan in the volume of about 40 ml/kg while breathing an oxygen-air mixture. After a 2-hour period of hemorrhagic shock, the kidneys were isolated from the 'hemorrhagic' animals and transplanted into recipient dogs that had previously undergone nephrectomy. The treatment of donor dogs with Perfortan enabled maintenance of ATP/ADP at a level two-fold higher, and decreased lactate/pyruvate ratios five-fold in the kidney tissue, in contrast to those in the dextran group. Correspondingly, the levels of creatinine and urea in the recipient blood serum were four-fold smaller and the kidney graft lifespan was twice as long if the donor dog was treated with Perfortan.

Sinchuk (1998) described similar shifts of hemodynamic and oxygen transport parameters in bleeding dogs treated with Perfortan or crystalloid solution (with subsequent dextran 60 infusions in both groups) 1–1.5 hours after blood losses of 25–45 ml/kg. He did not find any differences in oxygen regimes after plethoric infusion (30 ml/kg) of Perfortan or dextran 60 during acute lethal methemoglobinemia induced by nitrate poisoning. In this situation, 50 per cent isovolemic blood replacement with Perfortan had big advantages in comparison with dextran 60: cardiac output increased 1.5-fold ($P < 0.05$), arterial blood pressure was increased by 21 mmHg ($P < 0.05$), arterial $PO_2$ reached 270 mmHg, and the pH was 7.35. This compared with a $PaO_2$ of 92 mmHg and a pH of 7.27 with dextran 60 ($P < 0.06$).

We (Kuznetsova, 1997; Ivanitsky, 2001) suggest that an improvement in oxygen delivery by Perfortan is due to:

- the additional $O_2$ capacity of the PFC emulsion
- the faster $O_2$ and $CO_2$ consumption and release by the PFC emulsion
- enlarged gas gradients and diffusion surfaces
- a vasodilatation effect (probably connected with NO dissolution in PFCs).

Vasodilatation may be an important condition for providing oxygen delivery by even a very small quantity of erythrocytes (Winslow, 2003). Moreover, PFC particles can go through narrowed vessels that are impassable by erythrocytes, which are 70–100 times larger. Perfortan seemed to improve oxygen delivery together with the circulating erythrocytes, forming a reversible gas-carrying conveyer.

Due to a lipophilic relationship with biostuctures, PFCs and their emulsions have a biological activity which is responsible for some unexpected effects: prolongation of cardioplegic preservation (Beloyartsev et al., 1986), alterations in macrophage activities (Golubev, 1998), diminution of the secondary alteration during inflammation (Moiseenko, 1999; Orlov et al., 2004), and a decrease in transplant rejection (Shumakov et al., 1999). According to Islamov et al. (1986), when a cardioplegic medium contained Perfortan, both ischemic contracture and a decrease in pH in the tissue of isolated arrested hearts were delayed for at least twice as long. Reperfusion by Perfortan after total ischemia of isolated rabbit heart provided a two-fold higher resuscitation of contractility amplitude than that achieved with Tirode solution (Figure 26.3). The drug infusion in doses exceeding 2 ml/kg causes an induction of cytochrome P450 synthesis de novo and hence activates the monoxygenase system of the liver for the period of PFD retention (Obraztsov et al., 1994).

**CLINICAL TRIALS WITH PERFORTAN**

During the three stages of preregistration clinical trials (1984–1994), Perfortan was administered intravascularly into 964 patients (Krylov et al., 1985), in dosages ranging from 4 to 30 ml/kg depending on the disease (Table 26.2).

At massive blood replacement of more than 40 per cent of the circulating volume, Moroz et al. (1995, 1999) used Perfortan in doses of 1350–3600 ml, with the fraction of inhaled $O_2$ ($FIO_2$) being 0.4–0.6. When hemoglobin (Hb) concentration in the blood fell to 3.5–7.5 g/dl (238 wounded and sick), they added separate plasma expanders or freshly frozen plasma (200 ml per 450 ml of Perfortan). In critical situations, Perfortan permits the delay, reduction (by two to three times) or avoidance of donor blood transfusions. Various side effects were found in about 8 per cent of patients; these included transient itching, hyperemia and dizziness, pain in the kidneys, and even hypotension and pulmonary complications (Maevsky et al., 2001).

**CURRENT USAGE OF PERFORTAN**

Since its approval in 1997, Perfortan has been used for many clinical indications (Table 26.3). According to an All-Russian questionnaire (performed
Figure 26.3 Reperfusion restoration of mechanical activity of rabbit heart with different perfusion medium after 40 minutes of total ischemia: (a) Trote salt solution; (b) Perftoran supplemented with 2.5 mM calcium chloride. Continuous lines with dark marks show the level of diastolic tension; broken lines with open marks show the level of systolic tension; crosshatched regions show amplitudes of heart contractilities. $F_{%}$ is isometric tension relative of the initial level.

Table 26.2 Patient distribution according to indications, doses of Perftoran and frequency of side effects during clinical trials ($n=964^*$)

<table>
<thead>
<tr>
<th>Indications</th>
<th>Doses (ml/kg body weight)</th>
<th>Summary doses (l)</th>
<th>Patient distribution (%)</th>
<th>Frequency of side reactions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Acute blood loss, hemorhagic shock</td>
<td>6-30</td>
<td>1-5</td>
<td>22</td>
<td>2</td>
</tr>
<tr>
<td>2. Polytrauma, shock</td>
<td>4-12</td>
<td>0.4-1.2</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>3. Toxic shock</td>
<td>4-8</td>
<td>0.4-1.0</td>
<td>12.7</td>
<td>0</td>
</tr>
<tr>
<td>4. Limb ischemia</td>
<td>4-6</td>
<td>0.4-0.8</td>
<td>20.7</td>
<td>20</td>
</tr>
<tr>
<td>5. Cardiosurgery</td>
<td></td>
<td>1.0-2.0</td>
<td>11.1</td>
<td>0</td>
</tr>
<tr>
<td>6. Kidney transplantation</td>
<td>30</td>
<td>1.0-2.0</td>
<td>4.8</td>
<td>0</td>
</tr>
<tr>
<td>7. Burns, oncology and others</td>
<td>2-8</td>
<td>0.1-1.0</td>
<td>8.2</td>
<td>27</td>
</tr>
<tr>
<td>Total frequency of side effects</td>
<td></td>
<td></td>
<td></td>
<td>10**</td>
</tr>
</tbody>
</table>

*According to the original reports submitted in Russian Pharmaceutical Committee.
** Excluding cardioplegia and kidney transplantation patients.

by Evgeny Giburt at the Blood Center of the Russian Ministry of Health in 2002, positive effects of Perftoran were reported in 88.3 per cent of cases, negative effects in 3.3 per cent, the absence of any effect in 8.3 per cent, and side effects in 4 per cent of cases. The most frequent indication was bleeding (37 per cent), so the main Perftoran consumers were regional blood transfusion stations.

Perftoran was initially developed as a blood substitute to be used instead of allogeneic blood following massive blood losses, with simultaneous breathing of oxygen. In practice, Perftoran turned out to be useful even if the falling level of hematocrit and hemoglobin did not reach the transfusion trigger. As demonstrated by Tikanadze (1997), Perftoran administration ($n=32$) in doses of 900 ml (100-120 drops/min) together
Table 26.3 The percentage of patients treated with Perforan, by indication. Total number of patients = 3528, including 1921 Perforan-treated patients in comparative studies (according to Russian Scientific literature 1997–2004)

<table>
<thead>
<tr>
<th>Indications</th>
<th>Distribution of patients with Perforan (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Blood losses, multiple organ dysfunction</td>
<td>37</td>
</tr>
<tr>
<td>2. Limb ischemia</td>
<td>14</td>
</tr>
<tr>
<td>3. Dysfunction of inflammatory response</td>
<td>8</td>
</tr>
<tr>
<td>4. Detoxification</td>
<td>4</td>
</tr>
<tr>
<td>5. Lung function damage</td>
<td>6</td>
</tr>
<tr>
<td>6. Cranial-cerebral trauma</td>
<td>7</td>
</tr>
<tr>
<td>7. Burns, thermal shock</td>
<td>3</td>
</tr>
<tr>
<td>8. Kidney transplantation</td>
<td>2</td>
</tr>
<tr>
<td>9. Cardiosurgery</td>
<td>3</td>
</tr>
<tr>
<td>10. Oncology</td>
<td>2</td>
</tr>
<tr>
<td>11. Local application: wound and ulcer healing, lavage of lungs, spinal cord and peritoneum</td>
<td>14</td>
</tr>
</tbody>
</table>

with crystalloids and colloids at $F_1O_2 = 0.4$ after the cessation of gastroduodenal bleeding of 1500–2500 ml provided the following: higher cardiac output due to an increase of the heart stroke volume to 60–68 ml (as opposed to 46–52 ml in the control group; $P < 0.05$); an increase in arterial and central venous blood pressure; and enhancement of arterial and venous PO$_2$, which were also more sustainable than those in the control group of 30 patients. According to Lasarenko et al. (2002), Perforan was infused at the beginning of gastroduodenal and colon operations in doses of 400 ml (25 patients) or 800 ml (14 patients) after blood losses of 1000 or 2000 ml, respectively. Perforan administration augmented microcirculation by 15–30 per cent ($P < 0.05$) in the liver, intestine, skeletal muscle and peritoneum; increased erythrocyte elasticity from 36 to 78 per cent of the normal level ($P < 0.05$); and decreased the blood viscosity from 87 to 54 cP/s at 1/c ($P < 0.05$) when the normal level was 32 cP/s at 1/c. In all these cases, Perforan infusions were accompanied by acceleration of platelet aggregation and disaggregation, diminution of acidosis, and inhibition of peroxidative waste production in the blood by 1.5–2.0 times (Sofronov et al., 1999; Sofronov and Selivanov, 2003).

During lung resection with artificial ventilation ($F_1O_2 = 0.5$) when intraoperative blood losses were 400 ml (after hemodilution, hematocrit was 32–35), Perforan administration (0.06 ml/kg) augmented saturation of HbO$_2$ in arterial blood to a significantly higher level than that in the control group treated with crystalloids (Biryukov and Petrova, 2001). As shown by Zakharov et al. (2001), inclusion of Perforan in doses of 4–6 ml/kg in conventional transfusion therapy 1, 2 and 3 days after a hemorrhagic shock and additional operation bleeding increased the efficiency of reanimation treatment, and shortened the reanimation period and duration of artificial ventilation.

Usenko et al. (2002) gained much clinical experience in Perforan application when treating bleeding, cranial-cerebral traumas, and burn shock. They adjusted Perforan doses to the volume of blood losses (VBL) in the following ratios: 2–4 ml/kg for 20 per cent VBL, 4–7 ml/kg for 20–40 per cent VBL, 7–10 ml/kg for 42–70 VBL, and 10–15 ml/kg if VBL exceeded 70 per cent. On Perforan administration they noted a decrease in arterial-venous shunting in the lungs, and an increase in PaO$_2$ and O$_2$ extraction from blood.

As a result, sequelae dropped by 12.5 per cent and morbidity by 5–8.5 per cent. Usage of donor blood was reduced by 1.5 times. In most cases a positive effect was achieved after Perforan application in doses of 4–6 ml/kg when the supplementary oxygen capacity of PFC emulsion was insignificant. These doses of Perforan accelerated patients’ resuscitation after cranial-cerebral traumas, and also the restoration of their mental activities. Side effects occurred in about 1 per cent of cases.

**CLINICAL IMPLICATIONS**

In compliance with the experimental data and the preregistration clinical trials, Perforan efficacy was revealed not only as a blood replacement but also for treating polytrauma, different kinds of shock and brain injuries, and for the elimination of edema after cranial-cerebral traumas. It promotes rapid recovery from coma owing to fat or air embolism of the cerebral vessels, and prevents the development of the multiple organ dysfunction syndrome and the respiratory distress syndrome of adults (Sofronov et al., 1999; Usenko et al., 2002; Kligunenko et al., 2004). In cardiopulmonary bypass with hemodilution by Perforan (45 patients) during reconstruction
operations on the heart, Kryuchenkov (1998) found a more pronounced antiischemia effect (the lactate level decreased three- to five-fold), improvement of tissue oxygenation ($O_2$ delivery and extraction increased two-fold) and diminution of blood viscosity and erythrocyte injuries in comparison with control groups (60 patients, hemodilution with crystalloids or with mixture of colloids and banked erythrocytes). Moroz et al. (1995) found augmentation of skin $PO_2$ by 30 per cent after the infusion of 400 ml of Perftoran for limb ischemia, while dextran 40 augmented skin $PO_2$ by only 6 per cent. Thermovision images supported resuscitation of the blood flow immediately on Perftoran administration (Ivanitsky et al., 2003; see Figure 26.4).

Repeated Perftoran infusion facilitates pain elimination at rest, and significantly enhances the distances for which patients can walk while remaining pain-free in 93 per cent of patients for about 6–9 months. Usenko et al. (2002) and Aliev et al. (2002) described the reduction of the ischemic area after acute myocardial infarct treated with small doses of Perftoran (100 ml). Infusion of 2000 ml of Perftoran into cadaver donors (no heartbeat) alleviated kidney transplant ischemic injuries. Reperfusion damage and rejection of kidney grafts also diminished after Perftoran infusion (4–6 ml/kg) into recipients (Onishenko et al., 1990). Sofronov et al. (1997) demonstrated that Perftoran decreased the symptoms of poisoning with carboxophos and neurotropic drugs. Stable antiinflammatory effects of Perftoran (1.5–3 ml/kg) were described by Moiseenko (1999) in chronic uveitis (39 patients). Combining Perftoran local lavage of injured spinal cord with intravenous administration, Katunyan et al. (2003) significantly improved the outcome of decompression operations and the neurologic resuscitation of patients after spinal cord trauma.

THE FUTURE OF PERFTORAN

We completely agree with Keipart (2003) that the most likely anticipated future PFC emulsion application (which has already been demonstrated by preclinical and first clinical efficacy data) will target tissue ischemia, with a focus on the vital organs. Since Perftoran enhancement is limited by the probability of side effects (about 4 per cent), which frequently result from violated conditions of storage, the possibility of decreasing the frequency of these side effects by technological modification and strict obedience regarding the rules of Perftoran usage will determine the imminent future of Perftoran application. It will lie in a wider scope of both previously mentioned and new indications, such as preoperative isovolemic blood replacement (during temporal autotransfusion), treatment of cerebral ischemia, reversal of myocardial ischemia, diminution of reperfusion injuries, resuscitation of emergency traumas, lung and peritoneal lavage, enhancement of sensitivity to radiation and chemotherapy, prolongation of the storage time of isolated organs prior to transplantation as well as detoxication, suppression of the hyperactive inflammatory response, and liver function correction.

SUMMARY

Perftoran can be qualified as an ‘antihypoxic’ and ‘anti-ischemic’ blood substitute with marked membranotropic effects. At present it is highly
advisable to use Perftoran at an early stage of blood replacement, when the joint functioning of Perftoran and the remaining erythrocytes can increase tissue oxygenation, delay and reduce allogetic blood usage, alleviate cerebral ischemic injuries, and prevent development of multiple organ dysfunction. Perftoran will target tissue ischemia and inflammation. Its further enhancement depends on the possibility of diminishing the frequency of side effects by technological modifications and stricter obedience regarding the rules of its usage.

EDITOR’S SUMMARY

Perftoran is a perfluorocarbon emulsion developed in Russia, with a similar composition to Fluosol. Perftoran is stabilized with Proxanol P268 instead of Pluronic F-68, both of which are copolymers, but the Russian studies found Proxanol P268 to be less toxic than Pluronic F-68 in animal tests. Perftoran contains no oncotic agents (starches), and therefore it can potentially be given in relatively large doses without concern of volume overload. Perftoran is bottled and frozen as a single solution – not three, as was the case for Fluosol. It is therefore more convenient to use.

Perftoran has a smaller particle size than Fluosol, to which the lower incidence of side effects such as anaphylaxis, flu-like symptoms and fever is attributed. In spite of its low O₂ capacity (6.9 ml/dl of O₂ at 760 mmHg PO₂), Perftoran was found to be efficacious in preclinical animal studies in a variety of species. Due to its low lipophilicity, its retention time in the body is quite long – 90 days in some studies. This was a concern, but no specific toxic effects have emerged from the studies.

Perftoran was approved for clinical use in Russia in 1997 after several trials involving 964 patients, some with massive blood replacement. The incidence of side effects is said to be 8 per cent. With increasing use in Russia, considerable clinical experience has now accumulated. Although it is being used in many different clinical indications, including acute and chronic anemia, its greatest application might be in oxygenation of specific tissues such as in limb ischemia, cerebral ischemia and coronary artery disease.

ACKNOWLEDGMENTS

We thank T. N. Kharybina and her colleagues in Pushchino Library and Professor G. A. Sofronov and his coworkers from the Military Medical Academy in Saint Petersburg for their help in researching information regarding applications of Perftoran.

REFERENCES


Perfluorocarbon-Based Oxygen Carriers


