INSULINOTERAPIA NEL DIABETICO CON IRC E NEL DIALIZZATO

Dott.sa Roberta MANTI
S. C. M.Metaboliche e Diabetologia
ASL TO 5 MONCALIERI

CONFLITTO DI INTERESSI

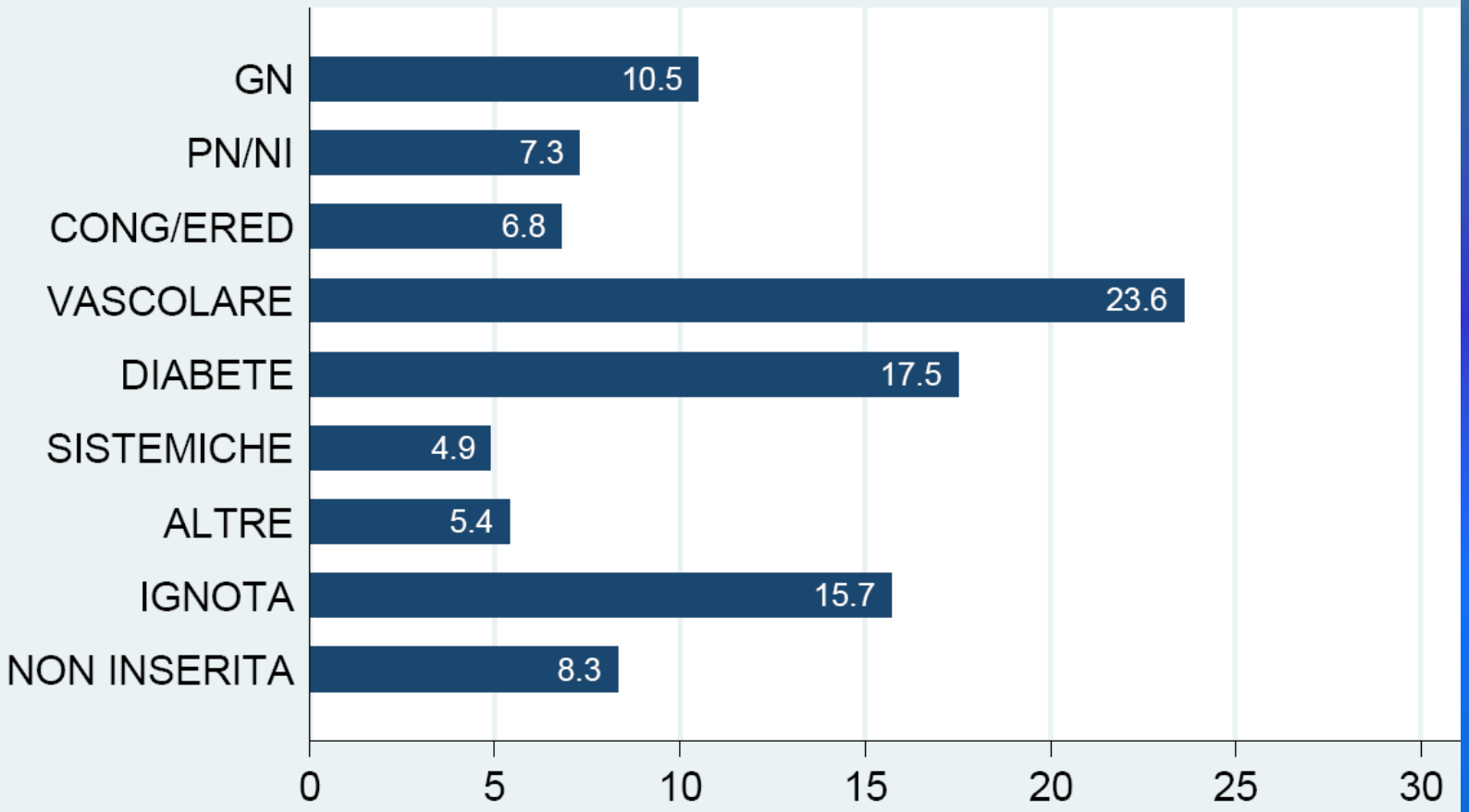
- ELI LILLY
- SANOFI AVENTIS
- NOVARTIS

Diabetes is the leading cause of CKD in developed countries and is rapidly becoming the leading cause in developing countries as a consequence of the global increase in type 2 diabetes and obesity. In the United States…diabetes accounts for 45% of prevalent kidney failure, up from 18% in 1980.

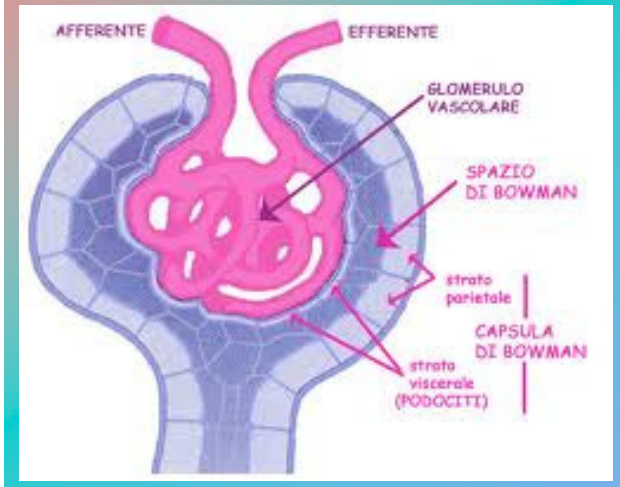
NKF KDOQI GUIDELINES

NEFROPATIA PRIMITIVA

CASI INCIDENTI 2006



Report Annuale RIDT 2008



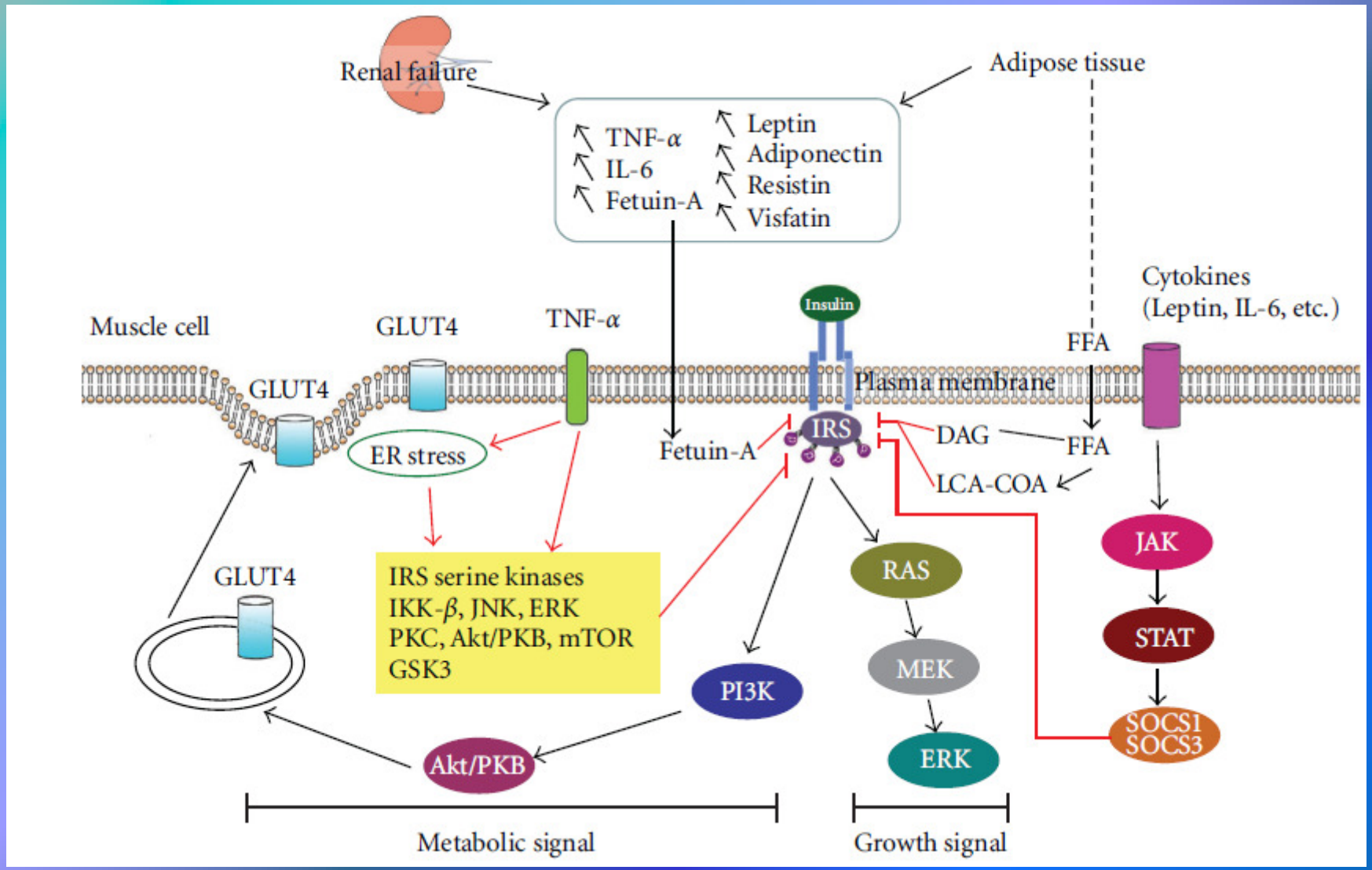
RENE….

… ruolo importante sull'omeostasi glicidica

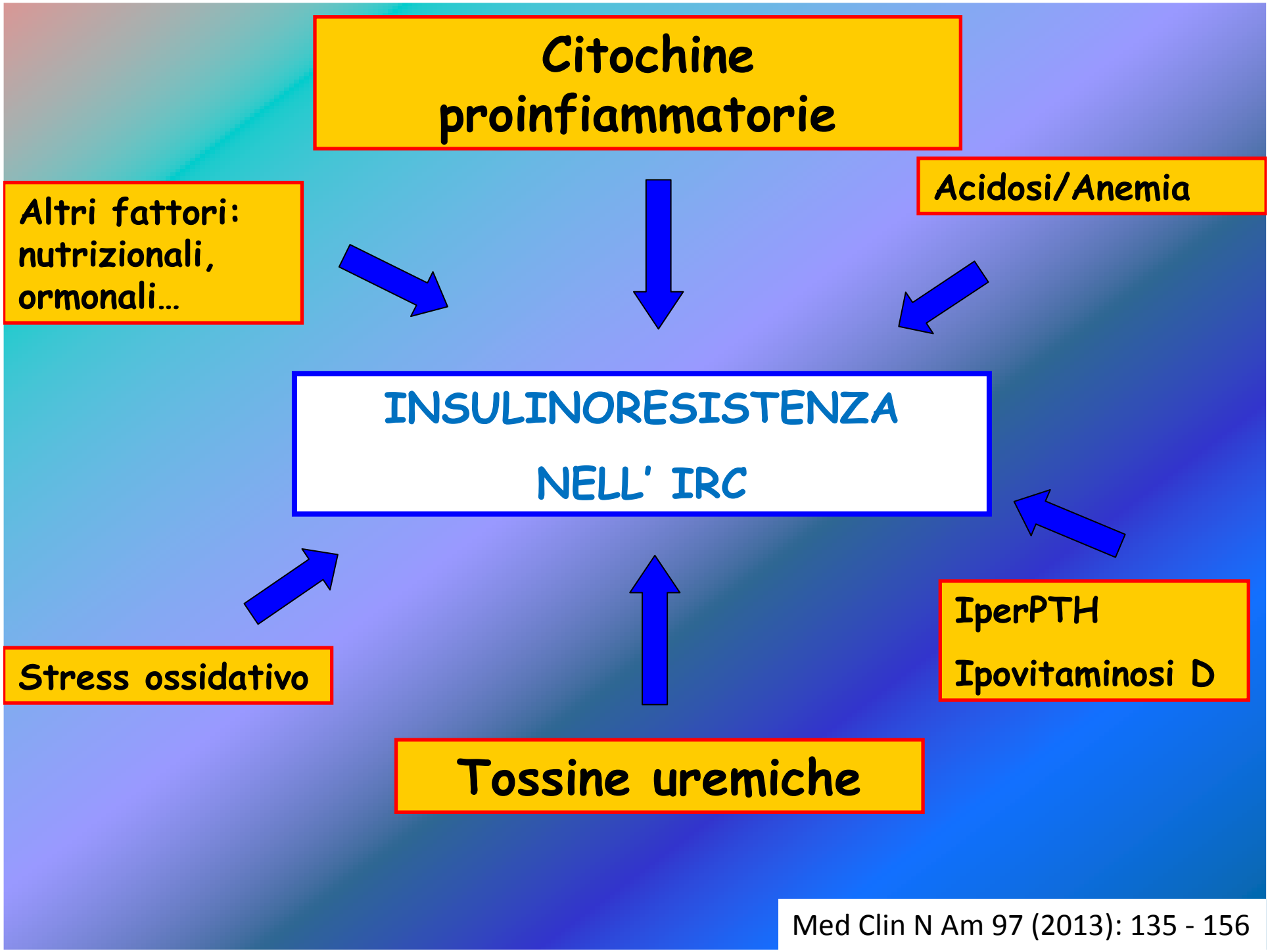
l'insufficienza renale è associata a multiple alterazioni del metabolismo dei carboidrati e dell'insulina, elementi che vanno considerati nell'approccio terapeutico, in particolare con insulina, al paziente diabetico con alterazione del GFR

XIX
CONGRESSO
NAZIONALE AMD
Roma, 29 maggio - 1 giugno 2013
Rome Marriott Park Hotel

INSULINORESISTENZA E IPERGLICEMIA



Journal BiomedBiotechnol 2012



Med Clin N Am 97 (2013): 135 - 156

Table 1. Determinants of glucose intolerance or "pseudodiabetes" in renal failure

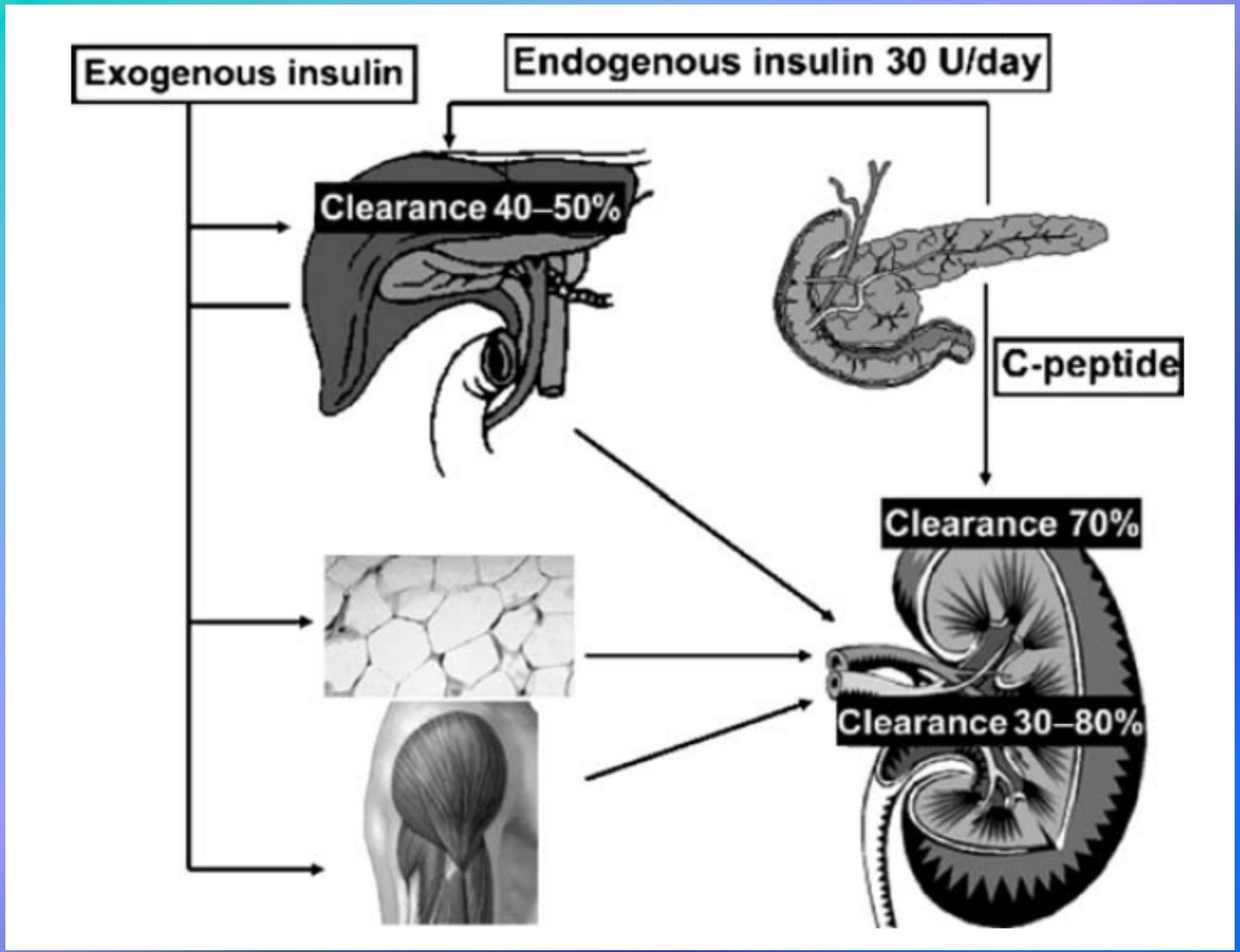
Acidemia
Insulin resistance in hepatic and peripheral tissues
Abnormal receptor binding
Postreceptor defect
Increased plasma levels of:
Glucagon[a]
Growth hormone
Parathyroid hormone
Increased plasma levels of substrates for hepatic gluconeogenesis derived from skeletal muscle
Potassium deficiency

[a] Increased tissue sensitivity also is present.

Kidney International, 42 (1992): 1266-1282

XIX
CONGRESSO
NAZIONALE AMD
Roma, 29 maggio - 1 giugno 2013
Rome Marriott Park Hotel

IPOGLICEMIA



Diabetes, Obesity and Metabolism, 10,2008: 811-823

- Diminuisce la clearance dell'insulina
- Diminuisce la gluconeogenesi
- Entrambe aumentano il rischio di ipoglicemia

Table 5. Causes of hypoglycemia in renal failure

Physiologic derangement	Clinical entity
Caloric deprivation	Dietary neglect, acute and chronic
	Prolonged fasting
	Chronic malnutrition
	Heart failure
	Neoplasms
	Adrenal, thyroid deficiency
Diminished hepatic release of glucose	Alcohol intake
	Oral hypoglycemic agents
	Beta-blockers, other medications (see Table 6)
	Hepatic disease
Reduced renal release of glucose	Renal failure
Excess peripheral utilization of glucose	Insulin therapy
	Sepsis

Kidney International, 42 (1992): 1266-1282

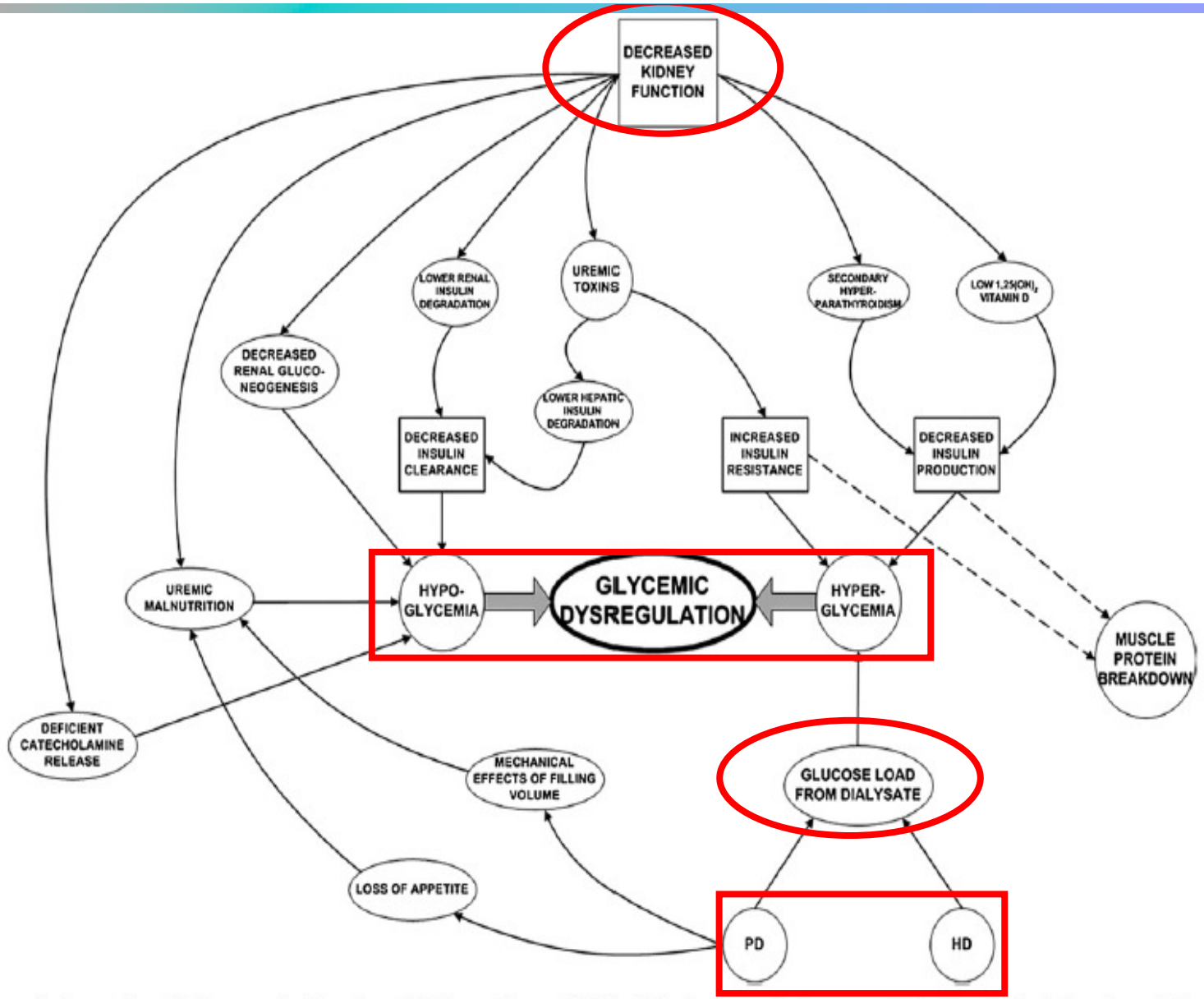
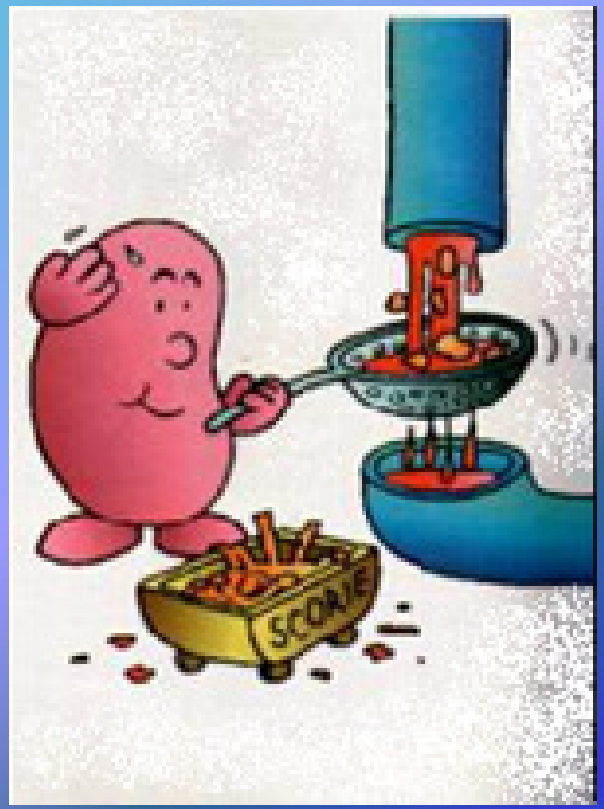
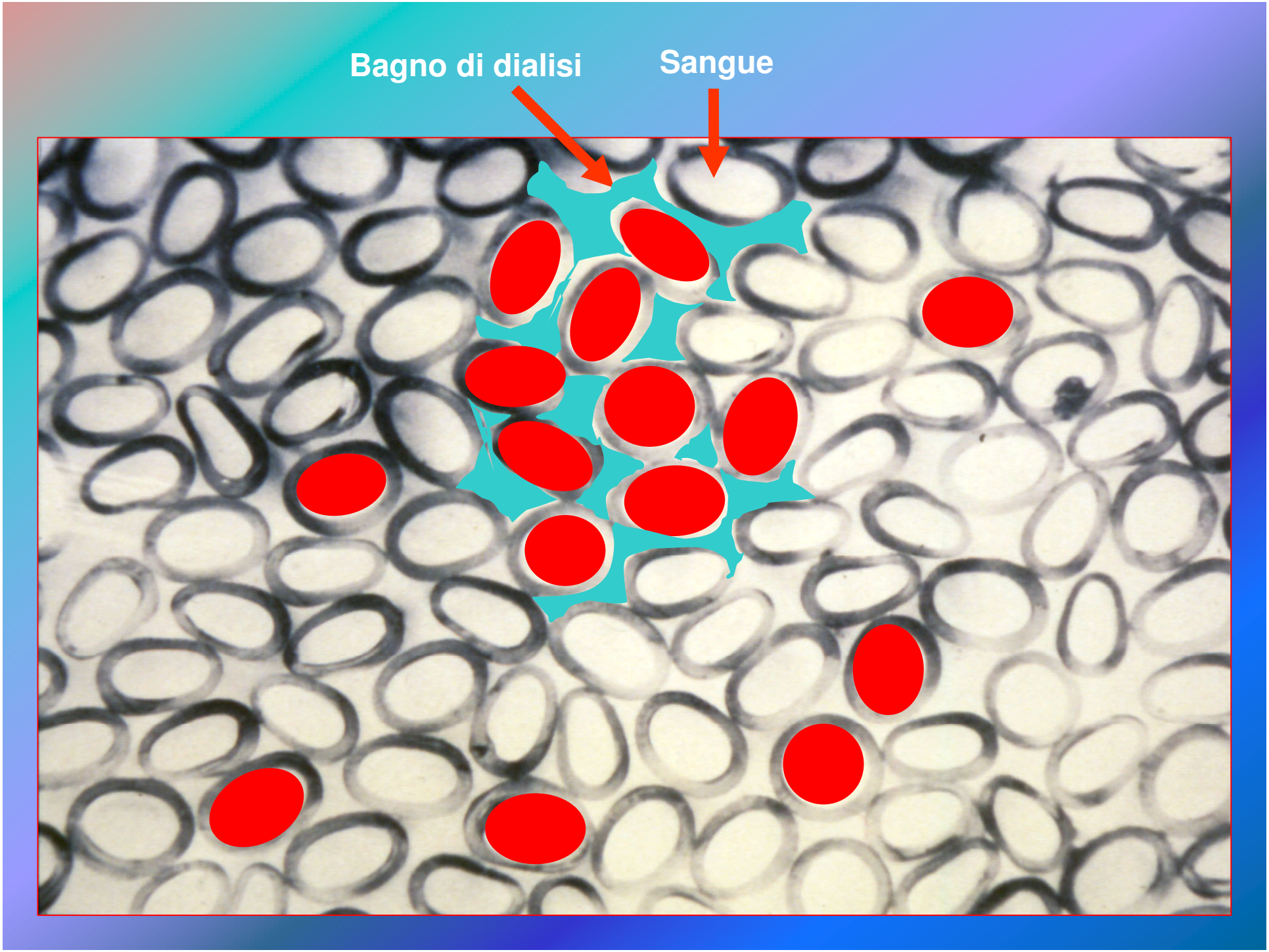


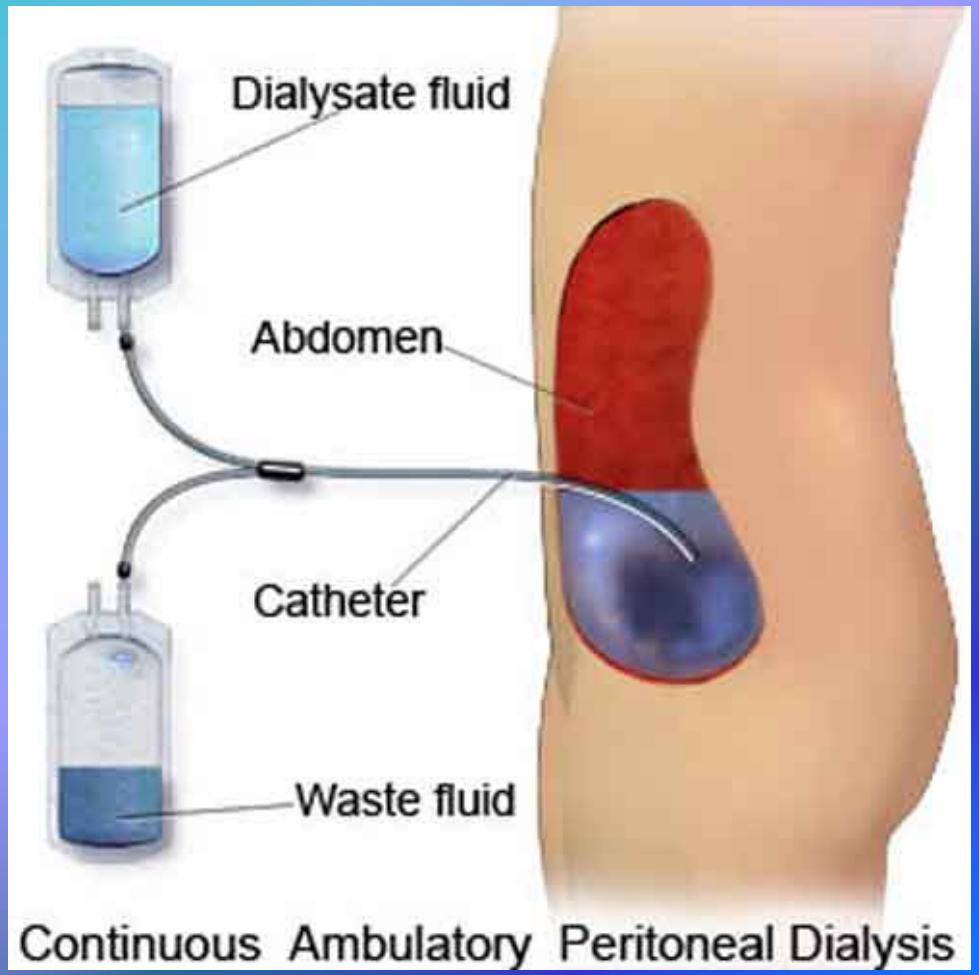
Fig. 1. Overview of glucose/insulin homeostasis in chronic kidney disease/ESRD. Disturbances of glucose metabolism include insulin resistance and glucose intolerance. Several factors contribute to hyperglycemia, which may coexist with hypoglycemia. *Abbreviations:* HD, hemodialysis; PD, peritoneal dialysis.

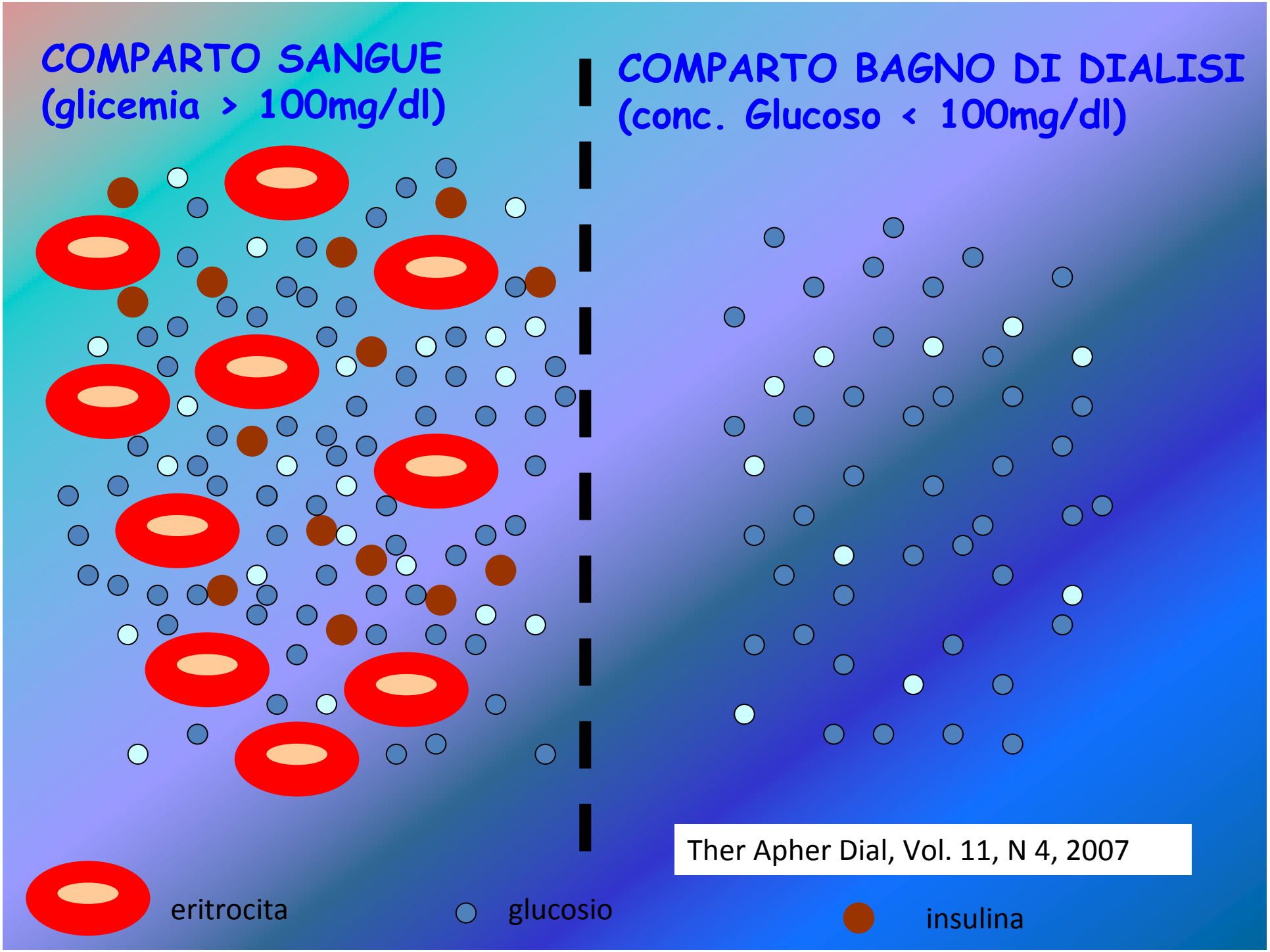
Med Clin N Am 97 (2013): 135 - 156

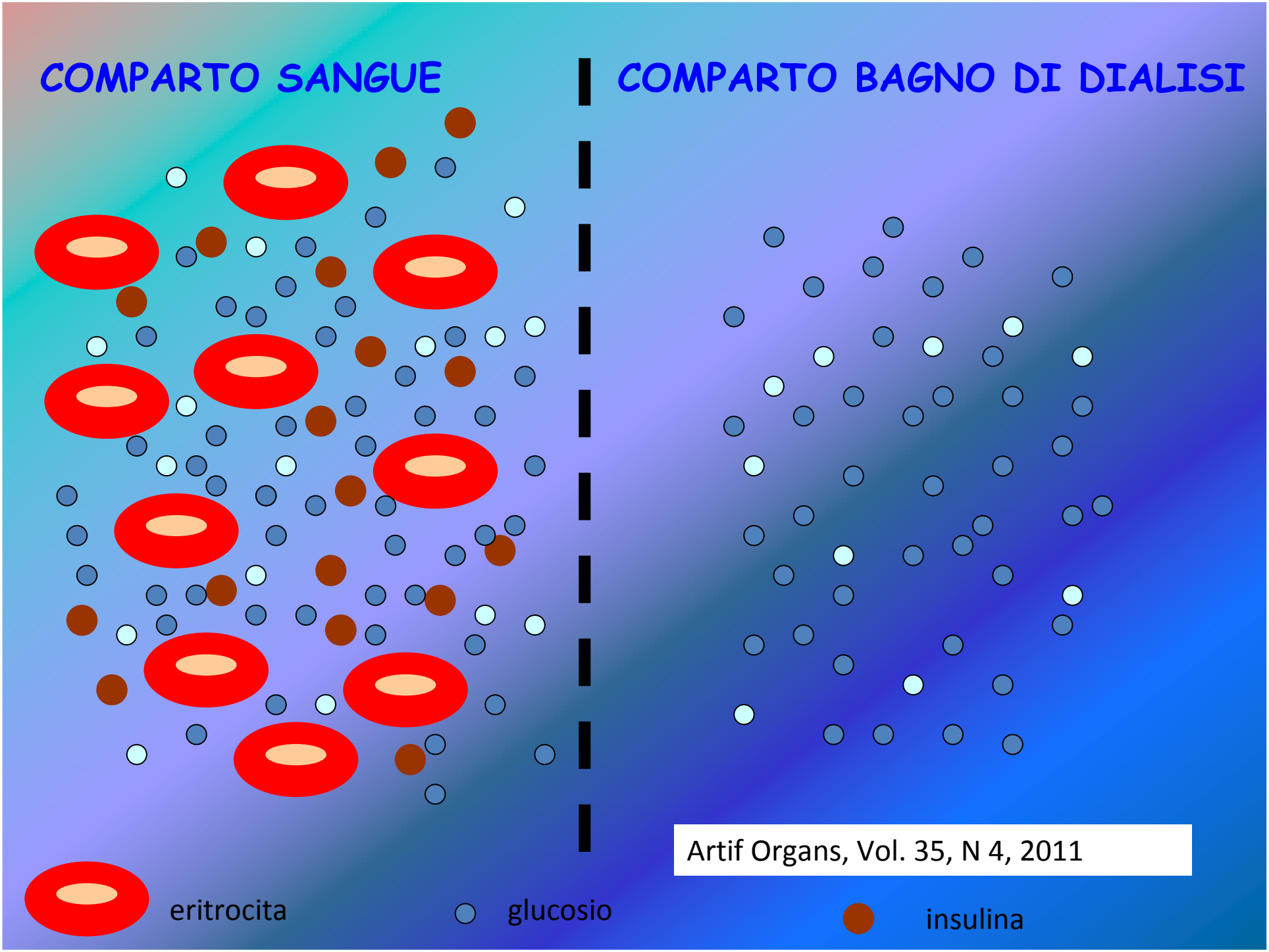


IN DIALISI….


Bagno di dialisi
Sangue


Dialysate fluid
Abdomen
Catheter
Waste fluid
Continuous Ambulatory Peritoneal Dialysis


COMPARTO SANGUE
(glicemia > 100mg/dl)
COMPARTO BAGNO DI DIALISI
(conc. Glucoso < 100mg/dl)
Ther Apher Dial, Vol. 11, N 4, 2007
eritrocita
glucosio
insulina


COMPARTO SANGUE
COMPARTO BAGNO DI DIALISI
Artif Organs, Vol. 35, N 4, 2011
eritrocita
glucosio
insulina

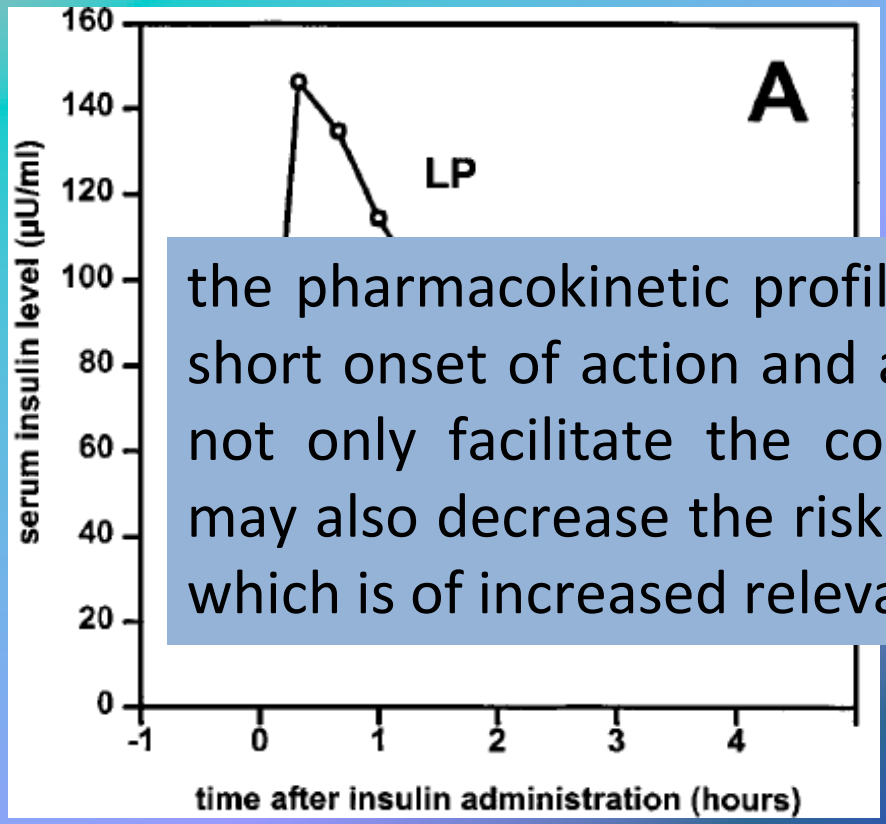

INSULINA

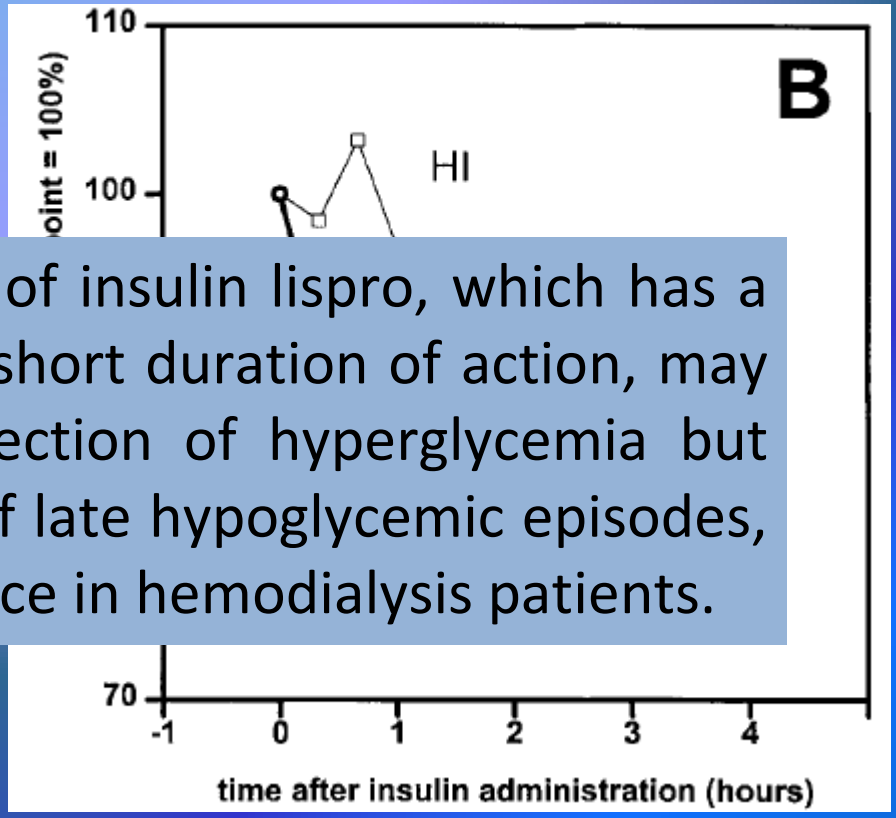
there are no randomized controlled trials of diabetes therapies in patients with CKD

Pilmore HL. Nephrology. 2010;15:412-418

The rationale for insulin analogues is based on structural changes in the insulin molecule to take advantage of the analogue's new pharmacokinetic properties, reproducing both basal (long-acting insulin analogues) and prandial (rapid-acting insulin analogues) insulin secretion more physiologically in response to glucose

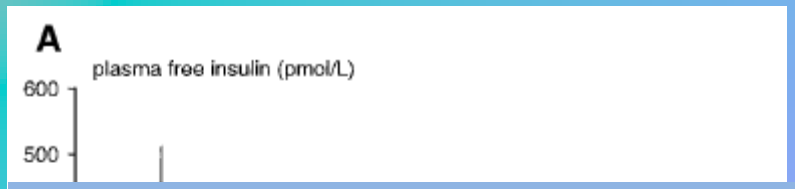
Diabetes, Obesity and Metabolism, 10, 2008: 811-823

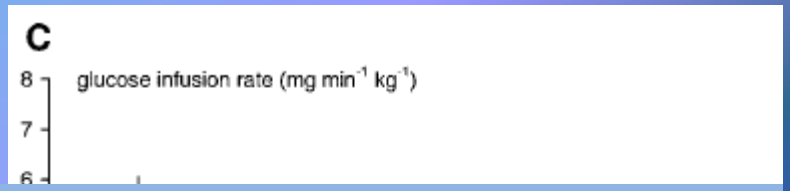




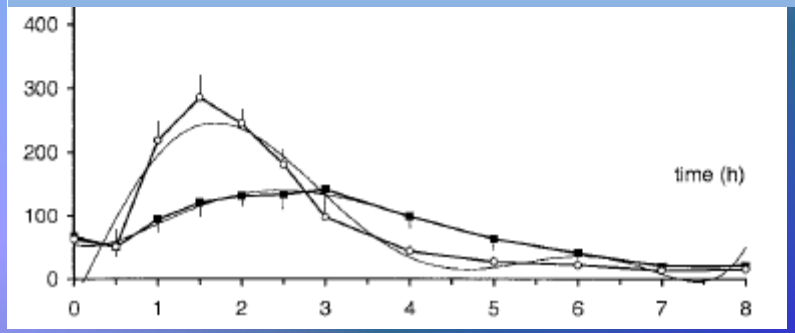
the pharmacokinetic profile of insulin lispro, which has a short onset of action and a short duration of action, may not only facilitate the correction of hyperglycemia but may also decrease the risk of late hypoglycemic episodes, which is of increased relevance in hemodialysis patients.

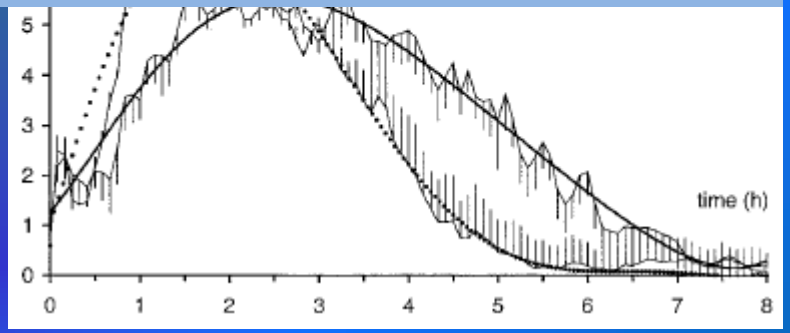
Nephrol Dial Transplant 1999 14 (S4): 5-6



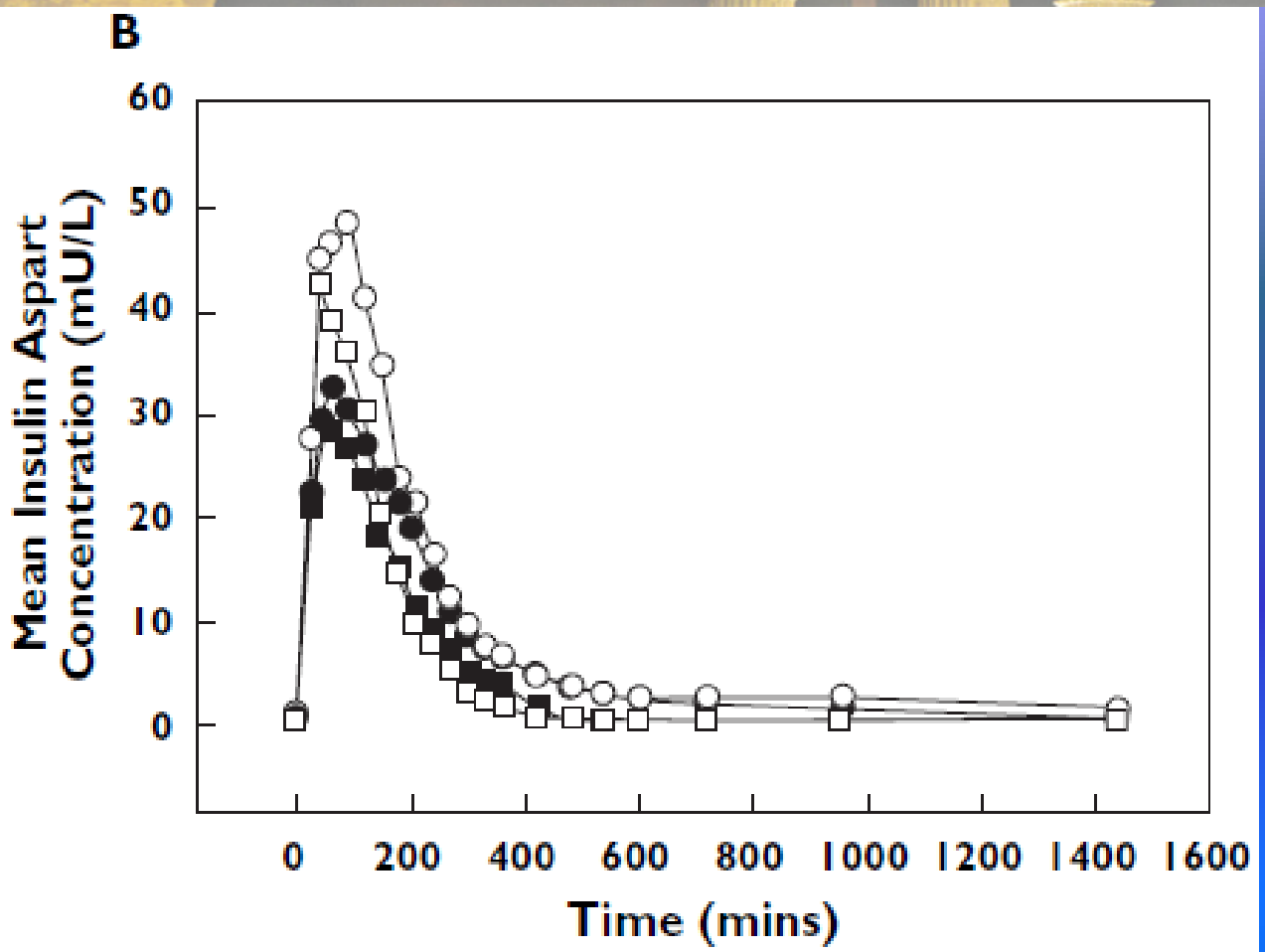


Although insulin levels were higher in patients with overt diabetic nephropathy, the metabolic response to regular insulin – although not to insulin lispro – was reduced. This finding would indicate that a higher dose of regular human insulin with the consequent higher risk of hypoglycaemia would be necessary in achieving the same metabolic effect in patients with overt diabetic nephropathy.





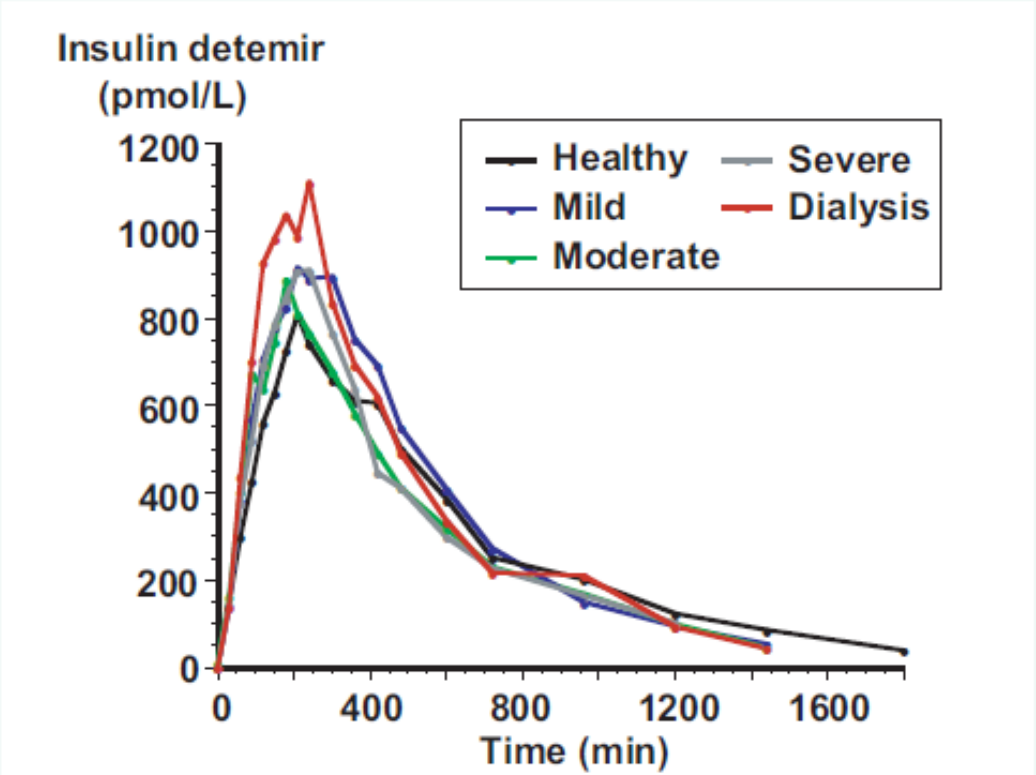
Diabetes Care 2001 ; 24:886-890



Rangel II (○), Rangel III (■), Rangel IV (□). Panel B: profiles for degree of renal impairment. Normal (●), mild (○), moderate (■), severe (□);

Br J Clin Pharmacol 2005 Nov;60(5):469-76

Insulin Detemir Profiles by Renal Function Group



Diabetologia 2002; 45: A259

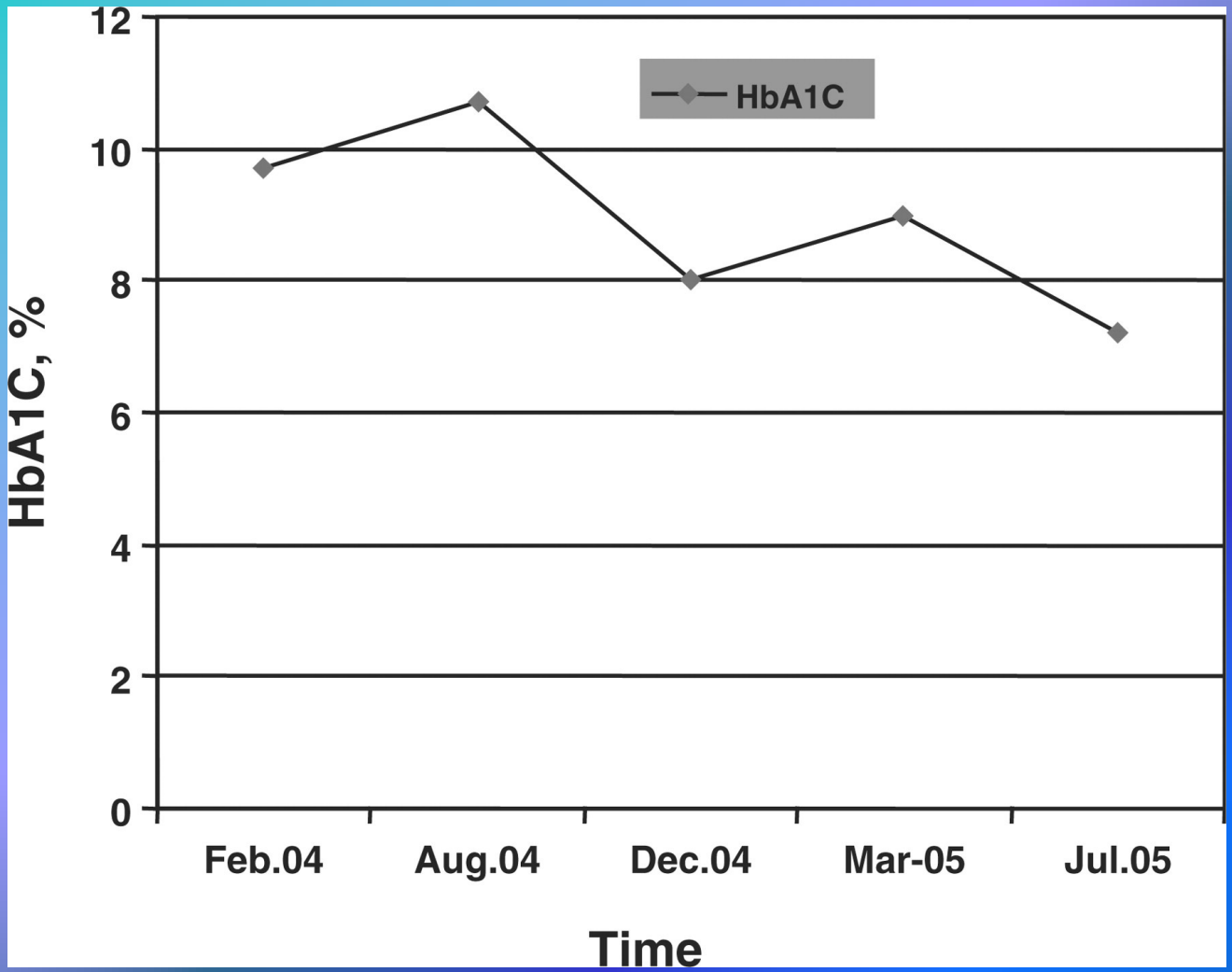
216-OR

Experience with Insulin Glargine in Patients with End-Stage Renal Disease

STEFAN PSCHERER, GERHARD SCHREYER-ZELL, MARTIN GOTTSMANN *Traustein, Zentrale, Germany*

Insulin glargine (LANTUS®) is a long-acting human insulin analog, but the efficacy of this insulin in patients with end-stage renal disease and chronic hemodialysis treatment (dialysate glucose concentration 5.6 mmol/L) has not yet been discerned. In a retrospective investigation of 20 patients with diabetes (Type 1, n=4; Type 2, n=16) and end-stage renal disease treated with insulin glargine, the level of glycemic control and the incidence of hypoglycemia were assessed. The patients had been on dialysis for a mean 43.1 ± 7.1 months. 19 of the patients had previously been on insulin therapy, either as conventional therapy (CT) or as intensified conventional therapy (ICT). One patient was on oral antidiabetic drugs (OADs) alone. All patients were transferred to insulin glargine: patients on CT were moved to ICT. In patients already on ICT, NPH insulin was replaced by insulin glargine, or the patients were treated with insulin glargine and OADs (in cases with an increased fasting plasma glucose). Prior to switching to insulin glargine all patients received counseling. The initial dose was individualized based on the patient's previous therapy regimen. The average duration of insulin glargine therapy subsequently was 9.9 ± 4.8 months. No dose reduction in insulin glargine was made before dialysis sessions. The level of glycemic control increased as demonstrated by a significant reduction in the patient's mean HbA_{1c} from 7.7 ± 1.3% to 6.8 ± 0.7% (p=0.005). Throughout the study there was no occurrence of severe hypoglycemia. The mean patient weight (dry weight post-dialysis) increased with treatment duration by 1.5 kg during insulin glargine therapy (Type 1 patients, 0.6 kg; Type 2, 1.7 kg). While all patients with diabetes and renal disease need careful surveillance of their glycemic status when on insulin therapy, this study suggests that insulin glargine is effective and well tolerated in patients with diabetes on chronic hemodialysis treatment.

62nd Sci Sess Am Diabetes Assoc (ADA), San Francisco (Jun 2002)
Diabetes 2002; 51(suppl 2): A53, abs 216-OR



Nephrol. Dial. Transplant. 2006;21:553-554

TABLE IV
RESULT OF THE QUESTIONNAIRE CONCERNING QUALITY OF LIFE

1. How was it to change to glargine from previous insulin treatment?

Easier	Unchanged	More difficult
75.0% (n=9)	25.0% (n=3)	0

2. How is your hypoglycemia compared with that with your previous insulin treatment?

Decreased	Unchanged	Increased
50.0% (n=6)	50.0% (n=6)	0

3. Has there been any change in your being active and positive using glargine, which has a low risk of hypoglycemia?

More active	Unchanged	Less active
50.0% (n=6)	50.0% (n=6)	0

4. How is your glycemic control, after changing to glargine from your previous insulin treatment?

Satisfied	Unchanged	Worse
66.7% (n=8)	33.3% (n=4)	0

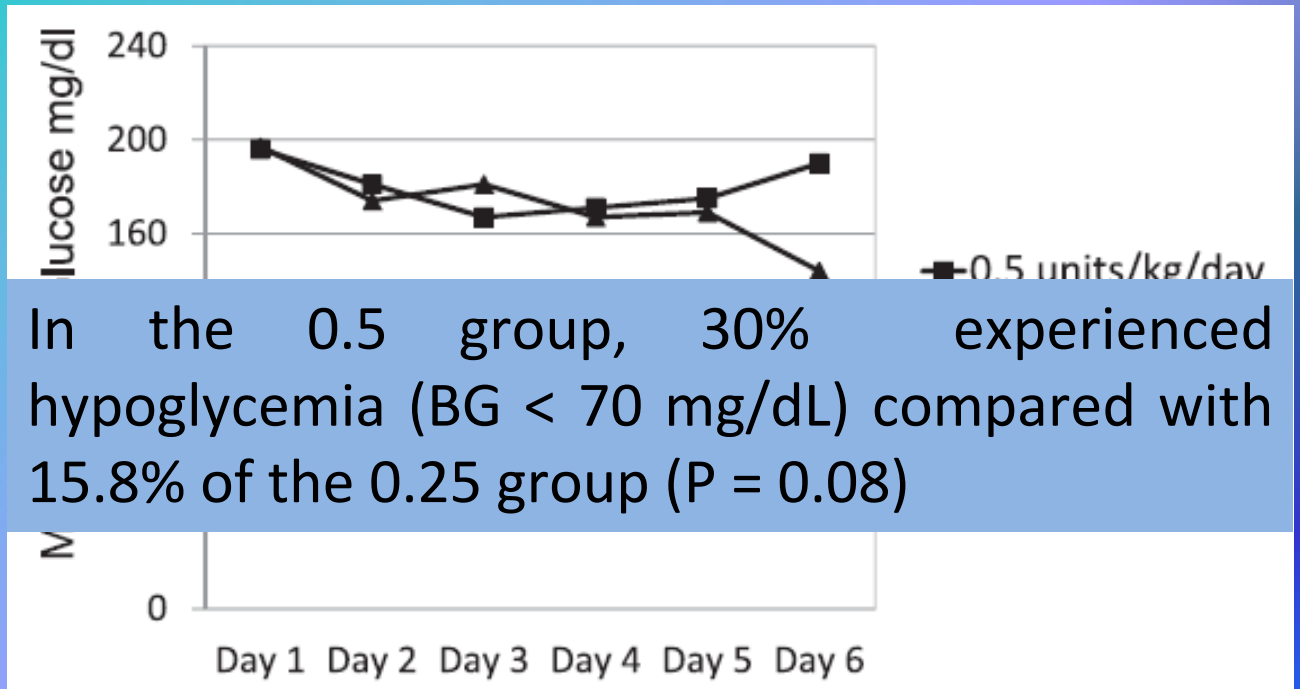
5. Do you want to go back to the previous insulin treatment?

No, I don't	No preference	Yes, I do
91.7% (n=11)	8.3% (n=1)	0

XIX
CONGRESSO
NAZIONALE AMD
Roma, 29 maggio - 1 giugno 2013
Rome Marriott Park Hotel

A Randomized Trial of Two Weight-Based Doses of Insulin Glargine and Glulisine in Hospitalized Subjects With Type 2 Diabetes and Renal Insufficiency

Diabetes Care 35:1970–1974, 2012



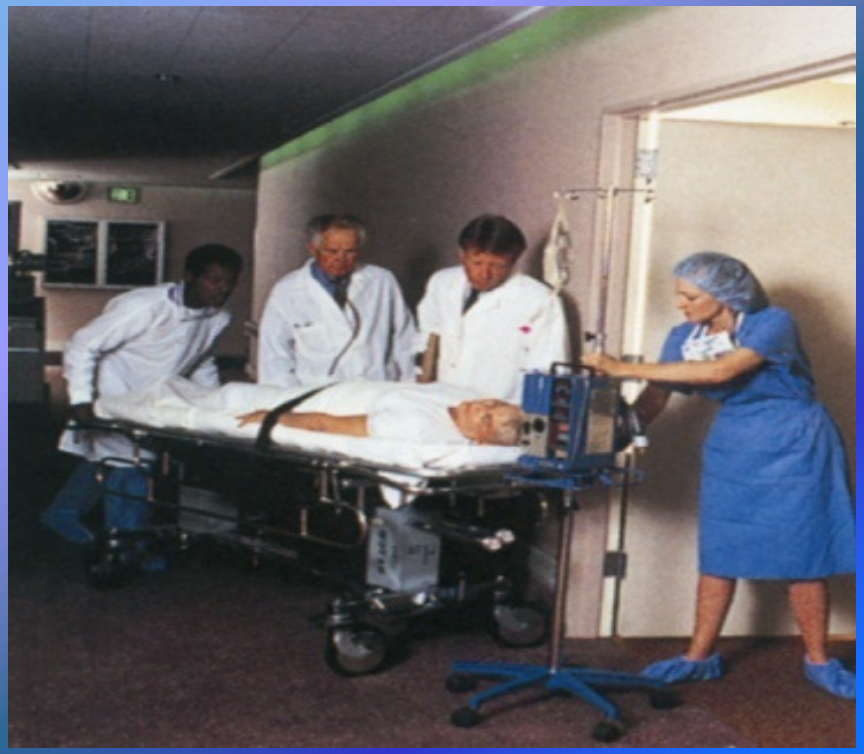
In the 0.5 group, 30% experienced hypoglycemia (BG < 70 mg/dL) compared with 15.8% of the 0.25 group (P = 0.08)

Figure 2—*Mean daily blood glucose: 0.5 vs. 0.25 units/kg/day.*

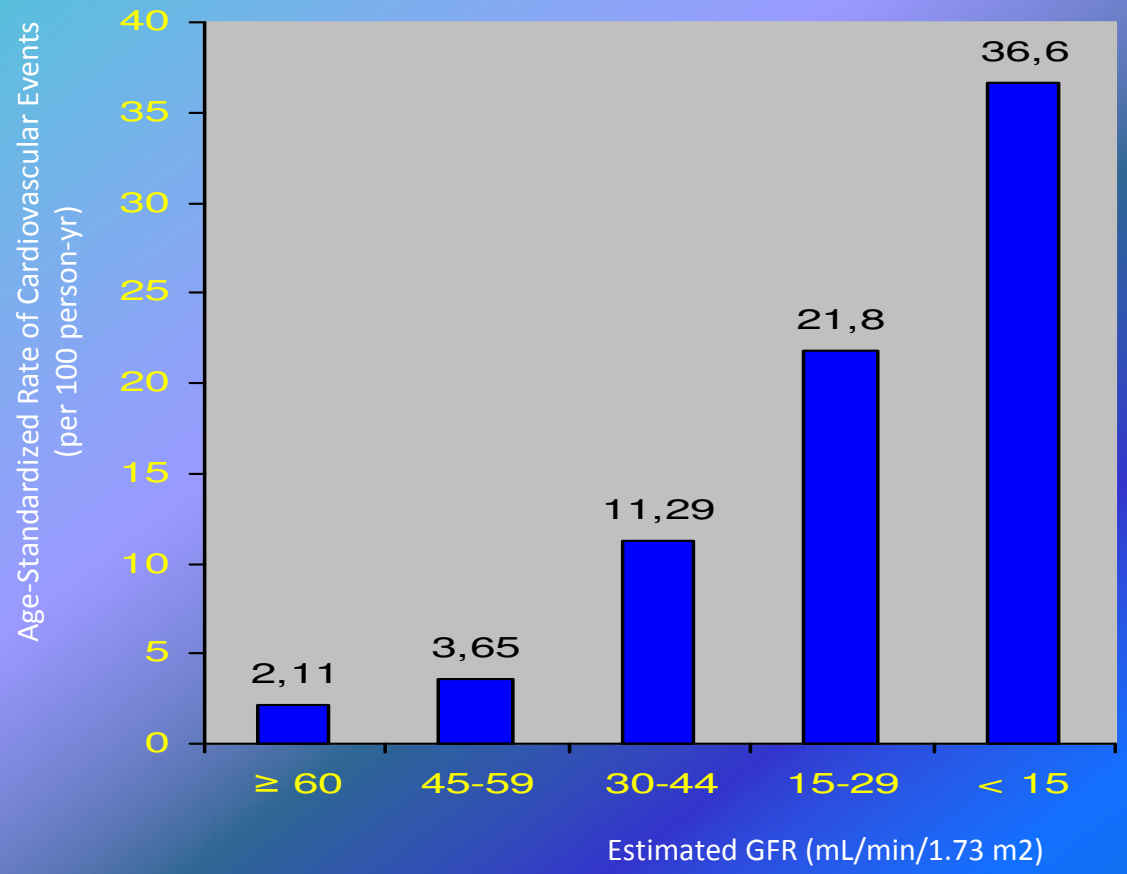
Diabetes Care 35:1970–1974, 2012

The Big Fear

Hypoglycaemia



CKD Predicts CVD



Go, et al., 2004

KDOQI Diabetes Guideline: 2012 Update

AJKD

Table 4. Dose Adjustment for Insulin Compounds and Oral Medicines for Diabetes in CKD

Medication Class and Agents	CKD stages 3, 4, and 5 ND
Insulin	
Glargine	No advised dose adjustment*
Detemir	No advised dose adjustment*
Neutral Protamine Hagedorn (NPH)	No advised dose adjustment*
Regular	No advised dose adjustment*
Aspart	No advised dose adjustment*
Lispro	No advised dose adjustment*
Glulisine	No advised dose adjustment*

*Adjust dose based on patient response.

GFR	Total Insulin Dose
>50	No variazione
30-50	Riduzione del 20%
15-29	Riduzione del 30%
<15 or Dialisi	Riduzione del 50%

Charpentier G,Diabetes Metab 2000; 26(4):73

Maryann E, SHM, 2008

GRAZIE PER L'ATTENZIONE