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PD
Chemical Peritonitis

Iraj Najafi MD
Professor of Internal Medicine
TUMS
2019

JASN

J Am Soc Nephrol. 2016 Nov; 27(11): 3238–3252.
Published online 2016 Jun 23. doi: 10.1681/ASN.2016010112

PMCID: PMC5084899
PMID: 27339663

The Current State of Peritoneal Dialysis

Rajnish Mehrotra,[⊠*†] Olivier Devuyst,[‡§] Simon J. Davies,[‖] and David W. Johnson[¶]

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J Am S

Changes in the worldwide epidemiology of peritoneal dialysis

Philip Kam-Tao Li, Kai Ming Chow, Moniek W.M. Van de Luijtgaarden, David W. Johnson, Kitty J. Jager, Rajnish Mehrotra, Sarala Naicker, Roberto Pecoits-Filho, Xue Qing Yu & Norbert Lameire

Affiliations | Contributions | Corresponding author

Nature Reviews Nephrology (2016) | doi:10.1038/nrneph.2016.181
Published online 28 December 2016

- Global burden of chronic kidney disease continues to increase, so does the need for a cost-effective RRT
- Patient outcomes with peritoneal dialysis are comparable to or better than those with hemodialysis, and PD is more cost-effective.
- These benefits have not, however, always led to increased utilization of peritoneal dialysis

World distribution of PD for RRT

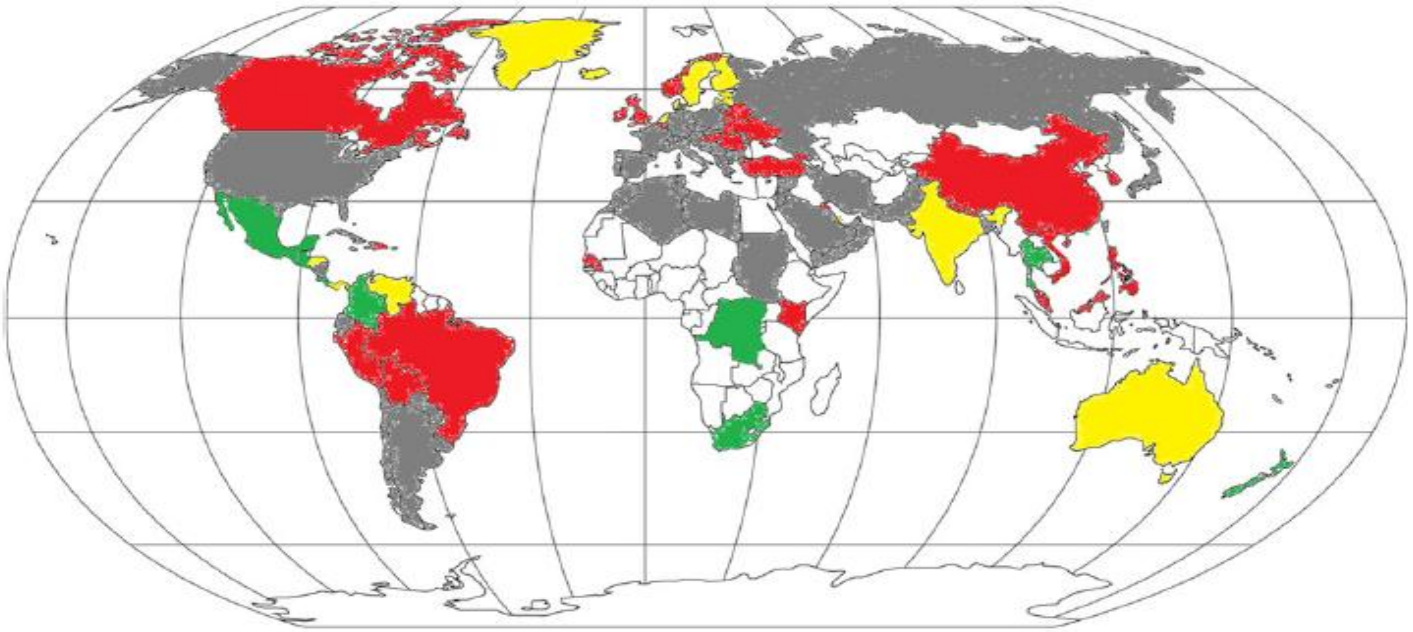
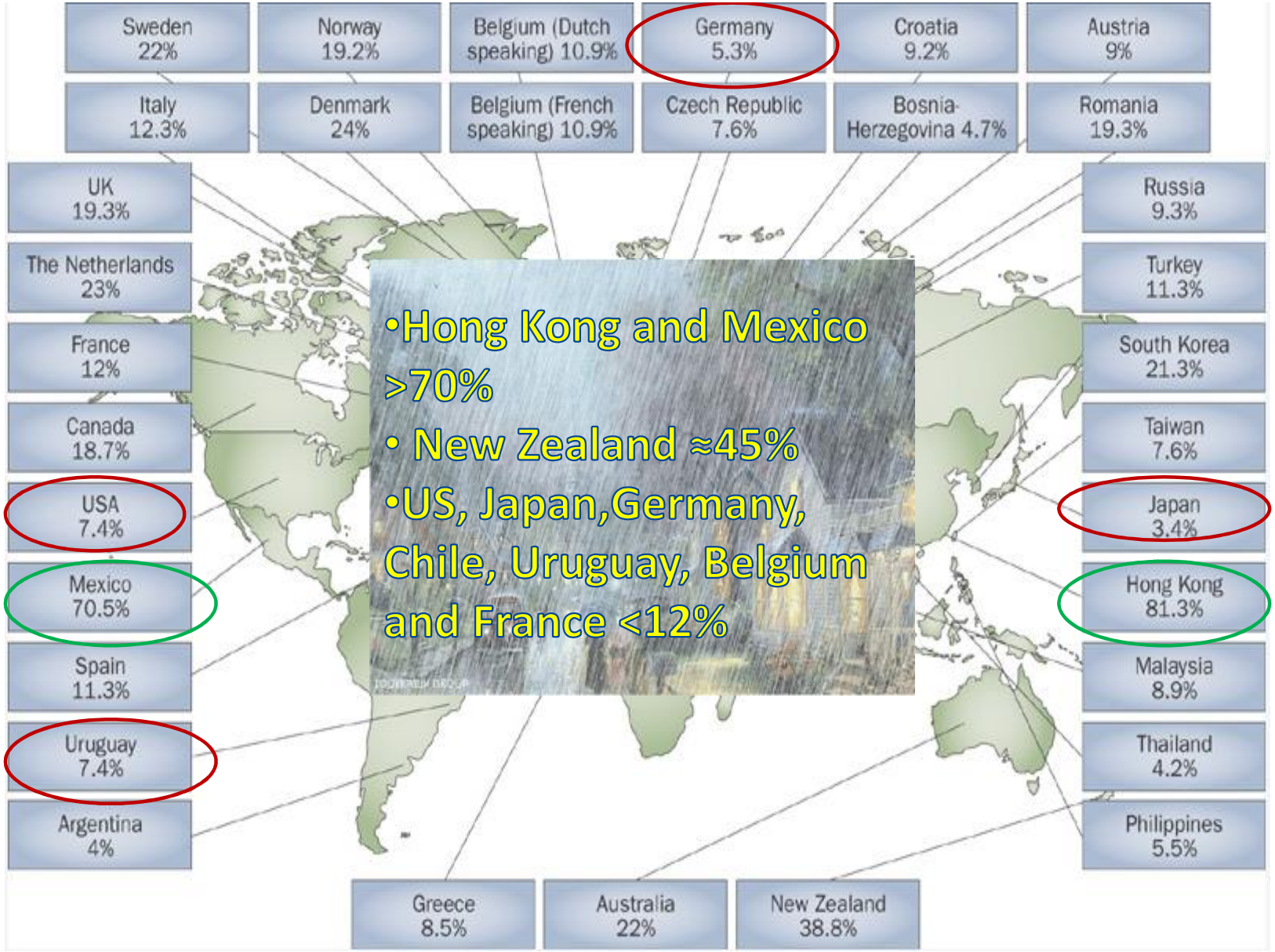


Fig. 2. Utilization of PD for chronic dialysis (prevalence) across the globe.


Sweden 22%
Norway 19.2%
Belgium (Dutch speaking) 10.9%
Germany 5.3%
Croatia 9.2%
Austria 9%
Italy 12.3%
Denmark 24%
Belgium (French speaking) 10.9%
Czech Republic 7.6%
Bosnia-Herzegovina 4.7%
Romania 19.3%
UK 19.3%
The Netherlands 23%
France 12%
Canada 18.7%
USA 7.4%
Mexico 70.5%
Spain 11.3%
Uruguay 7.4%
Argentina 4%
Russia 9.3%
Turkey 11.3%
South Korea 21.3%
Taiwan 7.6%
Japan 3.4%
Hong Kong 81.3%
Malaysia 8.9%
Thailand 4.2%
Philippines 5.5%
Greece 8.5%
Australia 22%
New Zealand 38.8%
•Hong Kong and Mexico >70%
• New Zealand ≈45%
•US, Japan,Germany, Chile, Uruguay, Belgium and France <12%

Changes in the worldwide epidemiology of peritoneal dialysis

- Use of this therapy is increasing in some countries, including China, the USA and Thailand, but has proportionally decreased in parts of Europe and in Japan.

- The variable trends in peritoneal dialysis use reflect the multiple challenges in prescribing this therapy to patients.

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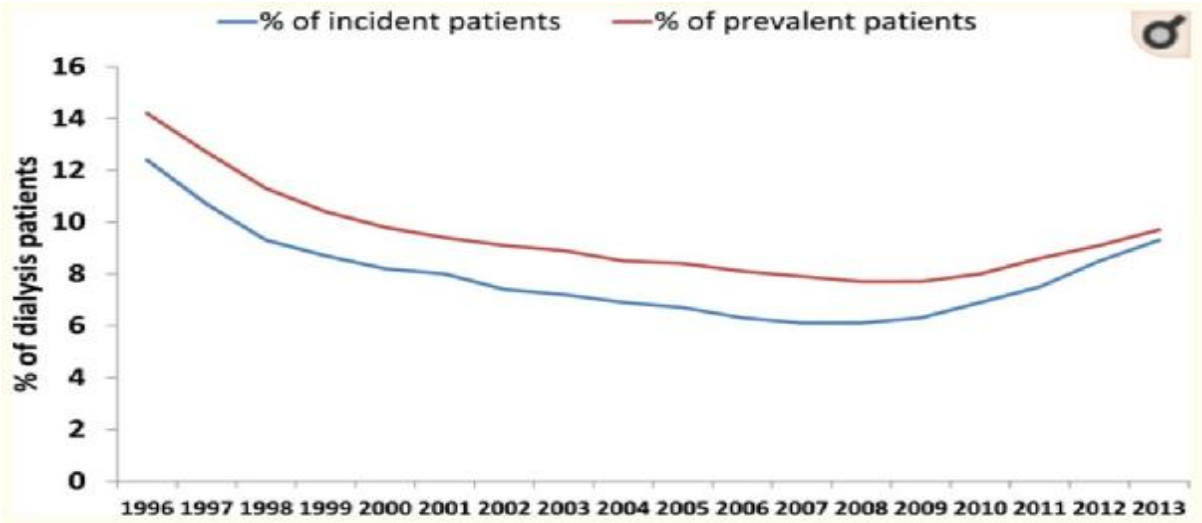

Figure 3.

Secular trends in the proportion of patients undergoing maintenance dialysis treated with PD in the United States (1996–2013). The blue line represents the proportion of all patients undergoing maintenance dialysis treated with PD 90 days from the date of first dialysis and the red line represents the proportion of all patients undergoing maintenance dialysis on December 31 of any calendar year.

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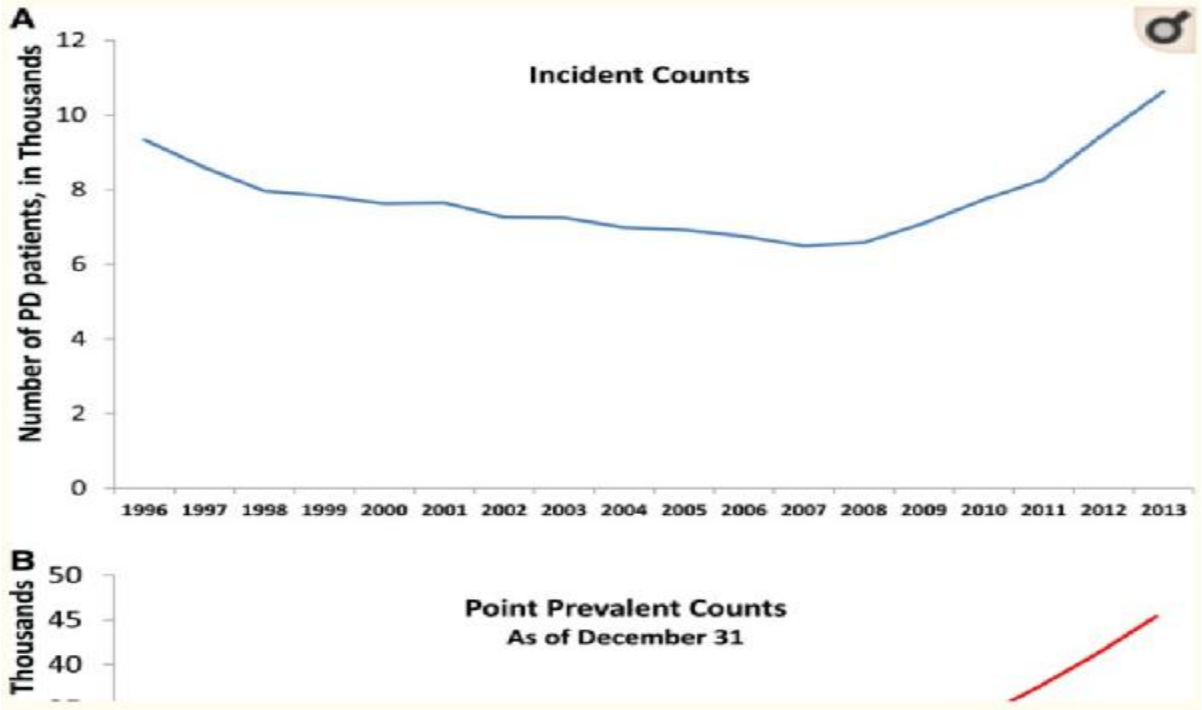


Changes in the worldwide epidemiology of peritoneal dialysis

- Each country has unique factors that will determine the areas that must be prioritized to improve the availability and effectiveness of peritoneal dialysis.

- The three main areas that could facilitate such improvement are :

Factors that could improve access to and expertise in peritoneal dialysis

Organization of health care

- Implementation of PD first or PD favored policies
- Setting of targets for PD use as a proportion of total dialysis
- Improvement of infrastructure in rural and developing areas

Financial Incentives

- Government reimbursement policies
- Fee-for-service payments to private centers for managing patients on PD
- Insurance coverage
- Penalties when targets for PD use are not achieved

Research and education

- Training and education networks for PD
- Research aimed at improving the PD technique

PD-First Policy

Peritoneal Dialysis International, Vol. 35, pp. 406–420
doi: 10.3747/pdi.2013.00204

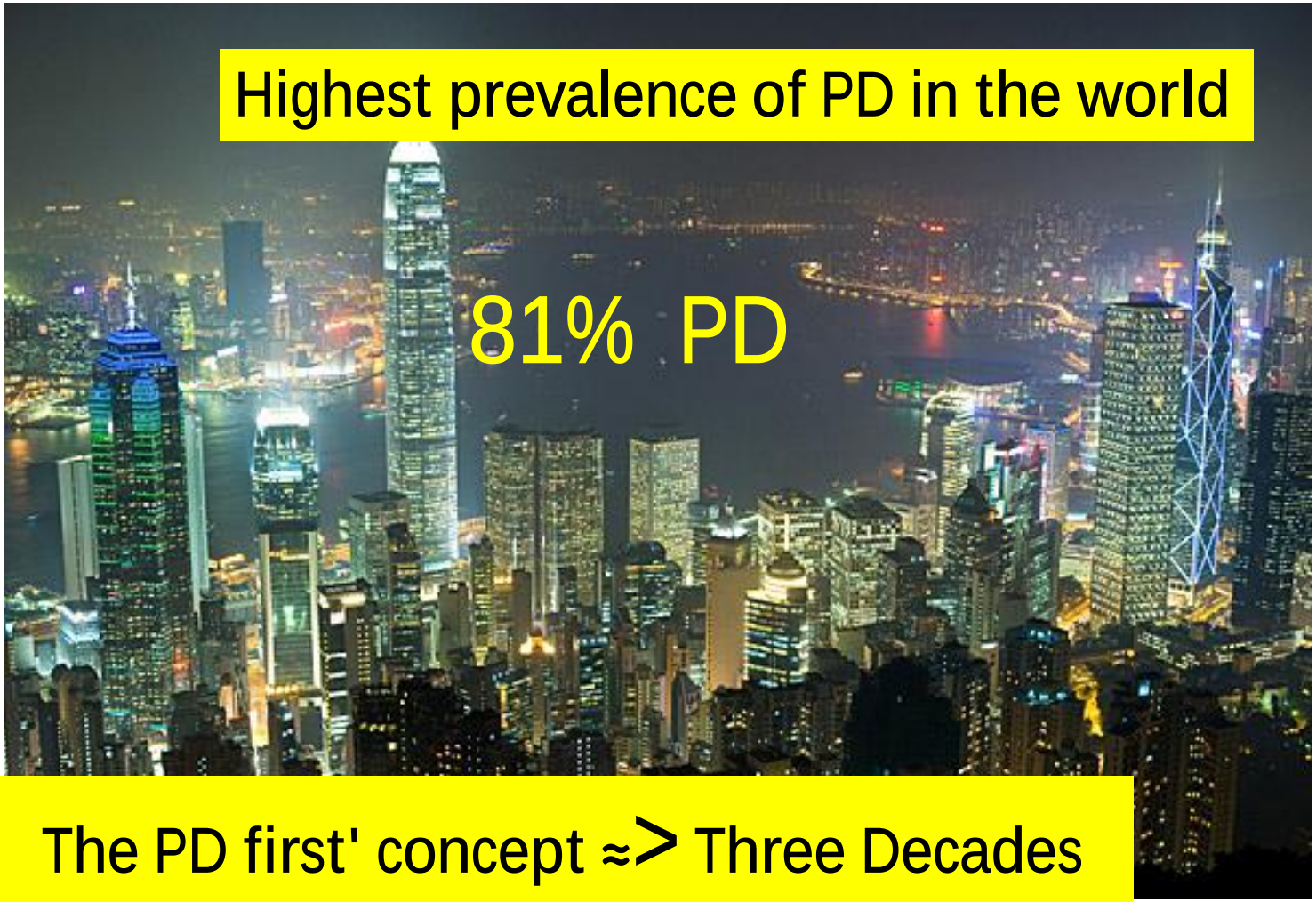
0896-8608/15 $3.00 + .00
Copyright © 2015 International Society for Peritoneal Dialysis

A GLOBAL OVERVIEW OF THE IMPACT OF PERITONEAL DIALYSIS FIRST OR FAVORED POLICIES: AN OPINION

Frank Xiaoqing Liu,[1] Xin Gao,[2] Gary Inglese,[3] Piyatida Chuengsaman,[4] Roberto Pecoits-Filho,[5] and Alex Yu[6]

Baxter Healthcare Corporation,[1] Deerfield, IL, USA; Pharmerit International,[2] Bethesda, MD, USA; Hollister Incorporated,[3] Libertyville, IL, USA; Banphaeo Hospital, Prommitr branch,[4] Bangkok, Thailand; Pontificia Universidade Católica do Paraná,[5] School of Medicine, Curitiba, Parana, Brazil; and Hong Kong Baptist Hospital,[6] Hong Kong, China

In Hong Kong



The PD first' concept ≈> Three Decades

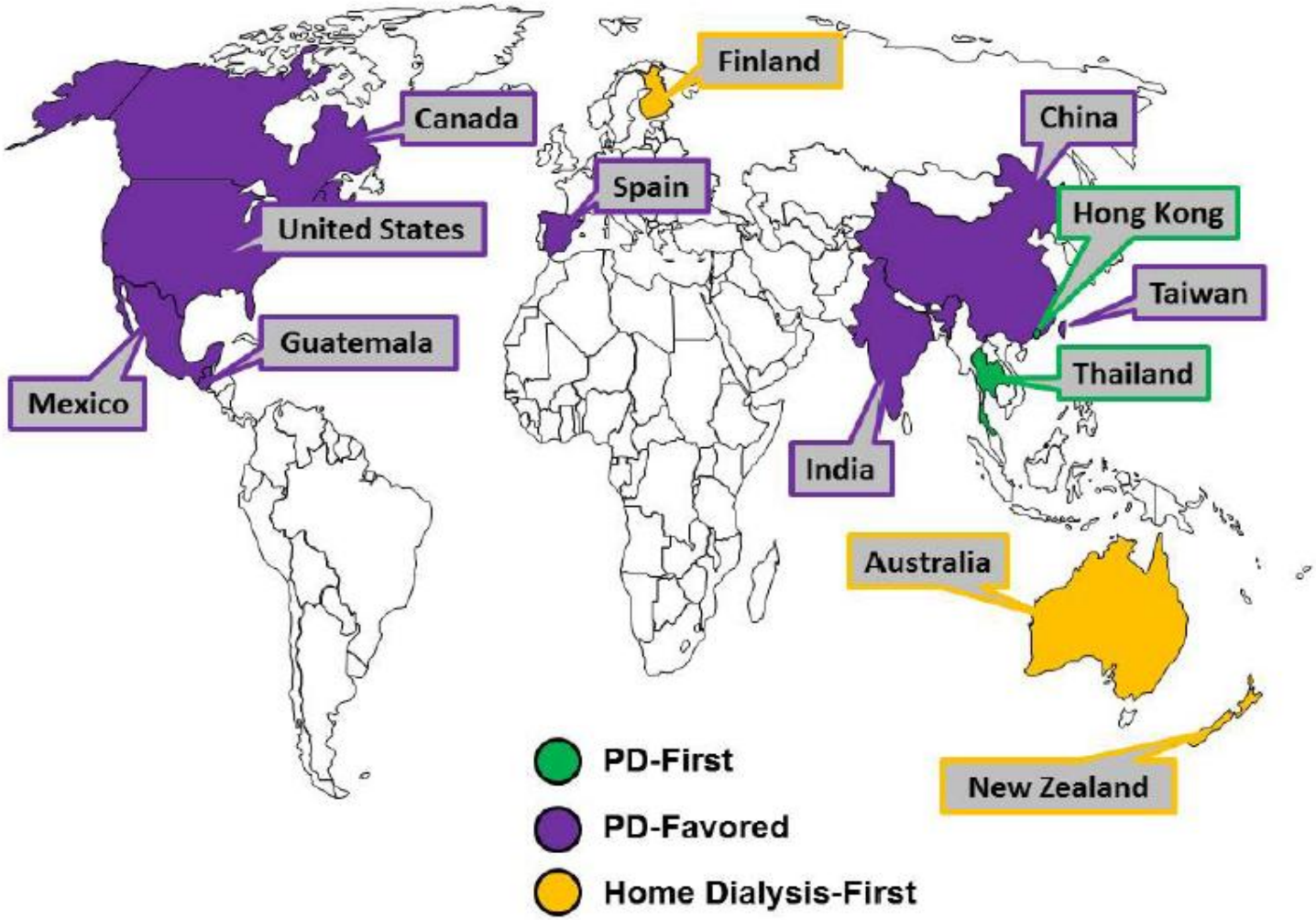


Figure 1 — Geographic summary of country-specific policy types. PD = peritoneal dialysis.

PD FIRST POLICY

Facts about PD First Policy in Thailand

Publication of
PD Technology and Training Center
Srinagarind Hospital, Faculty of Medicine
Khon Kaen University, Khon Kaen, Thailand

Supported by
National Health Security Office of Thailand

Our partners

Actual process of running PD first policy in Thailand

• Budgeting
• Formation of the first provider group (Phase I PD hospitals)
• Obtaining cheap PD solution supplies
• Training a new generation of medical personnel
• Learning form the success PD programs in Hong Kong and Singapore
• Setting up PD technology and training centers for problem solving
• Policy management by the national RRT committee
• Setting up regional RRT technology and training centers for quality control

Treatment of ESRD should provide the following

1) The best possible patient outcomes
2) The maximum medical, social, economic, and psychological rehabilitation
3) Few ill effects
4) The highest possible quality of life
5) Excellent patient compliance
6) Maximum opportunity for employment and education
7) Maintenance or "repair" of family dynamics
8) The least possible stress on patients, families, and the health care team

Quality of Life

"We should place the highest value not on living, but on living well."

Socrates

Given the similar survival data between HD and PD, quality of life ("living well") has become increasingly important in patients choice of dialysis

Patients often favor PD due to:

- Ø Flexibility of schedule,
- Ø Ability to perform dialysis at home,
- Ø Ability to dialyze while sleeping

Conventional Center Dialysis

Home Dialysis

Peritoneal Dialysis in 2019

- Is a cost-effective,
- Home-based therapy,
- Significant advantages particularly, regarding quality of life,
- Early patient outcome is at least similar to HD

(Waldum-Grevbo et al., 2015)

Peritoneal Dialysis in 2019

- Despite these benefits, only a small number of dialysis patients receive PD, in Europe about 13% and in the USA about 10%

- This discrepancy is in part explained by limitations of PD

  - Infectious complications, mainly peritonitis,
  - The PD fluid induced deterioration of the PD membrane
  - Lead to PD function deterioration and technique failure.

(Kramer et al., 2018)

Peritoneal Dialysis in 2019

- As with hemodialysis, the uremic toxin and water removal capacity is far below physiological renal function.

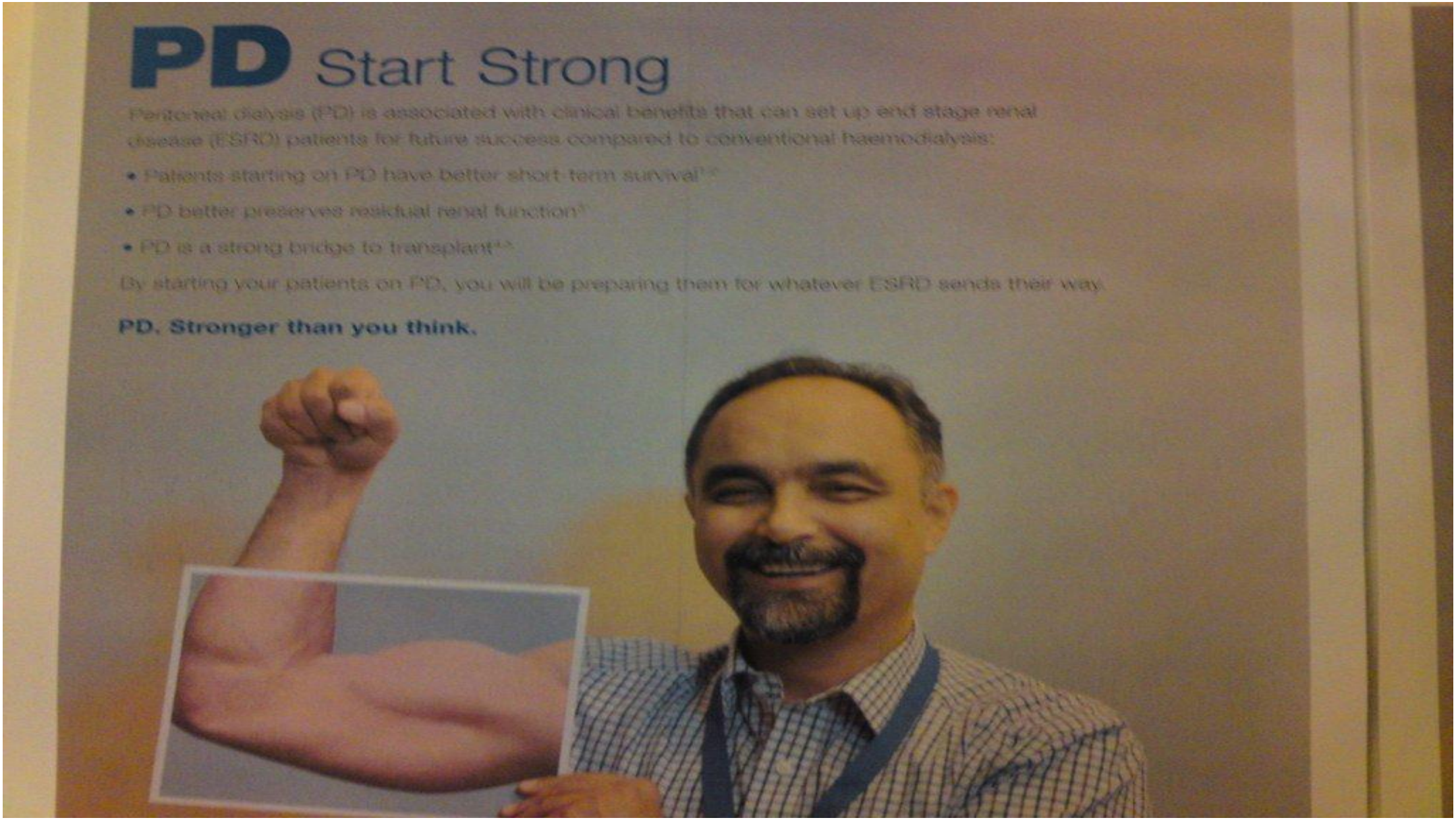
- Patients require strict dietary control and pharmacological treatment, but the vast majority of patients are salt, fluid, and toxin overloaded.

- Dietary phosphate and sodium contribute to high blood pressure CKD mineral bone disorder, and cardiovascular disease (CVD) (Ortega and Materson, 2011)

- Mortality rates of both hemodialysis and PD patients are 40-fold higher compared to the age-related healthy population (de Jager et al., 2009)

PD The Most Healthy Start

دیالیز صفاقی سالمترین روش درمانی برای شروع


PD Start Strong
Peritoneal dialysis (PD) is associated with clinical benefits that can set up end stage renal disease (ESRD) patients for future success compared to conventional haemodialysis:
• Patients starting on PD have better short term survival[1-4]
• PD better preserves residual renal function[5]
• PD is a strong bridge to transplant[1-3]
By starting your patients on PD, you will be preparing them for whatever ESRD sends their way.
PD. Stronger than you think.

PD a bridge to kidney transplantation

دیالیز صفاقی پلی برای پیوند کلیه

Iraj Najafi
PD congress Kish
Jan 2015

پلهای مطمئن

پلهای ترسناک

پل های خوف آور

پلهای خطرناک

پلهای دل و روده درار

پلهای زور به خود بیار

دیالیز صفاقی پلی مطمئن بسوی پیوند

Impact of Dialysis Modality on Kidney transplantation outcome

Iraj Najafi

Rasht 2016

J. Biomedical Science and Engineering, 2015, 8, 67-72
Published Online February 2015 in SciRes. http://www.scirp.org/journal/jbise
http://dx.doi.org/10.4236/jbise.2015.82007

Scientific Research Publishing

Impact of Dialysis Modality on Kidney Transplantation Outcomes

Imed Helal[1,2,3*], Imen Gorsane[1,3], Fethi Ben Hamida[1,2,3], Adel Kheder[1,2,3]

[1]Department of Medicine A (M8), Charles Nicolle Hospital, Tunis, Tunisia
[2]Laboratory of Kidney Pathology (LR00SP01), Charles Nicolle Hospital, Tunis, Tunisia
[3]Faculty of Medicine, University of Tunis El Manar, Tunis, Tunisia
Email: *imedhelal@voila.fr

Dialysis Modality and Outcomes in Kidney Transplant Recipients

Miklos Z. Molnar,[*†] *Rajnish Mehrotra,*[‡§] *Uyen Duong,*[*] *Suphamai Bunnapradist,*[§] *Lilia R. Lukowsky,*[*] *Mahesh Krishnan,*[‖] *Csaba P. Kovesdy,*[¶**] *and Kamyar Kalantar-Zadeh*[*‡§††]

Summary

Background and objectives The influence of pretransplant dialysis modality on post-transplant outcomes is not clear. This study examined associations of pretransplant dialysis modality with post-transplant outcomes in a large national cohort of kidney transplant recipients.

Design, setting, participants, & measurements Linking the 5-year patient data of a large dialysis organization to the *Scientific Registry of Transplant Recipients*, 12,416 hemodialysis and 2092 peritoneal dialysis patients who underwent first kidney transplantation were identified. Mortality or graft failure and delayed graft function risks were estimated by Cox regression (hazard ratio) and logistic regression (odds ratio), respectively.

Results Recipients treated with peritoneal dialysis pretransplantation had lower (21.9/1000 patient-years [95% confidence interval: 18.1–26.5]) crude all-cause mortality rate than those recipients treated with hemodialysis (32.8/1000 patient-years [30.8–35.0]). Pretransplant peritoneal dialysis use was associated with 43% lower adjusted all-cause and 66% lower cardiovascular death. Furthermore, pretransplant peritoneal dialysis use was associated with 17% and 36% lower unadjusted death-censored graft failure and delayed graft function risk, respectively. However, after additional adjustment for relevant covariates, pretransplant peritoneal dialysis modality was not a significant predictor of death-censored graft failure delayed graft function, respectively. Similar trends were noted on analyses using a propensity score matched cohort of 2092 pairs of patients.

Conclusions Compared with hemodialysis, patients treated with peritoneal dialysis before transplantation had lower mortality but similar graft loss or delayed graft function. Confounding by residual selection bias cannot be ruled out.

Clin J Am Soc Nephrol 7: 332–341, 2012. doi: 10.2215/CJN.07110711

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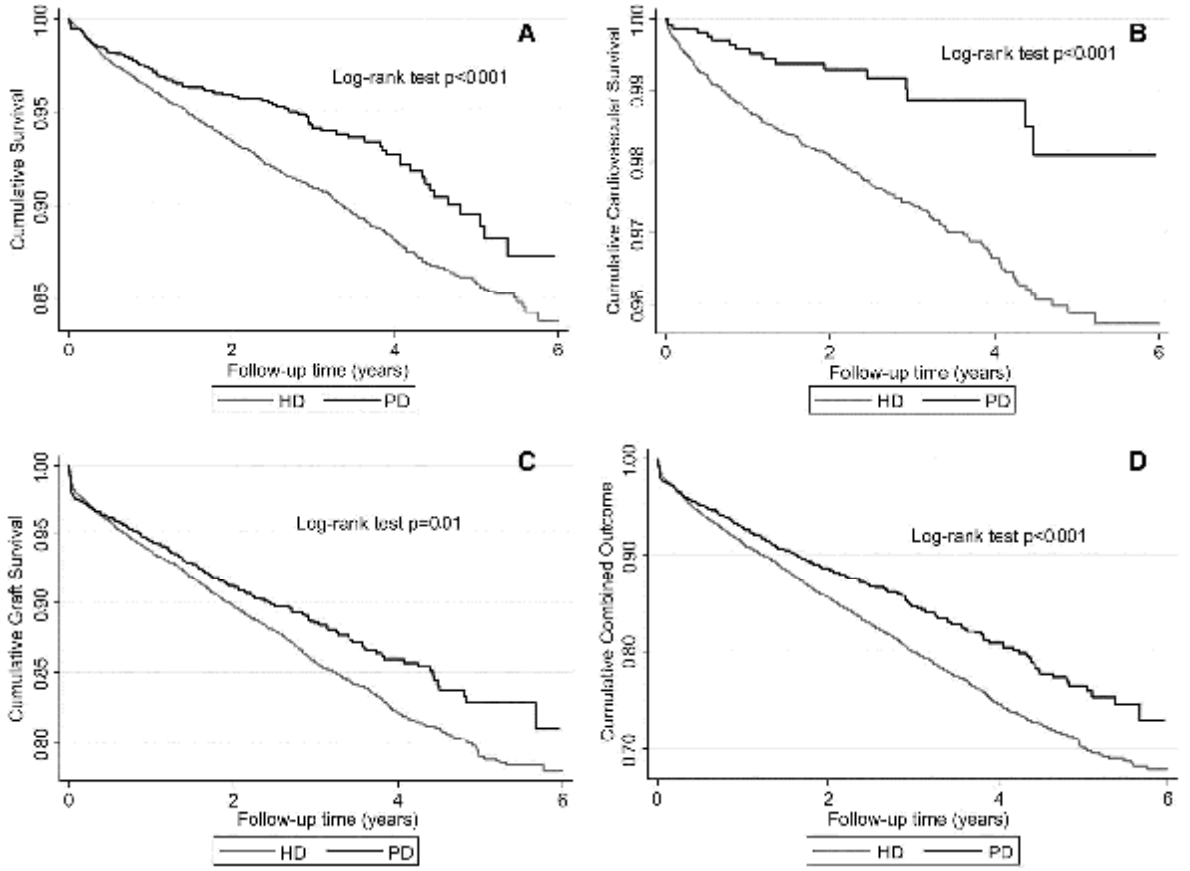
Association of pretransplant dialysis modality with post-transplant outcomes in the entire study cohort.



Miklos Z. Molnar et al. CJASN 2012;7:332-341

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CJASN

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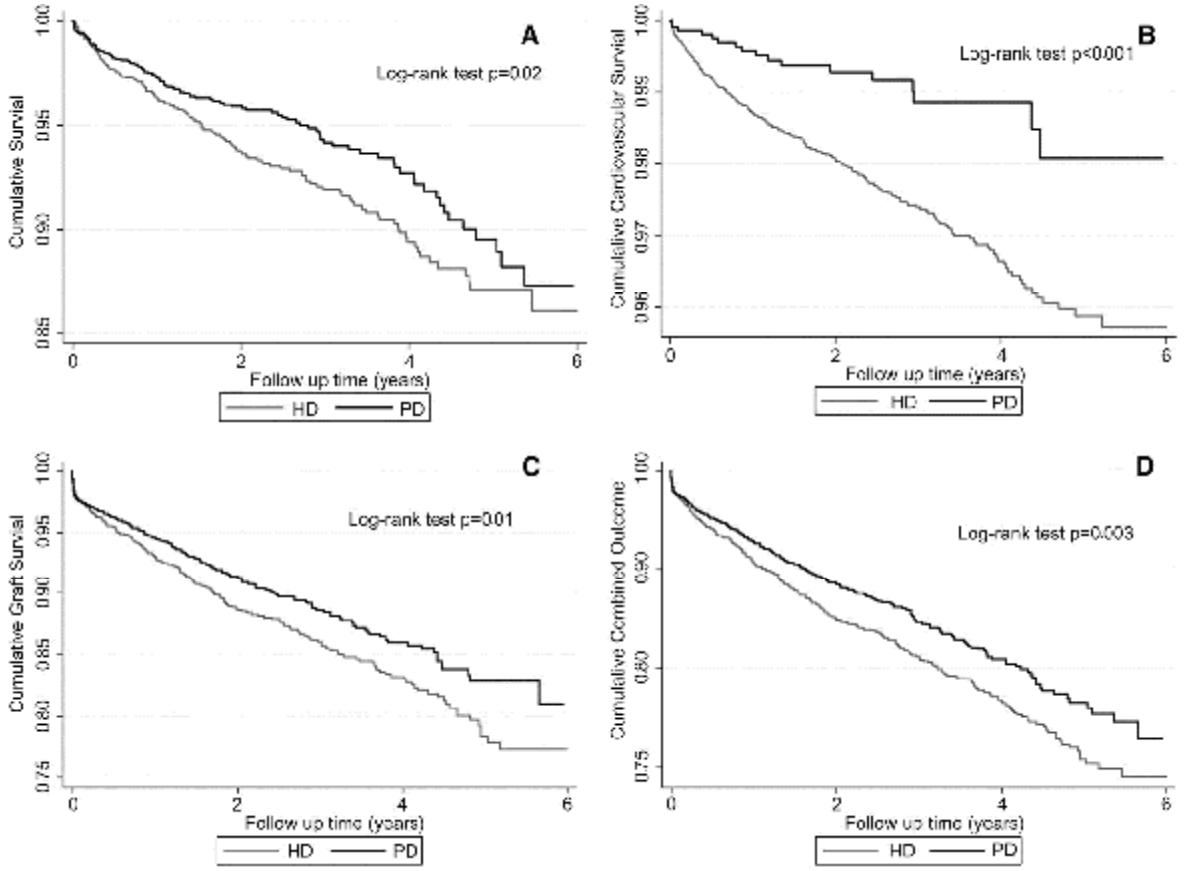

Miklos Z. Molnar et al. CJASN 2012;7:332-341

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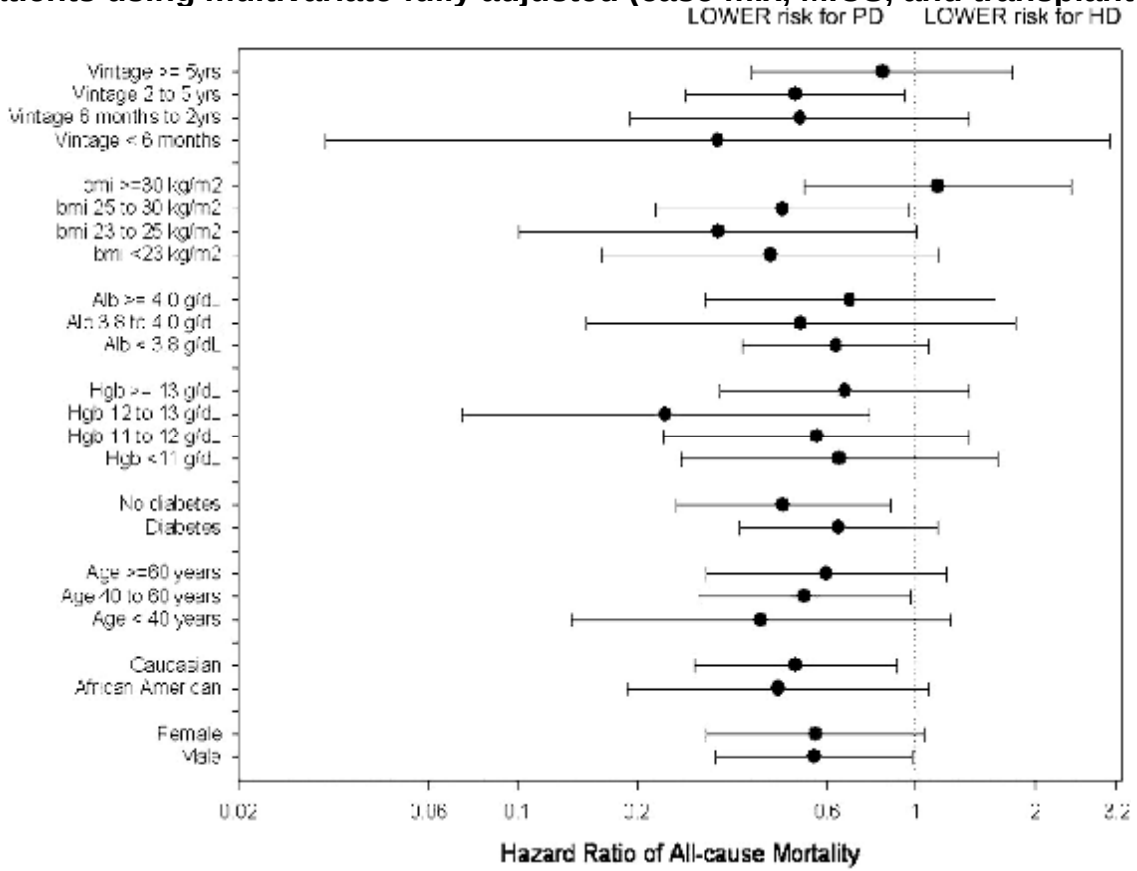
HR (and 95% CI as error bars) of all-cause mortality of patients treated with PD before transplantation compared with patients treated with HD (reference) in a different subgroup of patients using multivariate fully adjusted (case mix, MICS, and transplant ...



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CJASN

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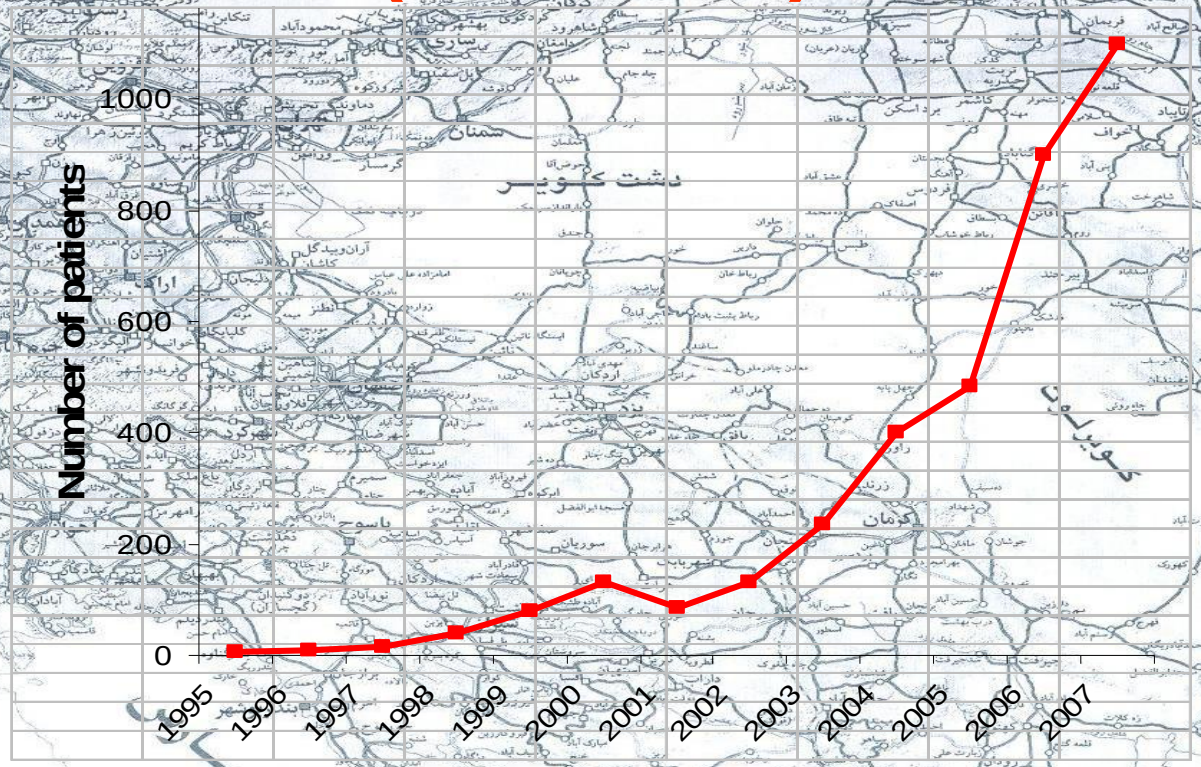
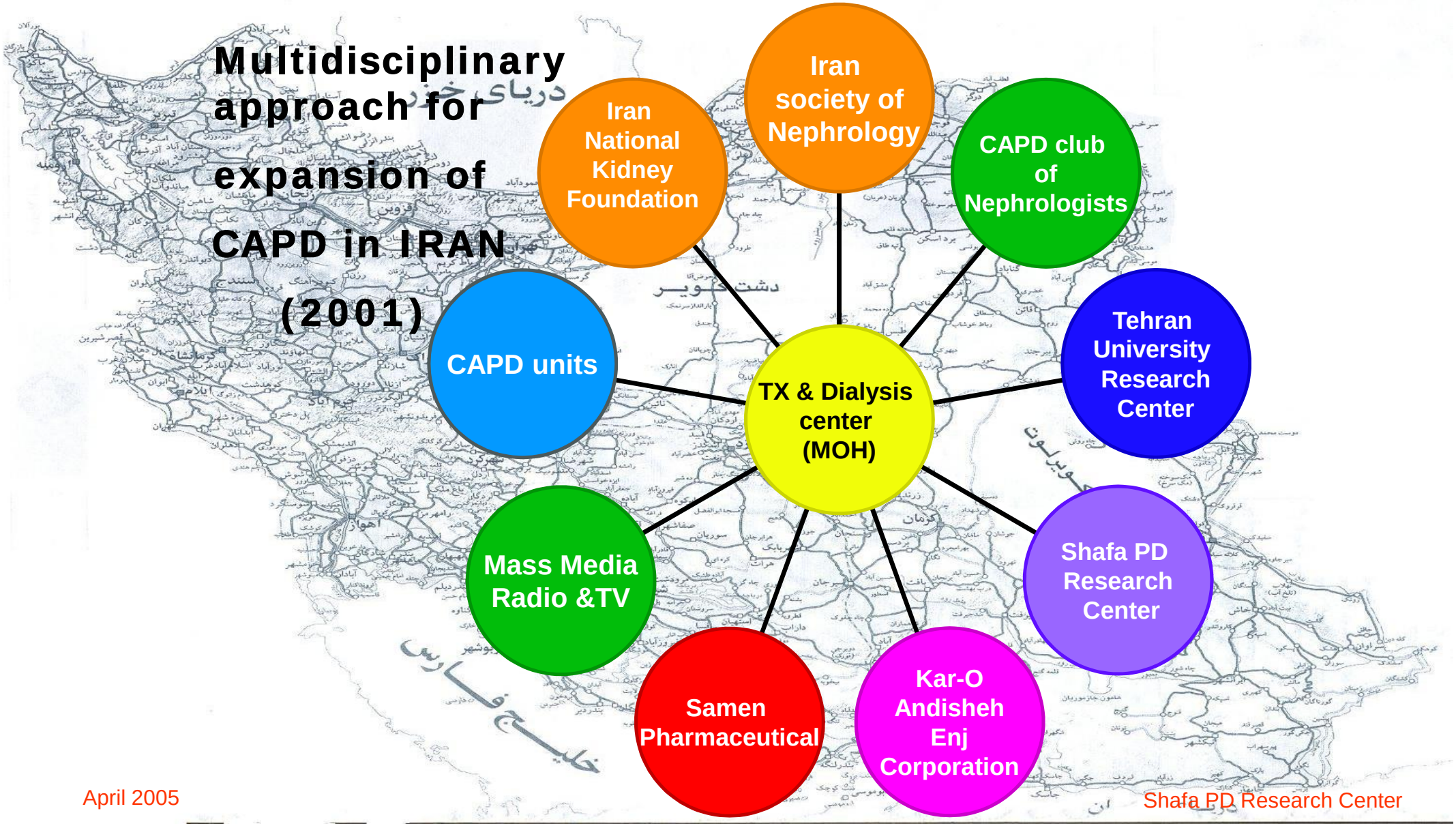
Growth of PD patient in IRAN (1995-2007)



April 2005

Shafa PD Research Center

Multidisciplinary approach for expansion of CAPD in IRAN (2001)



Interventional Program

İmprovement of Peritoneal Dialysis in the Country (Quantity and Quality)

A Comprehensive Computerized Registry System Designed for Peritoneal Dialysis

P.Hatamizadeh, I.Najafi

Shafa Peritoneal Dialysis Research Center

2004


Hakim
Your best approach to
Electronic Health Record
Press any key or click to continue ...
مرکز تحقیقات دیالیز صفاقی شفا
Dr A Shojaee

Peritoneal Dialysis International, Vol. 34, pp. 636–642
doi: 10.3747/pdi.2012.00054

0896-8608/14 $3.00 + .00
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SEVENTEEN YEARS' EXPERIENCE OF PERITONEAL DIALYSIS IN IRAN: FIRST OFFICIAL REPORT OF THE IRANIAN PERITONEAL DIALYSIS REGISTRY

Iraj Najafi,[1] Sudabeh Alatab,[1] Shahnaz Atabak,[2] Nader Nouri Majelan,[3] Houshang Sanadgol,[4] Khadijeh Makhdoomi,[5] Mohammad Reza Ardalan,[6] Jalal Azmandian,[7] Abbas Shojaee,[8] Amir Keshvari,[9] and Mostafa Hosseini[10]

Division of Nephrology,[1] Shariati Hospital, and Nephrology Research Center, Tehran University of Medical Sciences, Tehran; Division of Nephrology,[2] Modares Hospital, Shahid Beheshti University of Medical Sciences, Tehran; Division of Nephrology,[3] Sadoughi Hospital, Yazd University of Medical Sciences, Yazd; Division of Nephrology,[4] Ali-ebn Abitaleb Hospital, Zahedan University of Medical Sciences, Zahedan; Division of Nephrology,[5] Imam Khomeini Hospital, Urmiah University of Medical Sciences, Urmiah; Division of Nephrology,[6] Imam Hospital, Tabriz University of Medical Sciences, Tabriz; Division of Nephrology,[7] Shafa Hospital, Kerman University of Medical Sciences, Kerman; Pegahsoft,[8] Khorasan Science and Technology Park, Mashad; Division of Surgery,[9] Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran; and Department of Epidemiology and Biostatistics,[10] School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

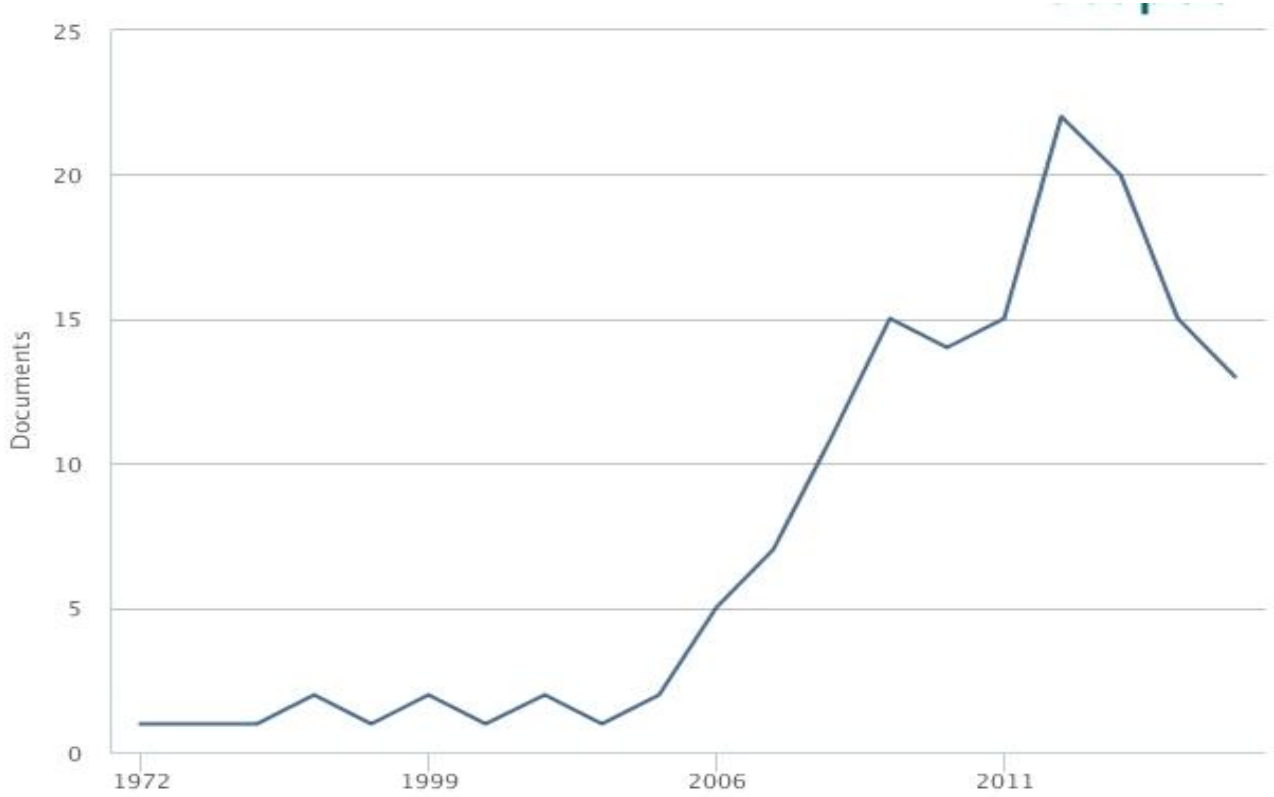
♦ ***Background:*** **To facilitate planning, national renal**

baseline serum hemoglobin and albumin were 10.7 g/dL and

Peritoneal Dialysis International

Downloaded from http://www.pdiconnect.com/t

International papers by year
PD in Iran



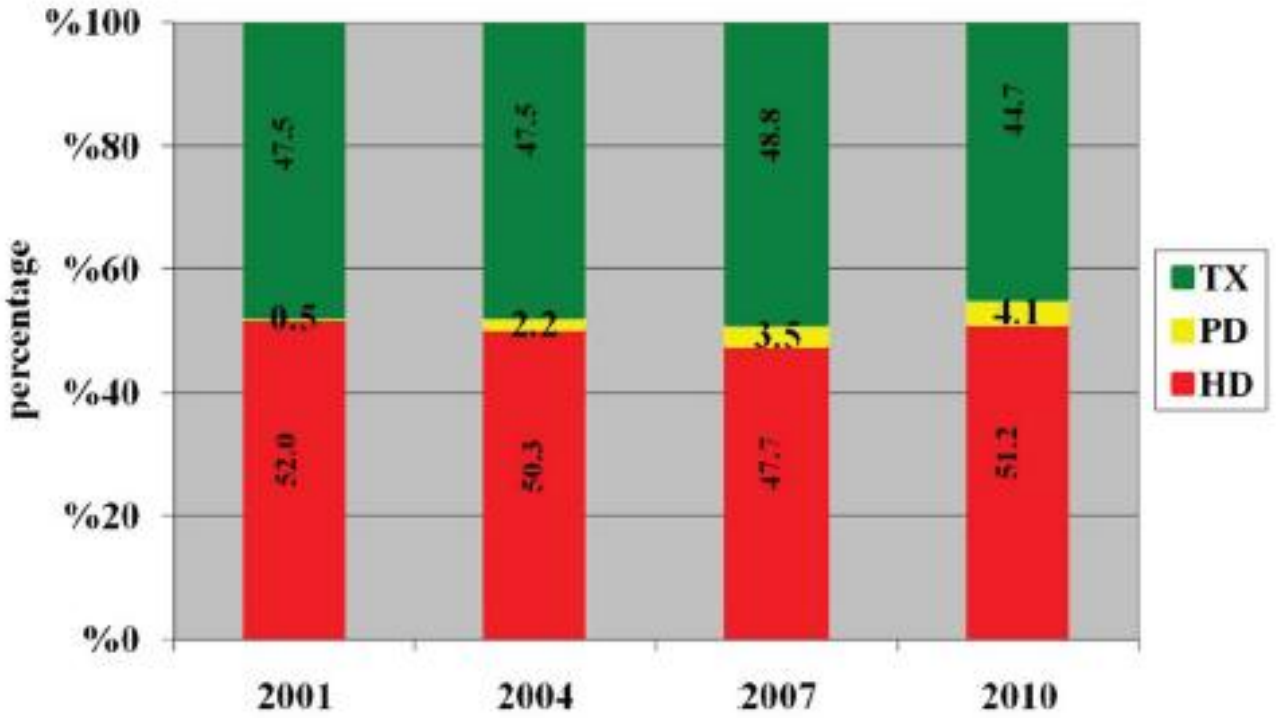
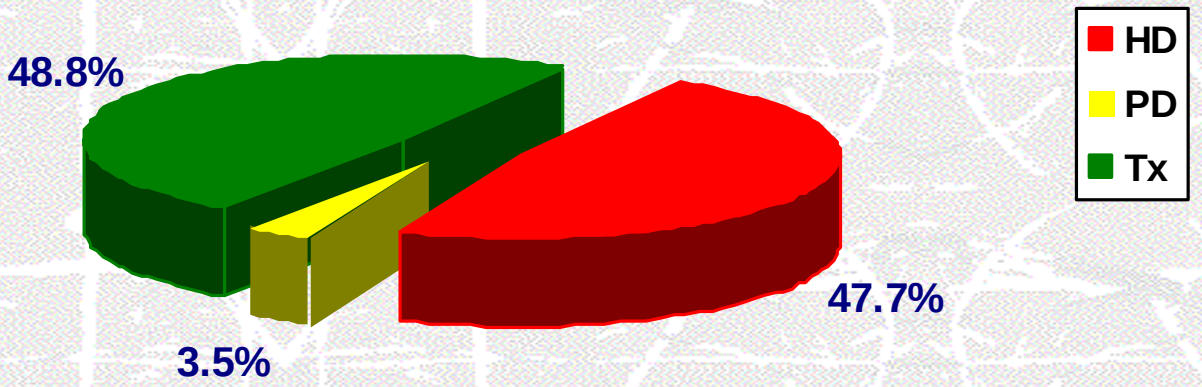


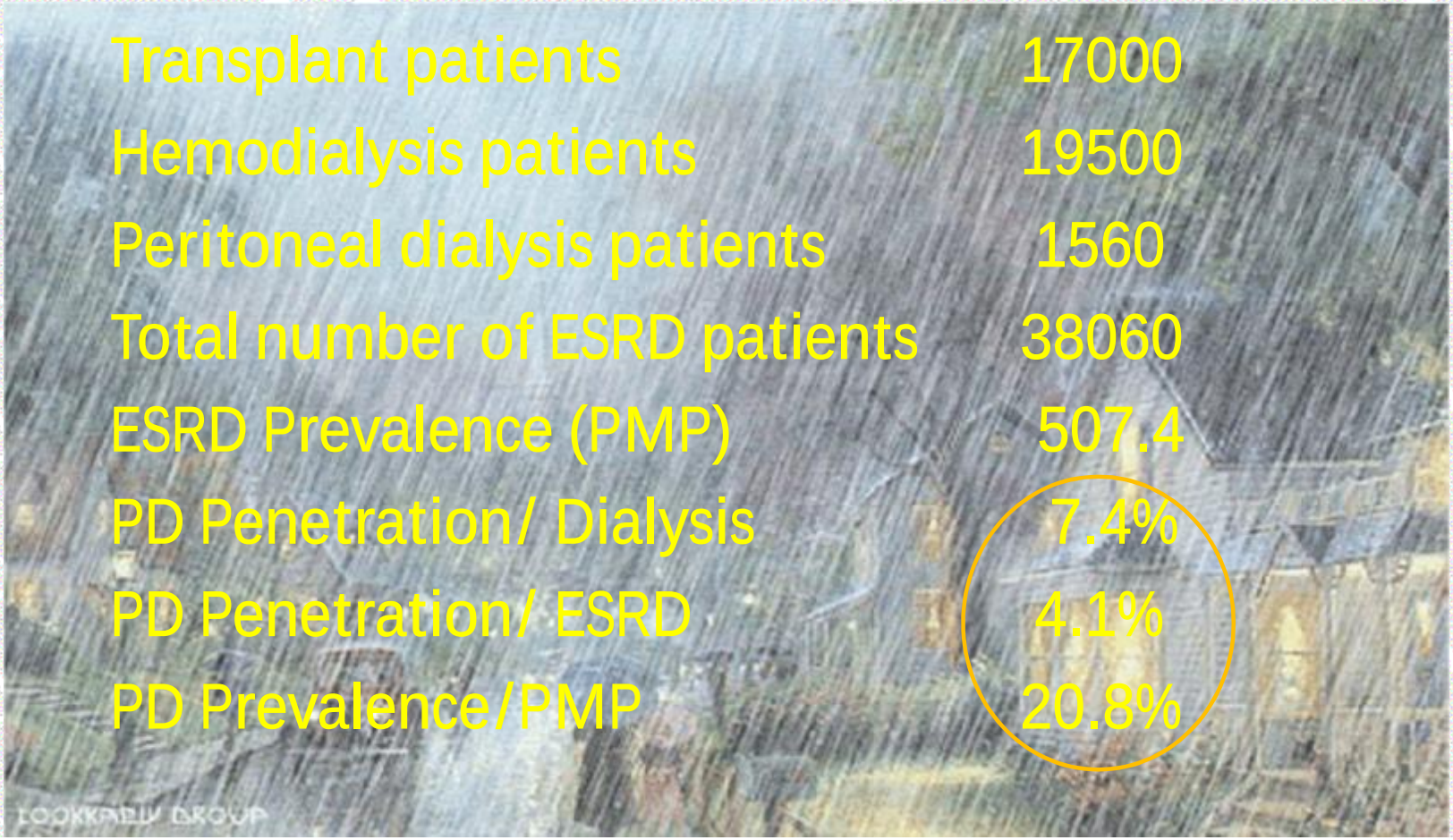
Figure 1 — End-stage renal disease requiring renal replacement therapy in Iran from 2001 to 2010. TX = transplantation; PD = peritoneal dialysis; HD = hemodialysis.

RRT in IRAN 2007

Total of patients : 32686



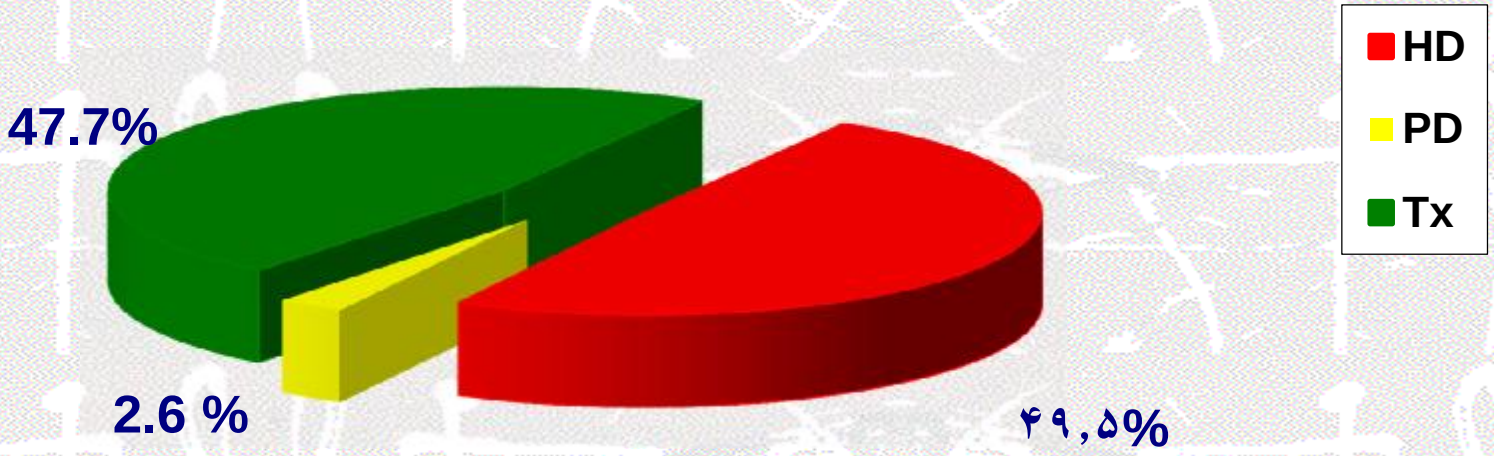
Different ESRD Modalitis in IRAN (2011)



Transplant patients	17000
Hemodialysis patients	19500
Peritoneal dialysis patients	1560
Total number of ESRD patients	38060
ESRD Prevalence (PMP)	507.4
PD Penetration/ Dialysis	7.4%
PD Penetration/ ESRD	4.1%
PD Prevalence/PMP	20.8%

RRT in IRAN 2017

Total of patients :64324



PD Numbers in IRAN
(2017)

Transplant patients	32000
Hemodialysis patients	30700
Peritoneal dialysis patients	1624
Total number of ESRD patients	64324
PD Penetration/ Dialysis	5.2%
PD Penetration/ ESRD	2.6%
PD Prevalence/PMP	20.3%

May 2017

IRAN CAPD REGISTRY

Latest Report (2016)

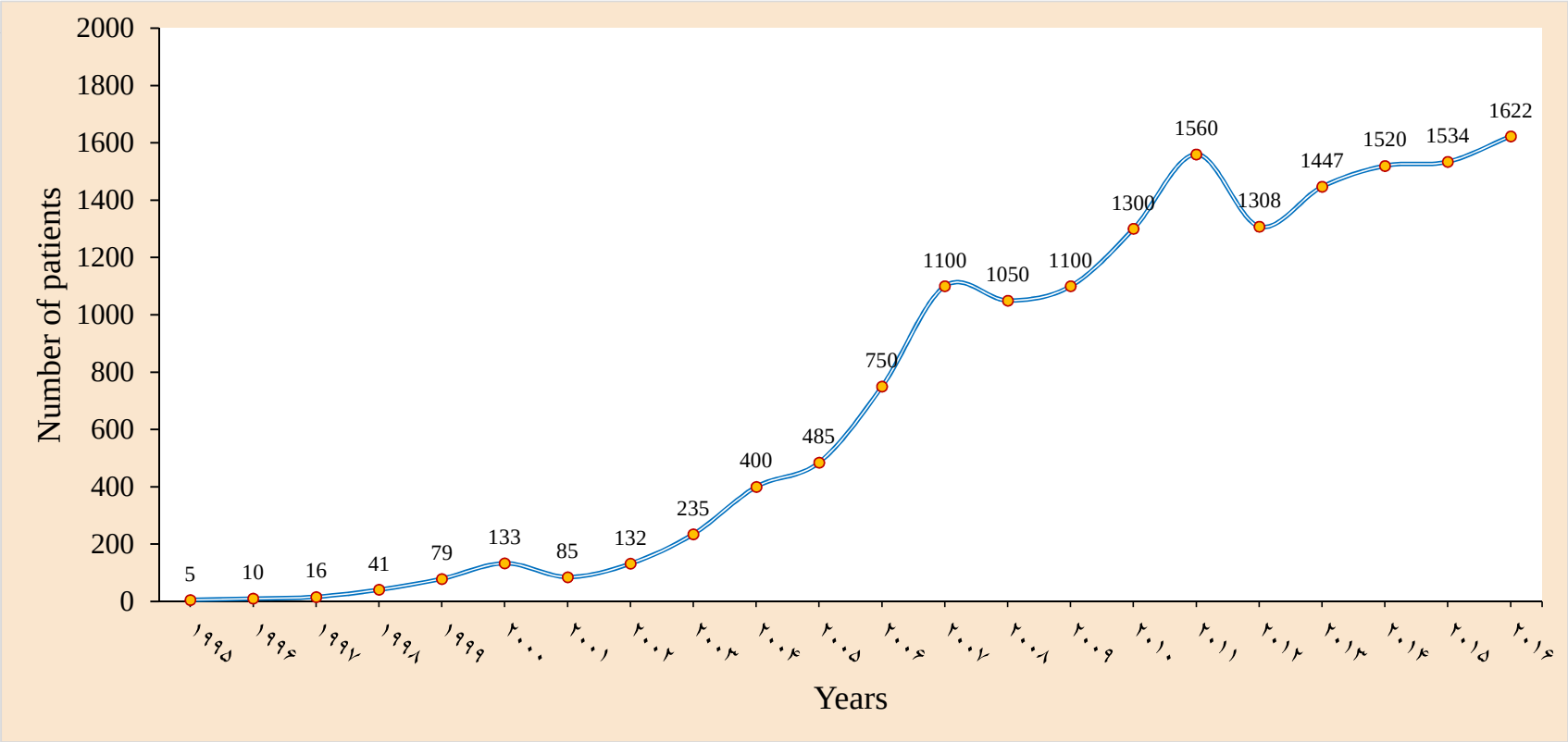
Descriptive Data

IRAJ NAJAFI

2017

MAY 2017

Growth of PD patient in IRAN
(1995-2016)



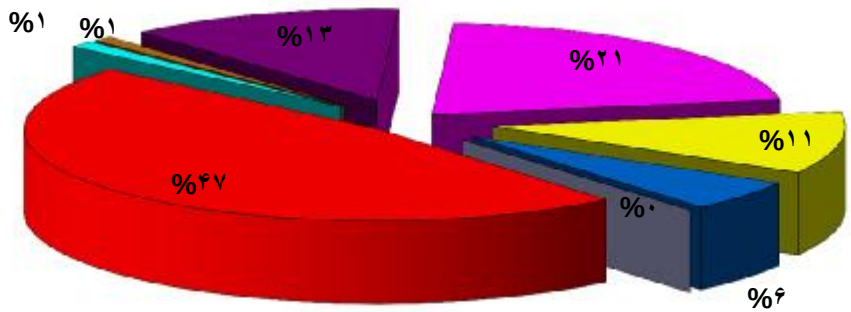
Iran CAPD Registry

Etiology of CKD	Before 2012	After 2012
DM	1285 (35.2)	186 (42.2)
HTN	843 (23.1)	134 (30.4)
Unknown	615 (16.9)	47 (10.7)
GN	248 (6.8)	12 (2.7)
APKD	150 (4.1)	17(4.1)
Stone	102 (2.8)	14 (3.2)
Other	217 (6.0)	16 (3.6)
Reflux	78 (2.1)	9 (2.0)
Familial	92 (2.5)	3 (0.7)
Toxin	16 (0.4)	2 (0.4)
Total	3646 (100.0)	406 (100.0)

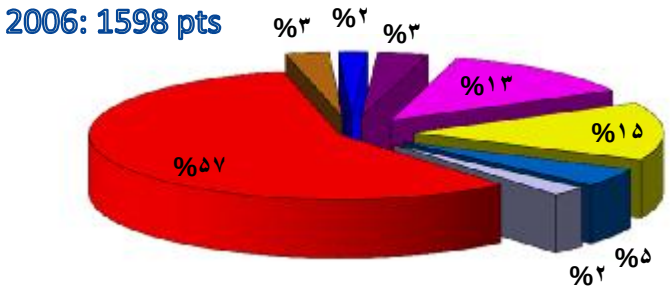
Iran CAPD Registry 2014

(Cause of Drop out N=803)

2014: 3395 pts

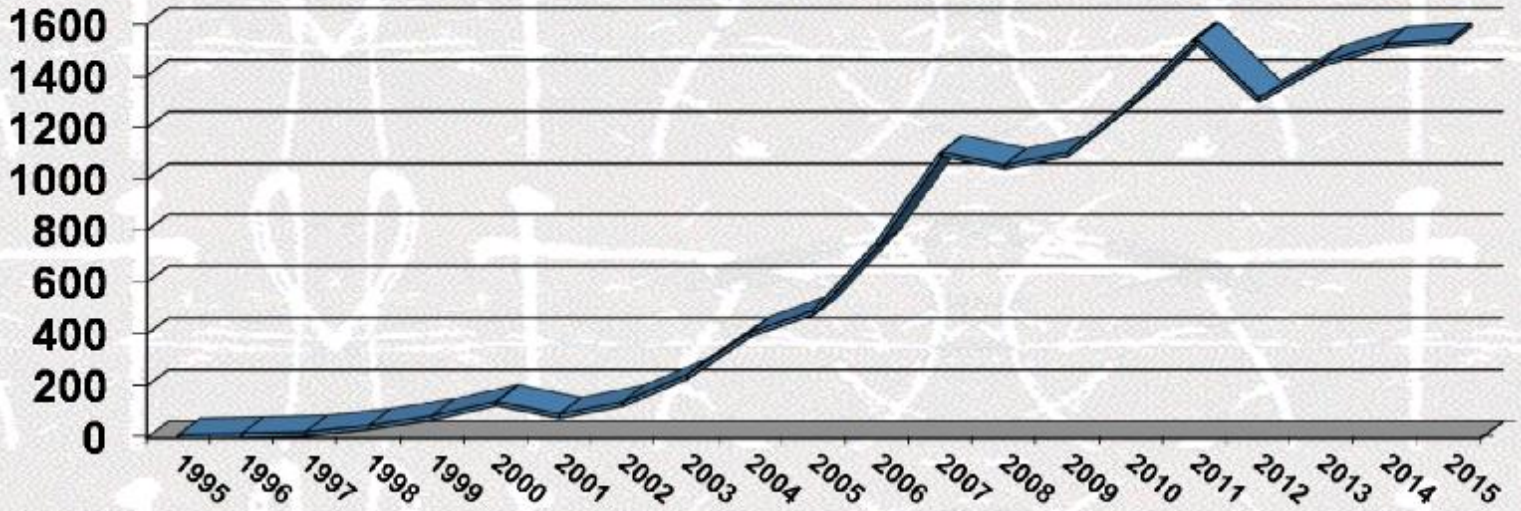


2006: 1598 pts



Growth of PD patient in IRAN

(1995-2014)



sluggish

Fast

Stagnation

September 2015

What is the probable reasons for PD stagnation in the last 7-8 years (2011-2019)

1) The Price of a single Glucose base solution has increased %800 something not happening in HD&TX
2) The cost of a patient on CAPD, is %20 higher than HD, makes no desire in MOH to expand the program
3) Questions regarding the Quality of our solutions?!
4) Local production of PD solutions exclusively by one producer with no competitors
5) PD continue to be free of charge for nephrologists and nurses with no reimbursement (the law has not get executed)

What is the probable reasons for PD stagnation in the last 7-8 years (2011-2019)

Could it be due to international sanctions against Iran?!

The issue that raise by local producer

PD as a Nauseating Bridges

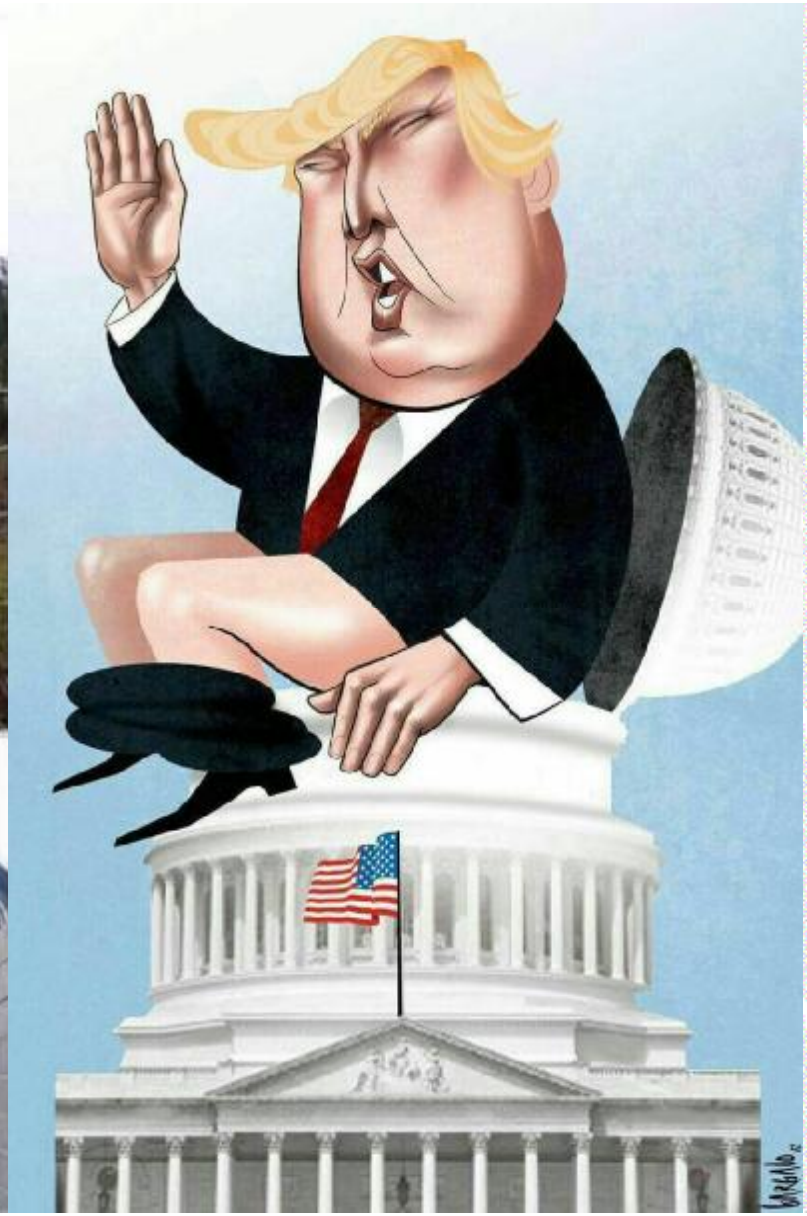
Due to international sanctions against Iran the availability pattern of our PD solutions .in market is sometimes make us filling sick

Hope to see

Iran nuclear deal with the 6 world powers

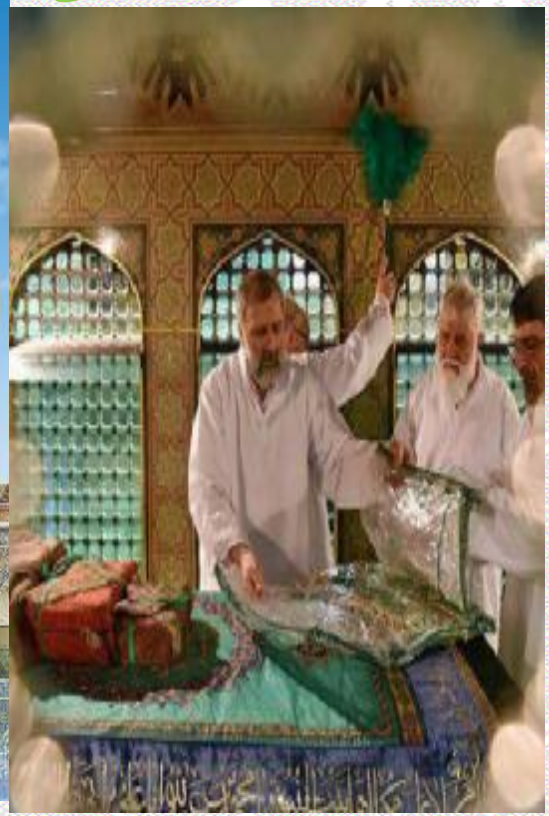
PD as a Safe and Healthy Bridge to TX

Do you ever look at stuff and wonder how it got there?



با شکوه ترین و بزرگترین موقوفه جهان

بارگاه ملکوتی ثامن الحجج امام رئوف حضرت رضا(ع)



Key strategies for facilitating PD utilization

- Implementation of policies and incentives that favor this modality
- Production and supply of peritoneal dialysis fluid at a low cost
- Training for nephrologists to enable increased utilization
- Ensure that rates of technique failure continue to decline
- Further growth in PD use is required to enable this modality to become an integral part of renal replacement therapy

PD Solutions

2,10,1394

Component of conventional PD solutions

- Glucose(13.6mg/ml, 22.7mg/ml, 38.6mg/ml)
- Sodium 132mmol/L
- Potassium 0mmol/L
- Calcium 1.25-1.75mmol/L
- Magnesium 0.25-0.75mmol/L
- Chloride 102mmol/L
- Lactate 35-40mmol/L
- pH 5.0-5.5

Composition of standard peritoneal dialysis solution

Na	**132 mmol/l**	
Ca	**1,25mmol/l**	
Mg	**0,5 mmol/l**	
Cl	**100 mmol/l**	
lactate	**35 mmol/l**	**ev. lactate/bicarbonate**
glucose	**1,36-4,25 g/dl**	
osmolarity	**347-486**	
pH	**5,2**	

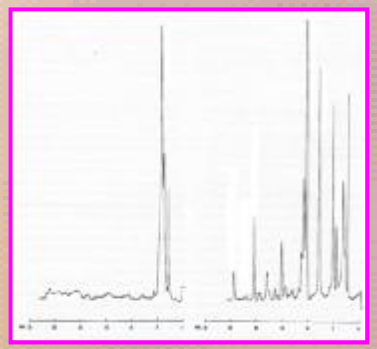
GDP (degradation products of glucose)

How do GDP's impact on peritoneal membrane function

Glucose

Heat Sterilisation

Glucose Degradation Products (GDP's)



Filter Heat

Proteins

AGE Formation

Modulation of Cell function

Fibrosis

Inflammation

Angiogenesis

Membrane structural and functional alterations

Heat sterilization effect

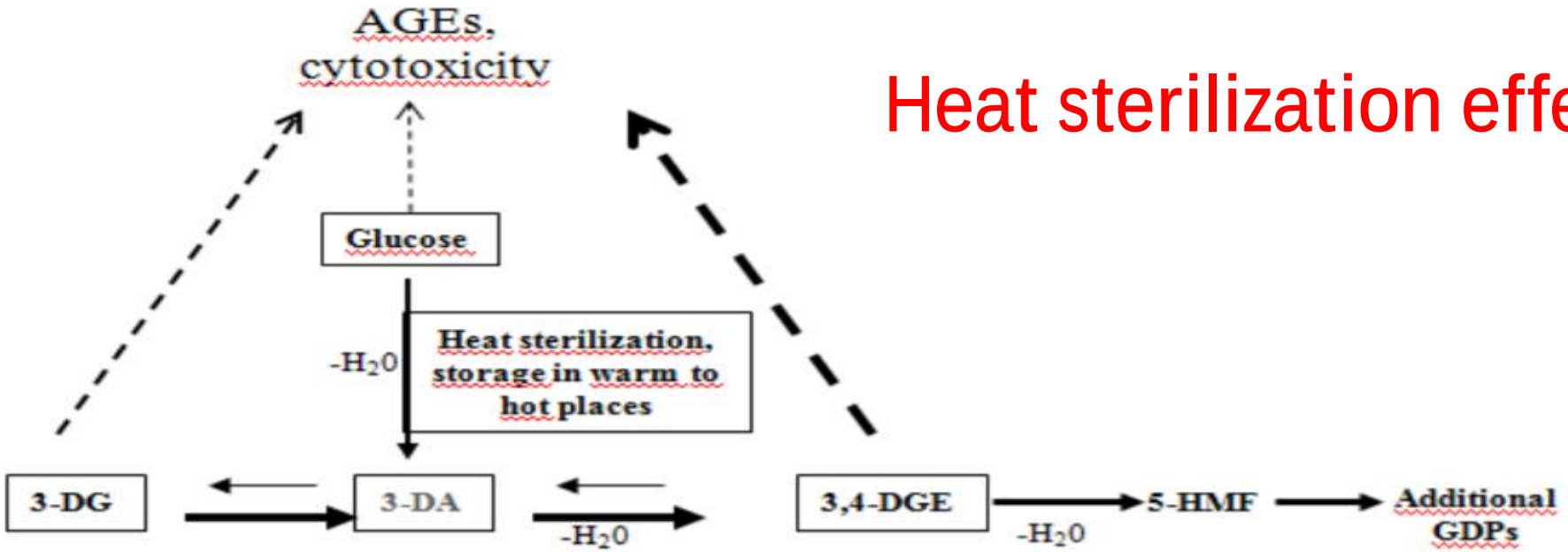
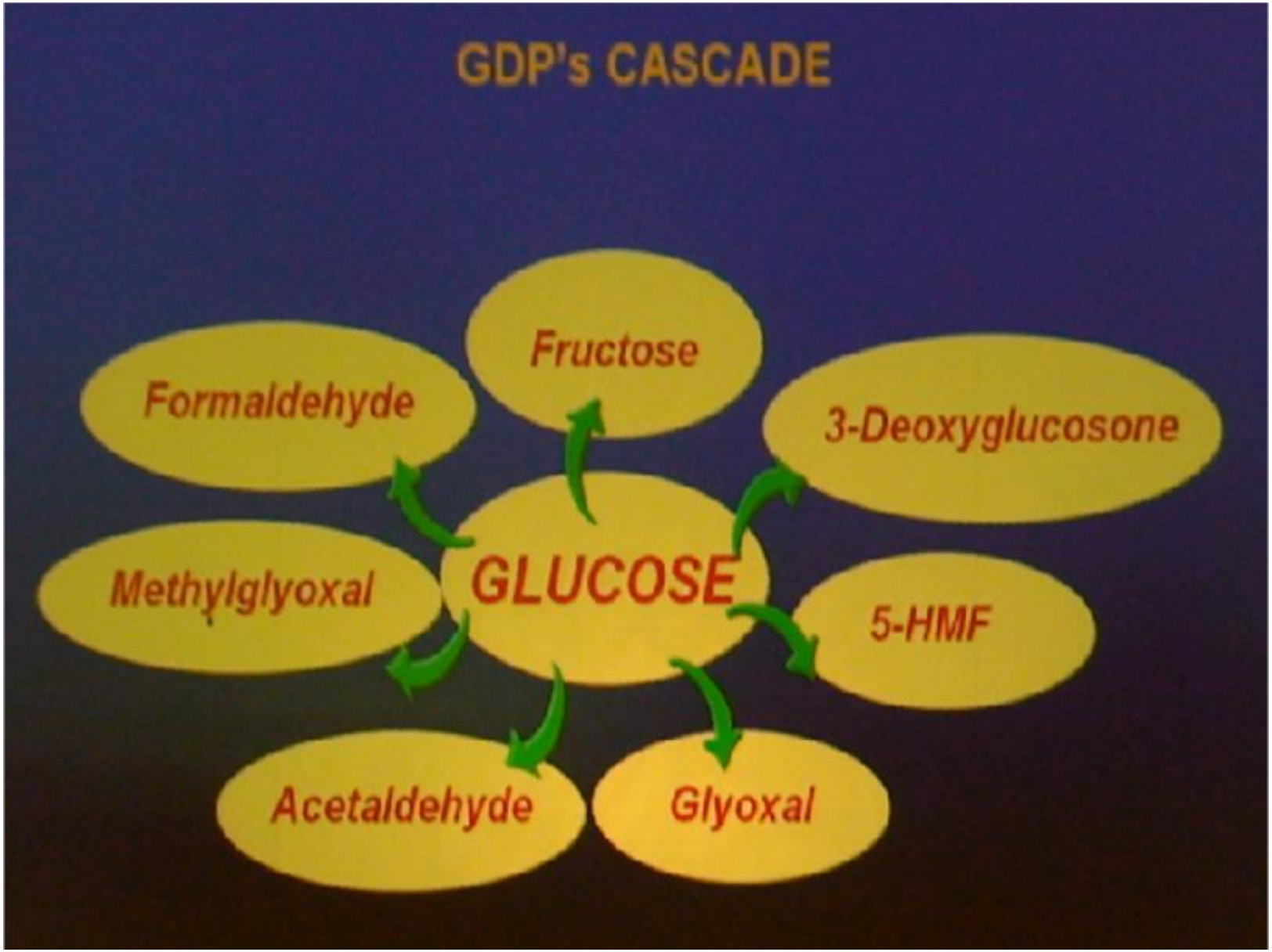
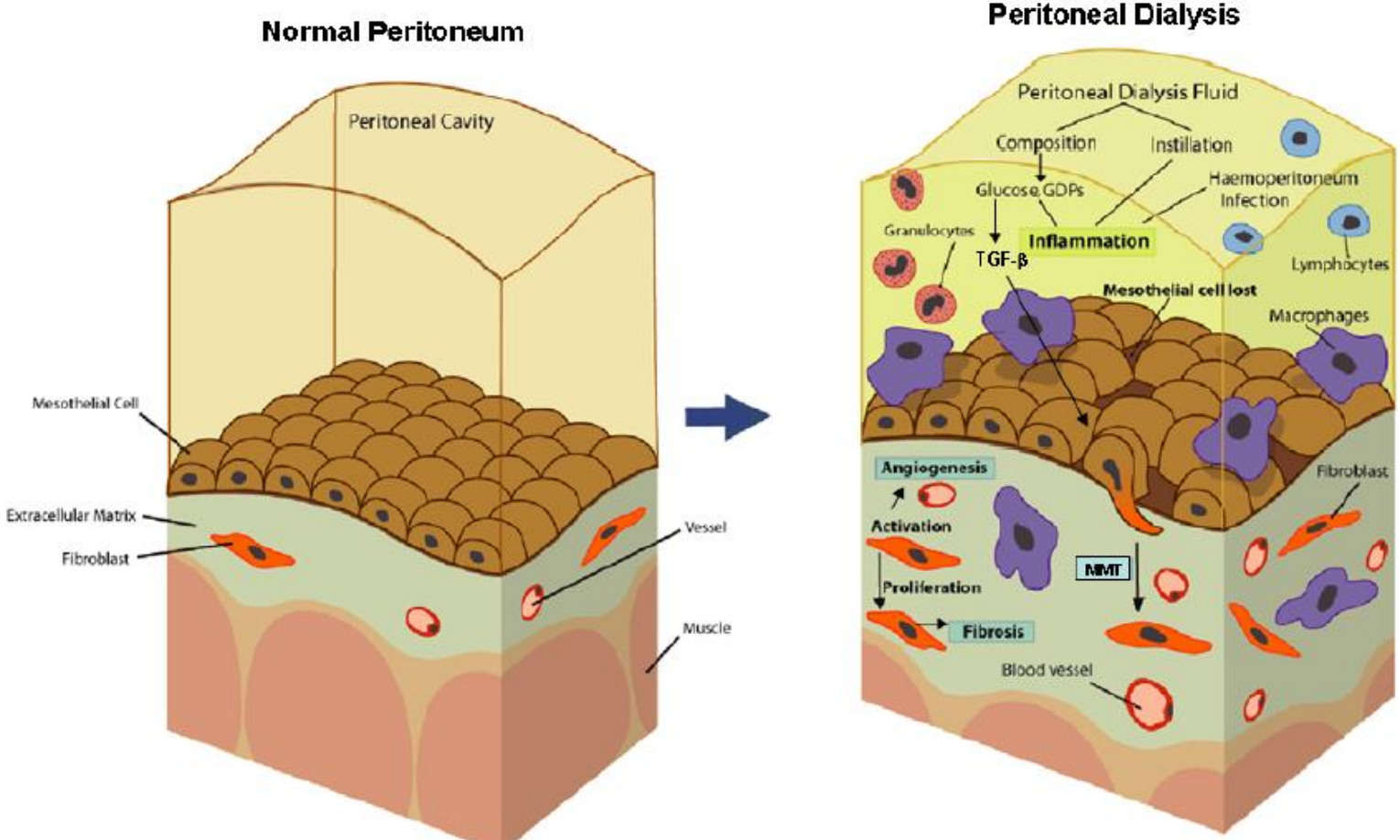
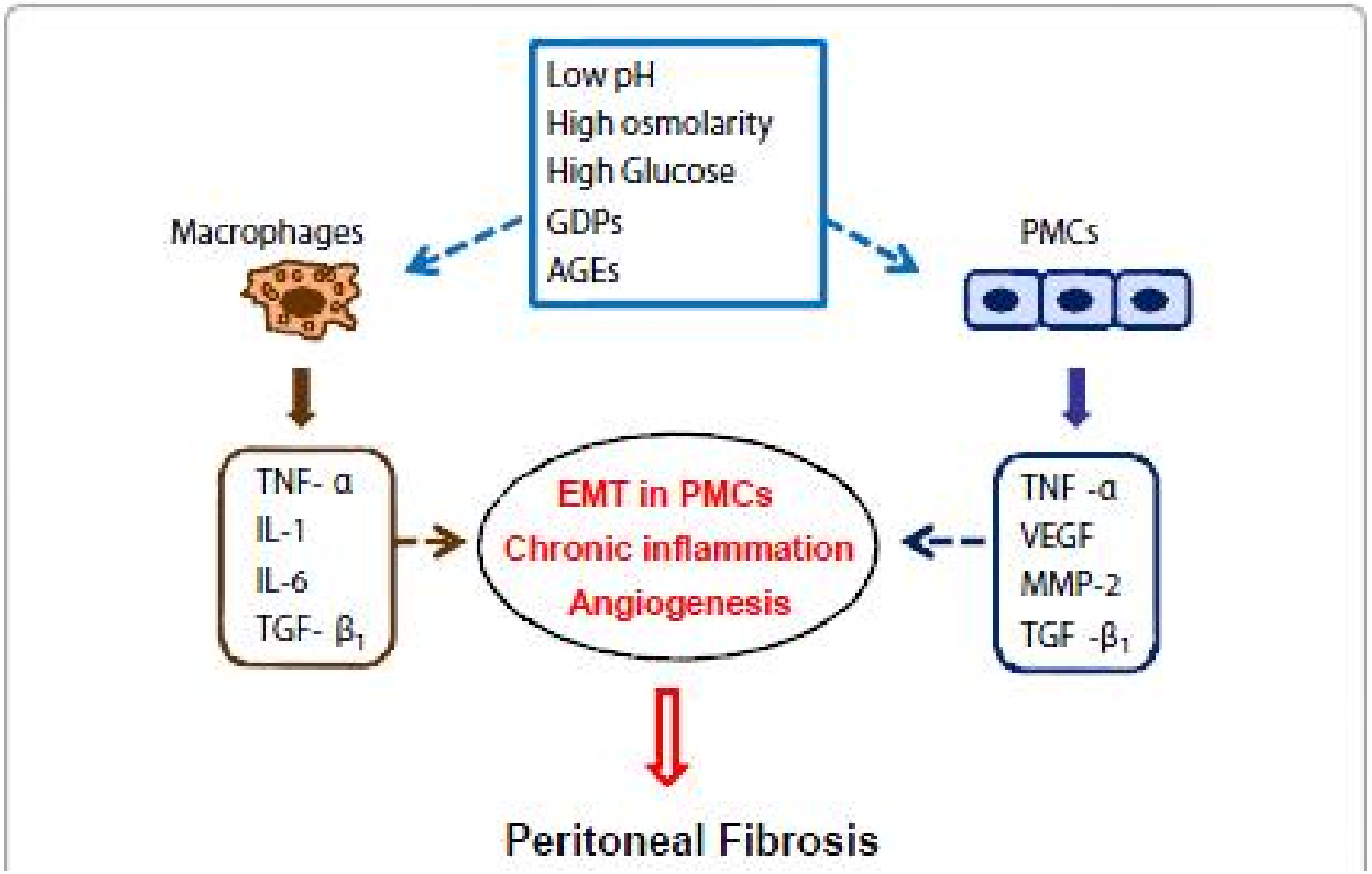


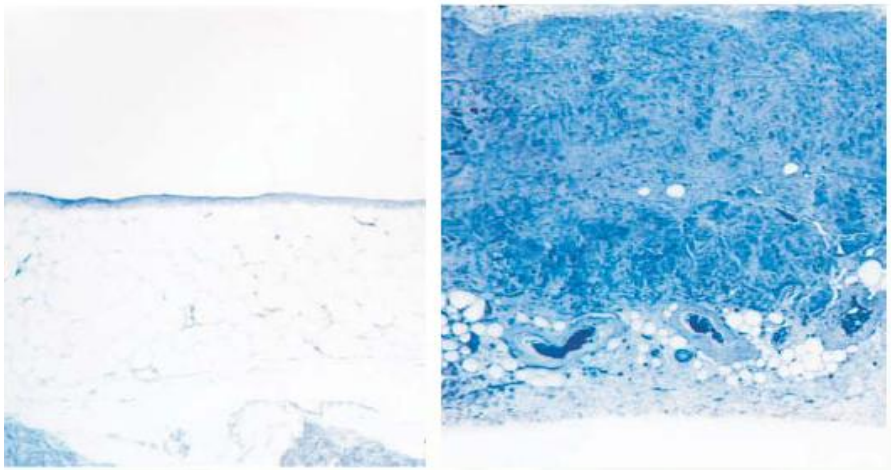
Fig. 2. **GDP generation from glucose in PD fluids during heat sterilization and storage.** Successive dehydration steps of the glucose molecule lead to initial GDPs and these are subsequently degraded into smaller molecules. There is a temperature-dependent balance between 3-DG, 3-DA and 3,4-DGE. Increasing temperature shifts the equilibrium to the right, towards the most toxic compound, 3,4-DGE. High concentrations of glucose are cytotoxic and lead to AGE formation, but 3-DG and, above all, 3,4-DGE lead to higher cytotoxicity and AGE generation. The thick dashed lines represent the ability to induce biological effects. 3-DG: 3-deoxyglucosone, 3-DA: 3-deoxyaldos-2-ene, 3,4-DGE: 3,4-dideoxyglucosone-3-ene, AGE: advanced glycation products. HMF: hydroxymethylfurfural. Adapted from reference (Ortiz, A. et al. 2006). Additional GDPs include furaldehyde, formaldehyde, acetaldehyde, methylglyoxal, glyoxal.


GDP's CASCADE
Fructose
Formaldehyde
3-Deoxyglucosone
GLUCOSE
Methylglyoxal
5-HMF
Acetaldehyde
Glyoxal


Normal Peritoneum
Peritoneal Cavity
Mesothelial Cell
Extracellular Matrix
Fibroblast
Vessel
Muscle
Peritoneal Dialysis
Peritoneal Dialysis Fluid
Composition
Instillation
Glucose,GDPs
Haemoperitoneum
Infection
Granulocytes
Inflammation
TGF-β
Lymphocytes
Mesothelial cell lost
Macrophages
Angiogenesis
Fibroblast
Activation
MMT
Proliferation
Fibrosis
Blood vessel


Low pH
High osmolarity
High Glucose
GDPs
AGEs
Macrophages
PMCs
TNF- α
IL-1
IL-6
TGF- β1
EMT in PMCs
Chronic inflammation
Angiogenesis
TNF -α
VEGF
MMP-2
TGF -β1
Peritoneal Fibrosis

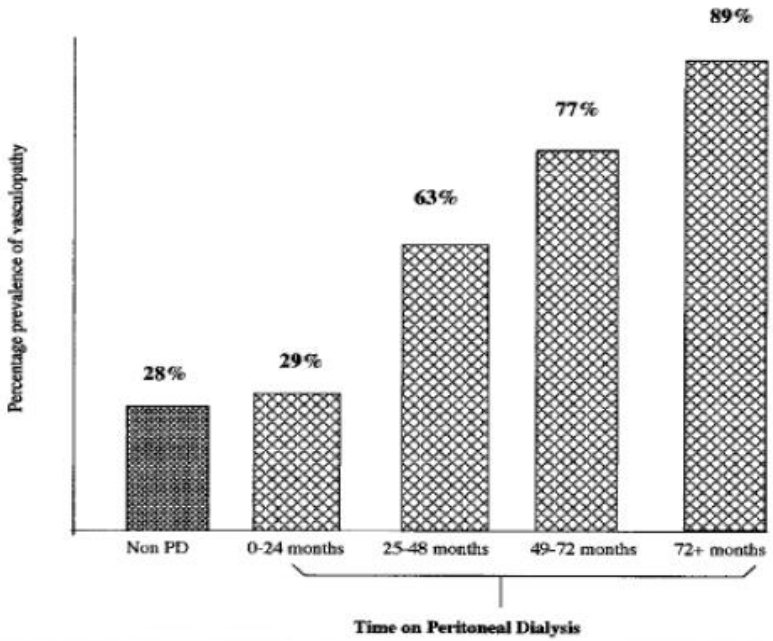
Morphologic Changes in Peritoneal Barrier: Peritoneal Biopsy Registry



Normal

After 9 years of PD

Compact Sub-mesothelial zone



- Peritoneal Biopsy Registry
- 20 Centers, 63% cases at Cardiff
- 130 PD patients

FRONTIERS IN PD

Williams JD et al: *J Am Soc Nephrol* 2002; 13: 470–479

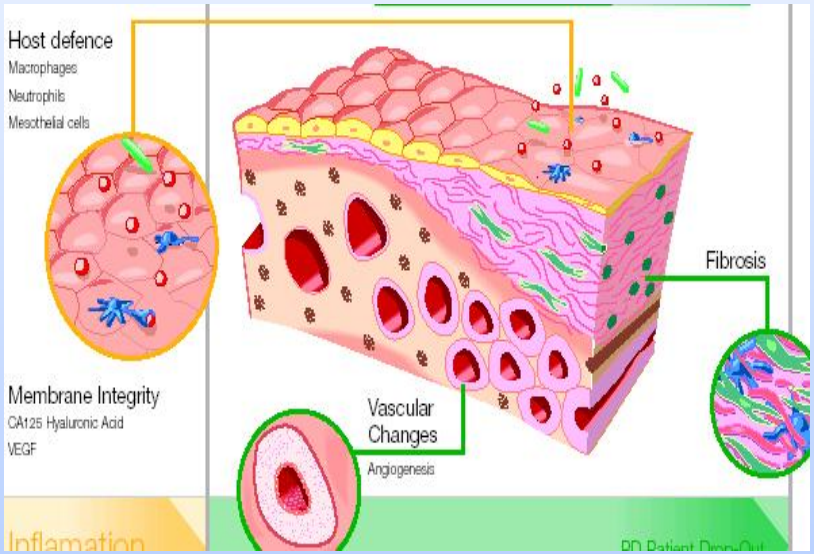
Membrane characteristics change
with time on therapy

1. Neo-angiogenesis
2. Vasculopathy
3. Interstitial fibrosis

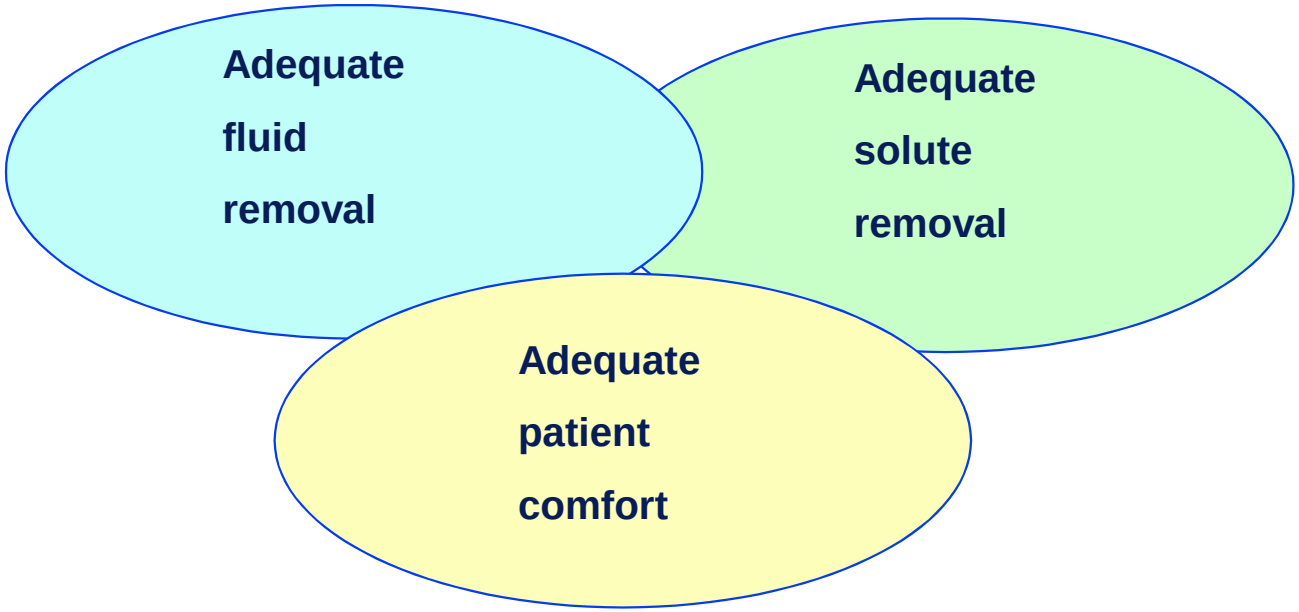
lead to ;

Ø Decreased ultrafiltration capacity

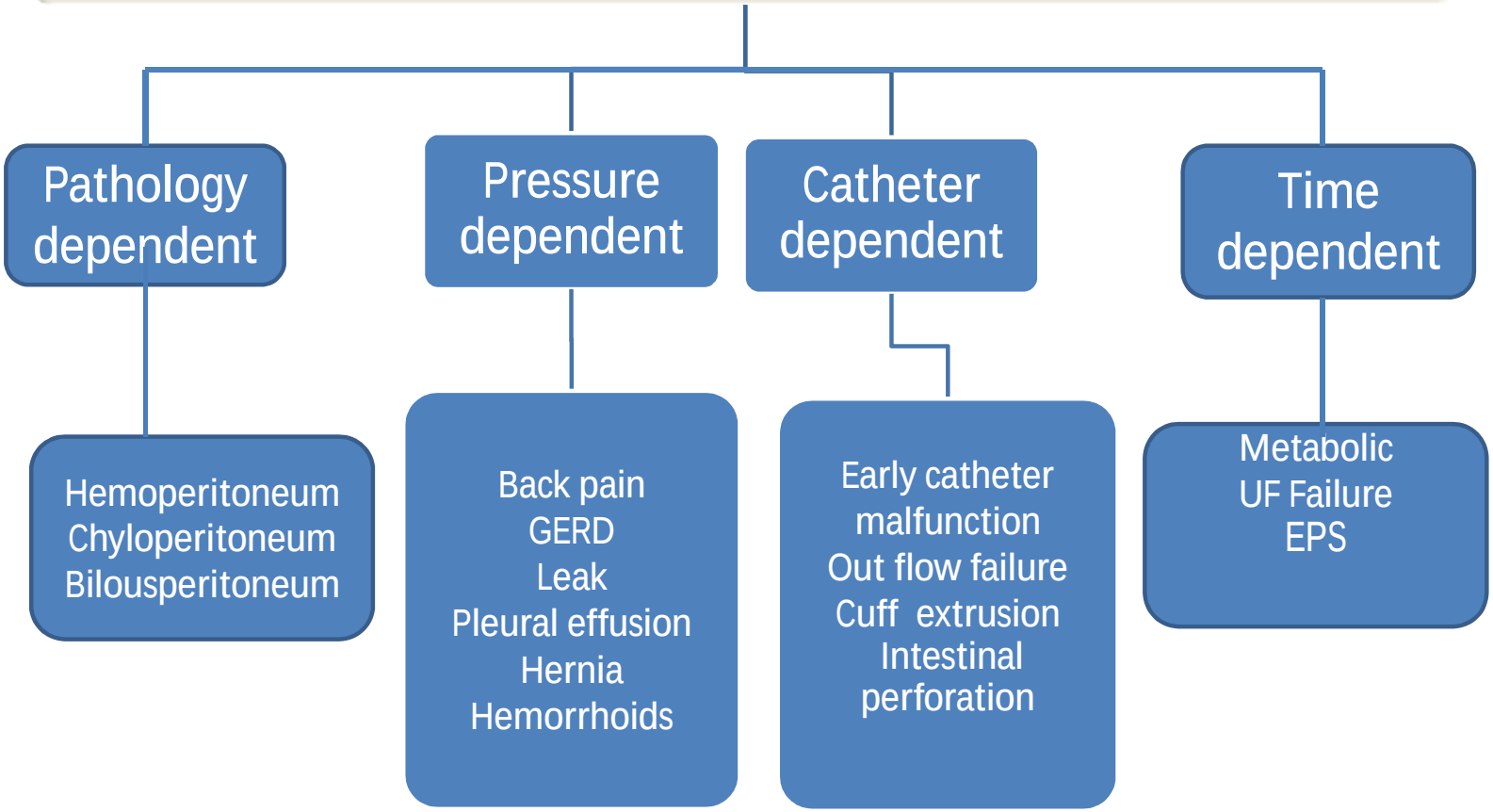
Ø Increase in the transport rate for small solutes



What is Adequacy?



Non-Infectious complications

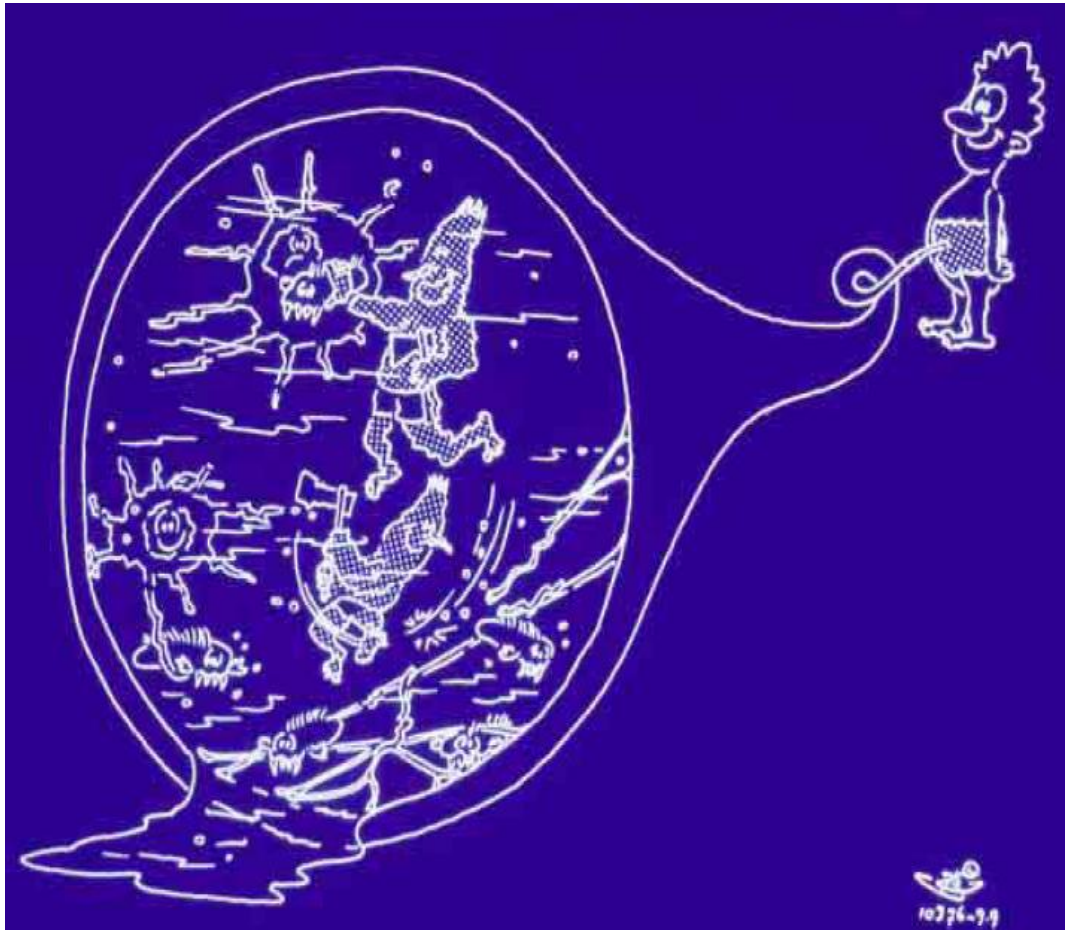


Biocompatible dialysis fluids for peritoneal dialysis

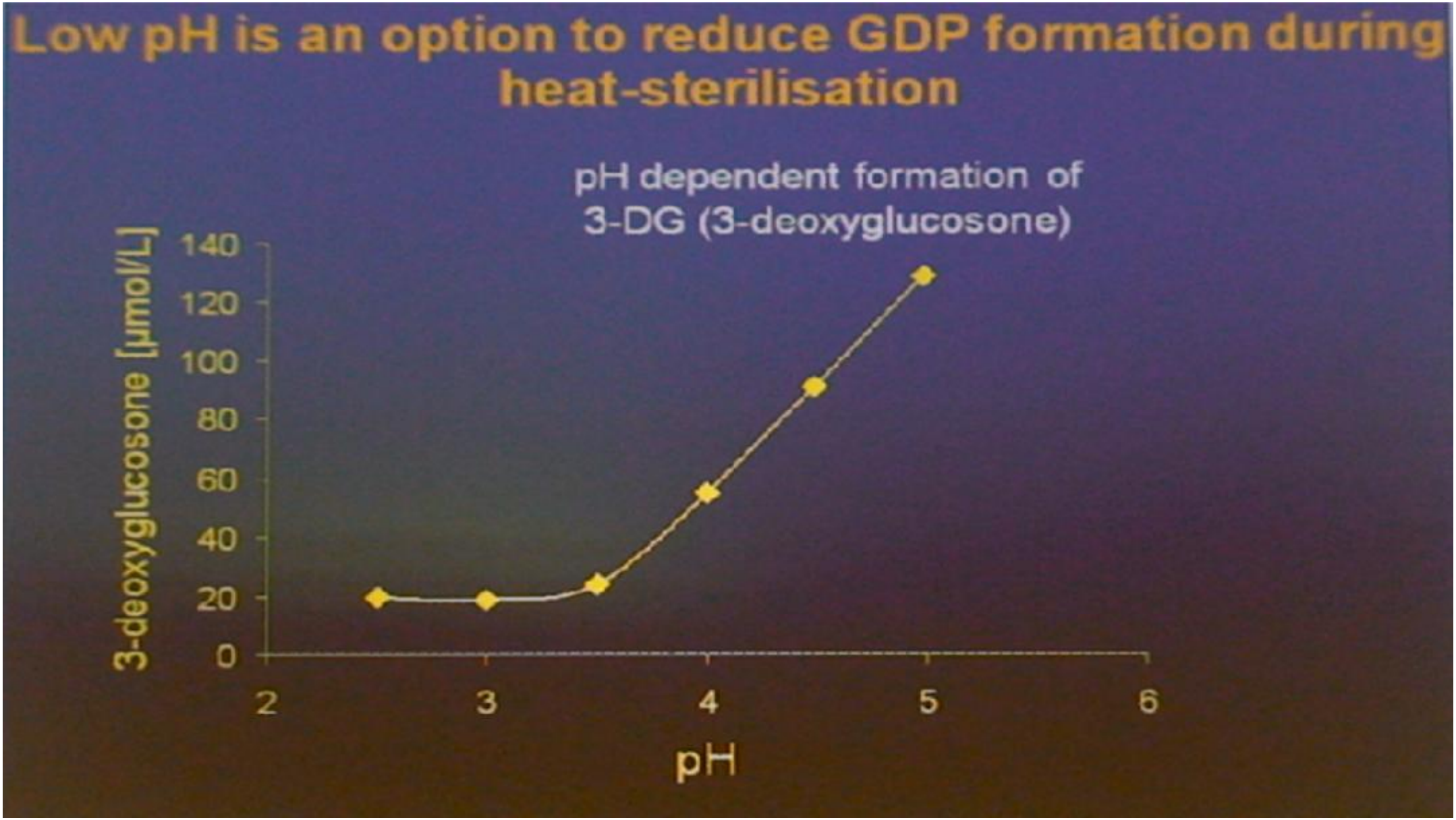
- The longevity of PD can be limited by membrane injury, which is partly as a result of biologically 'unfriendly' PD solutions, which are acidic and consist of high levels of glucose and toxic GDP.

- To overcome these hurdles, biocompatible PD solutions (i.e. with a neutral pH and low levels of GDP or with a glucose-alternative like icodextrin) have been manufactured with the aim of providing patient benefit.

Bicarbonate Vs Lactate Solutions



Low pH is an option to reduce GDP formation during heat-sterilisation

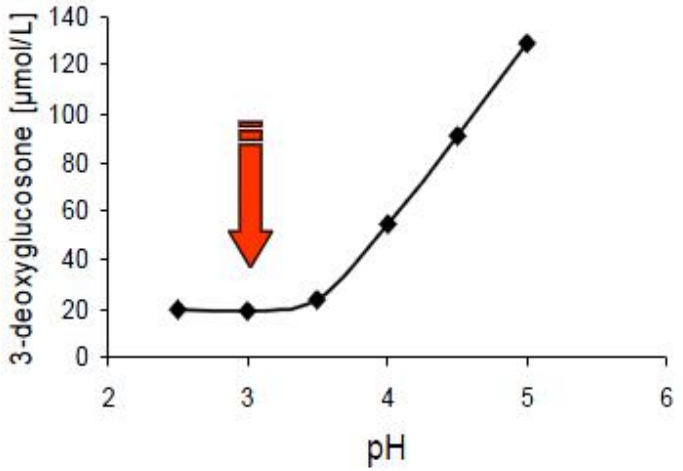


Methods to reduce the GDP load in PD

① (Filter sterilisation)

② Separation of glucose from catalysing substances during heat sterilisation

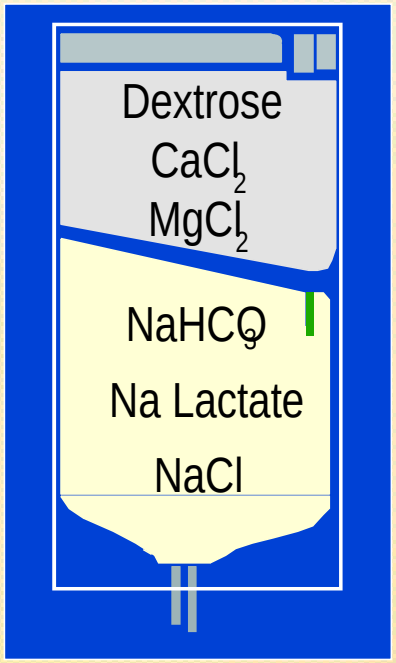
③ Lowering the pH during heat sterilisation



④ Increasing the glucose concentration during heat sterilisation

② - ④ can be achieved in multi-chamber bags

Physioneal® Bicarbonate-buffered PD Solution



Product Description

- Ca and Mg separated from bicarbonate during sterilization to prevent precipitate formation
- Dextrose separation during sterilization results in very low levels of GDPs
- pH 7.4

A Natural Solution for a Natural Membrane

Bicarbonate/Lactate PD Solutions

Physioneal® offers a:

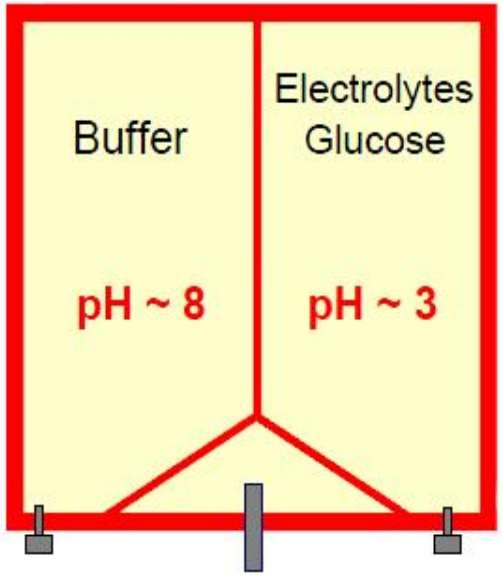
- *physiological pH*
- *physiological bicarbonate concentration*
- *physiological pCO_2*
- *reduced level of GDPs*

Coles GA., et al., NDT 1998; 13:3165-3171
Mactier RA., et al., KI 1998; 53:1061-1067
McKenzie R., et al., JASN 1998; 9:1499-1506
Topley N., et al., JASN 1999; 10, 230A (A1169)

PHYSIONEAL

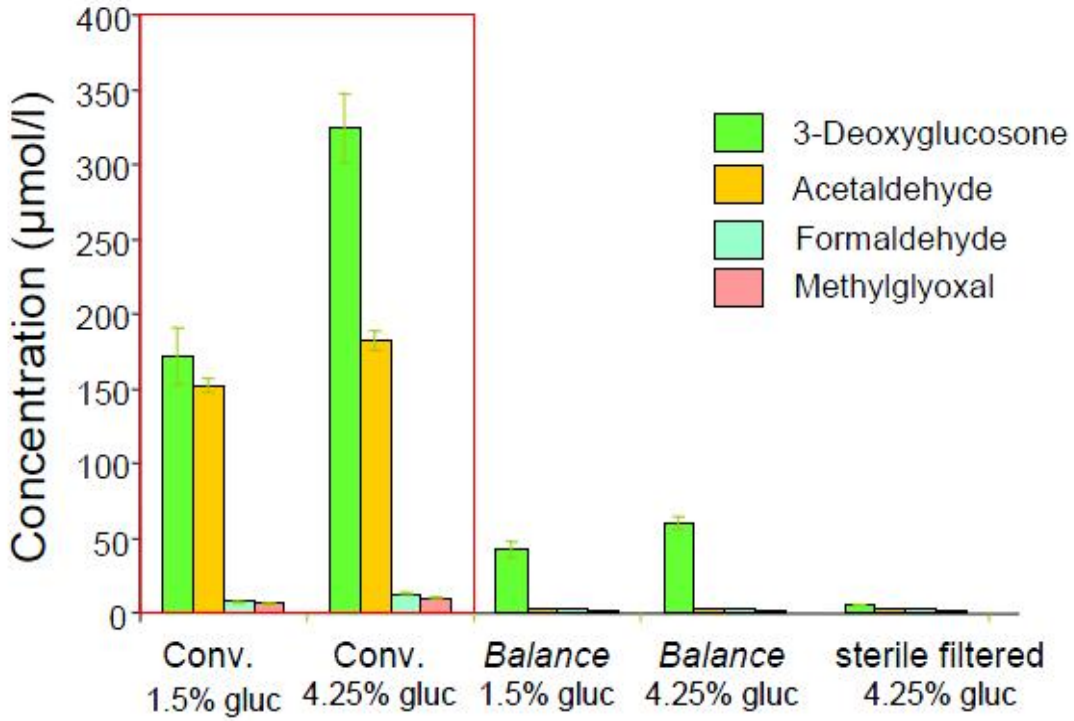
Dual-chambered PD fluid

CAPD *stay•safe* Balance



pH ~ 7.0

GDP concentration is substantially reduced in dual-chambered vs. conventional PD fluid



Tauer et al. *BBRC* 2001, 280(5): 1408-1414

PD Solutions

- Osmotic agent
- Buffer
- pH
- Electrolytes
- Biocompatible

New Generation Of PD solutions

Glucose Solutions

Alternative osmotic
No glucose

Bicarbonate/Lactate
pH 7.4
Low GDPs
pCO2 FS

Icodextrine
pH 5.5-6.1
Very low GDPs
Iso-osmolar

Amino acids
pH ~6.6
No GDPs

Extraneal ™ and GDPs

Ueda et al, *2000 Kidney Int 58: 2518-2524*

	<Concentration (㎜M)>	
	1.36% Glucose	*Extraneal*
Glyoxal	6.2 ±0.5	1.7 ±0.2
Methyl-glyoxal	7.8 ±0.6	1.8 ±0.2
3-deoxyglucosone	47.2 ±4.3	3.5 ±0.4
Total reactive carbonyl compounds	64.7 ±8.7	25.7 ±4.1

Extraneal ™ **contains significantly lower levels of carbonyl stress compounds even versus conventional 1.36% glucose solution**

Positive Lipid Profile

Icodextrin and Cholesterol

*P <.001 vs baseline; †P =.001 vs baseline.

Bredie, et al. *Perit Dial Int*. 2001;21:275-281.

Baxter

Nutrineal ® Characteristics

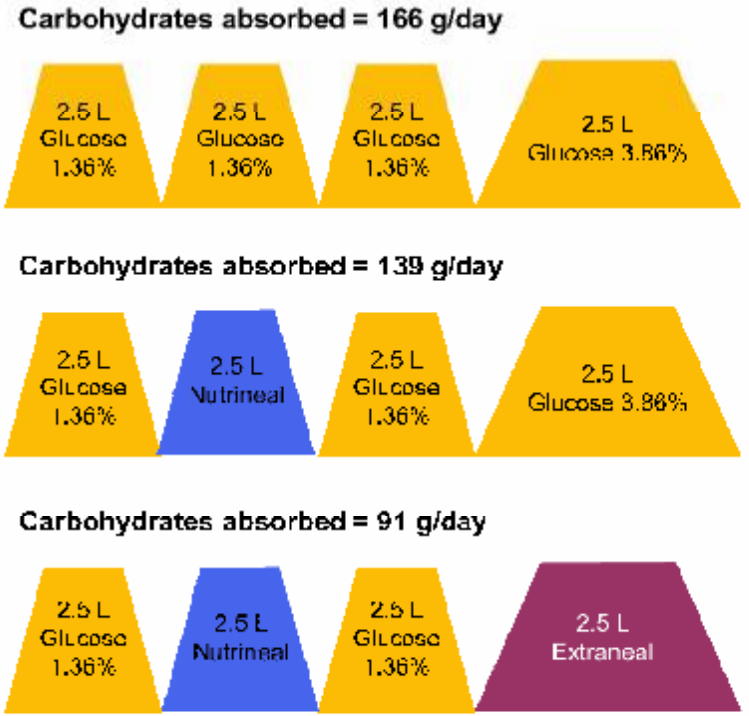
- Amino acids as osmotic agent
- No GLUCOSE
- No change in dialysis procedures
- More physiologic pH
- Osmolality equivalent to 1.5% glucose
- Clearance equivalent to 1.5% glucose
- 40 mEq/L lactate

Together, Extraneal and Nutrineal are strongest in reducing glucose load

Example in high average transporter:

In replacement of a 1.36% glucose bag, Nutrineal reduces carbohydrate exposure by 16%:

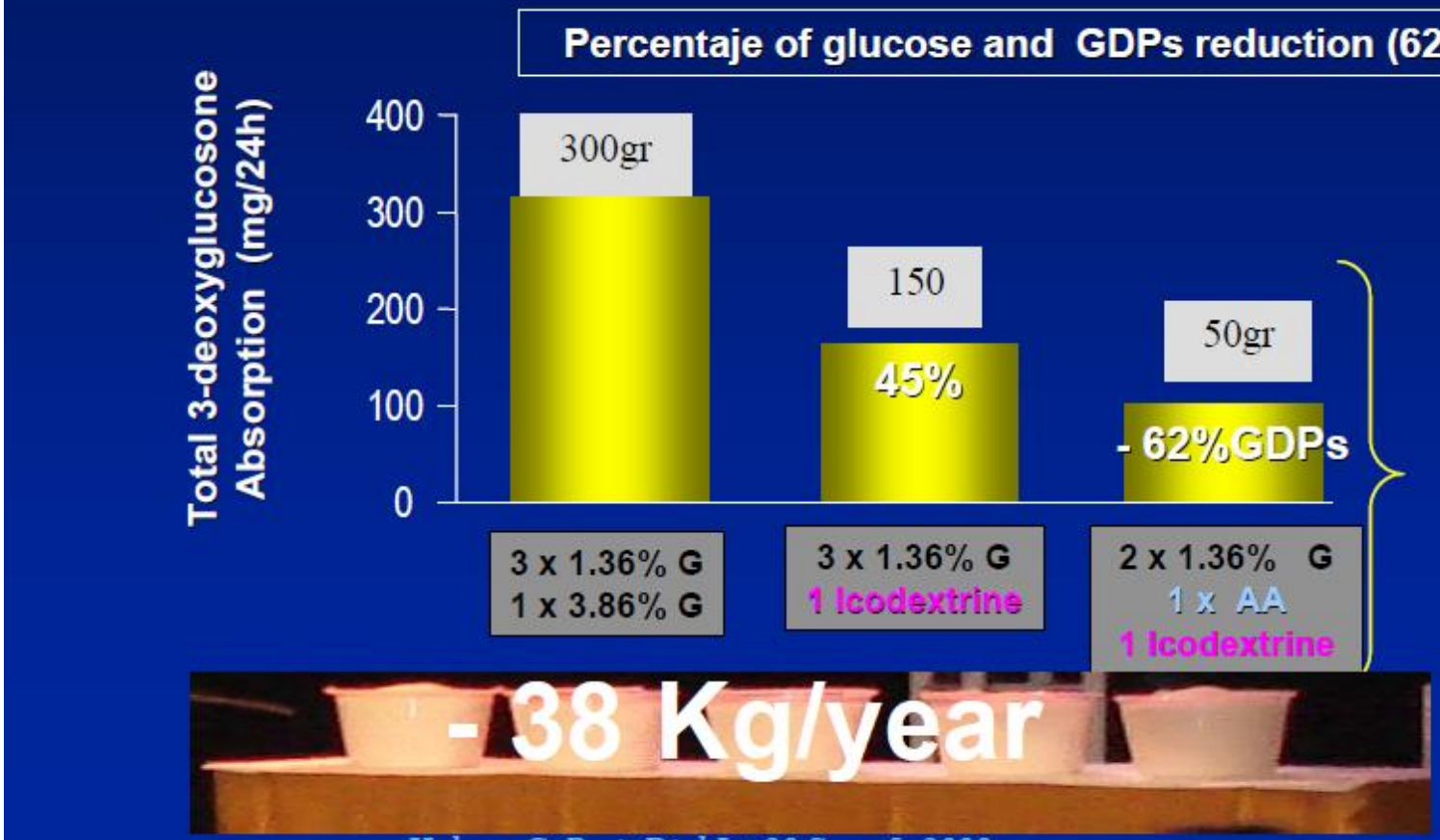
Together with Extraneal, Nutrineal reduces glucose load by more than 45%:



Mathematical modelling, Baxter internal data on file. Compare: Holmes CJ, et. al. "Strategies to reduce glucose exposure in peritoneal dialysis patients" PDI, May 2000- Vol 20-Supp;537-541

Baxter

Glucose and GDPs Levels in the new PD regimens



Holmes C. Perit Dial Int 20 Supp 5, 2000

Clinical advantages of new dialysis solutions

Physioneal

- ¯ Infusion pain
- ¯ Peritonitis
- - Glycemic control
- - Appetite
- - Patient acceptance

No ¯ UF

Extraneal

- ¯ Glucose load
- - Glycemic control
- - UF, control of fluid status
- ¯ Dyslipidemia
- - Quality of life
- - Time on PD

Nutrineal

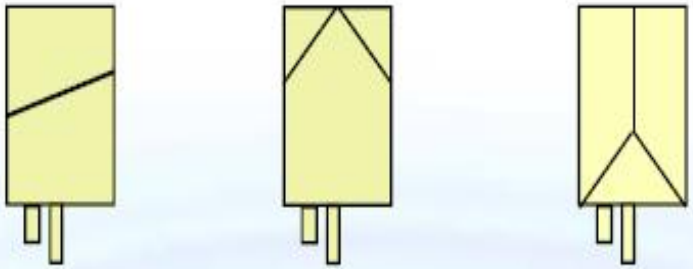
- ¯ Glucose load
- - Glycemic control
- - Protein intake, nutritional status

Pecoits-Filho, et al. *Kidney Int*. 2003;64(suppl 88):S100-S104.
Vardhan, et al. *Kidney Int.* 2003;64(suppl 88):S114-S123.

A New Generation of PD Solutions

Glucose based solutions

Alternative osmotic agents



Extraneal

Amino Acids

pH 7.0-7.4
Low GDP
HCO_3/lactate

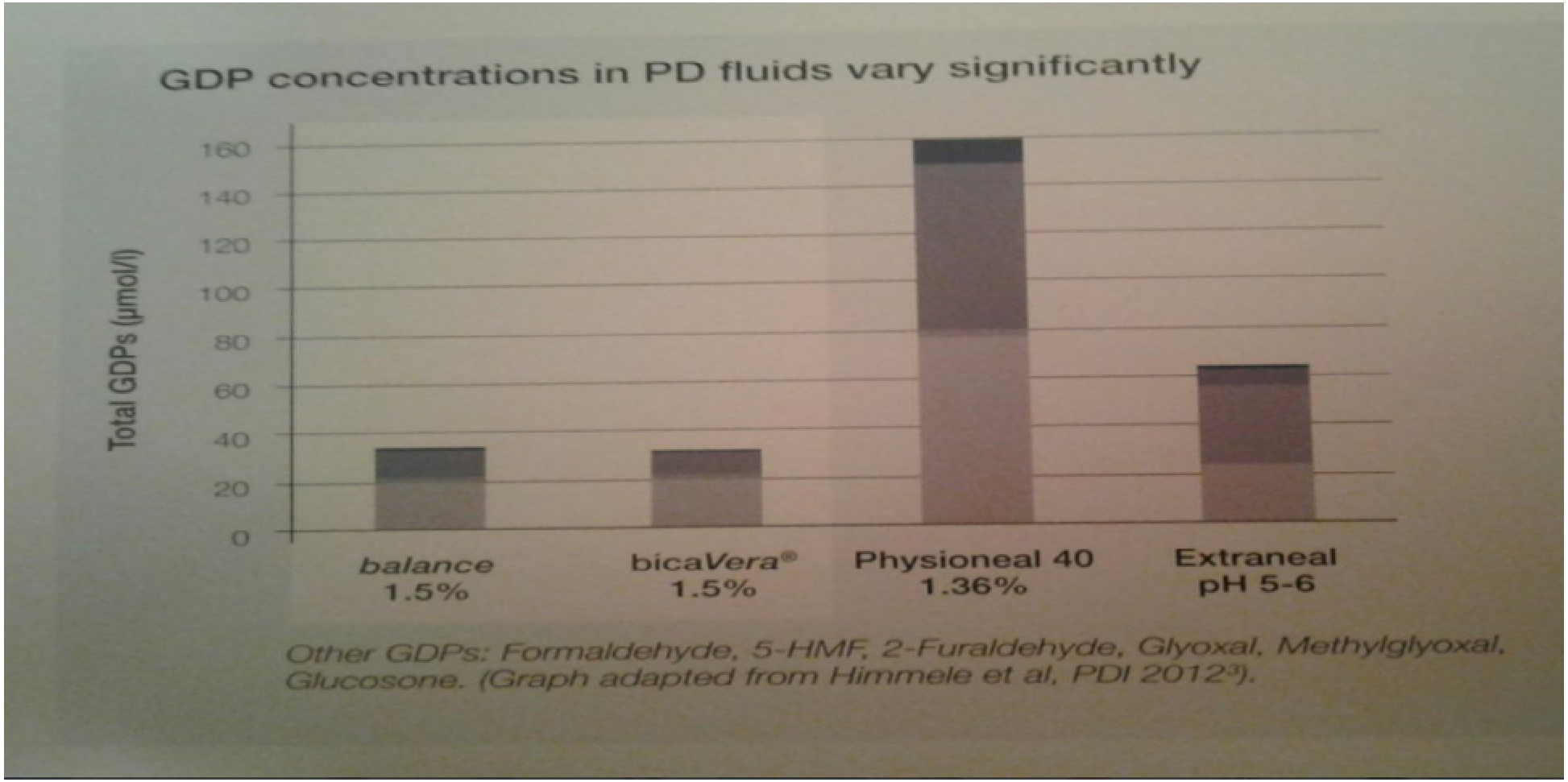
pH ~6.3
V. Low GDP

pH 7.0-7.4
V. Low GDP
HCO_3

pH 5.2
Low GDP
Iso-osmolar

pH ~6.7
No GDP
Glucose free

UltraLow GDP PD fluid



GDP	Conventional glucose[1]	Biocompatible glucose[1,2]	Icodextrin	Aminoacids
3-deoxiglucosone	172-425	10	4-11	<0.2
3,4-DGE[3]	10-125	0.2-0.5	3	<0.2
5-HMF	6-15	10 to 19	2	-
Methylglyoxal	2-12	<1	1.5	<0.2
Glyoxal	<3-14	<1	2.5	<0.2
Acetaldehyde	120-420	<2	37	-
Formaldehyde	7-13	<3	9	-

[1] The range represents the values for glucose solutions with concentrations around 1.5 to 4% and measurements made by different authors.
[2] Excludes Physioneal that has higher values.
[3] The wide range observed depends on the concentration of glucose as the time since the sterilization and storage conditions
Ref: (Erixon, M. et al. 2006)

Table 5. GDP content in µmol / L of different solutions PD

BIOCOMPATIBLE SOLUTIONS

- Improved local host defense (Mortier et al., 2003),
- Reduced mesothelial damage (Grossin et al., 2006)
- Reduced EMT (Bajo et al., 2011),
- less peritoneal GDP and AGE deposition, (Mortier et al., 2004)
- less TGF-β and VEGF signaling, (Mortier et al., 2005)
- less submesothelial fibrosis and angiogenesis, (Rippe, 2009)

Altogether resulting in preservation of peritoneal ultrafiltration capacity

BIOCOMPATIBLE SOLUTIONS

- Higher CA125 effluent concentrations (Haas et al., 2003; Szeto et al., 2007), a putative marker of mesothelial cell viability

- Lower hyaluronic acid and procollagen peptide concentrations, suggesting improved peritoneal membrane integrity (Williams et al., 2004)

- A declining incidence of encapsulating peritoneal sclerosis has been associated with low GDP fluid usage (Nakao et al., 2017)

- Residual renal function, a major predictor of patient outcome, was better preserved (Kim et al., 2008; Haag-Weber et al., 2010; Johnson et al., 2012b)

JASN

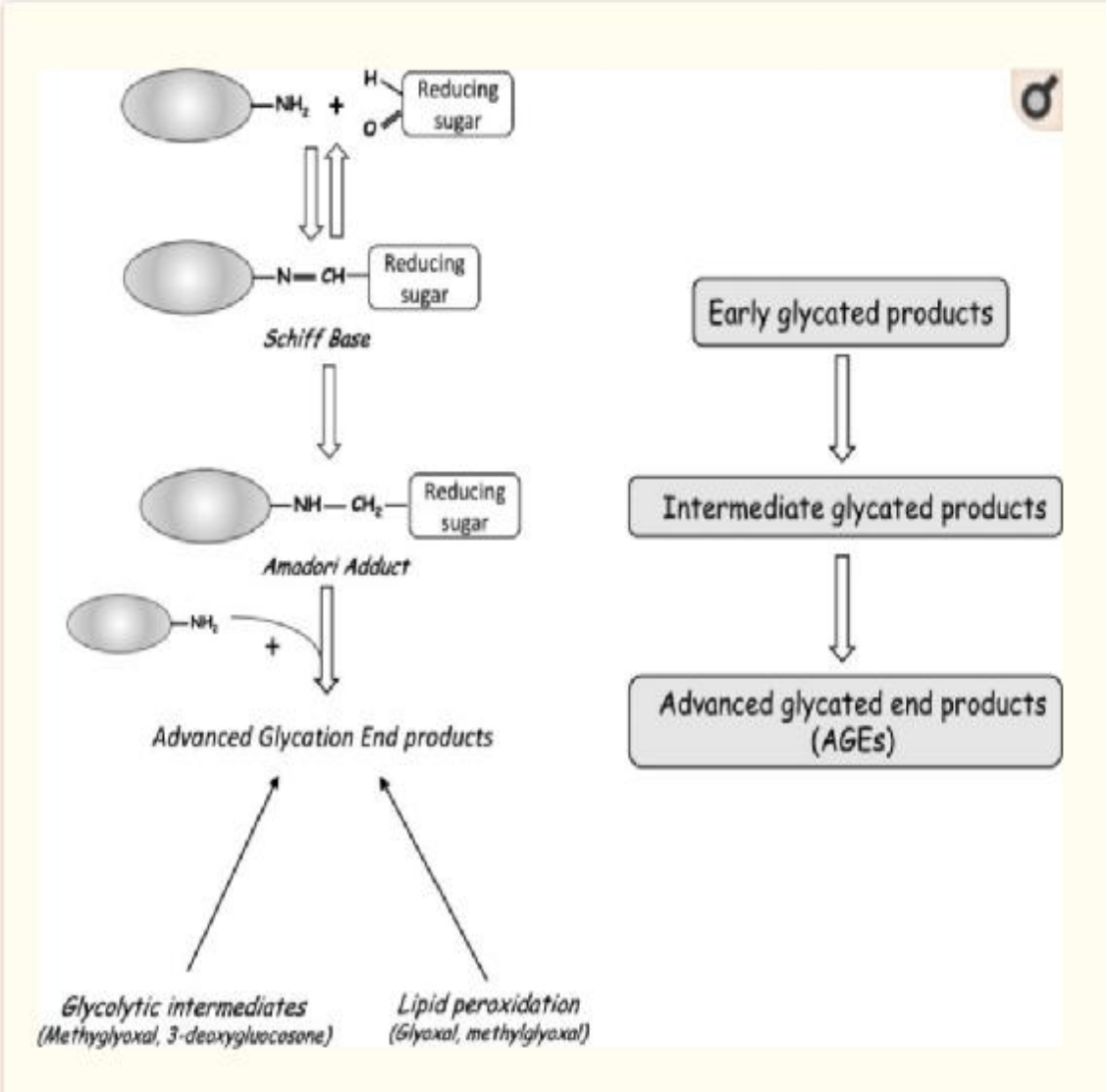
J Am Soc Nephrol. 2016 Feb; 27(2): 354–370.
Published online 2015 Aug 26. doi: 10.1681/ASN.2014101047

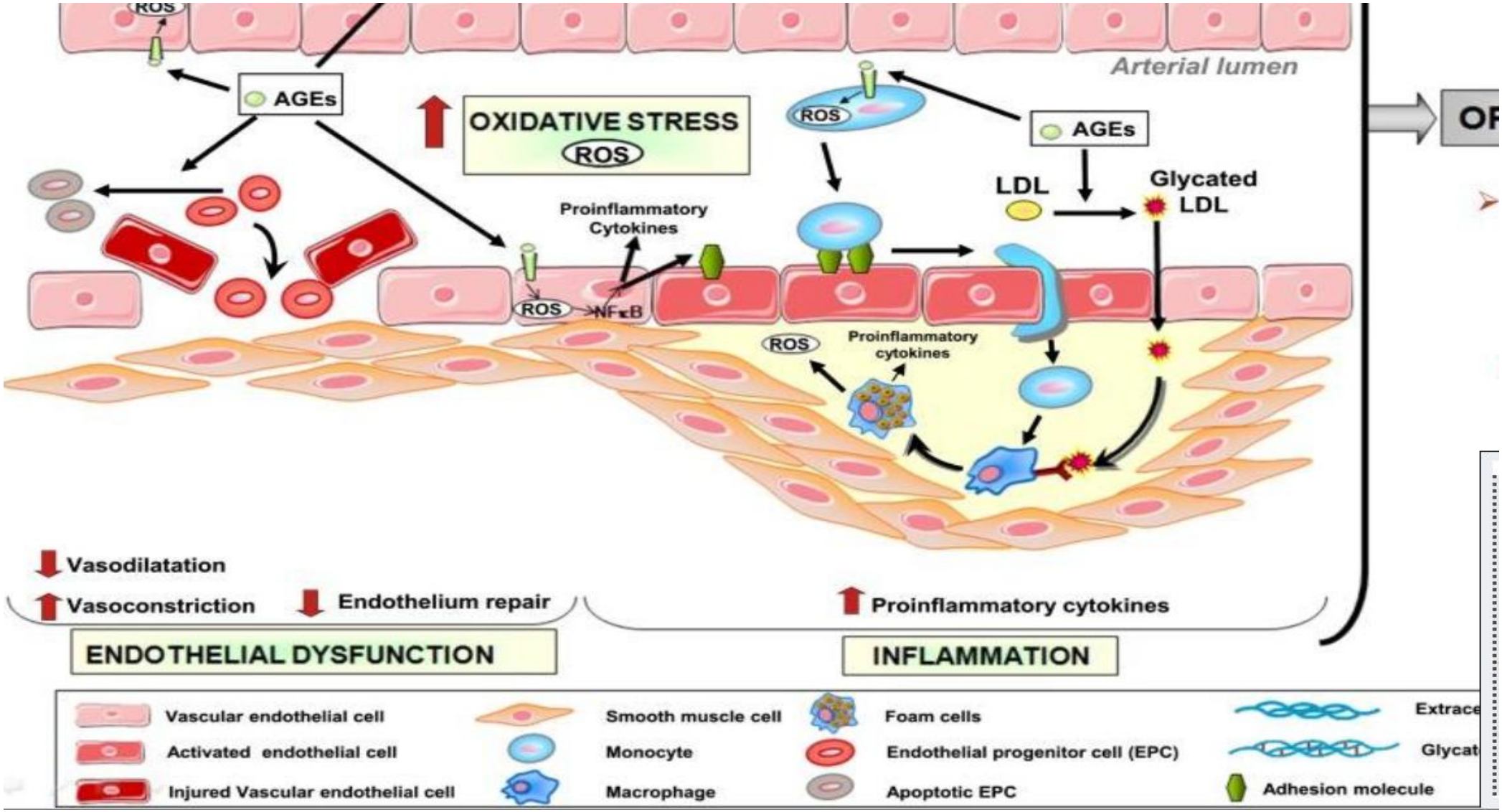
PMCID: PMC4731113
PMID: 26311460

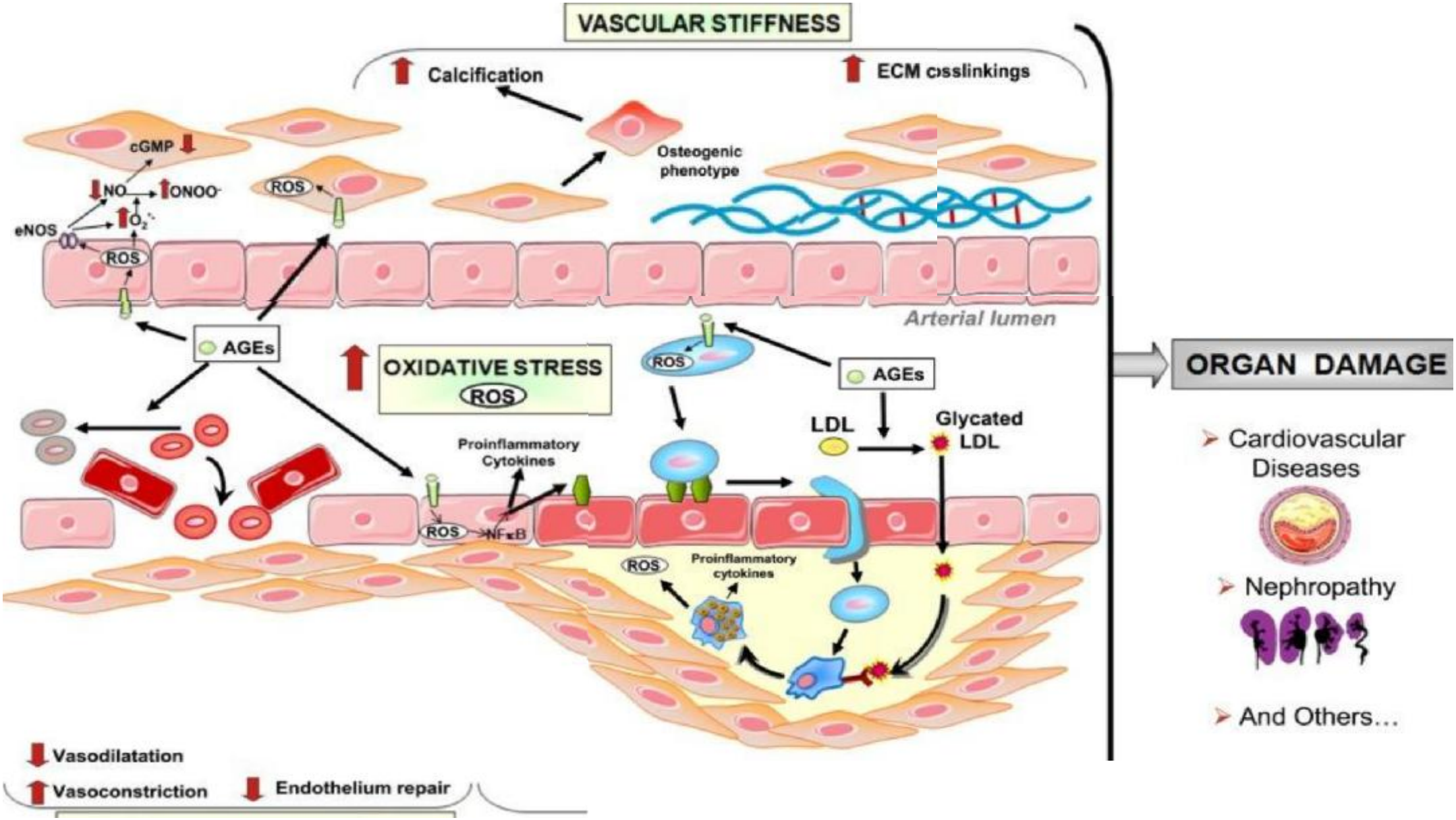
Uremic Toxicity of Advanced Glycation End Products in CKD

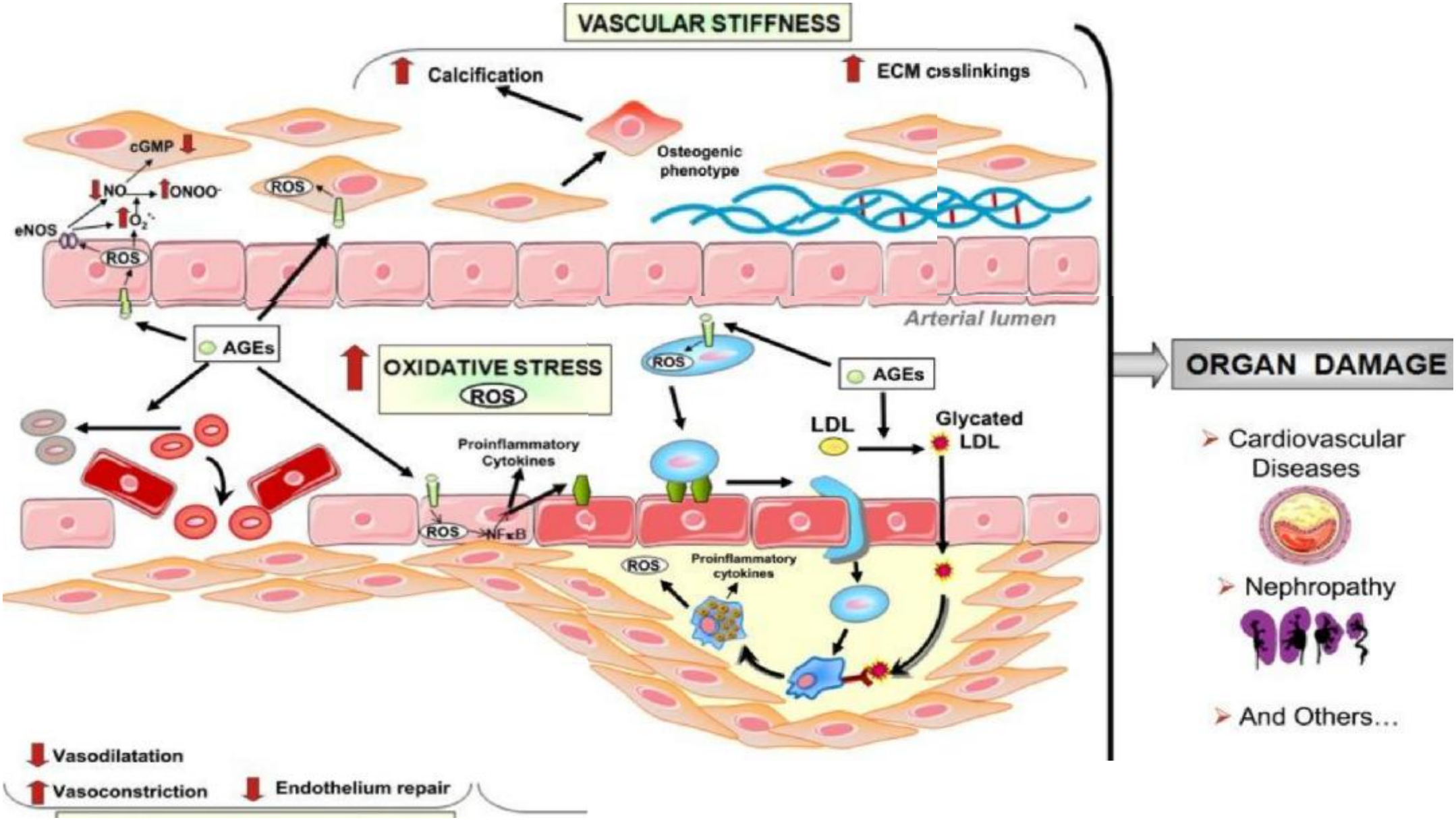
Andréa E.M. Stinghen,[*] Ziad A. Massy,[*†] Helen Vlassara,[‡§] Gary E. Striker,[‡§] and Agnès Boullier[✉*‖]

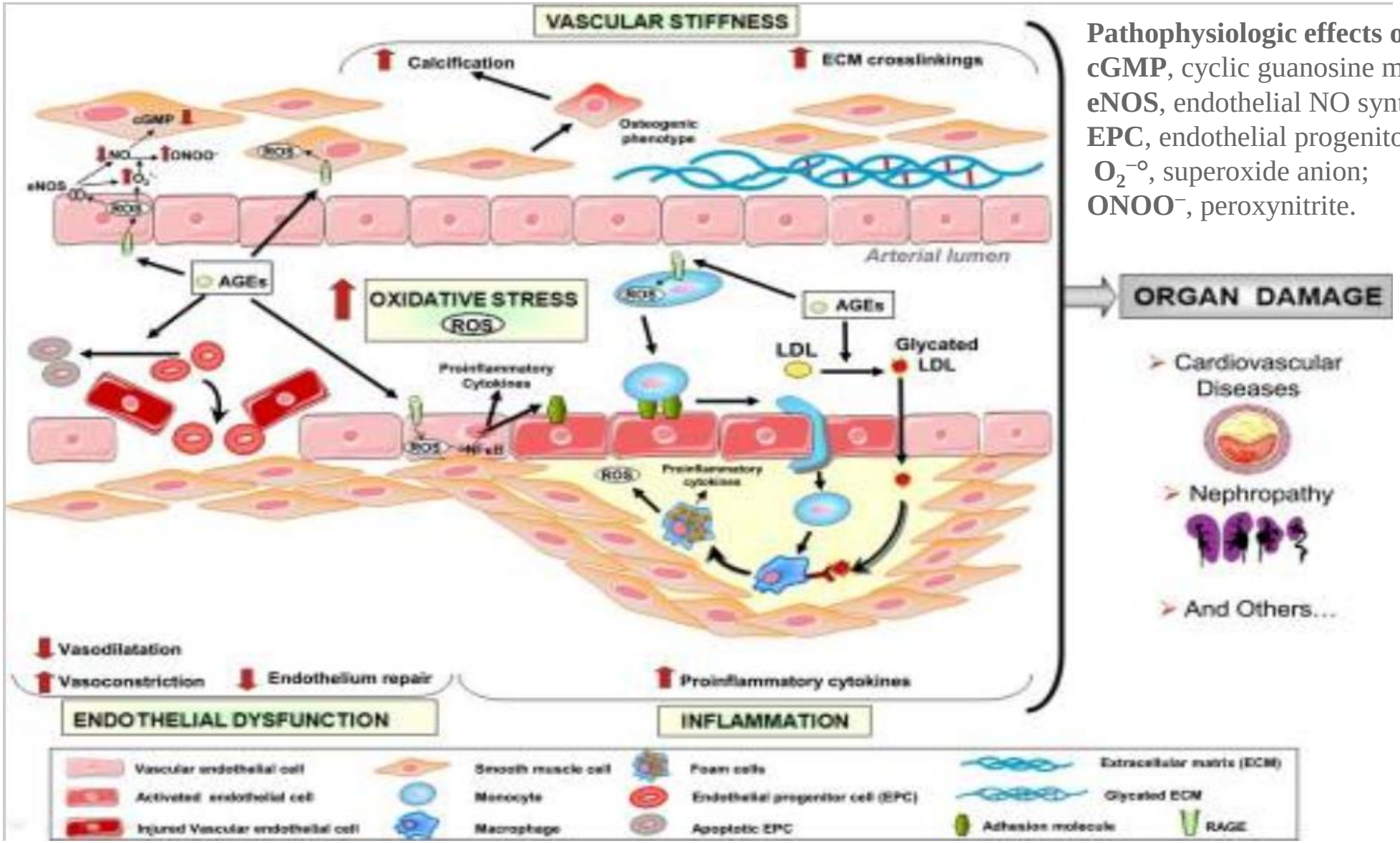
- Free amino group from a protein and a carbonyl group from a reducing sugar, unstable, Schiff base
- This base can be rearranged to form a more stable intermediate called an Amadori product
- Which in the presence of a transition metal, is oxidized to yield the final AGE




ROS
AGEs
OXIDATIVE STRESS
ROS
Arterial lumen
AGEs
LDL
Glycated LDL
Proinflammatory Cytokines
ROS
NF-κB
ROS
Proinflammatory cytokines
Vasodilatation
Vasoconstriction
Endothelium repair
Proinflammatory cytokines
ENDOTHELIAL DYSFUNCTION
INFLAMMATION
Vascular endothelial cell
Activated endothelial cell
Injured Vascular endothelial cell
Smooth muscle cell
Monocyte
Macrophage
Foam cells
Endothelial progenitor cell (EPC)
Apoptotic EPC
Adhesion molecule


VASCULAR STIFFNESS
Calcification
ECM osslinkings
Osteogenic phenotype
cGMP
NO
ONOO⁻
eNOS
$O_2^{\cdot-}$
ROS
Arterial lumen
AGEs
OXIDATIVE STRESS
ROS
AGEs
LDL
Glycated LDL
Proinflammatory Cytokines
NFκB
Proinflammatory cytokines
ORGAN DAMAGE
Cardiovascular Diseases
Nephropathy
And Others…
Vasodilatation
Vasoconstriction
Endothelium repair


VASCULAR STIFFNESS
Calcification
ECM osslinkings
Osteogenic phenotype
cGMP
NO
ONOO⁻
eNOS
$O_2^{\cdot-}$
ROS
Arterial lumen
AGEs
OXIDATIVE STRESS
ROS
AGEs
LDL
Glycated LDL
Proinflammatory Cytokines
NFκB
Proinflammatory cytokines
ORGAN DAMAGE
Cardiovascular Diseases
Nephropathy
And Others…
Vasodilatation
Vasoconstriction
Endothelium repair



Pathophysiologic effects of AGEs.
cGMP, cyclic guanosine monophos
eNOS, endothelial NO synthase;
EPC, endothelial progenitor cell;
$O_2^{-\circ}$, superoxide anion;
$ONOO^-$, peroxynitrite.

- The oxidative stress induced by reactive oxygen species (ROS) is associated with atherosclerosis and cardiovascular morbidity in patients with CKD.[32]
- AGEs increase the levels of ROS[33] through activation of NADPH oxidase[34] and mitochondrial pathways
- Circulating AGE levels are correlated with RAGE mRNA expression and oxidative markers, such as protein carbonyl formation, advanced oxidation protein product generation, and lipid peroxidation.[36]
- Reciprocally, high levels of ROS lead to increased levels of AGEs,[37]because another cause of AGE formation in uremia is the increased oxidative stress generated by an imbalance between oxidized glutathione and GSH levels as well as changes in antioxidant systems, such as superoxide dismutase (SOD)/peroxidase.[5]
- Furthermore, AGEs have been shown to increase the oxidation of LDLs[39]—a key stage in the development of atherosclerosis.[40] Glycated LDLs are, therefore, more susceptible to oxidation,[41] are less effectively cleared from the circulation, and also, promote the formation of antibodies that bind AGEs localized in the vessel wall, which amplifies the development of vascular inflammation and atherosclerosis.[42]

The role of Inflammation in PD

- RAGE ‹ AGE interaction activates transcription factor NF-κB, which leads to gene expression and the release of proinflammatory molecules, IL-1α , IL-6, TNF-α

- Differences in intraperitoneal chronic inflammation, particularly IL-6 production , are associated with peritoneal solute transfer rate, and strongly associated with PD clinical outcomes.

Volume Management

- Volume depletion puts residual kidney function at risk but equally volume excess is detrimental.
- Hypertension is associated with worse survival and there is evidence from bioimpedance data that over-hydration predicts worse survival.
- In anuric patients daily net fluid removal of <750–1000 ml is associated with higher mortality.
- There is evidence that automated PD and icodextrin use can improve the risks associated with fast peritoneal solute transfer rate.

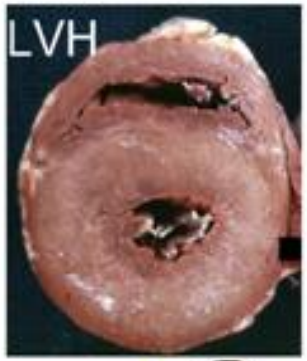
The dialysis patient today

Bone Disease

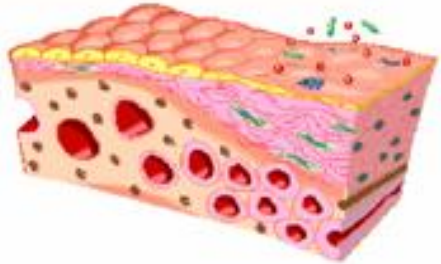
High BP

Inflammation

Anemia



Poor lipid profile



Malnutrition

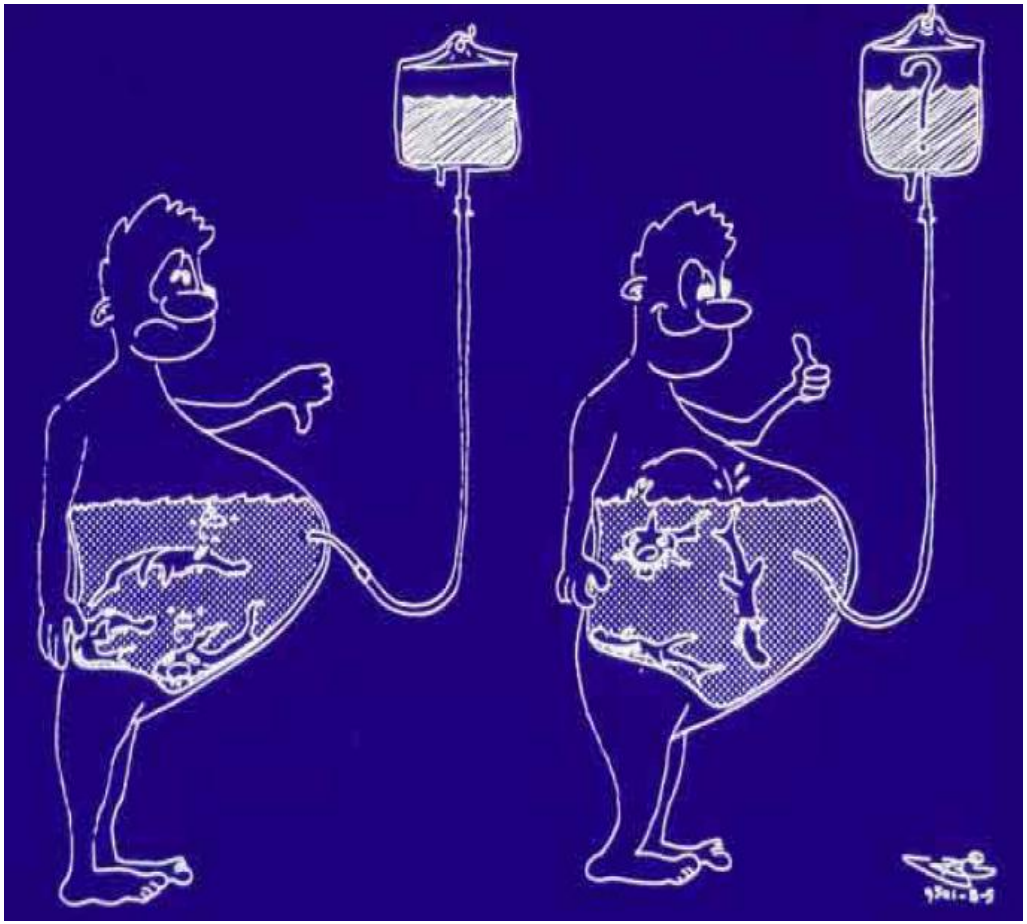
Kt/V

Inadequacy

Atherosclerosis

Failing membrane

Conventional Vs Biocompatible Solutions



Kidney Int. 2018 Aug;94(2):419-429. doi: 10.1016/j.kint.2018.02.022.

Neutral pH and low-glucose degradation product dialysis fluids induce major early alterations of the peritoneal membrane in children on peritoneal dialysis.

Schaefer B[1], Bartosova M[1], Macher-Goeppinger S[2], Sallay P[3], Vörös P[3], Ranchin B[4], Vondrak K[5], Ariceta G[6], Zaloszyc A[7], Bayazit AK[8], Querfeld U[9], Cerkauskiene R[10], Testa S[11], Taylan C[12], VandeWalle J[13], Yap Y[14], Krmar RT[15], Büscher R[16], Mühlig AK[17], Drozdz D[18], Caliskan S[19], Lasitschka F[20], Fathallah-Shaykh S[21], Verrina E[22], Klaus G[23], Arbeiter K[24], Bhayadia R[25], Melk A[25], Romero P[26], Warady BA[27], Schaefer F[1], Ujszaszi A[1], Schmitt CP[28].

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Neutral pH and low–glucose degradation product dialysis fluids induce major early alterations of the peritoneal membrane in children on peritoneal dialysis

Betti Schaefer[28], Maria Bartosova[28], Stephan Macher-Goeppinger, Peter Sallay, Peter Vörös, Bruno Ranchin, Karel Vondrak, Gema Ariceta, Ariane Zaloszyc, Aysun K. Bayazit, Uwe Querfeld, Rimante Cerkauskiene, Sara Testa, Christina Taylan, Johan VandeWalle, YokChin Yap, Rafael T. Krmar, Rainer Büscher, Anne K. Mühlig, Dorota Drozdz, Salim Caliskan, Felix Lasitschka, Sahar Fathallah-Shaykh, Enrico Verrina, Günter Klaus, Klaus Arbeiter, Raj Bhayadia, Anette Melk, Philipp Romero, Bradley A. Warady, Franz Schaefer, Akos Ujszaszi, Claus Peter Schmitt

Thus, in children

inflammation, fibroblast activation, epithelial-mesenchymal transition and marked angiogenesis, which determines the PD membrane transport function could be seen.

Kidney Int. 2018 Aug;94(2):246-248. doi: 10.1016/j.kint.2018.04.014.

Is the peritoneal dialysis biocompatibility hypothesis dead?

Blake PG[1].

Author information

Abstract

The peritoneal dialysis (PD) biocompatibility hypothesis is that conventional PD solutions with high levels of glucose degradation products (GDPs), glucose and lactate, and low pH cause morphological and functional damage to the peritoneal membrane and that this damage may be attenuated by biocompatible solutions. Functional findings from randomized trials have not supported this hypothesis, and now new data from a large European pediatric peritoneal biopsy study provide a morphologic correlate for this. The implications are discussed.

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Effects of Biocompatible versus Standard Fluid on Peritoneal Dialysis Outcomes

David W. Johnson[*†], Fiona G. Brown[‡], Margaret Clarke[§], Neil Boudville[‖], Tony J. Elias[¶], Marjorie W.Y. Foo[**], Bernard Jones[††], Hemant Kulkarni[‡‡], Robyn Langham[§§‖‖], Dwarakanathan Ranganathan[†¶¶], John Schollum[***], Michael Suranyi[†††], Seng H. Tan[‡‡‡§§§‖‖‖], David Voss[¶¶¶] and on behalf of the balANZ Trial Investigators

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OXFORD JOURNALS Nephrology Dialysis Transplantation

Nephrol Dial Transplant. 2012 Dec; 27(12): 4445–4453. PMCID: PMC3520083
Published online 2012 Aug 1. doi: 10.1093/ndt/gfs314 PMID: 22859794

The effect of low glucose degradation product, neutral pH versus standard peritoneal dialysis solutions on peritoneal membrane function: the balANZ trial

David W. Johnson,[1,2‡] Fiona G. Brown,[3,‡] Margaret Clarke,[4] Neil Boudville,[5] Tony J. Elias,[6] Marjorie W.Y. Foo,[7] Bernard Jones,[8] Hemant Kulkarni,[9] Robyn Langham,[10,11] Dwarakanathan Ranganathan,[2,12] John Schollum,[13] Michael G. Suranyi,[14] Seng H. Tan,[15,16,17] David Voss,[18] and on behalf of the balANZ Trial Investigators

The Effects of Biocompatible Compared with Standard Peritoneal Dialysis Solutions on Peritonitis Microbiology, Treatment, and Outcomes: the *bal*ANZ Trial

David W. Johnson[1,2], Fiona G. Brown[3], Margaret Clarke[4], Neil Boudville[5], Tony J. Elias[6], Marjorie W.Y. Foo[7], Bernard Jones[8], Hemant Kulkarni[9], Robyn Langham[10,11], Dwarakanathan Ranganathan[2,12], John Schollum[13], Michael G. Suranyi[14], Seng H. Tan[15,16,17], David Voss[18] and the *bal*ANZ Trial Investigators

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This Article

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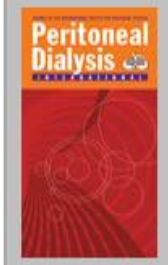

September–October 2012, 32 (5)

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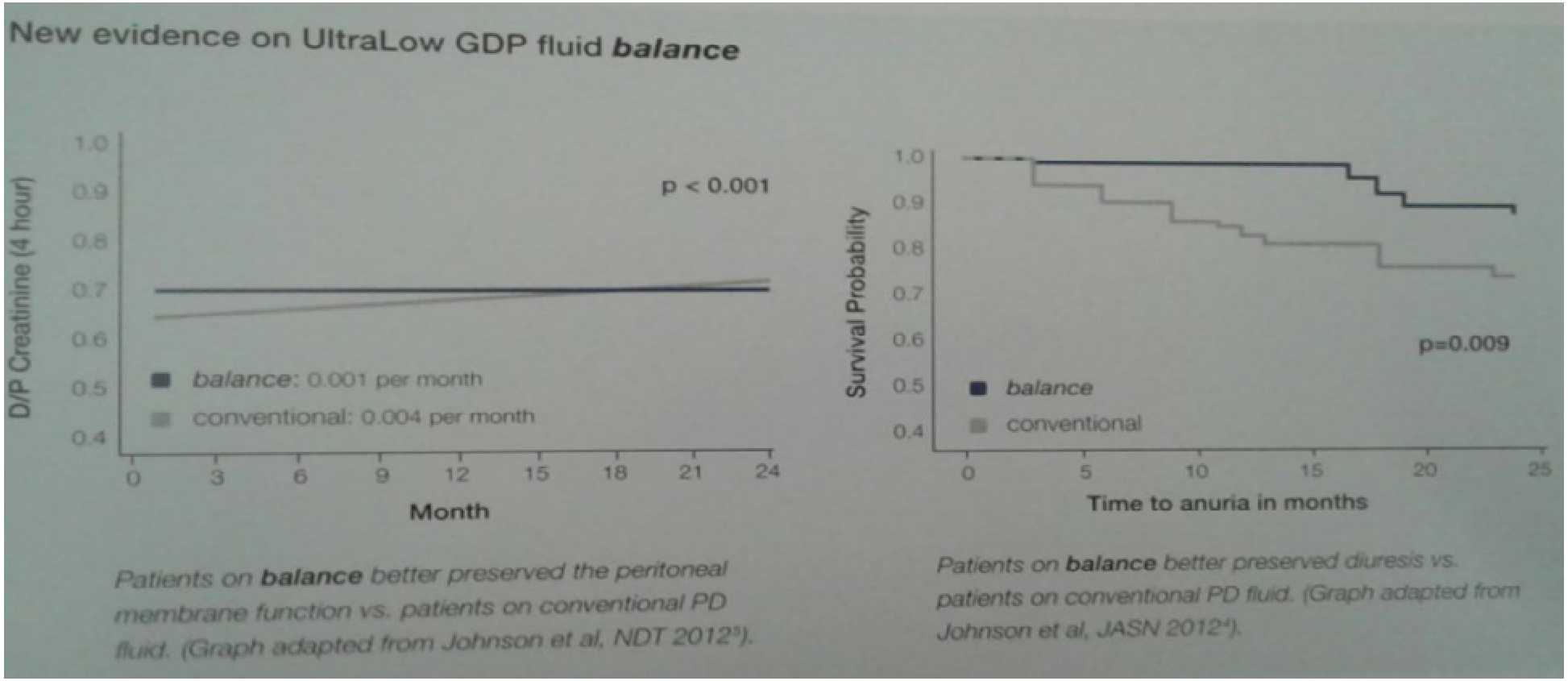
- Time to anuria,
- peritonitis rates,
- Severity of peritonitis when it does occur, and
- Stability of peritoneal membrane function.

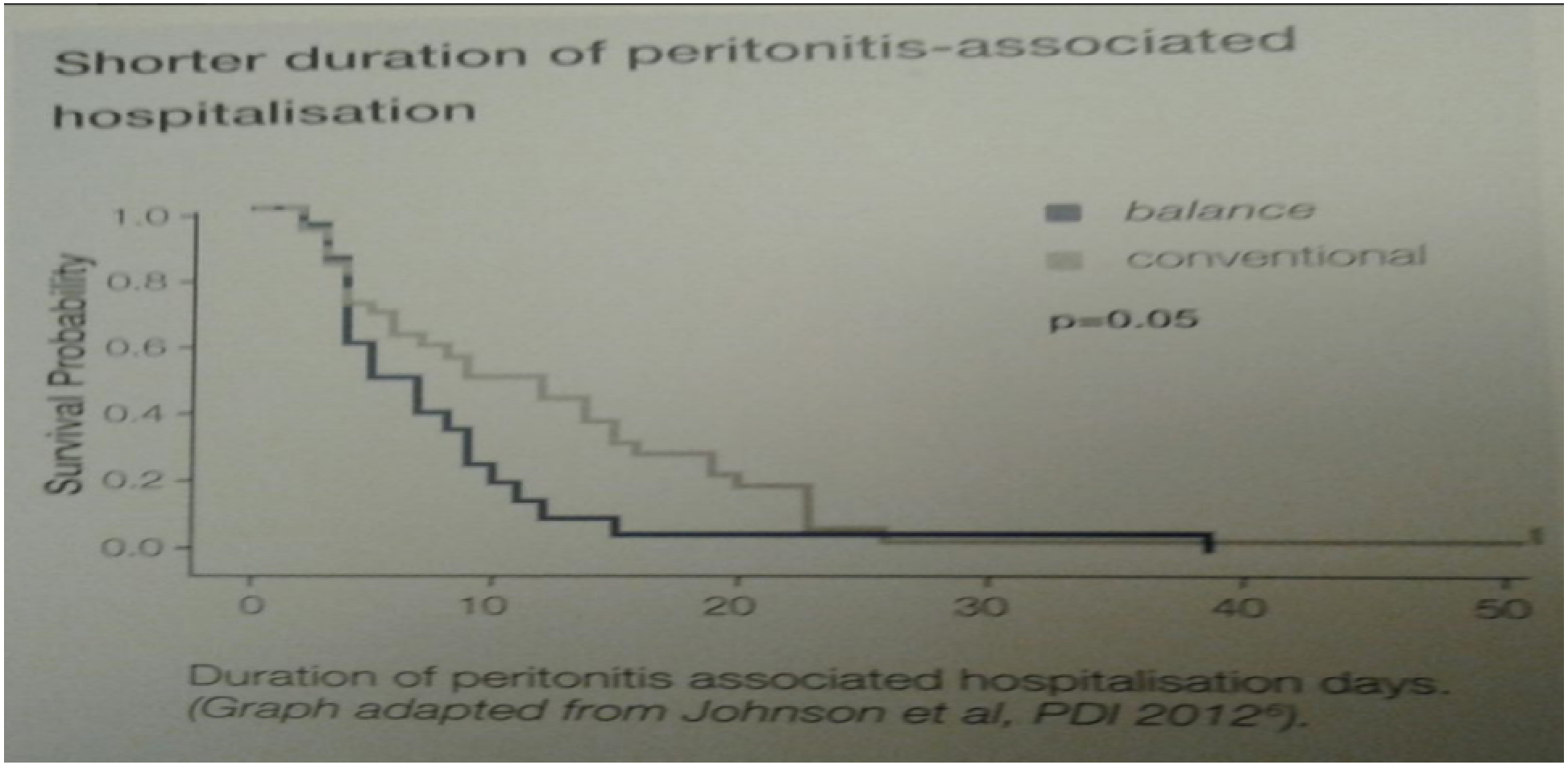
Balance PD solution



*Patients on **balance** better preserved the peritoneal membrane function vs. patients on conventional PD fluid. (Graph adapted from Johnson et al, NDT 2012[3]).*

*Patients on **balance** better preserved diuresis vs. patients on conventional PD fluid. (Graph adapted from Johnson et al, JASN 2012[4]).*

Balance PD solution



Associations Between Peritoneal Glucose Exposure, Glucose Degradation Product Exposure, and Peritoneal Membrane Transport Characteristics in Peritoneal Dialysis Patients: Secondary Analysis of the *bal*ANZ Trial

Melissa S. Nataatmadja[1], David W. Johnson[1,2,3⇑], Elaine M. Pascoe[2], Darsy Darssan[2], Carmel M. Hawley[1,2,3], Yeoungjee Cho[1,2,3], on behalf of the *bal*ANZ Trial Investigators

Conclusions:

Increases in peritoneal solute transport rate over time were not associated with peritoneal **glucose exposure**, although a strong and positive association with PD solution **glucose degradation product** content was identified.

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Clin J Am Soc Nephrol. 2015 Aug 7; 10(8): 1380–1388. PMCID: PMC4527022
Published online 2015 Jun 5. doi: 10.2215/CJN.05410514 PMID: 26048890

Effect of Neutral-pH, Low–Glucose Degradation Product Peritoneal Dialysis Solutions on Residual Renal Function, Urine Volume, and Ultrafiltration: A Systematic Review and Meta-Analysis

Seychelle Yohanna,[*] Ali M.A. Alkatheeri,[*†] Scott K. Brimble,[‡] Brendan McCormick,[§] Arthur Iansavitchous,[*] Peter G. Blake,[*] and Arsh K. Jain[✉*]

- **Neutral-pH, low-GDP solutions resulted in significantly greater urine volume beyond 6 months and improved preservation of RRF throughout all durations of treatment.** Peritoneal UF and peritoneal small-solute transport were not significantly different with the use of these solutions.

JOURNAL OF THE INTERNATIONAL SOCIETY FOR PERITONEAL DIALYSIS
Peritoneal Dialysis INTERNATIONAL

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Perit Dial Int. 2016 Mar-Apr; 36(2): 129–134. PMCID: PMC4803356
doi: 10.3747/pdi.2014.00038 PMID: 26475848

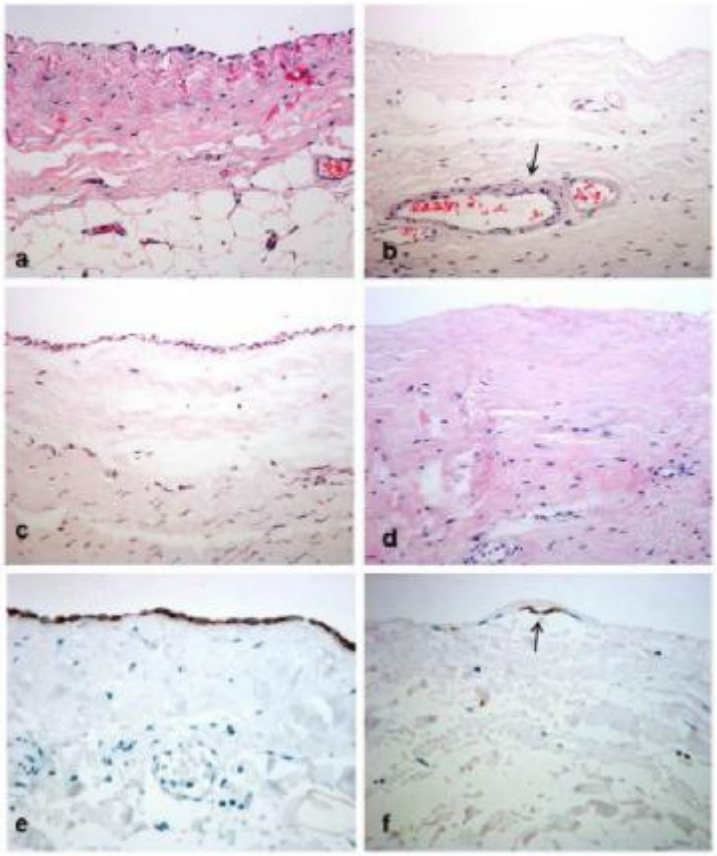
Biocompatible Dialysis Solutions Preserve Peritoneal Mesothelial Cell and Vessel Wall Integrity. A Case-Control Study on Human Biopsies

Gloria del Peso,[1] José Antonio Jiménez-Heffernan,[2] Rafael Selgas,[1] César Remón,[3] Marta Ossorio,[1] Antonio Fernández-Perpén,[4] José Antonio Sánchez-Tomero,[4] Antonio Cirugeda,[5] Erika de Sousa,[1] Pilar Sandoval,[6] Raquel Díaz,[1] Manuel López-Cabrera,[6] and María Auxiliadora Bajo[1]

In conclusion, the present study offers *in vivo* evidence in **human biopsies** that **biocompatible solutions are better tolerated** by the peritoneum in the medium and long term than conventional solutions.

As a result, we suggest that PD should be offered with biocompatible solutions.

- Peritoneal biopsies from patients receiving biocompatible solutions (a,c,e) showed better mesothelial cell preservation, less submesothelial thickness and hyalinizing vasculopathy when compared with patients treated with conventional fluids (b,d,f).
- Grade 1 hyalinizing vasculopathy lesions are seen on image b (arrow).
- A clear contrast among mesothelial cell preservation is evident on all images (a,b,c,d: hematoxylin and eosin, ×200).
- Immunohistochemistry for cytokeratins reveals a modified, superficial mesothelial cell (arrow) that contrasts with the well preserved layer seen on a biocompatible patient



Encapsulating Peritoneal Sclerosis
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PERITONEAL DIALYSIS IN JAPAN: THE ISSUE OF ENCAPSULATING PERITONEAL SCLEROSIS AND FUTURE CHALLENGES

Akira Saito

Department of Molecular Nephrology and Bioartificial Organs, Institute of Medical Science, Tokai University, Kanagawa, Japan

Encapsulating peritoneal sclerosis (EPS) is a life-threatening complication of peritoneal dialysis (PD). The overall prevalence of EPS in Japanese PD patients is 2.3%. Among patients on PD for less than 5 years, the rate is 0.9%; among patients on PD for 5 – 10 years, the rate is 3.8%; and among patients on PD for >10 years, it is 11.5%. Thus, the longer the treatment duration, the higher the prevalence of EPS.

KEY WORDS: Challenges; encapsulating peritoneal sclerosis; EPS; Japan.

Encapsulating peritoneal sclerosis (EPS), which was first reported by Gandhi and colleagues in 1980 (1), is a life-threatening complication of peritoneal dialysis (PD). Past surveys had indicated that the prevalence of EPS ranged from 0.4% to 2.8% (2–5). More recent re-

Ren Fail. 2017; 39(1): 32–39.
Published online 2016 Oct 24.
doi: 10.1080/0886022X.2016.1244075

PMCID: PMC6014288
PMID: 27774831

Risk factors of severe peritoneal sclerosis in chronic peritoneal dialysis patients

Sudabeh Alatab,[a] Iraj Najafi,[b] Gholamreza Pourmand,[a] Mostafa Hosseini,[c] and Soroosh Shekarchian[d]

Conclusion

We found that longer time being on PD, younger age, and higher UFF duration were the risk factors for EPS development.

Ren Fail. 2017; 39(1): 32–39.
Published online 2016 Oct 24. doi: 10.1080/0886022X.2016.1244075
PMCID: PMC6014288
PMID: 27774831

Risk factors of severe peritoneal sclerosis in chronic peritoneal dialysis patients

Sudabeh Alatab,[a] Iraj Najafi,[b] Gholamreza Pourmand,[a] Mostafa Hosseini,[c] and Soroosh Shekarchian[d]

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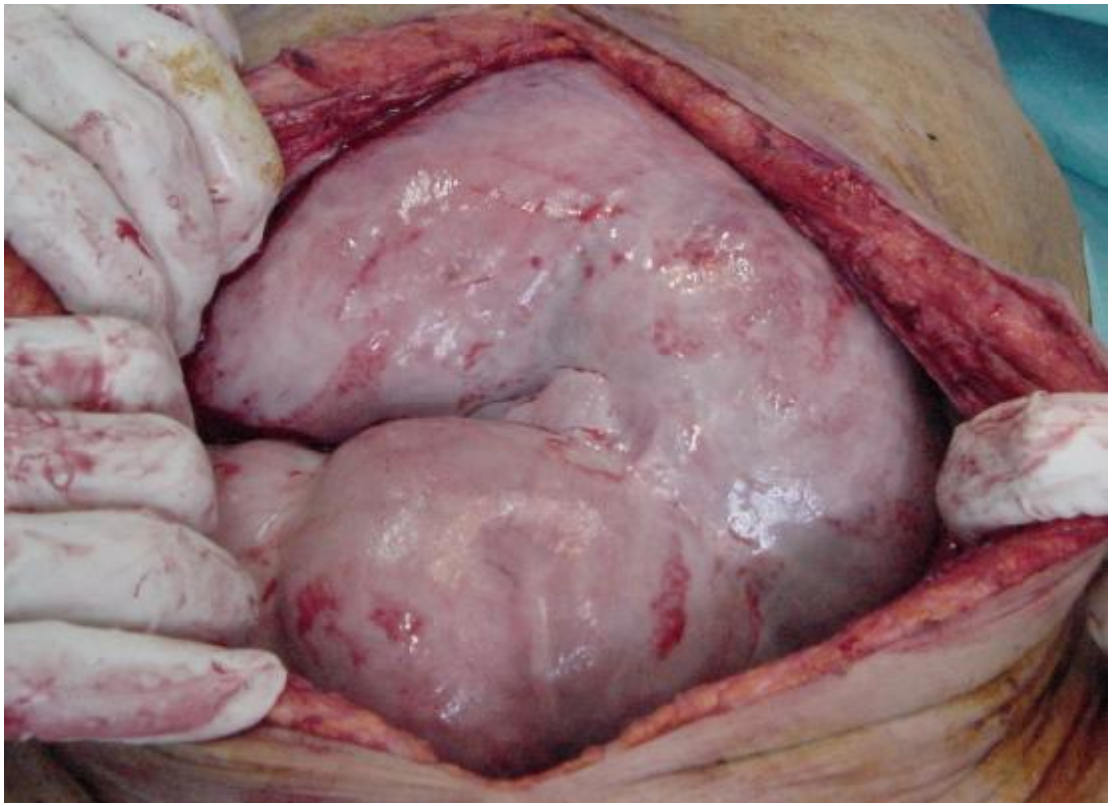
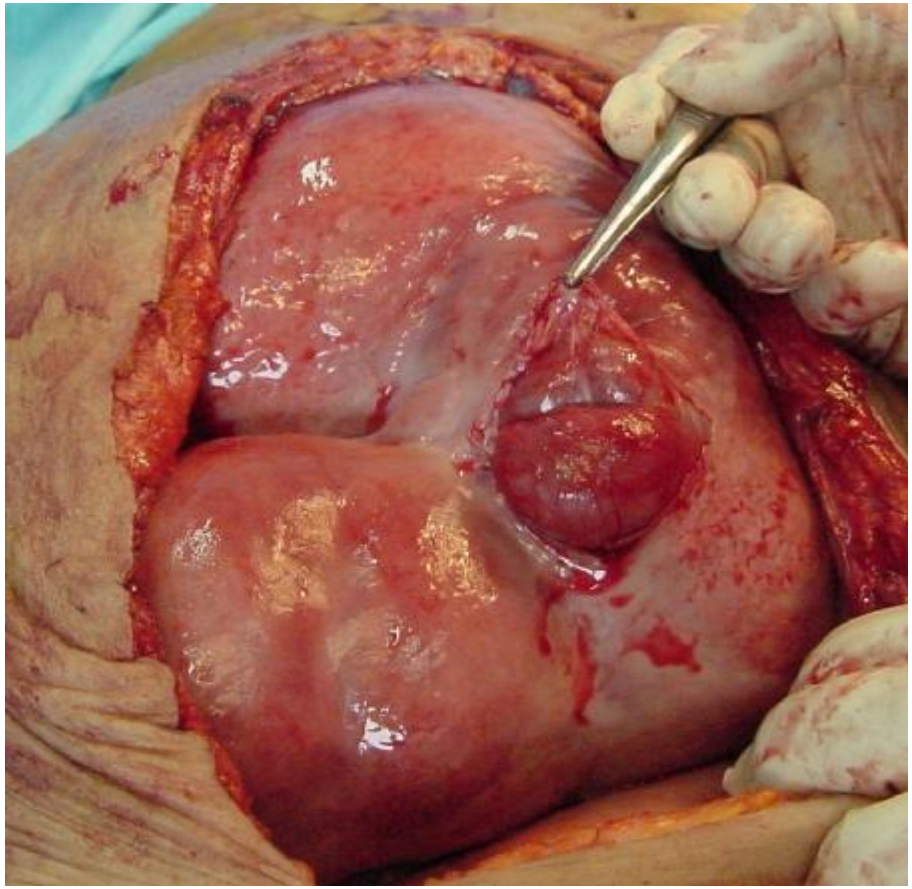
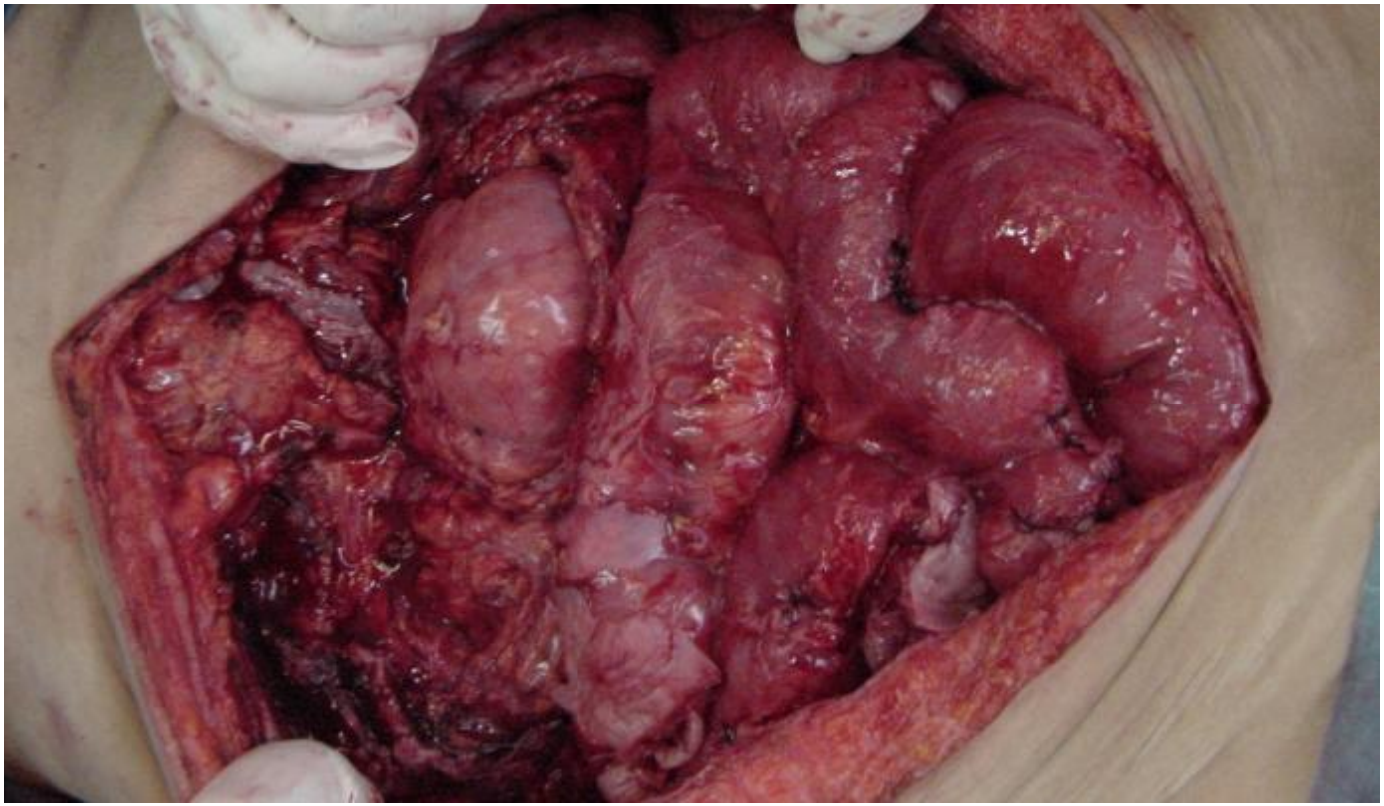
EPS

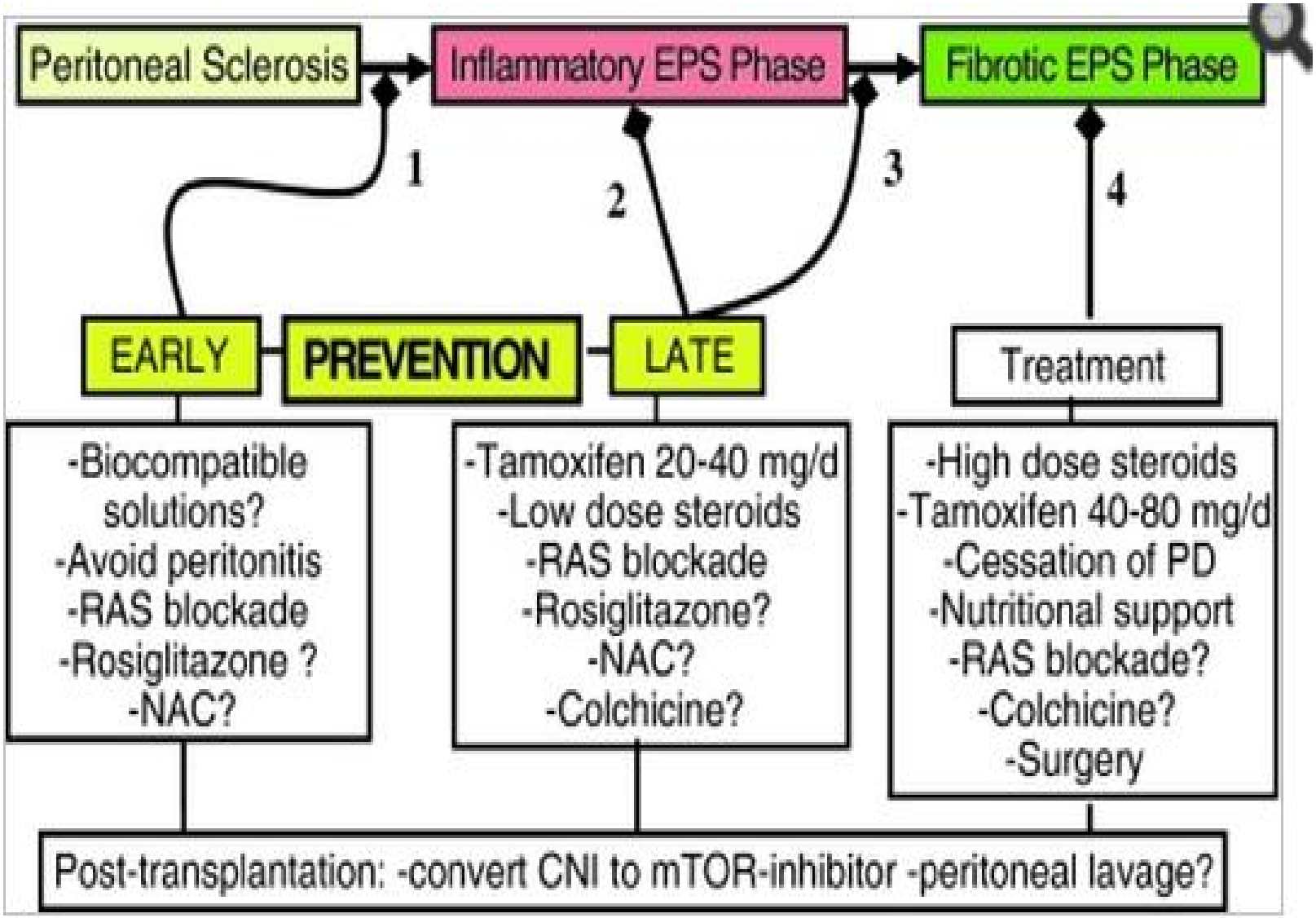


EPS



EPS after surgery




Peritoneal Sclerosis
Inflammatory EPS Phase
Fibrotic EPS Phase
1
2
3
4
EARLY
PREVENTION
LATE
Treatment
-Biocompatible solutions?
-Avoid peritonitis
-RAS blockade
-Rosiglitazone ?
-NAC?
-Tamoxifen 20-40 mg/d
-Low dose steroids
-RAS blockade
-Rosiglitazone?
-NAC?
-Colchicine?
-High dose steroids
-Tamoxifen 40-80 mg/d
-Cessation of PD
-Nutritional support
-RAS blockade?
-Colchicine?
-Surgery
Post-transplantation: -convert CNI to mTOR-inhibitor -peritoneal lavage?

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ISPD GUIDELINES/RECOMMENDATIONS

LENGTH OF TIME ON PERITONEAL DIALYSIS AND ENCAPSULATING PERITONEAL SCLEROSIS — POSITION PAPER FOR ISPD: 2017 UPDATE

Edwina A. Brown,[1] Joanne Bargman,[2] Wim van Biesen,[3] Ming-Yang Chang,[4] Frederic O. Finkelstein,[5] Helen Hurst,[6] David W. Johnson,[7] Hideki Kawanishi,[8] Mark Lambie,[9] Thyago Proença de Moraes,[10] Johann Morelle,[11] and Graham Woodrow[12]

Imperial College Renal and Transplant Centre,[1] Hammersmith Hospital, London, UK; University Health Network and the University of Toronto,[2] Toronto, ON, Canada; Renal Division,[3] Ghent University Hospital, Ghent, Belgium; Kidney Research Center,[4] Department of Nephrology, Chang Gung Memorial Hospital, Taoyuan, Taiwan; Yale School of Medicine,[5] New Haven, CT, USA; Central Manchester and Manchester Children's NHS Foundation Trust,[6] Manchester, UK; Department of Nephrology,[7] University of Queensland at Princess Alexandra Hospital, Brisbane, Australia; Tsuchiya General Hospital,[8] Faculty of Medicine, Hiroshima University, Japan; Institute for Applied Clinical Sciences,[9] Keele University, Stoke-on-Trent, UK; Pontificia Universidade Catolica do Parana,[10] Curitiba, Parana, Brazil; Division of Nephrology,[11] Cliniques universitaires Saint-Luc, Brussels, Belgium, et Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Brussels, Belgium; and St James's University Hospital,[12] Leeds, UK

TABLE 1
Studies Examining the Epidemiology of EPS*

Country	Time period	Study design	N	Prevalence	EPS epidemiology Incidence rate (/1,000 patient-yrs)	Risk with time	Reference
Iran	1995–2012	2-center, retrospective, observational cohort	464	8.9%	7	≥4 yrs: 8.6% ≥5 yrs: 10.8% ≥6 yrs: 23.3% ≥7 yrs: 25%	Alatab *et al.* 2017 (21)
Germany	1997–2015	Single-center, retrospective, observational cohort	745 (catheters)	4% (1995–2000) 0% (2001–2003) 5% (2004–2006) 11% (2007–2009) 15% (2010–2012) 5% (2013–2015) 15% (2010–2012)	NA	NA	Kitterer *et al.* 2016 (16)
Scotland	2000–2007	Scottish Renal Registry	1,238	2.8%	8.7 (by 2007) 13.6 (by 2014)	1 yr: 1.1% 3 yrs: 3.4% 4 yrs: 8.8% 5 yrs: 9.4% 7 yrs: 22.2%	Petrie *et al.* 2016 (24)
Italy	1979–2013	Single-center, retrospective, observational cohort	920	2.8%	9.5	<2 yrs: 3% 2–4 yrs: 3% 4–6 yrs: 4% 6–8 yrs: 6% 8–10 yrs: 8% 10–12 yrs: 18% 12–14 yrs: 75% >14 yrs: 67%	Vizzardi *et al.* 2016 (27)
Japan	1987–2013	Single-center, retrospective, observational cohort	270	4.8%	NA	NA	Yamakatsu *et al.* 2015 (33)
Spain	1980–2012	Single-center, retrospective, observational cohort	679	2.9% (overall) 5.6% (1980–1990) 3.9% (1991–2000) 0.3% (2000–2012)	NA	NA	De Sousa-Amorim *et al.* 2014 (17)
Japan	2008–2012	Multicenter, prospective observational cohort (56 centers)	1,338	1.0%	2.3	<3 yrs: 0.3% 5 yrs: 0.6% 8 yrs: 2.3% >8 yrs: 1.2%	Nakayama *et al.* 2014 (18)
Korea	2001–2011	Single-center, retrospective, observational cohort	606	1.3%	1.4	NA	Hong *et al.* 2013 (34)
Italy	1986–2011	Italian Registry of Pediatric Chronic	712 (children)	1.9%	NA	<5 yrs: 0.45% ≥5 yrs: 21.1%	Vidal *et al.* 2013 (26)

TABLE 1 (cont'd)

Country	Time period	Study design	N	Prevalence	EPS epidemiology Incidence rate (/1,000 patient-yrs)	Risk with time	Reference
USA	1998–2003	Single-center, retrospective, observational cohort	76	18.4% (>5 yrs)	NA	NA	Gayomali *et al.* 2011 (37)
Netherlands	1 January 1996 – 1 July 2007	Multicenter case-control study	2,022	2.7%	NA	NA	Korte *et al.* 2011 (29)
USA	1979–2009	Single-center, retrospective, observational cohort	676	1.2%	NA	≥6 yrs: 15% ≥9 yrs: 38%	Bansal *et al.* 2010 (22)
Canada	1974–2008	Single-center, retrospective, observational cohort	1,966	1.1%	NA	NA	Trigka *et al.* 2011 (38)
Ireland	1989–2008	Single-center, retrospective, observational cohort	615	1.98%	3.2	≥6 yrs: 20% ≥8 yrs: 100%	Phelan *et al.* 2010 (25)
Australia and New Zealand	1995–2007	Binational Registry (ANZDATA)	7,618	0.4%	1.8	3 yrs: 0.3% 5 yrs: 0.8% 8 yrs: 3.9%	Johnson *et al.* 2010 (13)
Slovenia	1983–2003	Single-center, retrospective, observational cohort	423	1.2%	NA	NA	Lindic *et al.* 2009 (39)
Scotland	2000–2007	Scottish Renal Registry	1,238	1.5%	4.9	<1 yr: 0% 1–2 yrs: 0.6% >2–3 yrs: 2.0% >3–4 yrs: 3.5% >4–5 yrs: 8.1% >5–6 yrs: 8.8% >6 yrs: 5%	Brown *et al.* 2009 (7)
Turkey	1989–2003	Single-center, retrospective, observational cohort	104 (children)	1.9%	NA	NA	Ekim *et al.* 2005 (40)
Korea	1981–2002	Multicenter, retrospective observational cohort (7 centers)	4,290	0.79% (center variation 0.28–2.86%)	NA	NA	Kim *et al.* 2005 (28)
Japan	April 1999–March 2003	Multicenter, prospective observational cohort (57 centers)	1,958	2.5%	NA	3 yrs: 0% 5 yrs: 0.7% 8 yrs: 2.1% 10 yrs: 5.9% 15 yrs: 5.8% >15 yrs: 17.2%	Kawanishi *et al.* 2004 (11)

Non-Infectious complications

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Complication	Centers		
	Shariati 138 pt	Shafa 360 pt	Other Studies
Catheter Malfunction	20.2%	9.7%	5-20%
Hernia	5.7%	5.27%	10-15%
Hemoperitoneum	6.5%	4.72%	2.2%
Leak	15.2%	10.5%	11%
EPS	2.9%	2.22%	0.7-7.3%

Indian J Nephrol. 2011 Apr-Jun; 21(2): 112–115.

Unpublished Data Shafa PD research center 2014 Dec

Nephrology (Carlton). 2017 Nov;22(11):907-912. doi: 10.1111/nep.12911.

Risk factors for encapsulating peritoneal sclerosis: Analysis of a 36-year experience in a University Hospital.

Nakao M[1], Yamamoto I[1], Maruyama Y[1], Morishita M[1], Nakashima A[1], Matsuo N[1], Tanno Y[1], Ohkido I[1], Ikeda M[1], Yamamoto H[1], Yokoyama K[1], Yokoo T[1].

Author information

Abstract

AIM: Encapsulating peritoneal sclerosis (EPS) is a rare but serious complication that occurs in peritoneal dialysis (PD) therapy. The present study aimed to identify the risk factors, especially peritonitis and biocompatible PD fluid.

CONCLUSION:

- Both the longer duration of peritonitis and higher D/P Cr, as well as the longer PD duration, were risk factors for EPS development.
- **Use of biocompatible PD fluid contributed to the decrease in EPS development.**

Original Article

Systemic Infusion of Autologous Adipose Tissue-Derived Mesenchymal Stem Cells in Peritoneal Dialysis Patients: Feasibility and Safety

Sudabeh Alatab, M.D., Ph.D.[1#], Soroosh Shekarchian, M.D.[2#], Iraj Najafi, M.D.[3], Reza Moghadasali, Ph.D.[2, 4], Naser Ahmadbeigi, Ph.D.[5], Mohammad Reza Pourmand, M.D., Ph.D.[6], Tina Bolurieh, M.Sc.[2], Neda Jaroughi, M.Sc.[2], Gholamreza Pourmand, M.D.[1*], Nasser Aghdami, M.D., Ph.D.[2*]

1. Urology Research Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Regenerative Biomedicine, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran
3. Urology Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
4. Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran
5. Cell-based Therapies Research Center, Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, Iran
6. Department of Pathobiology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

Conclusion: This study, for the first time, showed the feasibility and safety of AD-MSCs in PD patients and the potentials for positive changes in solute transport

Further studies with larger samples, longer follow-up, and randomized blind control groups to elucidate the most effective route, frequency and dose of MSCs administration, are necessary

Epidemiology

- This entity has a various rate of occurrence between 0.7 to 7.3%.

- The highest frequencies are observed in the Japanese reports, while very low prevalence is seen in United States, Canada, and Europe.

- Its annual incidence in chronic ambulatory peritoneal dialysis (CAPD) patients is 0.37 per 1000 patient years with the male to female ratio of 5:2

Biocompatible dialysis fluids for peritoneal dialysis

Published:
26 October 2018

Authors:
Htay H, Johnson DW, Wiggins KJ, Badve SV, Craig JC, Strippoli GFM, Cho Y

Primary Review Group:
Kidney and Transplant Group

What is the issue?

Peritoneal dialysis is a form of dialysis therapy for people with kidney failure delivered at home. Patients are required to use peritoneal dialysis solutions to perform the dialysis by putting solution in their abdomen. Peritoneal dialysis uses the lining of the abdomen called the “peritoneal membrane” as a filter, across which toxins and fluids are removed from the body. The longevity of peritoneal dialysis can be limited by peritoneal membrane injury, which is partly as a result of biologically 'unfriendly' peritoneal dialysis solutions, which are acidic and consist of high levels of glucose and toxic glucose breakdown products. To overcome these hurdles, biocompatible peritoneal dialysis

Am score 14
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Biocompatible dialysis fluids for peritoneal dialysis

- The longevity of PD can be limited by membrane injury, which is partly as a result of biologically 'unfriendly' PD solutions, which are acidic and consist of high levels of glucose and toxic GDP.

- To overcome these hurdles, biocompatible PD solutions (i.e. with a neutral pH and low levels of GDP or with a glucose-alternative like icodextrin) have been manufactured with the aim of providing patient benefit.

Biocompatible dialysis fluids for peritoneal dialysis

- We identified 42 studies (3262 participants) examining the effects of these solutions on patient outcomes.

- Neutral pH, low GDP PD solutions resulted in better preservation of a patient's own kidney function including urine output.

- Patients on (icodextrin) achieved greater fluid removal with their dialysis and were 70% less likely to experience uncontrolled episodes of fluid overload.

Biocompatible dialysis fluids for peritoneal dialysis

- No significant harms were identified with any of the biocompatible peritoneal dialysis solutions.

- Many of the studies were limited by small size, short follow-up duration, suboptimal methodological quality, and inconsistent reporting of outcomes.

- Consequently, the effects of biocompatible peritoneal dialysis solutions on the length of time that a patient is able to either remain on peritoneal dialysis or stay alive are uncertain

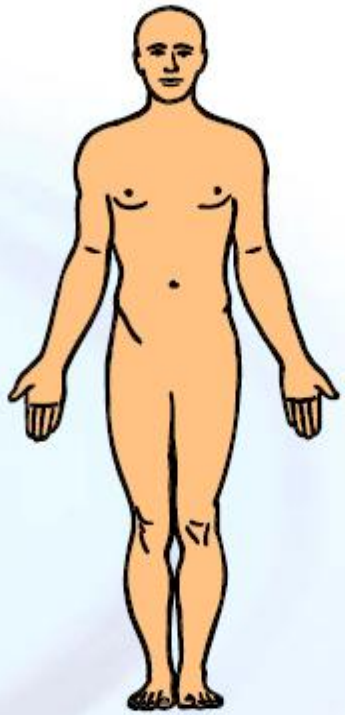
Biocompatible dialysis fluids for peritoneal dialysis

- Compared with peritoneal dialysis patients treated with conventional peritoneal dialysis solutions, those treated with biocompatible solutions experience important benefits including better preservation of their own kidney function and urine volume with neutral pH, low glucose breakdown product peritoneal dialysis solutions and more effective prevention of fluid overload due to increased dialysis-related fluid removal with icodextrin. Whether these benefits help patients to stay on peritoneal dialysis longer or live longer are uncertain and require further study

Slowing down progression of co-morbidities

Advanced solutions in combination may help to slow down the progression of co-morbidities by:

- Minimising glucose load
- Optimising fluid balance
- Delivering 25% of daily protein needs
- Improving hyperlipidaemia
- Reducing hypertension
- Improving blood sugar control
- Preserving RRF

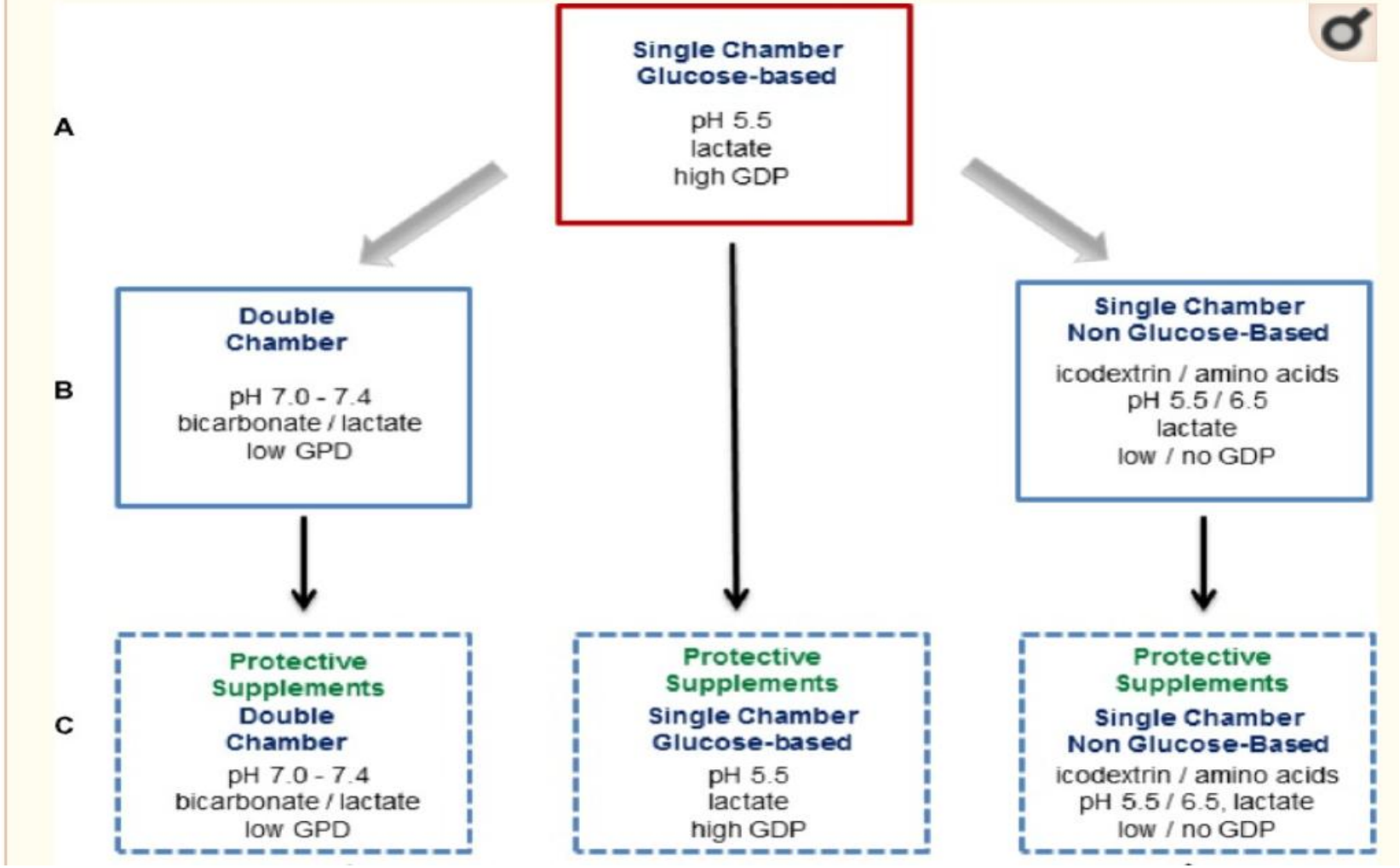


Front Physiol. 2018; 9: 1853.
Published online 2019 Jan 7. doi: 10.3389/fphys.2018.01853
PMCID: PMC6343681
PMID: 30700974

Biocompatible Peritoneal Dialysis: The Target Is Still Way Off

Maria Bartosova and Claus Peter Schmitt*

▸ Author information ▸ Article notes ▸ Copyright and License information Disclaimer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icodextrin / amino acids
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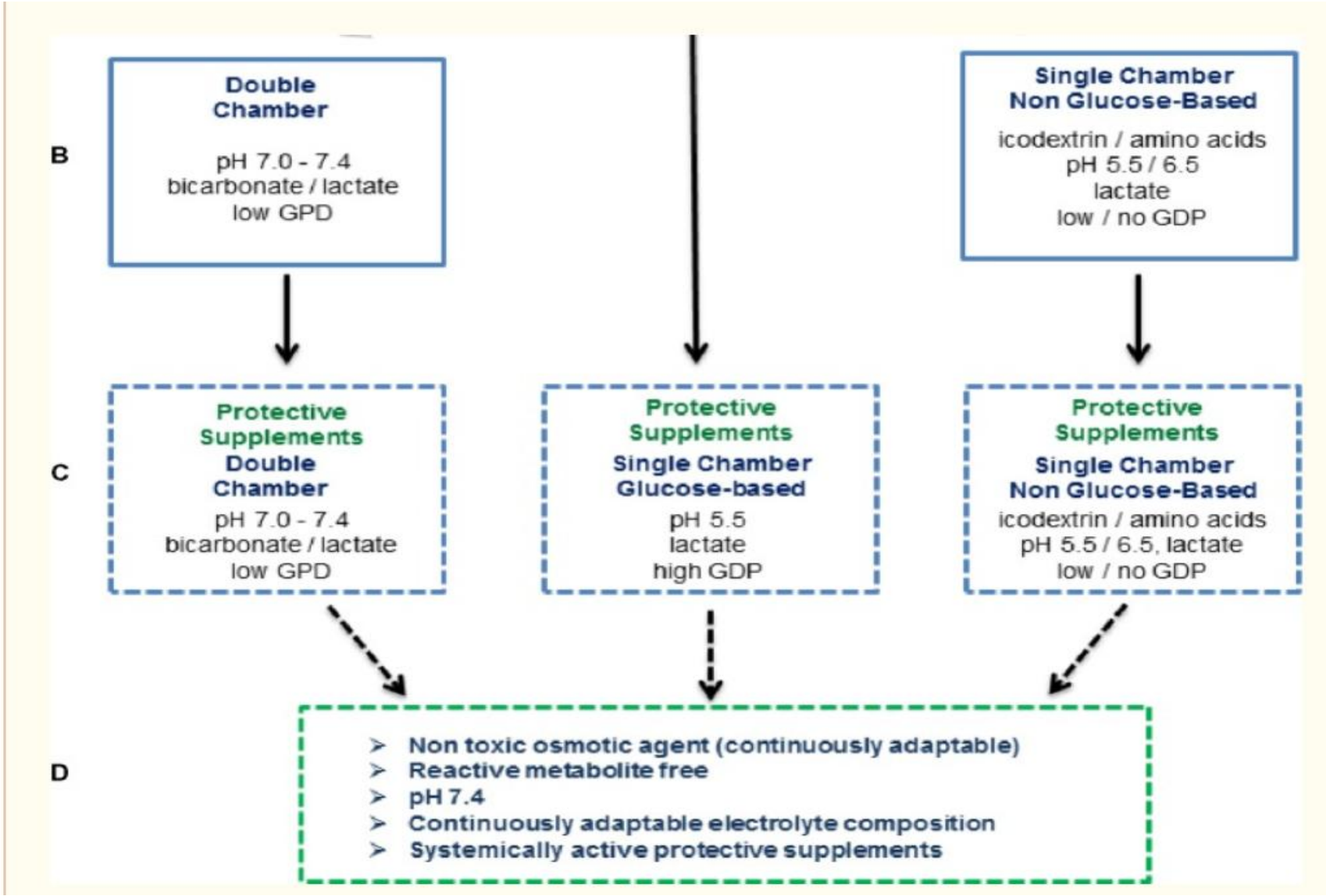
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C
Protective Supplements
Double Chamber
pH 7.0 - 7.4
bicarbonate / lactate
low GPD
Protective Supplements
Single Chamber Glucose-based
pH 5.5
lactate
high GDP
Protective Supplements
Single Chamber Non Glucose-Based
icodextrin / amino acids
pH 5.5 / 6.5, lactate
low / no GDP
D
Non toxic osmotic agent (continuously adaptable)
Reactive metabolite free
pH 7.4
Continuously adaptable electrolyte composition
Systemically active protective supplements

Perit Dial Int. 2009 Mar-Apr;29(2):204-16.

Evaluation of taurine as an osmotic agent for peritoneal dialysis solution.

Nishimura H[1], Ikehara O, Naito T, Higuchi C, Sanaka T.

- 3.5% taurine-based PD fluid achieved equivalent ultrafiltration as glucose-based PD fluid and induced less mesothelial and fibroblast-like cell proliferation in rats

- L-carnitine has a dose-dependent osmotic effect similar to glucose.
- L-carnitine increased the expression of AQP1, significantly improved viability, and prevented glucose-induced apoptosis.

AJKD
AMERICAN JOURNAL OF KIDNEY DISEASES
Official Journal of the National Kidney Foundation

To read this article in full, please review your options for gaining access at the bottom of the page.

Effect of an L-Carnitine–Containing Peritoneal Dialysate on Insulin Sensitivity in Patients Treated With CAPD: A 4-Month, Prospective, Multicenter Randomized Trial

Mario Bonomini, MD, Lorenzo Di Liberato, MD, Goffredo Del Rosso, MD, Antonio Stingone, MD, Giancarlo Marinangeli, MD, Agostino Consoli, MD, Silvio Bertoli, MD, Amedeo De Vecchi, MD, Emanuele Bosi, MD, Roberto Russo, MD, Roberto Corciulo, MD, Loreto Gesualdo, MD, Francesco Giorgino, MD, Paolo Cerasoli, MD, Augusto Di Castelnuovo, PhD, Maria Pia Monaco, MD, Ty Shockley, ScD, Claudia Rossi, PhD, Arduino Arduini, MD

Conclusions

The use of L-carnitine in dialysis solutions may represent a new approach to **improving insulin sensitivity** in nondiabetic peritoneal dialysis patients.

JOURNAL OF THE INTERNATIONAL SOCIETY FOR PERITONEAL DIALYSIS
Peritoneal Dialysis INTERNATIONAL
CURRENT SEARCH ARCHIVES SUBSCRIBE PDI IN PRESS SUBMIT

Perit Dial Int. 2013 Jan-Feb; 33(1): 15–27.
doi: 10.3747/pdi.2012.00148
PMCID: PMC3598258
PMID: 23349194

Hyperbranched Polyglycerol Is an Efficacious and Biocompatible Novel Osmotic Agent in a Rodent Model of Peritoneal Dialysis

Asher A. Mendelson,[1] Qiunong Guan,[2] Irina Chafeeva,[3] Gerald A. da Roza,[1] Jayachandran N. Kizhakkedathu,[3,4] and Caigan Du[2,5]

CONCLUSIONS

- A novel HPG-based PD solution can achieve successful UF and waste removal while **reducing peritoneal injury and inflammation**.
- This preliminary study suggests that HPG may be a promising alternative to glucose in the development of **next-generation PD solutions** for patients with end-stage renal disease.

J Transl Med. 2016; 14: 338.
Published online 2016 Dec 13. doi: 10.1186/s12967-016-1098-z
PMCID: PMC5153908
PMID: 27964722

Hyperbranched polyglycerol is superior to glucose for long-term preservation of peritoneal membrane in a rat model of chronic peritoneal dialysis

Caigan Du,[#1,5] Asher A. Mendelson,[#2,6] Qiunong Guan,[1] Ghida Dairi,[1] Irina Chafeeva,[3] Gerald da Roza,[2] and Jayachandran N. Kizhakkedathu[3,4]

Conclusion

- Present study clearly suggests that HPG is a promising novel osmotic agent for use in PD
- Currently we are investigating the metabolic and pharmacokinetic pathways of HPG in order **to ensure that our novel solution is safe** for long-term use in patients

BCPT
Basic & Clinical Pharmacology & Toxicology

Original Article

Peritoneal and Systemic Responses of Obese Type II Diabetic Rats to Chronic Exposure to a Hyperbranched Polyglycerol-Based Dialysis Solution

Bo La Han, Qiunong Guan, Irina Chafeeva, Asher A. Mendelson, Gerald da Roza, Richard Liggins, Jayachandran N. Kizhakkedathu, Caigan Du

First published: 12 May 2018 | https://doi.org/10.1111/bcpt.13038 | Cited by: 1

Conclusions

Compared to **physioneal or icodextrin** solutions, the HPG solution had **less adverse effects** locally on the **PM** and systemically on distant organs (e.g. **kidneys**) and the plasma oxidative status in rats with MetS.

Kidney Int. 2016 Mar;89(3):625-35. doi: 10.1016/j.kint.2015.12.005. Epub 2016 Jan 8.

The dipeptide alanyl-glutamine ameliorates peritoneal fibrosis and attenuates IL-17 dependent pathways during peritoneal dialysis.

Ferrantelli E[1], Liappas G[2], Vila Cuenca M[1], Keuning ED[1], Foster TL[1], Vervloet MG[3], Lopéz-Cabrera M[2], Beelen RH[4].

- It **reduced peritoneal thickness**, αSMA expression and angiogenesis.
- **Attenuate the IL-17 pathway** expression, transforming growth factor β, IL-6, and the transcription factor retinoic acid receptor-related orphan receptor gamma T

Kidney Int. 2016 Mar;89(3):625-35. doi: 10.1016/j.kint.2015.12.005. Epub 2016 Jan 8.

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- Thus, intraperitoneal administration of Ala-Gln, a stable dipeptide commonly used in parenteral nutrition, ameliorates PD-induced peritoneal damage in animal models, in part by modulating IL-17 expression.

- Hence, Ala-Gln supplementation of dialysate may be a potential strategy to ameliorate peritoneal deterioration during PD.

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PLoS One. 2016; 11(10): e0165045. PMCID: PMC5074513

Published online 2016 Oct 21. doi: 10.1371/journal.pone.0165045 PMID: 27768727

Addition of Alanyl-Glutamine to Dialysis Fluid Restores Peritoneal Cellular Stress Responses – A First-In-Man Trial

Klaus Kratochwill,[1,2,3] Michael Boehm,[1] Rebecca Herzog,[1,2,3] Katharina Gruber,[1] Anton Michael Lichtenauer,[1,3] Lilian Kuster,[1,3] Dagmar Csaicsich,[1] Andreas Gleiss,[4] Seth L. Alper,[5] Christoph Aufricht,[1] and Andreas Vychytil[6,*]

Conclusions

- A single dwell of AlaGln-supplemented glucose-based PDF increased peritoneal cell HSP expression and enhanced stimulated *ex-vivo* cytokine release.
- AlaGln attenuated peritoneal effluent inflammatory markers in patients with prior peritonitis.

Primary outcome data

Parameter (unit)	Placebo Mean ± SD (*n*) Median (range)	AlaGln Mean ± SD (*n*) Median (range)	Difference AlaGln–placebo LS mean (95% CI)	*P* value (1-sided)
CA-125 appearance rate (U/min), FAS	253.9 ± 103.1 (38) 250.6 (98.6–555.4)	302.3 ± 141.7 (39) 273.8 (119.9–764.6)	46.7 (23.5–69.9)	0.0001
CA-125 appearance rate (U/min), PP	253.4 ± 104.5 (37) 248.8 (98.6–555.4)	303.8 ± 143.3 (38) 274.5 (119.9–764.6)	48.0 (24.3–71.6)	0.0001
Stimulated IL-6 release (1 h) ([$\log_{10}$] pg/ml), FAS	1.36 ± 0.55 (38) 1.25 (0.23–2.74)	1.52 ± 0.48 (40) 1.47 (0.66–2.74)	0.15 (0.04–0.26)	0.0040
Stimulated IL-6 release (1 h) ([$\log_{10}$] pg/ml), PP	1.36 ± 0.56 (37) 1.25 (0.23–2.74)	1.53 ± 0.49 (39) 1.48 (0.66–2.74)	0.16 (0.05–0.26)	0.0033

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PLoS One. 2016; 11(10): e0165045.
Published online 2016 Oct 21. doi: 10.1371/journal.pone.0165045
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- In the intensive care setting, both CSR and patient outcome were shown to deteriorate in parallel with systemic glutamine (Gln) depletion and to improve with Gln supplementation.
- A recent Cochrane meta-analysis of 53 randomized controlled trials concluded that Gln supplementation reduced infection rate and length of hospital stay in critically ill patients.
- The relevant cellular processes underlying dysfunctional CSR and impaired host defense in these patients and in patients undergoing PD are likely closely linked by a common pathomechanism, such as injury induced chronic inflammation.

PLoS One. 2016; 11(10): e0165045.
Published online 2016 Oct 21. doi: 10.1371/journal.pone.0165045
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Addition of Alanyl-Glutamine to Dialysis Fluid Restores Peritoneal Cellular Stress Responses — A First-In-Man Trial

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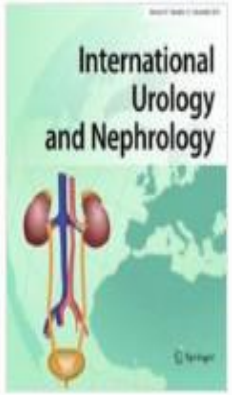
- We recently demonstrated that Gln depletion during PDF exposure aggravated mesothelial cell injury and suppressed CSR
- PDF supplementation with Gln or with its stable dipeptide, alanyl-glutamine (AlaGln), restored CSR and enhanced both heat shock protein (HSP) expression and cytoprotection in *in-vitro* and *in-vivo* models of PD
- As AlaGln is already used clinically for parenteral nutrition, this approach is particularly attractive for translation from bench-to-bedside in PD.

Conclusions

A novel AlaGln-supplemented PDF, compared with treatment with a dual-chamber PDF, improves important biomarkers of mesothelial cell status, peritoneal immune competence, and systemic inflammation in PD patients



International Urology and Nephrology

December 2015, Volume 47, Issue 12, pp 2047–2051 | Cite as

Effect of bevacizumab, a vascular endothelial growth factor inhibitor, on a rat model of peritoneal sclerosis

Authors Authors and affiliations

Sibel Ada, Sibel Ersan, Aykut Sifil, Mehtat Unlu, Efsun Kolatan, Mehmet Sert, Sulen Sarioglu, Osman Yilmaz, Taner Camsari

Conclusion

Histopathologically, bevacizumab was proven to **attenuate fibrotic process** in experimental peritoneal sclerosis model.

Conclusions

The noninferiority of the low-sodium PD solution for total Kt/V_{urea} could not be proved; however, it showed **beneficial clinical effects on sodium removal and BP**

Kidney Int. 2016 Apr;89(4):761-6. doi: 10.1016/j.kint.2015.12.032. Epub 2016 Jan 21.

Increasing sodium removal on peritoneal dialysis: applying dialysis mechanics to the peritoneal dialysis prescription.

Fischbach M[1], Schmitt CP[2], Shroff R[3], Zaloszyc A[4], Warady BA[5].

- PD prescription can be adapted to promote small pore transport to achieve improved sodium and fluid management. Both adequate dwell volume and dwell time are required for small pore transport.

- The dwell volume determines the amount of "wetted" peritoneal membrane being increased in the supine position and optimized at dwell volumes of approximately 1400 ml/m.

- Diffusion across the recruited small pores is time-dependent, favored by a long dwell time, and driven by the transmembrane solute gradient.

- In adapted automated PD, **sequential short- and longer-dwell exchanges, with small and large dwell volumes**, respectively, are used.

- A crossover trial in adults and a pilot study in children suggests that sodium and fluid removal are increased by adapted automated PD, leading to improved blood pressure control when compared with conventional PD.

Pharmacologic therapies targeting AQP1

- Steroids may be efficacious in humans as illustrated by comparing ultrafiltration in patients before and after kidney transplantation.

- Another potential agent is an arylsulfonamide, AqF026, the first pharmacologic agonist of AQP1 that interacts with an intracellular loop involved in the gating of the channel.

- These enhances AQP1-mediated water transport and net ultrafiltration in rodents.

Kidney Int. 2016 Apr;89(4):761-6. doi: 10.1016/j.kint.2015.12.032. Epub 2016 Jan 21.

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- A crossover trial in adults and a pilot study in children suggests that **sodium and fluid removal are increased by adapted automated PD**, leading to improved blood pressure control when compared with conventional PD.

Key strategies for facilitating PD utilization

- Implementation of policies and incentives that favor this modality
- Production and supply of peritoneal dialysis fluid at a low cost
- Training for nephrologists to enable increased utilization
- Ensure that rates of technique failure continue to decline
- Further growth in PD use is required to enable this modality to become an integral part of renal replacement therapy

ESRD Costs

How novel and original must be each new man's view of the universe — for though the world is so old — and so many books have been written — each object appears wholly undescribed to our experience — each field of thought wholly unexplored — The whole world is an America — a New World.

HENRY DAVID THOREAU
Journals

Total Medicare spending in 2010 rose 6.5 percent, to $522.8 billion. Expenditures for ESRD rose 8.0 percent, to $32.9 billion. These numbers include the new Medicare Part D prescription drug benefit, as the USRDS Coordinating Center now receives up-to-date data on Part D use in the ESRD population.

These expenditures cover 488,938 patients in the prevalent Medicare ESRD population, along with 105,436 non-Medicare patients; these latter patients cost an additional estimated $14.5 billion (data from Table p.a in the Précis).

Medicare HMO costs for ESRD rose to $3.38 billion in 2010, 7.1 percent higher than in 2009. This annual increase is the lowest since 2003, when the new Medicare hierarchical payment model, with disease burden risk adjusters, was implemented for Medicare Advantage (HMOs). Fee-for-service Medicare inpatient expenditures per person per year (PPPY) rose nearly 5.3 percent in 2010, down from their 18 percent growth in 2008, while PPPY costs by modality remained nearly stable, rising just 1.4 percent for hemodialysis patients. Interestingly, there were large increases across modalities in 2007–2008, from 8.9 percent for peritoneal dialysis patients to 7.7 percent for both hemodialysis and transplant patients. These year-to-year variations will need more complete assessment — including consideration of cause-specific hospitalizations — to define their exact source. With 2010 the last year before the start of the new bundled prospective payment system, some providers may have reduced expenditures in the months prior to January 1, 2011, in anticipation of the changing incentives.

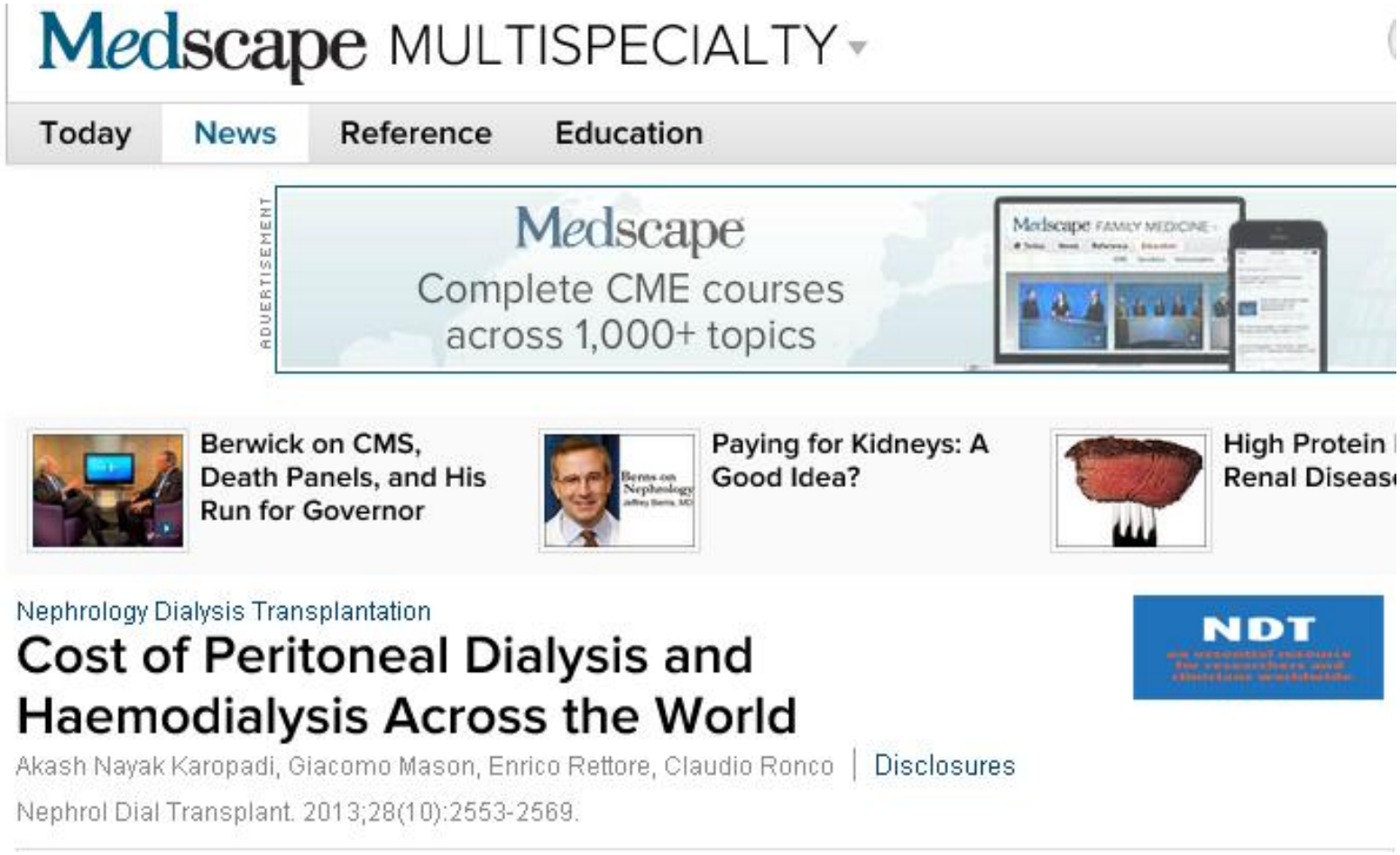
Recent attention to therapies using erythropoiesis stimulating agents (ESAs) has raised awareness of their costs to the healthcare system. After increasing each year since 1992 (including growth of 11–19 percent in 2002–2004) to reach nearly $2 billion, Medicare ESA costs were stable in 2004–2008, rose 4.9 percent in 2009, and changed little in 2010. Costs for IV vitamin D rose 12 percent in 2008, 5.7 percent in 2009, and 2.2 percent in 2010, reaching $519 million. And IV iron costs rose 6.6 percent in 2010, reaching a new high of $304 million.

The Average Sale Price payment system for injectables was introduced in 2004, as investigations showed that many providers had very profitable discount agreements, accounting for significant margins paid under the Medicare system. The composite rate payment was thus rebased, and the margins generated for injectables were addressed by allowing providers to receive only 6 percent above the sale price, monitored under quarterly reporting to CMS. There have been other

Overall annual cost of care for

- In-center Hemodialysis: US$ 51,252
- Satellite Hemodialysis: $ 42,057
- Home/self-care hemodialysis: $ 29,961
- Peritoneal dialysis :$ 26,959 ($P < 0.001$)

- After adjustment for the effect of other important predictors of cost, such as comorbidity, these differences persisted.



øOur final calculations included 46 countries (20 developed and 26 developing)

Table 1. Studies comparing HD and PD costs (arranged according to the country and year of publication)

Source	Country	Year of publication	HD/PD cost ratio	Methodological notes
North America				
McMurry *et al.* [24]	USA	1997	1.43	CB
Bruns *et al.* [25]	USA	1998	1.52	CB
Shih *et al.* [6]	USA	2005	1.2	CB
Berger *et al.* [26]	USA	2009	1.37	CB
USRDS Annual Report [2]	USA	2012	1.3	CB
BC Renal Council Project [27]	Canada—British Columbia	1994	1.77	CB
Goeree *et al.* [28]	Canada—Ontario	1995	1.98	CB
Coyte *et al.* [29]	Canada—Ontario	1996	1.6	CB
Lee *et al.* [30]	Canada—Alberta	2002	1.9	CB

Cost of Peritoneal Dialysis and Haemodialysis Across the World

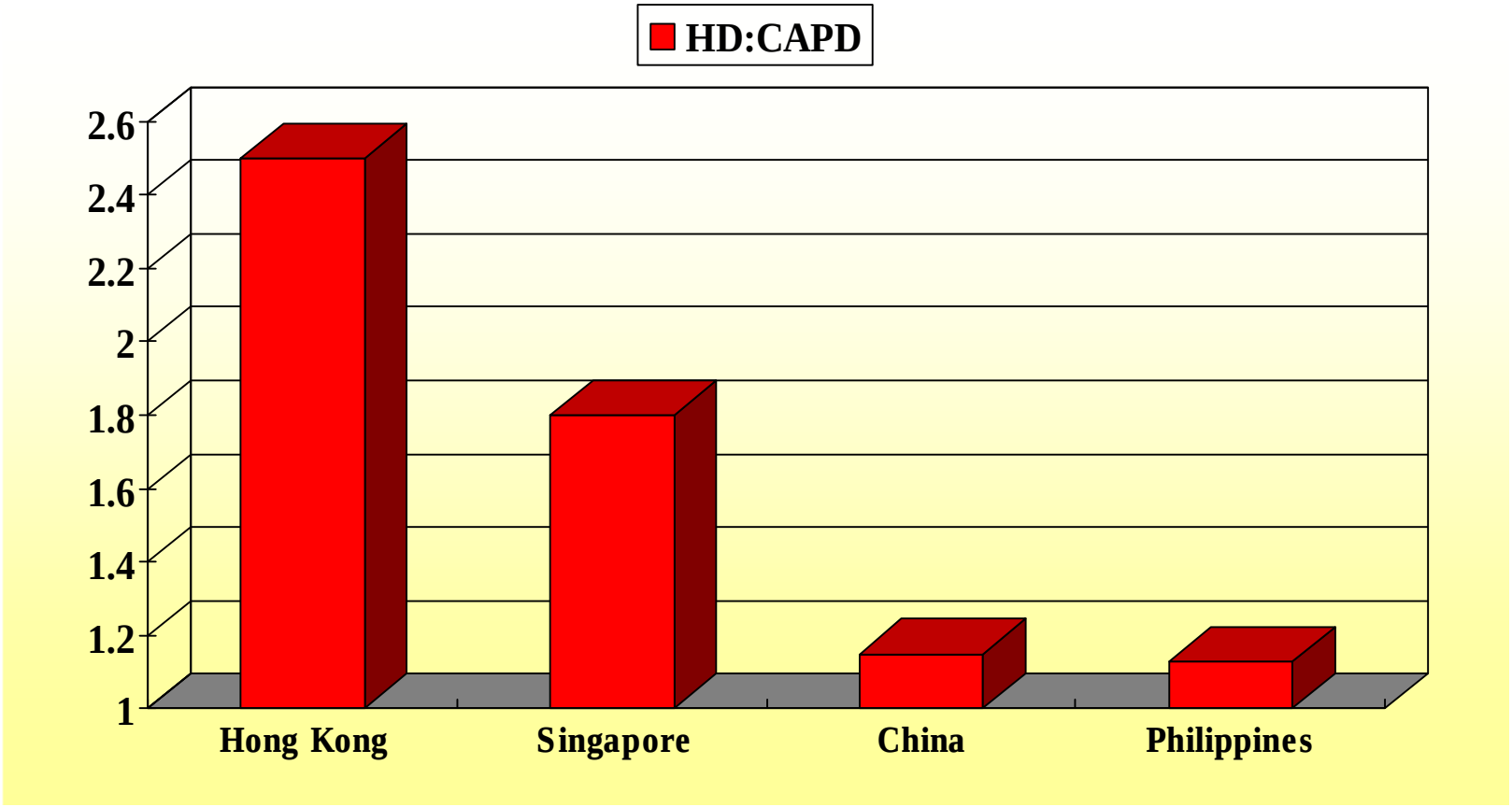
Akash Nayak Karopadi, Giacomo Mason, Enrico Rettore, Claudio Ronco

DisclosuresNephrol Dial Transplant. 2013;28(10):2553-2569.

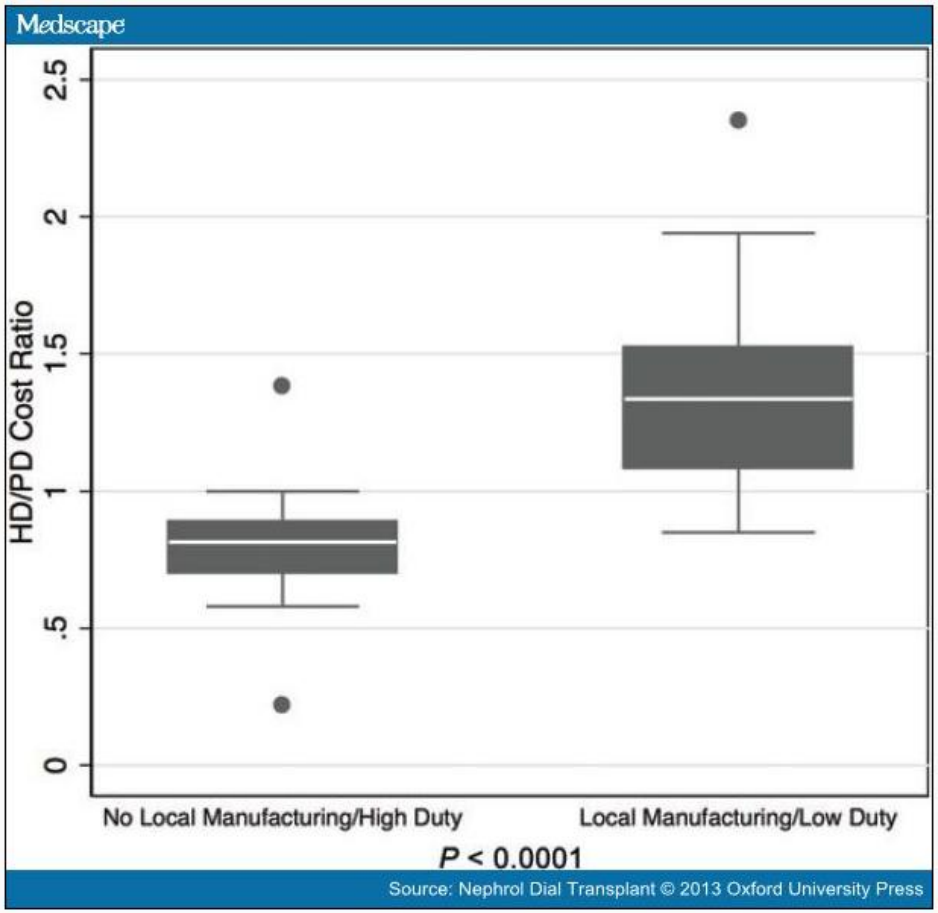
- Most developed countries can provide PD at a lesser expense to the healthcare system than HD.

- The evidence on developing countries is more mixed, but in most cases PD can be provided at a similar cost where economies of scale have been achieved, either by local production or by low import duties on PD equipment.

Cost Ratio: HD vs PD



The Roll of Local Manufacturing of PD solutions



Cost of Peritoneal Dialysis and Haemodialysis Across the World

[CLOSE WINDOW]

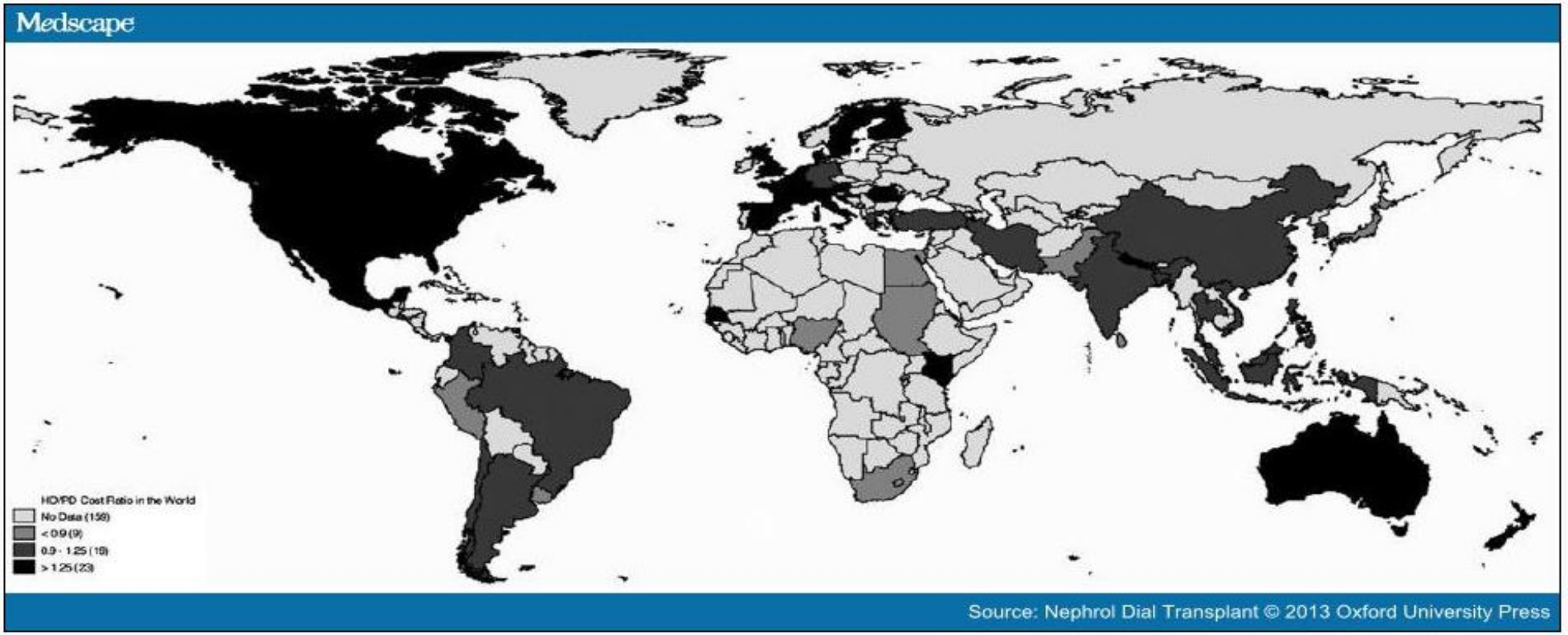


Figure 1.

Map summarizing the HD/PD ratios in 51 countries (survey data included). Countries are placed in three categories: (i) HD/PD ratio <0.90. (ii) HD/PD ratio between 0.90 and 1.25. (iii) HD/PD ratio >1.25. Map was generated using Stata 12 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP.)

Conclusion

PD

is overall more cost-effective than

HD

Economy of RRT Modalities in Iran
(Hemodialysis vs. Peritoneal Dialysis)

Authors: Farhang ZangnehH., Manbachi M., Najafi I., Mehran Nikoo H., Keyvani M.

INTRODUCTION

Health care expenditure in European countries varies between 11% of Gross Domestic Product (GDP) (Germany) and 6% of GDP (Luxemburg) whereas in Iran, this figure sums up to about 4% of the GDP. On the other hand, dialysis costs (in comparison to the total health budget) vary between 36% in France and 19% in Germany, while not more than 0.04% of the general population (on the average) is under dialysis. In previous studies performed by the MOH in Iran, CAPD (with an annual cost of around 70 million Rials) was introduced more expensive than hemodialysis (with an annual cost of around 48 million Rials) in the governmental sector. As this report contradicts completely with the information from other regions of the world, where CAPD is at least 30% less expensive than hemodialysis, we decided to have a second thought on this issue in Iran.

MATERIAL AND METHODS

According to the international guidelines, we have classified all the related expenses into six general categories, summarized as below:

7th EuroPD meeting; Prague, Oct 2005 poster presentation

Economy of RRT Modalities in Iran

(Hemodialysis vs. Peritoneal Dialysis)

Authors: Farhang ZangnehH., Manbachi M., Najafi I., Mehran Nikoo H., Keyvani M.

Annual Costs Per Patient (in Rials and US Dollar)	Hemodialysis	CAPD
Hardware & Services	11,927,644	891,694
Physicians & Nurses	11,576,500	4,052,137
Pharmaceuticals	28,632,302	13,898,446
Consumables	32,189,820	71,892,493
Complications	1,190,000	1,173,699
Others	16,315,760	2,025,113
Total (Rials)	**101,832,027**	**93,933,582**
Total (US $)	**11,572**	**10,674**

Comment: The extended calculations can be found *here*.

Convince the Ministry

Table 1. Studies comparing HD and PD costs (arranged according to the country and year of publication)

Source	Country	Year of publication	HD/PD cost ratio	Methodological notes
Abraham *et al.* [80]	Sri Lanka	2008	0.85	B
Van Bui *et al.* [17]	Vietnam	2008	Similar cost	B
Naidas *et al.* [18]	Philippines	1998	1.14	CE
Prodjosudhadi *et al.* [10]	Indonesia	2006	1.03	B
Morad *et al.* [81]	Malaysia	2005	1.08	B
Hooi *et al.* [82]	Malaysia	2005	1.06	CE
Lim *et al.* [83]	Malaysia	1999	0.81	CE
Teerawattanon *et al.* [84]	Thailand	2007	1.07	CU
Neil *et al.* [16]	Thailand	2009	1.13	CB
Li and Chow [4]	Japan	2001	1.09	B
Fukuhara *et al.* [15]	Japan	2007	0.85	CB
Yu *et al.* [85]	Hong Kong	2007	2.35	B
Neil *et al.* [16]	Singapore	2009	1.38	CB
Utas *et al.* [12]	Turkey	2008	1.16	CB
Erek *et al.* [13]	Turkey	2004	1.02	CB
Najafi *et al.* [11]	Iran	2010	1.08	B

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PD cost in Iran

- The cost of PD comparing HD now in Iran is 20% more expensive.

430,000,000 as compared with 350,000,000 Rials

$ 12,500 PD vs 10,150 HD

12 years ago it was reversed

PD cost in Iran

Therefore, in the healthcare reform process, cost-effective care of patients on Peritoneal dialysis is of utmost importance to assure its

expanding feature

PD - Iran perspective

- PD remains underutilized as an initial modality in the majority of new end-stage renal disease (ESRD) patients in the Iran.

- Currently, almost 97% of all incident dialysis patients start in-center HD, a good numbers of them with a central venous catheter.

- The quality of life, is inferior in HD versus PD

PD - Iran perspective

- Although the reasons are not entirely clear, it appears the increased HD utilization has been driven by :

1) Ease of HD initiation,
2) Physician experience and training,
3) Misinformation about contraindications to PD,
4) Inadequate pre-ESRD patient education,
5) Large in-center HD capacity with prior financial incentives favoring HD,
6) Lack of PD related infrastructure to assure successful PD program utilization,
7) Questions regarding the quality of local manufactured PD solutions,
8) Higher cost of PD comparing HD

PD Infrastructure in Iran

- Aside from governmental and healthcare system support, the key infrastructural features that allow for successful PD programs include:
  - Adequate pre- ESRD CKD education,
  - Adequate physician knowledge,
  - Nurse training in PD,
  - Adequate support staff,
  - Adequate size of program,
  - Continuous quality monitoring programs

Many of infrastructural are lacking in Iran

Barriers to PD in Iran

The Iran ESRD marketplace has traditionally been better suited to support in-center HD

With reimbursement for dialysis services favoring HD

- The dialysis organizations
- Policy makers, and other
- Stakeholders

Have created the infrastructure to support in-center HD with less of a focus on home modalities

How to increase PD utilization

- PD utilization can be effectively promoted by governments; the implementation of a PD first programme (Hong kong, Thailand, Singapore)

- Encouragement of local manufacturing or production of CAPD bags (India over the last decade)

- Slashing of import duties on CAPD bags (in Nepal and Malaysia).

Governmental Policy

Should be PD-first , favored policy in Iran

Actual process of running PD first policy in Thailand

• Budgeting
• Formation of the first provider group (Phase I PD hospitals)
• Obtaining cheap PD solution supplies
• Training a new generation of medical personnel
• Learning form the success PD programs in Hong Kong and Singapore
• Setting up PD technology and training centers for problem solving
• Policy management by the national RRT committee
• Setting up regional RRT technology and training centers for quality control

PD First save a lot of money

- Currently, the USA spends nearly 18% of its GDP on healthcare

- Neil *et al*. USA could realize aggregated savings of over USD 1.1 billion in 5 years just on Medicare costs if PD utilization were increased to 15% (from the current 7%).

PD-First Policy

Global overview of PD First policy

&

Iran perspective

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