B BRAUN
SHARING EXPERTISE

H. EPARIN-INDUCED
E. XTRACORPOREAL
L. DL
P. RECIPITATION

BACK TO BALANCE

HYPERPROTEINEMIA

WHEN THE BALANCE IS LOST

Whether by genetic predisposition or due to permanent malnutrition, disturbances of the lipometabolism are caused when a healthy balance in the absorption, processing and/or degradation of lipids supplied to the body is lost. Left untreated, this imbalance can cause occlusion of the arteries, leading to death in the worst case. Lipoprotein apheresis is the ultima ratio therapy when a healthy lifestyle and medication are no longer sufficient to attain the desired treatment outcome. Demand for this form of therapy is rising dramatically: Germany alone now has more than 3,000 patients undergoing apheresis treatment, with more patients in Italy and other countries around the world.

Cholesterol does not dissolve easily in water. This is why it is transported in the body with the help of lipoproteins. These have varying densities ranging from very low-density lipoproteins (VLDLs) through low-density lipoproteins (LDLs) to high-density lipoproteins (HDLs). LDLs are associated with the development of cardiovascular diseases, whereas HDLs appear to play a protective role in this context.

PCSK9 inhibitors are a new class of medicinal product, which are used in this treatment. The PCSK9 enzyme binds to LDL receptors in the bloodstream and prevents them from returning to the membrane surface after intracellular transport. The use of PCSK9 inhibitors enables more LDL receptors to reach the cellular surface and thus remove LDL cholesterol from the bloodstream. This leads to a reduction in LDL cholesterol levels.[1]

Cholesterol is not the only problem, however. While examinations for excessive levels of cholesterol are now common practice in many parts of the world, another lipoprotein with harmful effects – lipoprotein(a) (or Lp(a)) – is still barely known to the public. At the same time, Lp(a) plays an important role in disorders of the cardiovascular system of the patients affected. Roughly half of the some

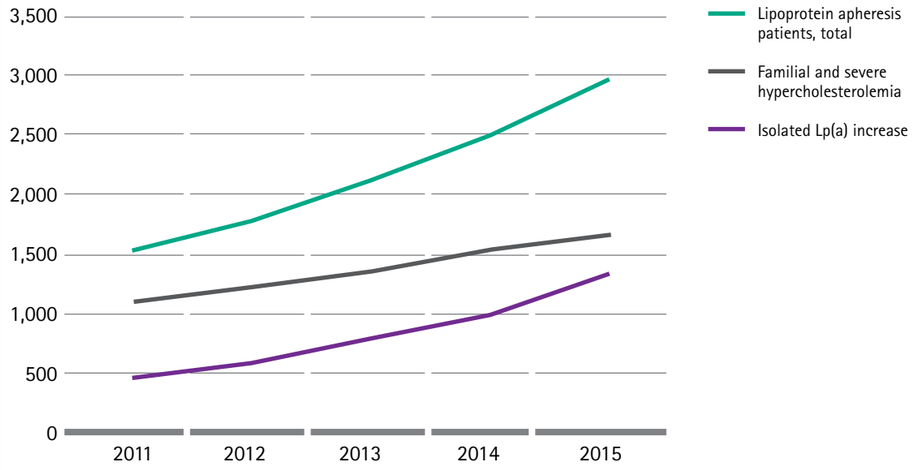
20%

ONE OUT OF FIVE IN THE TOTAL POPULATION HAS INCREASED LIPOPROTEIN(A) VALUES.[2]

3,000 APHERESIS PATIENTS

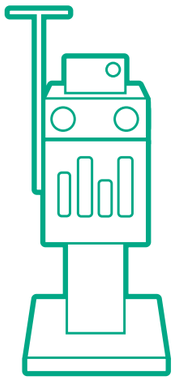
with hyperlipoproteinemia currently being treated in Germany suffer from an isolated Lp(a) increase (Fig. 1). The physiological role of LP(a) here is not yet fully understood. Cardiovascular diseases are hardly ever observed in patients with a complete lack of the ability to form Lp(a). A pharmacological method for treating an elevated Lp(a) level specifically does not currently exist. However, lipoprotein apheresis does offer affected patients an effective form of treatment.

FIG. 1: DEVELOPMENT OF LIPOPROTEIN APHERESIS PATIENTS IN GERMANY[3]



THE PROCEDURE MAKES THE DIFFERENCE

H.E.L.P. APHERESIS BASED ON LIPOPROTEIN PRECIPITATION



Apheresis is the only effective form of treatment (ultima ratio therapy) for severe disturbances of the lipometabolism

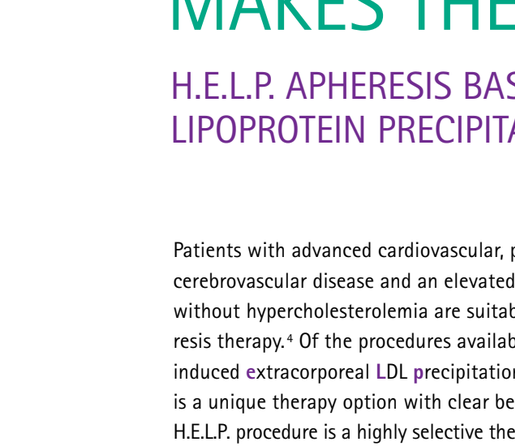
Patients with advanced cardiovascular, peripheral or cerebrovascular disease and an elevated Lp(a) value without hypercholesterolemia are suitable for apheresis therapy.[4] Of the procedures available, **h**eparin-induced **e**xtracorporeal **L**DL **p**recipitation (**H.E.L.P.**) is a unique therapy option with clear benefits. The H.E.L.P. procedure is a highly selective therapeutic approach used to reduce LDL cholesterol and Lp(a) while keeping HDL at a high level. In addition to LDL-C and Lp(a), there is also a significant reduction in other arteriosclerosis-inducing factors like fibrinogen or the acute phase protein CRP of approx. 60%[5] (see Fig. 2).

H.E.L.P. apheresis lowers the blood and plasma viscosity by 20% after just one treatment, due to the reduction of high fractions of lipids such as total cholesterol, LDL or triglycerides and fibrinogen. The aggregation of erythrocytes will also be significantly reduced, leading to improved microcirculation.[6]

H.E.L.P. can also be used for microcirculation disorders when conventional therapies are unsuccessful. Examples here are acute hearing loss or dry age-related macular degeneration (AMD). [7, 8]

In H.E.L.P. apheresis, there are no contraindications against ACE inhibitors, and patient tolerance to the treatment is good.[9] The H.E.L.P. therapy is an established course of treatment, and its efficacy and good tolerability can be demonstrated in more than

500,000 TREATMENTS PERFORMED.

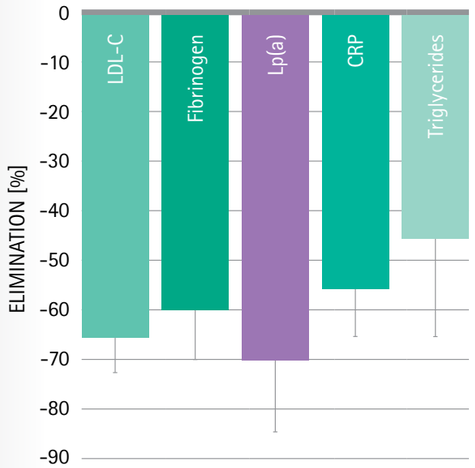


PCSK9 inhibitors are a promising new form of medication but cannot help patients with an isolated elevated Lp(a) level.

THE BENEFITS AT A GLANCE:

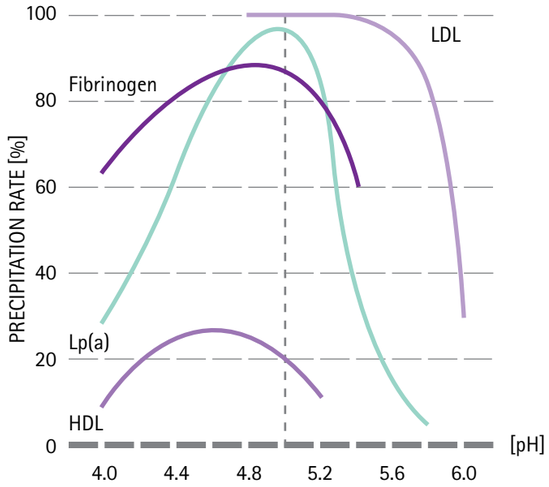
- Reduction in the atherogenic causal factors LDL cholesterol and lipoprotein(a)
- No contraindications against ACE inhibitors
- Good patient tolerance
- High HDL preservation
- Reduction of inflammatory mediators (CRP)
- Fibrinogen reduction
- 500,000 treatments performed
- Reduction of plasma viscosity

FIG. 2: MEDIUM REDUCTION IN SPECIFIC PLASMA COMPONENTS DUE TO UNIQUE H.E.L.P. TREATMENT WITH 3 L PLASMA VOLUME[5]



Effective treatment of disturbances of the lipometabolism while reducing inflammation parameters and improving microcirculation.

FIG. 3: PRECIPITATION BEHAVIOR AS A FUNCTION OF PH VALUE[10]



The reduction in the plasma pH value leads to precipitation of various relevant blood plasma proteins at a pH value of 5.12.

H.E.L.P.
LIPOPROTEIN PRECIPITATION

THIS IS HOW THE H.E.L.P. PROCEDURE WORKS

In the first stage of the H.E.L.P. procedure (Fig. 4), the plasma is separated from the remaining blood components. Following that, heparin and an acetate buffer are added, causing the plasma's pH value to drop. This alters the surface charge of the LDL, the LP(a) and other substances, resulting in increased binding to the heparin used. The resulting precipitates are filtered out and then removed from the plasma circuit.

The excess heparin is eliminated by adsorption. Removal of the buffer solution by dialysis then restores the physiological pH value. The cleaned blood is returned to the patient at the end of the treatment. There is no contraindication against ACE inhibitors. To date, more than 500,000 H.E.L.P. treatments have been performed successfully.

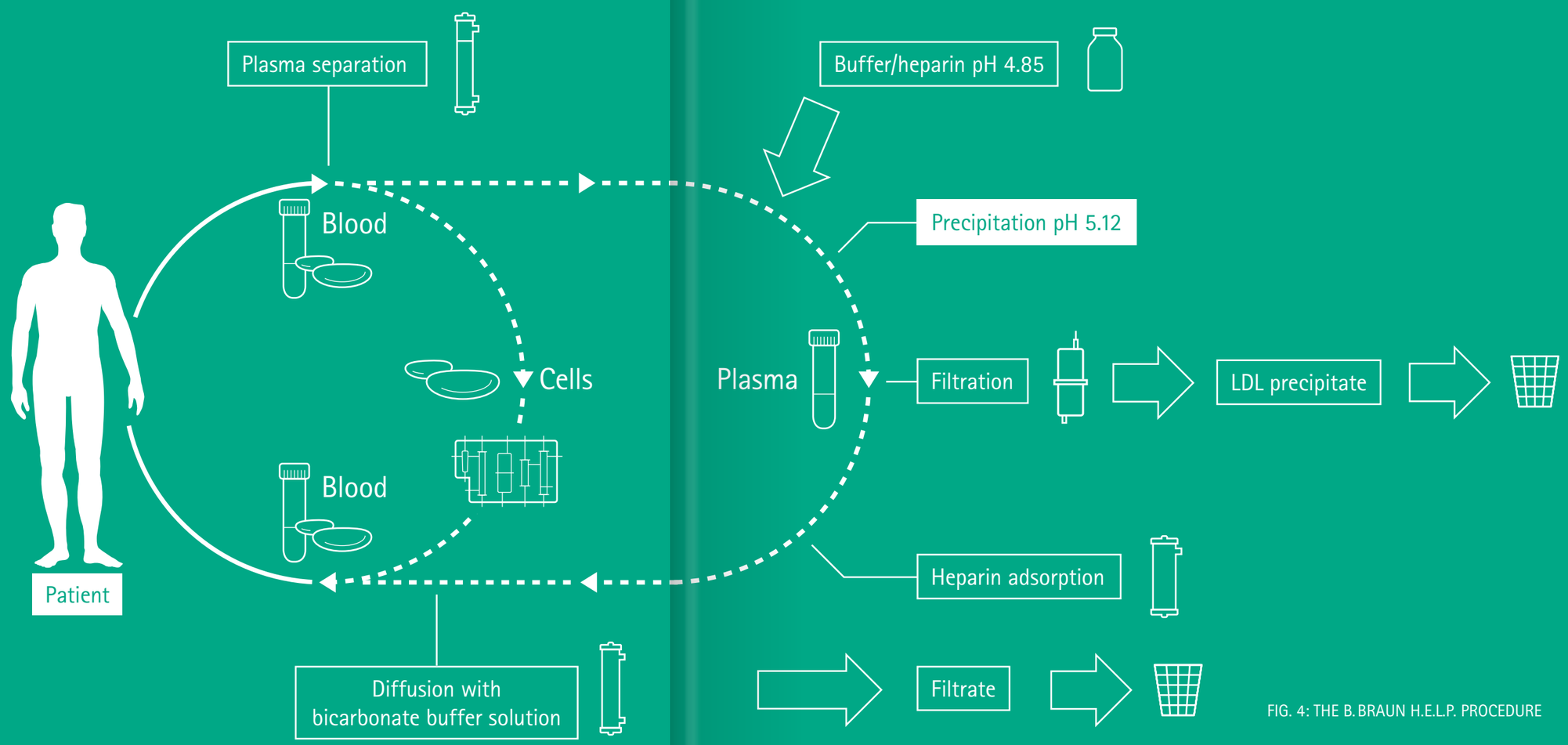
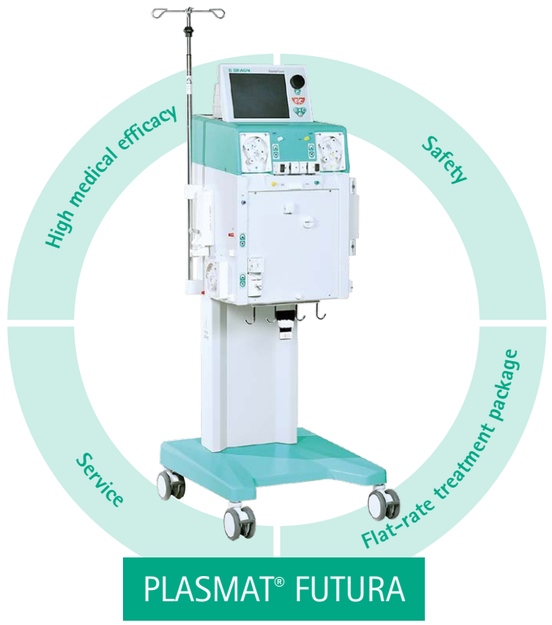


FIG. 4: THE B. BRAUN H.E.L.P. PROCEDURE

THE B. BRAUN H.E.L.P. SYSTEM

MUCH MORE THAN JUST AN APHERESIS PROCEDURE

Therapy with the H.E.L.P. system goes far beyond the mere treatment process itself: Our comprehensive range of products is supported by the B. Braun network of expertise, service, training and induction strategies.



High medical efficacy and **safety** formed the basic elements in the development of our H.E.L.P. concept. The Plasmat® Futura and all the associated components and consumables are an expression of this philosophy.

The Plasmat® Futura apheresis system and all the components and consumables are designed for perfect compatibility. The **pre-connected treatment set** leads to an efficient setup of the system.

The H.E.L.P. therapy is offered as a **flat-rate treatment package**, including machine and service components, as well as all the consumables necessary for performing the therapy.

Lipoprotein apheresis is more than just a product solution, however. The H.E.L.P. therapy comes with a comprehensive **service and training** package. Our experienced application consultants will assist you in the **introduction, organization and planning of treatments**.

SEE FOR YOURSELF!
H.E.L.P. HELPS!

ARRIVING AT THE GOAL FASTER

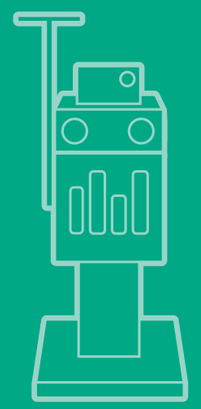
B. BRAUN'S H.E.L.P. APHERESIS FOR A MORE EFFICIENT HYPERLIPOPROTEINEMIA THERAPY

EXPERIENCE GAINED FROM MORE THAN HALF A MILLION TREATMENTS and the findings of various clinical studies prove the efficiency and effectiveness of H.E.L.P. apheresis. This well-tolerated therapy reduces the incidence of cardiovascular event rates in a large number of high-risk patients.

The H.E.L.P. procedure is used in numerous treatment centers around the world. Find more information on our website:

WWW.BBRAUN.COM

NO CONTRAINDICATION AGAINST ACE INHIBITORS: H.E.L.P. apheresis is an extremely gentle procedure. HIGH EFFICACY WITH ISOLATED INCREASED LP(A) VALUES: No pharmacological alternative. ULTIMA RATIO THERAPY FOR SEVERE DISTURBANCES OF THE LIPOMETABOLISM: If it is not possible to lower the LDL cholesterol level sufficiently despite maximum dietic therapy and medication documented for 12 months, then lipoprotein apheresis is the only remaining effective treatment option. REDUCTION OF OTHER ATHEROSCLEROSIS-INDUCING FACTORS like fibrinogen or of the acute phase protein CRP by about 60%.[11] IMPROVEMENT IN MICROCIRCULATION: For use with dry age-related macular degeneration and/or acute hearing loss when conventional therapies are unsuccessful. EFFICACY PROVEN IN MORE THAN 500,000 TREATMENTS: Years of clinical experience and carefully conducted clinical trials prove that H.E.L.P. is a safe, gentle and effective procedure.[9] REDUCTION IN MORTALITY: Studies and data from the German lipoprotein apheresis registry show that after the beginning of apheresis therapy, the event rates fall by more than 70% as compared to the period before lipoprotein apheresis.[12, 13]



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3 KBV Qualitätsberichte 2012-2016 (Berichtszeiträume 2011-2015)

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