

ALIVER Project overview

Development of DIALIVE, a novel Liver Dialysis Device for the treatment of patients with Acute on Chronic Liver Failure (ACLF)



Improvement of Albumin for Liver Support

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ALBUTEC GMBH

KICK OFF MEETING LONDON JANUARY 23RD 2017



Albumin is an important component of the endogenous “public transport system”

Blood circuit transports oxygen, nutrients, electrolytes, hormones, toxins etc.

Current perception of albumin as merely a provider of colloid osmotic pressure is incomplete

Albumin makes 60% of plasma proteins (40 g/l)

Albumin transports toxins, hormones, nutrients, electrolytes,

Albumin's transport function is affected in Liver failure

Albumin Synthesis is decreased (Hepatocellular Dysfunction, Acute Phase Response)

Albumin Recycling is decreased

Albumin Oxidation Level increased (Non-Mercaptalbumin)

Kobalt Binding is decreased (IMA)

Albumin Binding Function (ABiC) at the Benzodiazepine Binding Site is decreased, correlates with CHILD and MELD (Klammt et al.) and Survival

Changes are in part reversible or irreversible

Improving Albumin Dysfunction is associated with improved Survival

Albumin Dysfunction can be improved by infusion, exchange therapy, plasma adsorption or albumin dialysis

Albumin Dialysis and plasma adsorption can potentially improve reversible dysfunction

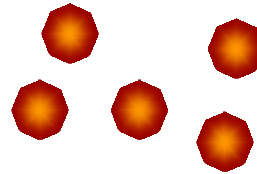
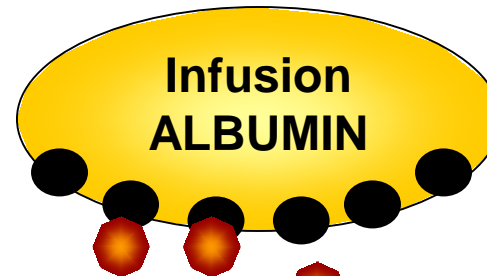
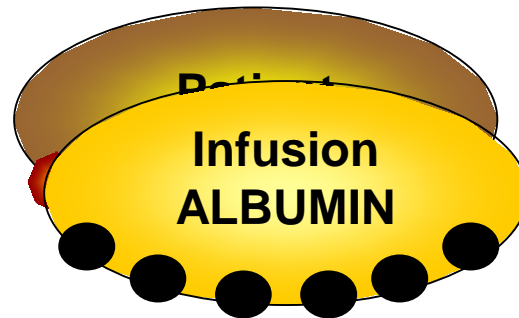
- hemodynamics, renal function, encephalopathy improved
- survival improvement in tightly defined groups (AAH)

Infusion/Exchange therapy can resolve potentially irreversible dysfunction

- HRS I, SBP, Large Volume Paracentesis for Infusion
- Plasma Exchange for ALF

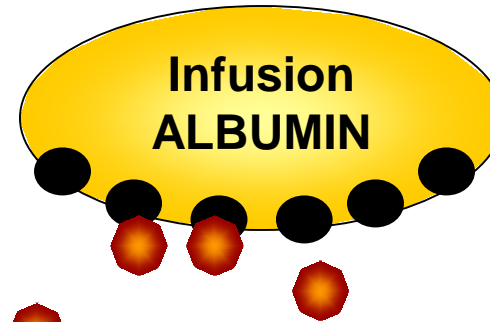
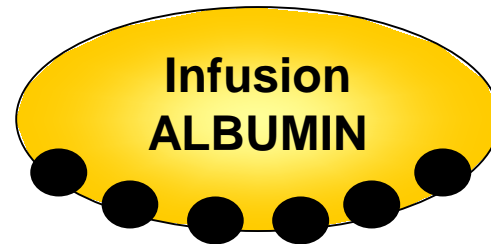
Albumin Therapy (Goal)

Create Binding Sites
with:

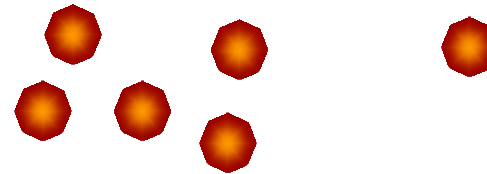


Albumin Therapy (Goal)

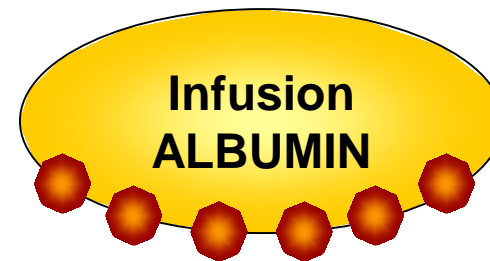
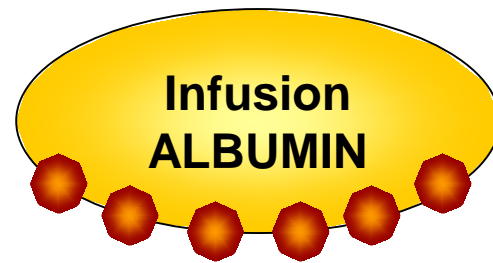
Create Binding Sites
with



Free, biologically active toxins
are supposed to be bound



Albumin Therapy (Goal)

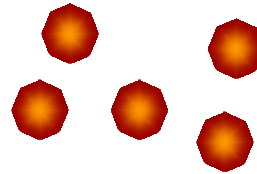
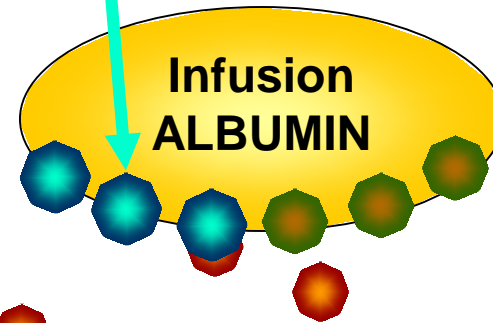
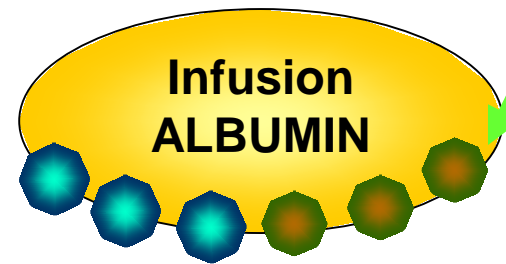


Should „immobilize“ Toxins from
Circulation



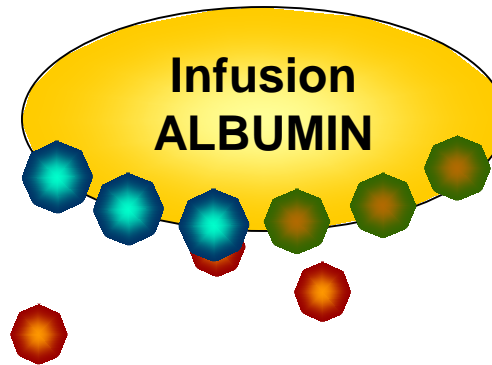
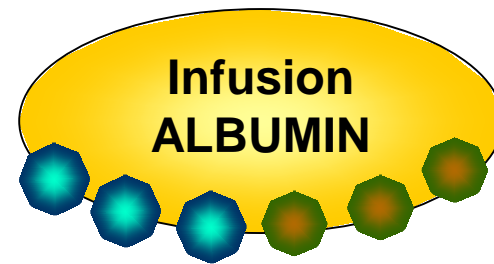
Problem of Albumin Therapy

Stabilizers occupy
Binding Sites



Problem of Albumin Therapy

Stabilizers occupy
Binding Sites



Toxins remain biologically
active

BLOOD SIDE

DIALYSATE SIDE

Albumin
from patient

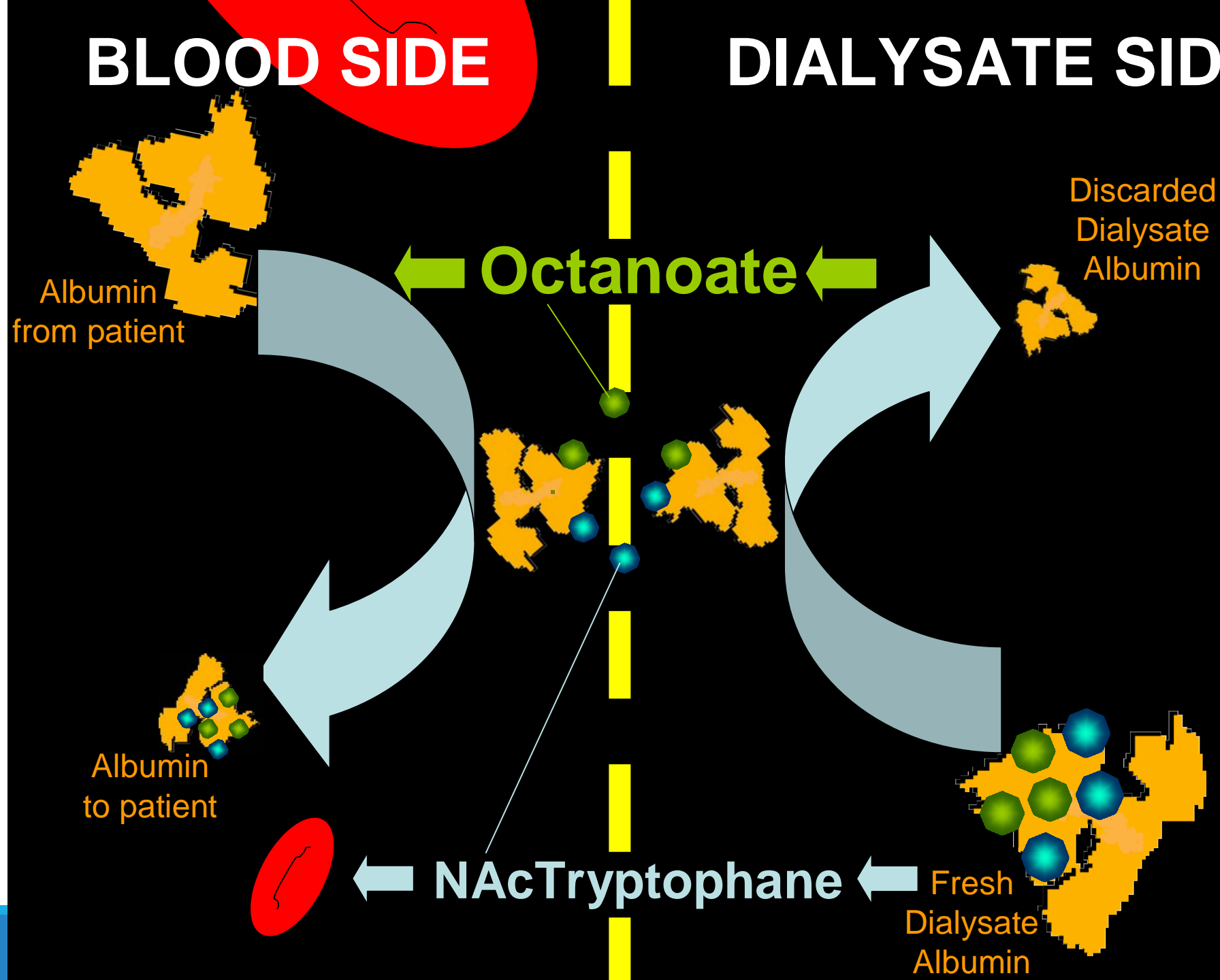
Albumin
to patient

Octanoate

Discarded
Dialysate
Albumin

NAcTryptophane

Fresh
Dialysate
Albumin



Octanoate and Tryptophane:

Induce hepatic coma:

-Mullen et al. 2000

- **Induce vasodilation and hypotension**

- Kristev et al. 1992

- Blei et al. 1994

- **Deteriorate ammonia metabolism**

- Mitkov 1988

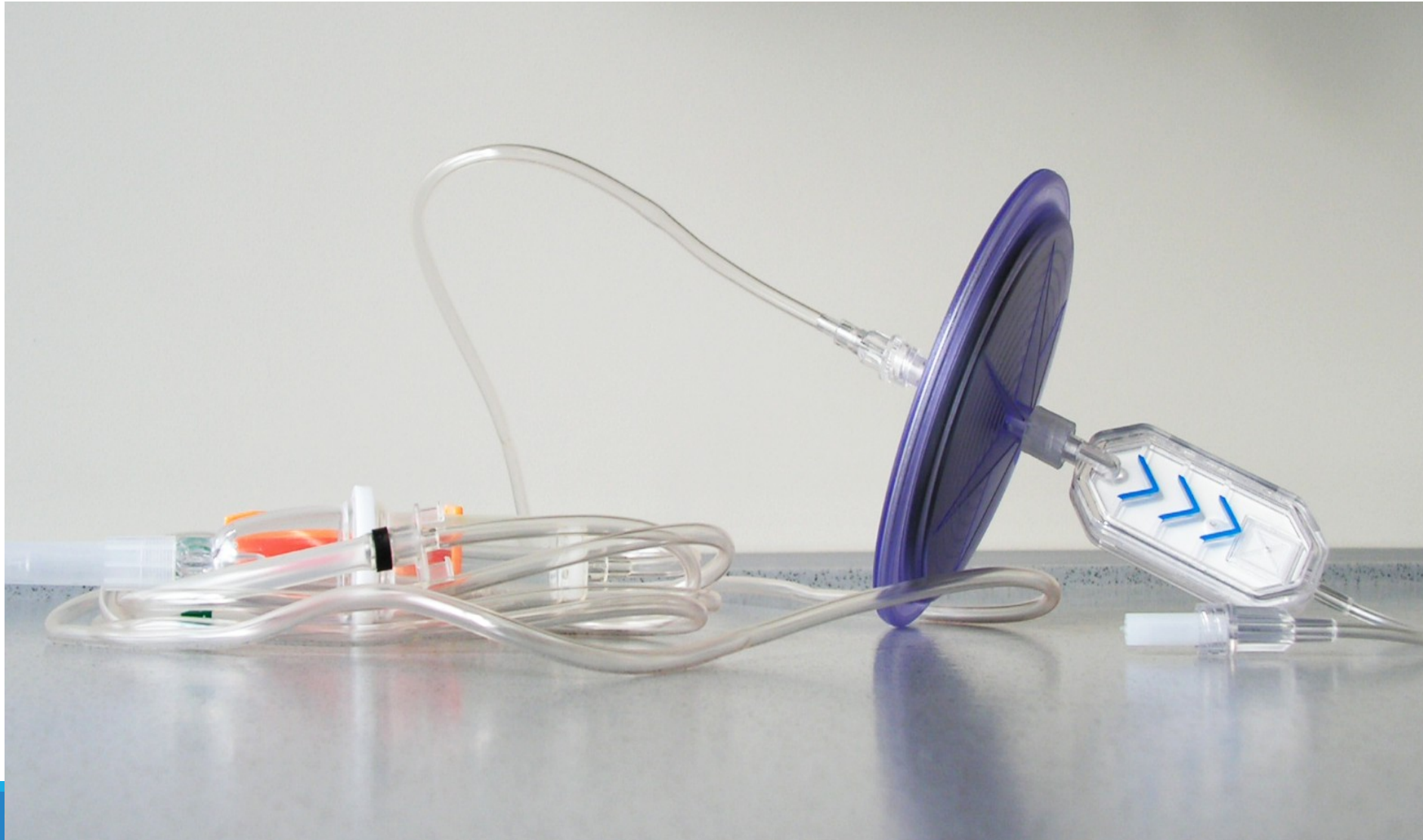
- **Inhibit mitochondrial respiration**

- Parker 1983

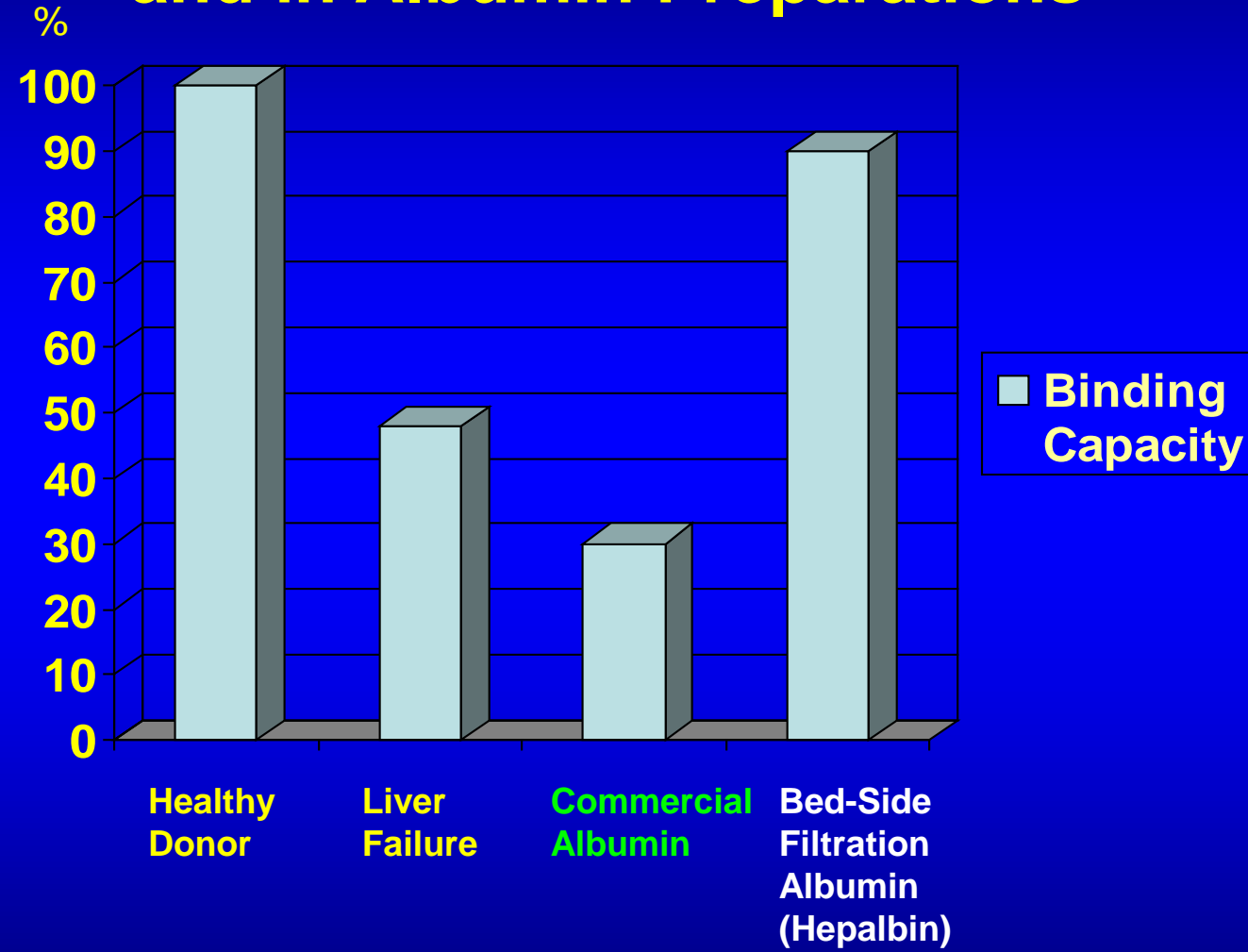
- **Induce Astrocyte Swelling**

- Olson 1989

New Device: Bed-side Removal of Caprylate and Tryptophane

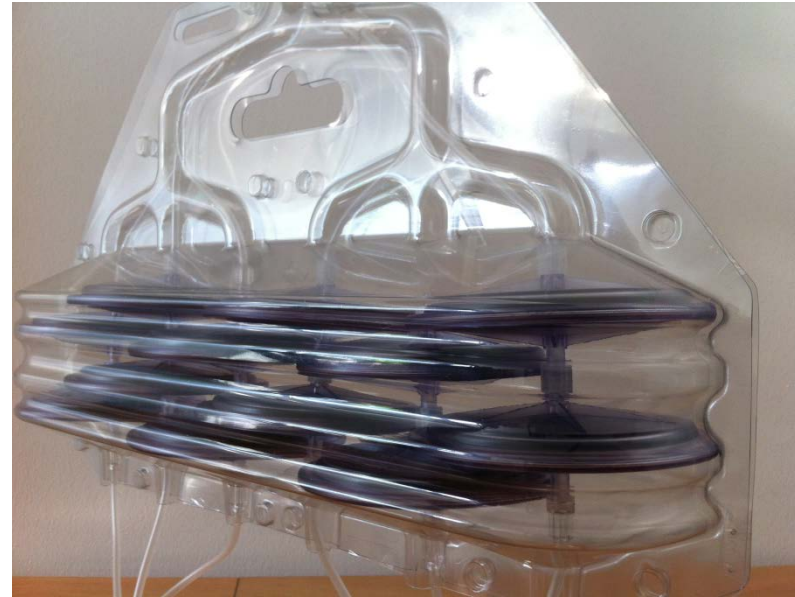


Albumin Binding Capacity in Health, Disease and in Albumin Preparations





**-Cross over Design: First Day
MARS Tx or New Adsorbent,
next Day alternative
Adsorbent**



Deligandized Albumin

Reduced Patient exposure to Octanoate in i.v. Therapy

- hemodynamics, renal function, improved more

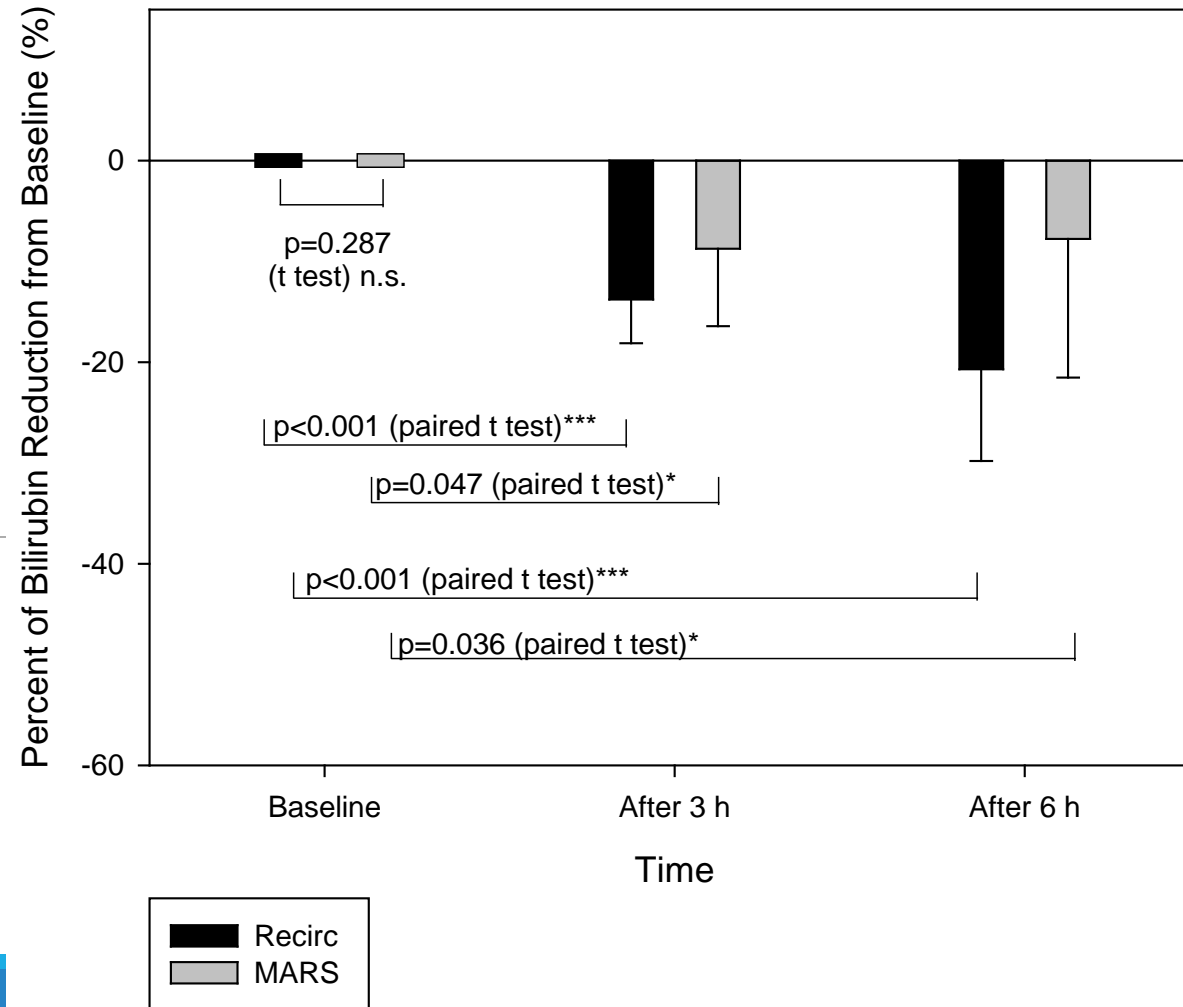
Provides more Binding Sites and is more effective in Albumin Dialysis

- improved Albumin Binding in vivo, enhanced toxin reduction

Should be tested in Exchange Therapy

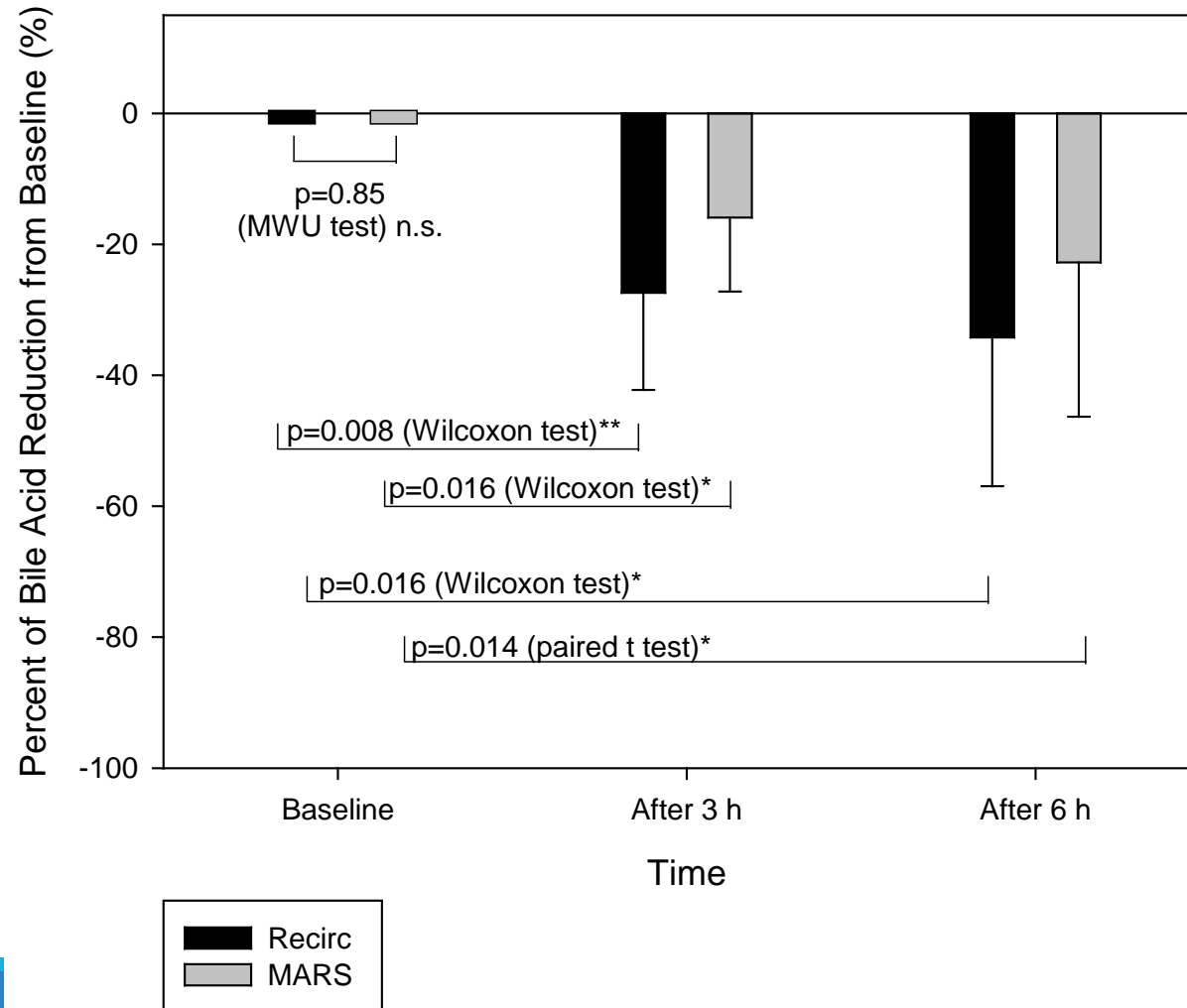
Results I

Reduction of Total Bilirubin



Results II

Reduction of Total Bile Acids



Results III

Improvement of Albumin Binding Function (ABiC)

