



ANTE  
Associazione Nazionale Tecnici Emodialisi



# Abbinamento emoadsorbimento + emodialisi (HA-HD): una nuova opportunità da esplorare? In quali pazienti?

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# Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention

Ron T Gansevoort, Ricardo Correa-Rotter, Brenda R Hemmelgarn, Tazeen H Jafar, Hidde J Lambers Heerspink, Johannes F Mann, Kunihiro Matsushita, Chi Pang Wen

www.thelancet.com Vol 382 July 27, 2013

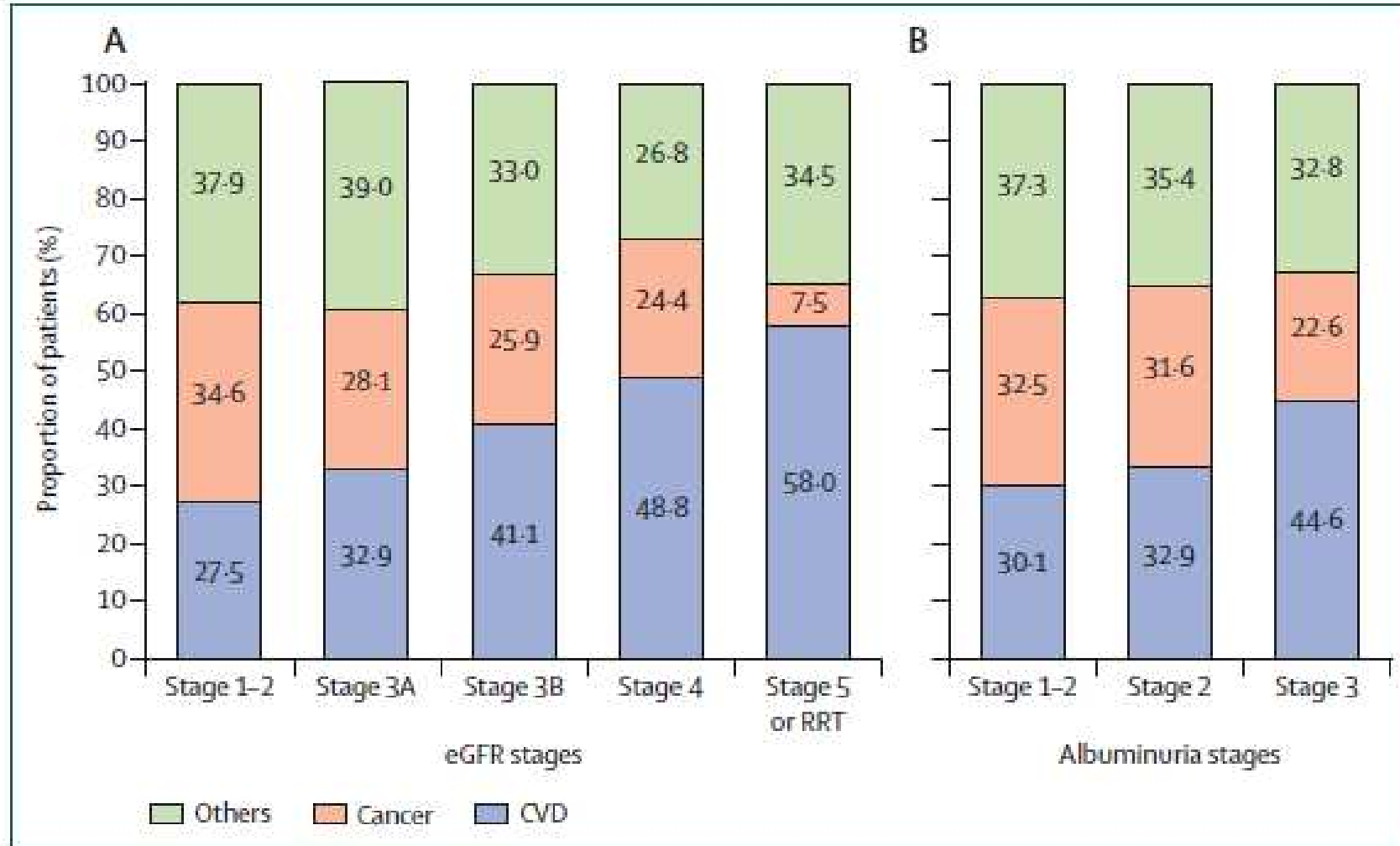
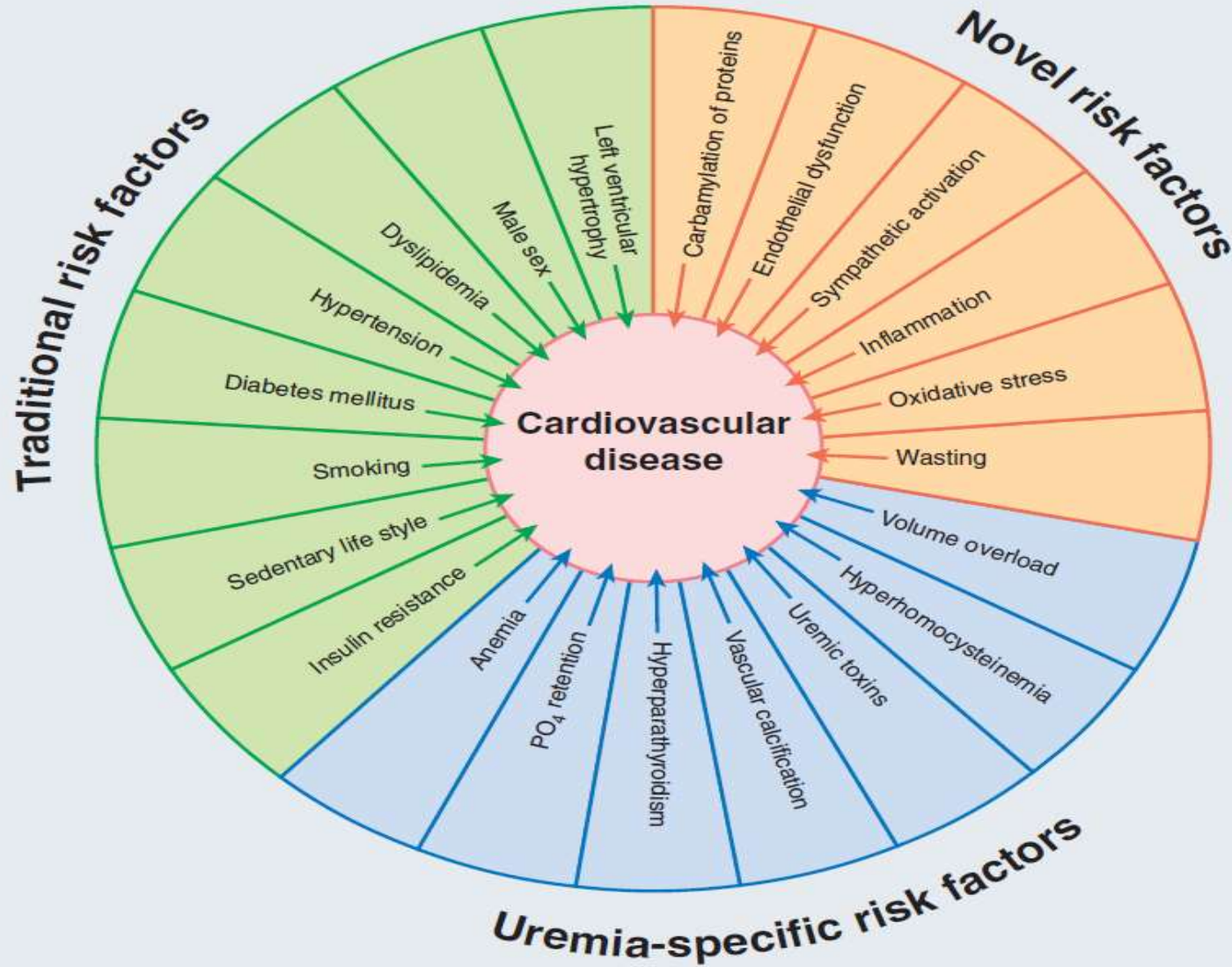
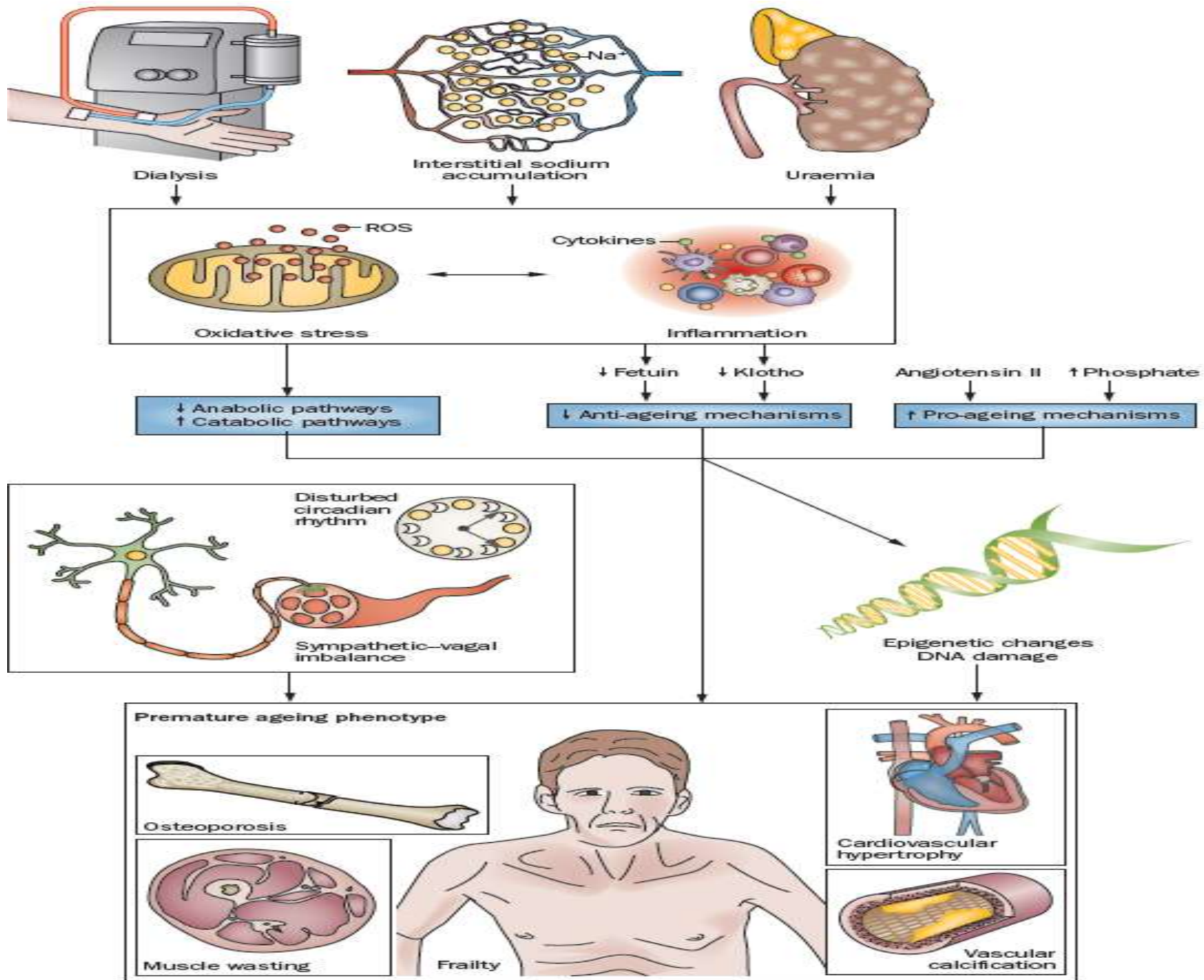


Figure 3: Causes of death per chronic kidney disease stage (Canadian data)

# Risk Factors in Chronic Kidney Disease





**Box 1 | Aetiologies of uraemic ageing**

Increased allostatic load

- Persistent inflammation
- Oxidative stress
- Increased carbonylation and glycation of proteins
- Sympathetic-vagal imbalance

Pro-ageing factors

- Hyperphosphataemia
- Angiotensin II activation
- Sodium accumulation

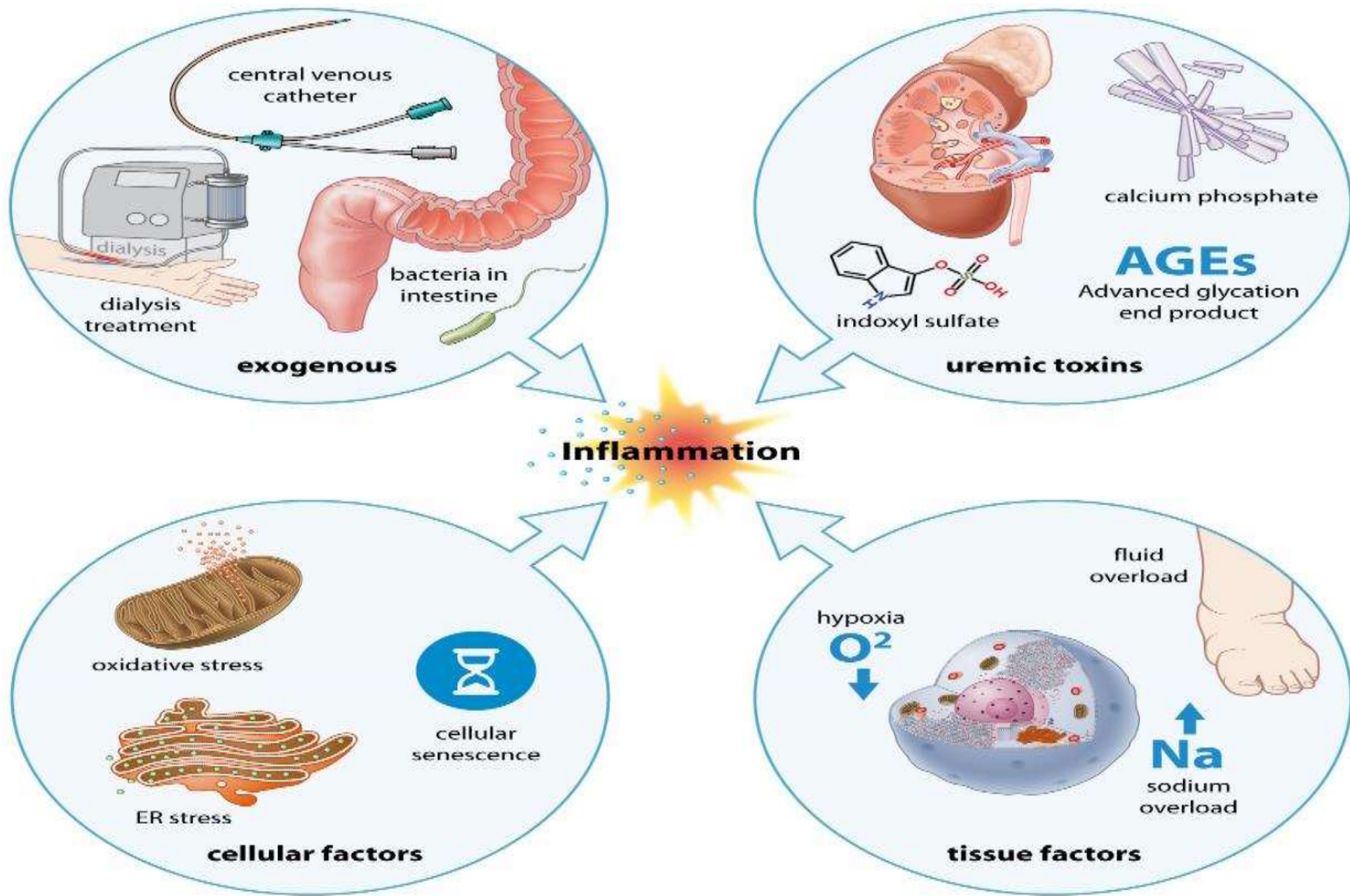
Defective anti-ageing mechanisms

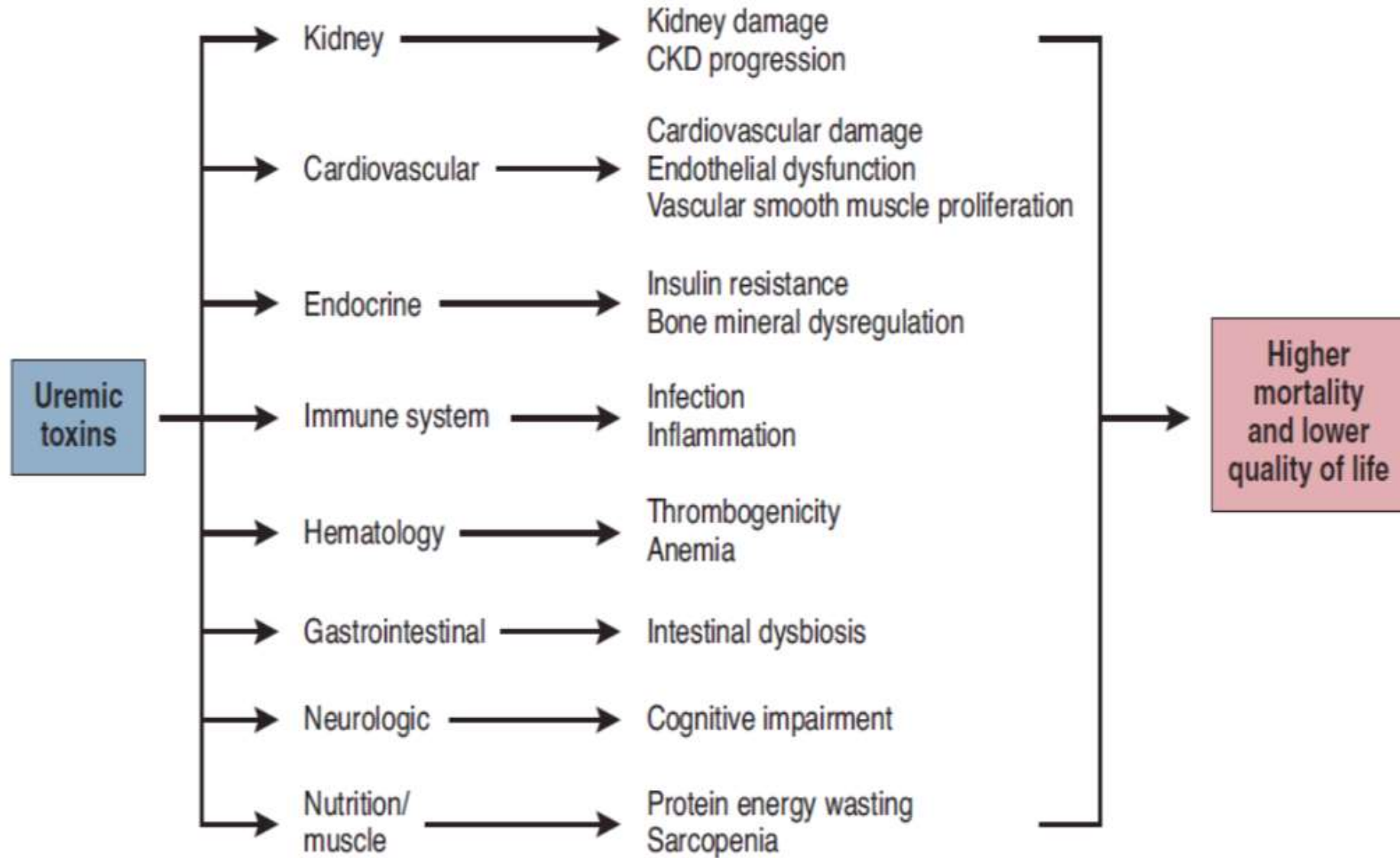
- Klotho deficiency
- Vitamin D deficiency
- Hypogonadism
- Nuclear lamina defects

Use of drugs such as steroids

## Chronic kidney disease and premature ageing

Jeroen P. Kooman, Peter Kotanko, Annemie M. W. J. Schols, Paul G. Shiels and Peter Stenvinkel





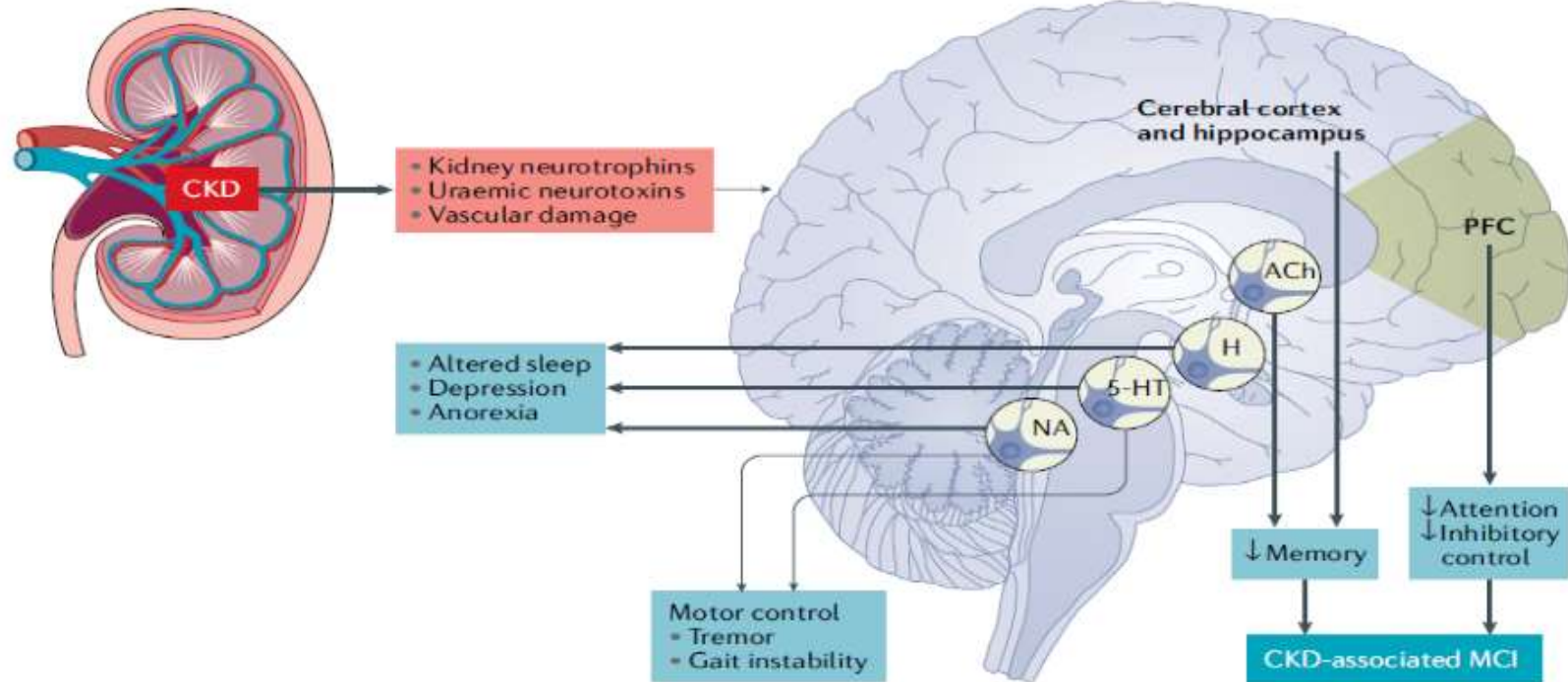
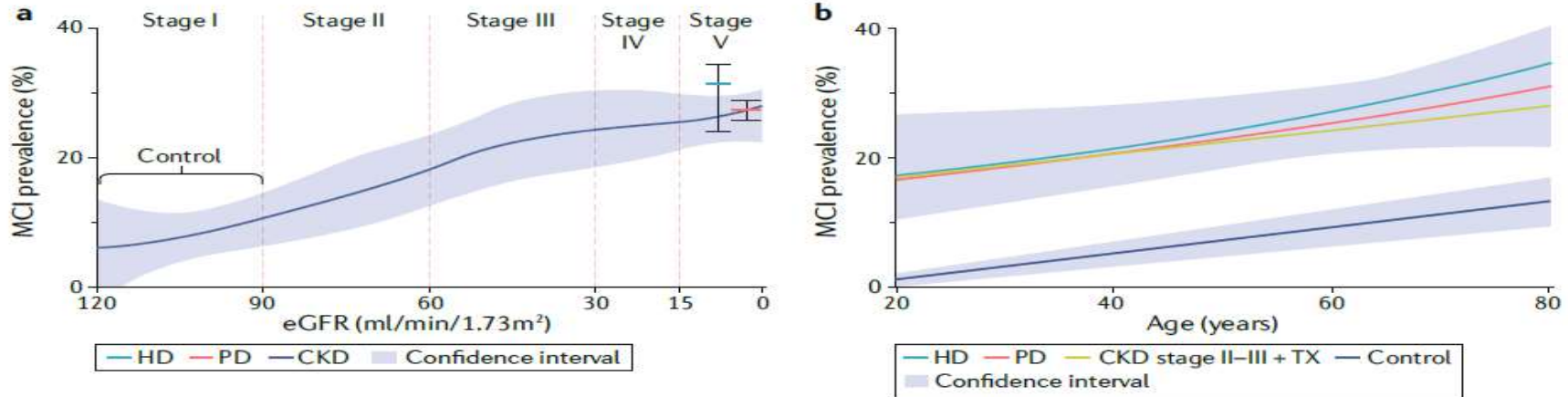
**Classification of Uremic Toxins and Their Role in Kidney Failure**

*CJASN* 16: 1918–1928, 2021.

*Matthiel M, Rosner, Thiago Reis, Faeg Mustafa-Syed, Raymond Vanholder, Colin Hutchison, Peter Steenvinkel, Peter L. Mankeslajn, Mario Cuzzocani, Laurent Juliant, Koushik Kashant, Manish Kaushik, Hiroki Kawasaki, Ziad Massy, Tammy Lisa Siech, Ji Zhai, and Claudio Ronco*

# Mechanisms of cognitive dysfunction in CKD

Davide Viggiano<sup>1,2,3</sup>, Carsten A. Wagner<sup>3,4</sup>, Gianvito Martino<sup>5\*</sup>, Maiken Nedergaard<sup>6</sup>,  
Carmine Zoccali<sup>8</sup>, Robert Unwin<sup>7,8,9</sup> and Giovambattista Capasso<sup>1,2,9,10</sup>



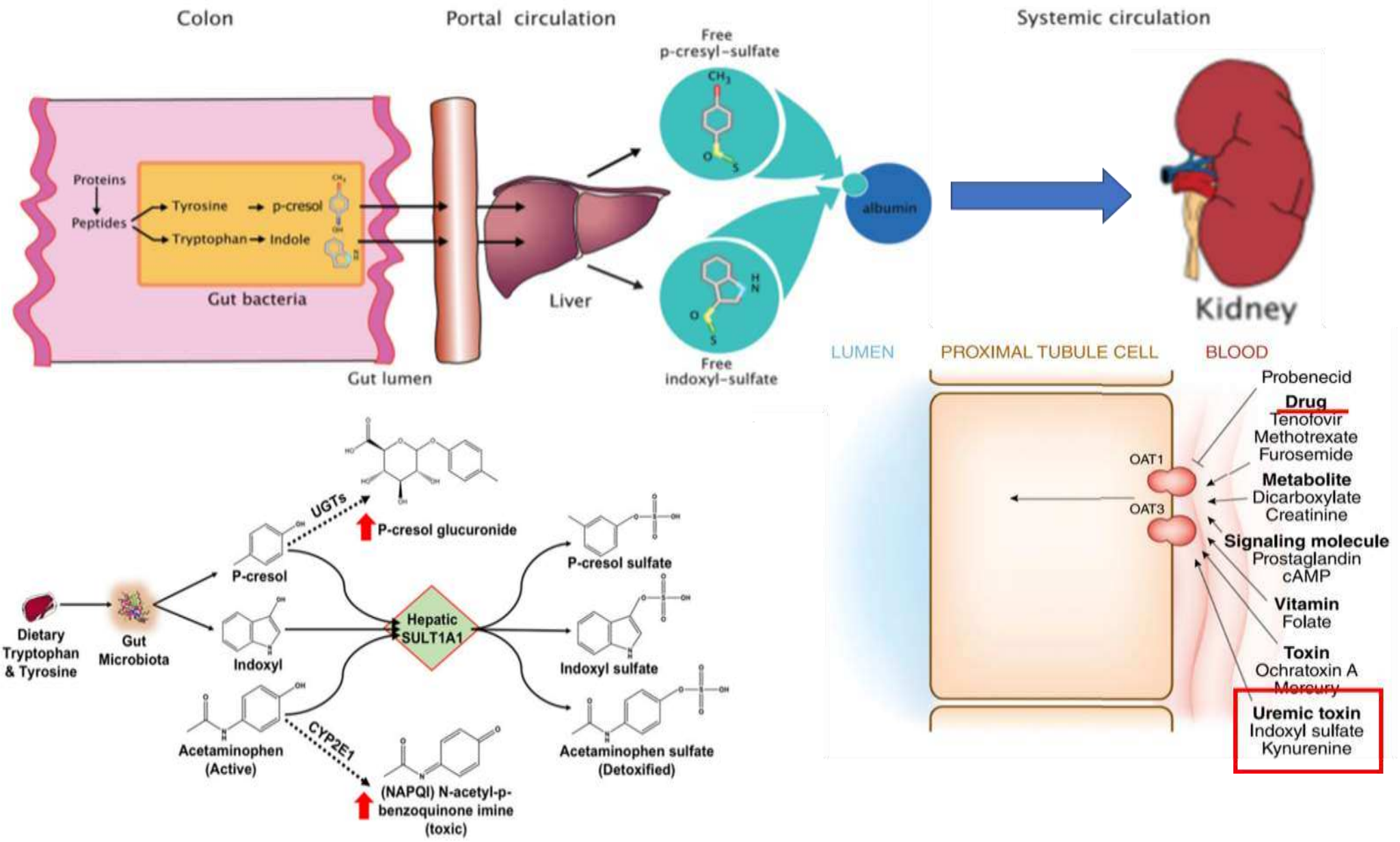
Review on uremic toxins: Classification, concentration, and interindividual variability

*Kidney International, Vol. 63 (2003), pp. 1934-1943*

KAYMOND VANHOLDER, RITA DE SMET, GRIET GLOREUX, ANGEL ARGILÉS, ULRICH BAURMEISTER, PHILIPPE BRUNET, WILLIAM CLARK, GERALD COHEN, PETER PAUL DE DEYN, REINHOLD DEPPISCH, BEATRICE DESCAMPS-LATSCHA, THOMAS HENLE, ACHIM JORRES, HORST DIETER LENKE, ZIAD A. MASSY, JUTTA PASSLICK-DEETJES, MARIANO RODRIGUEZ, BERND STEGMAYR, PETER SUENVINKEL, CIRO TETTA, CHRISTOPH WASSER, and WALTER ZIDEK, For the EUROPEAN UREMIC TOXIN WORK GROUP (EUTOX)

<i>Small water-soluble solutes</i>	< 500 Da	<i>Protein-bound solutes</i>	variable	<i>Middle molecules</i>	500-15000 Da
asymmetric dimethylarginine		3-deoxyglucosone		$\beta_2$ -microglobulin	
benzylalcohol		CMPF		$\beta$ -endorphin	
creatinine		fructoselysine		clara cell protein	
guanidine		glyoxal		complement factor D	
guanidinoacetic acid		hippuric acid		cystatin C	
guanidinosuccinic acid		homocysteine		degranulation inhibiting protein I	
hypoxanthine		indole-3-acetic acid		endothelin	
methylguanidine		indoxyl sulfate		hyaluronic acid	
myoinositol		methylglyoxal		interleukin 1 $\beta$	
orotic acid		N-carboxymethyllysine		interleukin 6	
orotidine		p-cresol		$\kappa$ -Ig light chain	
oxalate		pentosidine		$\lambda$ -Ig light chain	
pseudouridine		phenol		leptin	
symmetric dimethylarginine		p-OH-hippuric acid		methionine-enkephalin	
urea		quinolinic acid		parathyroid hormone	
uric acid		spermidine		retinol binding protein	
xanthine		spermine		tumor necrosis factor $\alpha$	



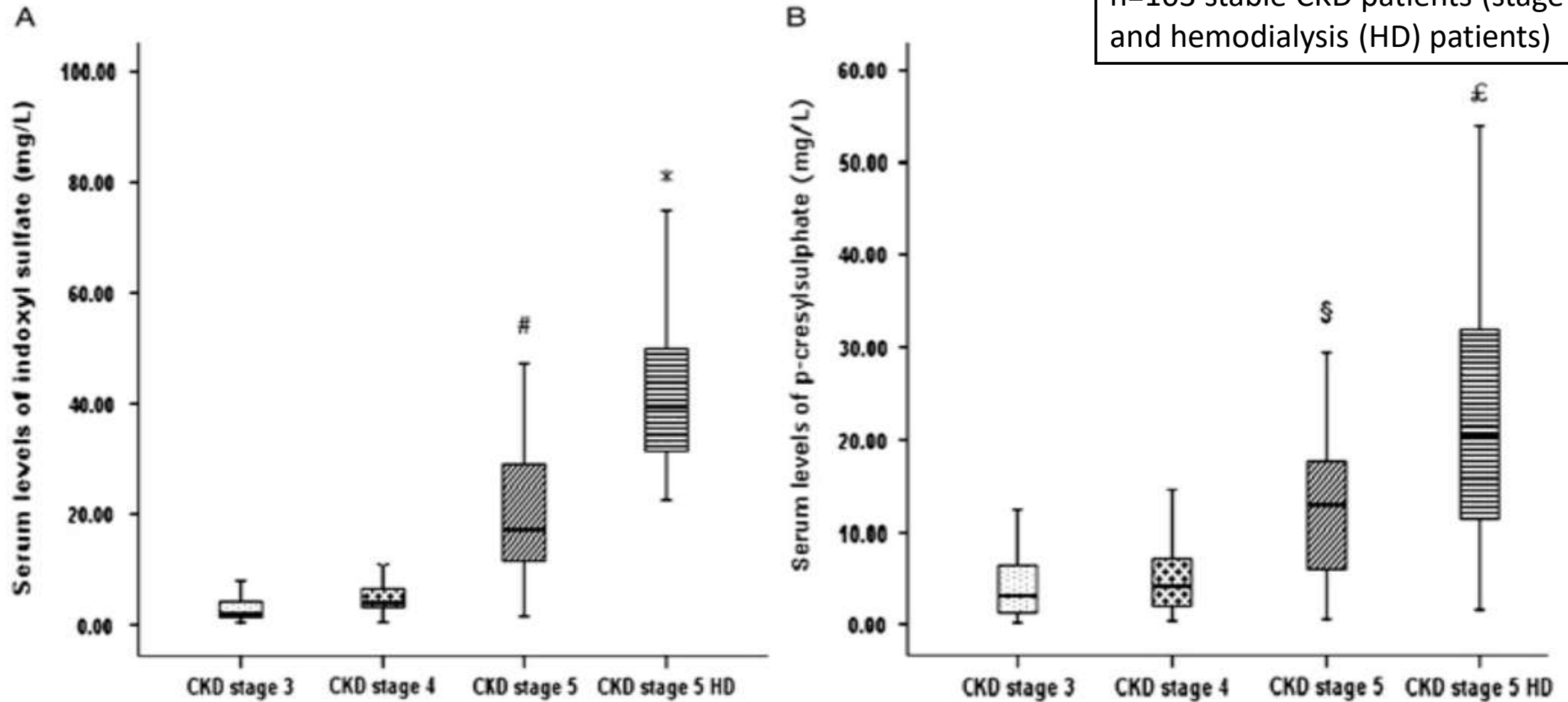


**Microbiota-Derived Uremic Retention Solutes: Perpetrators of Altered Nonrenal Drug Clearance in Kidney Disease**  
*Expert Rev Clin Pharmacol.* 2018 January ; 11(1): 71-82.

# PBUTs levels and CKD

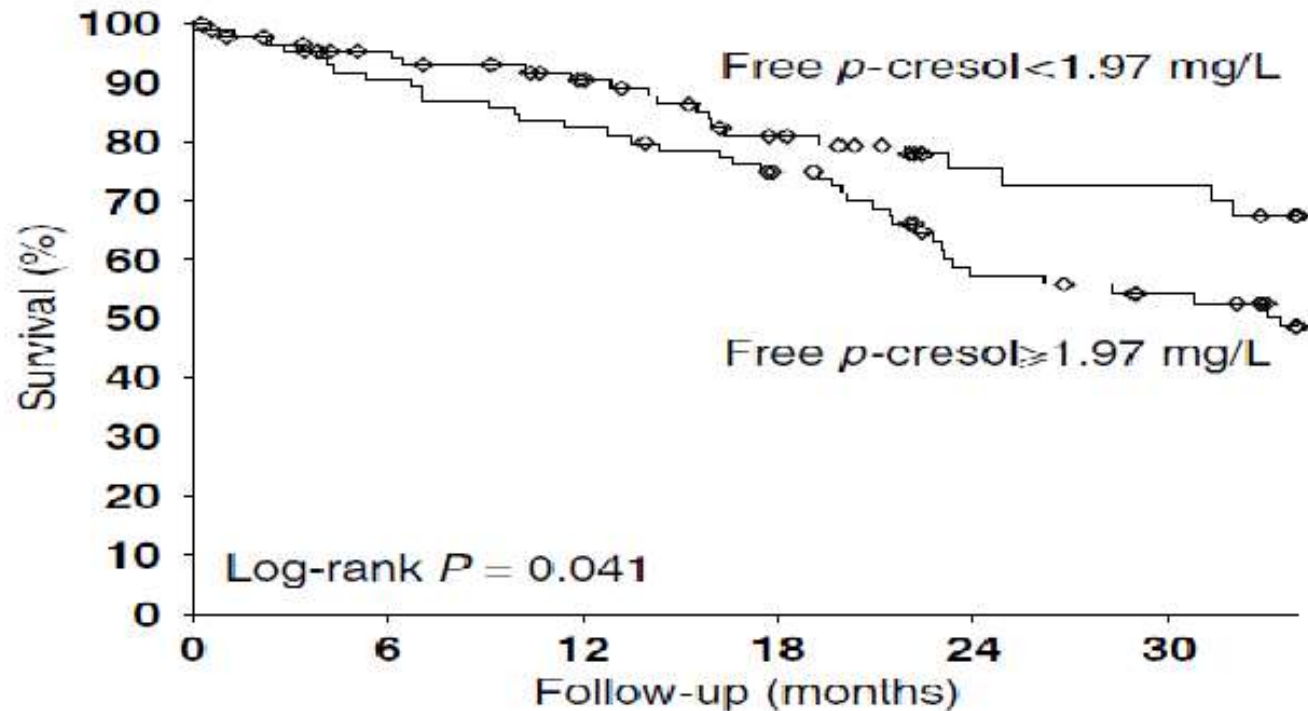
## *p*-Cresylsulfate and Indoxyl Sulfate Level at Different Stages of Chronic Kidney Disease

n=103 stable CKD patients (stage 3–5 and hemodialysis (HD) patients)



# PBUTs: why so dangerous?

...because they are associated mortality...

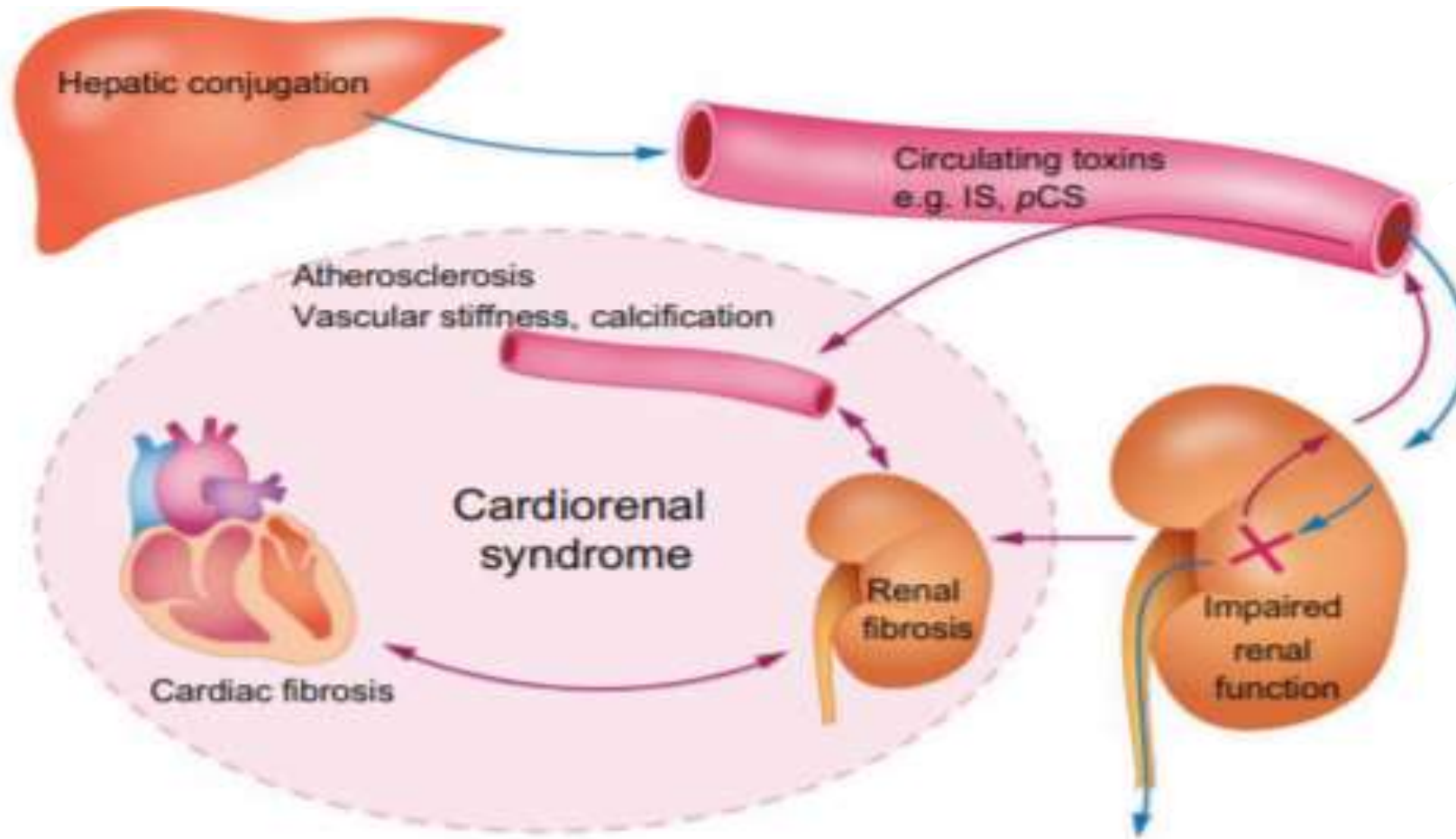


n=175 patients with stage 5D chronic kidney  
Follow-up: 36 months  
Two Belgian HD center

In conclusion, our data suggest for the first time that free serum levels of the protein-bound uremic retention solute *p*-cresol are associated with mortality in patients treated with HD.

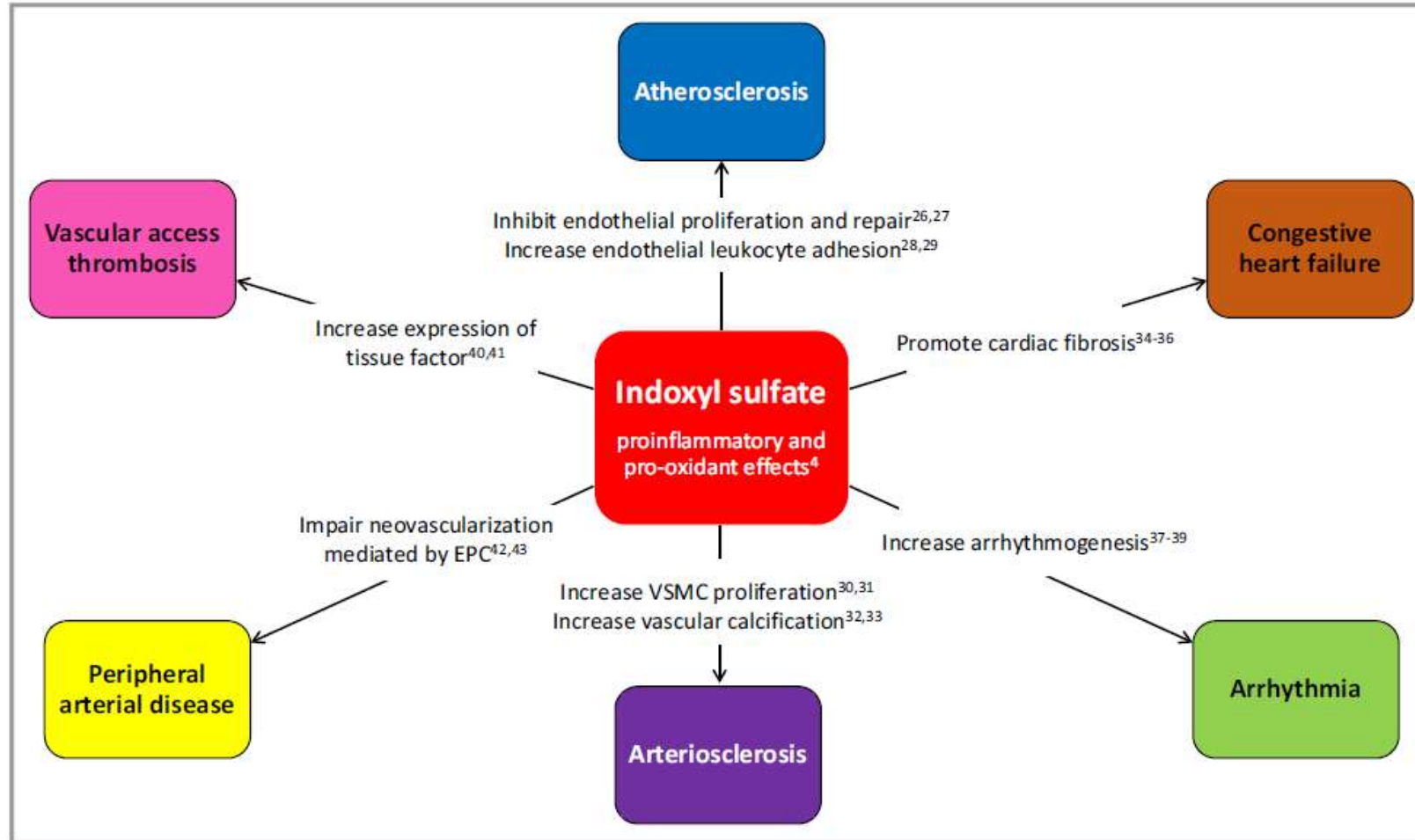
# PBUTs: why so dangerous?

...because they are the "missing link" with  
cardiorenal syndrome...



# PBUTs: why so dangerous?

... because they are associated mortality.....



**Figure 1.** Role of indoxyl sulfate in the pathogenesis of various forms of cardiovascular disease in chronic kidney disease. EPC indicates endothelial progenitor cell; VSMC, vascular smooth muscle cell.

# PBUTs: why so dangerous?

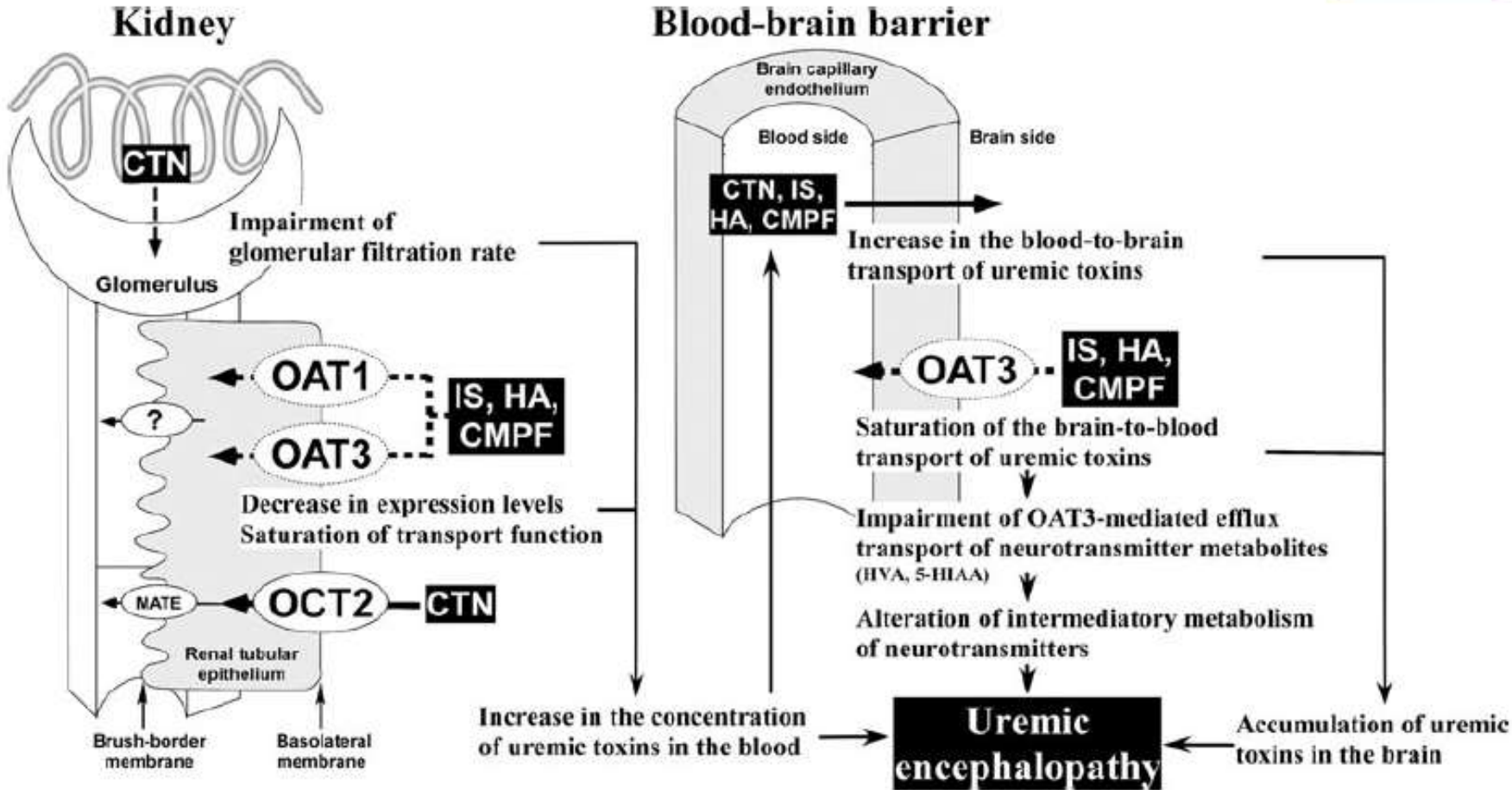
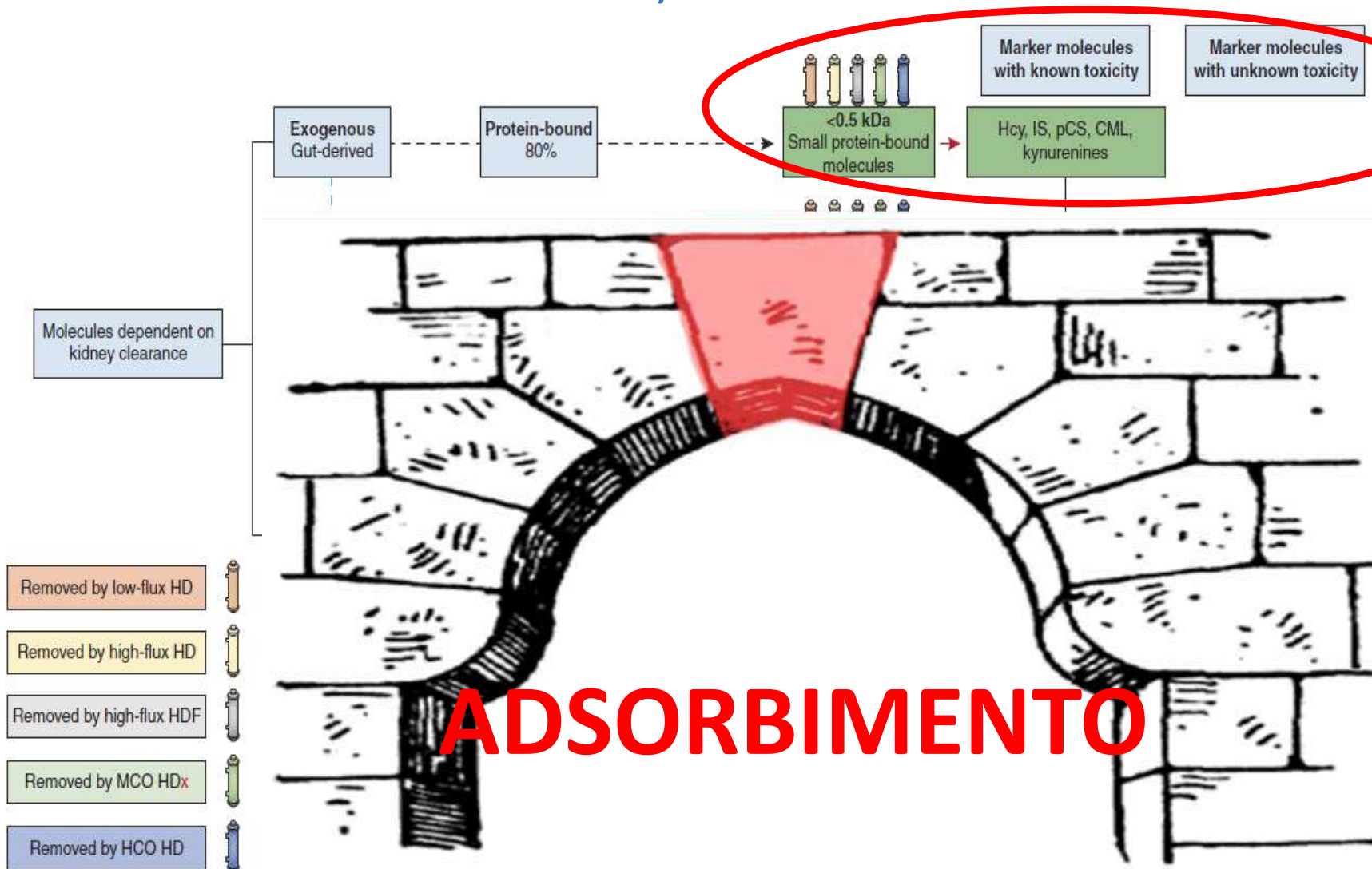


Fig. 5 Putative mechanisms of uremic encephalopathy with regard to dysfunction of organic anion transporters (OATs) caused by uremic toxins.

Roles of organic anion/cation transporters at the blood-brain and blood-cerebrospinal fluid barriers involving uremic toxins

# PBUTs: why so dangerous?

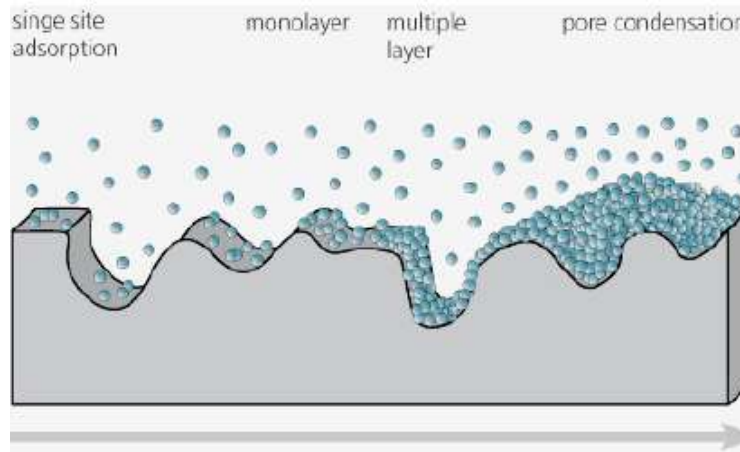
...because they are poorly filtrated by dialysis membranes ...



**ADSORBIMENTO**

# L'adsorbimento è un fenomeno di superficie

Processo chimico per cui un elemento (soluto) aderisce ad un altro elemento (adsorbente) con una struttura molecolare adeguata ad essere complementare al soluto.



La specificità dell'adsorbimento è il risultato di diversi gradi di affinità tra le molecole ed il materiale sorbente.



# L'adsorbimento è un fenomeno di superficie

## Blood-Membrane Interactions During Dialysis

Zhongping Huang,\* Dayong Gao,† Jeffrey J. Letteri,‡ and William R. Clark†§  
 \*Department of Mechanical Engineering, Widener University, Chester, Pennsylvania, †Department of Biomedical Engineering, University of Washington, Seattle, Washington, ‡Gambro Renal Products, Lakewood, Colorado, and §Nephrology Division, Indiana University School of Medicine, Indianapolis, Indiana  
 Seminars in Dialysis—Vol 22, No 6 (November–December) 2009 pp. 623–628

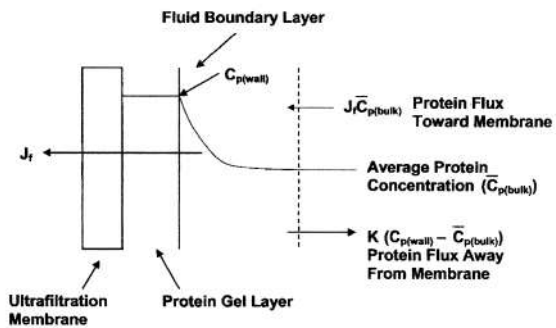
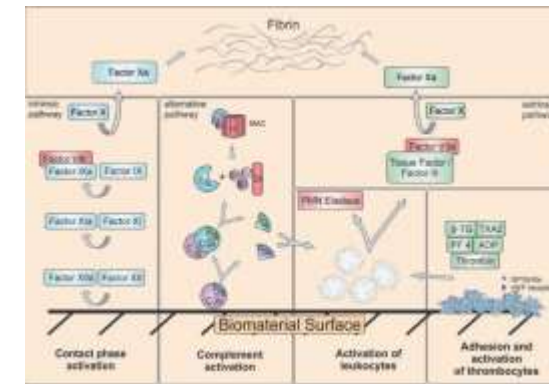
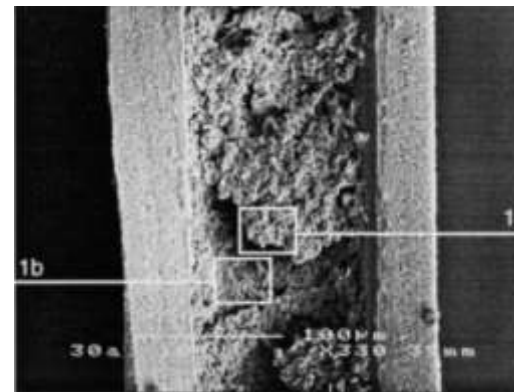


FIG. 3. Depiction of the phenomena of secondary membrane formation and concentration polarization during hemofiltration. In the figure,  $J$  represents fluid flux while  $C$  represents protein concentration. Reprinted with permission from Clark et al. (47).

Protein layer

Exposure of blood to artificial membrane surfaces almost immediately leads to the adsorption of plasma proteins. The initial adsorption influences all subsequent events and determines the thrombogenicity and biocompatibility of the material.



membrane permeability

thrombogenicity

Time-dependent loss of efficiency

# L'adsorbimento è un fenomeno di superficie

.....si dice che una membrana è adsorbente quando le sue proprietà di adsorbimento possono essere considerate come un reale metodo di depurazione...

There are two steps of plasma protein membrane adsorption:

- 1) the first occurs **on the membrane surface** as a result of preferential competitive adsorption of **high molecular weight proteins**, such as albumin, fibrinogen/fibrin, immunoglobulins. **This process has no relevant effect on their plasma concentrations.**
- 2) the second adsorption is **in the body of the membrane** of proteins with **low- and medium-molecular weights** (such as  $\beta_2$ microglobulin). This is slower, depends on membrane structure and thickness, and **can be quantitatively important, contributing to relevant decreases in plasma concentrations.**

## Haemodialysis membranes

Claudio Ronco<sup>1</sup> and William R. Clark<sup>2\*</sup>

NATURE REVIEWS | NEPHROLOGY

VOLUME 14 | JUNE 2018 | 395

# L'adsorbimento in emodialisi

## MEMBRANE



## HFR



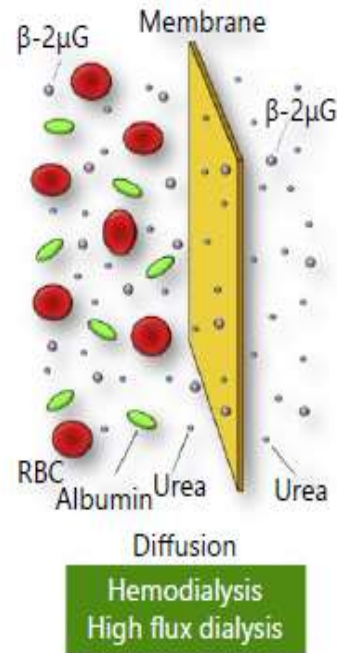
## DEVICES



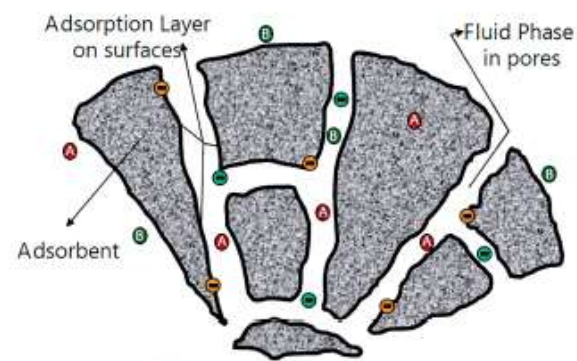
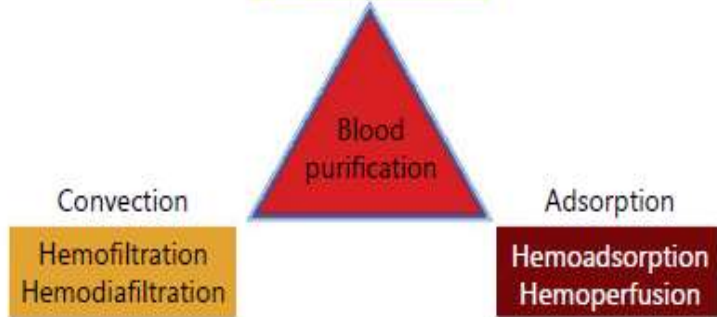
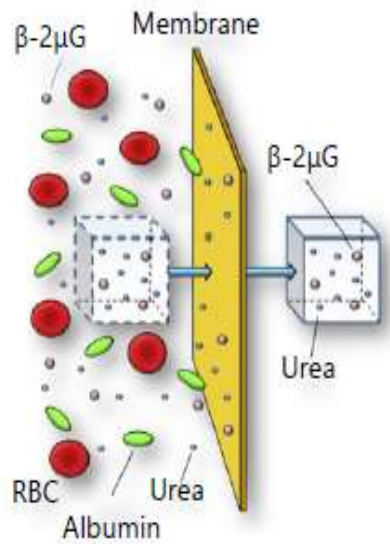
## The Promise of Adsorption for Chronic Dialysis Patients

Claudio Ronco<sup>a,b</sup>

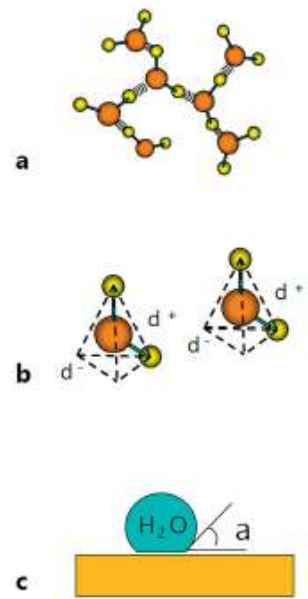
<sup>a</sup>Director of International Renal Research Institute of Vicenza and IRRV Foundation at San Bortolo Hospital, Vicenza, Italy; <sup>b</sup>Department of Medicine, University of Padova, Padova, Italy



Adsorption is a mass separation process by a solid agent, it differs significantly from the classic mechanisms of convection and diffusion based on separation by a barrier (dialysis membrane). This modality of solute removal goes beyond membrane characteristics and permeability.



- Co-ions
  - Matrix with fixed charges
  - Counterions
- Binding mechanisms:  
A) Van der Waals forces  
B) ionic bonds  
C) hydrophobic bonds



# L'adsorbimento è un fenomeno di superficie

	Example	Sorption principle	Substances bound
Activated charcoal		Van der Waals Hydrophobic Interactions	Creatinine Beta2 microglobulin PBUT
Non-ionic organic polymer	Resins	Van der Waals Hydrophobic	PBUT Cytokines
Organic ion exchanger	Resins	Ionic bonds	Ions
Crystalline ion exchanger	Zirconium FeOOH	Ionic bonds	Ions
Specific binders	Ninhydrin	Covalent bonds	Urea

Pores are divided based on their inlet size:

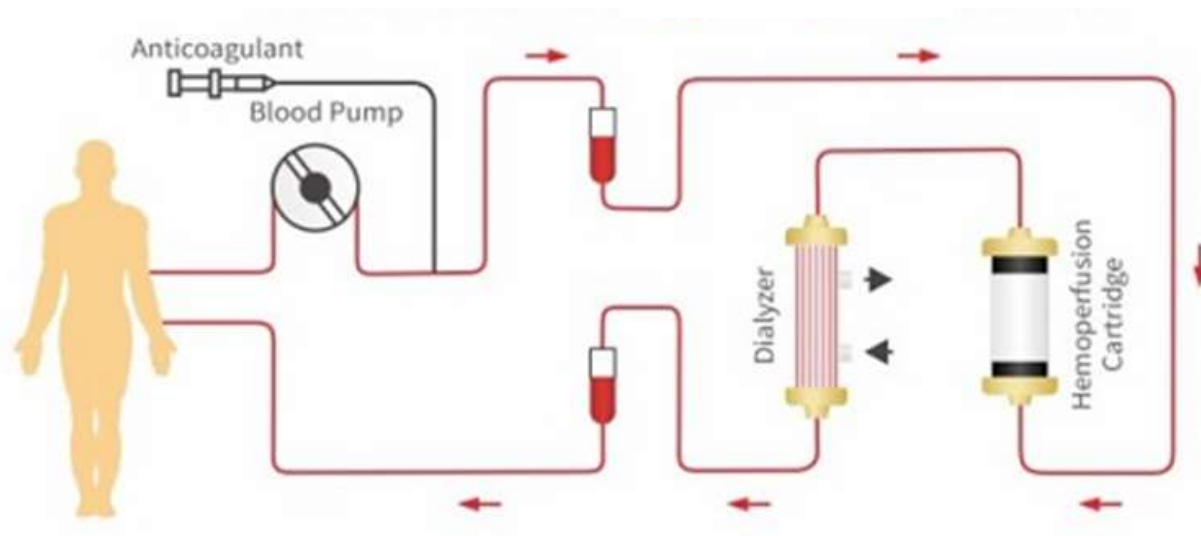
- micropores (< 2 nm)
- mesopores (2-50 nm)
- macropores (> 50 nm)



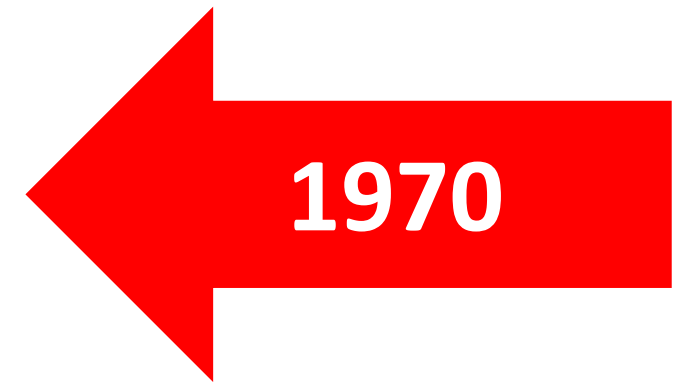
**For removal of uremic toxins without albumin removal,  
mesopores appear the most relevant**

**Adsorption is limited by saturation of the sorbents.**

# Emoadsorbimento + Emodialisi (HA-HD)



The "*new*" concept of sorbent in hemodialysis....



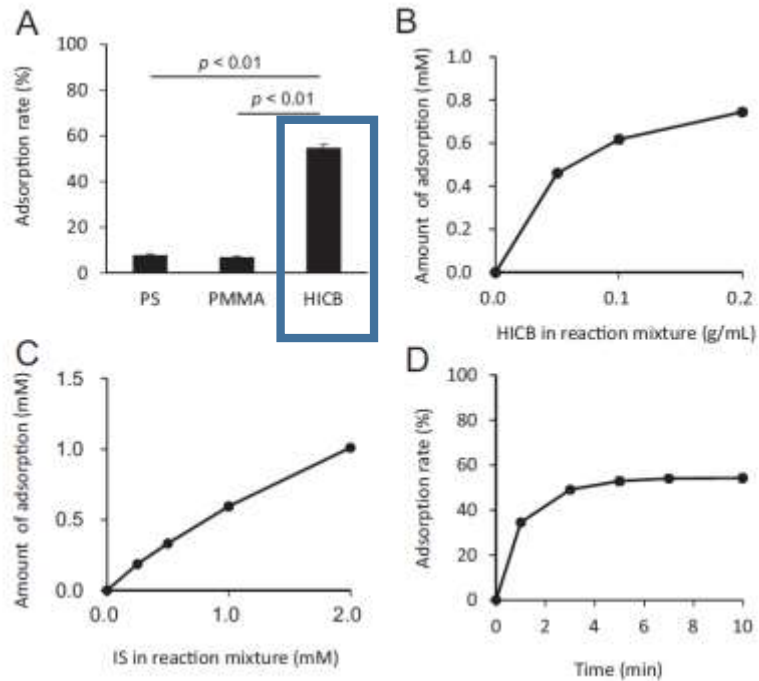
# The "new" concept of sorbent in hemodialysis....

## Adsorption of Protein-Bound Uremic Toxins Through Direct Hemoperfusion With Hexadecyl-Immobilized Cellulose Beads in Patients Undergoing Hemodialysis

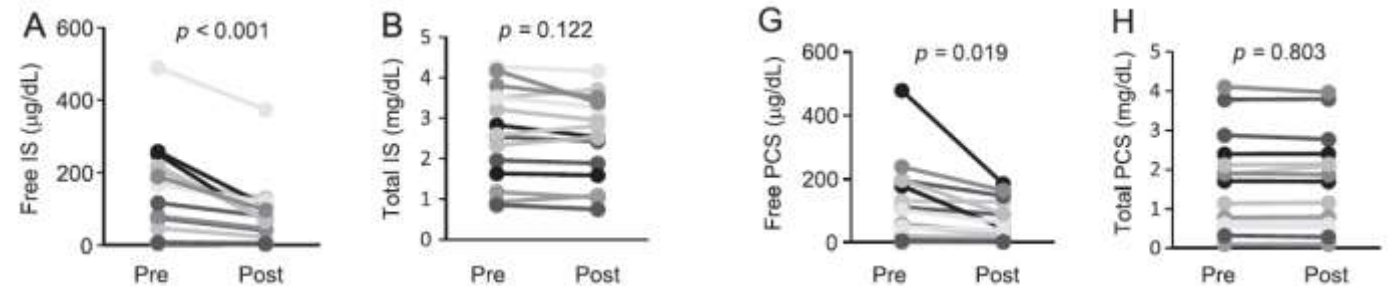
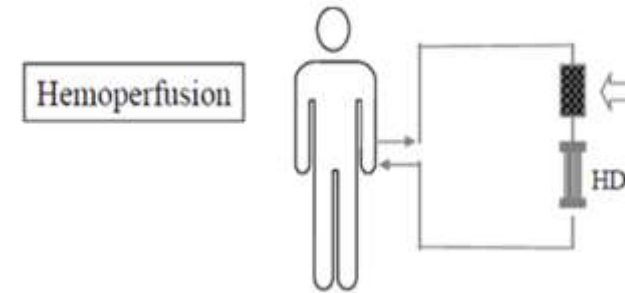
*Artificial Organs* 2018, 42(1):88–93

\*†Suguru Yamamoto, \*Mami Sato, \*Yoko Sato, \*Takuya Wakamatsu, \*Yoshimitsu Takahashi, ‡Akira Iguchi, §Kentarō Omori, ‡Yasushi Suzuki, ¶Isei Ei, \*Yoshikatsu Kaneko, \*Shin Goto, ||Junichiro J. Kazama, \*#Fumitake Gejyo, and \*Ichiei Narita

### Adsorption of IS in vitro



### Adsorption of PBUTs in vivo



In clinical studies, passing the adsorber column decreased the serum level of free IS and PCS significantly, but not protein-bound IS and PCS.



# The "new" concept of sorbent in hemodialysis....

Article

## Efficacy of Divinylbenzenic Resin in Removing Indoxyl Sulfate and P-cresol Sulfate in Hemodialysis Patients: Results from an In Vitro Study and an In Vivo Pilot Trial (xuanro4-Nature 3.2)

Maria Teresa Rocchetti <sup>1,†,\*</sup>, Carmela Cosola <sup>1,†,\*</sup>, Ighli di Bari <sup>1</sup>, Stefania Magnani <sup>2</sup>, Vanessa Galleggiante <sup>2</sup>, Letizia Scandiffo <sup>2</sup>, Giuseppe Dalfino <sup>1</sup>, Giuseppe Stefano Netti <sup>1,‡</sup>, Mauro Atti <sup>2</sup>, Roberto Corciulo <sup>1</sup> and Loreto Gesualdo <sup>1,\*</sup>

Toxins 2020, 12, 170; doi:10.3390/toxins12030170

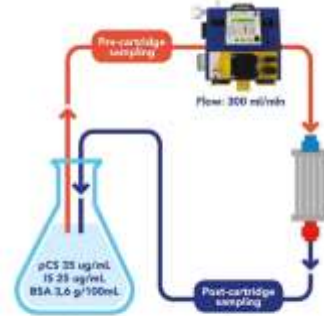


Figure 1. In vitro experiment. Recirculation of an experimental solution in a disc-shaped resin containing the resin sorbent to be tested. Solution samples to be tested, solution samples to be tested were collected after passing through the resin after 1, 3, and 6 hours.

### Uremic Toxins Removal - %Reduction Rate

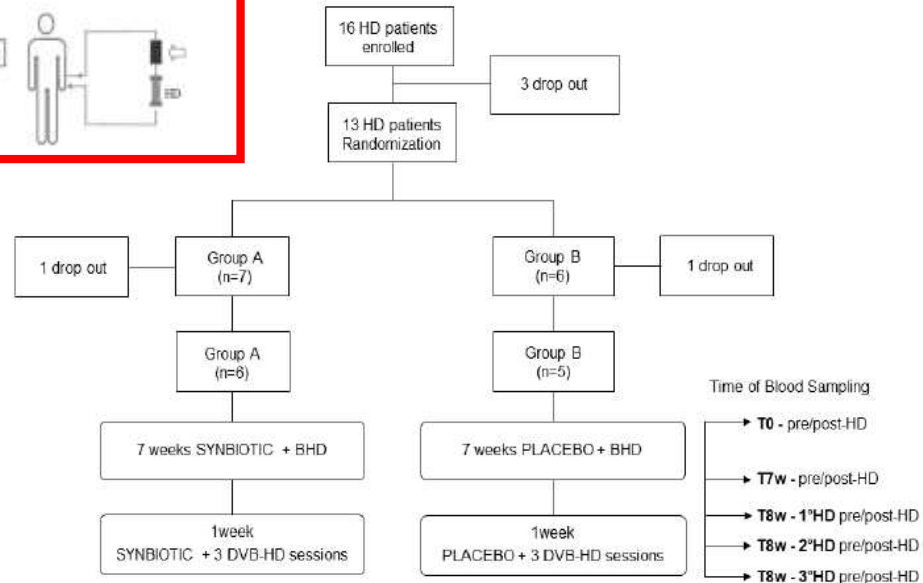
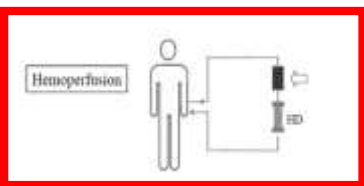
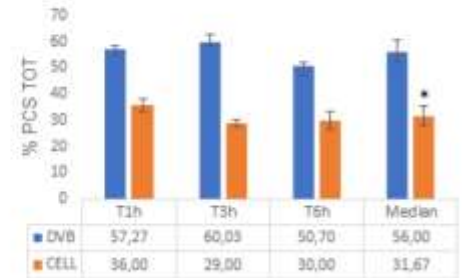
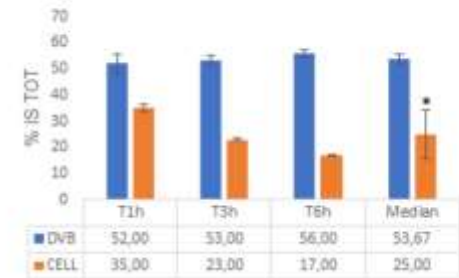
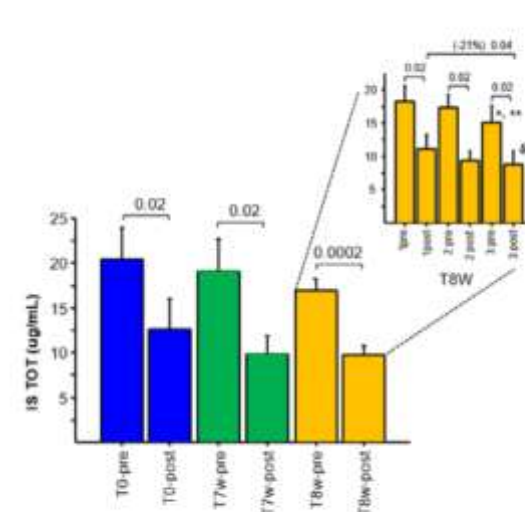
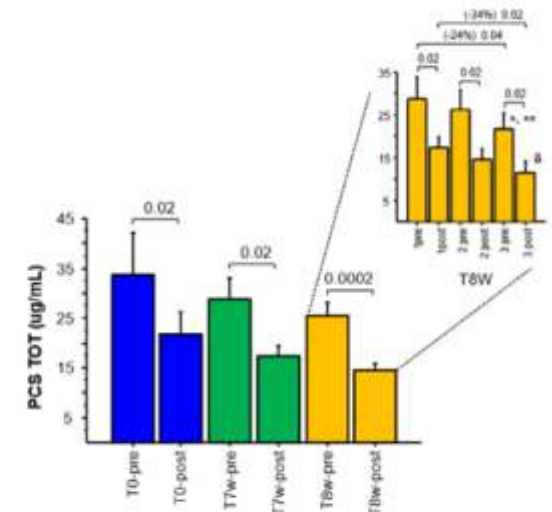


Figure 3. Study Design.

### (A) SYNBIOIC



\*: -24% from baseline, T0-pre, p=0.02  
 \*\*: -24% from T7w-pre, p=0.04  
 ⚡: -31% from baseline, T0-post, p=0.04



\*: -35% from baseline, T0-pre, p=0.04  
 \*\*: -25% from T7w-pre, p=0.02  
 ⚡: -47% from baseline, T0-post, p=0.04

# The "new" concept of sorbent in hemodialysis....

## The Effect of Combination Use of Hemodialysis and Hemoperfusion on Microinflammation in Elderly Patients with Maintenance Hemodialysis

Blood Purification

Jun Li<sup>a</sup> Hui Li<sup>b</sup> Wenjiao Deng<sup>a</sup> Lixin Meng<sup>a</sup> Wenya Gong<sup>a</sup> Huitian Yao<sup>a</sup>

Aim of the study was to investigate the effects of hemodialysis (HD) combined with hemoperfusion (HP) on microinflammatory state in elderly patients with MHD.

150 elderly patients with MHD were randomly divided into the control group and the observation group.

Groups	CRP, mg/L	Hcy, $\mu$ mol/L	IL-6, ng/L	TNF- $\alpha$ , ng/L
Control group (n = 75)				
Difference before and after treatment	0.96 $\pm$ 1.14	0.52 $\pm$ 2.35	2.45 $\pm$ 3.83	1.80 $\pm$ 0.97
CV, %	134	129	154	183
Observation group (n = 75)				
Difference before and after treatment	9.61 $\pm$ 3.48	30.82 $\pm$ 9.62	38.26 $\pm$ 10.89	22.85 $\pm$ 6.41
CV, %	21.12	27.84	30.37	36.70
t	12.33	14.67	16.29	19.81
p value	0.035	0.023	0.041	0.029

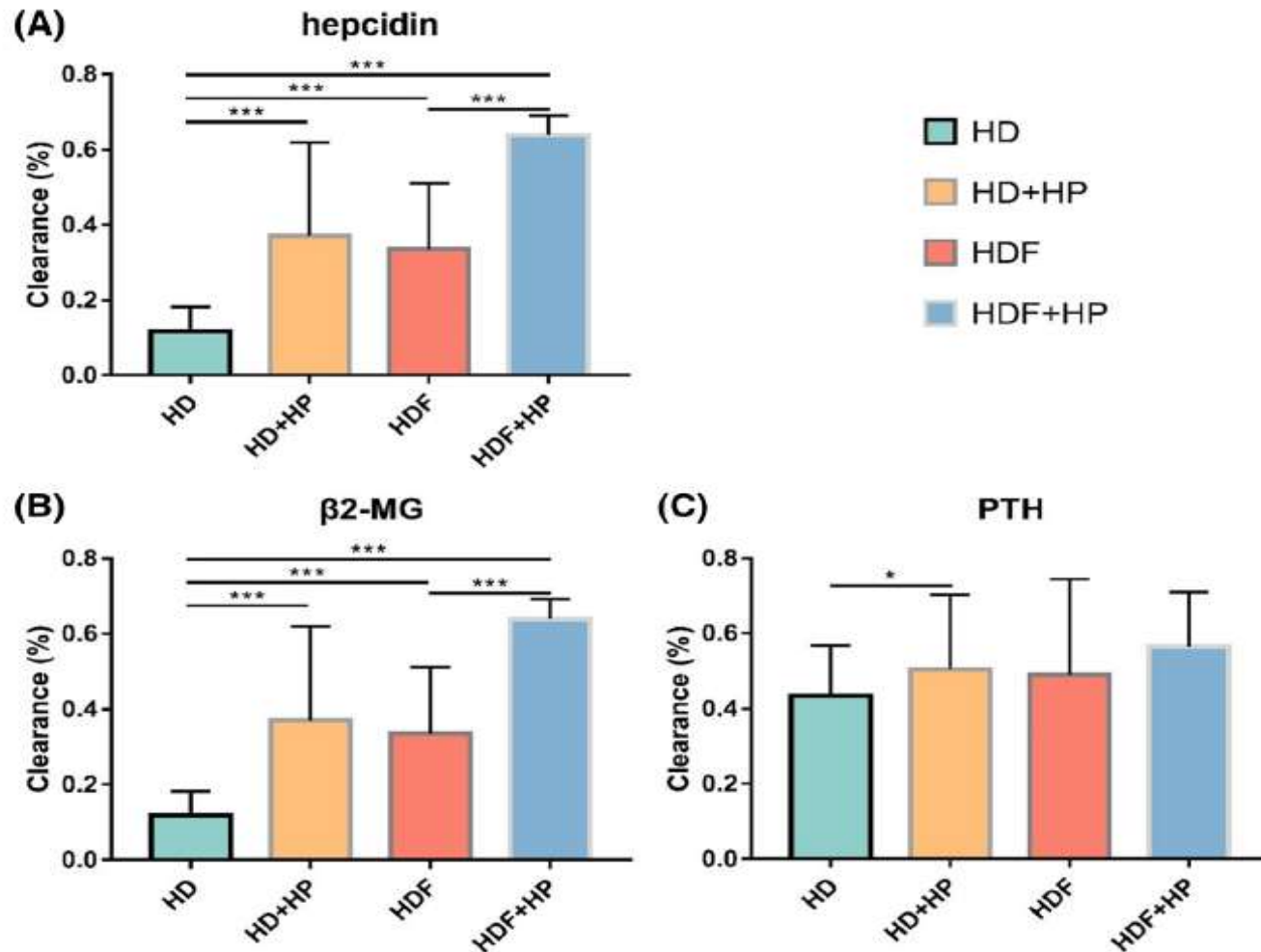
Clinical effect of HD combined with HP in elderly patients is significant, which can effectively reduce the incidence of adverse reactions and inflammation in the patients and improve the quality of life and nutritional indicators of the patients.

**Comparison of the differences of inflammatory levels between the 2 groups before and after treatment**

## Effect of different hemodialysis modalities on hepcidin clearance in patients undergoing maintenance hemodialysis

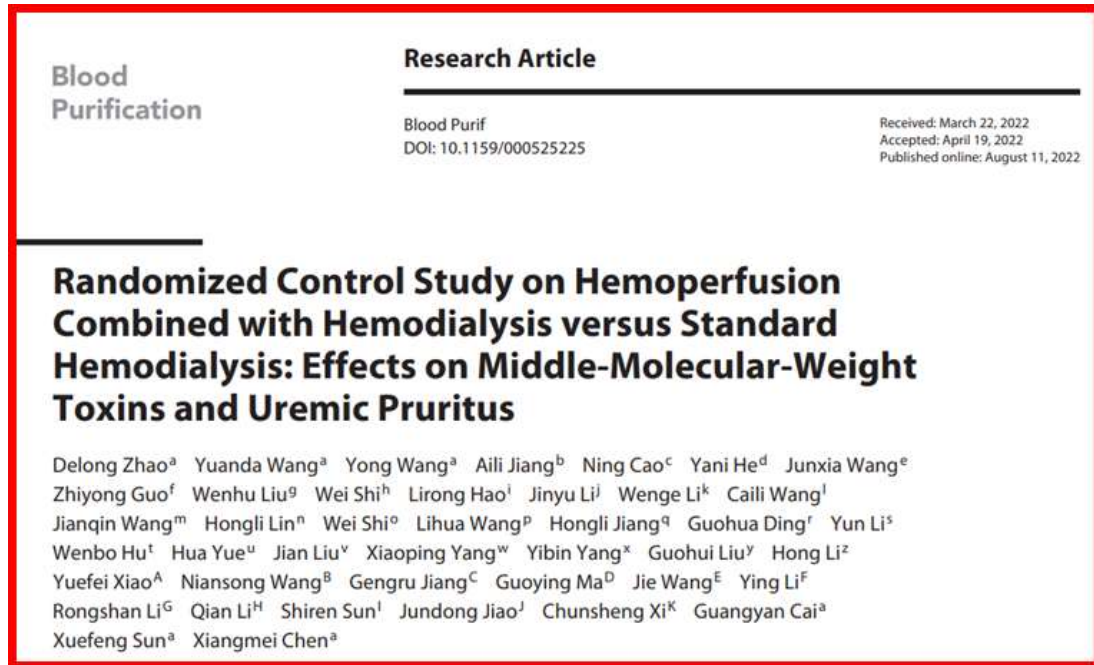
Ling Sun<sup>1</sup> | Rui-Xue Hua<sup>2</sup> | Yu Wu<sup>2</sup> | Lu-Xi Zou<sup>2</sup> 

**Materials and Methods:** In a longitudinal interventional study of 26 stable MHD patients, the serum hepcidin,  $\beta$ 2-microglobulin ( $\beta$ 2-MG), and intact parathyroid hormone (iPTH) were measured before and after one treatment session of hemodialysis (HD), hemodiafiltration (HDF), HD + HP, and HDF + HP, separately. One-way analysis of variance (ANOVA) was used to identify the effect of dialysis modalities on the intra-dialysis clearance ratios.



The combined dialysis modalities of regular HD/HDF plus HP could achieve better clearance ratios of hepcidin than HD/HDF alone during one treatment session, thereby, the combined dialysis modalities might improve iron utilization, and benefit anemia management in MHD patients.

# The "new" concept of sorbent in hemodialysis....

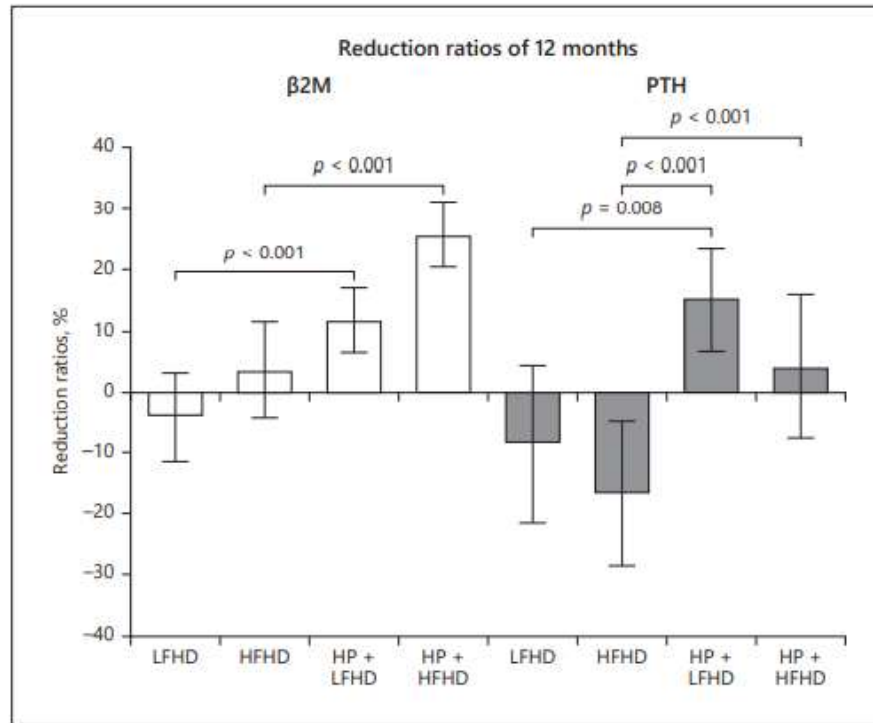


438 MHD patients from 37 HD centers in China with end-stage kidney disease (63.9% males, mean age 51 years) suffering from chronic intractable pruritus were enrolled in the study.

Eligible patients were randomized into four groups:

1. low-flux hemodialysis (LFHD)
2. high-flux hemodialysis (HFHD)
3. HP + LFHD
4. HP + HFHD

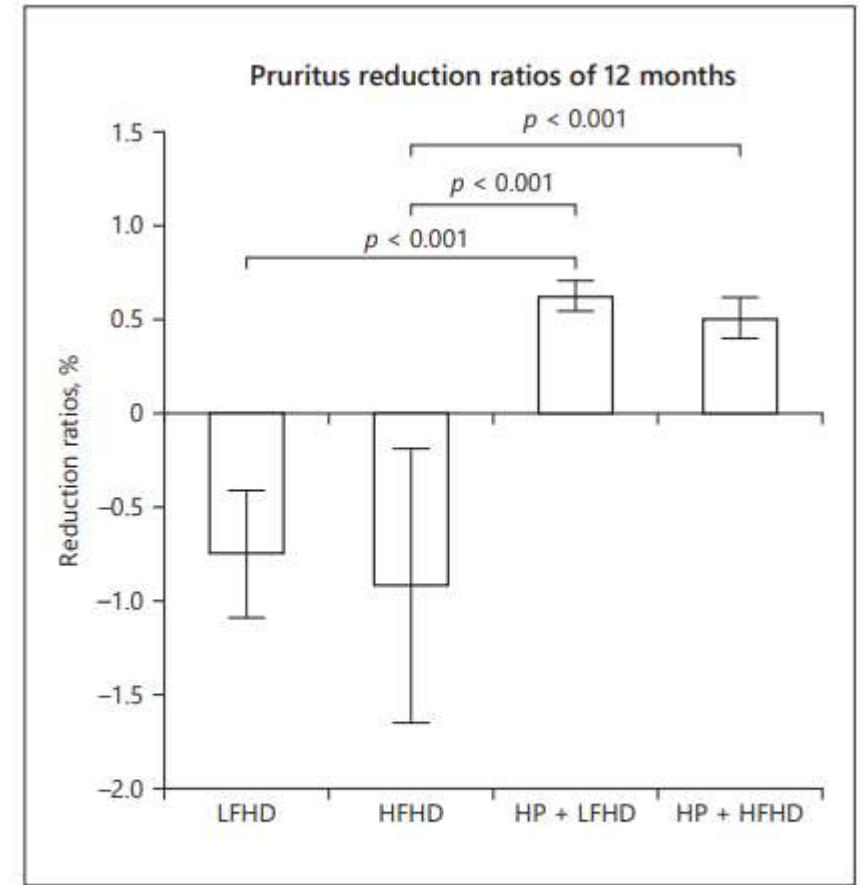
Beta-2 microglobulin ( $\beta$ 2M) and parathyroid hormone (PTH) were measured at baseline, 3-6, and 12 months. At the same time points, the pruritus score was evaluated.



**Fig. 3.** Reduction ratios of  $\beta 2M$  and PTH: intergroups analysis. LFHD, low-flux hemodialysis; HFHD, high-flux hemodialysis; HP, hemoperfusion;  $\beta 2M$ ,  $\beta 2$ -microglobulin; PTH, parathyroid hormone.

In the two groups HP + LFHD and HP + HFHD, there was a significant decrease of  $\beta 2M$  and PTH levels after 12 months compared to the control groups. No significant differences were noted between HP + LFHD and HP + HFHD.

Pruritus score reduction was 63% in the HP + LFHD group and 51% in the HP + HFHD group, respectively.



**Fig. 5.** Reduction ratios of pruritus: intergroups analysis. LFHD, low-flux hemodialysis; HFHD, high-flux hemodialysis; HP, hemoperfusion.

**Conclusion:** The long-term HP + HD can reduce  $\beta 2M$  and PTH levels and improve pruritus in MHD patients independently on the use of high- or low-flux dialyzers, showing that the results are linked to the effect of adsorption.

## Additional hemoperfusion is associated with improved overall survival and self-reported sleep disturbance in patients on hemodialysis

Yan Hong Gu<sup>1,\*</sup>, Xiu Hong Yang<sup>1,\*</sup>, Li Hua Pan<sup>1,\*</sup>, Xiao Li Zhan<sup>1</sup>, Li Li Guo<sup>2</sup> and Hui Min Jin<sup>1</sup>

158 patients who underwent routine hemodialysis divided into two groups:

1. 80 patients => HD
2. 78 patients => HD+HP

Hemoperfusion was performed 1-2 times biweekly, with each session lasting 2 h.

Self-reported sleep disturbance was evaluated before and after the observational time (2-year period).

Sleep quality was measured using the Pittsburgh Sleep Quality Index.

## Improving Pruritus & Sleep

	Baseline		P	End of treatment		P
	HD	HD + HP		HD	HD + HP	
Patients (n)	80	78		68	75	
Age (years)	62.5 ± 11.5	63.9 ± 12.8	NS	64.1 ± 10.6	65.6 ± 11.8	NS
Male (%)	41.25	43.56	NS	42.65	41.33	NS
Diabetes (%)	40	39.74	NS	41.18	40.0	NS
HD duration (years)	4.4 ± 0.5	4.8 ± 0.6	NS	6.3 ± 0.7	6.5 ± 0.8	NS
Low-incomes (%)	28.75	14.10	<0.05	25.0	12.0	<0.05
Pruritus score	7.3 ± 1.5	7.2 ± 1.4	NS	7.2 ± 0.9	5.9 ± 1.1	<0.01
Sleep medication	37	34	NS	28	19	<0.05
<b>Laboratory parameters</b>						
CRP (mg/L)	13.1±0.7	12.7±0.8	NS	12.7±0.5	9.6 ± 0.4	<0.01
Albumin (g/dL)	31.1±1.5	31.0±1.6	NS	30.0±2.1	31.4±1.5	NS
Hemoglobin (g/dL)	9.8 ± 2.3	9.2 ± 2.7	NS	10.6±0.6	10.8±0.7	NS
Hypercalcemia (%)	8.75	8.97	NS	8.82	1.33	<0.05
Hyperphosphatemia (%)	75.0	76.9	NS	63.2	42.7	<0.05
iPTH (pg/mL)	601 ± 23.9	607 ± 23.5	NS	618 ± 29.4	449 ± 27.3	<0.01
<b>Sleep parameters</b>						
Sleep duration (min)	360 ± 16.6	370 ± 15.1	NS	368 ± 25.2	418 ± 22.7	<0.05
Sleep efficiency (%)	76 ± 5.5	78 ± 6.9	NS	78.5±5.4	88.2±3.5	<0.01

**Tab. 1** Characteristics of the HD versus HD + HP groups at baseline and at the 2-year follow-up.

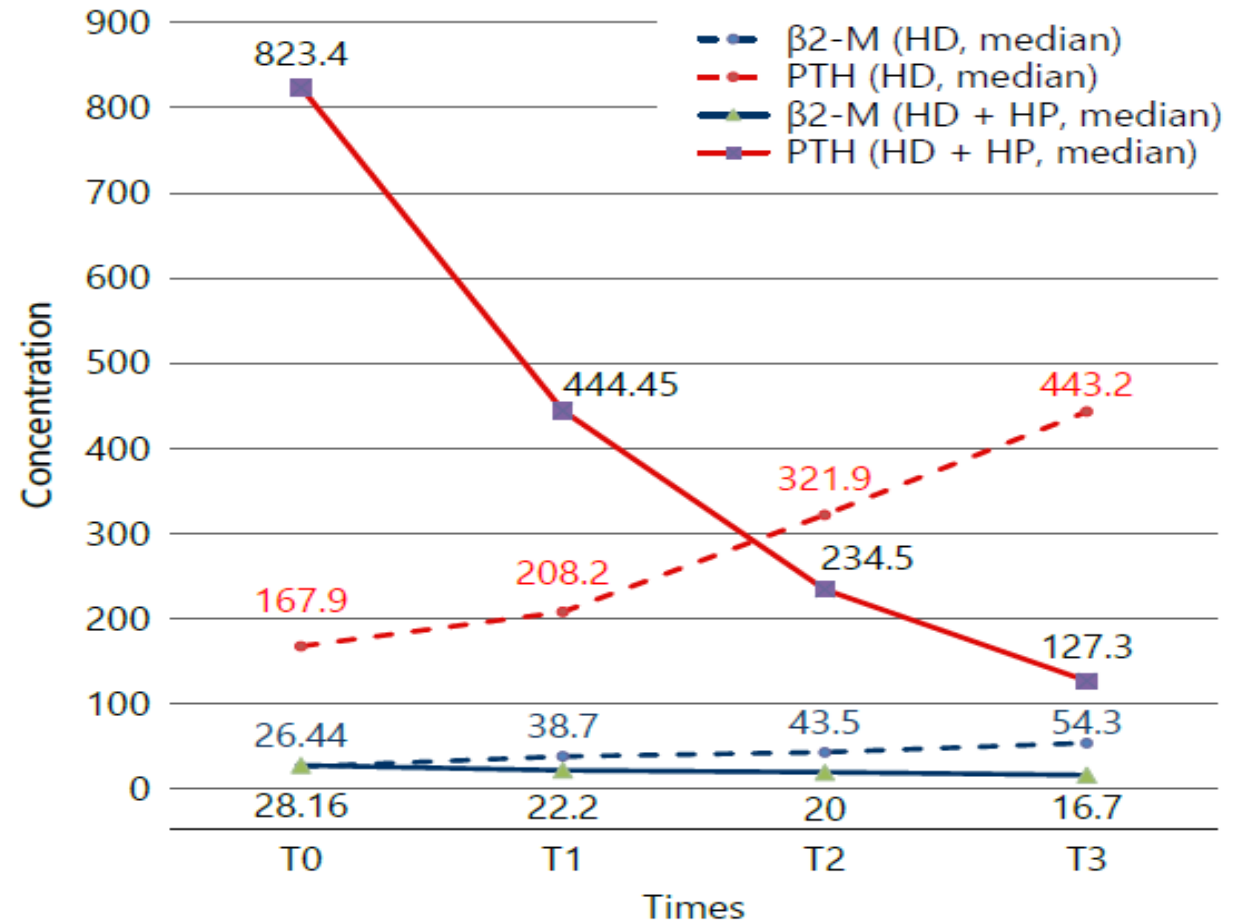
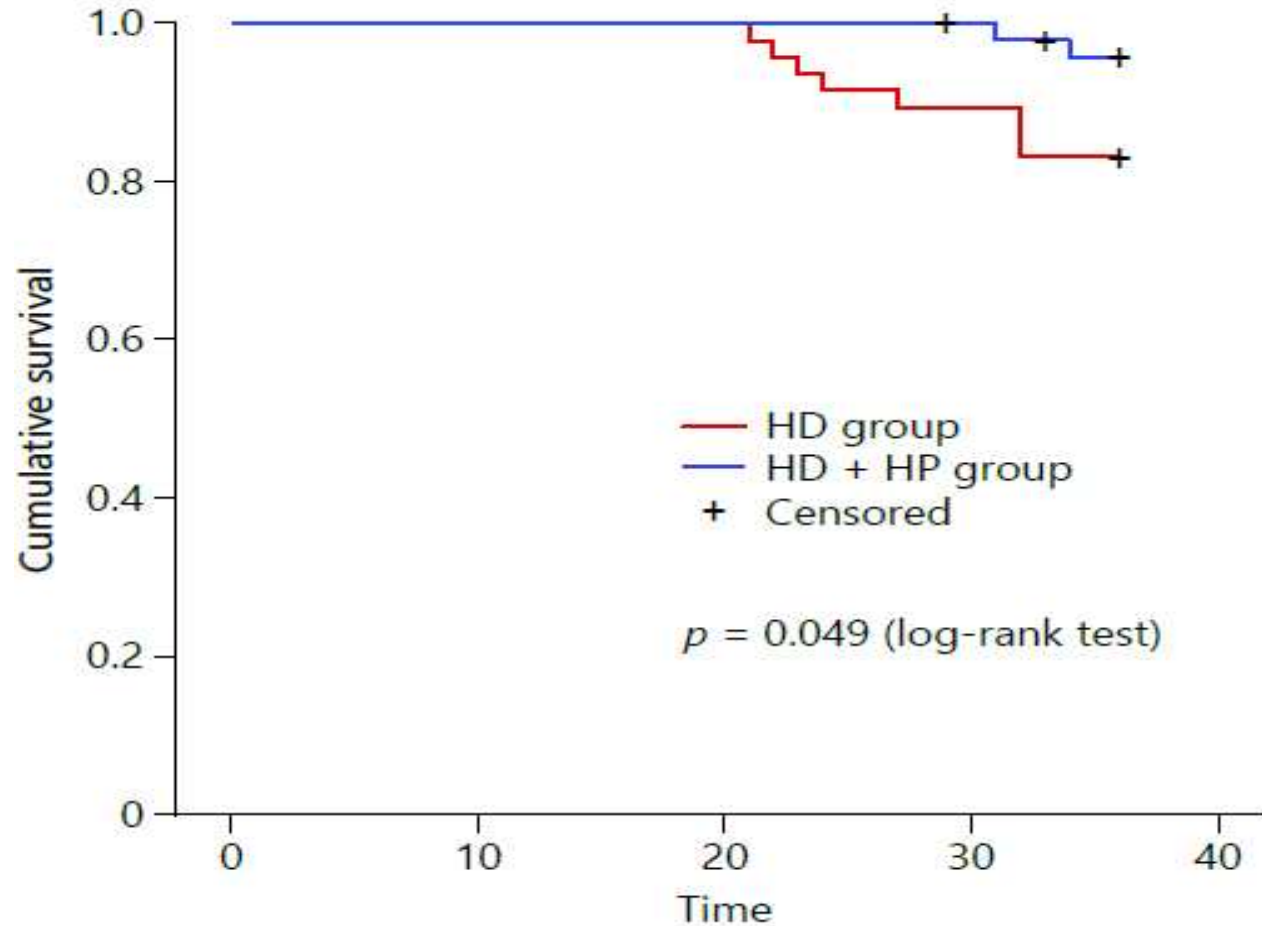
# A Combination of Hemodialysis with Hemoperfusion Helped to Reduce the Cardiovascular-Related Mortality Rate after a 3-Year Follow-Up: A Pilot Study in Vietnam

Dung Nguyen Huu<sup>a</sup> Quyên Dao Bui Quy<sup>b</sup> Hai Nguyen Thi Thu<sup>a</sup>

*Blood Purif* (2021) 50 (1): 65–72.

93 maintenance hemodialysis patients with PTH  $\geq 600$  pg/ml were divided into 2 groups:

- 46 patients => HD + HP for consecutive 3 years
- 47 patients => HD for consecutive 3 years



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# Hemoperfusion in Maintenance Hemodialysis Patients

Wei Lu<sup>a</sup> Gengru Jiang<sup>a, b, c</sup> on behalf of Shanghai HP-HD Consensus Group

<sup>a</sup>Renal Division, Department of Internal Medicine, Xin Hua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; <sup>b</sup>Centre for Rare Disease, Shanghai, China; <sup>c</sup>Shanghai Medical Association Society of Nephrology, Shanghai, China



# 1. Patients

2. Treatment frequency

3. Treatment methods

4. Adverse reactions

- severe uremic pruritus
- severe uremia-related sleep disorders
  - protein-energy wasting
  - microinflammatory state
- severe secondary hyperparathyroidism
  - severe hyper $\beta_2$ -microglobulin
  - refractory hypertension
  - restless legs syndrome
- uremic peripheral neuropathy

1. Patients

**2. Treatment frequency**

3. Treatment methods

4. Adverse reactions

Individualized HP treatment frequency should be determined according to patients' complications and severity

**Once a week or once every 2 weeks**

1. Patients
2. Treatment frequency
- 3. Treatment methods**
4. Adverse reactions

### ***Treatment Mode***

HP can be combined with three blood purification methods, i.e., LF-HD, HF-HD, and HDF.

### ***Each HP Treatment Duration***

The recommended HP treatment duration is 2.0–2.5 h each time. In practice, it should be the treatment duration recommended in the product manual of each brand of perfusion device.

### ***Blood Flow during HP Treatment***

When HP is combined with HD or HDF, the blood flow should be controlled at 150–250 mL/min.

### ***Hemoperfusor Connection with Dialyzer or Filter in Group Treatment***

It is recommended that the hemoperfurors be connected in series, in front of a dialyzer or filter.

### ***Start Time of HP Treatment in the Treatment Group***

For group treatment, HD and HP devices should be combined in series. After 2.0–2.5 h of the first group treatment, the HP device should be removed, but HD treatment should continue; alternatively, 2.0 h–2.5 h before the end of HD treatment (the second group treatment), the HP device should be installed, and the group treatment should be performed again.

1. Patients
2. Treatment frequency
3. Treatment methods
- 4. Adverse reactions**

- Abnormal biocompatibility
- Adsorbent particle embolization
  - Air embolism
- Blood coagulation dysfunction
  - Hypotension

*HP Is Not Recommended, or HP Treatment Should Be Suspended, in the following Circumstances*

(1) Platelet count  $<60 \times 10^9/L$ ; (2) white blood cell count  $<4 \times 10^9/L$ ; (3) hypotension (predialysis blood pressure  $<90/60$  mm Hg); (4) active hemorrhage; and (5) unstable hemodynamics or vital signs.



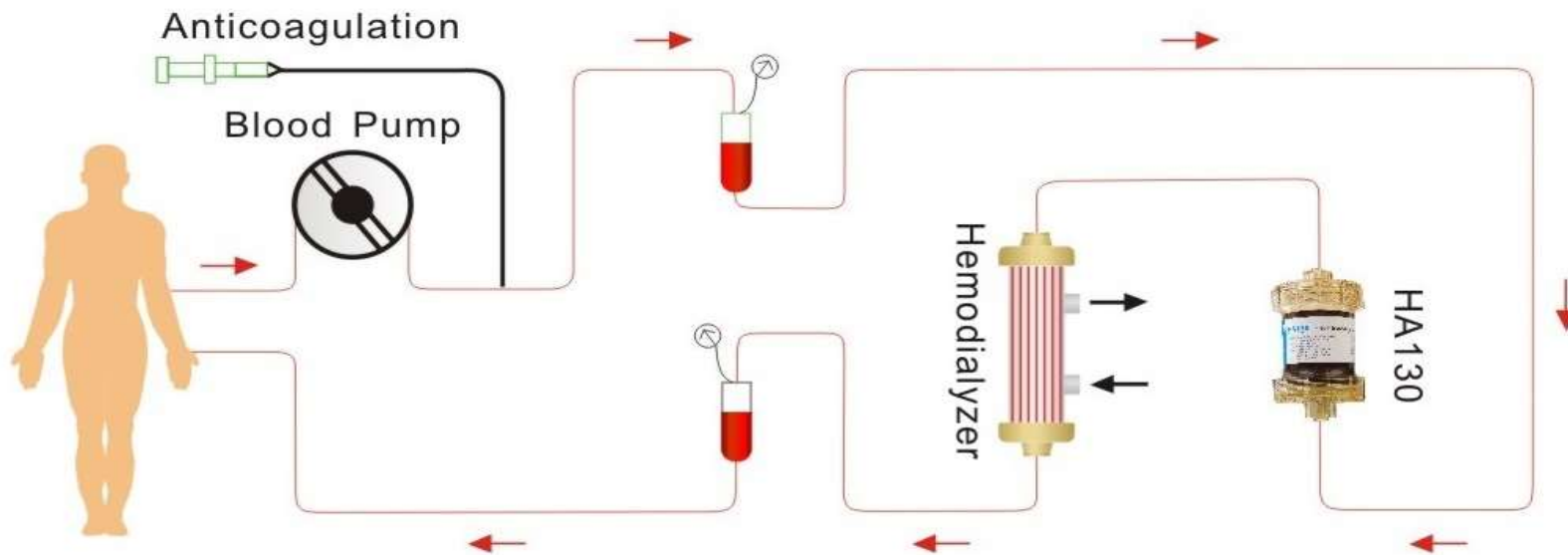
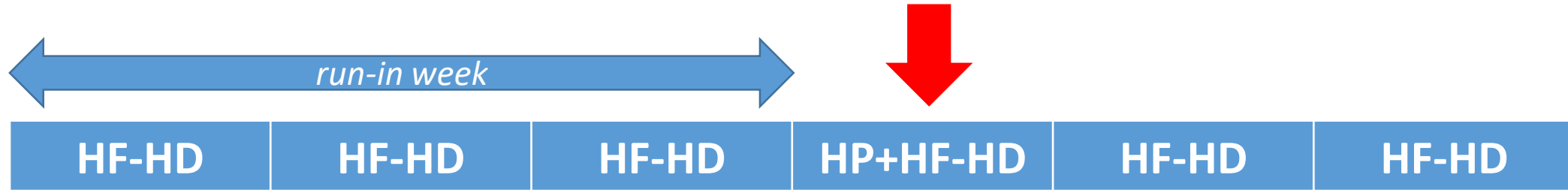
## Effects of Sequential therapy with Hemoperfusion (HP) and Hemodialysis (HD) on uremic toxin removal

**Study Design:** Multicenter, prospective and observational study aimed to evaluate the efficacy of a coupled hemoperfusion (HP)-hemodialysis (HD) system aimed to enhance the removal of small-medium-large size molecules and protein-bound uremic toxins (PBUT).

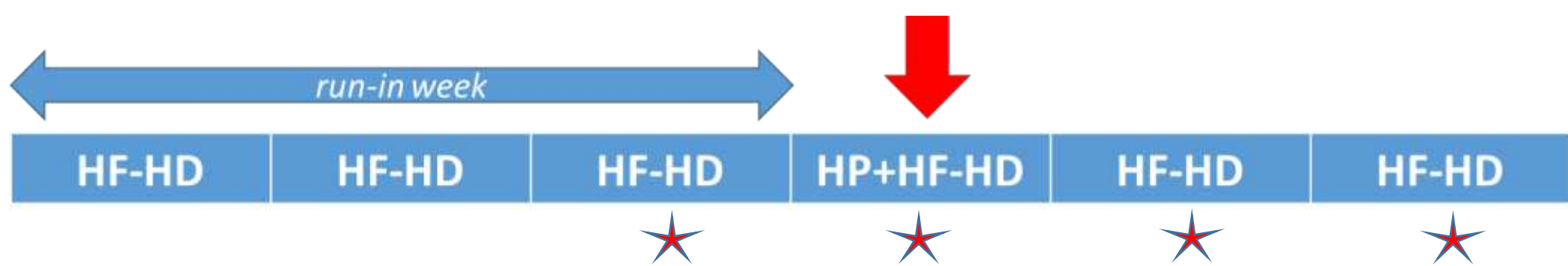
**Population:** 18 patients undergoing high-flux hemodialysis (HF-HD) were enrolled in the study. Patients in on-line hemodiafiltration (OL-HDF) were enrolled as control group.



**Method:** Run-in phase of 3 HD sessions (1 week) performed with HF-HD (polysulfone membrane). After the run-in week, only at the first dialysis of the following week (HP-HD week), HP device will be added to standard HF-HD, maintaining the usual prescription of dialytic parameters. The same variables will be also applied to the second and third dialysis of the HP-HD week, but without addition of the HP device.



**4 hr HF-HD + HP**  
**Qb 300 ml/min**  
**Qd 500 ml/min**



★ the following parameters have been collected: real duration of dialysis (min), dialyzer, Qb, Qd, recirculation index, arterial and venous pressure, transmembrane pressure (TMP), initial and final hematocrit, initial and final body weight, volume of blood processed, Kt/V, circuit clotting, heparin dose.

At the start and at the end of all the above-reported HD sessions, the following lab tests have been performed: creatinine, red/white blood cell count, sodium, potassium, calcium, phosphate, uric acid, albumin, total proteins, cholesterol, HDL, LDL, triglycerides, albumin, CRP,  $\beta$ 2-microglobulin, myoglobin, kappa and lambda FLCs.

## Samples

Before and after each dialysis session, analysis of serum levels of the following uremic toxins (UTs): 1-methyladenosine, trimethylamine-N-oxide (TMAO), indoxyl sulfate, p-cresyl sulfate, phenyl sulfate and 4-ethylphenyl sulfate.

Mass Removal (MR) of the above-mentioned UTs has been evaluated using the following formula:

$$MR = [Body\ Volume\ before\ HD\ (ml) \times UTs\ before\ HD\ (ng/ml)] - [Body\ Volume\ after\ HD\ (ml) \times UTs\ after\ HD\ (ng/ml)]$$

where:

- Body Volume before HD (ml) = 1000 x Body Weight before HD (Kg) x (1/13)
- Body Volume after HD (ml) = 1000 x Body Weight before HD (Kg) x (1/13) x [Hct before HD (%) / Hct after HD (%)]

# Take home points

**Dialysis adequacy should not be based only on  $Kt/V$  urea, but consider the kinetics of other retention solutes that are associated with adverse clinical outcomes.**

**Relevance of PBUT (IS, pCS) in CKD progression and ESRD-associated cardiovascular and neurological alterations.**

**PBUT are not removed (if not the unbound free fraction) by conventional diffusive and convective strategies.**

**Adsorption (HP + HD) can be a good therapeutic option for ESRD: promising results from first clinical trials aimed to evaluate HD complications.**