DIABETIC NEPHROPATHY

CD POTGIETER

GAMARA

Incidence

ESRD programme in USA 35% = Diabetes mellitus
63% = Type II D.M.

Epidemiology

- Diabetic Nephropathy usually after 10 years of Diabetes duration.
- Cumulative proteinuria in type I D.M. is 40% after 20 years duration.
- Type II D.M. = 40% will develop Diabetic Nephropathy

Pathogenesis of Diabetic Nephropathy

Daibetic milieu -

- Hyperglycaemia
- Insulien deficiency
- Increased growth hormone and glucagon
- Increased ketones

- Hyperglycaemia - increased advanced glycosylation end-products, of tissues (AGE)
- Contributing factors
  - Hypertension (less with Renal artery stenosis)
  - Intraglomerular hypertension (Angiotensin 2)
- Dietary protein excess
- Alterations renin angiotensin axis
- Altered prostaglandin production
- Elevated kinin production
- Elevated Atrial Natuiretic levels

Diabetic Nephropathy

What is the natural history of Diabetic Nephropathy?

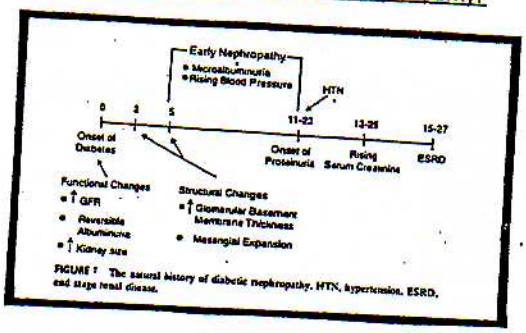

FIGURE 1 The natural history of diabetic nephropathy. HTN, hypertension. ESRD, end stage renal disease.

Onset

- Functional changes
- Hyperfiltration
- Elevation in blood pressure
- Type 1 D.M.: 17 ± 6 years after onset - frank proteinuria
- Proteinuria - 50% reach ESRD in 7 to 10 years
- Type 2 D.M. - Time of onset is unknown ! Perhaps similar natural history as type 1 D.M.

Functional changes of early Diabetic Nephropathy

- Increased kidney size
- Albuminuria reverses with blood sugar control
- Glomerular hyperfiltration
- Increased GFR
- Intraglomerular hypertension (A 2)
- Hypertension

Pathology

Onset: Normal morphology

1½ to 2½ years: Glomerular basement membrane thickening.

Nodular glomerulosclerosis

Diffuse glomerulosclerosis

Capsular drop

Fibrin cap

Mesangial matrix expansion

Afferent and Efferent arteriolar hyalinosis

Interstitial fibrosis and tubular atrophy

Microalbuminuria and Early Diabetic Nephropathy

- Subclinical elevation of urinary albumin excretion in type 1 diabetics predicts diabetic Nephropathy.
  - Normal 24h urine protein excretion = less than 30mg/24h
  - Micro-albuminuria: > 30mg/24h - <300mg/24h (albumin)
- Overt Nephropathy: > 300mg/24h
- Type 2 D.M. - microalbuminuria also predicts diabetic nephropathy but is a better predictor of cardiovascular mortality.
- Due to premature cardiovascular deaths in type 2 D.M. there is discrepancy between numbers of patients with early nephropathy and those that develop ESRD
- Elevated blood pressure - precede and predicts diabetic nephropathy.

Overt Diabetic Nephropathy

- Persistent proteinuria (>300mg/24h)
- Renal function inevitably declines
- Average time of ESRD is 10 years after onset of proteinuria
- Other complications of D.M. urological tract: Neurogenic bladder, Urinary tract infection and papillary necrosis
- Insulin requirements decrease with ESRD. Reason: kidney responsible for 30 to 40% of Insulin catabolism
- Type 4 renal tubular acidosis - hyperkalemia and metabolic acidosis despite relatively well - preserved GFR

Screening for Diabetic Nephropathy

- Type 1 D.M. with greater than 5 years duration - annual screen for microalbuminuria
- Use: 24h urine collection, overnight urine collection: creatinine ratio.
- Transient causes of microalbuminuria:
  - * Hyperglycaemia
  - * Uncontrolled On
  - * Congestive cardiac failure
  - * Urinary tract infection
  - * Excessive physical exercise
- Persistent microalbuminuria should be confirmed with 3 additional collections over 3 to 6 months.
- Type 2 DM - screen for microalbuminuria of DM and thereafter yearly.

Proteinuria in D.M. (>300mg / 24h)

- Type 1 D.M. with diabetic nephropathy ∴ 90 - 95% will also have diabetic retinopathy
- Absence of diabetic retinopathy - suspect another cause of proteinuria than D.M.
- Always consider other systemic diseases as possible causes of proteinuria.
- If in doubt - Renal biopsy. — indication

NB.

Treatment of progressive Diabetic Nephropathy

1. Improve glycaemic control
2. Anti-hypertensive therapy (135/85)
3. ACE - inhibitors (Type 1 D.M.)
4. Restriction of dietary protein intake.
5. Treat dyslipidemia
6. Other treatment eg: aldose reductase inhibitors etc - Not been proven efficaciuous.
7. Early referral to nephrologist
8. Avoid Nephrotoxins (eg. Radiological contrast media)
9. Renal replacement therapy earlier than non diabetics.
10. Vascular disease - IHD, CVA
11. Live related donor transplant is the best
12. Atherosclerosis = major risk

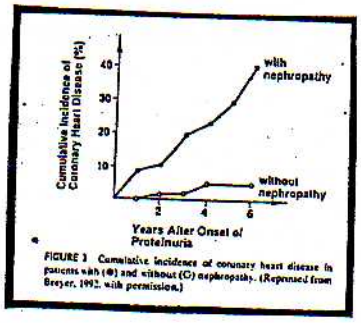

FIGURE 1 Cumulative incidence of coronary heart disease in patients with (●) and without (○) nephropathy. (Reprinted from Breyer, 1992, with permission.)