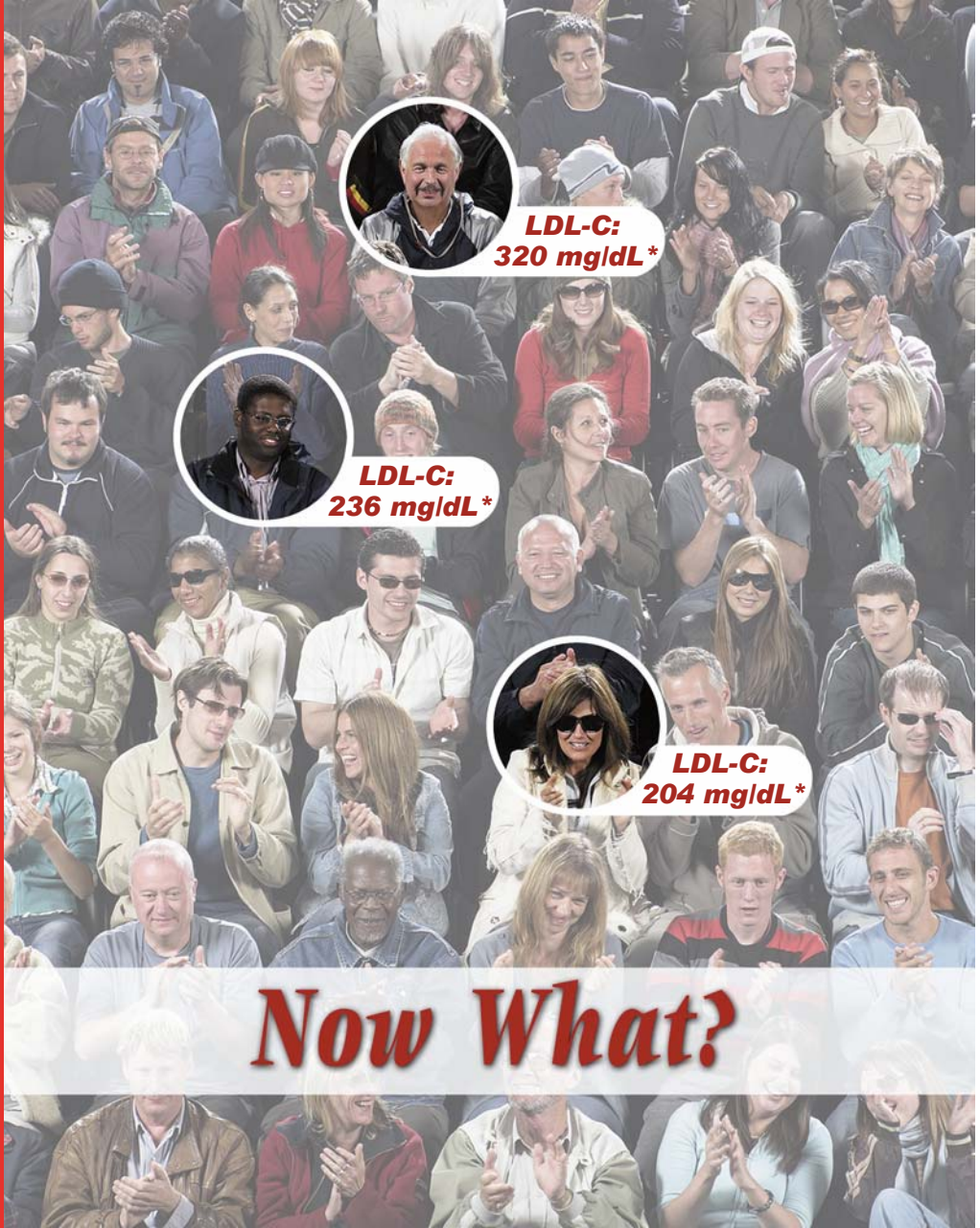


Diet and Maximum Drug Therapy Have Fallen Short...



**LDL-C:
320 mg/dL***

**LDL-C:
236 mg/dL***

**LDL-C:
204 mg/dL***

Now What?

The LIPOSORBER® Patient Guide

* THE LDL-C NUMBERS SHOWN IN THE PHOTOGRAPH ARE HYPOTHETICAL AND DO NOT CORRESPOND IN ANY WAY TO, OR WITH, THE INDIVIDUALS IN THE PHOTOGRAPH OR THEIR HEALTH.

Why has your doctor prescribed LIPOSORBER[®] treatment for you?

You are being considered as a candidate to receive LIPOSORBER treatment. The LIPOSORBER is a device that will selectively remove Low Density Lipoprotein (LDL) from the bloodstream. The technique of removing only harmful LDL from the blood and returning other blood components (blood cells, proteins, antibodies and HDL) is called *LDL apheresis*.

Familial Hypercholesterolemia (FH) is a treatable genetic disorder

Elevated LDL levels have been long recognized as one of the principal causes of heart and vascular disease. Most people receiving LIPOSORBER treatment have inherited a genetic condition (familial hypercholesterolemia or *FH*) causing LDL levels to rise dramatically, often to levels greater than 200 mg/dl. If untreated, 50% of FH patients experience cardiac and vascular illness by the age of 55 years if there is one gene affected and by age 20 years or less if two genes are affected.¹

Can I reduce my future risk of a heart attack?

Numerous scientific studies have demonstrated that lowering LDL levels will prevent heart or vascular disease progression and reduce future heart attacks, heart and vascular surgery and cardiac death. Published studies show reductions from 20-50% as compared to untreated patients.² In most instances LIPOSORBER treatment will be combined with medication therapy to insure the maximum LDL lowering effect. Some patients

with cholesterol-lowering medication side effects may be treated with LIPOSORBER treatment, since this involves only the selective removal of LDL from the bloodstream by a mechanical (filtering) method rather than the use of a medication.

Current national guidelines by experts (National Cholesterol Education Program – NCEP) now recommend that patients with heart and vascular disease have their LDL cholesterol levels reduced below 70 mg/dL for maximum benefit and protection against future cardiac events. In addition, the target of treatment for patients without heart and vascular disease is 100-130 mg/dL depending on the presence of other cardiac risk factors.³

What are the FDA criteria for LIPOSORBER treatment?

The LIPOSORBER system has been approved by the FDA for patient use since 1996. To date, there have been more than 25,000 treatments across 50 centers nation-wide.⁴ The FDA criteria for treatment are:

- ◆ LDL cholesterol greater than 200 mg/dL and documented coronary heart disease⁵
- ◆ LDL cholesterol greater than 300 mg/dL without coronary heart disease⁵

In order to qualify for LIPOSORBER treatment, a patient must first be on maximum medication and diet therapy for 6 months. Although most patients continue to receive maximum doses of lipid lowering therapies during LIPOSORBER treatment, medication doses may be lowered if there are medication side effects.

Case History, Mr. B.




- ◆ Father, grandfather and 2 paternal siblings developed heart disease at less than 55 years old
- ◆ Patient has a total cholesterol of 405 mg/dL, LDL cholesterol of 278 mg/dL before medication use, *after* medication, total cholesterol 290 mg/dL , LDL cholesterol 215 mg/dL
- ◆ First heart attack while taking a medication, age 42
- ◆ Angioplasty/Stent placed, age 42
- ◆ Recurrent angina cardiac bypass surgery, age 48
- ◆ Currently taking 3 cholesterol medications: statin, absorption inhibitor, niacin: LDL cholesterol 205 mg/dL

What is involved in a LIPOSORBER treatment ?

The LIPOSORBER System is a type of “apheresis” or “extracorporeal” (blood treated outside the body) therapy to remove LDL from the blood. The patient sits in a comfortable chair. The patient’s blood is withdrawn through a needle in the arm which then runs through the LIPOSORBER system. The LIPOSORBER separates components (cells, plasma) from the whole blood removing only LDL through a filter (column). The rest of the plasma components and the whole blood are returned to the patient through the needle in the opposite arm. Placement of needles in the arms and the momentary discomfort of a needle stick is the most common “side effect” of the procedure. In some patients with small veins or those patients that have difficulty with needle placement, a fistula (a surgical connection of a vein to an artery) may make the procedure easier.



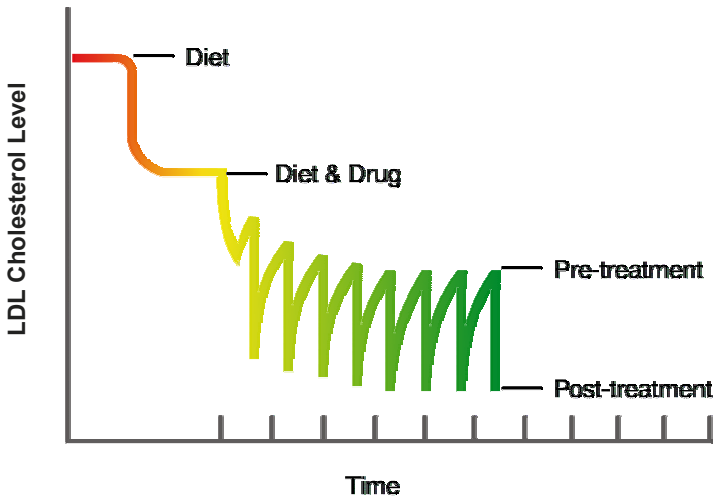
LDL and HDL go in...

-  Dextran Sulfate - cellulose beads
-  LDL
-  HDL

*Only HDL
returns to you...*



Studies have shown that the LIPOSORBER system will lower LDL cholesterol approximately 70-83% after a single treatment.⁶ The liver will continue to produce LDL following LIPOSORBER treatment and it will take approximately 2 weeks to regain the baseline level. In order to maintain lowest possible LDL levels over time, patients will typically require treatment every 2 weeks.



During the treatment approximately 1 pint of blood is continuously treated by the LIPOSORBER outside of the body. It will therefore take approximately 2-3 hours of treatment to filter the entire blood volume in a patient.

Do insurance policies cover LIPOSORBER treatment?

Most insurance policies including Medicare cover LIPOSORBER treatment. Manufacturer's complementary insurance consultation is available to verify proper pre-authorization of coverage.

Safety of LIPOSORBER Treatment

Note: A detailed explanation of risks and adverse reactions associated with LIPOSORBER treatment should be provided by your physician.

Selectivity:

Although LIPOSORBER treatment is very selective in removing LDL cholesterol, there are other components of your plasma that are partially removed. These components include HDL cholesterol, fibrinogen, and plasma proteins. The following chart shows the mean reductions in the clinical trial in the United States.

<i><u>Plasma Component</u></i>	<i><u>After-Treatment Reduction</u></i>
LDL cholesterol	73-83%
Lp(a)	53-76%
Triglycerides	47-68%
HDL cholesterol	4-13%
Fibrinogen	29%
Plasma Proteins	15%

U.S. Clinical Trial Data, December 1988 – September 1991, 4,936 treatments in 74 patients.

In most cases, these reductions do not pose a risk to your health. However, your physician will determine the levels of these plasma components before and after treatment periodically to check for any changes of clinical importance.

Adverse Reactions:

Out of 4,936 treatments during U.S. clinical trial, the most common adverse reactions were:

- ◆ Drop in blood pressure (hypotension): 0.8%*
- ◆ Nausea/vomiting: 0.5%
- ◆ Flushing/blotching: 0.4%

U.S. Clinical Trial Data, December 1988 – September 1991, 4,936 treatments in 74 patients.

* A group of medications used in patients with heart and vascular disease called ACE inhibitors (Lisinopril, Captopril, Enalapril, etc.) causes acute drop in blood pressure in LIPOSORBER patients. Substitute medications such as the ARB class of medications are permissible and a discussion with your physician is necessary before starting LIPOSORBER treatment.

Further Information

For further information, please refer to your physician and/or our website at www.liposorber.com. For your insurance coverage verification, the manufacturer provides complementary professional consultation upon request.

Citations:

- 1 Mabuchi H. *Familial Hypercholesterolemia*. 1991 Mar; p25.
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Hoeg JM, et al. *Arterioscler Thromb*. 1994 Jul; 14(7):1066-74.
- 2 Mabuchi H. *Saishin-Igaku*. (14)1134:56-6.
- 3 Grundy SM, et al. *Circulation*. 2005; 112:e297.
- 4 Data from Kaneka Pharma America Sales Record.
- 5,6 U.S. Clinical Trial Data, December 1988 – September 1991, 4,936 treatments in 74 patients.

Special thanks to the following healthcare professionals for their clinical advice:

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