An update of Pediatric PD in Asian perspectives

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Taiwan

Presentations of the Awards for the Best Abstracts submitted to the Special Pediatric Peritoneal Dialysis Symposium on February 9, 1990 at the 10th Annual Peritoneal Dialysis Conference in Dallas, Texas. The award winners were Dr. Eileen D. Brewer (far left) and Dr. Ching-Yuang Linn (second from left). The awards were presented by Dr. Alexander (second from right) and Mr. Larry Rohrer (far right) from Baxter Healthcare who sponsored the symposium.

content

1. Survival analysis of PD patients in Taiwan
2. What phosphate level should we aim for in children with ESRD?
3. The mechanism of modulating prognosis in PD patients with peritonitis
4. An update of pediatric PD in Asian perspectives

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Survival analysis of Pediatric Dialysis Patients in Taiwan

Study population

- from 1995 to 2004
  data from the Taiwan Renal Registry.
- A total of 264 HD and 110 PD patients
  aged <18 years at initiation of dialysis
- continuous follow up to 2009

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incidence of Pediatric ESRD

USA:	8.12 / million (1995-2004)
ERA-EDTA Registry:	9.9 / million (2000)
	6.5 / million (2007)
Taiwan	8.12 / million (1995-2004)
	Age-related population

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Statistical analysis

Statistical analysis were performed using the SAS/STAT software, Version 9.1.3 (SAS Institute Inc., Cary, NC, USA).

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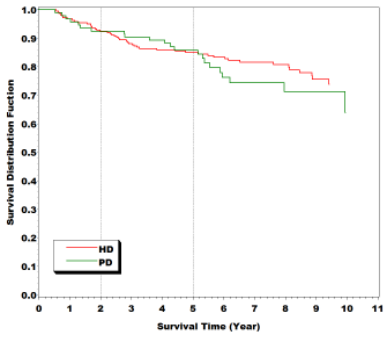
according to different modality – H.D; P.D
survival rates among children with ESRD in Taiwan



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1. The death rate for pediatric was 24.45 per 1000 patient-years.
2. The median survival time of RRT patients from onset of RRT until death is 2.78 years (HD 2.55 years, PD 3.59 years) P=0.590.
3. No significant difference was observed between HD and PD group in terms of gender (P=0.715) and number of co-morbidities (P=0.464)

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Mode of treatment

The overall 1-, 3-, 5-, 7-, and 10-year survival rates for PD patients were 97.3%, 89.1%, 84.7%, 73.8% and 64.8% respectively, and were 96.2%, 88.3%, 85.5%, 82.3%, 75% for HD patients.

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Table 1. Comparisons between HD and PD patients for demographic and clinical characteristics

	HD treatment		PD treatment		P-value
	N	%	N	%	(X^2-test)
Age					
0~4	9	50.0	9	50.0	< 0.001
5~9	16	51.6	15	48.4	
10~14	60	60.0	40	40.0	
15~19	179	79.6	46	20.4	
Gender					
Female	111	42.1	44	40.4	0.715
Male	153	58.0	66	60.0	
Total	264		110		
Survival Status					
Survival	212	80.3	85	77.3	0.509
Death	52	19.7	25	22.7	

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Using “15-19 years” as a reference group, the relative risk (RR) of the youngest group (0-4 years) was 5.83 (95% CI: 2.21-15.36) for HD, and 4.41 (95% CI: 1.07-18.23) for PD. Co-morbidity affected mortality in HD children (HR: 1.97, 95% CI: 1.10-3.56), but did not affect PD children (HR: 0.52, 95% CI: 0.02-1.36).

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Table 2. Stratified analysis of Cox proportional hazards model for pediatric dialysis patients

	HD treatment		PD treatment	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (yr)				
0~4 vs 15~19	5.83 (2.21~15.36)	< 0.001	4.41 (1.07~18.23)	0.040
5~9 vs 15~19	1.88 (0.65~5.44)	0.243	2.10 (0.52~8.51)	0.300
10~14 vs 15~19	1.58 (0.80~3.10)	0.185	1.91 (0.67~5.49)	0.227
Sex				
Male vs Female	0.84 (0.47~1.50)	0.551	1.46 (0.57~3.72)	0.429
Comorbidity				
1+ vs 0	1.97 (1.10~3.56)	0.024	0.52 (0.20~1.36)	0.184

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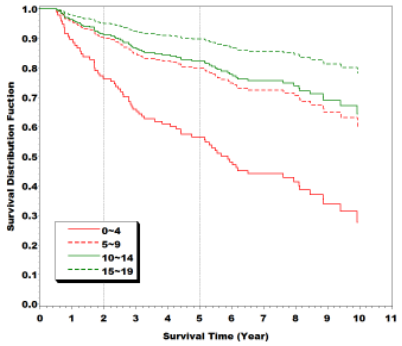
adjusted survival rates among children with ESRD in Taiwan from 1995 to 2004 according to age at dialysis initiation



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Cause of death

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1. The Causes of death of PD patients were not different from HD patients: cardiovascular (12.0% vs. HD 13.5%, P=1.000), cerebrovascular disease (16.0% vs. HD 7.7%, P=0.426) and infection (16.0% vs. HD 13.5%, P=0.741)
2. More pediatric dialysis patients died from cerbrovascular disease (17.8% vs. 7.8%, P=0.021). The types of cerebrovascular diseases were not different between pediatric and adult patients (87.5% of death due to cerebral hemorrhage in pediatric group vs. 82.3% in adult group, P=0.99.)
3. The lethal cerebrovascular events all occurred during the initial 5 years of dialysis.

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Comparison of causes of death between pediatric and adult dialysis patients

Cause (disease)	Pediatric N (%)	Adult N (%)	P-value*
cardiovascular	10 (22.2)	4720 (32.3)	
Non-cardiovascular	35 (77.8)	9906 (67.7)	0.200
cerebrovascular	8 (17.8)	1133 (7.8)	
Non-cerebrovascular	37 (82.2)	13493 (92.3)	0.021
infectious	11 (24.4)	3289 (22.5)	
Non-infectious	34 (75.6)	11337 (77.5)	0.722

*: Fisher’s Exact test

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Summary

1. Taiwanese pediatric PD and HD patients have similar survival
2. Age at initiation of dialysis is an important factor affecting survival since the highest mortality rate is in the youngest patients (0-4 years).
3. Infection, cardiovascular disease, cerebrovascular disease are the most common causes of death in children on chronic dialysis in Taiwan,
4. Higher propotion of pediatric dialysis patients suffered from cerebrovascular death than adult dialysis population. Hemorrhagic stroke is the main type of cerebrovascular disease.

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What phosphate level should we aim for in children with ESRD?

What phosphate level should we aim for?

- There is an association between phosphate levels and coronary artery calcification in young adults without kidney disease
- In CKD patients, phosphate levels within the normal range are associated with a greater prevalence of vascular and valvular calcification
- No clinical trials addressing the issue of plasma phosphate levels and mortality rate in children
- One interesting study: use of type of phosphate binder, even with phosphate levels in the normal range and below levels currently recommended for phosphate binder use, is associated with decreased mortality rate in patients on HD

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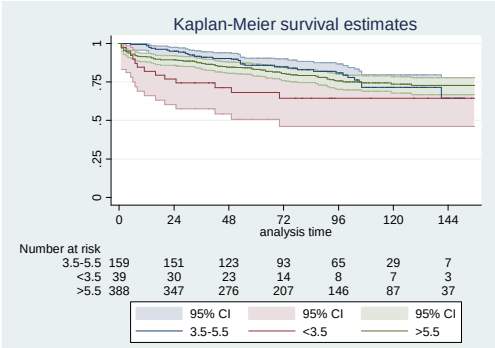
Adjusted survival rates among age less than 20 years old with ESRD in Taiwan from 1995 to 2008 according to serum phosphate level.



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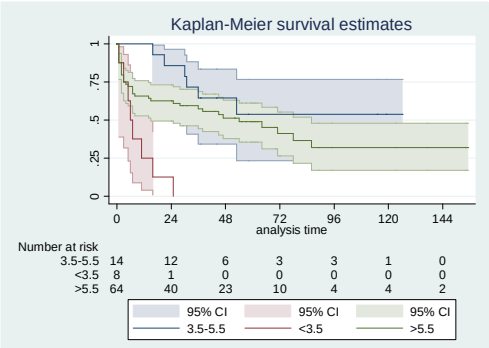
Adjusted survival rates among age less than 6 years old with ESRD in Taiwan from 1995 to 2008 according to serum phosphate level.



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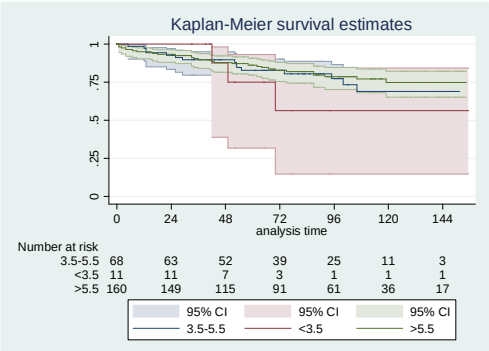
Adjusted survival rates among age between 6 to 17 years old with ESRD in Taiwan from 1995 to 2008 according to serum phosphate level.



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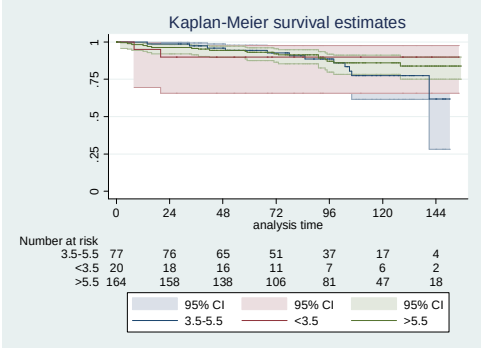
Adjusted survival rates among age between 17 to 20 years old with ESRD in Taiwan from 1995 to 2008 according to serum phosphate level.



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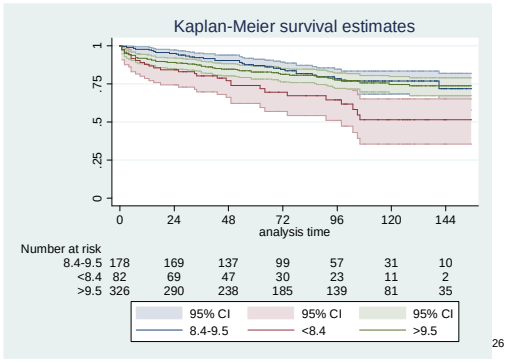
Adjusted survival rates among age less then 20 years old with ESRD in Taiwan from 1995 to 2008 according to serum Ca level.



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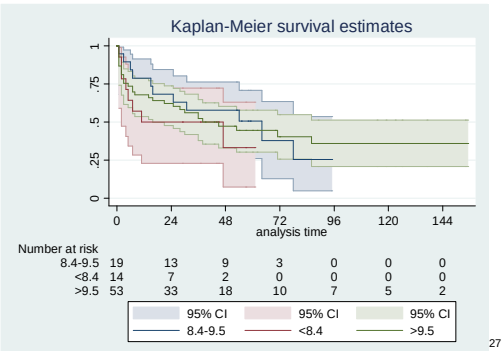
Adjusted survival rates among age less then 6 years old with ESRD in Taiwan from 1995 to 2008 according to serum Ca level.



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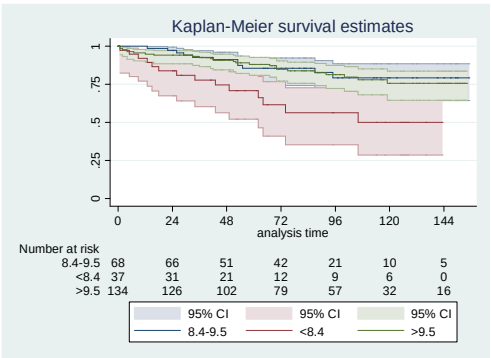
Adjusted survival rates among age between 6 to 17 years old with ESRD in Taiwan from 1995 to 2008 according to serum Ca level.



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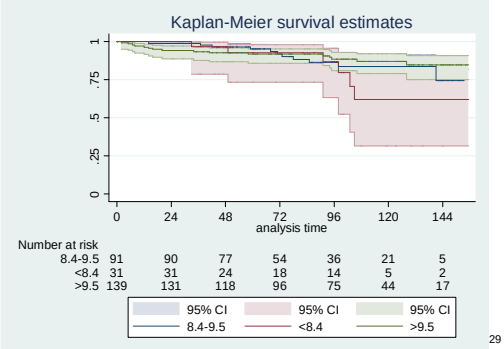
Adjusted survival rates among age between 17 to 20 years old with ESRD in Taiwan from 1995 to 2008 according to serum Ca level.



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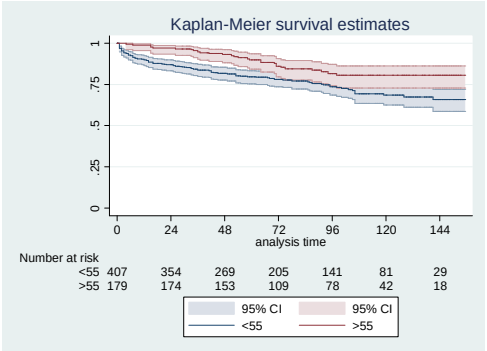
Adjusted survival rates among age less than 20 years old with ESRD in Taiwan from 1995 to 2008 according to serum CaxP level.



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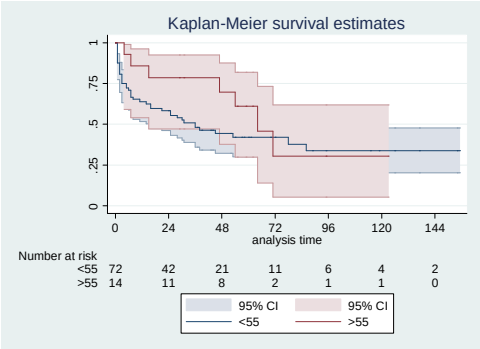
Adjusted survival rates among age less than 6 years old with ESRD in Taiwan from 1995 to 2008 according to serum CaxP level.



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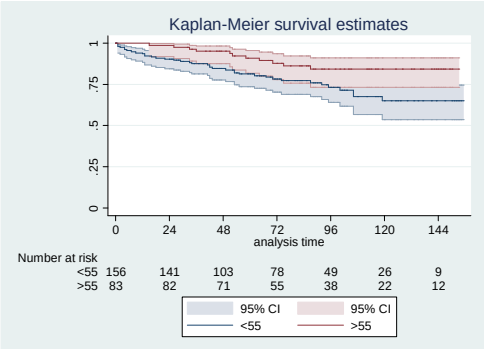

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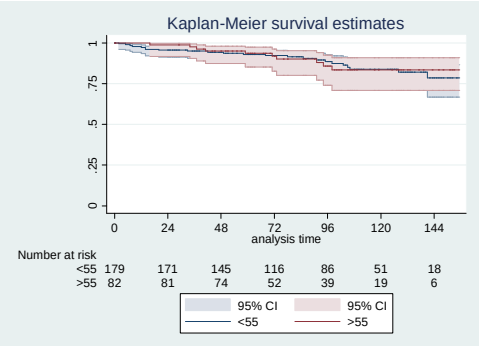

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So what phosphate level should we aim for in children with ESRD?

- Plasma phosphate varies throughout childhood
- Falling steeply from birth until the age of 1-2 years and then continuing to fall more slowly until the age of 7 years
- The optimum target is not clear
- It makes sense, therefore, to try to keep the plasma phosphate around the 50th centile

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How to improve PD quality?

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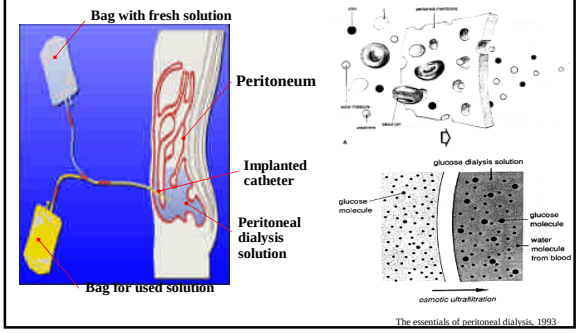
The Mechanism of Modulating Prognosis in Peritoneal Dialysis Patients with Peritonitis

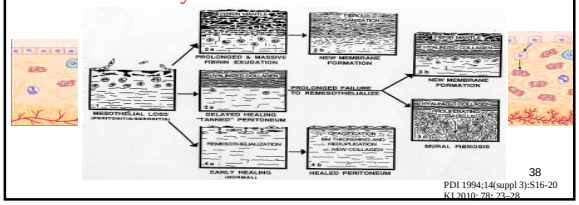
Peritoneal dialysis (PD)



The essentials of peritoneal dialysis, 1993

PD-related Peritonitis

- Peritonitis
  - The most serious complication of PD
  - Leading cause of morbidity and mortality
  - Morbidity: may compromise the efficiency of dialysis and lead to technique failure
  - Mortality: 41.5% Cardiovascular events



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PDI 1994;14(suppl 3):S16-20
KI 2010; 78: 23–28

Decreased Antimicrobial, Phagocytotic Activity, Interleukin-1, Gamma-Interferon Production in Peritoneal Macrophages in Continuous Ambulatory Peritoneal Dialysis Patients During Peritonitis

CHING-YUANG LIN, TUNG-PO HUANG

Am J Nephrol 1990:10:368

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Percent (%) of Staphylococcus aureus killed by peritoneal macrophages from same patients during and without peritonitis

Case	peritonitis	peritonitis
1	24	52
2	28	46
3	32	56
4	26	48
5	22	54
6	30	56
7	32	48
8	34	48
9	36	50
10	28	52
11	29	58
12	30	57
Mean ± SD t test	29.25 ± 3.85 p<0.001	52.08 ± 3.93

Abbreviation used: c, with; s, without

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IL-1 activity in supernatants of LPS-stimulated peritoneal macrophages from same patients during and without peritonitis

	IL-1 activity (Thymocyteproliferation cpm)	
Case	peritonitis	peritonitis
1	601	1890
2	489	2854
3	407	1817
4	846	2137
5	642	1772
6	391	802
7	763	2451
8	609	1871
9	784	2203
10	490	1629
11	504	1013
12	329	2582
Mean ± SD t test	571.25 ± 158.34 p<0.001	1918 ± 571.02

1×10^6 peritoneal macrophages incubated with 10 μ g of LPS (from Salmonella typhimurium) supernatants were tested for IL-1 activity a thymocyte proliferation assay (6-8 week-old C3H/HeJ mice thymocytes Abbereviation used: c, with; s, without)

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Gamma-interferon IFN-r production in supernatants of PMA and PHA stimulated peritoneal macrophages from same patients during and without peritonitis

Case	IFN-r (IU / ml)	
	c peritonitis	s peritonitis
1	0	400
2	0	800
3	0	800
4	0	800
5	400	1600
6	800	3200
7	0	400
8	200	800
9	200	800
10	400	1600
11	0	800
12	800	3200
Mean ± SD t test	233.33 ± 292.50 p<0.001	1266.67 ± 935.71

Addreviation used: c, with; s, without

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Antibody dependent cell-mediated cytotoxicity (ADCC) in peritoneal macrophages and peripheral blood monocytes during and without peritonitis

Case	Peritoneal macrophages (E/T: 50/1)		Peripheral monocytes (E/T: 20/1)		
	c peritonitis	s peritonitis	c peritonitis	s peritonitis	controls
1	3.0	21.4	14.6	11.5	53.1
2	1.8	18.4	16.6	14.0	56.5
3	2.4	23.6	14.2	10.9	56.5
4	3.1	23.6	11.8	10.3	44.0
5	5.6	43.3	10.4	9.2	45.9
6	7.2	55.6	11.2	8.1	50.5
7	9.0	48.5	19.4	17.8	49.2
8	6.7	46.2	17.3	14.2	42.3
9	12.0	62.4	18.9	15.8	57.1
10	6.2	42.6	19.1	17.0	51.4
11	10.6	86.8	16.4	12.8	67.1
12	5.0	38.4	12.6	11.2	43.6
Mean ± SD	6.05 ± 3.13[a]	42.57 ± 19.01[a,b]	15.18 ± 3.04[d]	12.73 ± 2.95[b,c]	51.43 ± 6.88[c,d]

Mean value in the same column followed by a common letter are significantly difference a, b, c, d. p<0.001
Abbreviation used: c, with; s, without

Phagocytosis index (%) in peritoneal macrophages from same atients during and without peritonitis.

Case	c peritonitis	s peritonitis
1	2.78	36.42
2	4.47	47.24
3	26.85	45.29
4	11.68	59.52
5	24.63	55.50
6	25.89	46.75
7	35.41	52.53
8	41.56	76.19
9	35.58	72.41
10	39.88	75.29
11	42.17	66.28
12	46.75	94.33
Mean ± SD t test	29.25 ± 3.85 p<0.001	52.08 ± 3.93 p<0.001

Addreviation used: c, with; s, without

Serial Peritoneal Macrophage Function Studies in CAPD Patients with Peritonitis

Ching-Yuang Lin, Tung-Po Huang

Advances in Peritoneal Dialysis 1990:115-119

Serial PM function study in CAPD patients before and during peritonicis

	Peritoniris (day)					
	Before	3rd	10th	20th	30th	60th
B.A. (%)						
LPO group	58±8	60±8[a,b]	40±4[a]	46±4[b]	50±6	54±4
HPO group	44±4[c,d]	30±4	22±2[c]	28±2[d]	32±3	38±3
P.I. (%)						
LPO group	42±4	60±6[e,f]	24±2[g]	36±3[f]	40±3	40±3
HPO group	36±3[g,h]	22±1[g]	20±1[h]	26±1	28±1	32±2
H_2O_2 (μ mH_2O_2/ μ gDNA)						
LPO group	9.2±2.0	16.2±2.4[i,j]	4.3±0.6[i]	6.2±0.2[j]	8.2±1.2	10.3±1.1
HPO group	7.4±0.5[k]	4.1±0.1	2.6±1.0[k]	4.5±0.1	5.3±0.2	6.2±0.3
IL-1 (pg/ml)						
LPO group	142±24	274±40[l,m,n]	69±12[l]	98±18[m]	124±21[n]	148±20
HPO group	102±18[o,q]	68±10	42±6[o]	56±8[q]	68±8	88±7
TNF-α (pg/ml)						
LPO group	345±42	614±56[r,s]	186±11[r]	286±28[s]	305±32	356±28
HPO group	254±21[t,u]	184±12[t]	112±10[u]	154±8	182±7	214±10
IFN-r (U/ml)						
LPO group	21±3	44±4[v,w,x]	10±2[v]	16±2[w]	20±3	24±3
HPO group	16±2[y,z]	10±1	2.2±0.3[y]	8.1±0.5[z]	12±1	14±1

Student's t test: a,c,e,h,i,l,m,p,r,s,u,v,w,y: P<0.01
b,d,f,g,j,k,n,q,t,x,z: P<0.05

Comparison of the change of peritoneal macrophages (PM) obtained from patients without peritonitis and added to dialysate with and without peritonitis

n=14	PM s peritonitis added to dialysate		PM c peritonitis added to dialysate	
	c peritonitis	s peritonitis	c peritonitis	s peritonitis
Cytokines production				
IFN-r (U/ml)	14.2±4.2[a]	31.7±6.8[a,b,c]	0.7±0.2[b,d]	9.4±.8[c,d]
TNF (U/ml)	202.8±26.4[e]	304.1±31.2[e,f,g]	152.1±10.4[f,h]	255.6±24.8[g,h]
IL-1 (U/ml)	161.7±18.2	192.4±19.4[i]	64.1±9.6[i,j]	155.9±14.2[j]
Phagocytosis index (%)	40.2±3.4	48.2±3.8[k,l]	31.1±2.6[k]	39.2±3.0[l]
Bactericidal activity (%)	42.8±4.2[m]	54.6±5.1[m,n,o]	30.4±3.2[n,p]	40.2±3.8[o,p]

Decreased Size of Peritoneal Macrophage during Peritonitis in Continuous Ambulatory Peritoneal Dialysis Patients

Wen-Tse Chen, Yasushi Kobayashi, Tung-Po Huang, Ching-Cheng Chiu, Ching-Yuang Kin

Am. J. Nephrol 1991:11:374-379.

Objectives

To improve the prognosis of PD-related peritonitis

Improve the outcome — Peritoneal Immune Response

Reduce the mortality — Mechanism of Cardiotoxicity

Long-term and successful peritoneal dialysis

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To improve the prognosis of PD-related peritonitis

Improve the outcome

- **Functional distinct type of peritoneal T cells** → **Peritoneal Th1/Th2 immune response and outcome** → **Cytokine and transcriptional regulation of T cell immune response**
- **Functional chemotaxis** → **Peritoneal mesothelial cells-T cells interaction** → **Migration regulate T cell Immune response**

Reduce the mortality

- **PD-related peritonitis Induced cardiotoxicity** → **Cellular mechanism For cardiotoxicity**

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To improve the prognosis of PD-related peritonitis

Improve the outcome

- **Functional distinct type of peritoneal T cells** → **Peritoneal Th1/Th2 immune response and outcome** → **Cytokine and transcriptional regulation of T cell immune response**
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Reduce the mortality

- **PD-related peritonitis Induced cardiotoxicity** → **Cellular mechanism For cardiotoxicity**

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Table. Baseline characteristics of patients with rapid versus delayed response to peritonitis treatment

Group	Rapid response (n=26)	Delayed response (n=14)
Men, n (%)	14 (54)	7 (50)
Age, y	46.3±15.2 (8-62)	47.1±13.4 (9-58)
Years on CAPD	2.63±1.21 (0.8-5.3)	2.65±1.03 (0.9-4.7)
Peritonitis rates (episode/yr)	0.52±0.3	0.49±0.2
Underlying disease, n (%)		
CGN	13 (50)	7 (50)
PCK	1 (4)	1 (7)
HUS	2 (8)	2 (14)
Reflux nephropathy	4 (15)	1 (7)
Obstructive nephropathy	3 (12)	0 (0)
Hypoplasic/dysplasic	2 (8)	1 (7)
Unknown	1 (4)	2 (14)
Serum albumin, g/dL	3.89±0.26 (3.3-4.4)	3.86±0.31 (3.3-4.6)
Adequacy of dialysis before peritonitis		
Kt/Vurea (per week)		
Renal	0.20±0.28	0.21±0.29
Total	2.23±0.20	2.20±0.18
wCCr (L/wk/1.73m^2)		
Renal	8.16±11.62	8.57±12.23
Total	63.56±13.93	64.31±12.92

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Table. Organisms isolated during peritonitis episodes in rapid and delayed response groups

Organisms	Rapid response (n=26)	Delayed response (n=14)
Gram-positive organisms		
Staphylococcus epidermidis	9	4
Other coagulase-negative Staphylococcus spp	3	2
Staphylococcus aureus	5	3
Streptococcus spp	2	-
Enterococcus spp	1	1
Total	20 (76.9%)	10 (71.4%)
Gram-negative organisms		
Psudomonas aeruginosa	1	2
Escherichia coli	3	2
Klebsiella spp	2	-
Total	6 (23.1%)	4 (28.6%)

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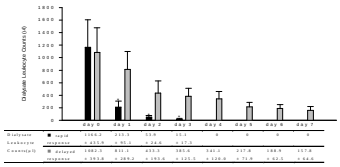
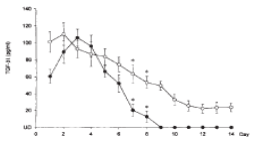
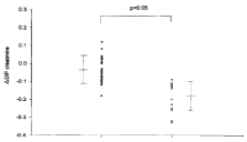
Leukocyte counts in the peritoneal dialysate effluent during peritonitis (PPDE)





TGF-β1 level in PPDE

rapid response (●)
delayed response (○)



Peritoneal equilibration test

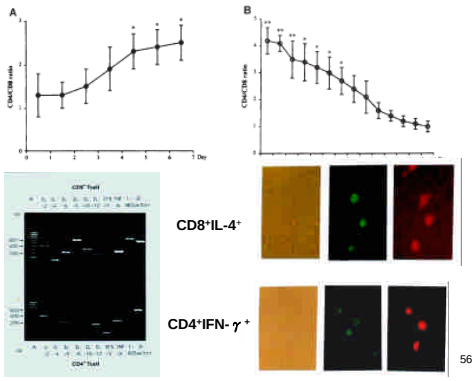
rapid response (●)
delayed response (○)

54

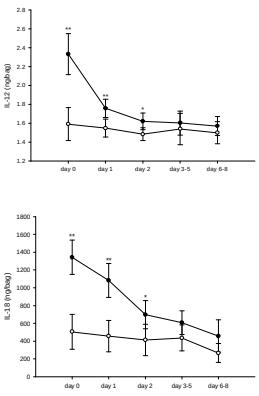
a progressively decreasing CD4/CD8 ratio in PDE correlates with the persistent expression of TGF-β1 in the dialysate, which may play a pathogenetic role in the outcome of peritonitis

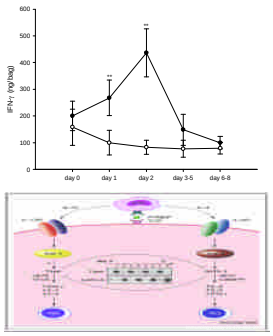
55

CD4/CD8 ratio in PPDE



56





- **Levels of IL-12, IL-18, IFN-γ in PPDE** ● = rapid clinical response; ○ = delayed clinical response.

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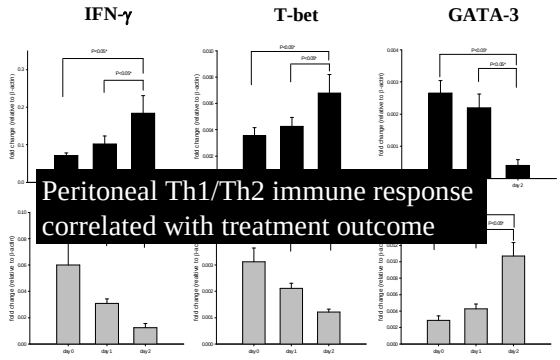

Changes in mRNA expression in peritoneal T cells from PPDE.
Upper panel= rapid clinical response ; Lower panel=delayed clinical response.

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1. local IL-12 and IL-18 production is part of a protective early immune response to PD-related peritonitis and correlates with type 1 T-cell polarization
2. Our results may have implications in designing therapeutic interventions aimed at manipulation of early cytokine cascades and type 1/type 2 T-cell balance in patients with peritonitis.

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To improve the prognosis of PD-related peritonitis

To improve the outcome of PD-related peritonitis

To reduce the mortality of PD-related peritonitis

Functional distinct type of peritoneal T cells

Peritoneal Th1/Th2 immune response and outcome

Cytokine and transcriptional regulation of T cell immune response

Functional chemotaxis

Peritoneal mesothelial cells-T cells interaction

Migration regulate T cell Immune response

PD-related peritonitis Induced cardiotoxicity

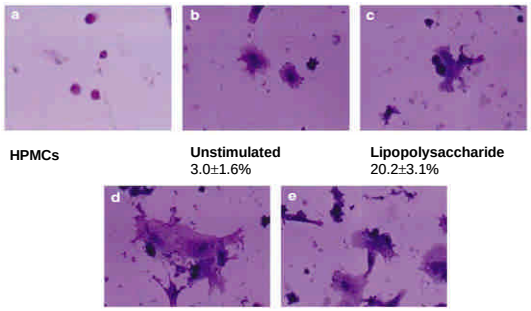
Cellular mechanism For cardiotoxicity

60

Interaction between Peritoneal Mesothelial Cells and T cells?

61

Human Peritoneal Mesothelial Cells (HPMCs)



HPMCs

Unstimulated
3.0±1.6%

Lipopolysaccharide
20.2±3.1%

Rapid-response PPDE
19.1±2.9%

Delayed-response PPDE
18.2±3.3%

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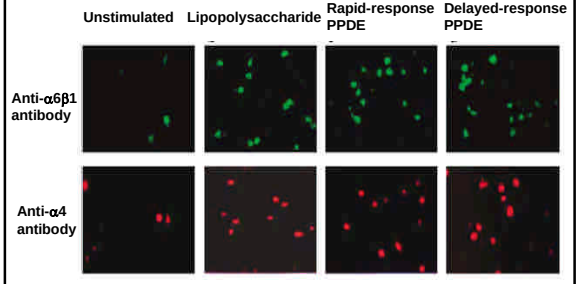

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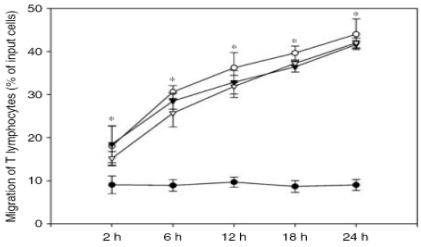
HPMCs
T lymphocytes



- **Effect of HPMC pre-stimulation on T lymphocyte migration.** (●), control; (○) LPS 10 μg/ml ; (▼) Rapid response PDE 1000 μg/ml; (▽) Delayed response PDE 1000 μg/ml.*P<0.05 versus control.

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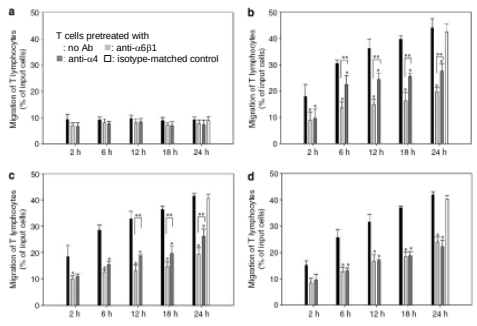
HPMCs without pre-stimulation LPS 10 μg/ml

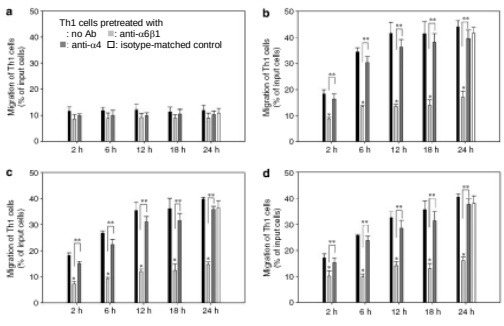


Rapid-response PPDE 1000 μg/ml Delayed-response PPDE 1000 μg/ml

Inhibition of T cell migration across HPMCs by anti-integrin antibodies.

65

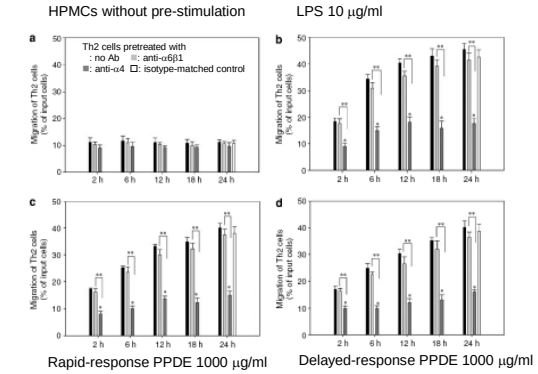
HPMCs without pre-stimulation LPS 10 μg/ml



Rapid-response PPDE 1000 μg/ml Delayed-response PPDE 1000 μg/ml

Inhibition of Th1 cell migration across HPMCs by anti-α6β1 antibodies.

66

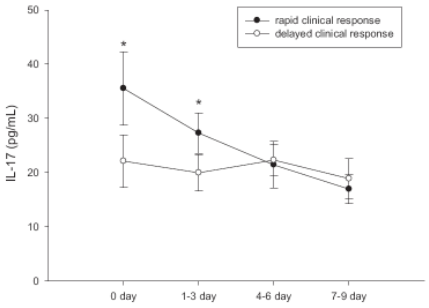


Inhibition of Th2 cell migration across HPMCs by anti-α4 antibodies.

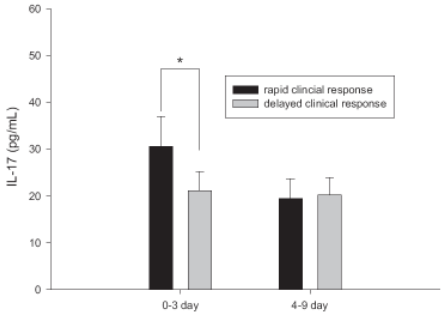
1. integrins play an important role in T-lymphocyte adherence and migration across HPMCs, which are important in regulating the traffic of T lymphocytes into the peritoneal cavity.
2. Different T-cell subsets express different integrins; this may mediate the polarized Th1/Th2 immune reaction in peritonitis.
3. Th-subset recruitment and the outcome of peritonitis could be affected by manipulating the expression of different integrins or by blocking the function of different integrins.

Kinetics and Involvement of Interleukin-17 in the Outcome of Peritonitis in Non-diabetic Patients Undergoing Peritoneal Dialysis

Levels of IL-17 in PDE during peritonitis

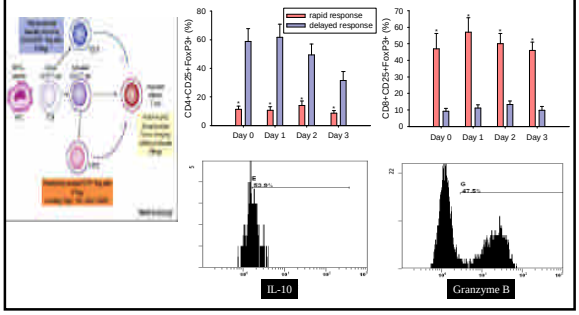


Levels of IL-17 in PDE during the early and late phases of peritonitis

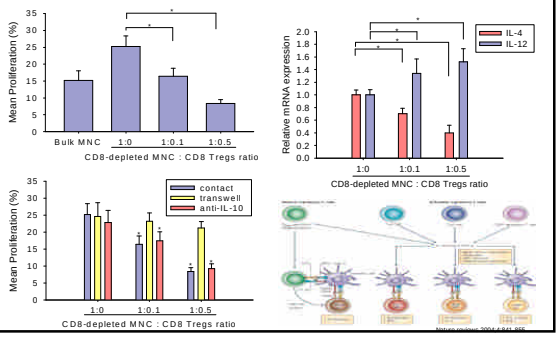


local IL-17 production is part of a protective early immune response to PD-related peritonitis. High levels of IL-17 in PDE during the early phase of peritonitis correlated with a favorable outcome.

- The role of regulatory T cells and correlation with outcome



Peritoneal Tregs Regulate Peritoneal Immune Defense Response



Innate and adaptive immune response during PD-related peritonitis will enhance our understanding of the basis of peritonitis outcome and facilitate the development of new strategies for peritonitis treatment and prevention.

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Migration regulate T cell Immune response

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Mechanism of
PD-related Peritonitis Induced Cardiotoxicity?

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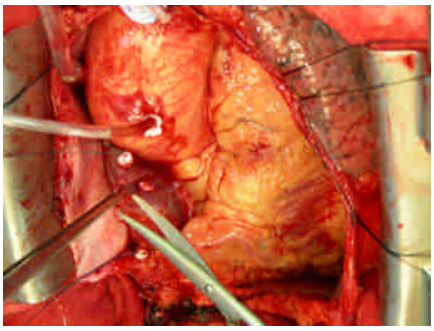
Excision of the tip of right atrial appendage



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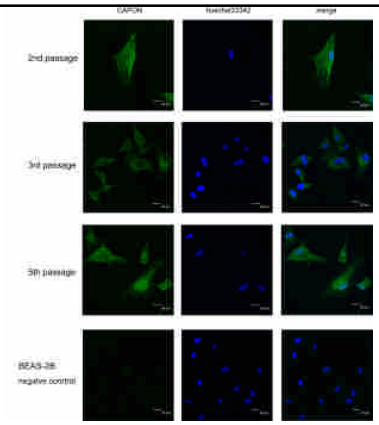
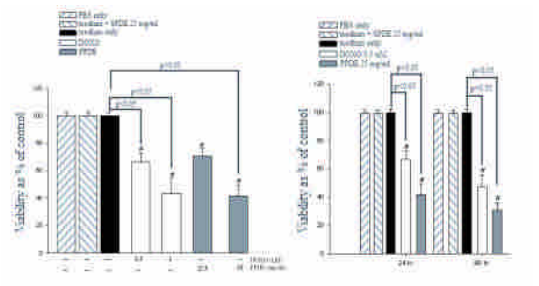


79



- Cell viability reduced after treatment with PPDE.
  Human cardiomyocytes were treated with PDE during peritonitis. Cell viability was determined by MTT assay.

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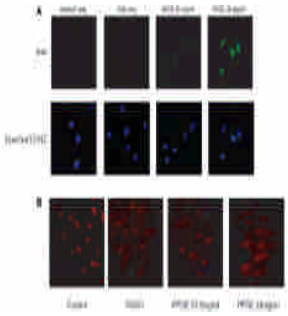

TABLE 1. Dose dependent manner of PPDE induced cell apoptosis in cultured human cardiomyocytes

	% of apoptosis		
Treatment	0	12.5 mg/ml	25 mg/ml
Medium only	1.0 ± 2.7	10.4 ± 2.8	11.8 ± 3.2
PBS only	2.2 ± 3.1	10.2 ± 3.2	10.8 ± 3.6
Medium + DOXO	9.7 ± 2.4	28.5 ± 4.1*	41.2 ± 4.5*
Medium + SPDE	0.7 ± 2.5	10.2 ± 2.7	12.4 ± 3.5
Medium + PPDE	9.7 ± 2.6	32.4 ± 3.8*	48.6 ± 4.8*

TABLE 2. Time dependent manner of PPDE induced cell apoptosis in cultured human cardiomyocytes

	% of apoptosis		
Treatment	0	24 h	48 h
Medium only	1.0 ± 2.7	11.5 ± 2.7	12.1 ± 3.2
PBS only	2.2 ± 3.1	10.4 ± 2.6	11.5 ± 3.4
Medium + DOXO	9.7 ± 2.4	34.8 ± 3.6*	42.2 ± 4.2*
Medium + SPDE	0.7 ± 2.5	12.2 ± 3.2	13.6 ± 3.2
Medium + PPDE	9.7 ± 2.6	48.2 ± 4.7*	57.6 ± 4.4*

- **PPDE treatment induces apoptosis in cultured human cardiomyocytes.**

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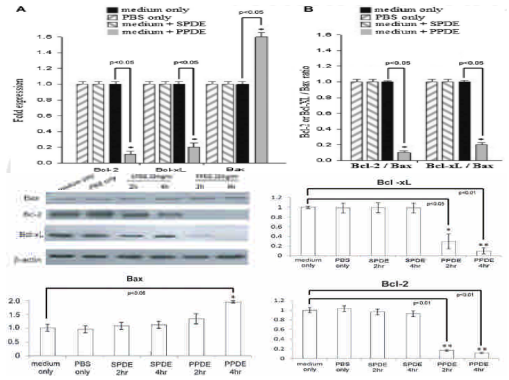

- **PPDE treatment upregulates Bax gene expression in cultured human cardiomyocytes.**

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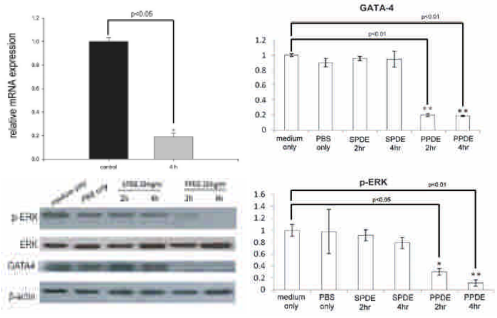

- **PPDE treatment reduces GATA4 expression, ERK phosyhorylation in cultured human cardiomyocytes.**

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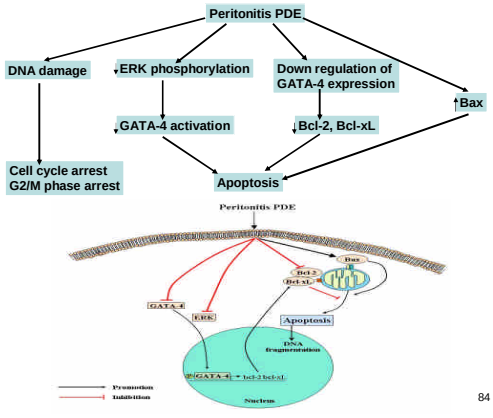

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1. PPDE contains potent pro-apoptotic factors that regulate expression of GATA-4 and Bcl-2 families, inducing cultured cardiomyocyte apoptosis.
2. Findings illustrate a pivotal role of apoptosis in PD peritonitis-associated cardiovascular events, explain high cardiac mortality in PD-related peritonitis.

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Summary

To improve the prognosis of PD-related peritonitis

Improve the outcome

↑ **Th1 immune response**
- ↑ IL-12, IL-18, IFN-γ
- ↑ T-bet ↓GATA-3
- ↑ Integrin α6β1
- ↓ Integrin α4

Reduce the mortality

↓ **Cardiomyocyte apoptosis**
- ↑ Bcl-2, Bcl-xL
- ↓ Bax
- ↑ GATA-4
- ↑ ERK phosyhorylation

Long-term and successful peritoneal dialysis

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An update of Pediatric PD in Asian perspectives

SWOT analysis & strategic thinking

To understand our environment in each Asian country

Understand our threat & weakness

Change to opportunity & establish strength

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Using innovation & strategy

planning & prospect

establish key performance index

From bench to clinic

To improve quality of pediatric PD

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All this we can do.

All this we will do.

We can do more better

in Pediatric PD

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Thank You for

Your Attention

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