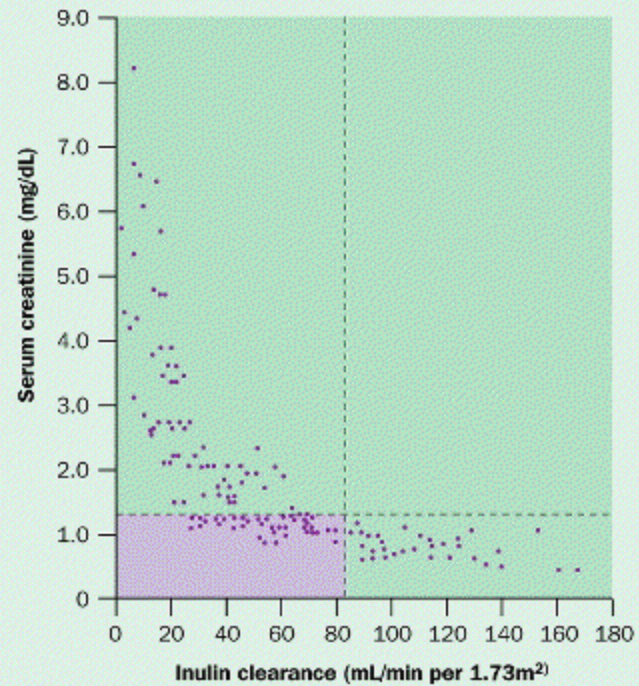


# ΧΡΟΝΙΑ ΝΕΦΡΙΚΗ ΑΝΕΠΑΡΚΕΙΑ

Δημήτριος Β. Βλαχάκος  
Καθηγητής

Μονάδα Νεφρολογίας και Υπερτάσεως  
Β' Προπαιδευτική Παθολογική Κλινική  
Πανεπιστημιακό Γενικό Νοσοκομείο «ΑΤΤΙΚΟΝ»

### Relationship between serum creatinine and glomerular filtration rate



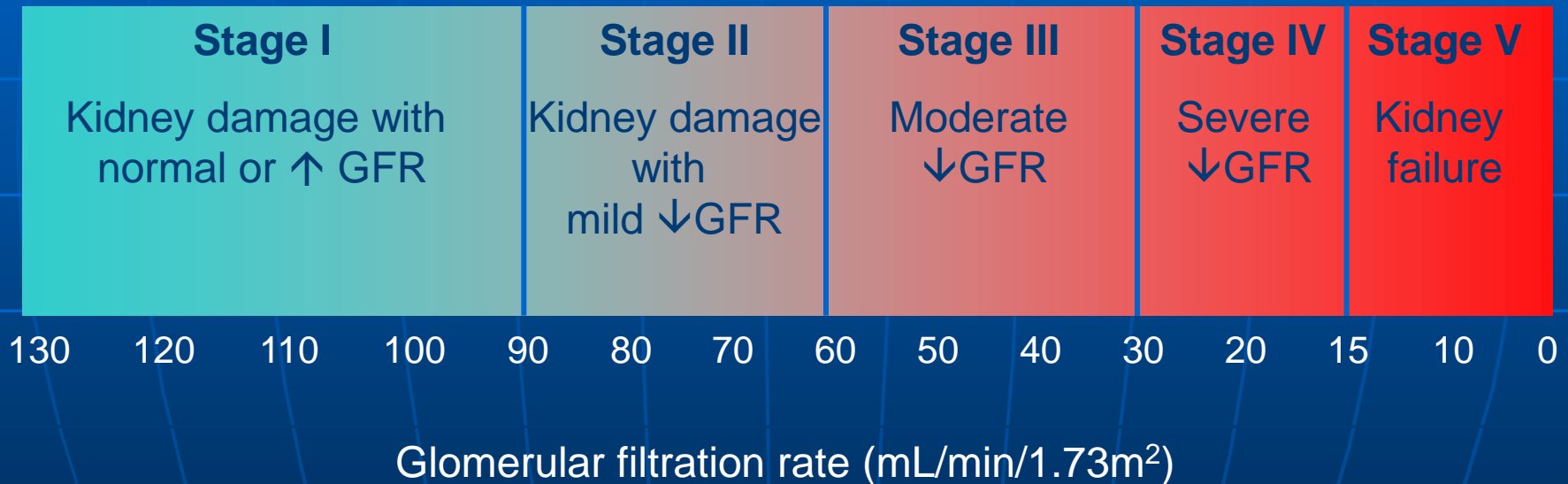
# Υπολογισμός νεφρικής καθάρσεως

(140-ηλικία σε έτη) X (Βάρος σε Kg)

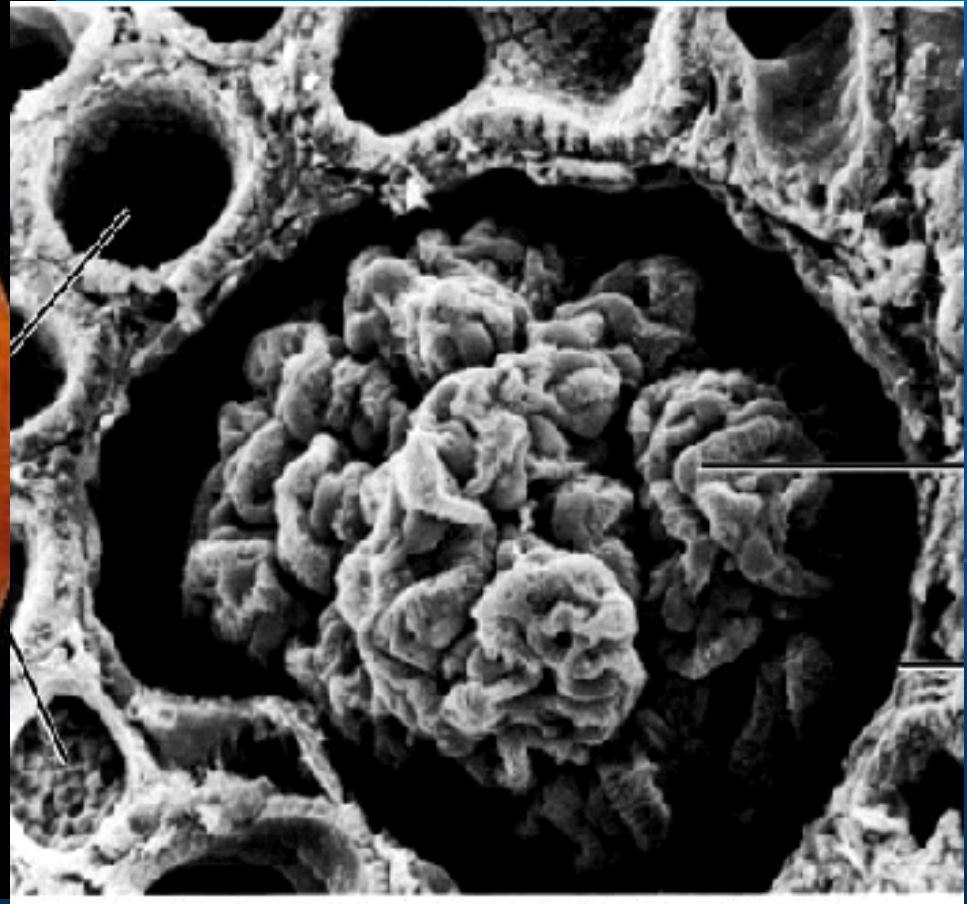
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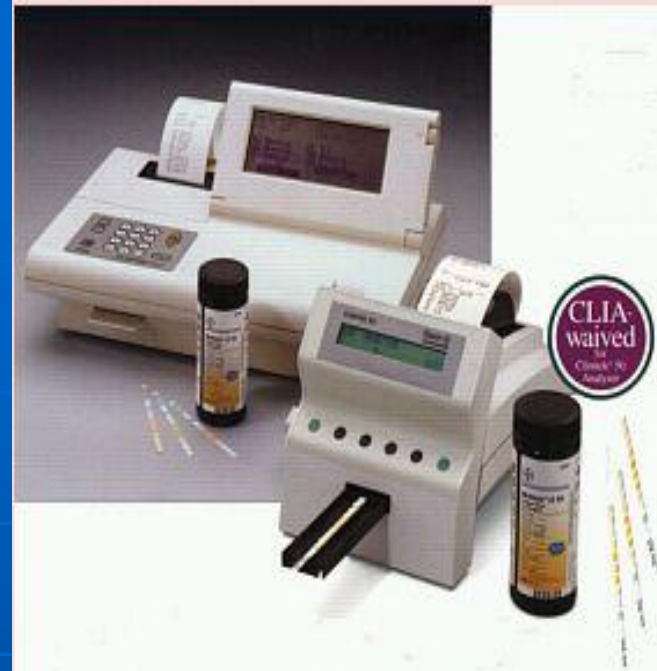
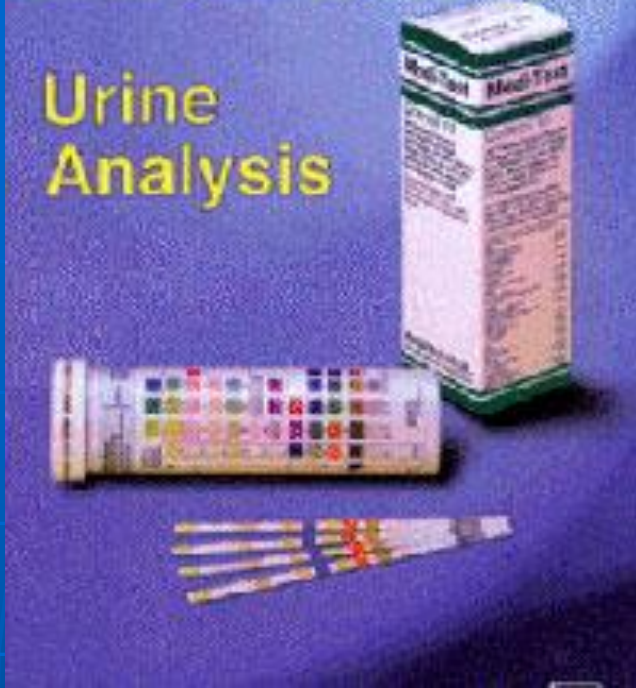
(72  ή 85  ) X (Κρεα,mg%)

# Stages of chronic renal disease



# Μικροαγγειοπάθεια





- **GLU (30 SEC)**
- **BIL (30 SEC)**
- **CET (40 SEC)**
- **DEN (45 SEC)**
- **BLD (60 SEC)**

- **Ph (60 SEC)**
- **PRO (60 SEC)**
- **URO (60 SEC)**
- **NIT (60 SEC)**
- **LEU (2 MIN)**

# Definitions of Microalbuminuria and Macroalbuminuria

Parameter	Normal	Micro-albuminuria	Macro-albuminuria
Urine AER ( $\mu\text{g}/\text{min}$ )	< 20	20 - 200	>200
Urine AER (mg/24h)	< 30	30 - 300	>300
Urine albumin/ Cr <sup>#</sup> ratio (mg/gm)	< 30	30 - 300	>300

AER=Albumin excretion rate

CR<sup>#</sup> =creatinine

## **Table 11. Definition of Chronic Kidney Disease**

### **Criteria**

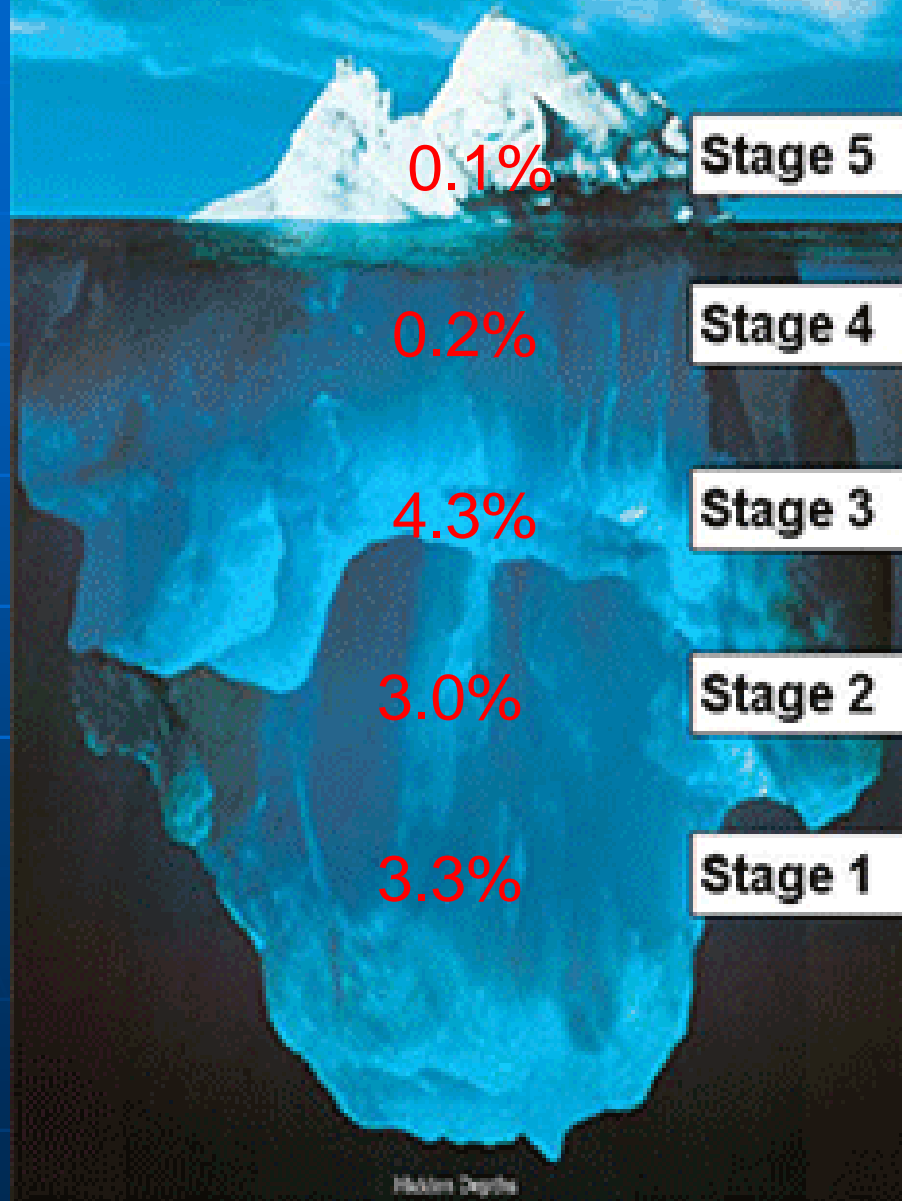
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- 1. Kidney damage for  $\geq 3$  months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by *either*:**
    - Pathological abnormalities; or**
    - Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests**
  - 2. GFR  $< 60$  mL/min/1.73 m<sup>2</sup> for  $\geq 3$  months, with or without kidney damage**
- 

**Methods to estimate GFR are discussed in Guideline 4. Markers of kidney damage are discussed in Guidelines 5–6.**



# Kidney Failure is the Tip of the Iceberg...



## Prevalence of Chronic Kidney Disease (CKD):

Kidney Failure/End-stage kidney disease (GFR <15): 400,000

GFR 15–29:  
300,000

GFR 30–59:  
7,400,000

Kidney damage & GFR 60–89:  
5,700,000

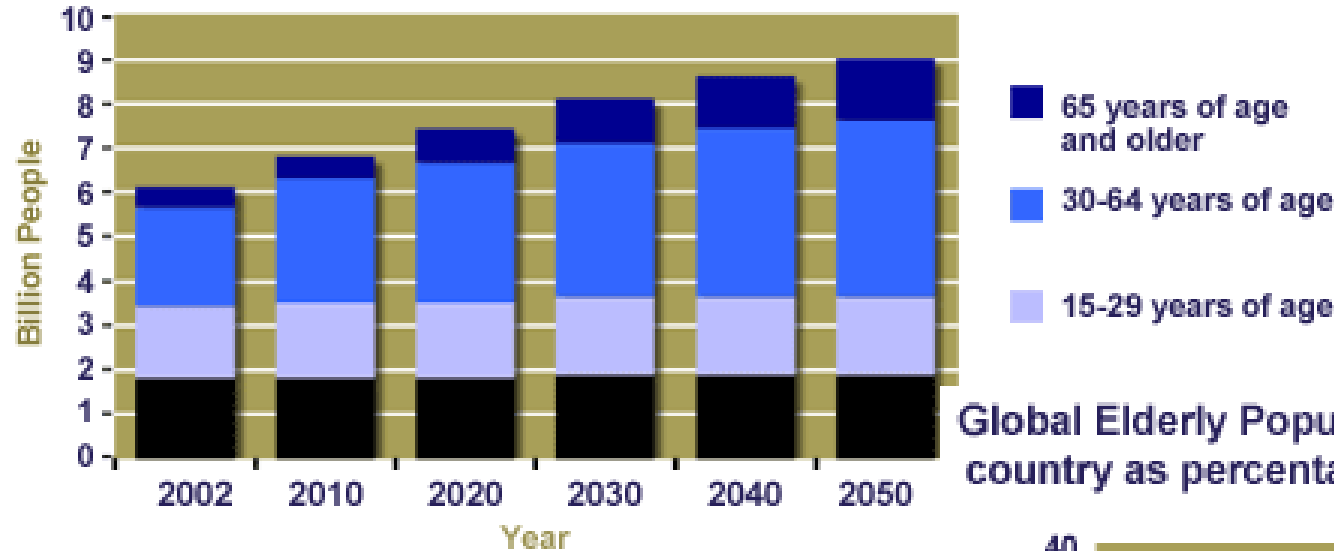
Kidney damage & GFR >90:  
5,600,000

**19 million Americans with CKD**  
**8 million Americans with GFR<60**

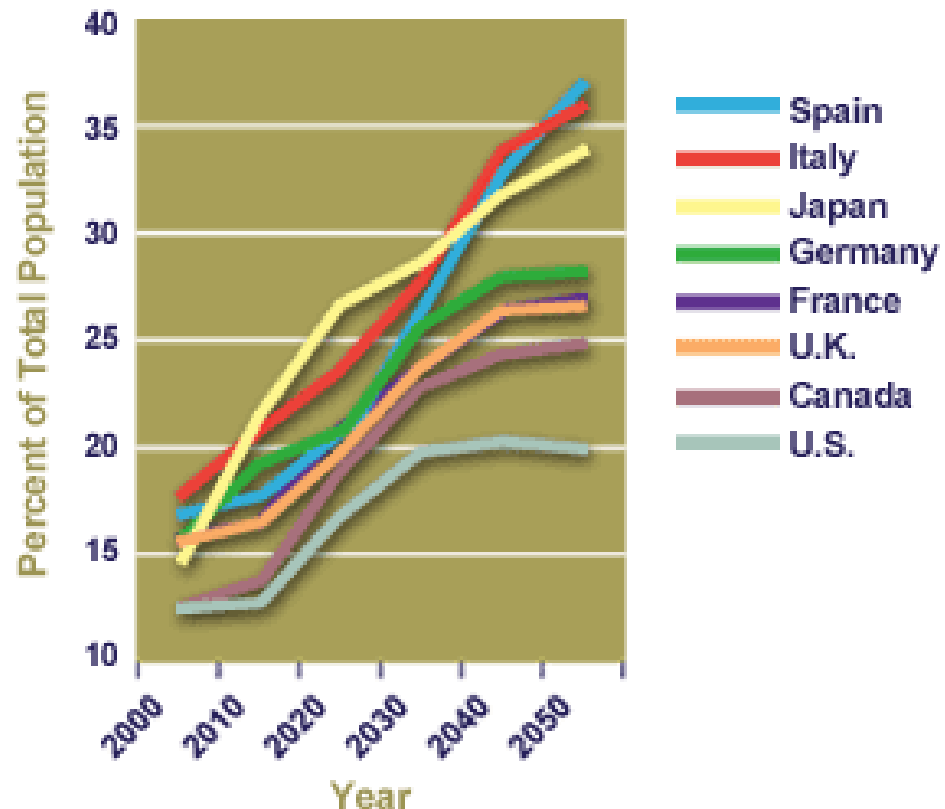
**Table 140. Simplified Classification of Chronic Kidney Disease by Diagnosis**

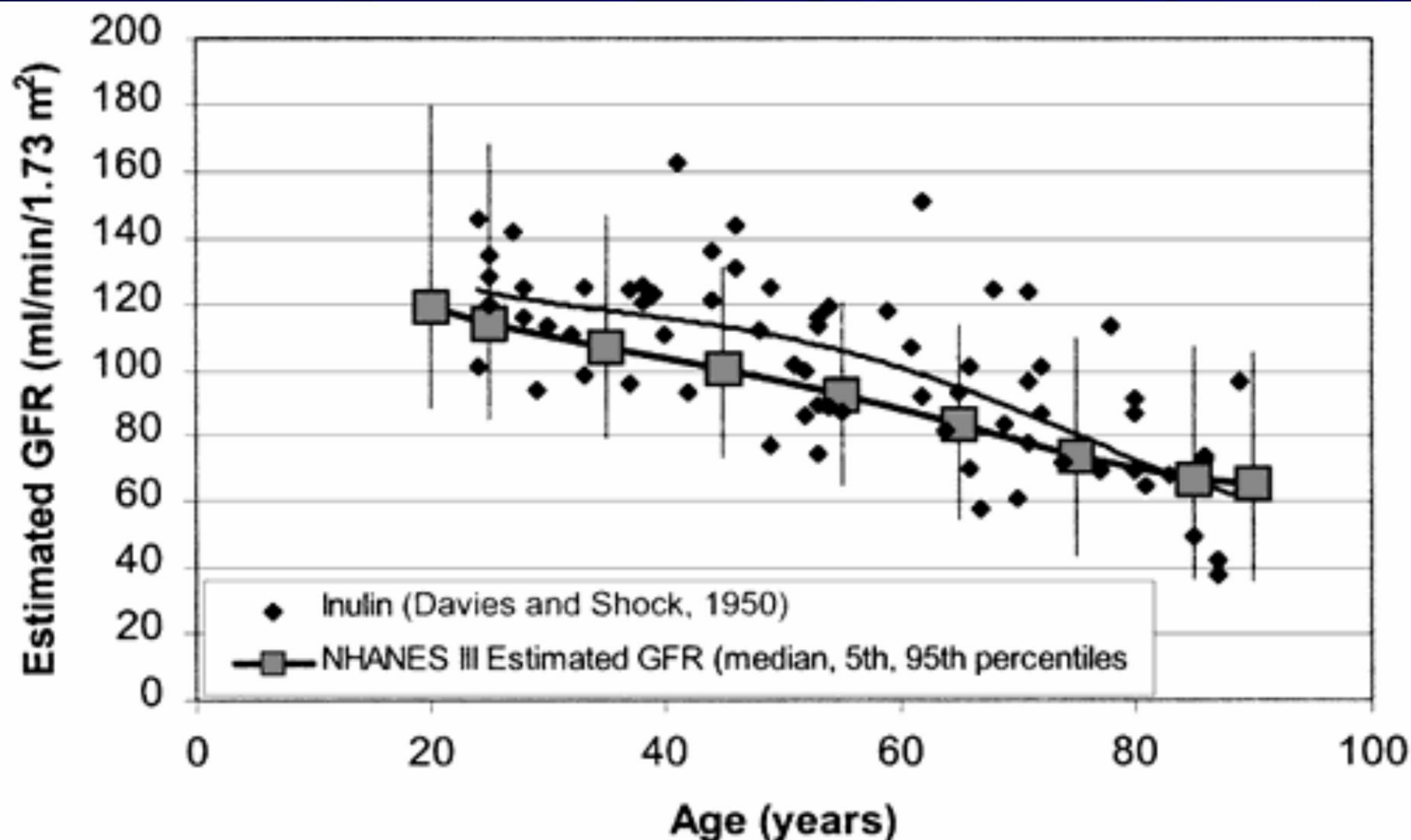
<b>Disease</b>	<b>Major Types (Examples)</b>
<b>Diabetic kidney disease</b>	Type 1 and type 2 diabetes
<b>Nondiabetic kidney diseases</b>	Glomerular diseases (autoimmune diseases, systemic infections, drugs, neoplasia)  Vascular diseases (large vessel disease, hypertension, microangiopathy)  Tubulointerstitial diseases (urinary tract infection, stones, obstruction, drug toxicity)  Cystic diseases (polycystic kidney disease)
<b>Diseases in the transplant</b>	Chronic rejection  Drug toxicity (cyclosporine or tacrolimus)  Recurrent diseases (glomerular diseases)  Transplant glomerulopathy

## Global Population Trends 2002 - 2050



## Global Elderly Population (over age 64) by country as percentage of total population

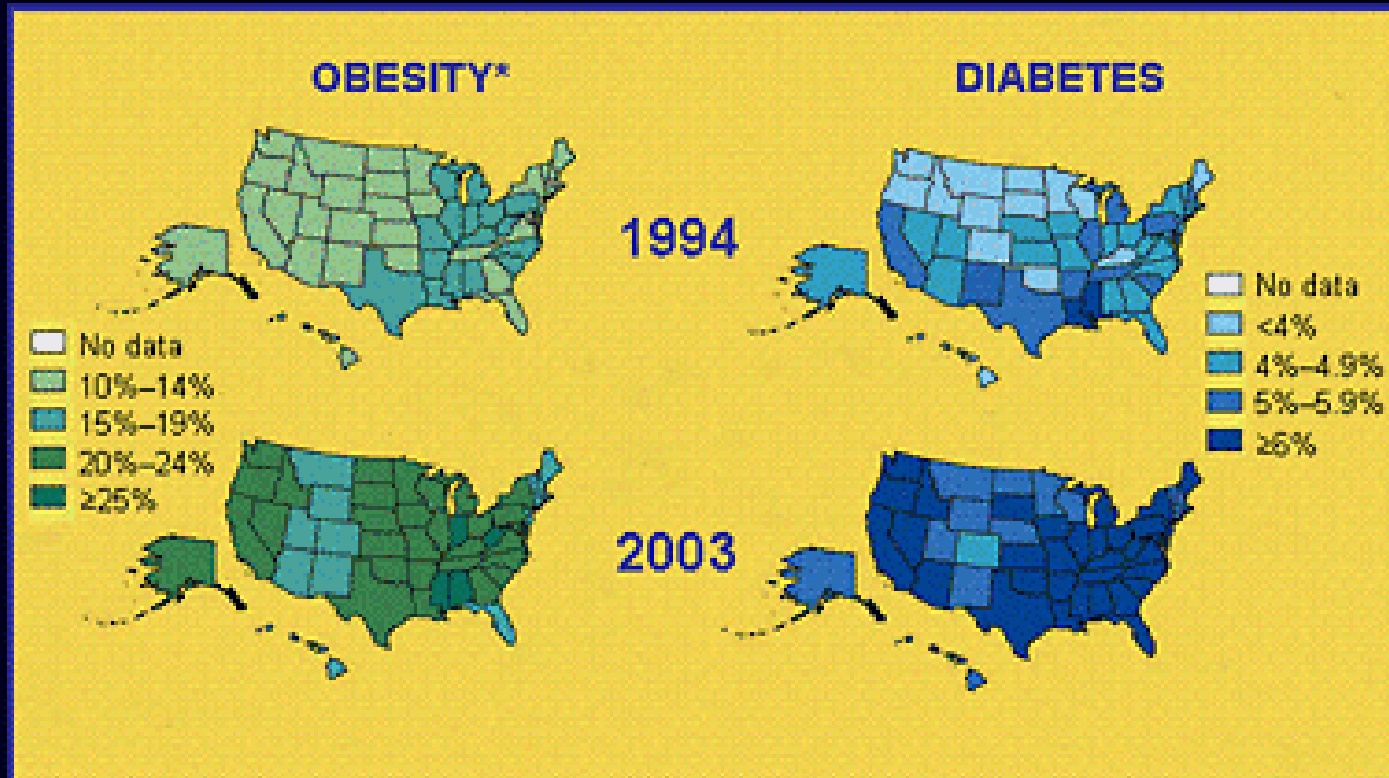




**Figure 9** GFR versus age. Estimated GFR percentiles for the US population using NHANES III serum creatinine, age, sex, and race data (see Part 10, Appendix 2) by age compared to a regression of inulin clearance measurement of GFR on age among 70 healthy male participants. (Data abstracted from Davies and Shock [72])

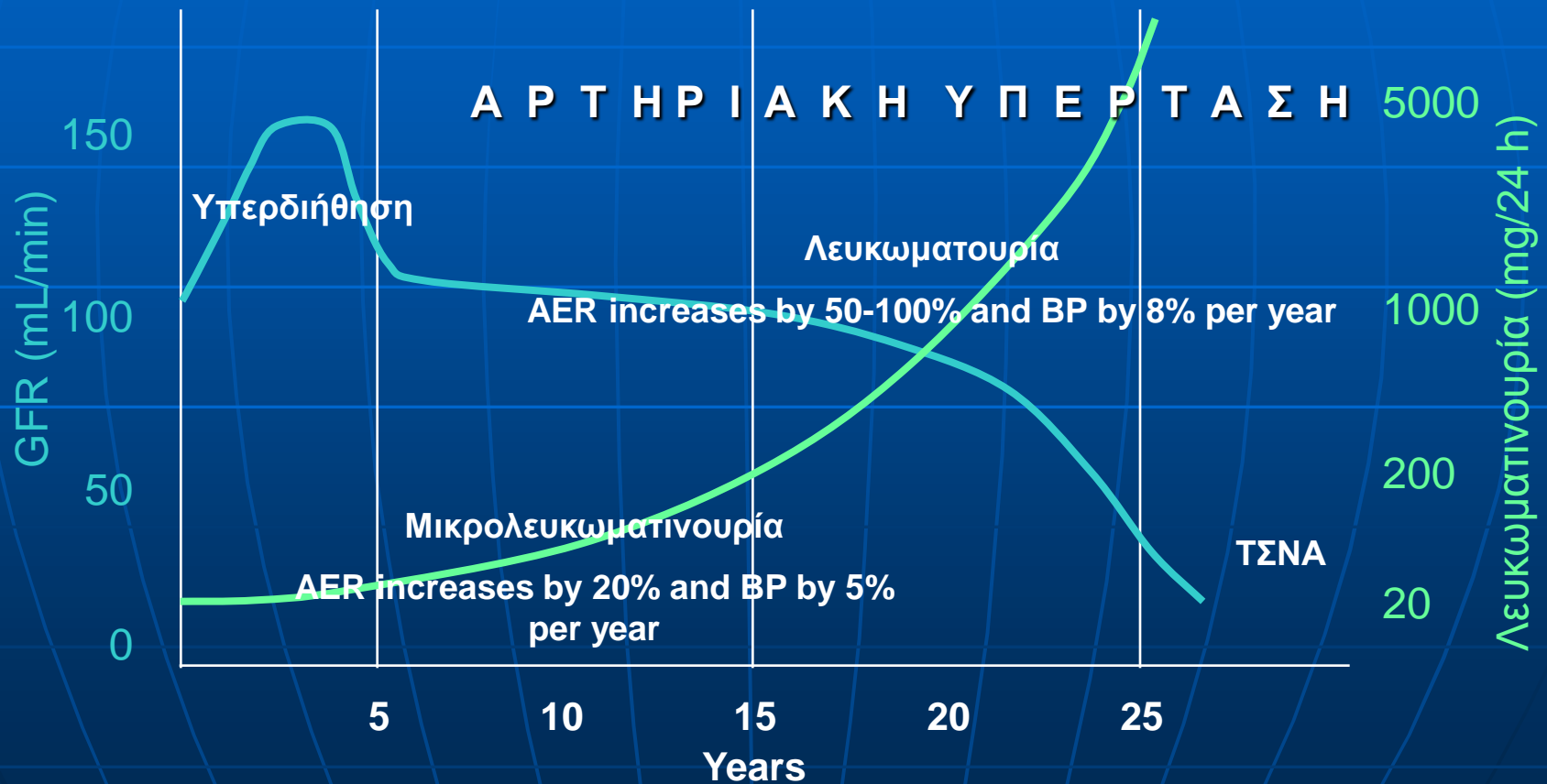
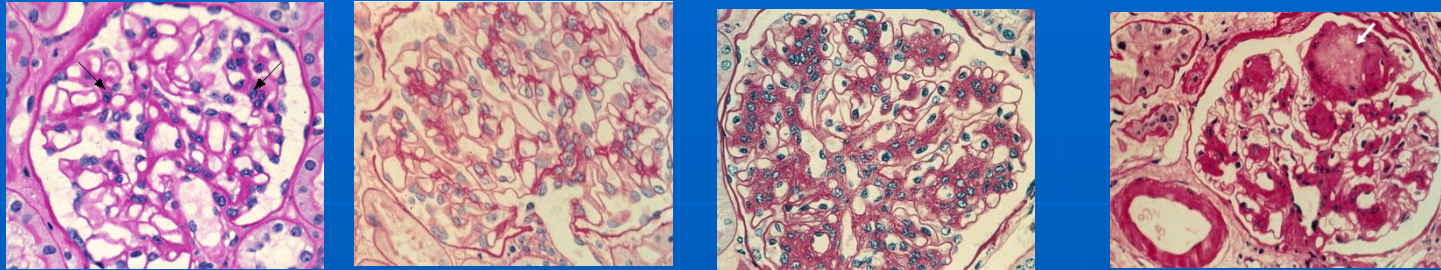


# Obesity and Diabetes Epidemics

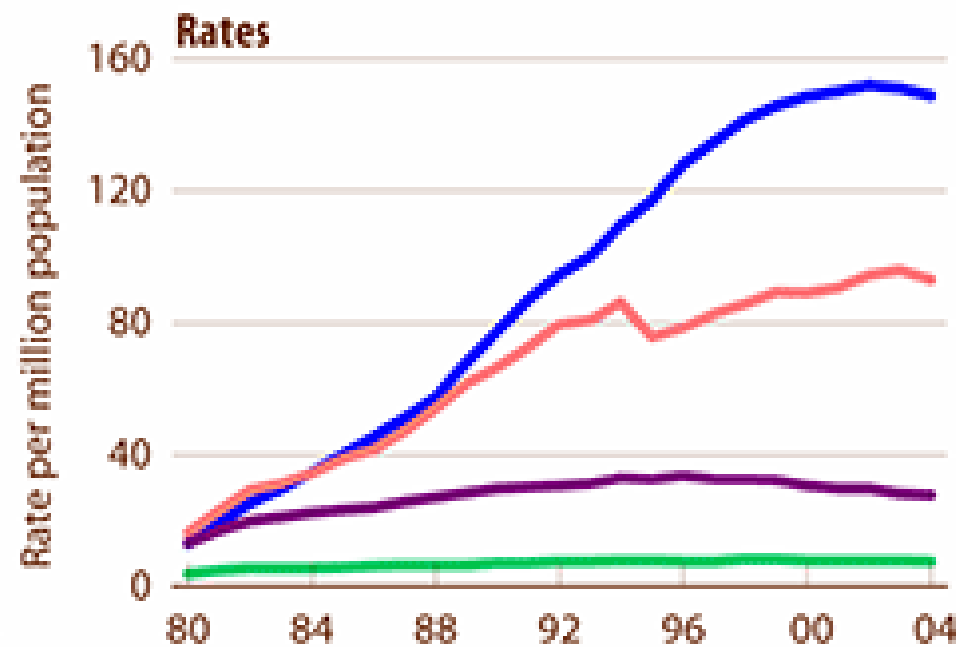
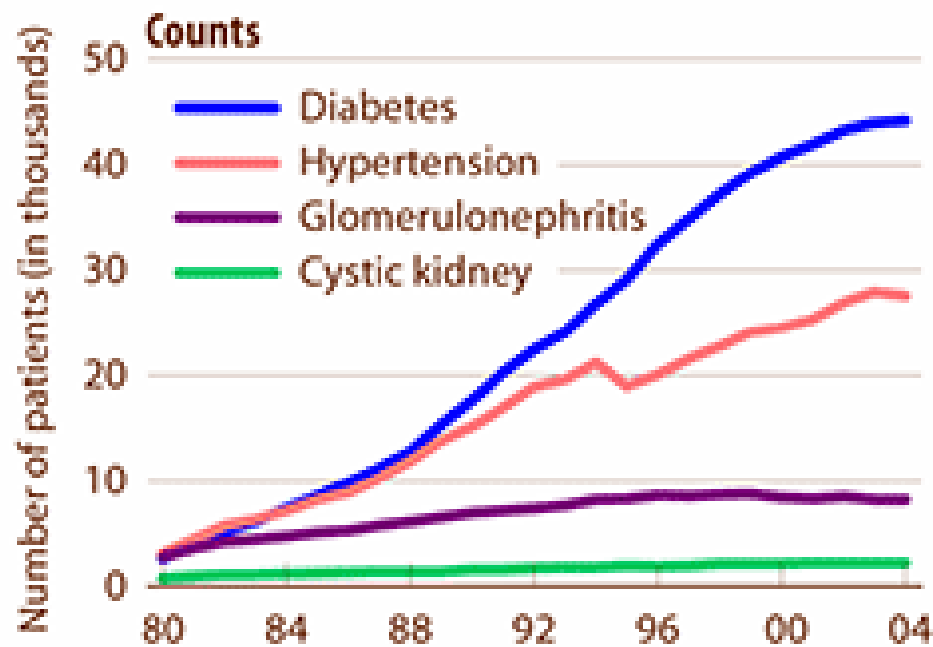


# Εξέλιξη της διαβητικής νεφροπάθειας

ΔΝ 10% σε Τύπου II και 30% σε Τύπου I

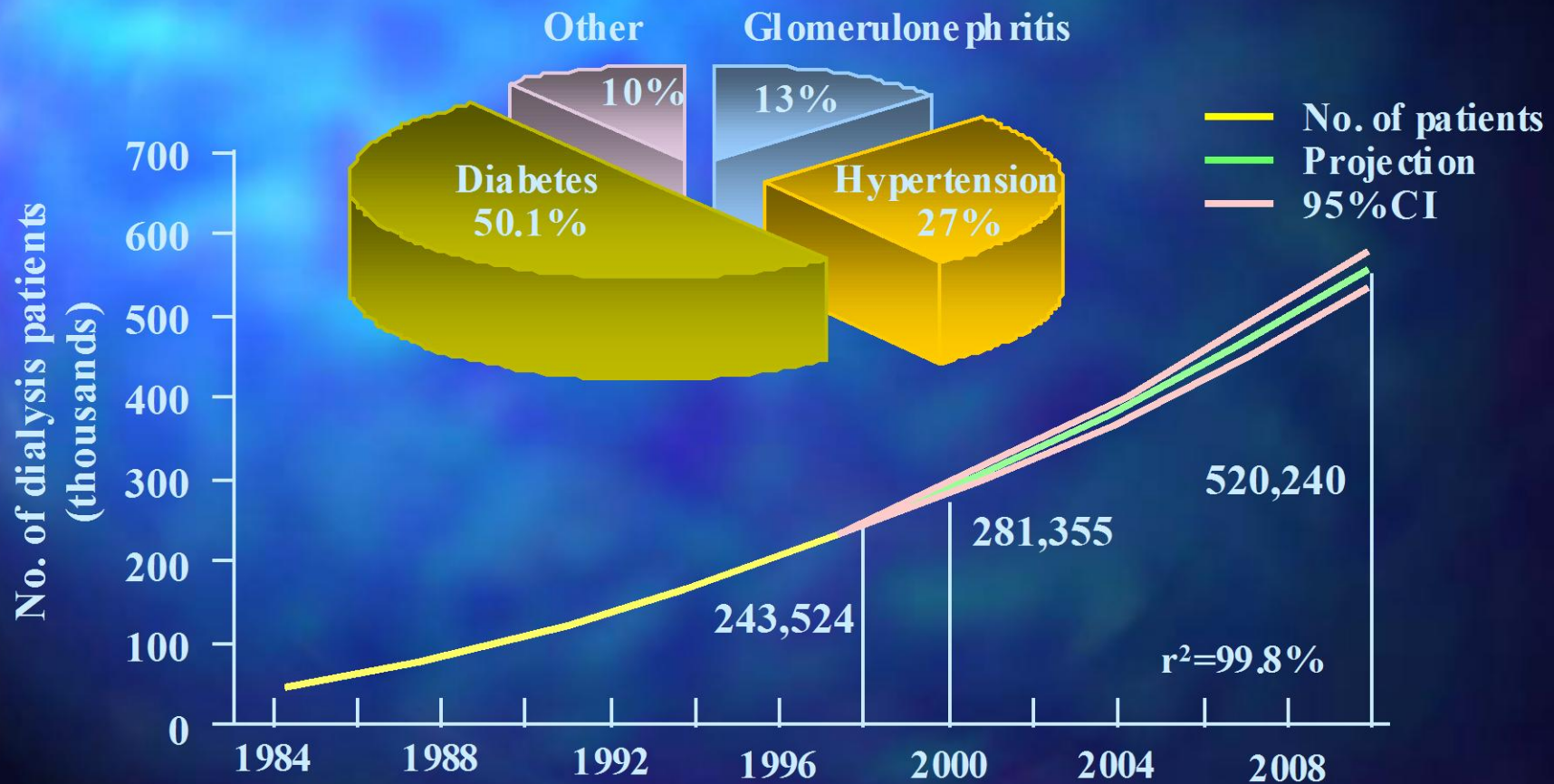


# Επιπλωλασμός της ΧΝΝ



# ΑΙΤΙΑ ΤΣΕΝΑ

Διάγνωση ασθενών που άρχισαν εξωνεφρική υποστήριξη





## Table 4

### Factors Associated with Accelerated GFR Decline

#### **Nonmodifiable**

Male gender, older age, etiology of kidney disease, African-American ethnicity, and decreased baseline level of kidney function

---

#### **Modifiable**

Increased levels of proteinuria, decreased serum albumin, increased blood pressure, poor glycemic control, and smoking

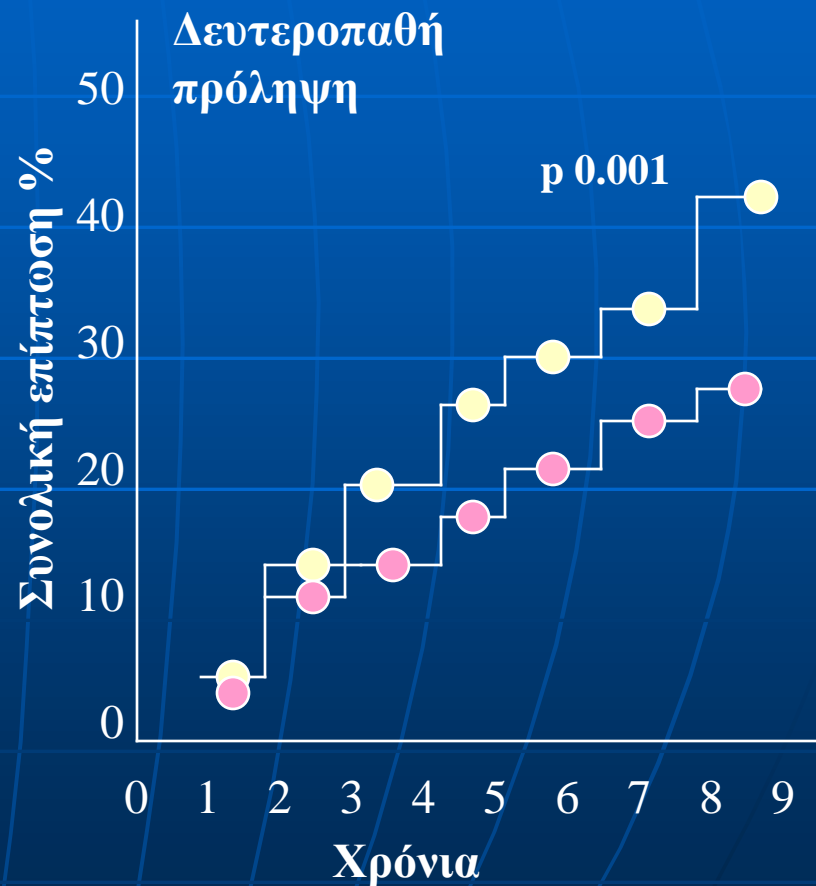
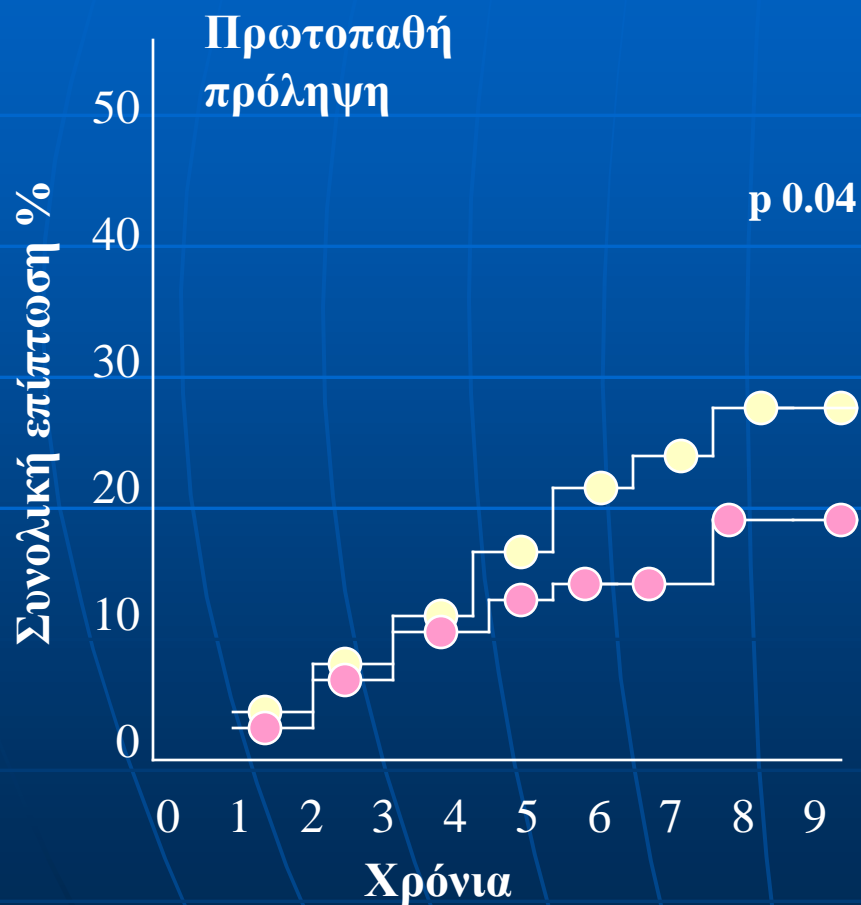
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*Source: Reference 1*

**Table 39. Types and Examples of Risk Factors for Chronic Kidney Disease**

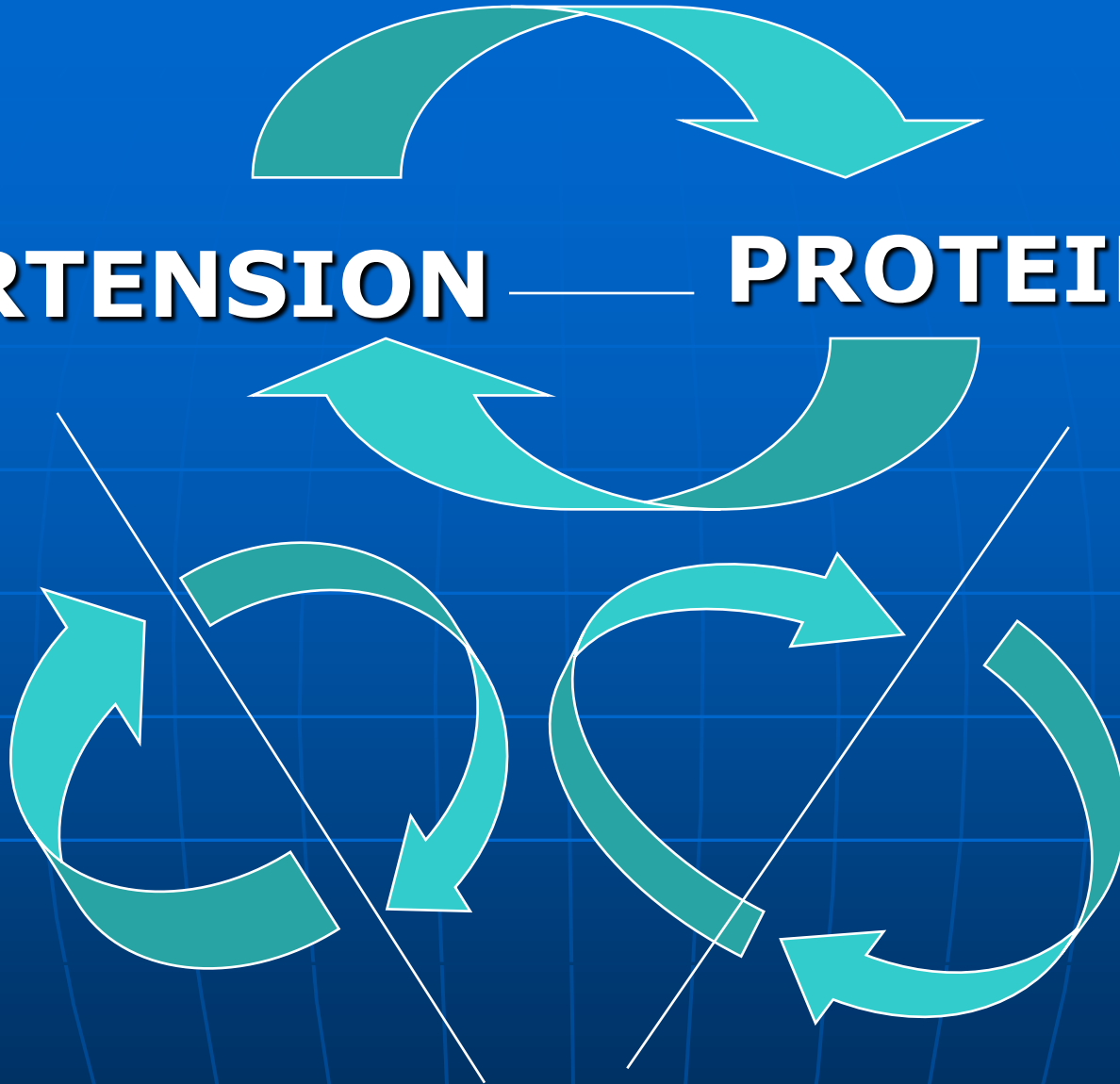
	<b>Definition</b>	<b>Examples</b>
<b>Susceptibility factors</b>	Increase susceptibility to kidney damage	Older age, family history
<b>Initiation factors</b>	Directly initiate kidney damage	Diabetes, high blood pressure, autoimmune diseases, systemic infections, urinary tract infections, urinary stones, lower urinary tract obstruction, drug toxicity
<b>Progression factors</b>	Cause worsening kidney damage and faster decline in kidney function after initiation of kidney damage	Higher level of proteinuria, higher blood pressure level, poor glycemic control in diabetes, smoking

# Διαβητική Νεφροπάθεια και ΣΔ Τύπου 1



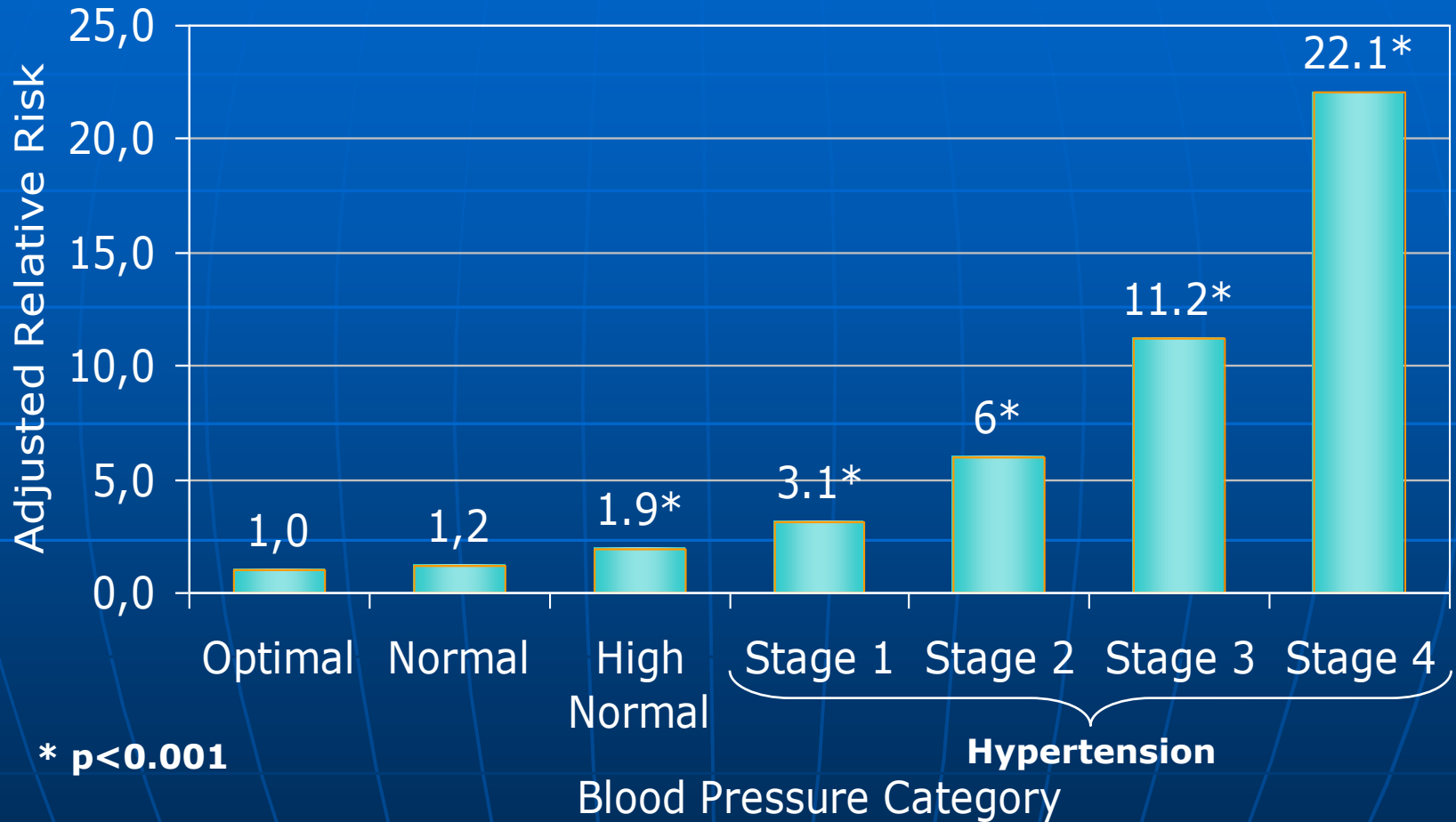
- Εντατικοποιημένη
- Συμβατική

**HYPERTENSION — PROTEINURIA**



**CKD**

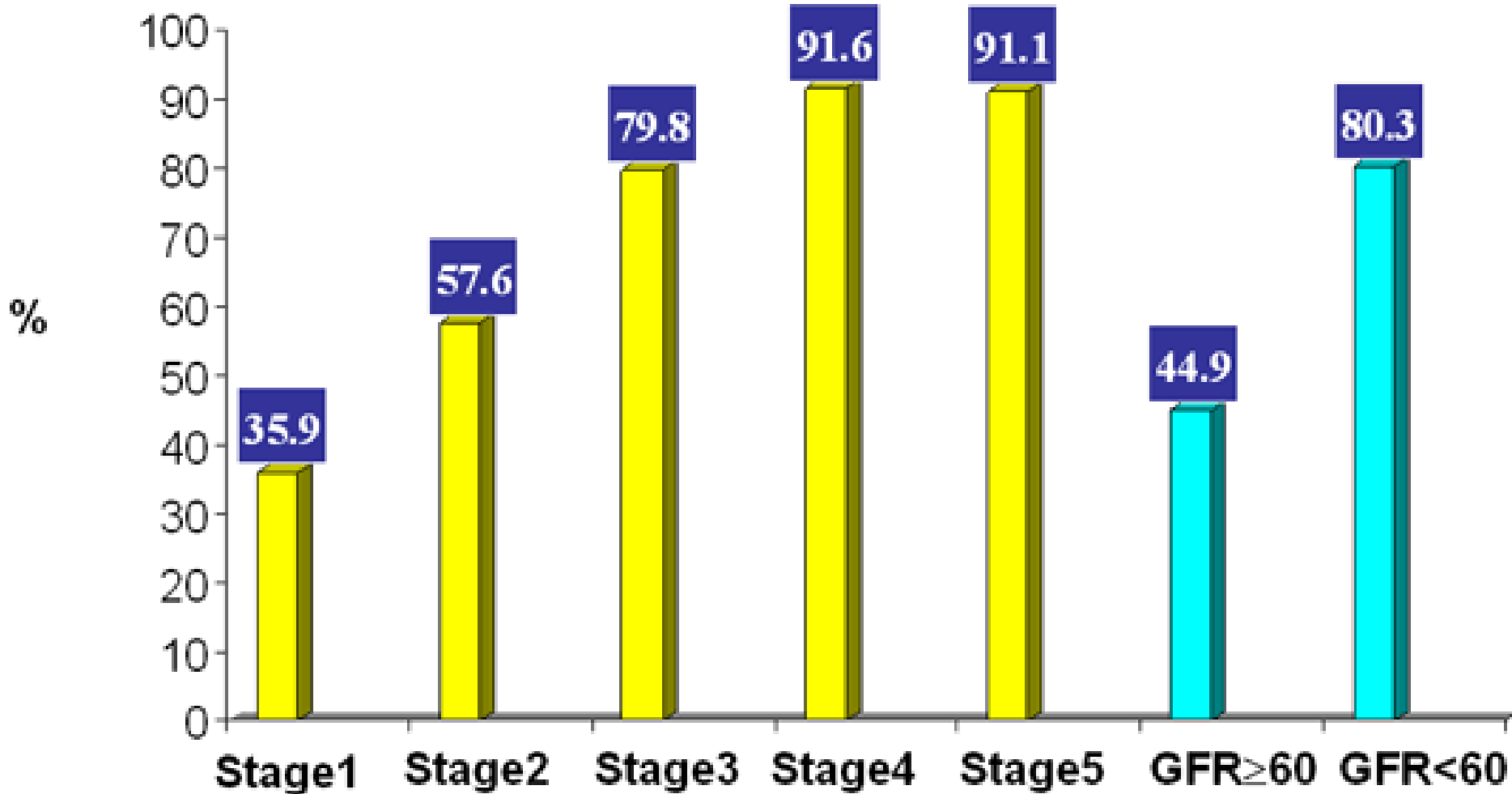
# ESRD Due to Any Cause In 332,544 Men Screened for MRFIT Adjusted Relative Risk<sup>§</sup>



§ Men with optimal blood pressure was the reference category.

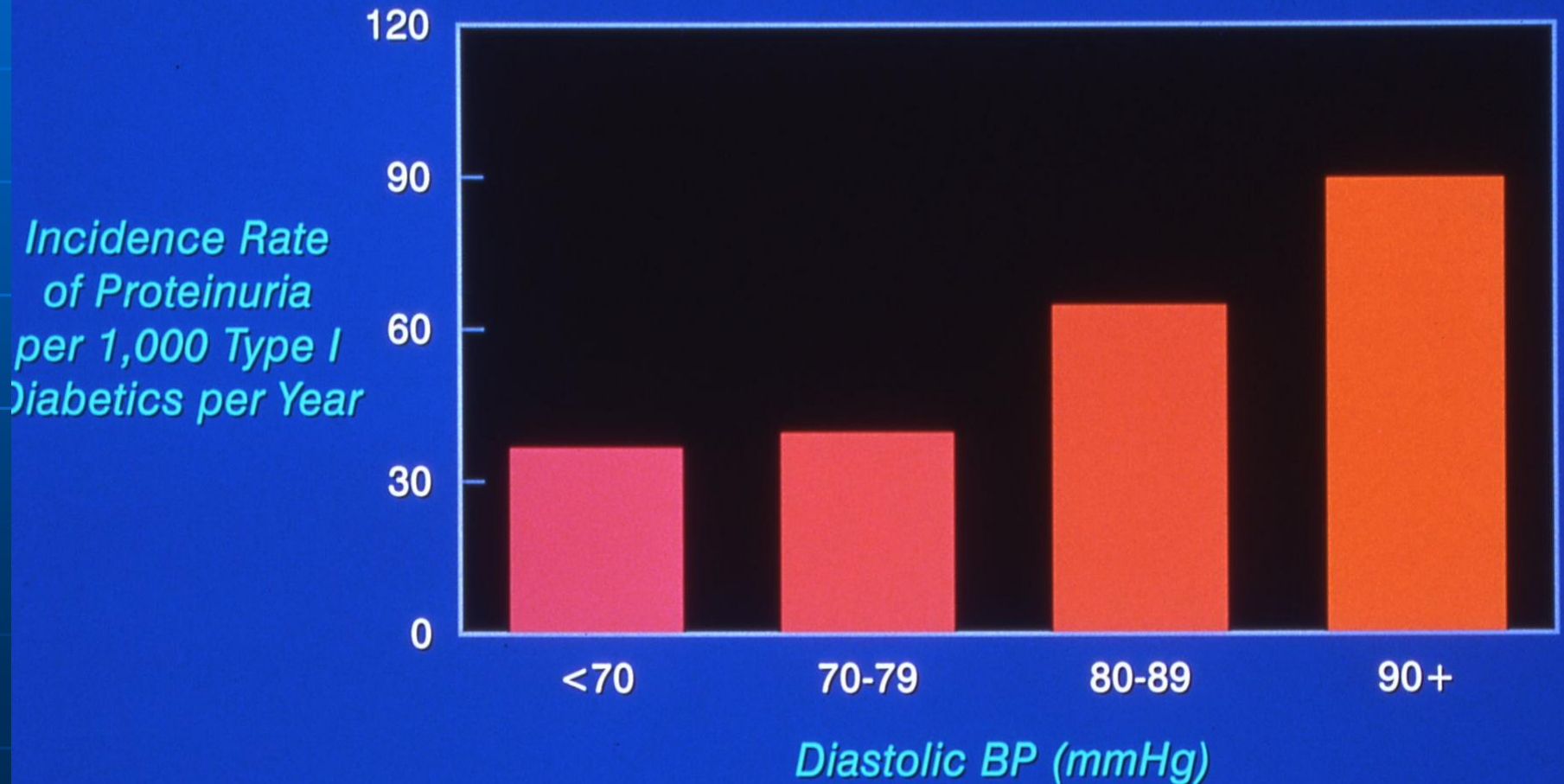
Klag MJ, et al. NEJM 1996;334:13-18.

# Hypertension and CKD



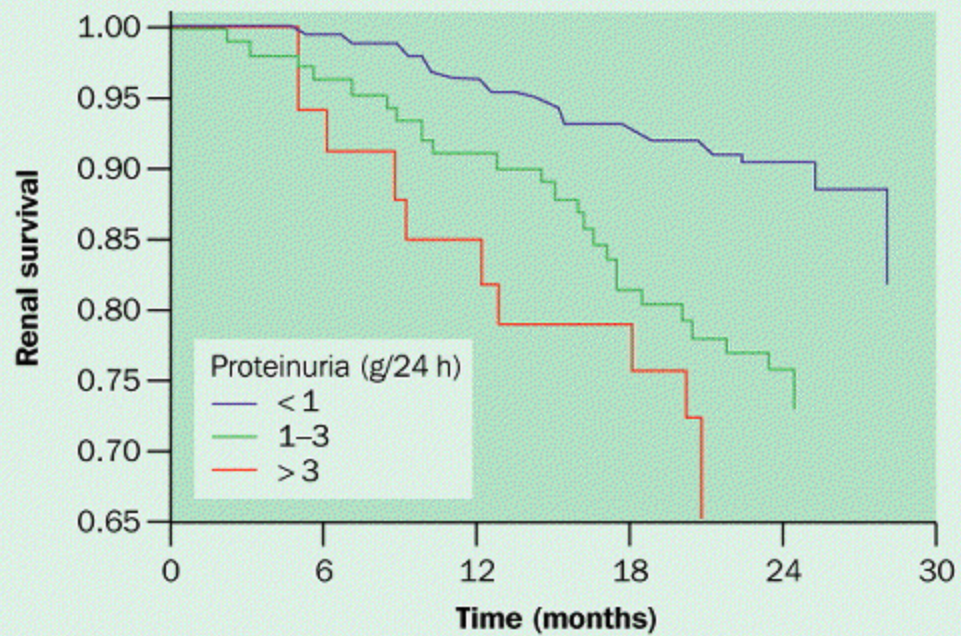


# Relationship between hypertension and diabetic nephropathy

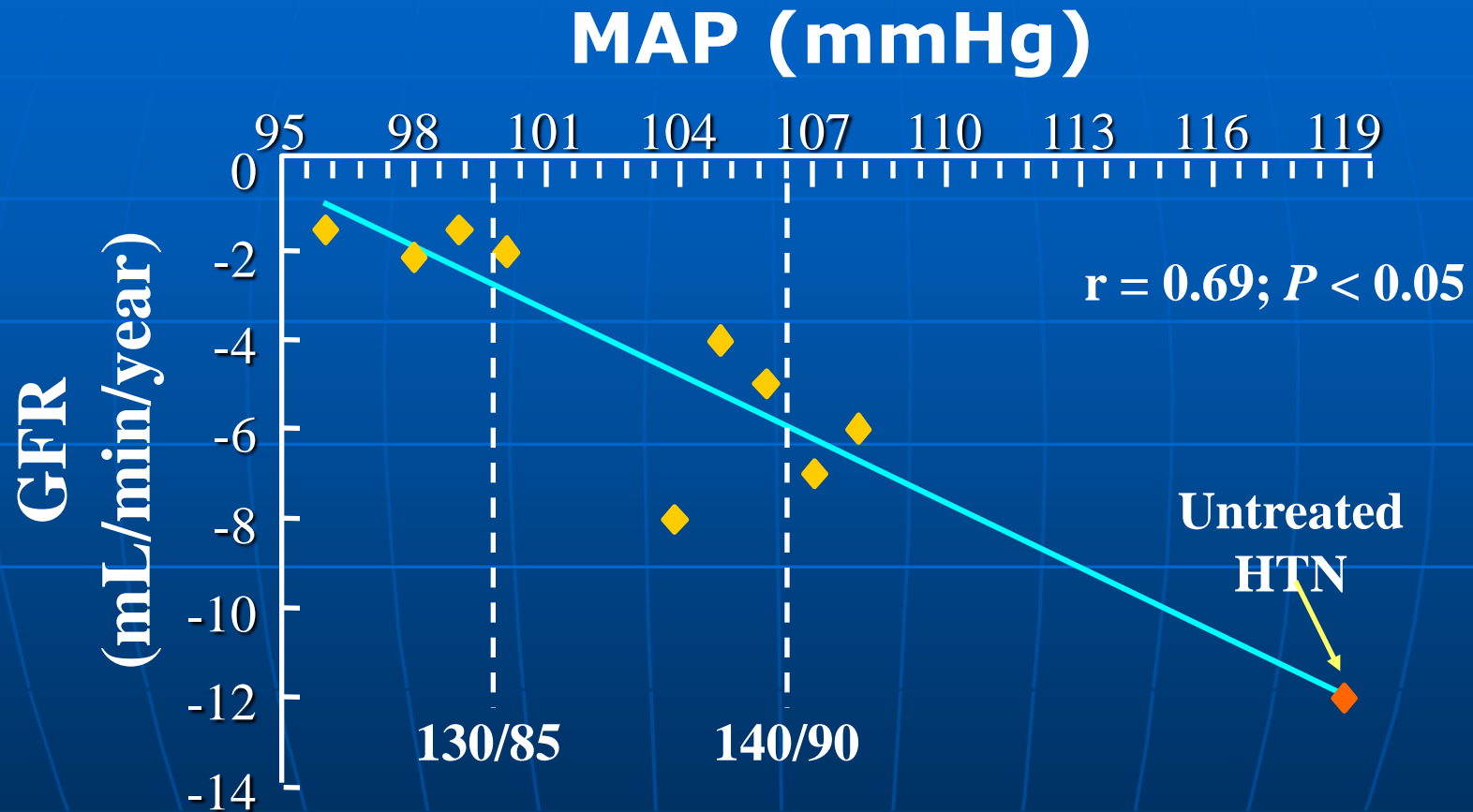




## Renal survival and level of proteinuria



# Meta Analysis: Lower Mean BP Results in Slower Rates of Decline in GFR in Diabetics and Non-Diabetics

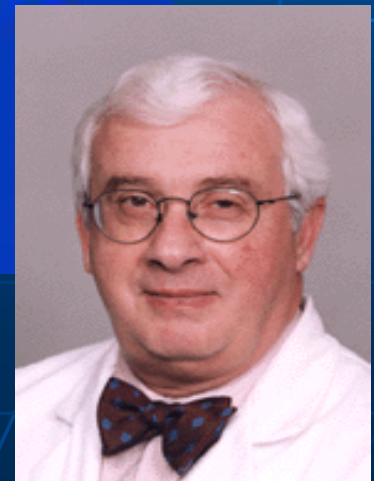


Bakris GL, et al. Am J Kidney Dis. 2000;36(3):646-661.

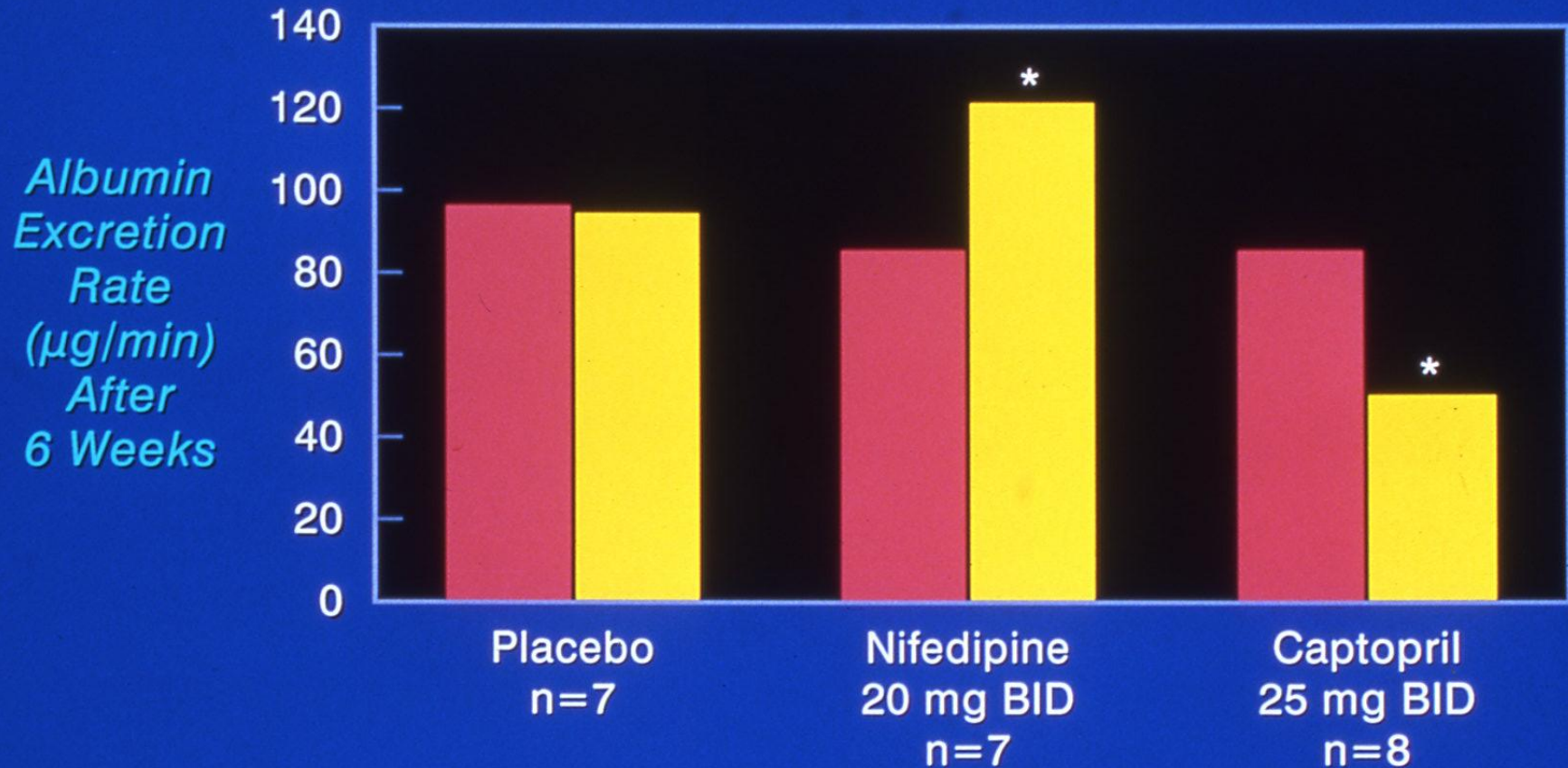
# Treatment of Patients with Kidney Disease

	<b>BP treatment goal</b>	<b># drugs required</b>
<b>&lt; 1 gm Proteinuria</b>	<b>&lt;130/80</b>	<b>~2-3</b>
<b>&gt;1gm Proteinuria</b>	<b>&lt;125/75</b>	<b>~3-4</b>

# Ενδοσπειραματική «υπέρταση»



# Effects of nifedipine and captopril in normotensive type I diabetic patients with incipient nephropathy

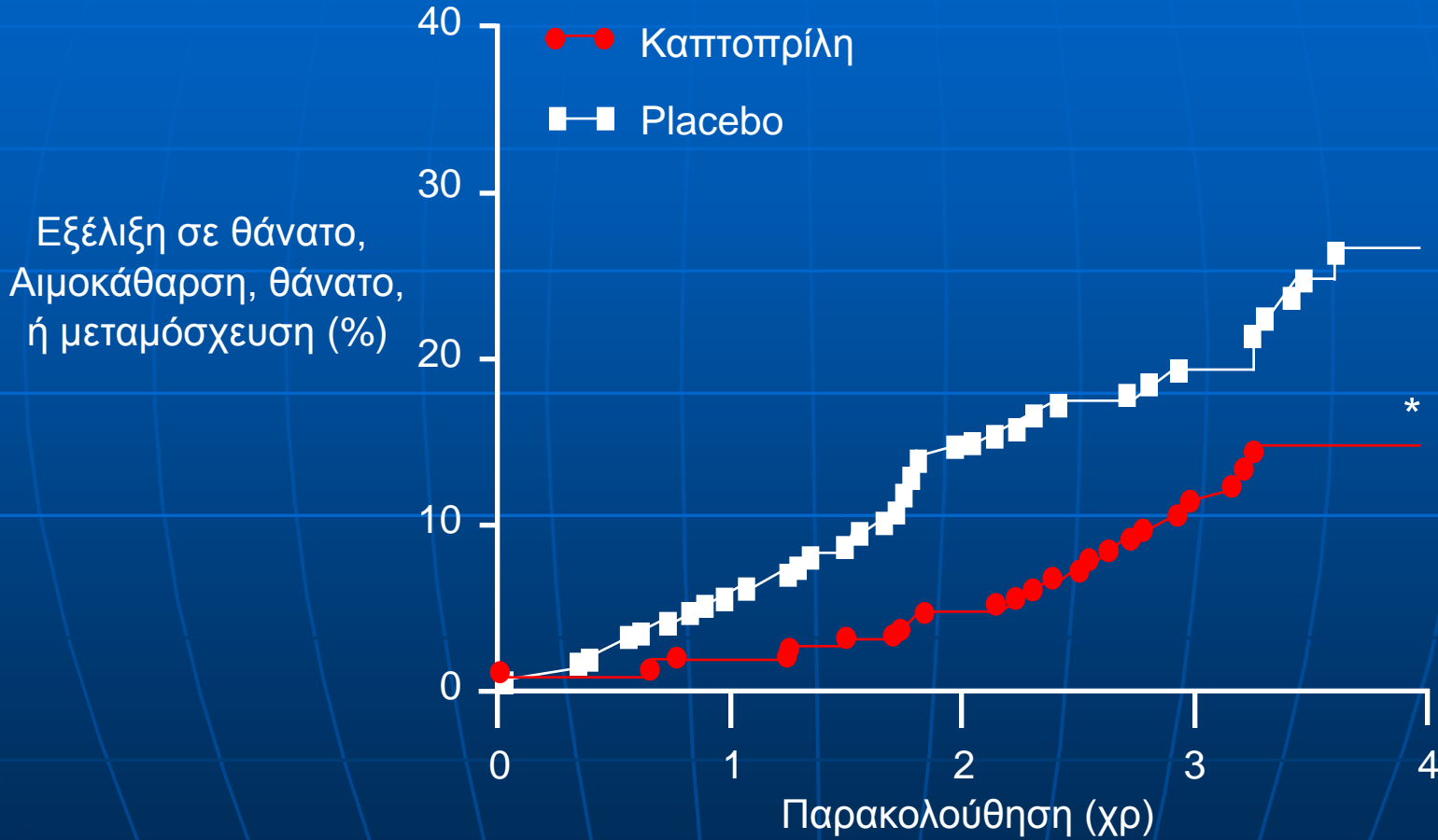


\*  $p < .05$ , baseline vs. treatment

Mimran A et al., *J Hypertens* 1988;6:919-23.

■ Baseline    ■ Treatment

# ΑΜΕΑ και Διαβητική Νεφροπάθεια στον ΣΔΤ1



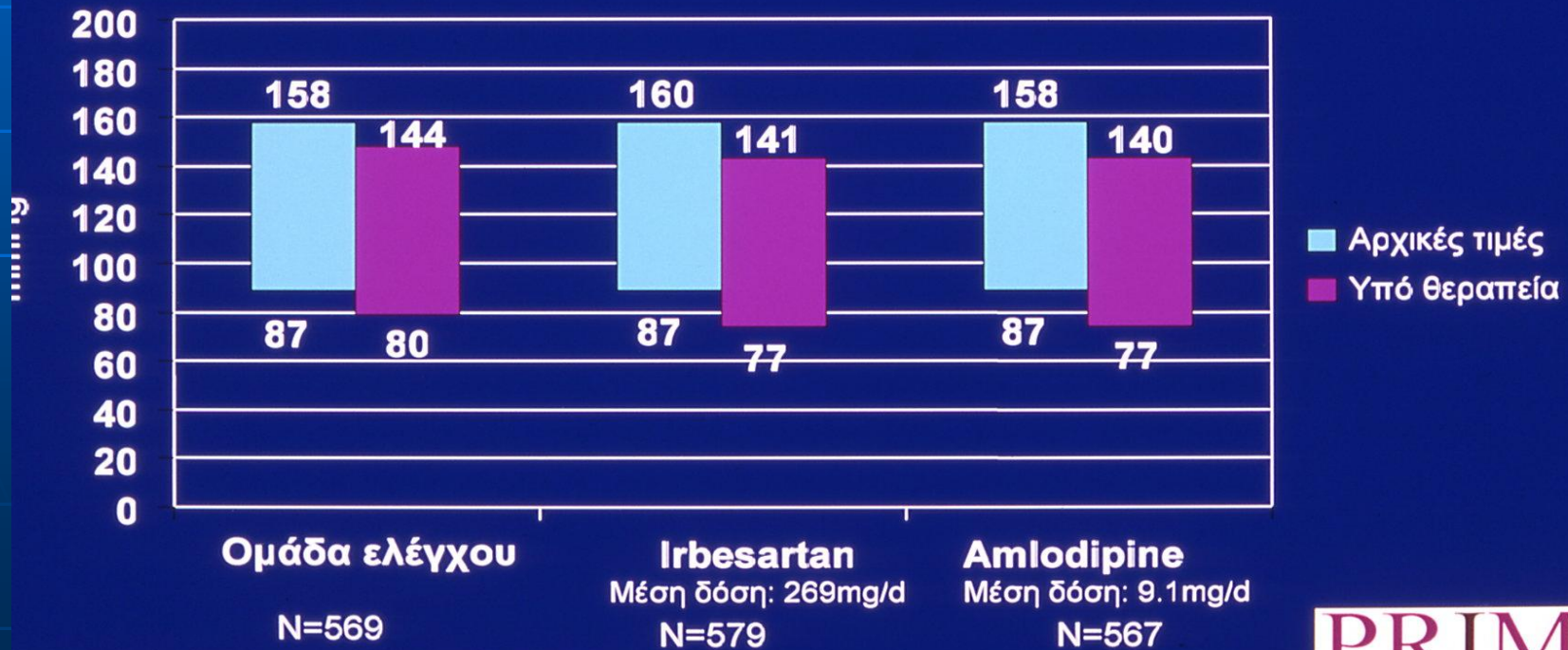
Collaborative Study Group  
\*  $p = 0.006$  vs placebo.

Lewis EJ et al. *N Engl J Med* 1993;329:1456-1462.

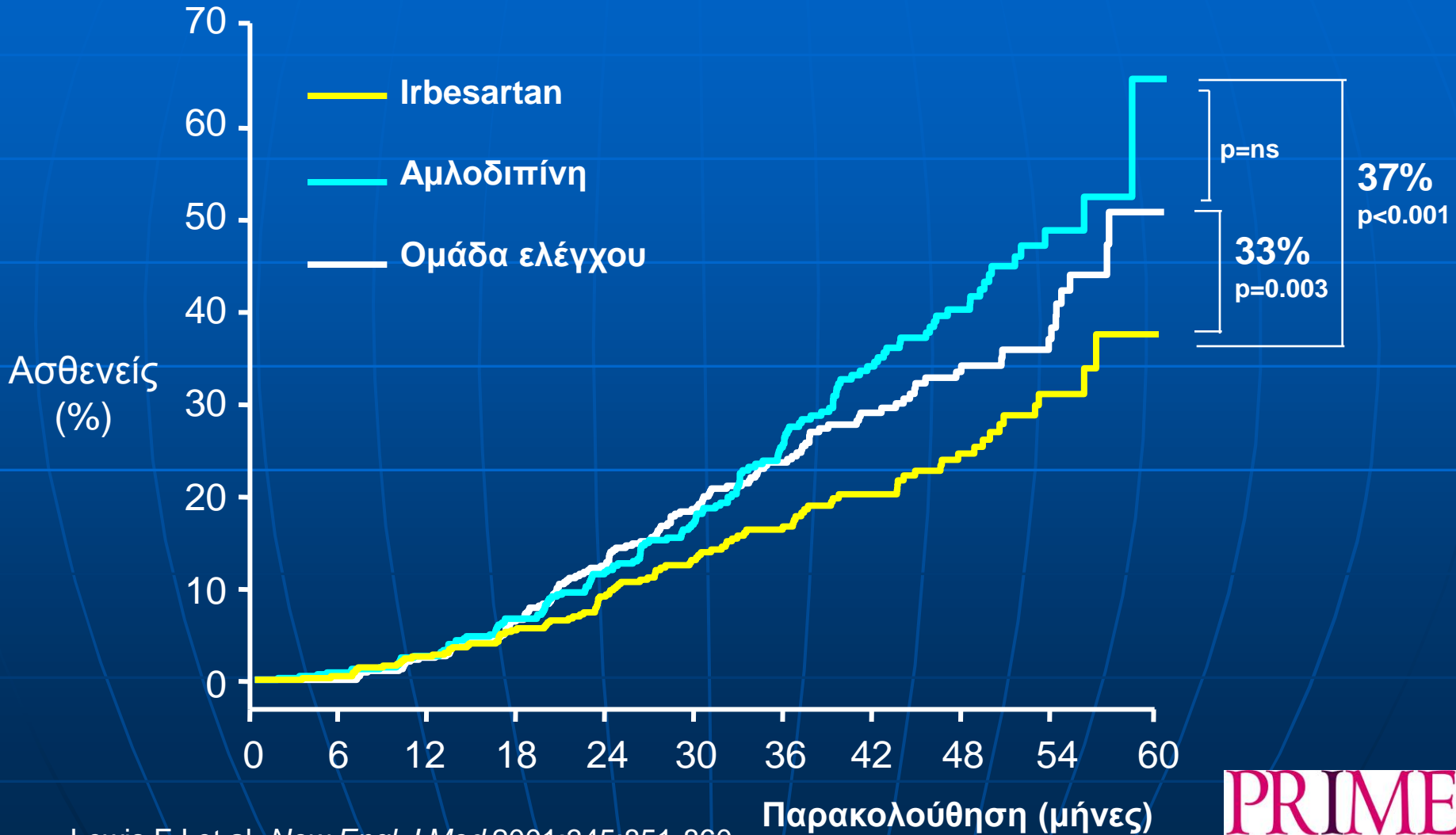
# Irbesartan vs Amlodipine in AODM

## IDNT: Επίδραση στην αρτηριακή πίεση

Παρόμοια μείωση της ΑΠ



# IDNT – time to duplication of serum creatinine

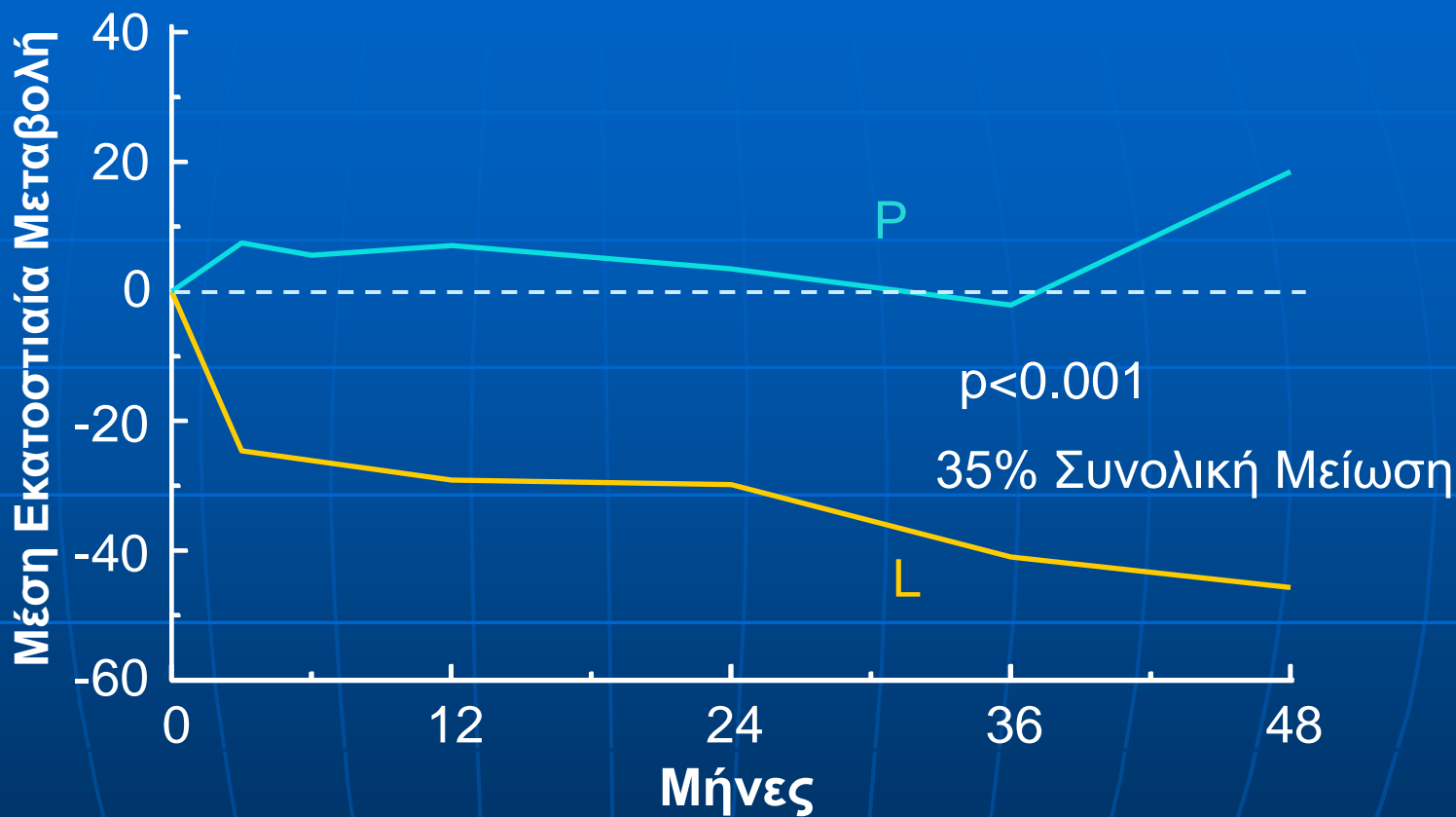


Lewis EJ et al. *New Engl J Med* 2001;345:851-860.



# RENAAL

## Μεταβολή της Πρωτεϊνουρίας από τις Αρχικές Τιμές

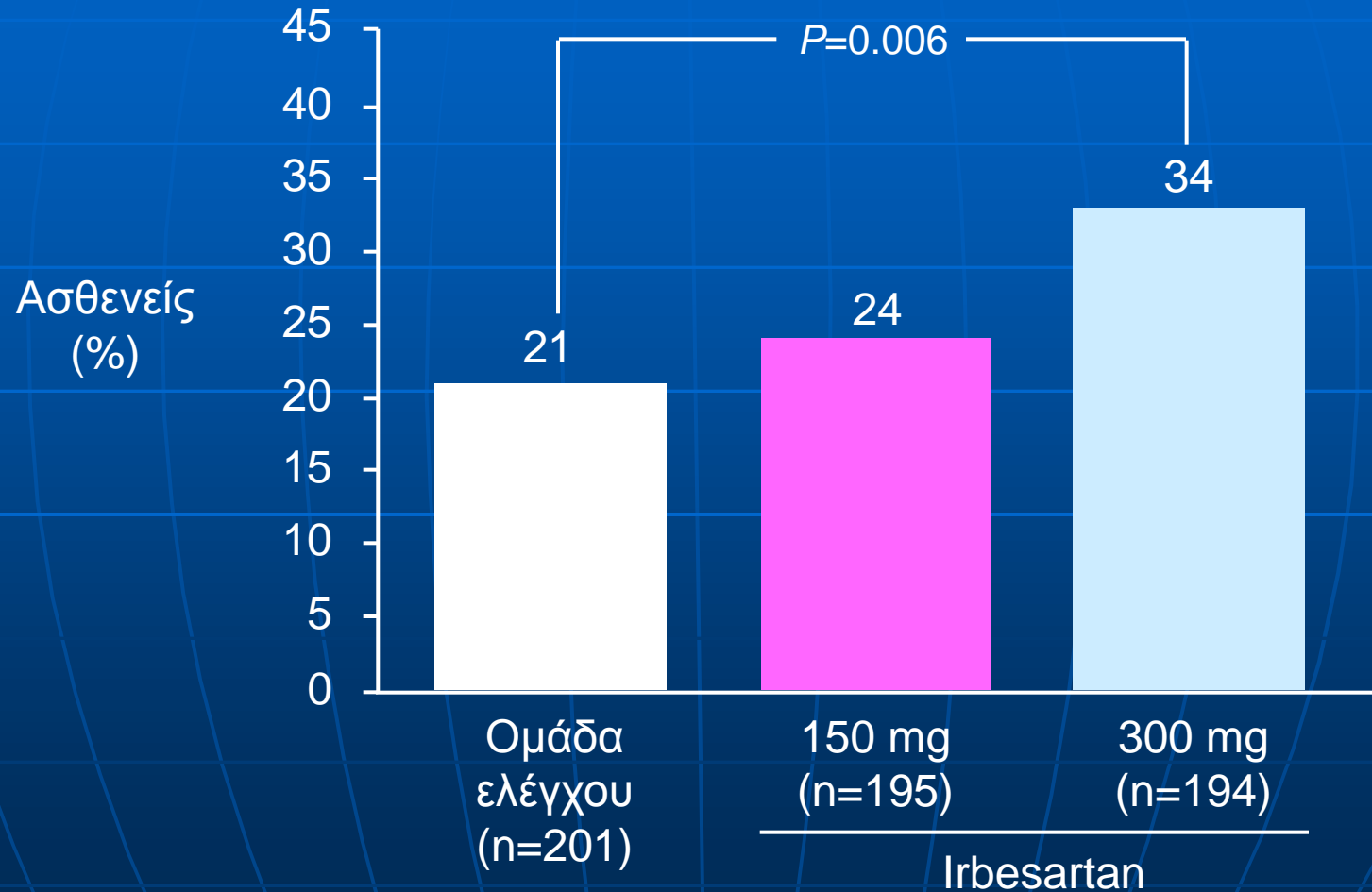


— P (+CT)	762	632	529	390	130
— L (+CT)	751	661	558	438	167

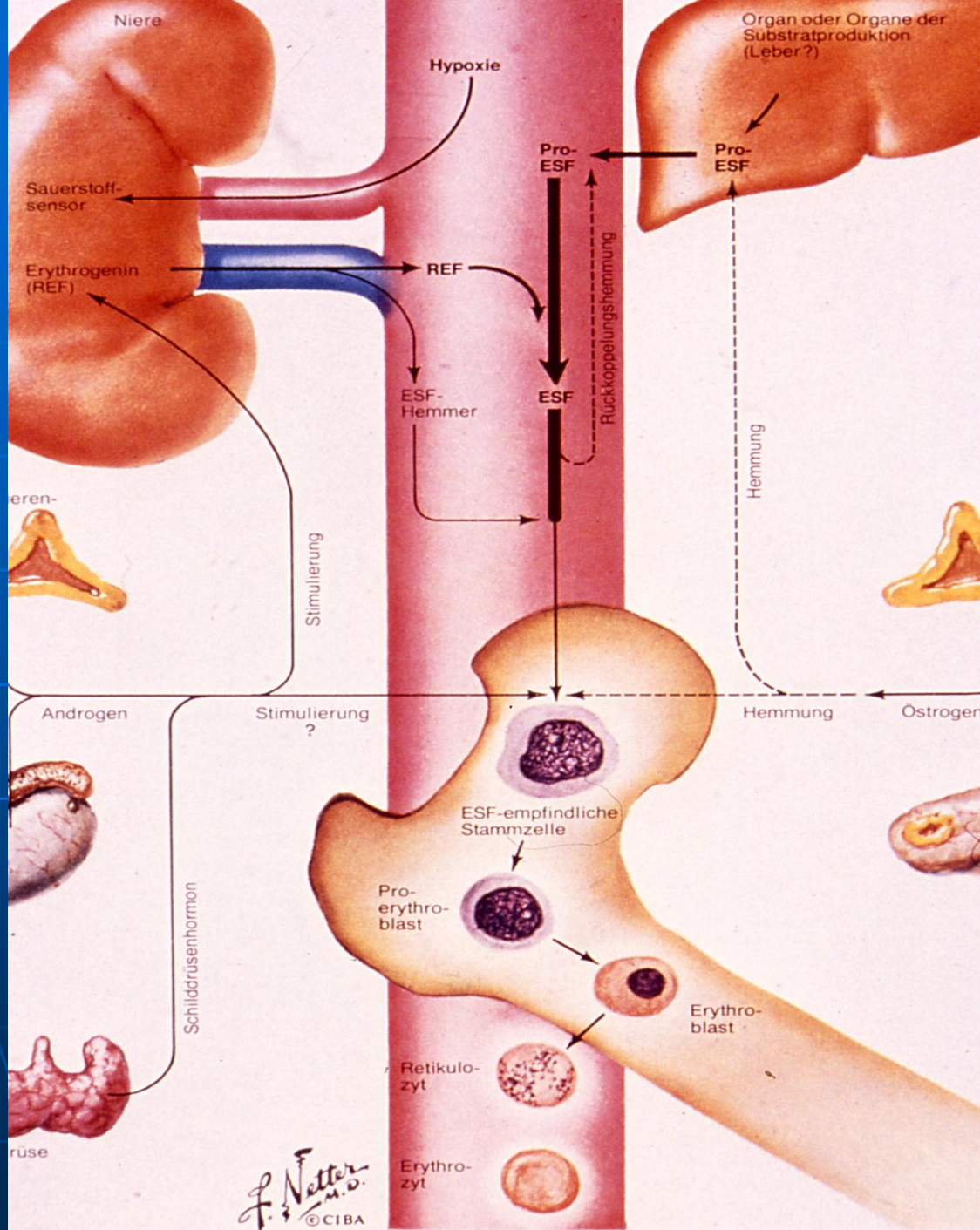
πρωτεϊνουρία μετρήθηκε με βάση την αναλογία λευκώματος ούρων/κρεατινίνης στα πρώτα πρωινά ούρα

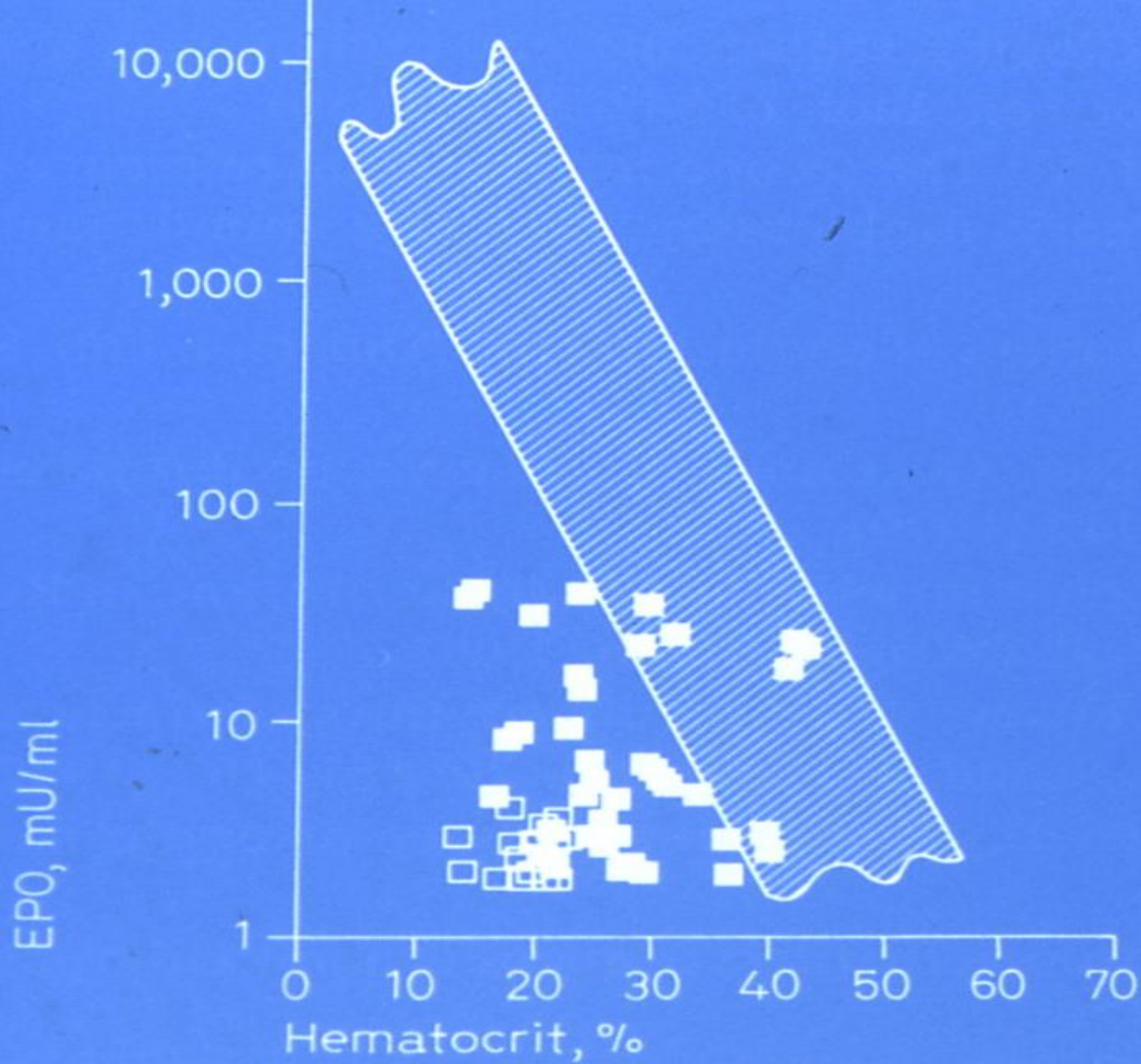
# IRMA 2: Αποτελέσματα

## Ομαλοποίηση της ταχύτητας απέκκρισης λευκωματίνης στα ούρα (UAE Rate)



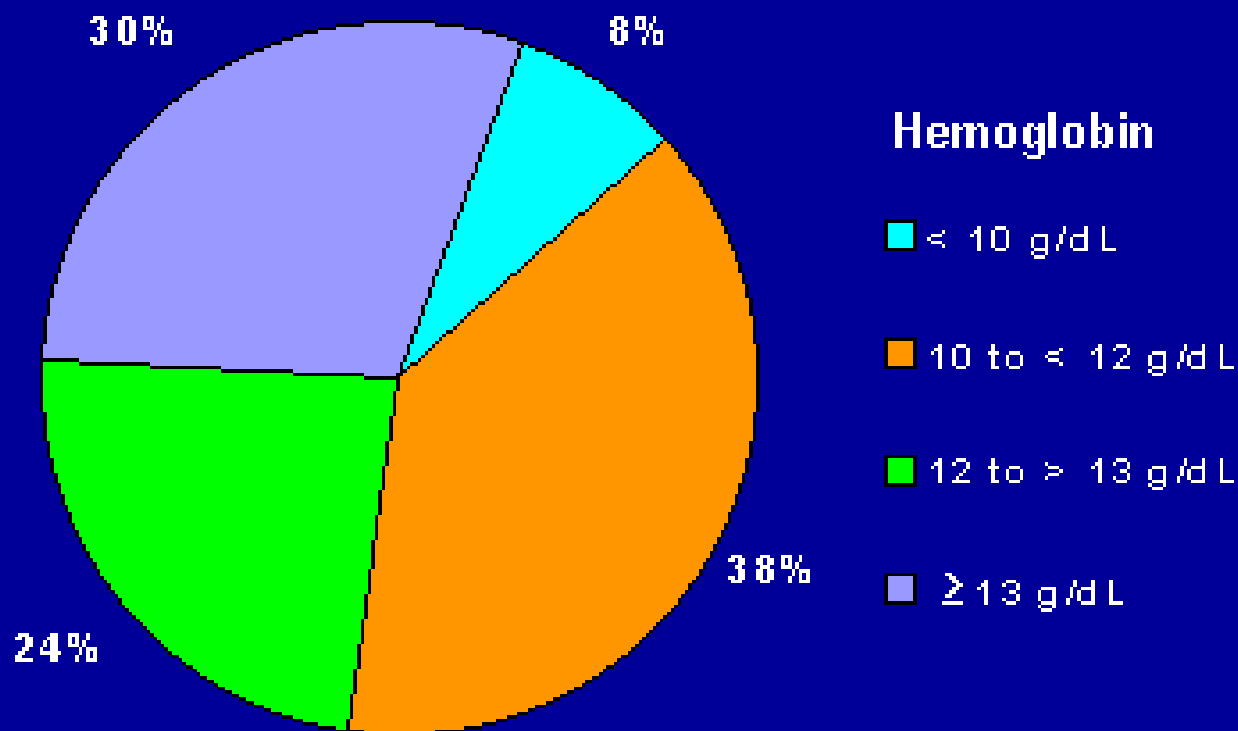
# ■ XNA KAI ANAIMIA

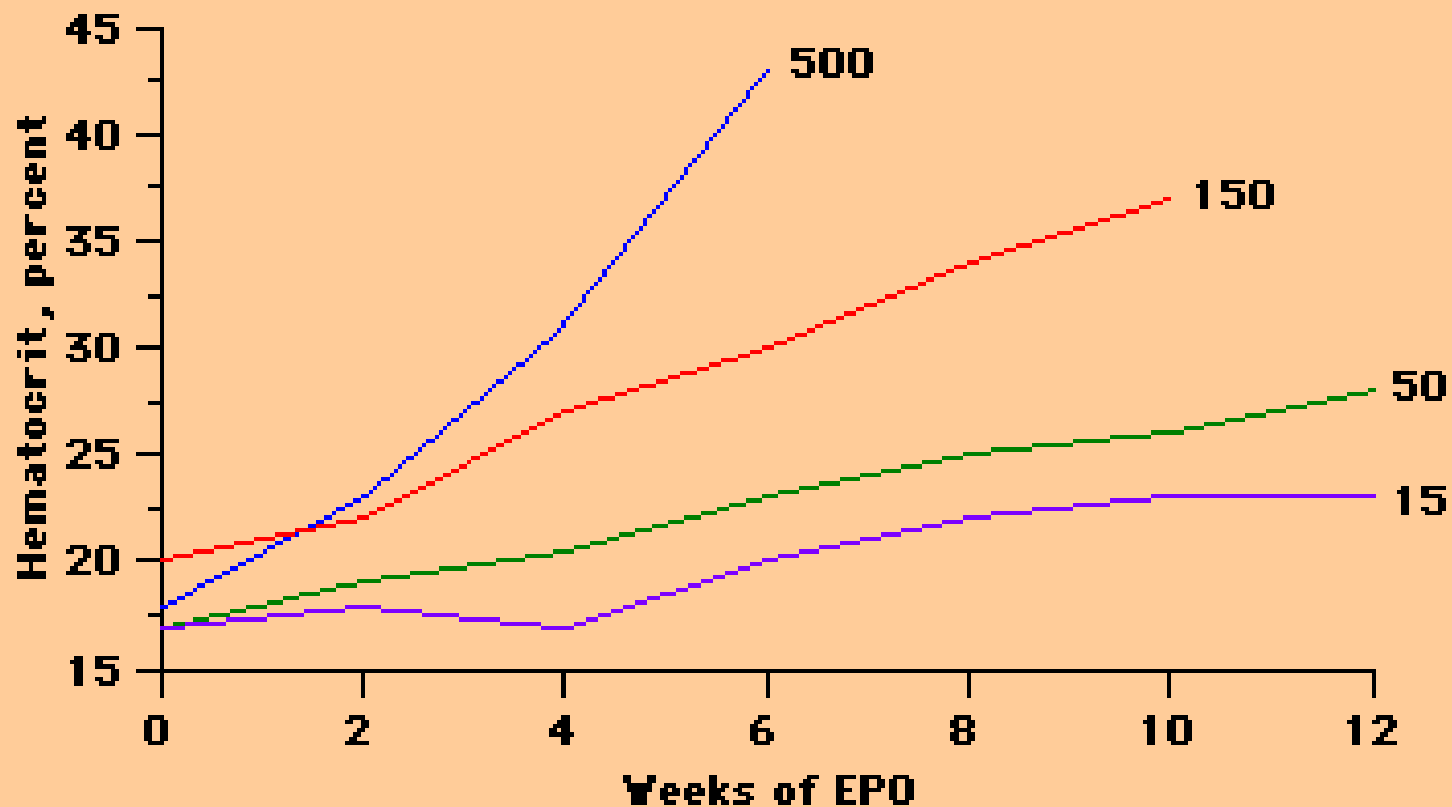




*Fig. 6.* EPO titers in patients with anemia secondary

# Prevalence of Anemia Among Patients With CKD: Preliminary PAERI Study Results



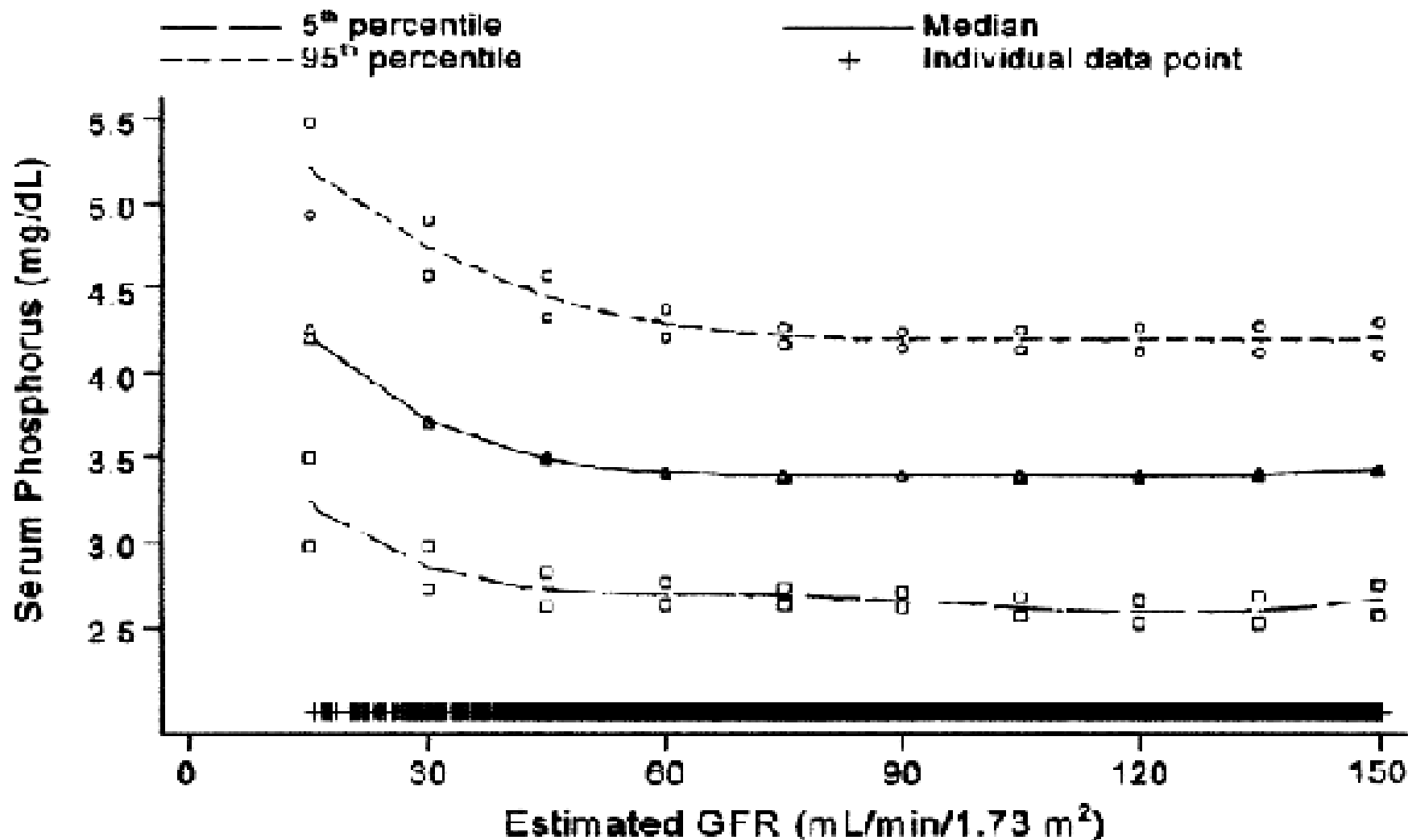


### **Dose response of EPO-induced correction of uremic anemia**

Slope of the rate of increase in the hematocrit in patients on maintenance dialysis given various doses (15 to 500 units/kg) of erythropoietin (EPO) three times per week. The response is fastest at the highest dose, but a gradual and adequate rise in hematocrit is achieved in most patients with 50 units/kg. (Data from Eschbach, JW, Egorie, JC, Downing, MR, et al. *N Engl J Med* 1987; 316:73.)

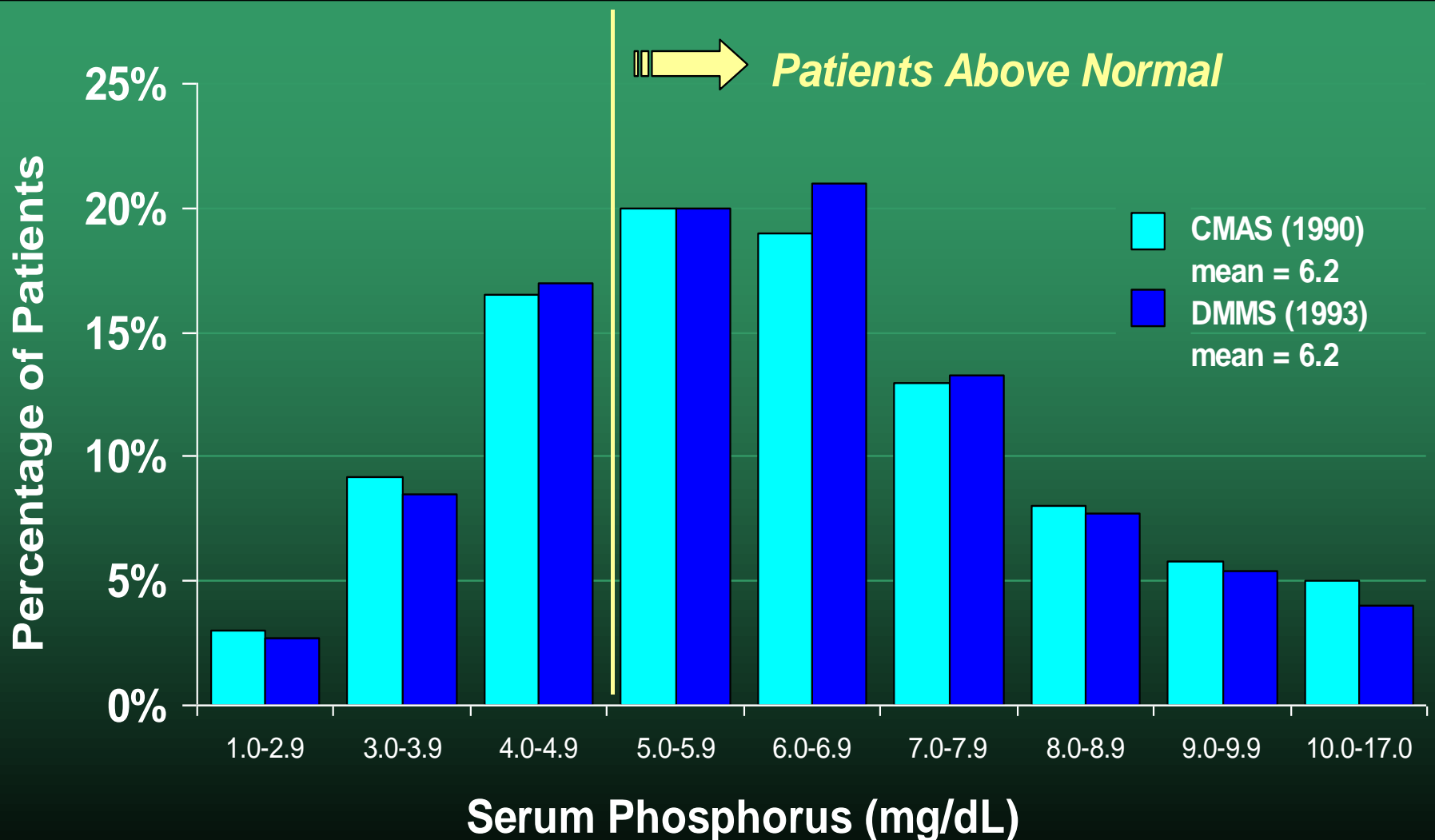
ΧΝΑ  
ΚΑΙ  
ΟΣΤΙΚΟΣ  
ΜΕΤΑΒΟΛΙΣΜΟΣ



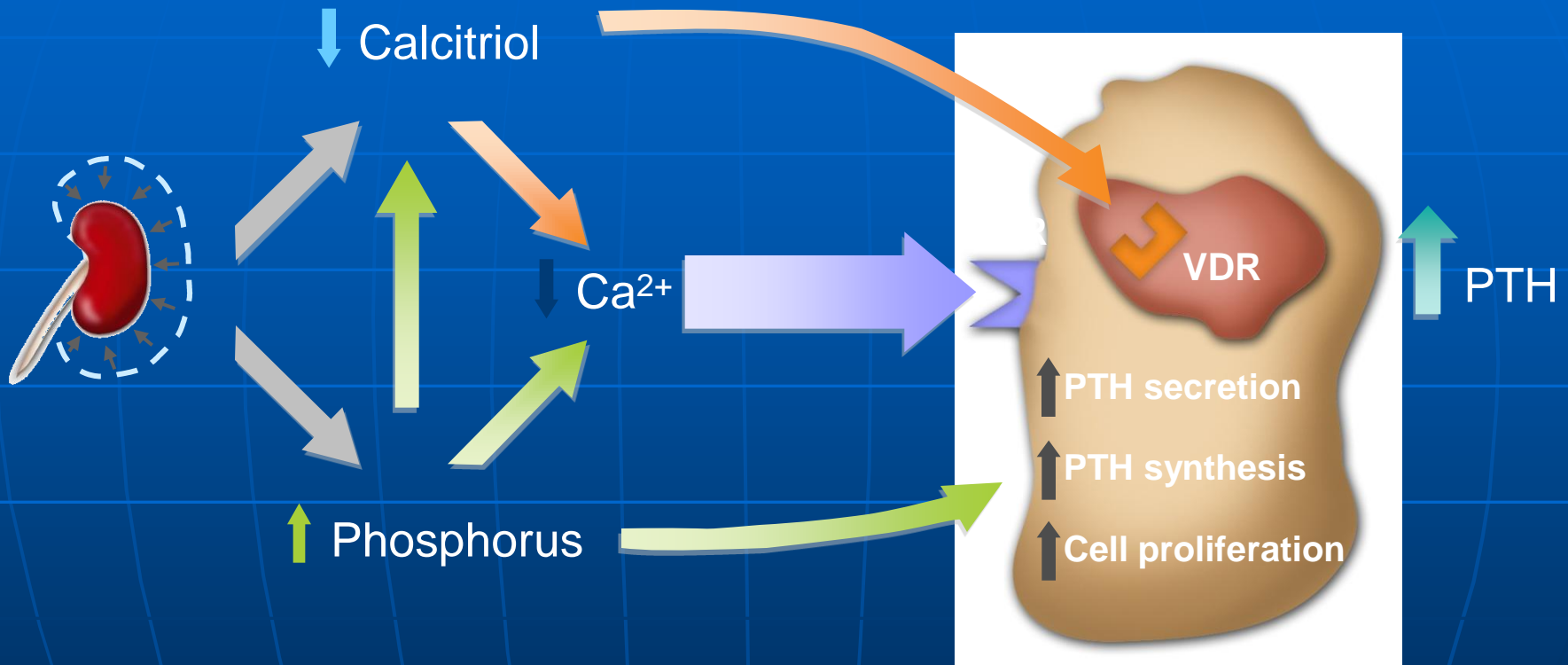


**Figure 41** Serum phosphorus levels versus GFR (NHANES III). Median and 5th and 95th percentiles of serum phosphorus among adult participants age 20 years and older in NHANES III, 1988 to 1994. Values are adjusted to age 60 years using a polynomial quantile regression. The estimated GFR for each individual data point is shown with a plus near the abscissa. 95 percent confidence intervals at selected levels of estimated GFR are demarcated with triangles, squares, and circles.

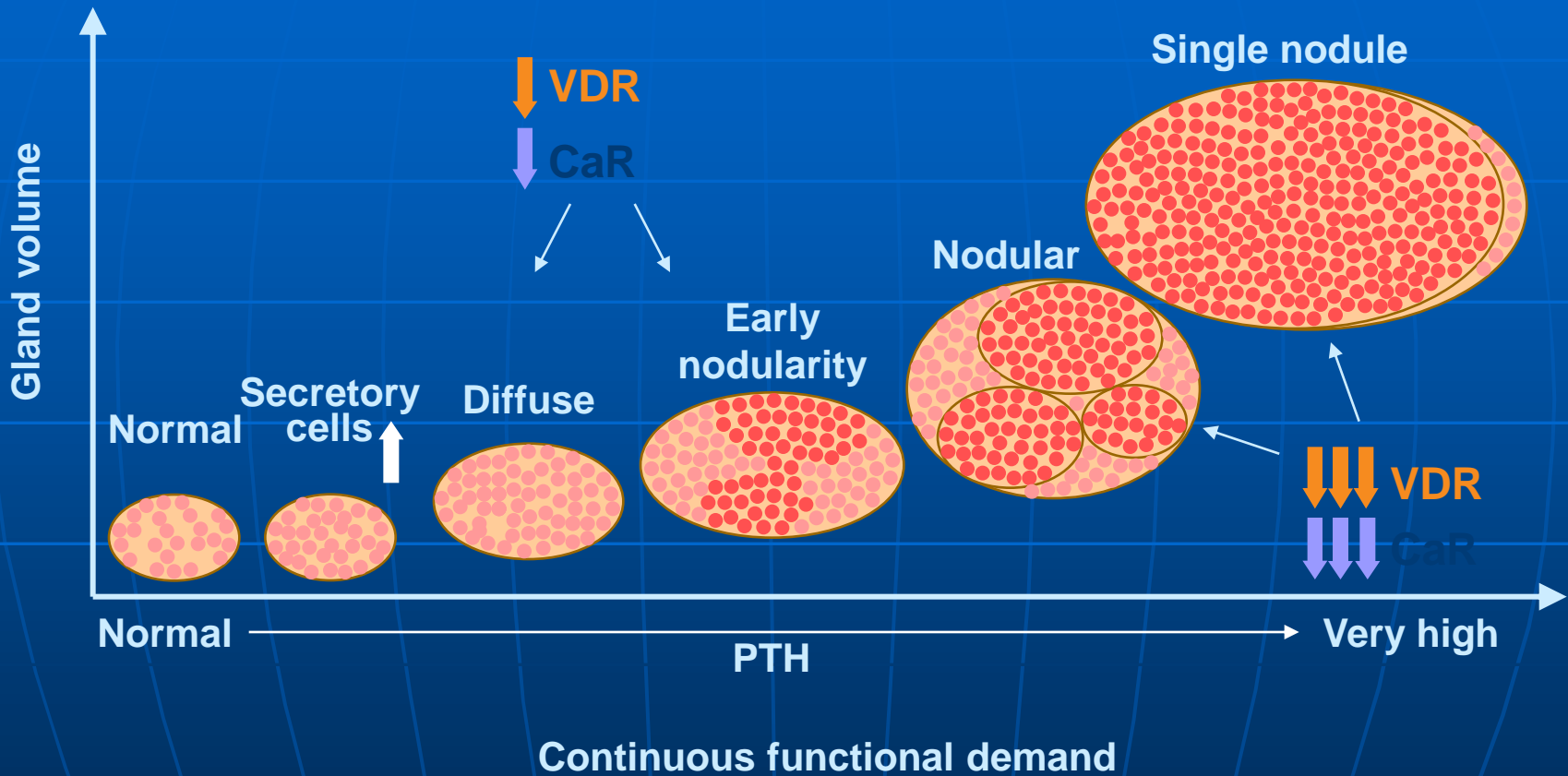
# In 70% of Dialysis Patients, Serum Phosphorus Exceeds 5 mg/dL (hyperphosphatemia)

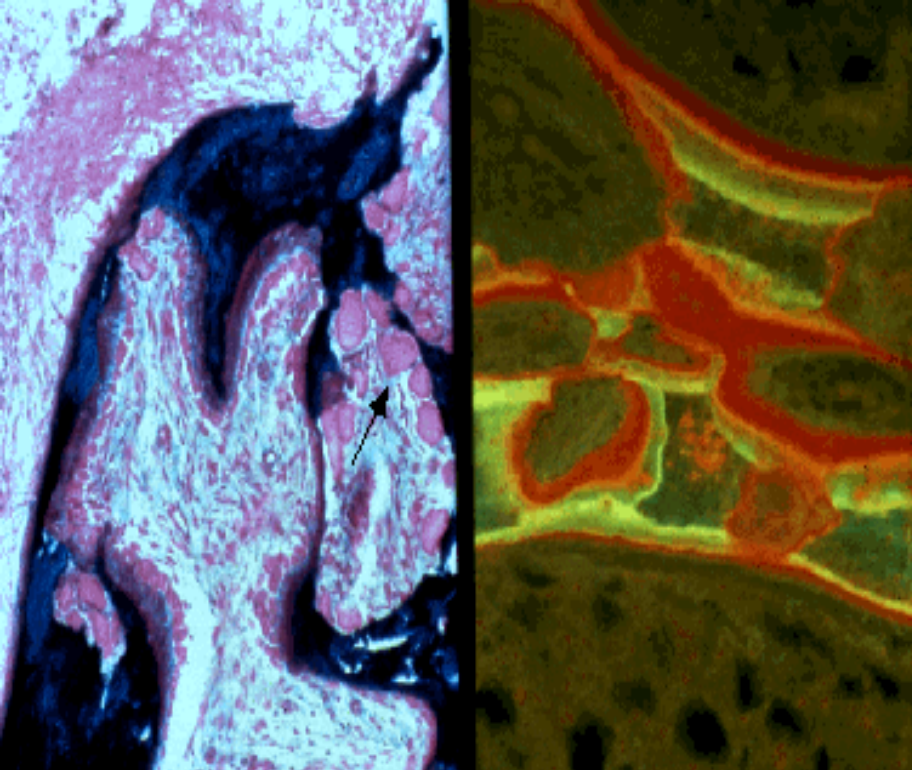


# Overview of SHPT pathogenesis

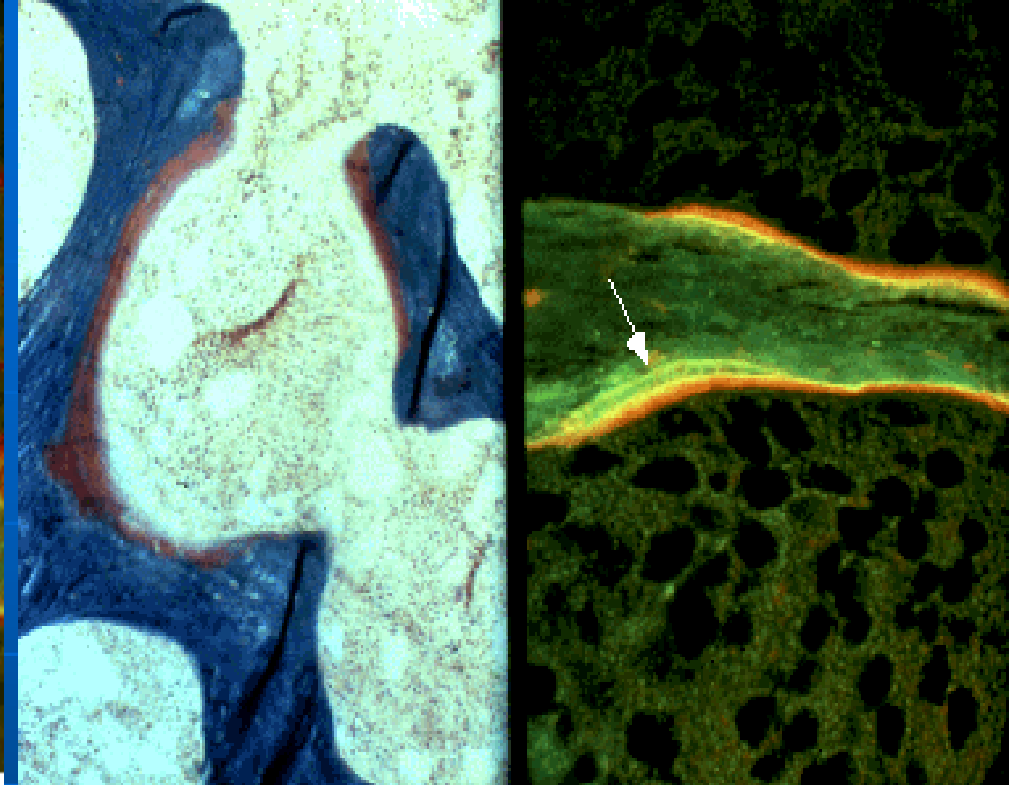


# Progression of SHPT: parathyroid hyperplasia



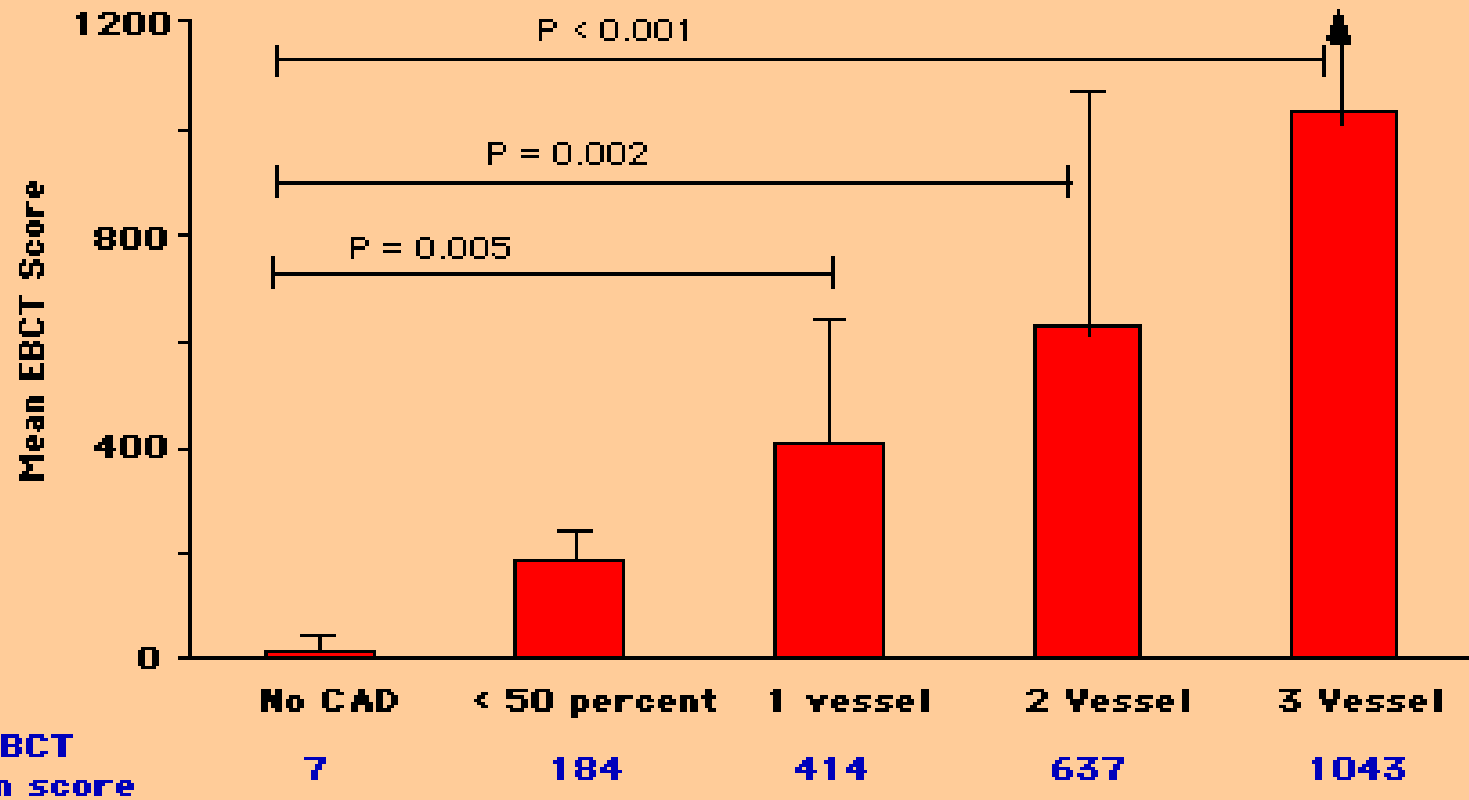


**Osteitis fibrosa** Bone biopsy from the iliac crest showing osteitis fibrosa due to severe secondary hyperparathyroidism. Left panel: Goldner Masson trichrome stain shows an increased number of multinucleate osteoclasts at the resorptive surfaces (arrow) and extensive bone marrow fibrosis (as shown by the light blue staining of the marrow) replacing normal marrow elements. The increased resorptive activity results in a thin and scalloped appearance to mineralized trabecular bone (blue). Right panel: Tetracycline labeling reveals a marked increase both in osteoid (orange-red staining) and in new bone formation (two distinct yellow-green bands below the majority of orange-red stained osteoid surfaces). Courtesy of L Darryl Quarles, MD.



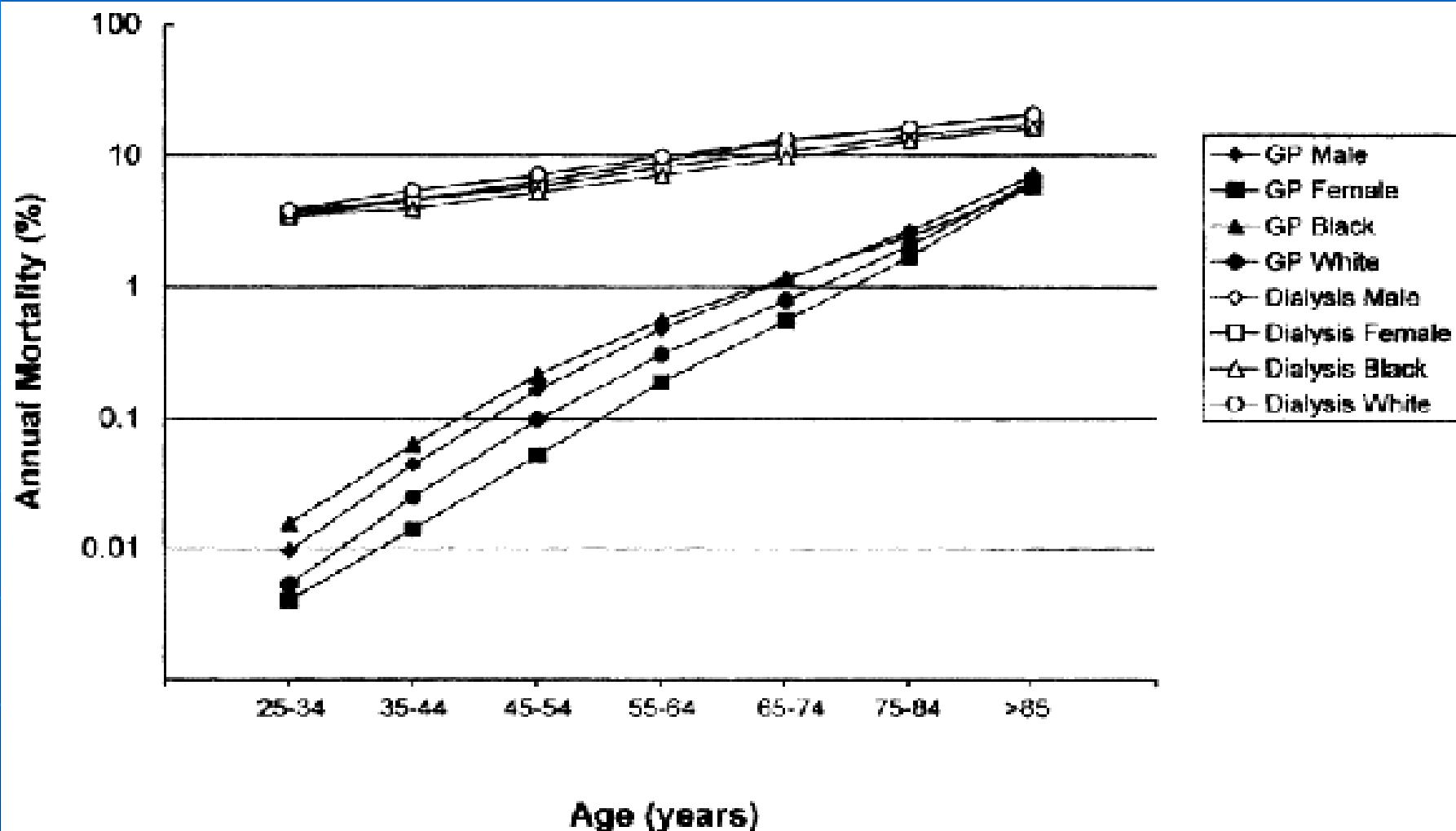
**Normal bone** Histologic appearance of normal bone. Left panel: Goldner Masson trichrome stain shows mineralized lamellar bone in blue and adjacent nonmineralized osteoid in red-brown. Osteoid usually comprises less than 25 percent of bone surfaces. The cellular area between the osseous structures is the marrow space. Right panel: Villanueva-stained section viewed under polarized light following time-spaced tetracycline labeling. Osteoid appears orange, mineralized bone is green, and tetracycline markers appear as luminescent yellow-green bands within bone and beneath osteoid (arrow). The distinct dual bands represent active mineralized bone formation. Courtesy of L Darryl Quarles, MD.

ΧΝΑ ΚΑΙ  
ΚΑΡΔΙΑΓΓΕΙΑΚΗ  
ΝΟΣΗΡΟΤΗΤΑ /  
ΘΝΗΣΙΜΟΤΗΤΑ



### EBCT calcium scores correlate with extent of coronary disease

Correlation of electron beam computed tomography (EBCT) calcium scores and the extent of coronary artery disease (CAD) as determined by angiography. The EBCT scores generally correlated with the amount of angiographic disease, with the highest scores in those patients with three-vessel disease by angiography. Patients with nonischemic cardiomyopathy (no CAD or <50 percent by angiography) had the lowest calcium scores. (Data from Budhoff, MJ, Georgiou, D, Brody, A. et al, Circulation 1996; 93:898.)



**Figure 6** Cardiovascular mortality in the general population (NCHS) and in ESRD treated by dialysis (USRDS). CVD mortality defined by death due to arrhythmias, cardiomyopathy, cardiac arrest, myocardial infarction, atherosclerotic heart disease, and pulmonary edema in the general population (data from NCHS multiple cause mortality data files, ICD-9 codes 402, 404, 410-414, and 425-429, 1993) compared to ESRD treated by dialysis (data from USRDS special data request HCFA form 2746, field numbers 23, 26-29, and 31, 1994-1996). Reprinted with permission [9].



# ΕΞΩΝΕΦΡΙΚΗ ΚΑΘΑΡΣΗ

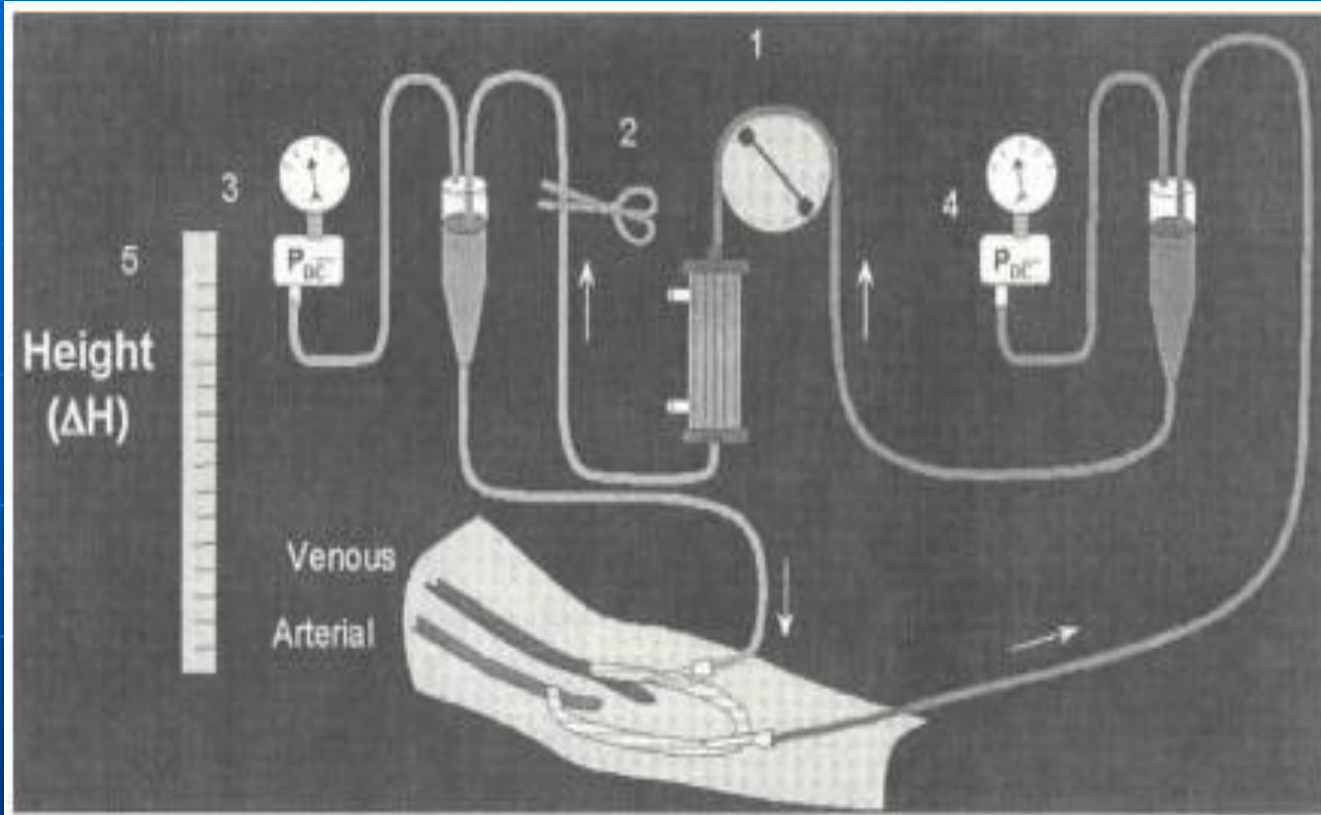
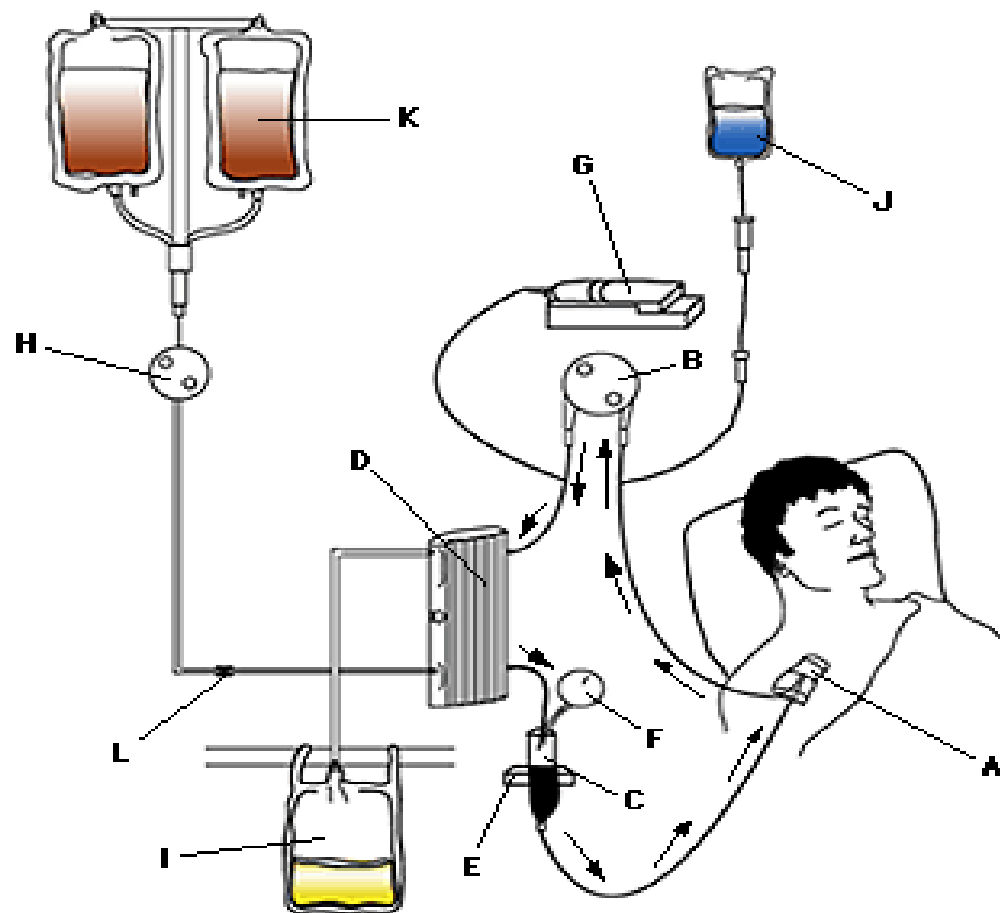


Fig III-1. Arterial and venous pressure monitoring.

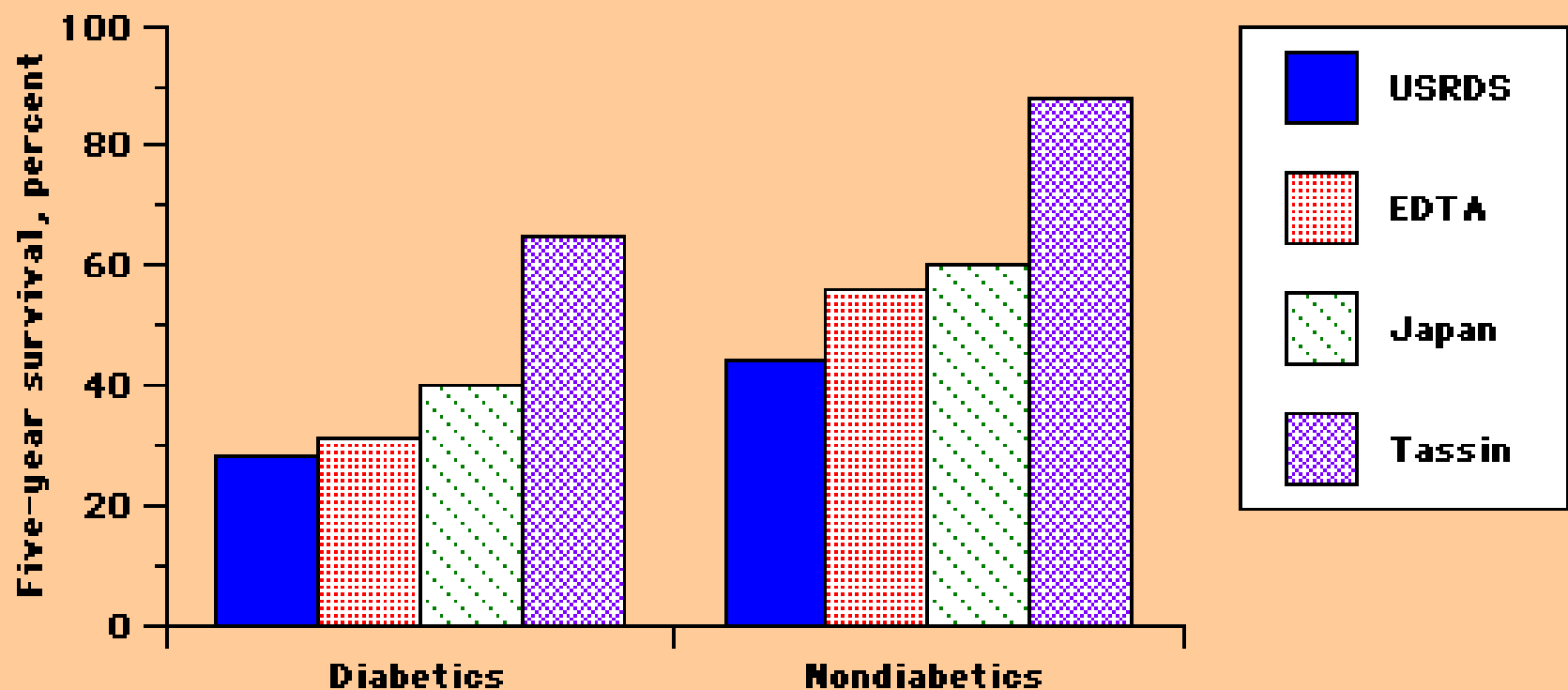


**Apparatus for CVVHD** Diagram of equipment used for the performance of continuous venovenous hemodialysis (CVVHD) or slow continuous hemodialysis. A: Double-lumen subclavian catheter; B: Blood pump; C: Venous bubble trap; D: Dialyser; E: Air embolus detector; F: Venous pressure monitor; G: Heparin infusion; H: Dialysate infusion pump; I: Dialysate collection bag; J: Saline infusion; K: Dialysate; L: Constricting clamp. (Reproduced with permission from Tam PY-W, Huraib S, Mahan B, et al. Clin Nephrol 1988; 30:79).

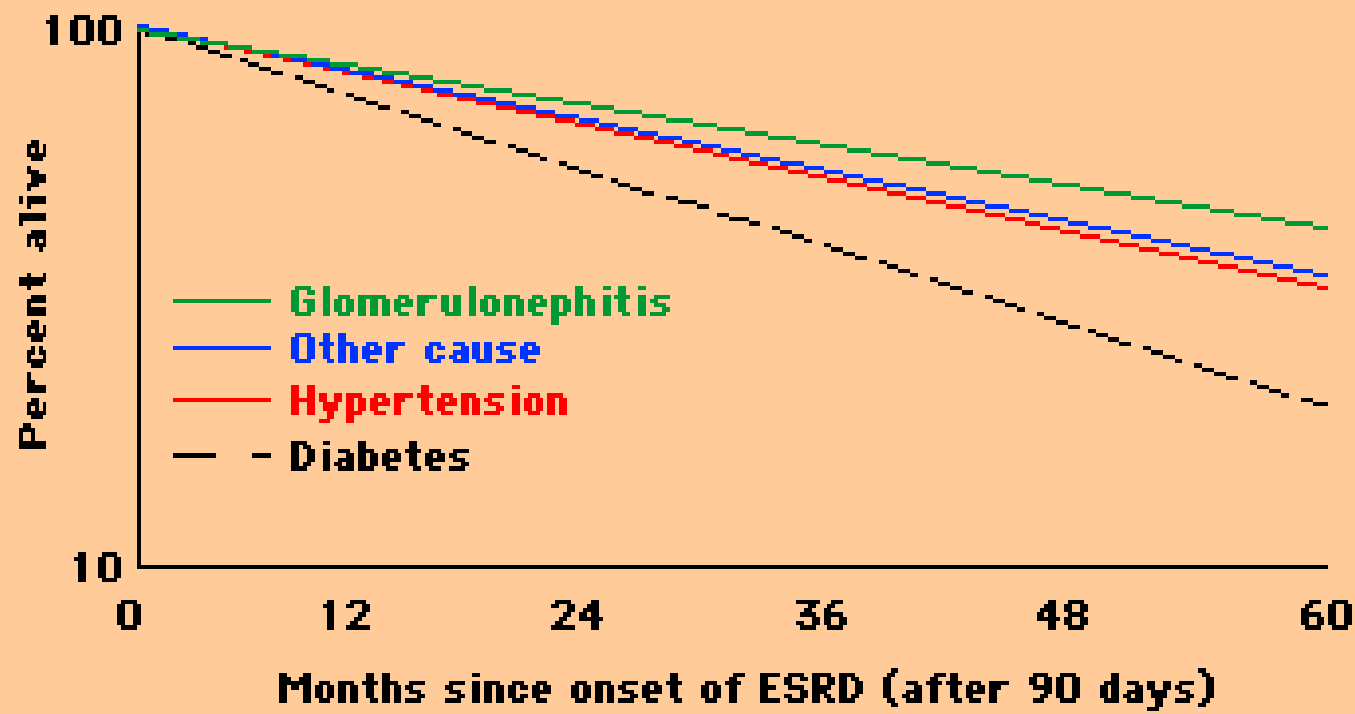


# ΦΙΛΤΡΟ ΑΙΜΟΚΑΘΑΡΣΗΣ



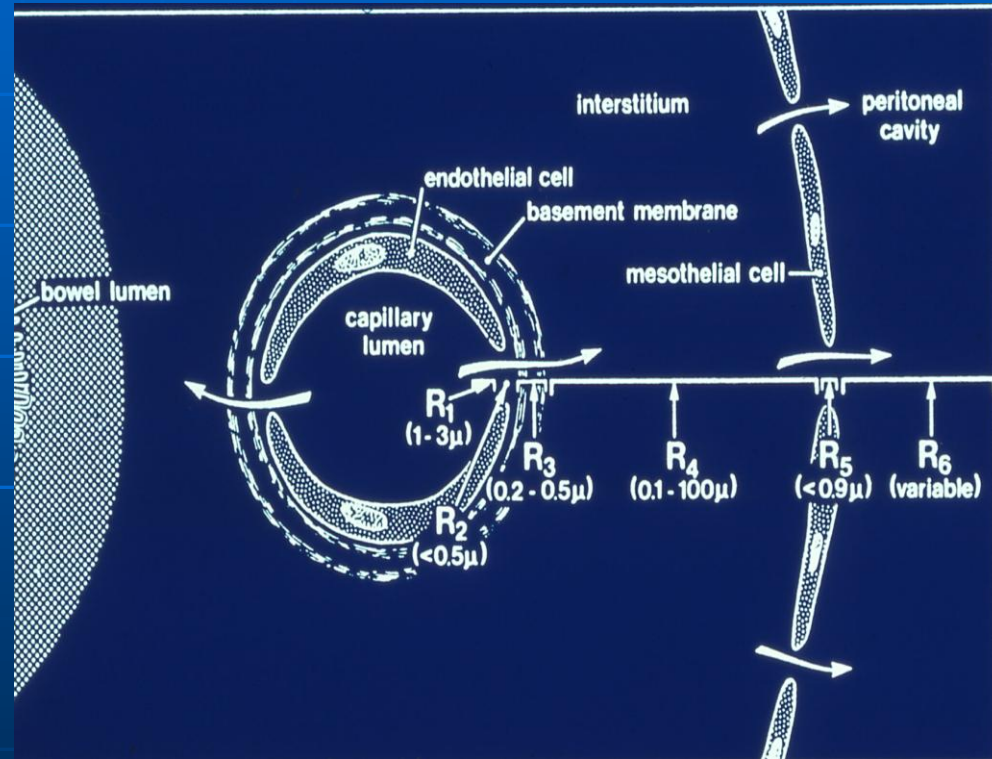
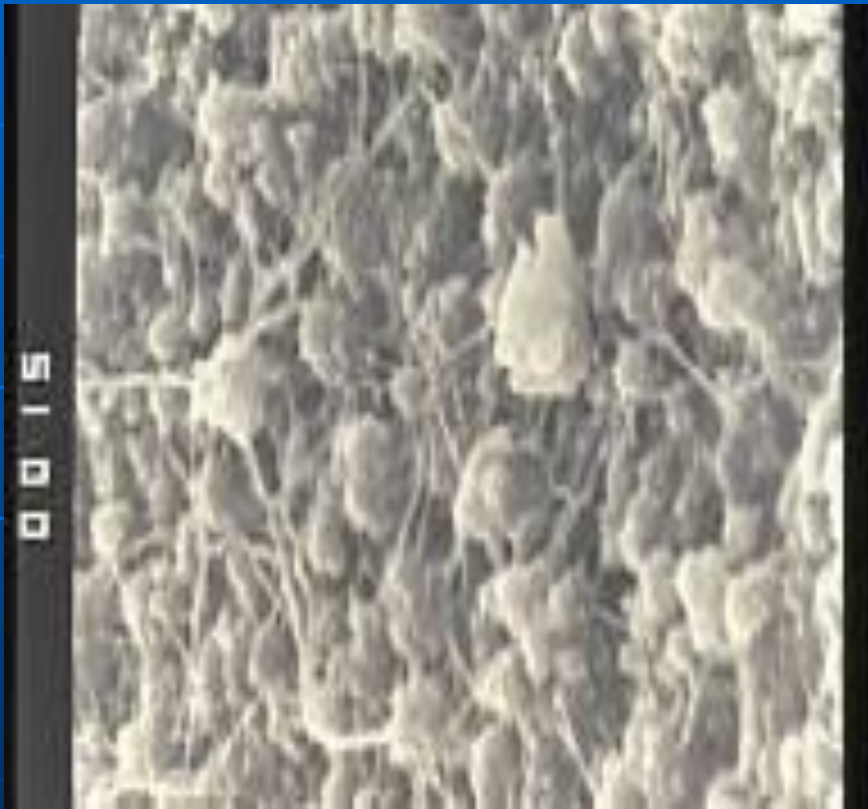


**Survival on dialysis according to site and disease** Five year patient survival rates after the institution of maintenance hemodialysis in the United States (from the US Renal Data System), Europe (from the European Dialysis and Transplant Association), Japan, and Tassin, France. Survival was lowest in the United States and highest in nondiabetics and in Tassin where the patients were more intensively dialyzed. (Data from Hull, AR, Parker, TF III, Am J Kidney Dis 1990; 15:375, and Charra, B, Calemard, E, Ruffet, M, et al, Kidney Int 1992; 41:1286.)



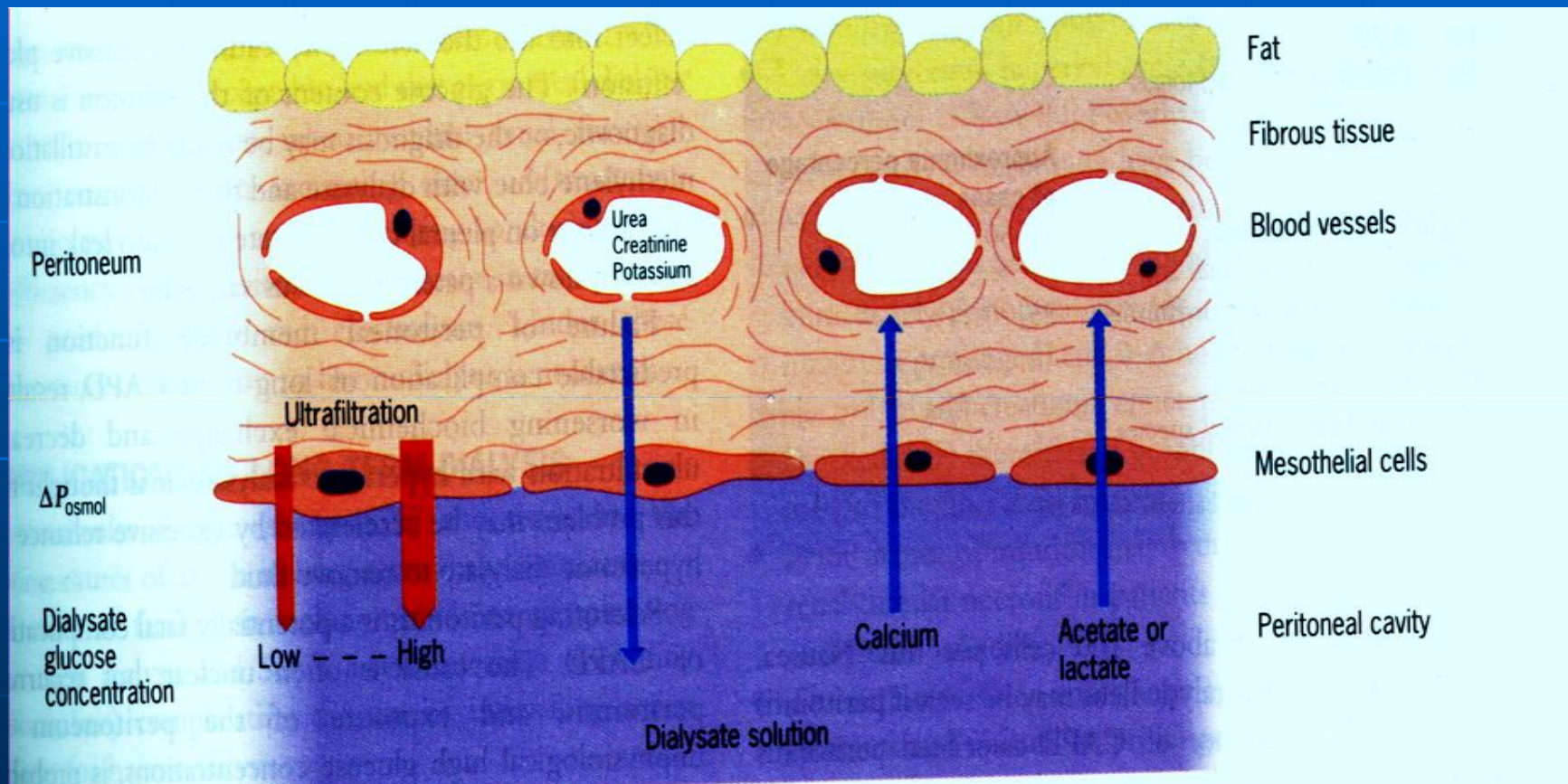
**Dialysis patient survival estimates by patient age** Kaplan-Meier survival curves (log scale) starting at day 91 following the onset of end-stage renal disease and censored at first transplant. The incident cohort is 1988, and the results are adjusted for the age, race, and sex characteristics of the 1992 incident cohort. Survival is highest in patients with glomerulonephritis and lowest in those with diabetes mellitus. (Data from the USRDS 1995 Annual Data Report).

# ΠΕΡΙΤΟΝΑΪΚΗ ΚΑΘΑΡΣΗ

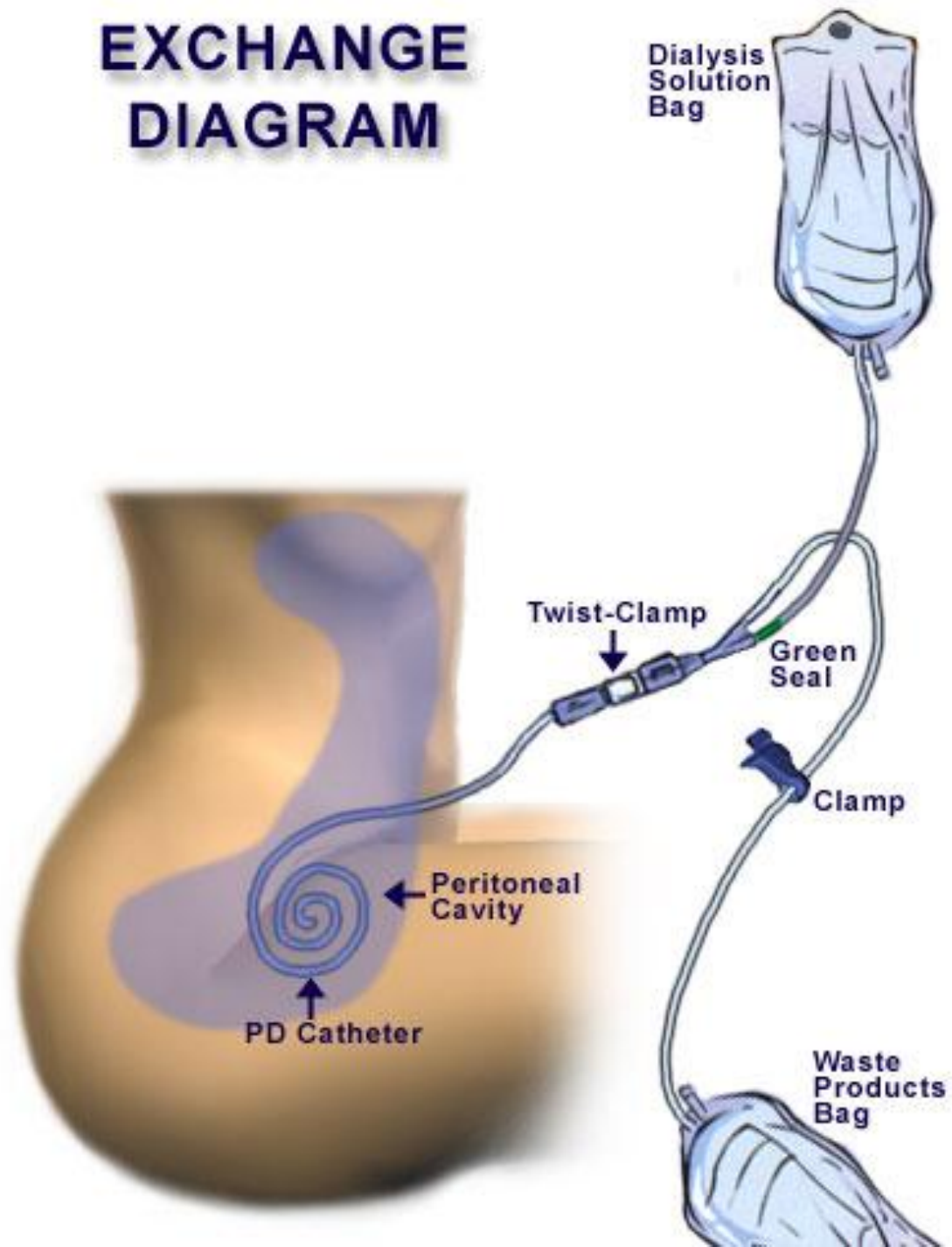




# Η ΠΕΡΙΤΟΝΑΪΚΗ ΜΕΜΒΡΑΝΗ



# EXCHANGE DIAGRAM



# ΕΙΔΗ ΠΕΡΙΤΟΝΑΪΚΗΣ ΚΑΘΑΡΣΗΣ ΑΥΤΟΜΑΤΟΠΟΙΗΜΕΝΗ



# **ΜΕΤΑΜΟΣΧΕΥΣΗ ΝΕΦΡΟΥ**

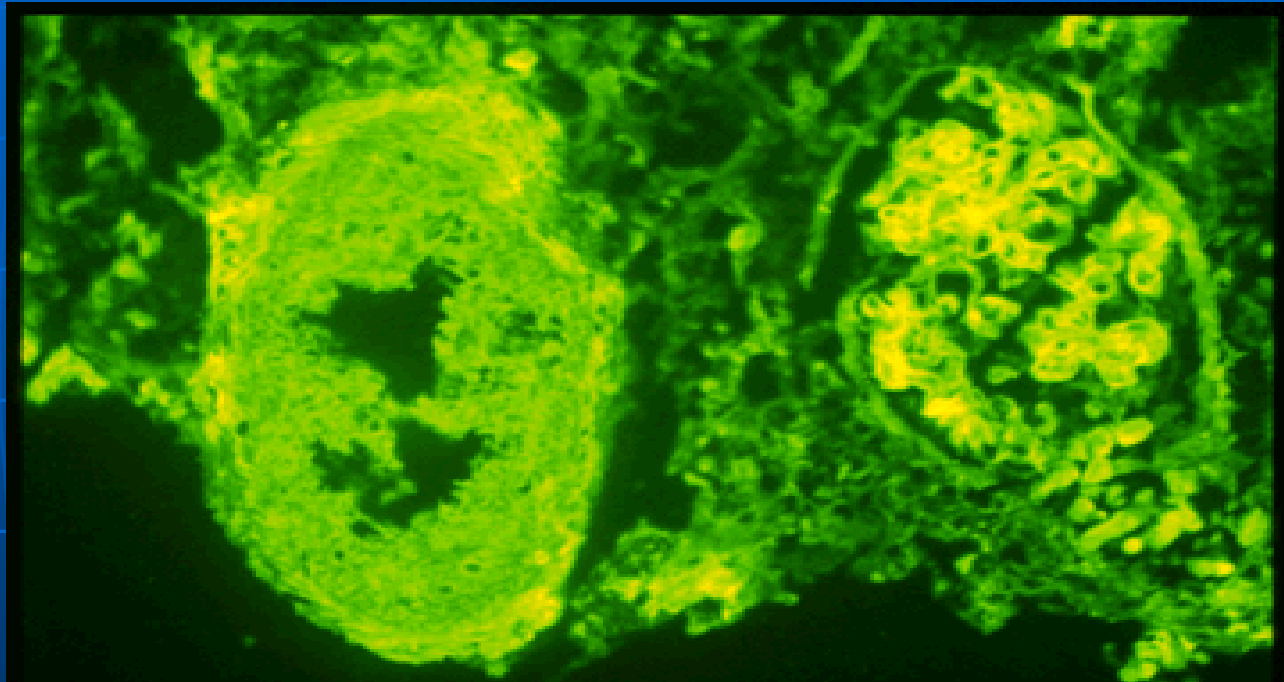
Πρώτη Μεταμόσχευση Νεφρού: 1954  
Dr. Murray, Brigham and Women's Hospital, Boston,  
MA, USA



# Πλεονεκτήματα νεφρικής μεταμόσχευσης

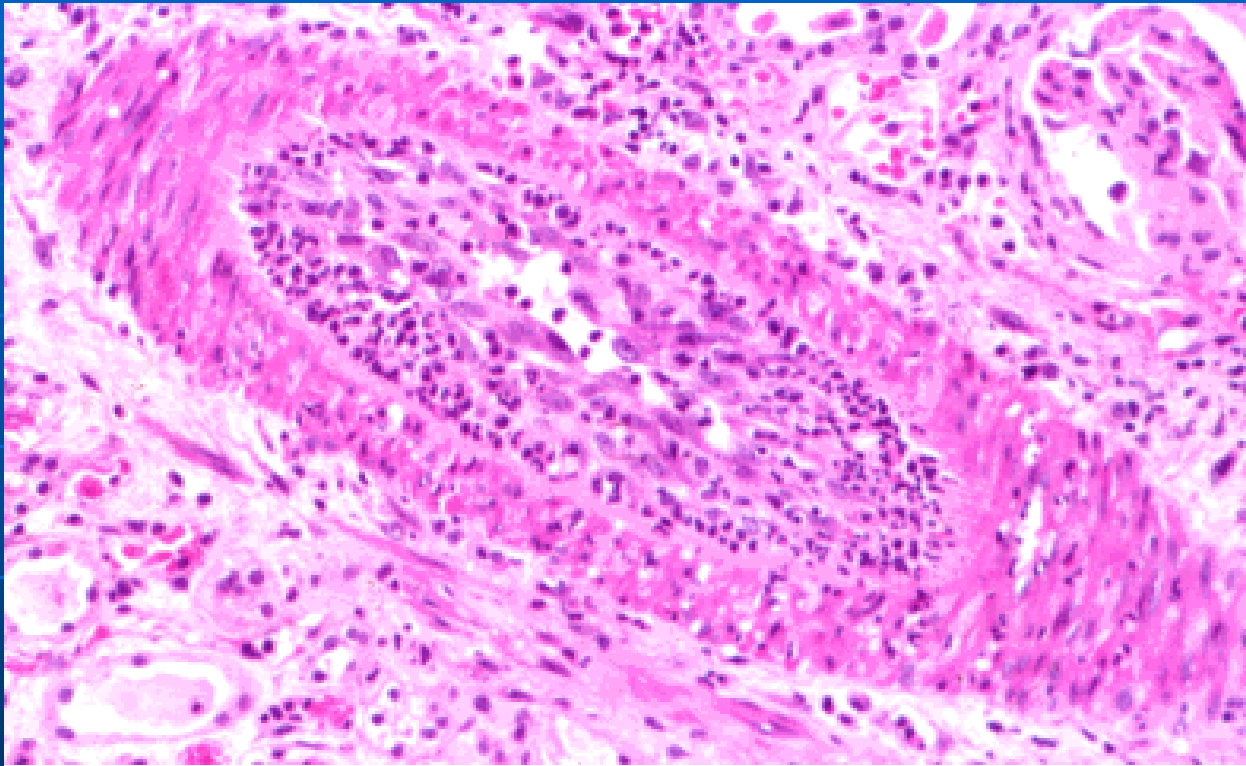
- Αποφυγή εξωσωματικής κάθαρσης
- Άρση διαιτητικών περιορισμών
- Βελτιωμένη ποιότητας ζωής
- Βελτιωμένη επιβίωση
- Χαμηλότερο κόστος

# Υπεροξεία απόρριψη



Immunofluorescence microscopy in hyperacute rejection showing extensive fibrin deposition in a glomerulus (right) and in the vascular wall and lumen of an artery (left). The arterial lumen is markedly narrowed due to intraluminal fibrin deposition. Courtesy of Helmut Rennke, MD.

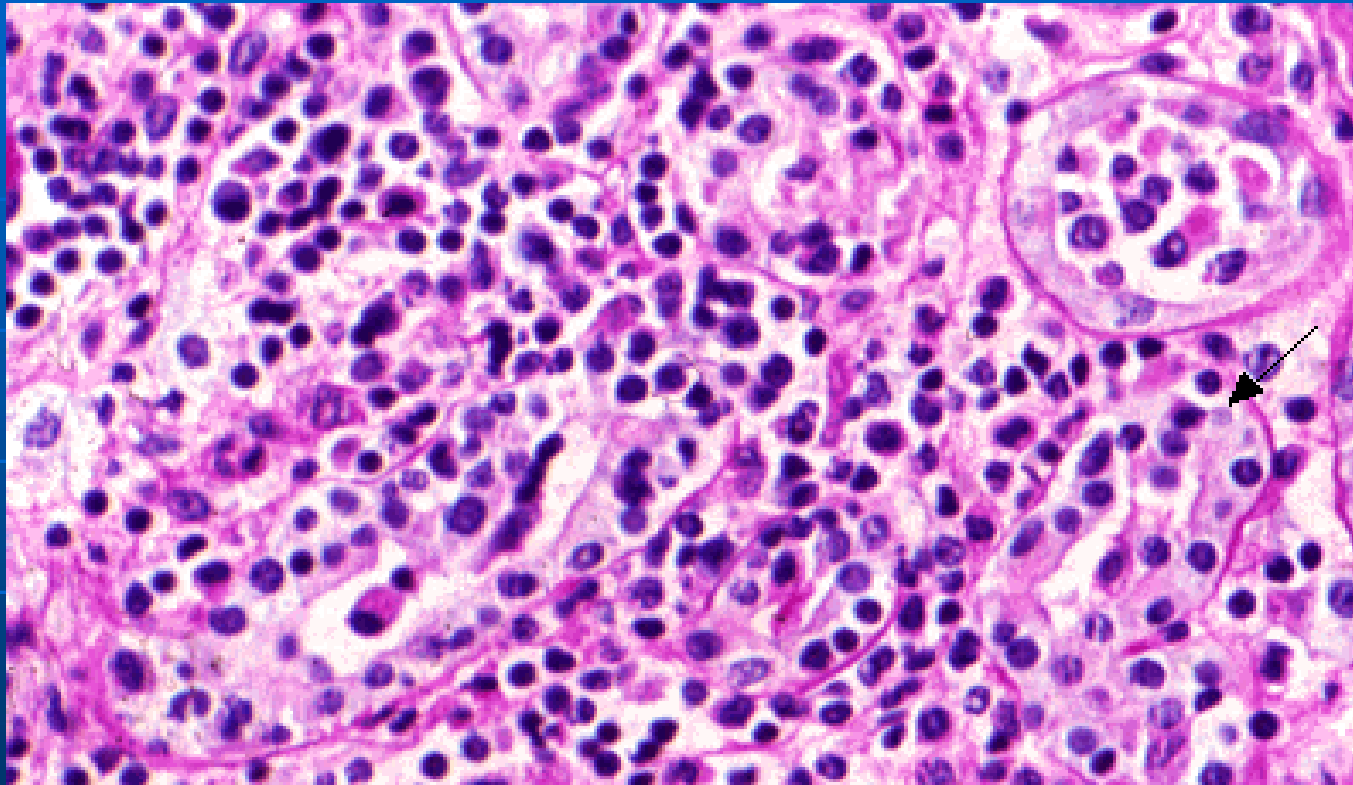
# Οξεία αγγειακή απόρριψη



**Acute vascular renal transplant rejection** Acute vascular rejection in a renal transplant. Note that the inflammatory infiltrate is limited to the expanded intima, and does not involve the entire vascular wall as in a systemic vasculitis. Courtesy of Helmut Rennke, MD.

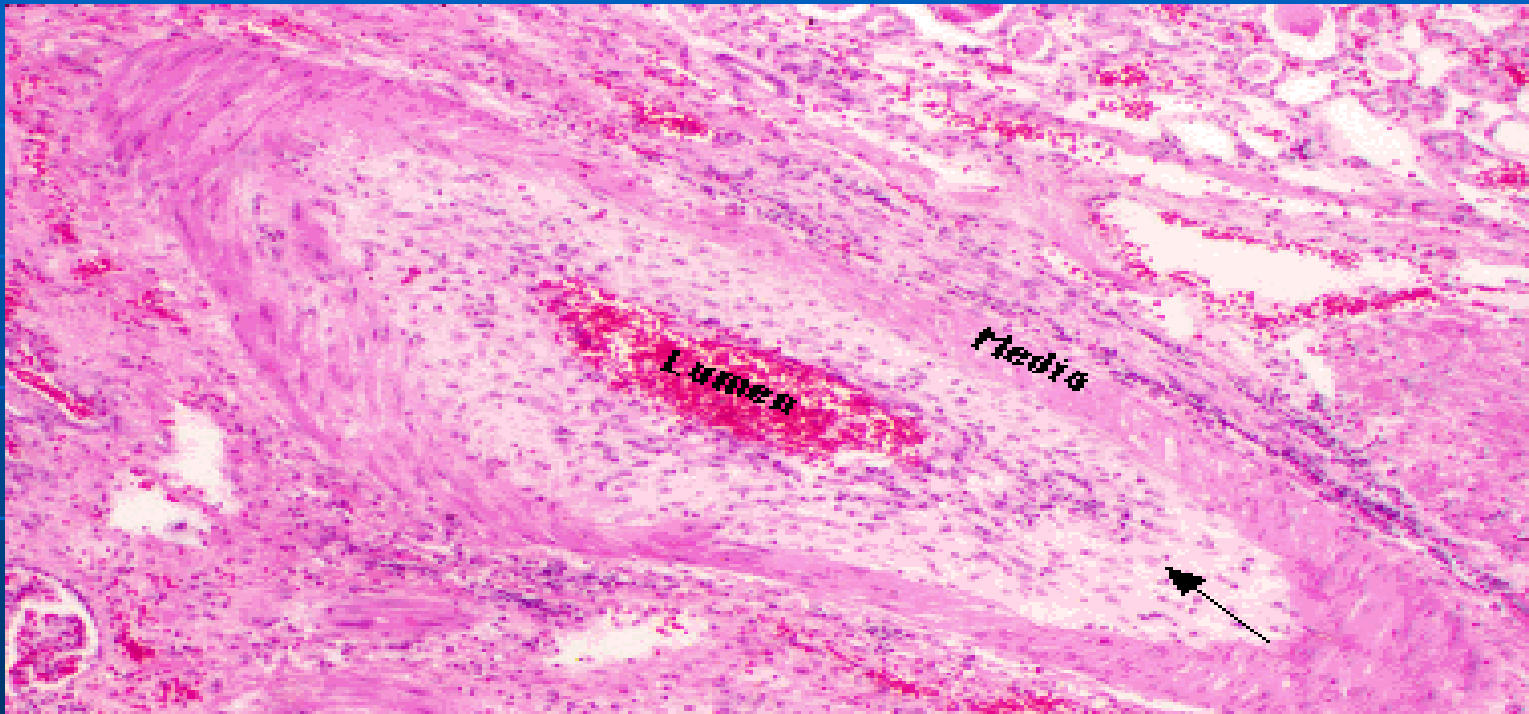


# Οξεία κυτταρική απόρριψη



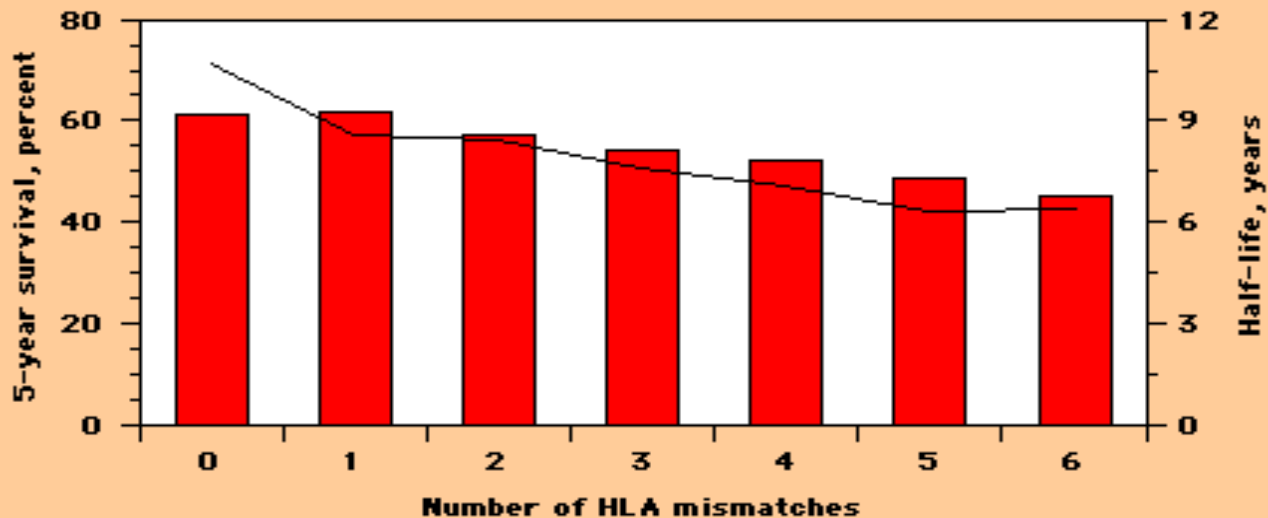
**Acute cellular renal transplant rejection** Acute cellular rejection in a renal transplant shows diffuse interstitial infiltrate of mononuclear cells, some of which are actively invading the tubules (arrow). Courtesy of Helmut Rennke, MD.

# Χρόνια απόρριψη



**Chronic renal transplant rejection** Light micrograph of an intermediate stage of chronic vascular rejection in an interlobular artery. The arterial lumen is narrowed by marked subintimal thickening with loose connective tissue (arrow). Courtesy of Helmut Rennke, MD.

# Ιστοσυμβατότητα και επιβίωση νεφρικού μοσχεύματος

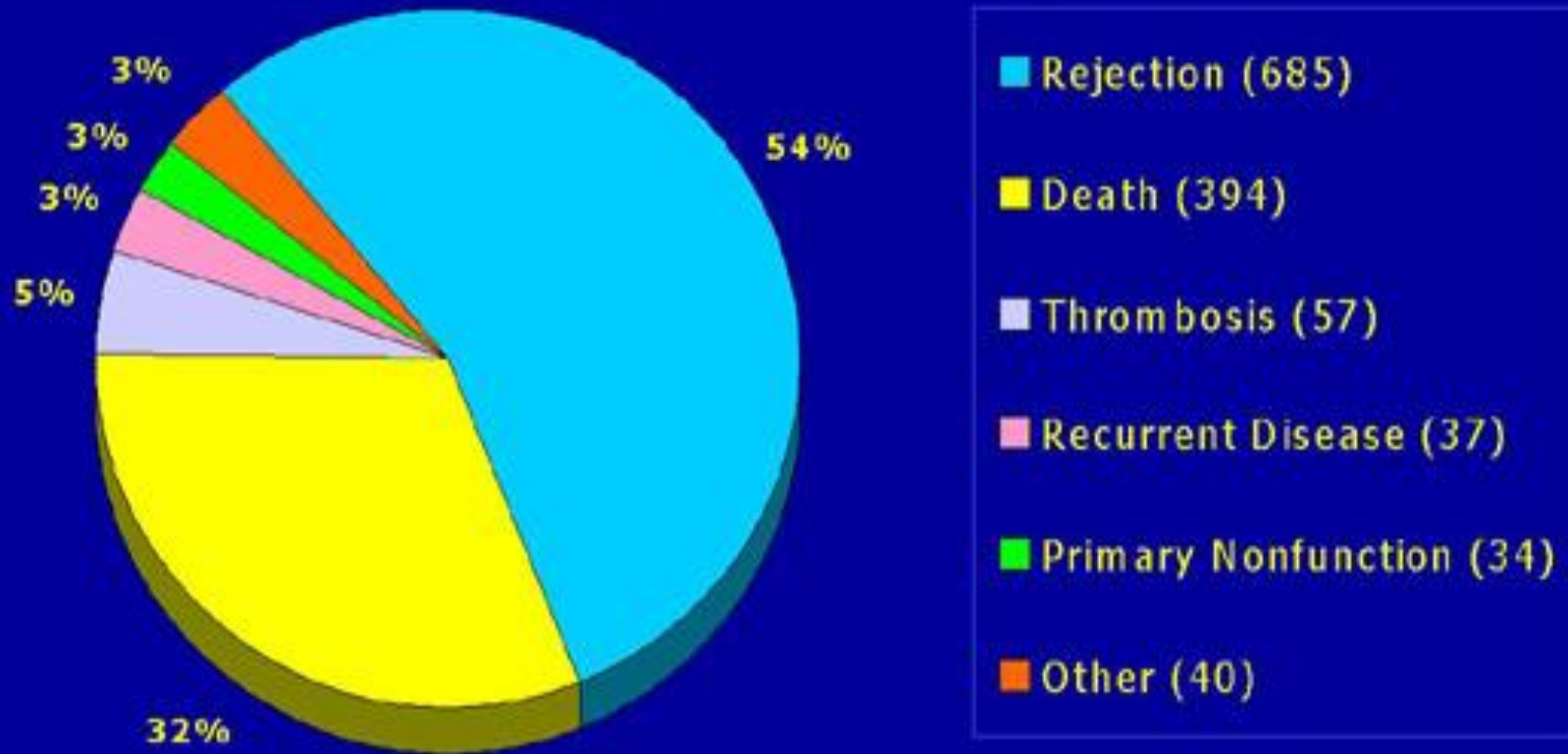


**HLA mismatches and renal graft survival** Five-year graft survival (columns) and the half-life of graft survival after the first year (line) in cyclosporine-treated cadaver recipients gradually decline with an increasing number of HLA-A,B,DR mismatches. The total number of patients exceeded 30,000, only 1928 of whom had 0 or 1 mismatches. (Data from Mitsuishi, Y, Terasaki, PI, *Kidney Int Suppl* 1992; 38:S172.)

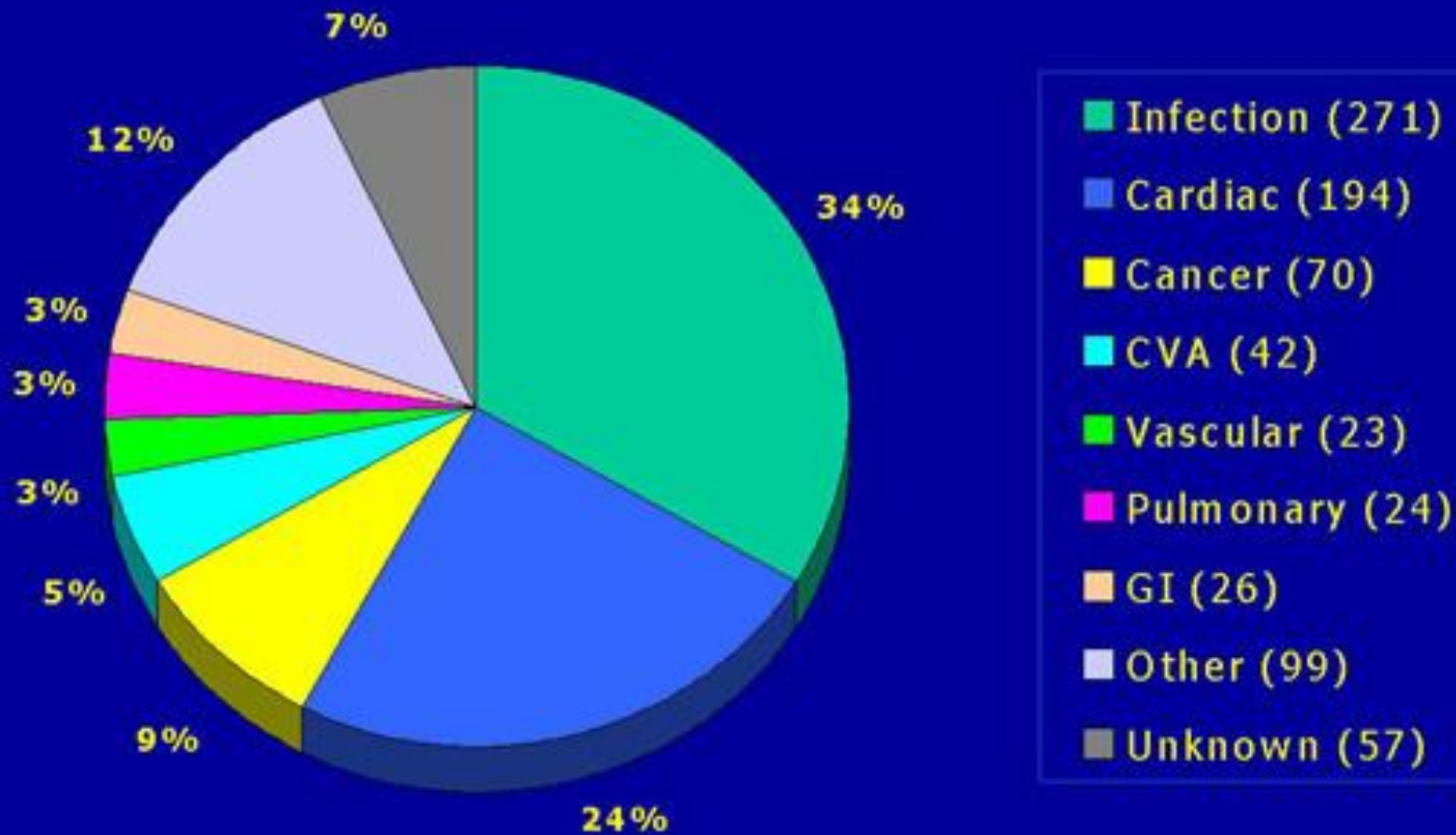
# Επιβίωση πτωματικών μοσχευμάτων



# Αίτια απώλειας μοσχευμάτων



# Αίτια θανάτου μεταμοσχευμένων νεφροπαθών



**ΕΥΧΑΡΙΣΤΩ  
ΓΙΑ ΤΗΝ  
ΠΡΟΣΟΧΗ ΣΑΣ**

