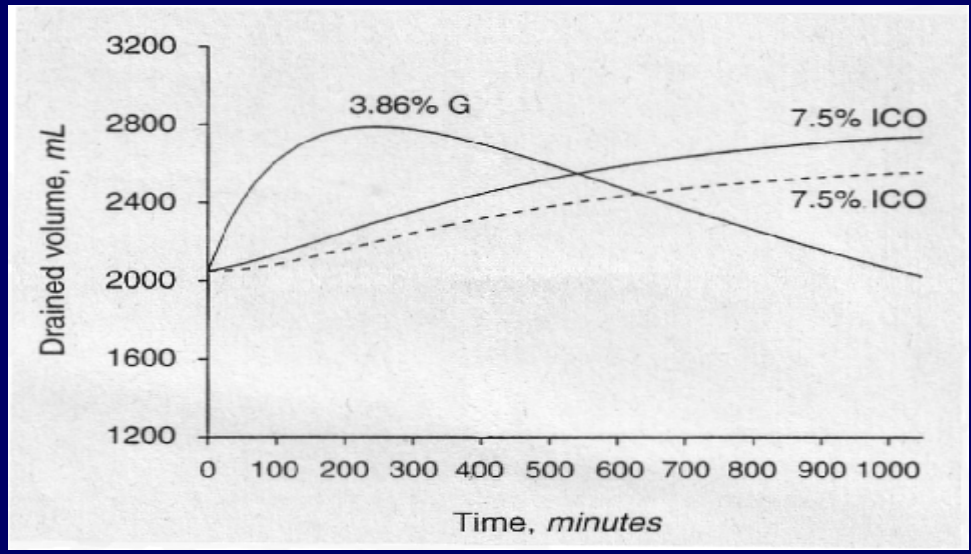
Icodextrin characteristics



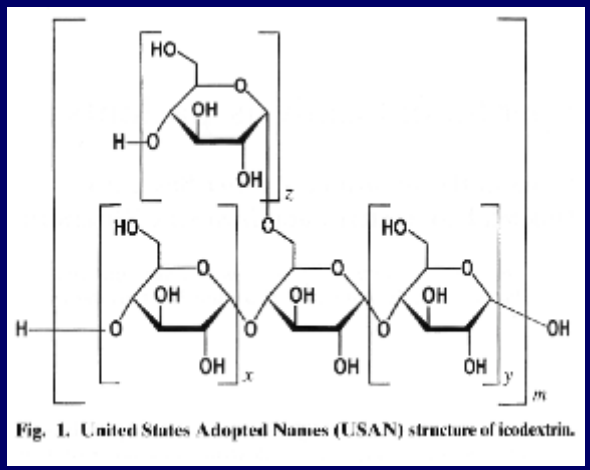


Fig. 1. United States Adopted Names (USAN) structure of icodextrin.

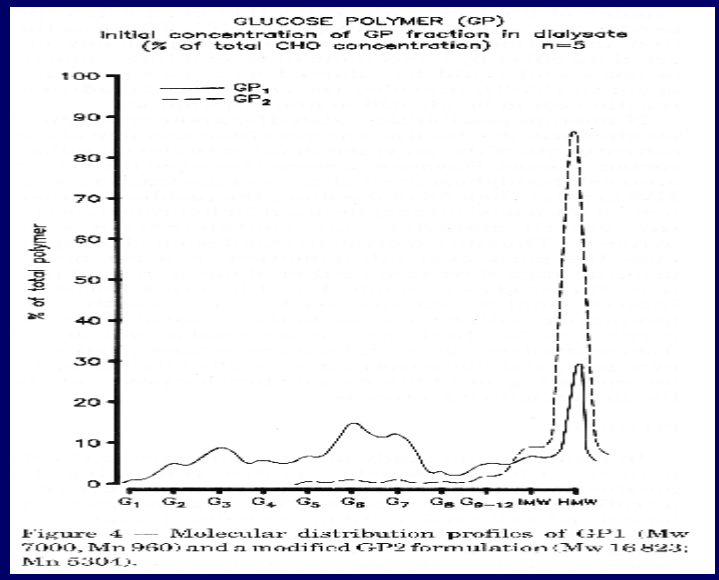
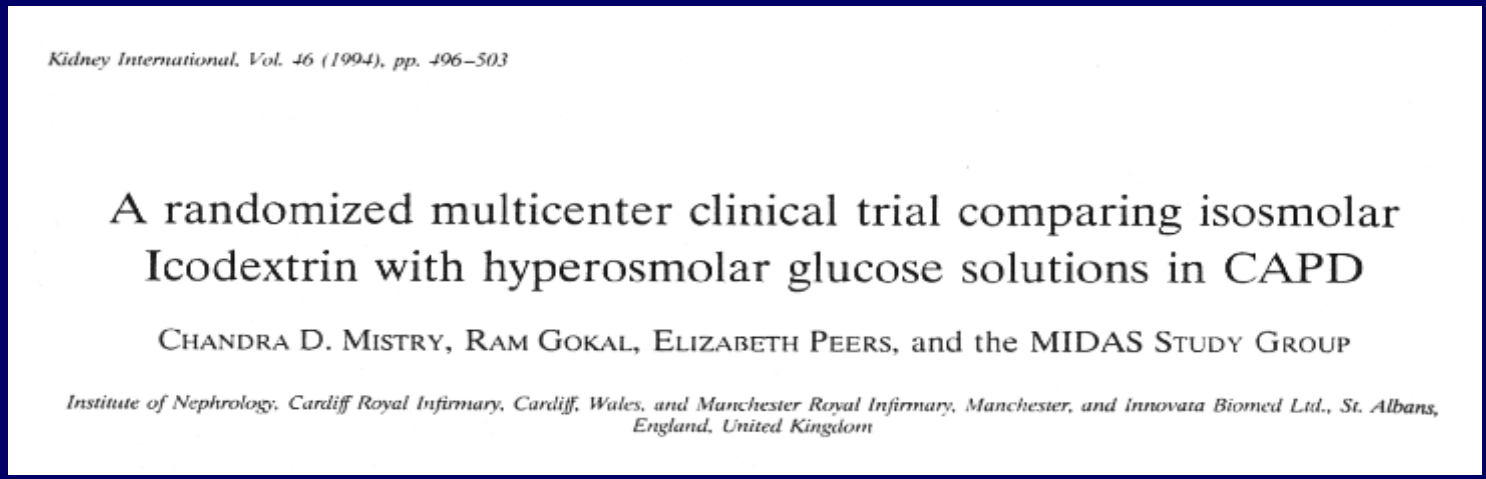


Figure 4 — Molecular distribution profiles of GP1 (Mw 7000, Mn 960) and a modified GP2 formulation (Mw 16 823; Mn 5304).

The MIDAS study



Kidney International, Vol. 46 (1994), pp. 496–503

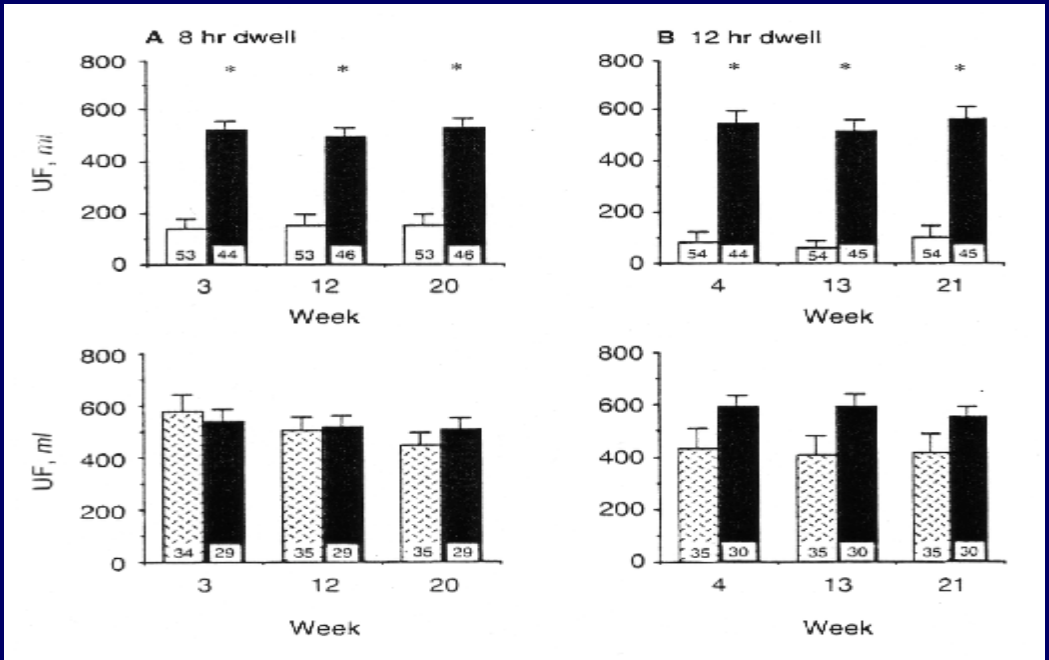
A randomized multicenter clinical trial comparing isosmolar Icodextrin with hyperosmolar glucose solutions in CAPD

CHANDRA D. MISTRY, RAM GOKAL, ELIZABETH PEERS, and the MIDAS STUDY GROUP

Institute of Nephrology, Cardiff Royal Infirmary, Cardiff, Wales, and Manchester Royal Infirmary, Manchester, and Innovata Biomed Ltd., St. Albans, England, United Kingdom

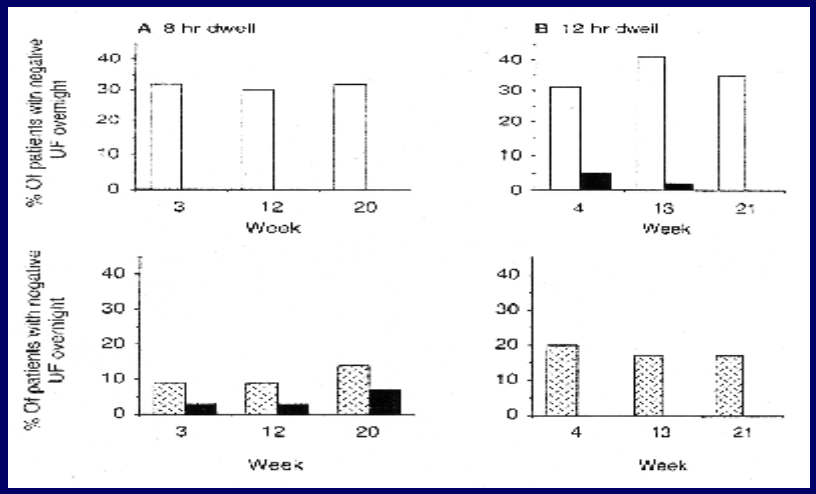
- 11 Centers.
- 106 patients treated with Icodextrin and 103 controls with glucose overnight.
- 6 months follow-up.

Results of MIDAS study



- Efficacy: ultrafiltration good and sustained, similar to G 3.86% at 8 hours.
- Safety: no adverse side effects at 6 months.

The problems reported by MIDAS



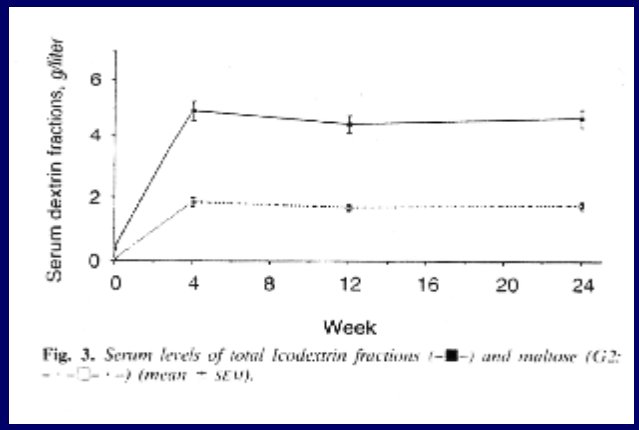
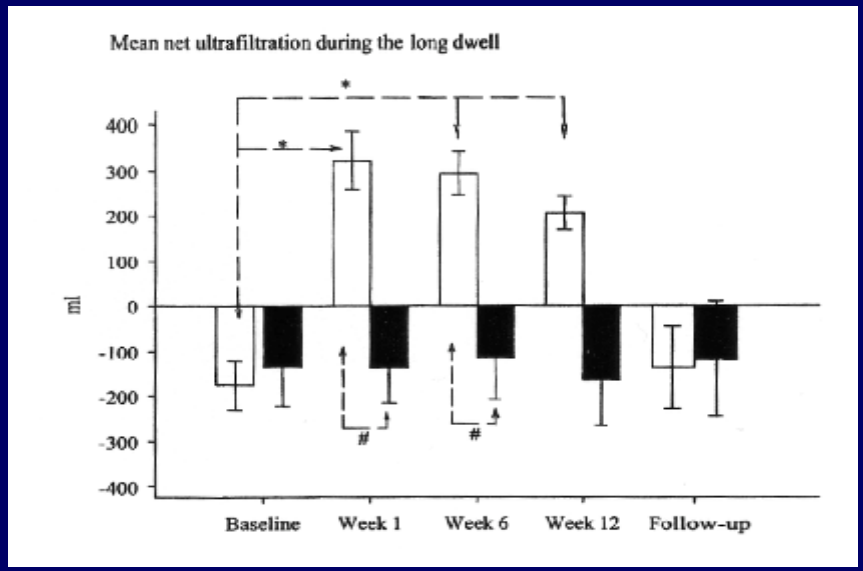
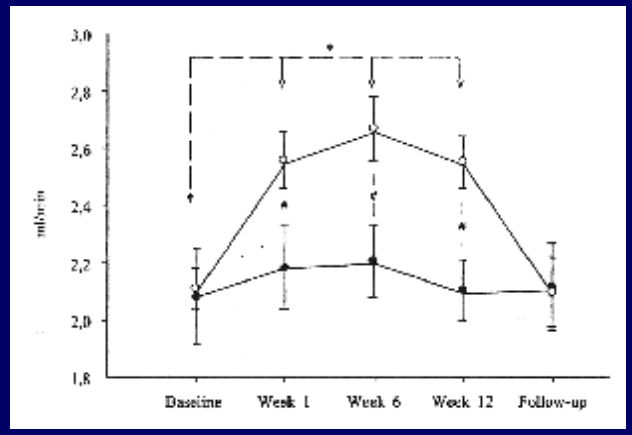


Fig. 3. *Serum levels of total Icodextrin fractions (–■–) and maltose (G2: - - -□- - -) (mean ± SEM).*

- Non responders: a small percentage of patients on Icodextrin with negative ultrafiltration.
- Absorption of 29±5g giving total plasma Icodextrin and maltose 14 and 30 times higher respectively.
- Mild hyponatremia.

Icodextrin in APD



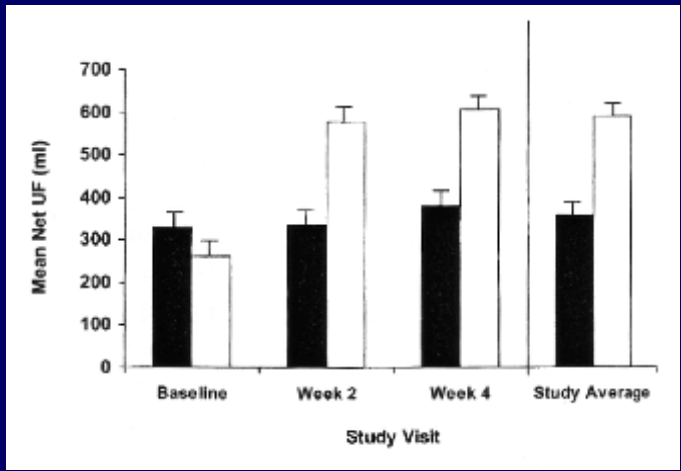


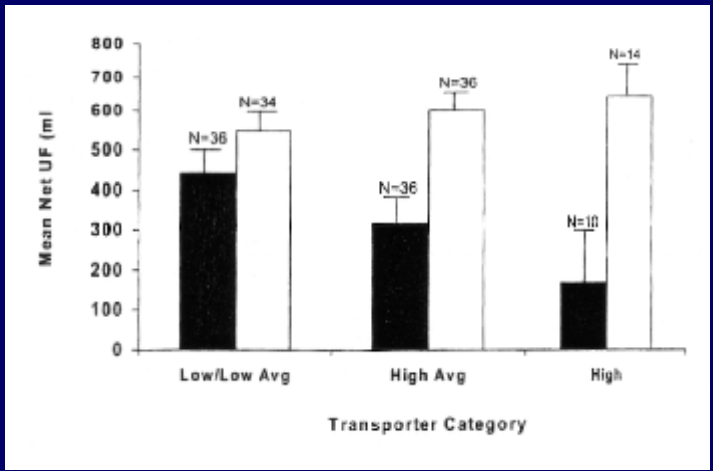
- Posthuma, Perit Dial Int 1997;17:602-7.
- Woodrow, Nephrol Dial Transplant 1999;14:1530-5.
- Plum, Am J Kidney Dis 2002;39:862-71.

A recent USA trial confirming MIDAS study

A Randomized Controlled Trial to Evaluate the Efficacy and Safety of Icodextrin in Peritoneal Dialysis

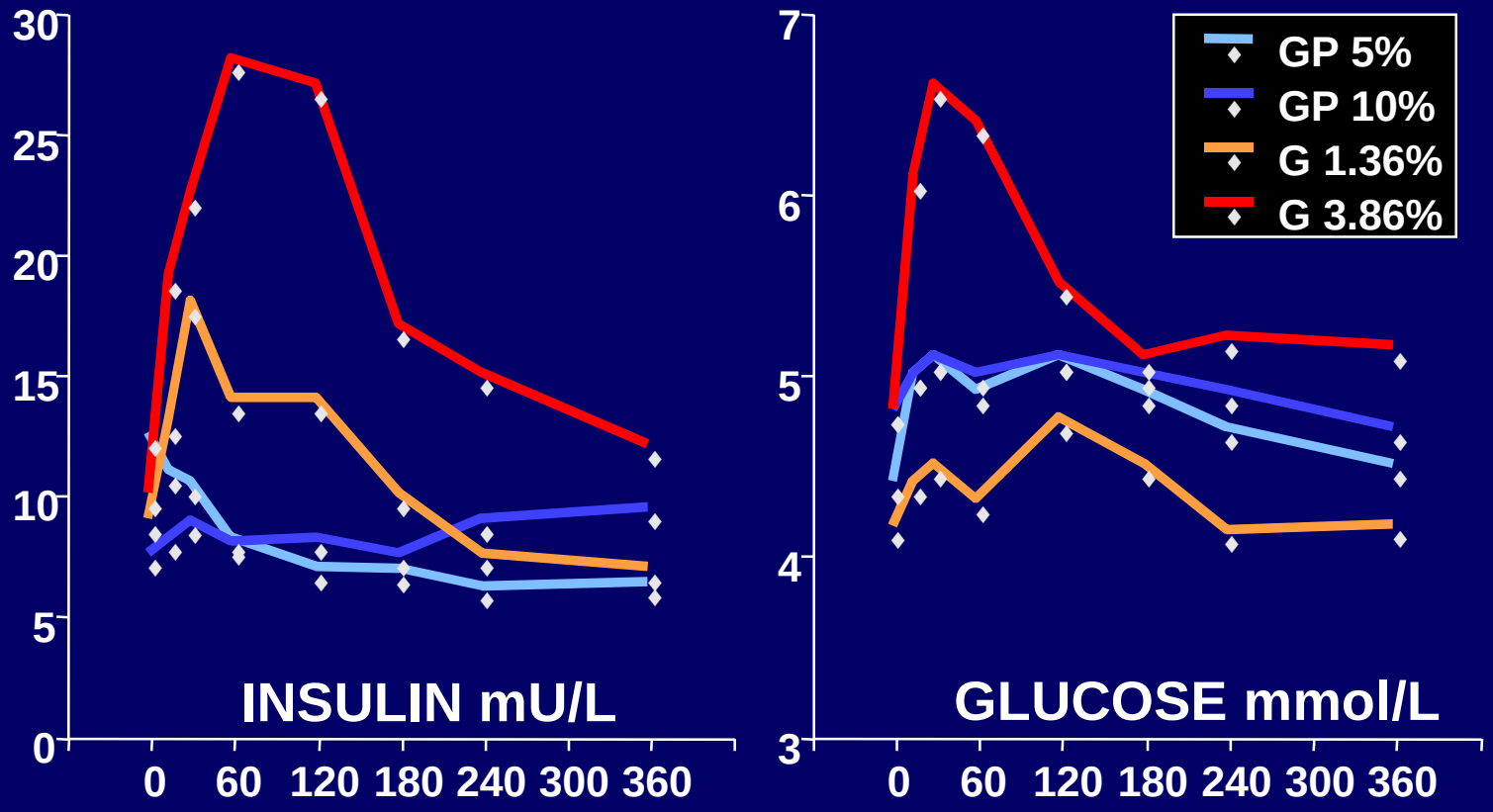
Marsha Wolfson, MD, Beth Piraino, MD, Richard J. Hamburger, MD, and A. Ross Morton, MD, for the Icodextrin Study Group





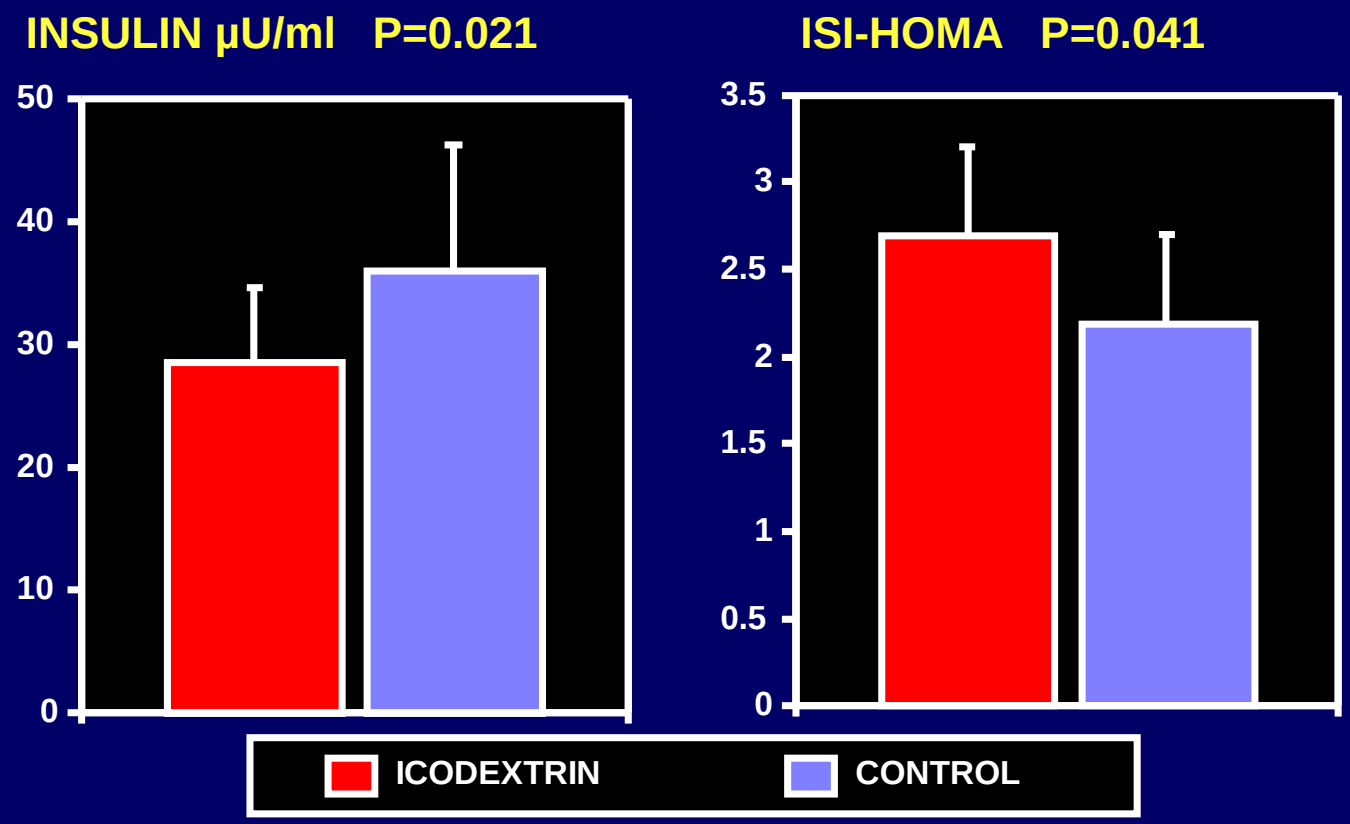
- 175+287 patients, 4 months+1 year follow-up, Wolfson, Am J Kidney Dis 2002;40:1055-65.

Insulin and glucose response to Icodextrin



- Mistry, MD Thesis, University of London 1988.
- Moberly, Kidney Int 2002;62(S81):S23-S33.

Hyperinsulinism reduction with Icodextrin



- Cross-sectional, 27 non-diabetics, 12h fasting.
  Amici, Adv Perit Dial 2001;17:80-3.

Icodextrin during peritonitis in CCPD

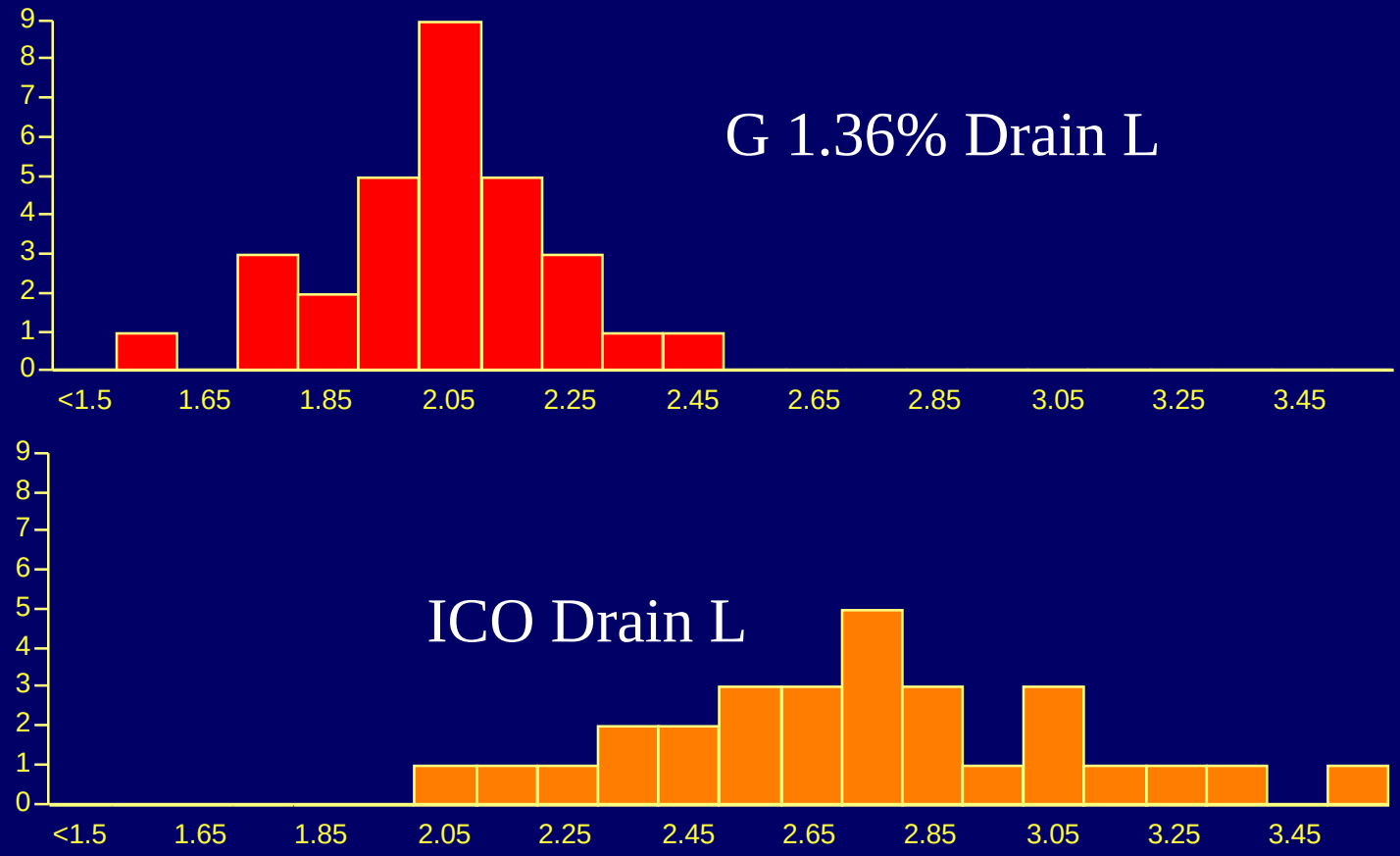
Table 3. Ultrafiltration volumes and used glucose concentrations in glucose- and icodextrin patients during peritonitis and non-peritonitis.

Daytime dwell PD fluid:		Glucose ($n=15$) UF (ml)	G (%)	Icodextrin ($n=14$) UF (ml)	G (%)
Daytime dwell:	peritonitis	$-736 \pm 81^{a,c}$	2.22 ± 0.23	296 ± 82	icodextrin
	non-peritonitis	-158 ± 97^{b}	2.13 ± 0.19	293 ± 61	icodextrin
	ΔP–NP (ml)	-578 ± 89^{c}		3 ± 72	
Total (24-h) ultrafiltration:	peritonitis	-72 ± 193^{b}	2.08 ± 0.24	1107 ± 202	2.14 ± 0.22
	non-peritonitis	571 ± 233^{b}	2.08 ± 0.22	1479 ± 159^{d}	2.24 ± 0.16
	ΔP–NP (ml)	-643 ± 213^{d}		-372 ± 181	

Note that, the glucose concentration given for the total ultrafiltration is only for the night-time dwells.
Abbreviations: Δ difference in ultrafiltration, UF: ultrafiltration, P: peritonitis, NP: non-peritonitis.
Mann–Whitney test: glucose vs icodextrin: $^{a}P<0.001$, $^{b}P<0.01$.
Wilcoxon test: P versus NP: $^{c}P<0.001$, $^{d}P<0.05$.

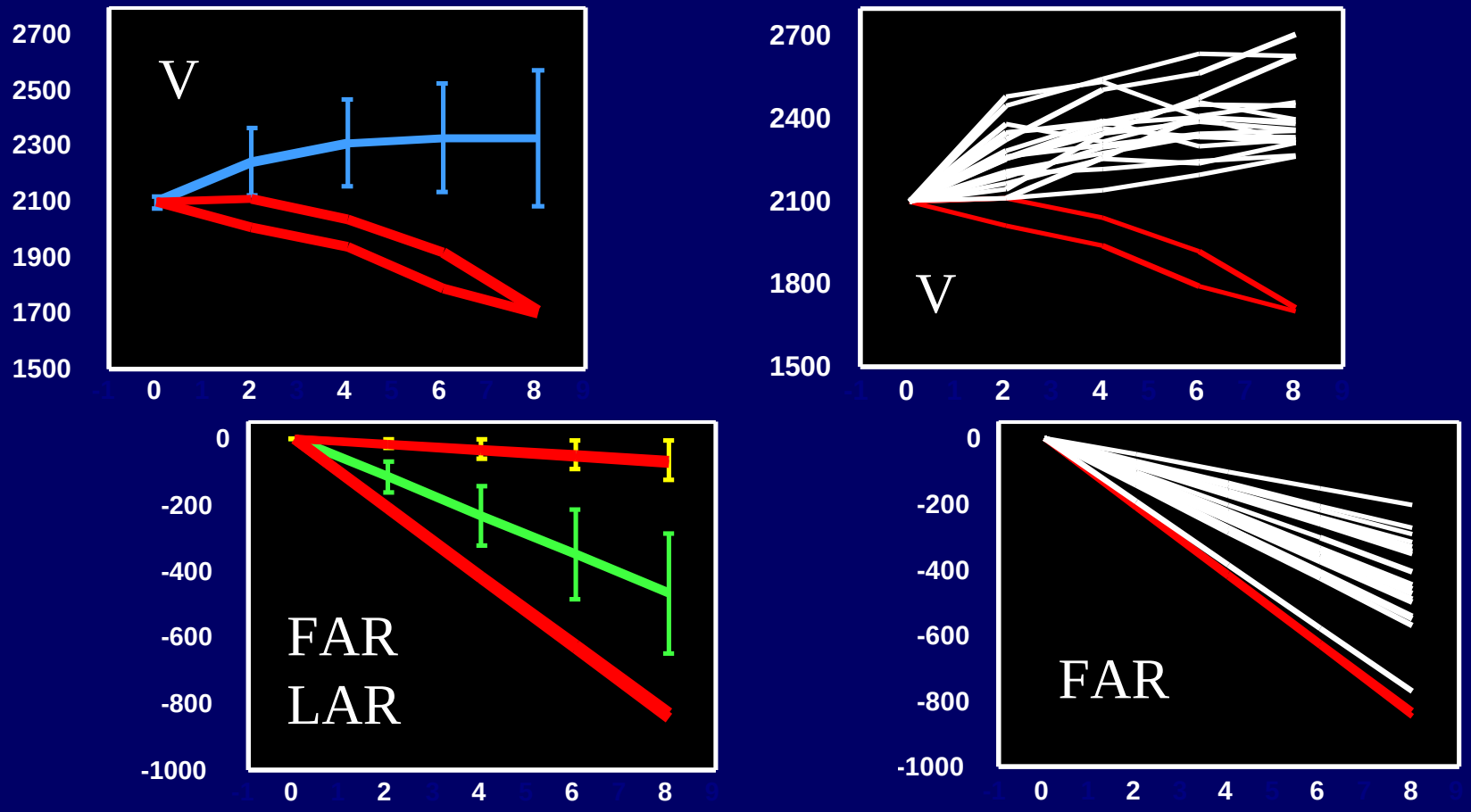
- Posthuma, Nephrol Dial Transplant 1998;13: 2341-4.

Icodextrin during peritonitis in CAPD



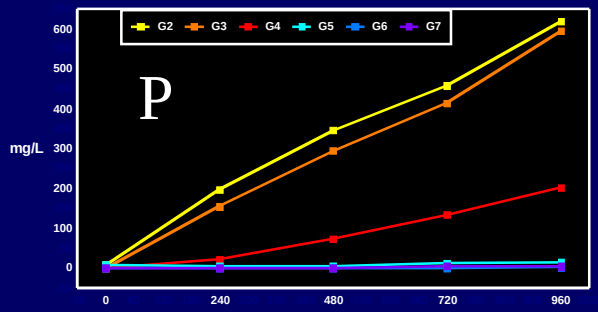
- Treviso peritonitis database, 30 episodes,
- G1.36% 6h 2.0±0.2 vs ICO 8h 2.7±0.3 L, p<0.001.

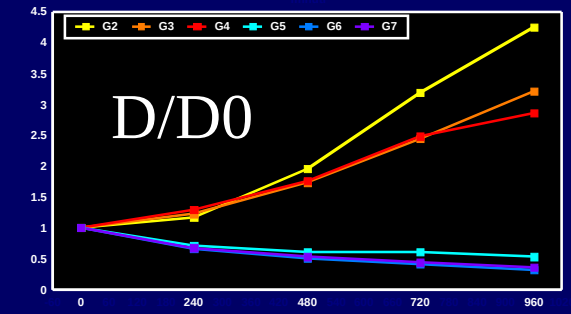
Absorption and non-responders

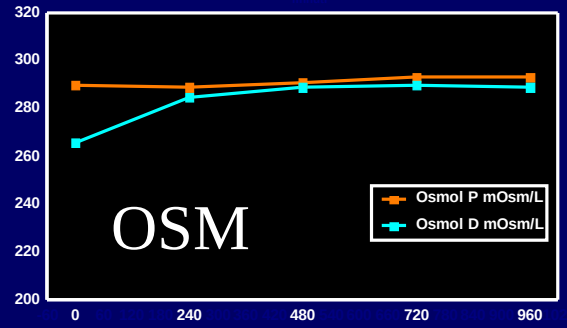


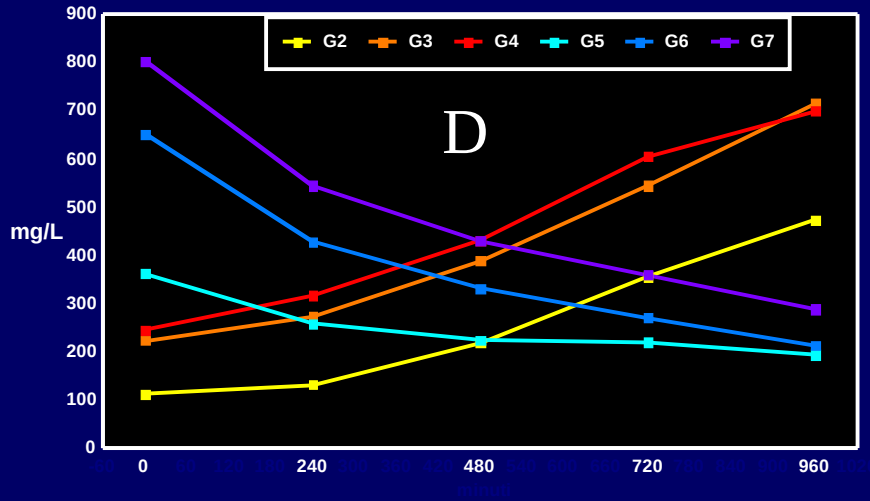
- 21 RISA-tested presumed non-responders. ICO D/D0 0.71±0.06. Only 2 patients (red lines) had negative UF, abnormal FAR and normal LAR.

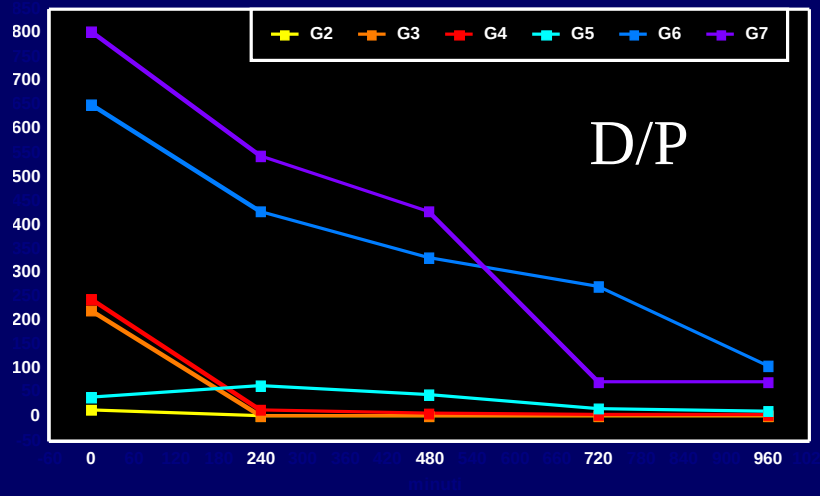
Icodextrin metabolytes and degradation











- The intraperitoneal depolymerization of Icodextrin is only 5.8 % after a 16-hour dwell.

Icodextrin interferences on laboratory assays and drugs

- No interference of Icodextrin and maltose on creatinine assay.
  Burke, Adv Perit Dial 1999;15:234-7.
- Reduced amylase levels in users.
  Wang, Perit Dial Int 2002; 22(S1):S17.
- Interference with glucose dehydrogenase assays.
  Wens, Perit Dial Int 1998;18:603-9.
- No interference with insulin, heparin, cefazolin, ceftazidime, gentamicin, netilmycin, vancomycin
  Choo, Perit Dial Int 1997;19(S1):S94.

Allergy to Icodextrin reports

Author	Year	Site	Details
Wilkie	1997	skin	hands and feet, exfoliative
Lam-Po-Tang	1997	skin	maculopapular rash, exfoliative erythema
Fletcher	1998	skin	erythematous macular rash
Queffeulou	1999	skin	generalized, psoriasiform, exfoliative
Divino-Filho	2000	skin	Baxter registry 108 cases
Goldsmith	2000	skin	blistering, exfoliative
Valance	2001	skin	psoriasiform, exanthematous pustulosis, hands and feet
Al-Hoquail	2001	skin	exanthematous pustulosis
Guerrero	2001	skin	hands and feet, exfoliative
Kanny	2002	skin	maculopapular eruption

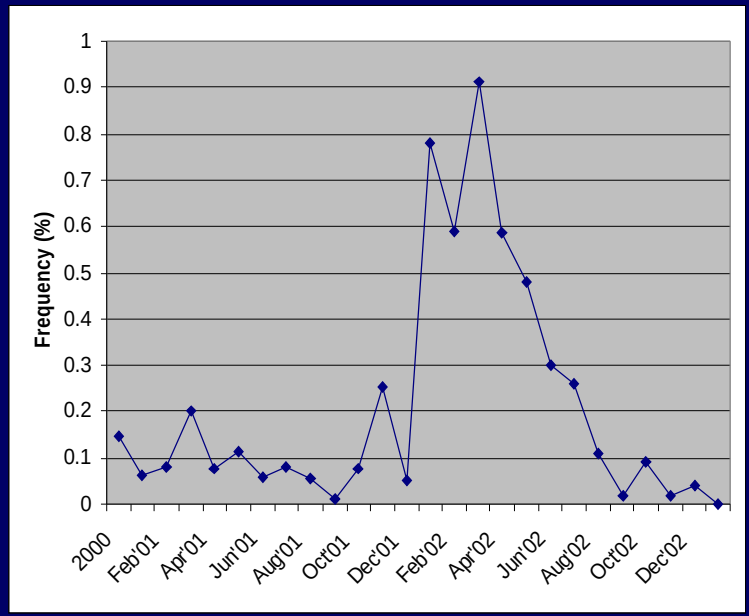
- Incidence is controversial: between 2.5 and 15%.

Icodextrin related peritonitis reports

Author	Year	Journal	Vol.	Page
Pinerolo	1999	Perit Dial Int	19	491-2
Del Rosso	2000	Nephrol Dial Transplant	15	927-8
Montagnac	2001	Nephrol Dial Transplant	16	435-6
Reichel	2001	Perit Dial Int	21	414-5
Fiedler	2002	Nephrol Dial Transplant	17	1708-9
Williams	2002	Perit Dial Int	22	89-90
Foggensteiner	2002	Perit Dial Int	22	471-6
Aanten	2002	Perit Dial Int	22	513-5
Tintillier	2002	Perit Dial Int	22	534-7
MacGinley	2002	Am J Kidney Dis	40	1030-5
Goffin	2002	Perit Dial Int	22	90-1
Goffin	2002	Perit Dial Int	22	723-6
Olszowska	2002	Pol Merkuriusz Lek	13	406-7
Marani	2002	Perit Dial Int	22	736-7
Enia	2003	Nephrol Dial Transplant	18	626
Boer	2003	Perit Dial Int	23	33-8
Basile	2003	J Nephrol	16	384-6

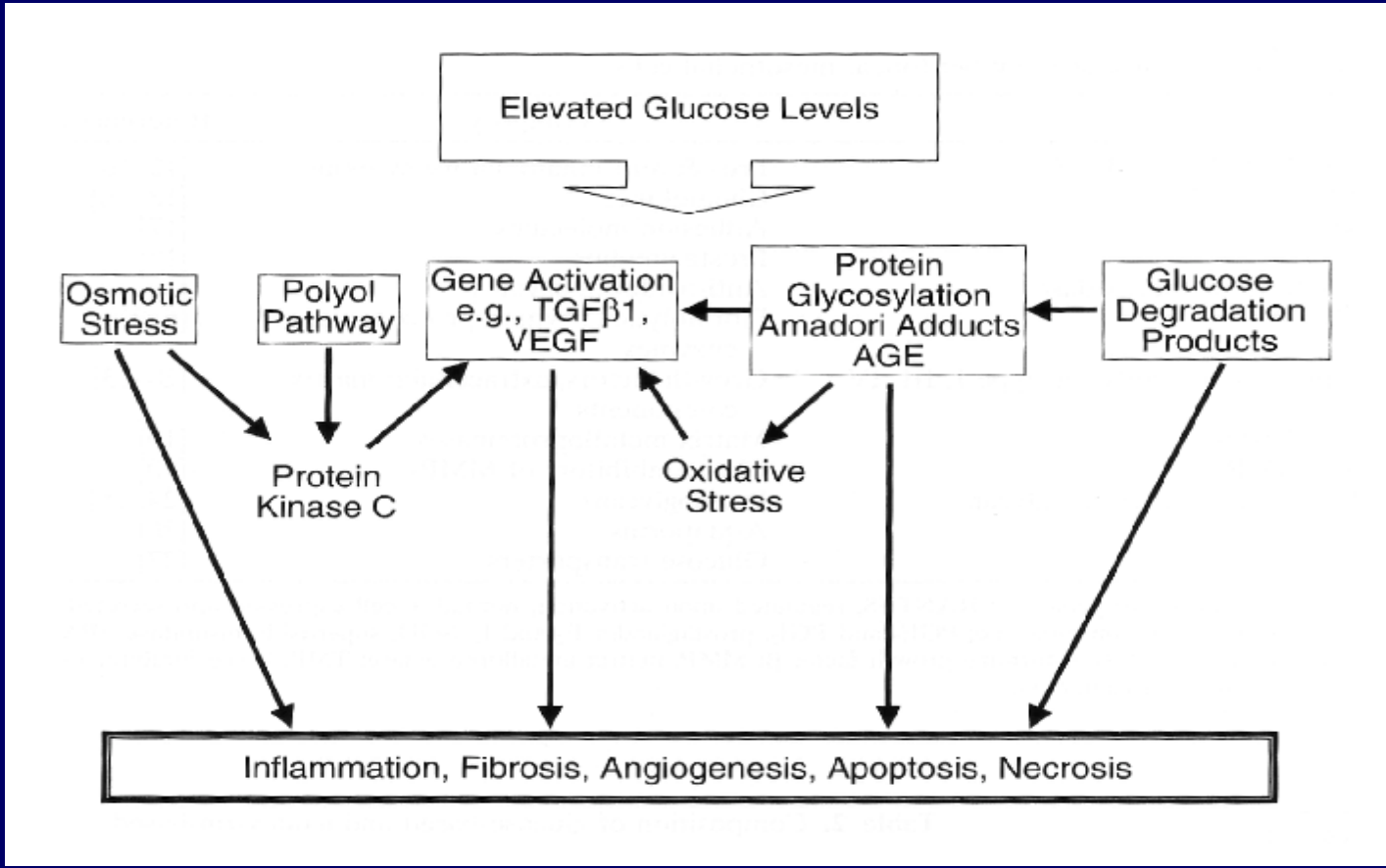
Pattern of Icodextrin related peritonitis

- **cloudy drain bags**
- **dialysate cell counts > 100 cells/µL with neutrophils, lymphocytes and macrophages**
- **negative cultures**
- **no loss of UF or hyperpermeability**
- **dialysate clears within 24-48h**
- **patients slightly symptomatic**
- **consistent with chemical peritonitis**



- Solution contaminated by gram+ bacterial capsule fragments (peptidoglycan).

Bioincompatibility of glucose



- Cooker, Kidney Int 2002;62(S81):S34-S45.

Biocompatibility of Icodextrin

- Less AGEs with alternative solutions.
  Dawnay, Perit Dial Int 1997;17:52-8.
- Less GDPs with alternative solutions.
  Schalkwijk, Perit Dial Int 2000;20:796-8.
- Higher mesothelial proliferation with ICO.
  Bajo, Perit Dial Int 2000;20:742-7.
- Normal cellular junctions and low TGFbeta1.
  Ito, Nephron 2003;93:c97-c105.

Bioincompatibility of Icodextrin

- No differences compared to glucose in glycation indices of in-vivo effluent.
  Ho-dac-Pannekeet, Perit Dial Int 1999;19(S2):S68-S74.
- Evidence of lipid peroxidation, DNA damage and cell senescence in rat peritoneum.
  Gotloib, Free Radic Biol Med 2003;34:419-28.
- Higher peritoneal protein excretion.
  Frajewicki, Nephron 2002;92:174-82.