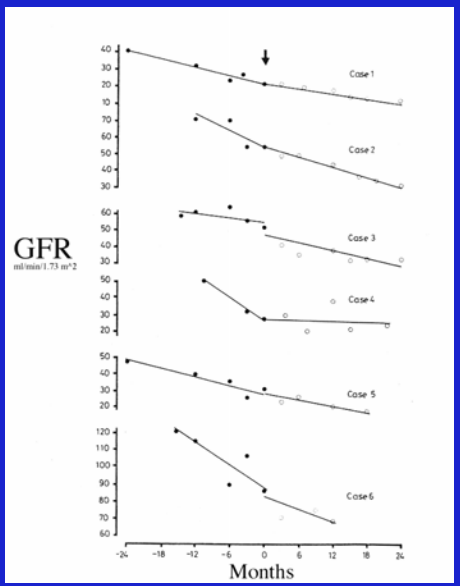
Renal injury often progresses after the initial cause of injury is removed

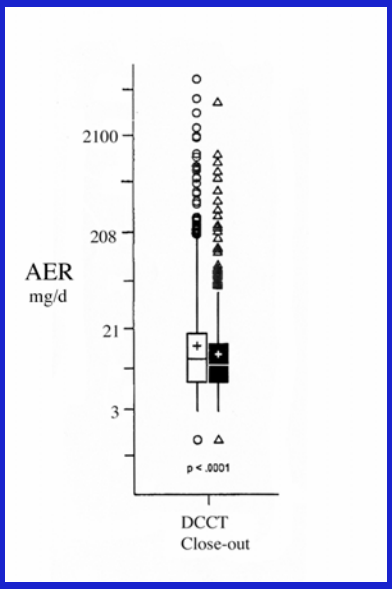


Viberti et al. BMJ 286:598 1983

At DCCT close-out, GFR was normal and median values for albumin excretion rate were low:

Conventional AER 9 mg/d (75th percentile 6-14 mg/d)

Intensive AER 10 mg/d (75th percentile 6-20 mg/d)



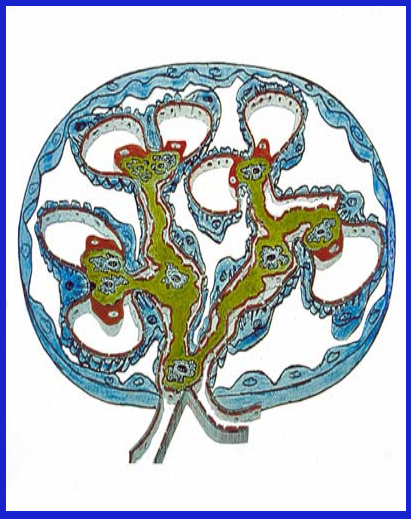
Patients who developed renal insufficiency*

AER at Close-out (mg/d)	Conventional n = 19	Intensive n = 5
> 1000	6	1
300 - 1000	-	2
40 - 300	4	2
< 40	9	-

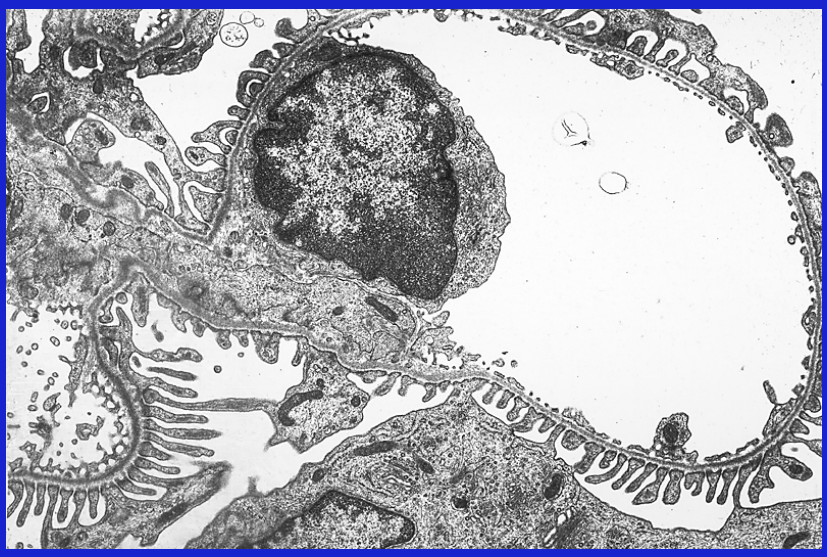
* Serum creatinine > 2.0 mg/dl or dialysis or kidney transplant by EDIC year 8

Patients who developed albuminuria > 300 mg/d

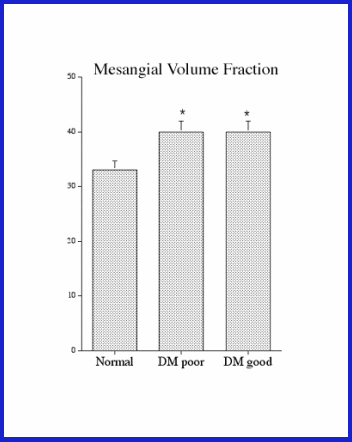
AER at Close-out (mg/d)	
>300	12
40 - 300	23
< 40	37

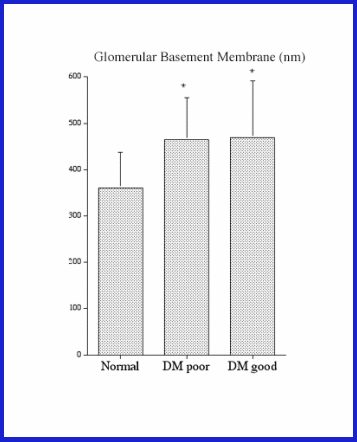


	Normal Human	Diabetes Micro-albuminuria
Glomerular Volume (10^6 μ^3)	3.2	3.6
GBM Thickness (nm)	330	600
Mesangial Fraction (% volume)	20	30



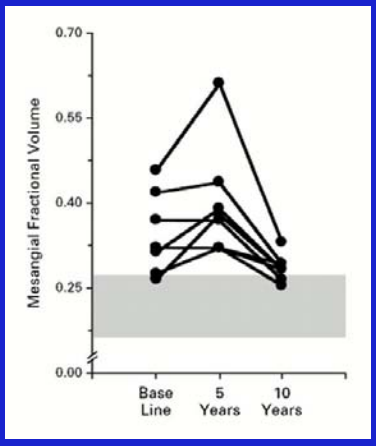
No reversal of lesions of diabetic nephropathy
after good control -- 2.5 years

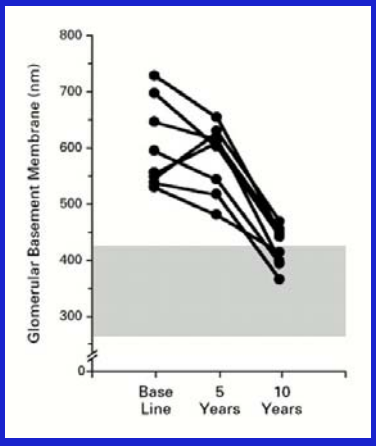




Kern Engerman 33:522 1990

Reversal of lesions of diabetic nephropathy after pancreas transplantation -- 10 years

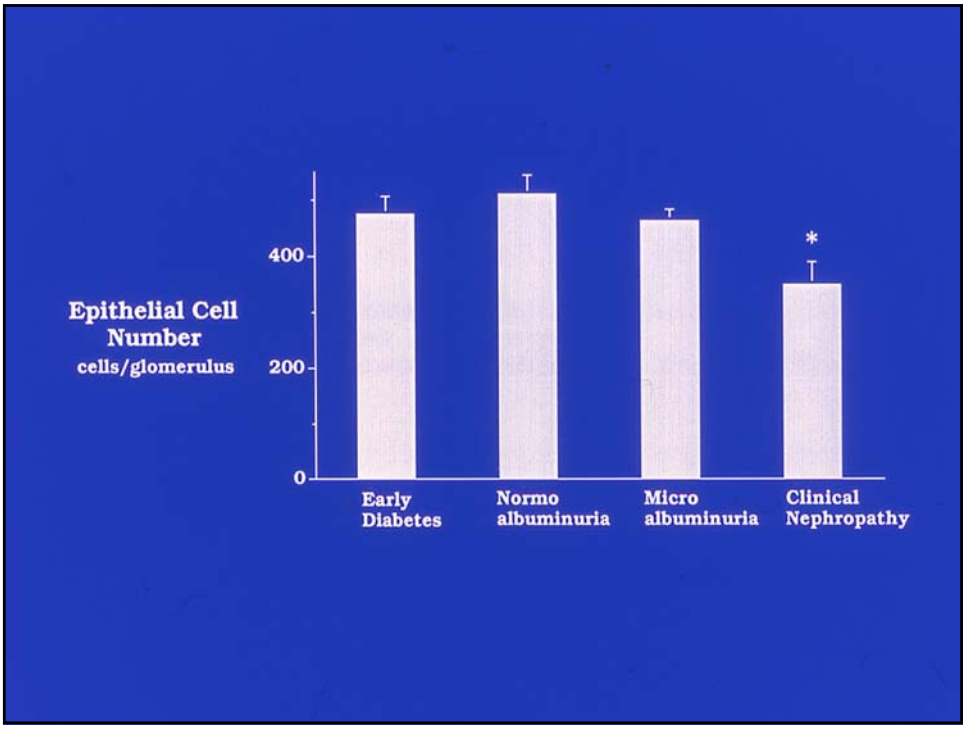


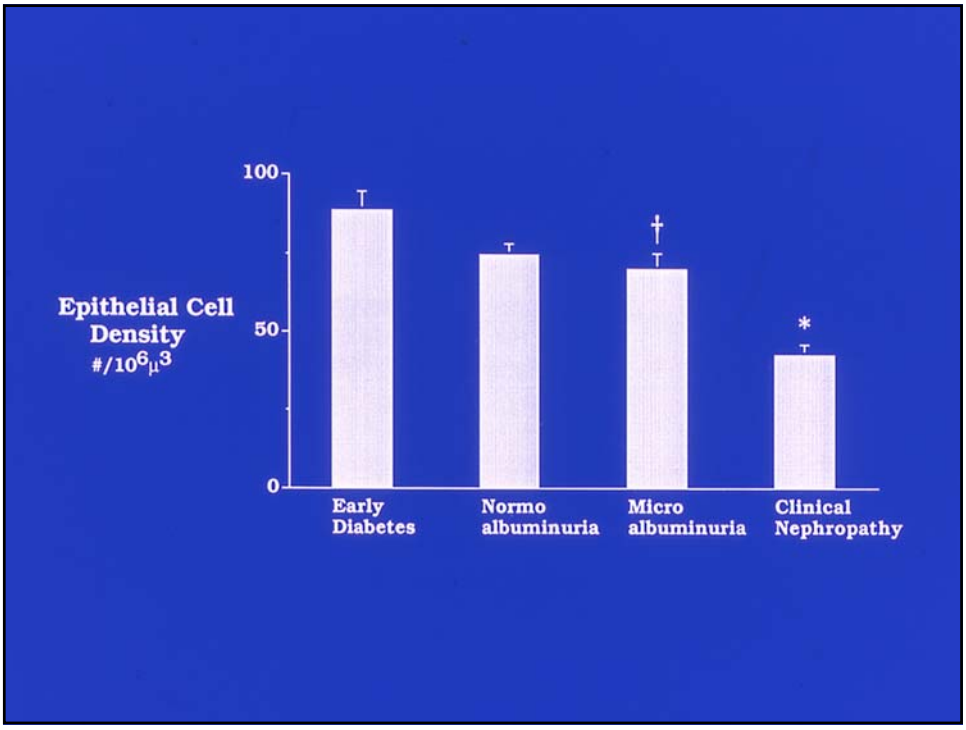


Fioretto et al., NEJM 339:69 1998

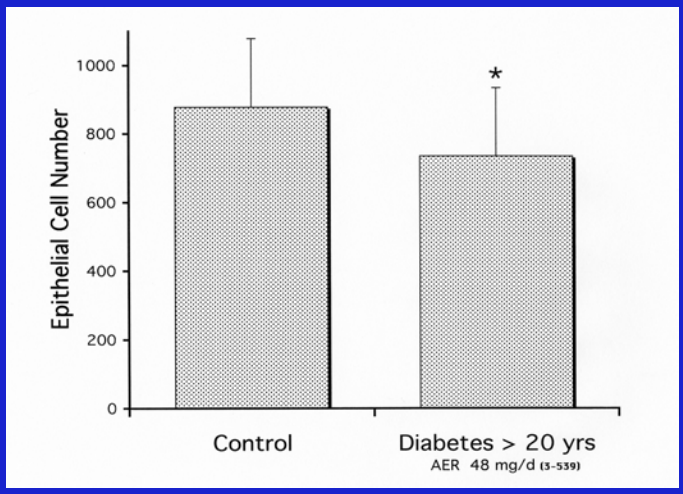
Visceral Epithelial Cells
Cannot Divide

	Normal	Compensatory Hypertrophy
Glomerular Volume $10^6 \mu^3$	1.3 ± 0.1	2.5 ± 0.2 *
Epithelial Cell Number	142 ± 11	129 ± 8
Epithelial Cell Density #/$10^6 \mu^3$	108 ± 9	52 ± 3 *


Epithelial Cell Number
cells/glomerulus
400
200
0
*
Early Diabetes
Normo albuminuria
Micro albuminuria
Clinical Nephropathy


Epithelial Cell Density
#/10⁶μ³
100
50
0
†
*
Early Diabetes
Normo albuminuria
Micro albuminuria
Clinical Nephropathy

Epithelial cell loss may begin while the albumin excretion rate is still low



Steffes et al., Kidney Int 59:2104, 2002

What's killing the visceral epithelial cells?

- effect of underlying matrix changes?
- direct effect of diabetes on these cells?

Why does angiotensin II blockade preserve epithelial cell function?