The clinical experiments have revealed a low percentage of side-effects: out of 434 cases, only 1.8% complained of fever and 1.16% of shivering, whilst the other complications are not worth mentioning. This solution gave encouraging results because of its positive pressure action and the increase in the volume of circulating plasma, against shock in burns, hemorrhages and other various causes. Even the elimination of burn toxin was speeded up. We were also able to demonstrate the characteristic action of the solution against dilution of the blood. Finally, administration of this remedy kept the circulation stable during operations, so that it could be used also during normal surgical operations as an antishock prophylaxis. In some cases where blood transfusions would have been necessary, this plasma expander allowed operations to be performed without blood transfusions. 273 operations on the abdomen, neck and thorax were performed in this way, obtaining worthwhile results.

Summarizing, it may be stated that our "recently isolated lower polymerized sodium alginate" which is an original product of our Clinic, has already given such favourable results that it may be favourably compared with Dextran and Periston. It also costs much less than other plasma expanders.

We hope that this new plasma expander may meet with world-wide acceptance.

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Preparation and Clinical Use of a Pasteurized Plasma Protein Solution (Pasteurisierbare Plasmaprotein-Lösung, PPL)

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1. Method of Preparation

A method for the preparation of a pasteurized plasma protein solution has been reported previously[1]. In general this method has remained unchanged. By complete desalting the euglobulins are precipitated from plasma. The proteins re-

Table I

Method of Preparation of PPL

Starting material:	ACD- or EDTA-plasma
Desalting column:	Filled with a mixture of cation-exchanger (H^+) and anion-exchanger (OH^-)
Desalted plasma:	pH 5.0–5.2 ω/cm 10^4–10^5
Filtration:	Through "Filtercel", fine grade, at pH 5.3
Additives:	5% glucose, 0.012% ascorbic acid, 0.004 m Na-caprylate, pH 7.5
Sterile filtration:	Through bacterial filters directly into the final containers
Heat treatment:	In the closed containers for 10 hours at 60° C

maining in solution after this procedure can be heated for 10 hours at 60° C, whereby the hepatitis virus, if present, is inactivated. Table I summarizes this method of preparation[2,3,4].

The addition of ascorbic acid, as introduced recently, prevents a discoloration of the final product due to oxidation of traces of hemoglobin to verdoglobin.

2. *Analytical Data*

The more important analytical data are compiled in table II.

Immuno-electrophoretic and serological investigations have shown that no new antigens are formed by heat treatment; furthermore, no indications for isoantigenicity have been found in PPL. The entire plasmatic clotting system has been eliminated.

Table II

Analytical Data

	Plasma	PPL	
		before heat treatment	after heat treatment
Protein content	100	70–75	70–75
Electrophoresis			
% albumin	54	66–70	66–70
% fibrinogen	6	0.4	0
% globulins	40	34–30	34–30
Total lipid content in percent of total protein	11–15	ca. 12	ca. 12
Cholesterol in percent of total protein	4	3	3
Plasminogen	1	0.5	0.5
Esterase	1	0.8	0
Prothrombin, antihemophilic globulins, Factors V and VII			0
Osmotic pressure, calculated for identical protein concentrations	1	1.25	1.05

Comparison of the salt contents of PPL with plasma and albumin preparations seems of particular interest (fig. 1).

In order to investigate the *stability* of PPL on prolonged storage, the turbidities, viscosities and sedimentation constants of preparations stored at room temperature over two years have been determined. In no case has there been any difference between the values obtained with old and with fresh preparations. The fact that the stored material causes no reactions in clinical tests is in accordance with these findings.

3. *Osmotic Activity and Price of PPL*

Results of *in vitro* measurements of osmotic pressure have already been mentioned (table II). They have been confirmed *in vivo* by volumetric measurements in

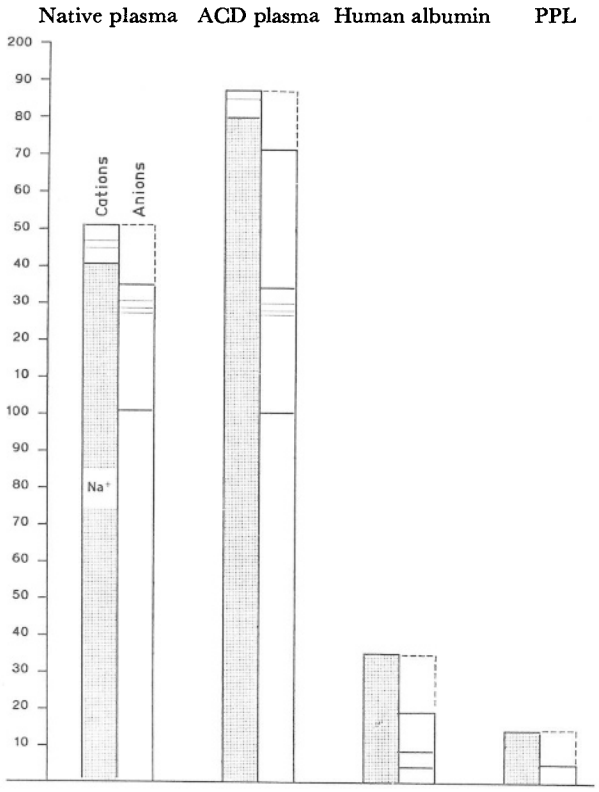

Fig. 1. Electrolyte content of native plasma, ACD plasma, human albumin and PPL m eq./liter at isooncotic concentration.

patients using radio isotopes[3]. A comparison of protein content and osmotic efficiency of PPL and other plasma expanders is presented in fig. 2.

In Switzerland the *costs of production* of iso-oncotic quantities of PPL, dried plasma and albumin are about the same.

4. Risk of Transmission of Hepatitis Virus

The results of an inquiry on the efficiency of heat treatment in eliminating the hepatitis virus are summarized in table III. It is particularly noteworthy that mainly *plasma of donors with a history of hepatitis has been used for the preparation of PPL.*

Table III

Risk of Transmission of Hepatitis by PPL

185 units of PPL have been transfused into 52 patients.
In no case was a hepatitis detected within the incubation period of 40–160 days.

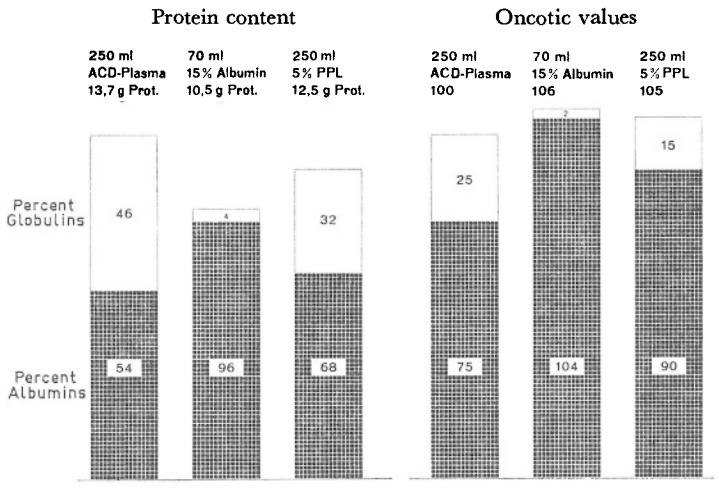

Fig. 2. ACD plasma, albumin and PPL solutions.

5. Tests, Indications and Tolerance

In table IV are compiled the tests carried out as a routine on PPL.

The indications for PPL are the same as for plasma, except for diseases with pronounced coagulation defects.

Table IV

Tests to be Performed on PPL before Release for Clinical Use

Every batch must be tested.	
Sterility test:	On Difco Fluid Thioglycollate medium
Test for pyrogens:	Three rabbits are injected intravenously with 5 ml PPL/kg each
Tolerance test:	Three mice are injected with 0.5 ml PPL intraperitoneally. They are observed over a period of 10 days
Clinical test:	Two bottles of every batch
All these tests are performed in this sequence after storage of the preparation for 6 weeks at room temperature.	
Screening test:	Careful visual control of all bottles during 8 weeks at room temperature

At the beginning of our trials with PPL, the rate of reaction was found to be 5.7 % from a total of 2229 reports received, representing about 50 % of the total number of units submitted to clinical trial. This rate was considered to be too high. A statistical analysis showed that this was mainly due to a few faulty batches. If these are not included in the calculation, the rate of reaction is decreased to 3.6 %. Since then another 1394 reports have been received, showing only 2.4 % of reactions. The assumption seems justified that the great number of transfusions for which no

written report has been received, has been performed without untoward reactions. Taking this into account, the rate of transfusion incidents is as low as 1.4 %.

The still decreasing tendency of the rate of incidents is due to improvements and increasing experience in production.

Of a total of 162 reactions, 124 were of febrile character, and 13 of an allergic nature. The remaining 25 patients showed pains in the back, nausea, uneasiness or dyspnoea.

6. Further Improvements of PPL-Production

The main disadvantage of the PPL-method stems from the fact, that up to now it has been connected with the loss of γ-globulins and fibrinogen. A pre-fractionation by means of polyphosphates will probably soon permit a recovery of both these products as well[5, 6].

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