

# CytoSorb®



## CytoSorb® Therapy

Indications and Set-up

# CytoSorb Therapy

## REGAIN CONTROL



*The statements in this document do not constitute diagnostic or therapeutic recommendations. It is a “best practice” collection, based on the current level of knowledge and expert opinion. The indication, conduction and termination of the CytoSorb therapy is the responsibility of the treating physician. The short set-up guide does not replace the instructions for use.*

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# The International CytoSorb Registry

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## Why join the Registry?



You want to optimize your CytoSorb therapy



You want to contribute to the improvement of international safety standards



You want to exchange your results and experiences worldwide



Little effort: No intervention, no randomization



Easy, quick and secure electronic data entry



Highest quality standard and independent scientific supervision by Center for Clinical Studies in Jena/Germany

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# 01 | The Therapy

# The Therapy

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The CytoSorb therapy is based on extracorporeal blood purification that effectively reduces excessive levels of inflammatory mediators.

In doing so, the goal is to reduce the overshooting systemic inflammatory response while the physiological immune response is maintained.

Patients with hyperinflammatory infectious and non-infectious conditions should benefit from CytoSorb therapy.

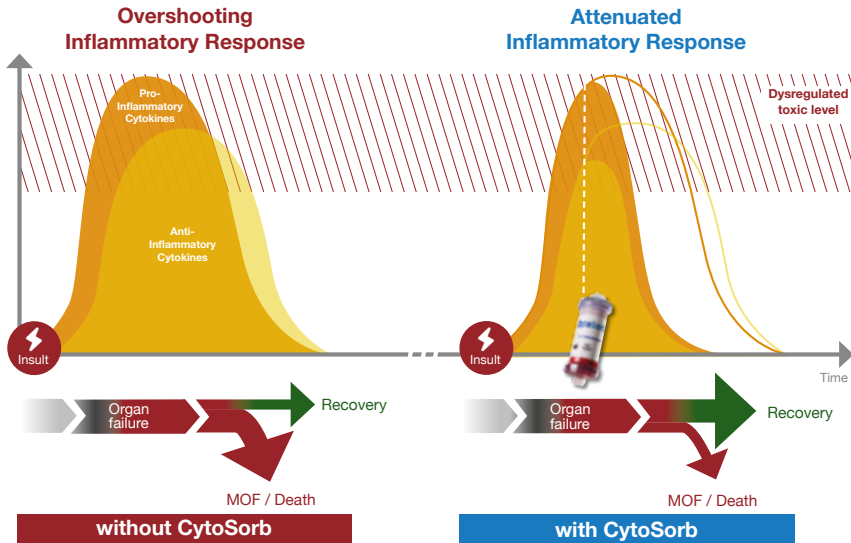
The life-threatening complications of the so called cytokine storm can potentially be avoided.

Stabilization following the hyper-inflammatory phase can be improved.





# The Therapy



# The Therapy

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## This is how CytoSorb modulates the immune response

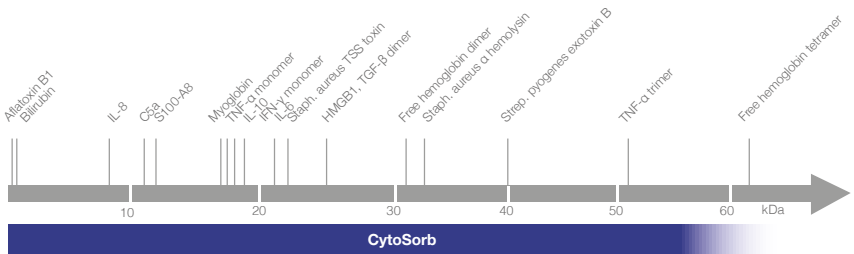
- Effective reduction of excessive cytokine levels
- Decreased de novo synthesis of inflammatory mediators
- Controlled attenuation of the overshooting immune response
- Re-targeting of the cellular immune defense to the focus of infection

## Your CytoSorb therapeutic goals

- Control the systemic inflammation
- Modulate the immune response
- Stabilize hemodynamics
- Improve the fluid balance
- Prevent and treat organ dysfunction and organ failure

## Adsorption spectrum of the CytoSorb adsorber

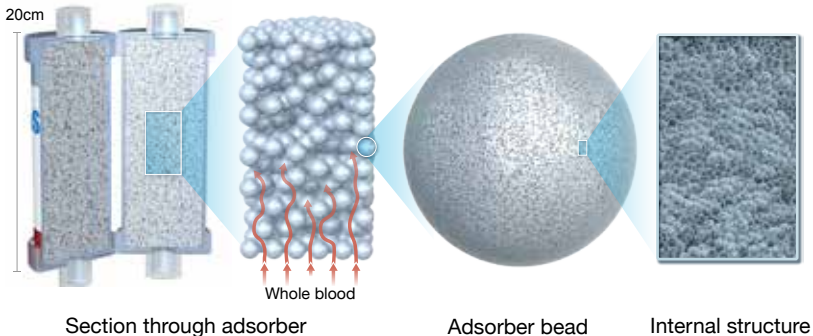
The CytoSorb adsorber adsorbs hydrophobic small and middle molecular substances dependent on their concentrations.



With high concentrations greater amounts of those substances can be removed very quickly, whereas elimination rates decrease with lower concentrations. This auto regulation based on physicochemical properties is supposed to prevent a complete removal of physiologic mediators.

# The Therapy

## Proprietary polymer technology



- High-tech polymer
- Size selectivity < 55 kD
- Low flow resistance
- Gamma sterilized, 3 years shelf life

- Recommended blood flow 150-500 ml/min
- Pre-filled with isotonic saline solution

# 02 | Sepsis Septic shock



## Basic prerequisites



- Onset of or ongoing acute systemic hyperinflammation
- Standard therapy according to sepsis guidelines established (e.g. 6 hr sepsis bundle, focus control)
- APACHE II > 25, platelets > 20,000/ $\mu$ l, no DNR order
- CytoSorb is to be employed as an adjunctive, not as a causative therapy
  
- Treatment duration and indication for exchange of adsorber depend on the clinical course. The maximum treatment time per adsorber is 24 hours
- Continuous treatment is recommended over intermittent
- Recommended blood flow rate 150 - 500 ml/min
- Anticoagulation with heparin or citrate, aPTT of 60 – 80 sec is sufficient for CytoSorb
- In stand-alone mode without hemofilter heparin anticoagulation only
- Contraindications for extracorporeal blood circuits apply

▶ See set-up page 34

# Sepsis / Septic shock

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## When should the therapy be started?



- Patient cannot be stabilized clinically with standard medical treatment
- Clinical picture of hyperinflammation
  - Onset of shock within the last 24 hrs  
(Norepinephrine > 0.3  $\mu\text{g}/\text{kg}/\text{min}$  or rapidly increasing)
  - Signs of capillary leak – e.g. positive fluid balance
- Development of at least one more organ dysfunction
  - Kidney, lung, liver, coagulation, neurologic impairment
- Systemic markers of infection:
  - PCT > 3  $\mu\text{g}/\text{l}$  in cases of bacterial or fungal sepsis
  - High IL-6 levels (e.g. > 500  $\text{pg}/\text{ml}$ ) can, if available, support the treatment decision, however low levels do not preclude reasonableness of treatment

**Early start of therapy:  
Better to avoid than have to treat organ failure**





## Why start early?

- Pre-clinical data and previous clinical experience point towards a survival benefit if CytoSorb therapy is started early <sup>(1-4)</sup>
- The guidelines, that are based on sound clinical evidence, should be followed first
- CytoSorb should be started if patients do not respond sufficiently to therapeutic guideline recommendations
- Insufficient therapeutic efficacy of the sepsis bundle is the recommended indication for start of CytoSorb therapy in septic shock

### References

1. Kogelmann K et al., Critical Care 2016 20(Suppl 2):94
2. Peng ZY et al., Kidney Int. 2012 Feb;81(4):363-9
3. Peng ZY et al., Crit Care Med. 2008, 36(5):1573-7
4. Sathe P et al., Critical Care 2015, 19(Suppl 1): P130

**Organ dysfunction caused by inflammation is potentially reversible and can be treated, in contrast to irreversible organ cell failure.**

# Sepsis / Septic shock

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## Signs of successful CytoSorb therapy



- Stabilization of the hemodynamic situation
  - Decreasing need for vasopressors
  - Stabilization of fluid balance
  - No further increase in lactate level
- Decrease in IL-6 level (if measured) and of WBC, PCT, CRP
  - When assessing the course of PCT, be aware of direct, partial PCT removal by CytoSorb
- Stabilization of other organ functions, e.g.
  - No further deterioration of liver function parameters
  - No further increase of ventilatory support necessary
  - Improvement in coagulation situation

## When should the therapy be terminated?



- Treatment should be continued until the clinical condition indicates that systemic hyperinflammation is under control
  - No need for catecholamines or rapidly decreasing dosage
  - Reversal of fluid balance, reduction in edema
  - Normalization of lactate level
- Improvement in impaired organ functions, e.g.
  - Marked reduction in ventilatory support
  - Return of spontaneous diuresis
  - Improvement in liver function parameters
- Deterioration after cessation of CytoSorb treatment (e.g. insufficient focus control or second hit) may indicate necessity to recommence CytoSorb therapy

# Sepsis / Septic shock

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## Possible patient groups



- Post-surgical patients with sepsis and onset of AKI
- Patients with severe concomitant diseases and impaired immune competence
  - Often elderly patients
  - Chronic diseases:
    - Chronic dialysis patients
    - Patients with chronic liver disease
- Patients with therapy refractory septic shock and multi-organ failure
- Patients suffering from sepsis caused by enterotoxins
- Patients with viral or fungal sepsis or by tropical diseases

# 03 | Cardiac surgery intraoperative

# Cardiac surgery: Intraoperative use

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## Basic prerequisites



- Installation must never be into the main-stream of a cardiopulmonary bypass (CPB)
- CytoSorb placement should be in a shunt off the main flow as is the current practice with hemoconcentrators
- Pressure or flow monitoring of CytoSorb line is recommended
- Recommended blood flow rate 150 - 500 ml/min
- Anticoagulation with heparin, ACT of 160 - 210 sec is sufficient for CytoSorb

▶ See set-up page 54

# Cardiac surgery: Intraoperative use

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## When should the therapy be started?



### **At the start of CPB**

Preemptive use in case of one or more of the following risk factors:

- Age > 75 yrs
- Preoperative activation of the immune system:
  - Endocarditis
  - Cardiac failure with inotropic therapy
  - Preoperative leukocytosis (> 12,000/ $\mu$ l)
  - Organ dysfunctions, e.g. kidney or liver
- Procedures with higher risk for complications and/or SIRS
  - Combination procedures (valve repair/-replacement, CABG)
  - Redo procedures
  - Aortic surgery with hypothermic circulatory arrest
  - LVAD implantation
- Long CPB duration expected (>120 min)
- High risk for postoperative need for ECMO

### **Anytime during CPB**

Patients with low primary risk but unexpected course

- Unexpected, significant prolongation of anticipated CPB time
- Intraoperative development of a severe SIRS
- Intraoperative complications with expected development of severe SIRS

# Cardiac surgery: Intraoperative use

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## When should the therapy be terminated?

At the end of CPB in cases of preemptive use and

- Uneventful intraoperative course
- No signs of hyperinflammation at end of CPB
- No undue hemodynamic instability at end of CPB

Postoperative continuation in ICU in cases of

- Ongoing or beginning SIRS intraoperatively
- Severe SIRS expected postoperatively





# 04 | Cardiac surgery postoperative

# Cardiac surgery: Postoperative use

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## Basic prerequisites

- Onset of or ongoing acute systemic hyperinflammation
- Standard therapy established and optimized
- Platelets > 20,000/ $\mu$ l, no DNR order
- In case of sepsis, Cytosorb is to be employed as an adjunctive, and not a causative therapy
- Treatment duration and indication for exchange of adsorber depend on the clinical course. The maximum treatment time per adsorber is 24 hours
- Continuous treatment is recommended over intermittent
- Recommended blood flow rate 150 – 500 ml/min
- Anticoagulation with heparin or citrate, aPTT of 60 – 80 sec is sufficient for CytoSorb
- In stand-alone mode without hemofilter heparin anticoagulation only
- Contraindications for extracorporeal blood circuits apply

**Early start of therapy:  
Better to avoid than have to treat organ failure.**

# Cardiac surgery: Postoperative use

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## When should the therapy be started?



Immediately upon arrival in ICU

- Postoperative continuation of intraoperative CytoSorb treatment
- Manifest severe SIRS upon arrival

Postoperative (0-48h) development of SIRS with or without proof of infection

- Patient cannot be stabilized clinically with standard medical treatment
- Impaired hemodynamics (shock)
  - Onset of shock (Norepinephrine > 0.3  $\mu\text{g}/\text{kg}/\text{min}$  or rapidly increasing)
  - Signs of capillary leak – e.g. positive fluid balance
- Onset of at least one more organ dysfunction, e.g.
  - Mechanical ventilation
  - Acute kidney failure with need for RRT
- Systemic markers of infection:
  - PCT > 3  $\mu\text{g}/\text{l}$  in cases of bacterial or fungal sepsis
  - High IL-6 levels (e.g. > 500  $\text{pg}/\text{ml}$ ) can, if available, support the treatment decision, however low levels do not preclude reasonableness of treatment

# Cardiac surgery: Postoperative use

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## In case of sepsis - why start early?



- Pre-clinical data and previous clinical experience point to a survival benefit if CytoSorb therapy is started early <sup>(1 - 4)</sup>
- The guidelines, that are based on sound clinical evidence, should be followed first
- CytoSorb should be started if patients do not respond sufficiently to therapeutic guideline recommendations
- Insufficient therapeutic efficacy of the sepsis bundle is the recommended indication for start of CytoSorb therapy in septic shock

### References

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**Organ dysfunction caused by inflammation is potentially reversible and can be treated, in contrast to irreversible organ cell failure.**

# Cardiac surgery: Postoperative use

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## Signs of successful CytoSorb therapy



- Stabilization of hemodynamic situation
  - Decreasing vasopressor need
  - Stabilization of fluid balance
  - No further increase in lactate level
- Decrease in IL-6 level (if measured) and of WBC, PCT (in case of sepsis), CRP
  - When assessing the course of PCT, be aware of direct, partial PCT removal by CytoSorb
- Stabilization of other organ functions, e.g.
  - No further deterioration in liver function parameters
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# Cardiac surgery: Postoperative use

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## When should the therapy be terminated?



- Treatment should be continued until the clinical condition indicates that systemic hyperinflammation is under control
  - No need for catecholamines or rapidly decreasing dosage
  - Reversal of fluid balance, reduction in edema
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stand-alone therapy

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CytoSorb in  
cardiopulmonary bypass





# 05 |

Set-up:

Short user guide

# Short user guide

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## Notes prior to treatment start

- Preparation and use of CytoSorb must always be carried out under hygienic conditions
- Before connecting CytoSorb the supply tubing system must be completely primed with sterile isotonic saline solution, ensuring there are no air bubbles
- **Under no circumstances must air enter the CytoSorb**
- Always pay attention to the prescribed running direction when installing CytoSorb
- The blood flow rate should be between 150-500 ml/min
- The maximum duration of usage of a CytoSorb adsorber should not exceed 24 hours
- It may be advisable to change the adsorber sooner if there is evidence of exhausted elimination capacity
- Check the extracorporeal circuit at regular intervals for signs of blood clots, the secure fit of the connections and air within the circuit

## Anticoagulation

- Anticoagulation must be effective at treatment start
- In intensive care patients an aPTT of 60 to 80 sec., and when used during heart surgery an ACT of 160 to 210 seconds, is sufficient for CytoSorb. Specifications of the device manufacturer have to be observed
- The aPTT and ACT should be checked regularly during therapy to ensure adequate anticoagulation

### **General materials required:**

- CytoSorb adsorber
- Mounting holder for CytoSorb
- 6 scissor clamps
- Isotonic saline solution with Luer Lock for flushing (2l NaCl 0.9%, sterile)

## Your notes

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06

Set-up:

CytoSorb as  
stand-alone therapy

stand-alone  
therapy

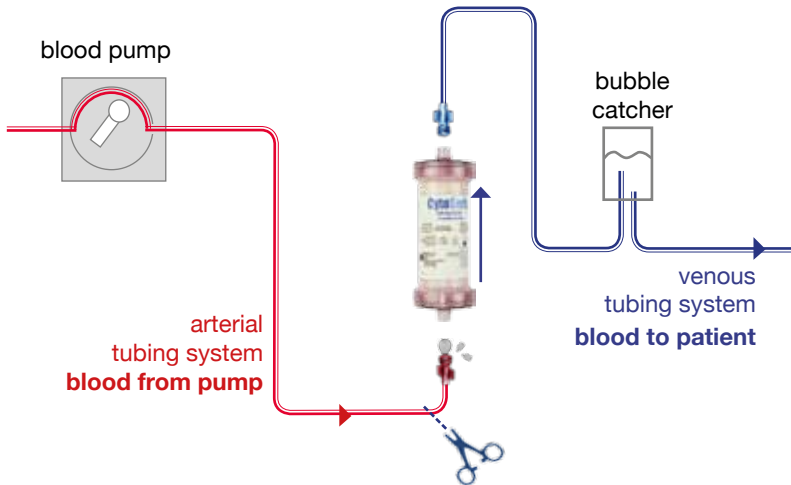
# CytoSorb as stand-alone therapy

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## Set-up

1. Set-up the device according to the manufacturer's instructions (dry)
2. Mount CytoSorb vertically into holder
3. Start blood pump and deaerate **arterial tubing system**
4. Stop blood pump and clamp **arterial tubing system** at **;** by using **scissors clamp**
5. Only remove the port plug on the CytoSorb inlet (**bottom**)
6. Connect CytoSorb bubble-free with **arterial tubing system** (observe flow direction)
7. Now remove the blood outlet port plug (top) and connect CytoSorb with **venous tubing system**
8. Remove scissor clamp from **arterial tubing system**
9. Start blood pump (approx. 100 ml/min) and rinse system with 2 liters of saline solution
10. Remove CytoSorb from the holder and deaerate it by tapping
11. Start patient treatment as prescribed

# Stand-alone set-up



# Your notes

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07

Set-up:

CytoSorb combined with  
renal replacement therapy

# CytoSorb combined with renal replacement therapy

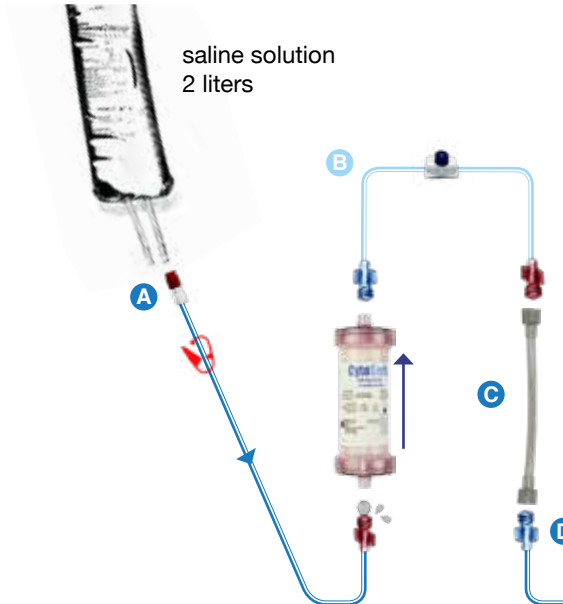
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## Set-up 1 of 2

1. Completely prepare the device according to manufacturer's instructions (incl. flushing). If necessary during ongoing renal replacement therapy first interrupt the treatment (return blood and disconnect patient according to the manufacturer's instructions for each device)
2. Connect saline solution with **A**, **deaerate** and close **red pinch clamp** on **A**
3. Connect **A** bubble-free with CytoSorb blood inlet (bottom) (observe flow direction)
4. Connect CytoSorb blood outlet (top) with **B**, **C**, **D** and **E**
5. Open **red pinch clamp** on **A** and rinse CytoSorb by gravity with 2 liters of saline and deaerate it by tapping
6. Close **red pinch clamp** on **A** and **blue pinch clamp** on **D**

Continued on next page ...

# Set-up before dialyzer



## Additional materials:

### Priming Adapter 1

- A** Red Luer Lock – Red DIN Lock
- C** DIN Lock color neutral –  
DIN Lock color neutral
- D** Blue DIN Lock – Blue Luer Lock
- E** 2 liters disposal bag

### Adapter 1



- B** Blue DIN Lock –  
Red DIN Lock



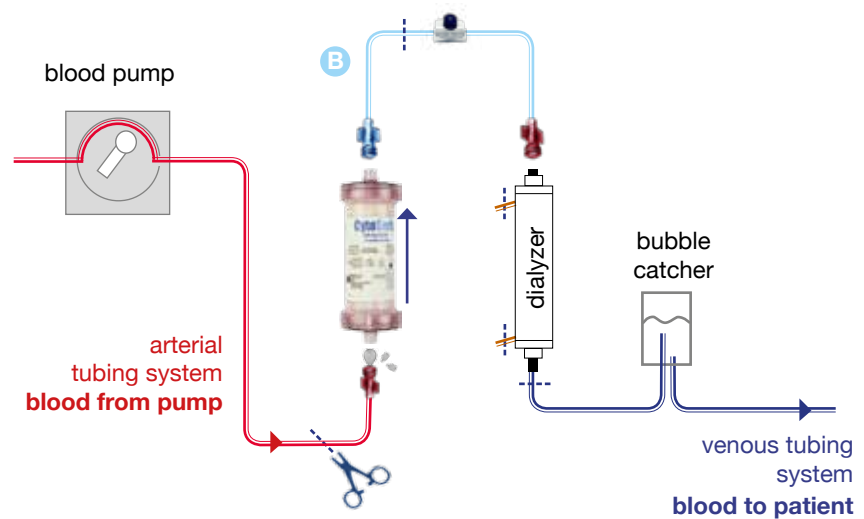
# CytoSorb combined with renal replacement therapy

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## Set-up 2 of 2

7. Stop blood pump
8. Clamp all tubes at the dialyzer at  by use of **scissor clamps**
9. Disconnect **A** from CytoSorb blood inlet (bottom) and discard it
10. Disconnect **arterial blood tube** from dialyzer blood inlet and connect bubble-free with CytoSorb blood inlet (bottom)
11. Disconnect **C** from **B** and discard **C**, **D** and **E**
12. Connect **B** bubble-free with dialyzer blood inlet
13. Remove all **scissor clamps** at  and start blood pump
14. Start patient treatment as prescribed

# Set-up before dialyzer




*possible configuration*

# CytoSorb combined with renal replacement therapy

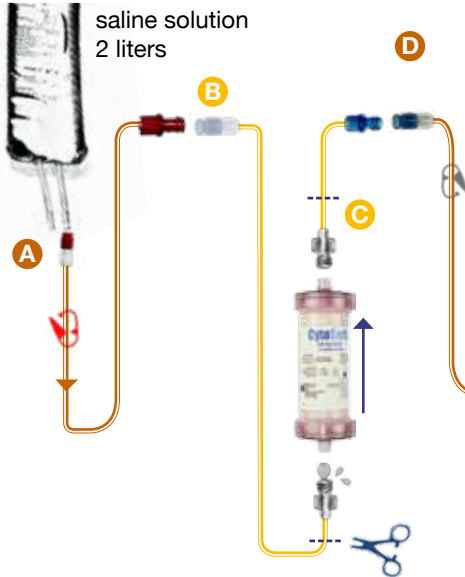
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## Set-up 1 of 2

1. Completely prepare the device according to manufacturer's instructions (incl. flushing). If necessary during ongoing renal replacement therapy first interrupt the treatment (return blood and disconnect patient according to the manufacturer's instructions of each device)
2. Connect saline solution with **A** and **B**, **deaerate** and close **red pinch clamp** on **A**
3. Connect **B** bubble-free with CytoSorb blood inlet (bottom) (observe flow direction)
4. Connect CytoSorb blood outlet (top) with **C**, **D** and **E**
5. Open **red pinch clamp** on **A** and rinse CytoSorb by gravity with 2 liters of saline and deaerate it by tapping
6. Close **red pinch clamp** on **A** and **blue pinch clamp** on **B** .  
Clamp **B** before and **C** after CytoSorb at  by using **scissor clamps**

Continued on next page ...

# Set-up after dialyzer



## Additional materials:

### Priming Adapter 2

- A** Red Luer Lock – Red Luer Lock
- D** Blue Luer Lock – Blue Luer Lock
- E** 2 liters disposal bag

### Adapter 2

- B** Color neutral Luer Lock – Color neutral DIN Lock
- C** Color neutral DIN Lock – Blue Luer Lock

# CytoSorb combined with renal replacement therapy

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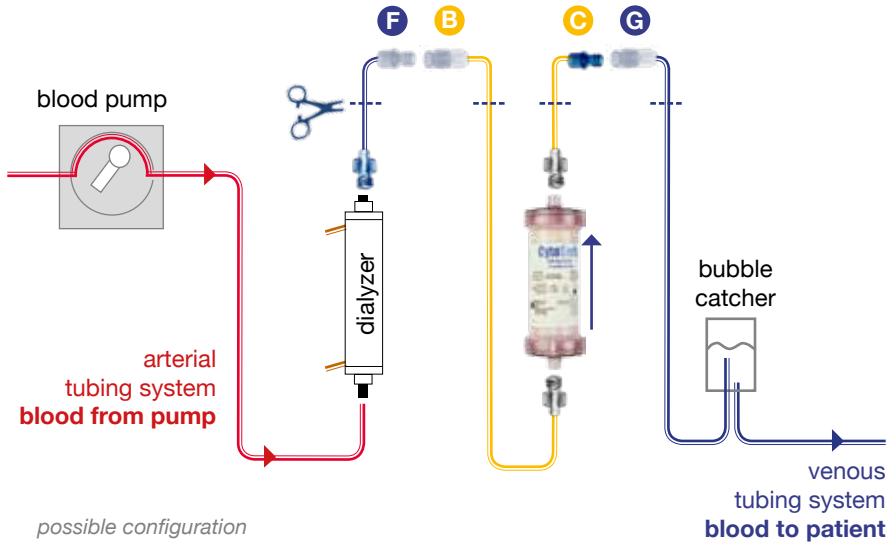
## Set-up 2 of 2

7. Stop blood pump
8. Clamp blood tubes at the dialyzer blood outlet **F** and before the venous bubble catcher **G** at **|** by use of **scissor clamps**
9. Disconnect saline solution and **A** from **B** and discard it
10. Connect **B** with blood tube from dialyzer blood outlet **F**
11. Connect **C** from CytoSorb blood outlet (top) with line to venous bubble catcher **G**
12. Remove all **scissor clamps** at **|** and start blood pump
13. Start patient treatment as prescribed.

**Cave:** If CytoSorb gets integrated after a dialyzer, postdilution in combination with a low blood flow may lead to clotting. Predilution configuration is recommended in this setting.





# Set-up after dialyzer

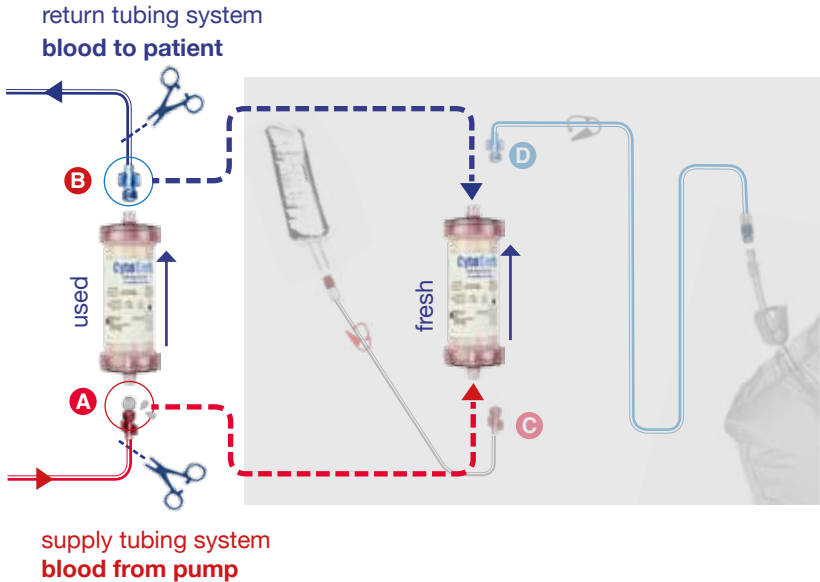


## CytoSorb exchange

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1. Prepare CytoSorb according to instructions for installation before or after dialyzer
2. Interrupt ongoing treatment (return blood and disconnect patient according to manufacturer's instructions for each device)
3. Stop blood pump
4. Clamp blood tubes directly before and after the used CytoSorb by using **scissor clamps** at 
5. Disconnect flushing tube **C** from blood inlet of the fresh CytoSorb (bottom) and discard it
6. Remove the **supply tubing system A** from the blood inlet of the **used** CytoSorb (bottom) and connect it to the blood inlet of the **fresh** CytoSorb (bottom)
7. Close the blood inlet of the used CytoSorb with the port plug of the fresh CytoSorb
8. Disconnect the flushing tube **D** from the blood outlet of the fresh CytoSorb (top) and discard it
9. Disconnect the **return tubing system B** from the used CytoSorb (top) and connect it to the blood outlet of the fresh CytoSorb (top)
10. Close the blood outlet of the used CytoSorb with the port plug of the fresh CytoSorb
11. Remove **scissor clamps** at  and start blood pump
12. Continue patient treatment as prescribed

# CytoSorb exchange



# Your notes

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08

Set-up:

CytoSorb in  
cardiopulmonary bypass

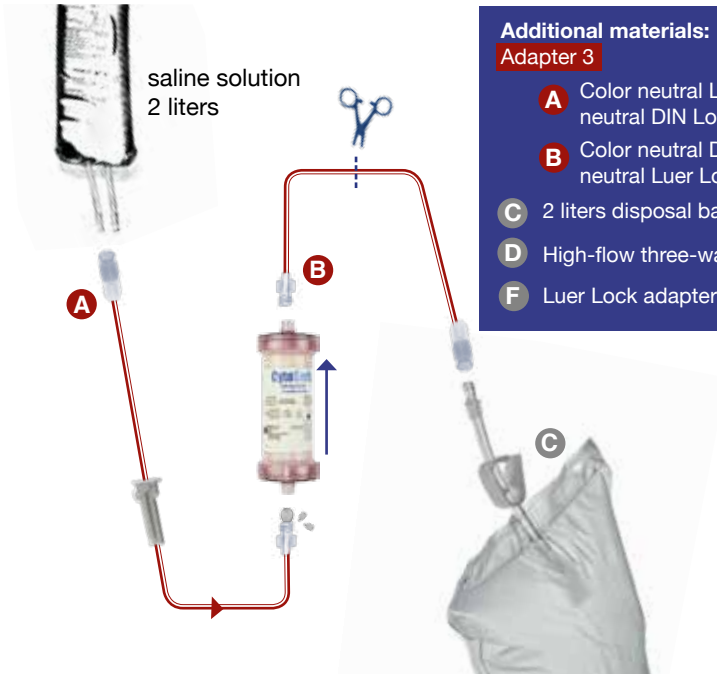
# CytoSorb in cardiopulmonary bypass

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## Set-up 1 of 2

1. Completely prepare the device according to manufacturer's instructions (incl. flushing)
2. Connect saline solution with **A**, **deaerate** and clamp with roller clamp on **A**
3. Connect **A** bubble-free with CytoSorb blood inlet (bottom) (observe flow direction)
4. Connect CytoSorb blood outlet (top) with **B** and **C**
5. Open roller clamp on **A** and and rinse CytoSorb by gravity with 2 liters of saline solution and deaerate it by tapping
6. Close roller clamp on **A**. Clamp line **B** with **scissor clamp** at **⋮**
7. Close pinch clamp on **C**

# CytoSorb in cardiopulmonary bypass



## Additional materials:

### Adapter 3

- A** Color neutral Luer Lock – Color neutral DIN Lock with roller clamp
- B** Color neutral DIN Lock – Color neutral Luer Lock
- C** 2 liters disposal bag
- D** High-flow three-way valve
- F** Luer Lock adapter for main tubing

# CytoSorb in cardiopulmonary bypass

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## Set-up 2 of 2

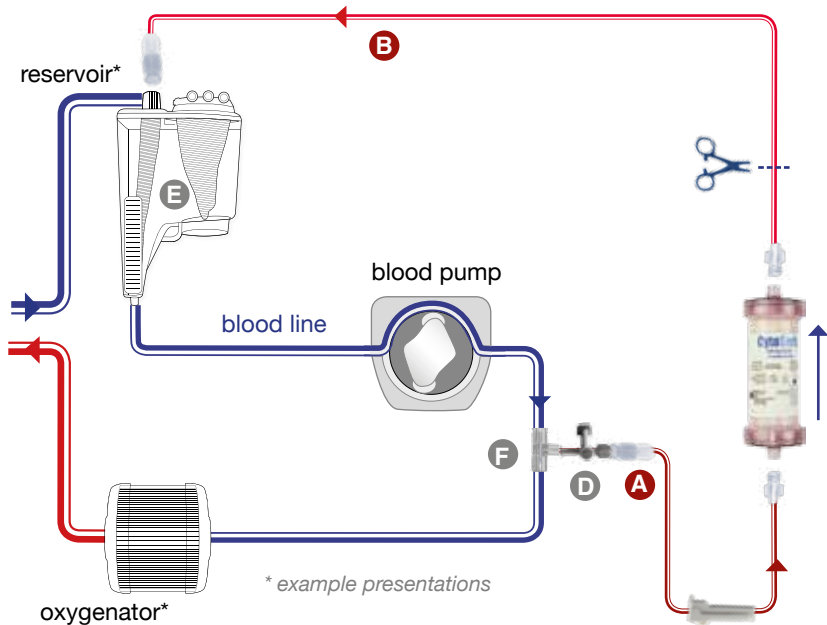
- Vertically install CytoSorb at the heart-lung-machine by using the holder
- Disconnect **A** from the saline bag and connect it bubble-free to a Luer Lock **D** on the **blood line** after the pump by use of a three-way high flow valve **F**
- Connect **B** via a Luer Lock connection to the reservoir **E**
- If necessary, regulate the flow via roller clamp on **A**

## NOTES

- For safety reasons, the installation of CytoSorb in cardiopulmonary bypass is always carried out via a Luer Lock branch between the pump and oxygenator, forming a reflux to the reservoir
- Due to the diameter of the Luer Lock connection the blood flow through CytoSorb is limited to 400 to 500 ml/min
- In order to avoid clotting, continuous blood flow has to be ensured after start of the CytoSorb therapy



# CytoSorb in cardiopulmonary bypass



# Your notes

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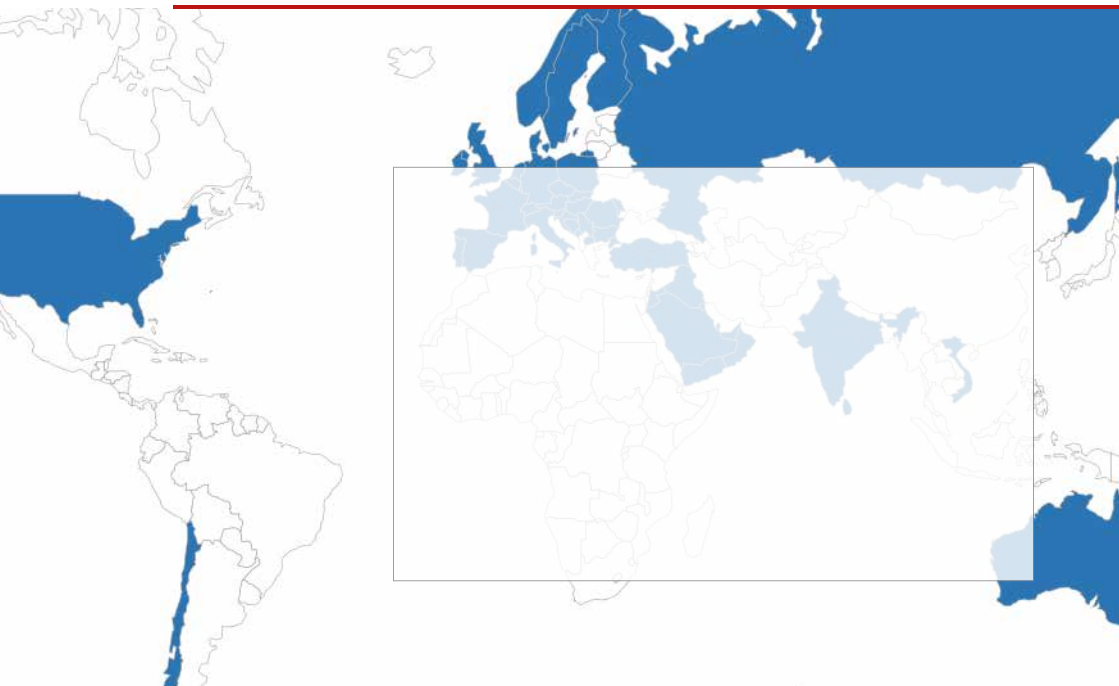
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## Your local CytoSorbents contact

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## SIRS and Sepsis

## REGAIN CONTROL



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