Persistent microscopic haematuria in childhood

Rachel Lennon
Professor of Nephrology & Consultant Paediatric Nephrologist, Manchester. UK

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Post Graduate Centre, Manchester Royal Infirmary

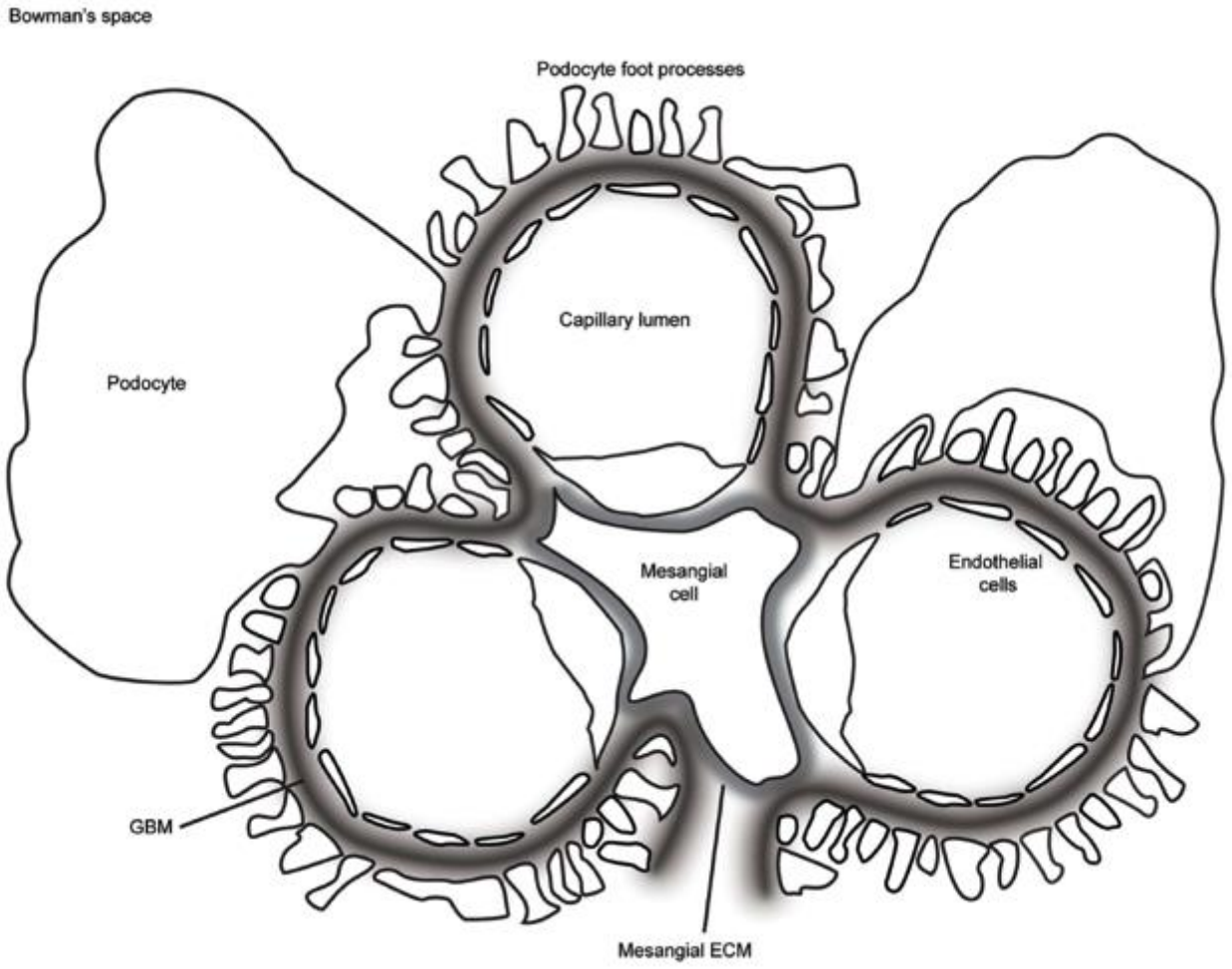
Causes of haemtauria in children

- Glomerular
  - Glomerulonephritis
    - C3 deposition
    - IgA disease (Henoch-Schönlein Pupura)
  - **Basement membrane glomerulopathy**

- Non-glomerular
  - Infection, hypercalciuria, renal stone disease, polycystic kidneys, tumours, arteriovenous malformation, loin-pain-haematuria syndrome, fabricated/induced illness

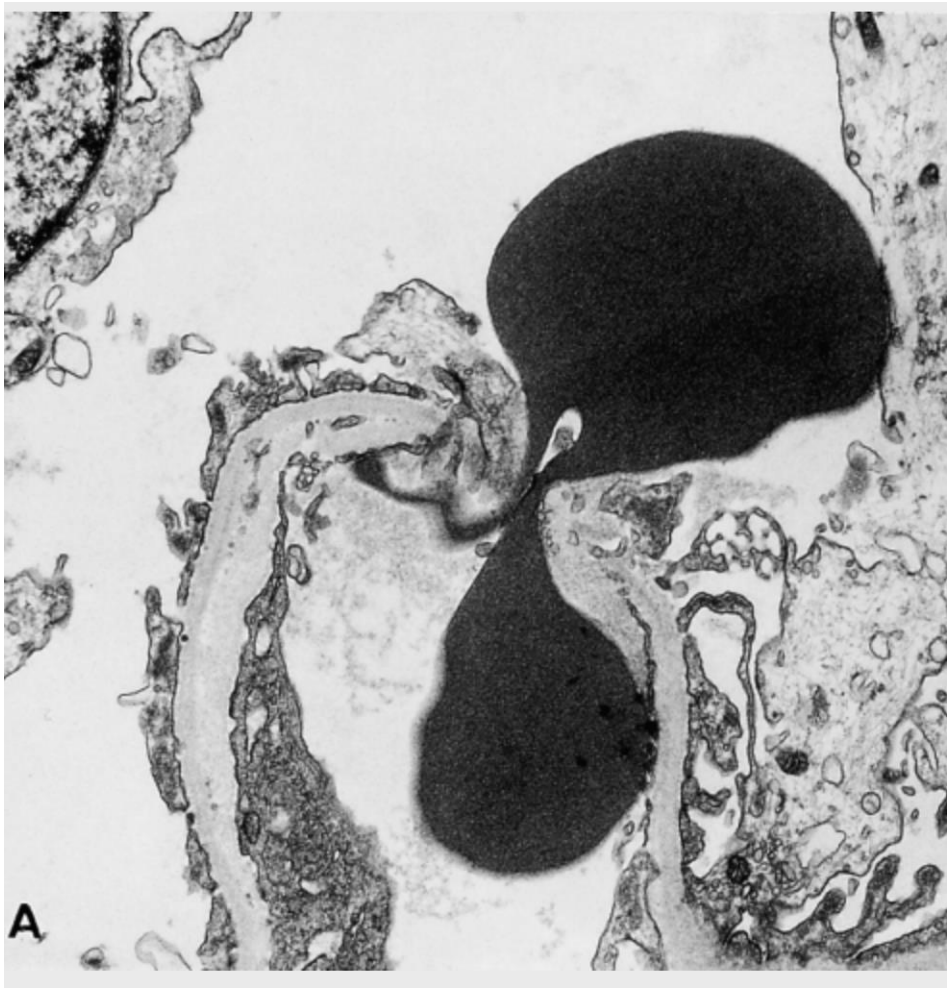
- 1% general population, 30-50% familial condition

A specialised capillary wall



Lennon R, Randles MJ, Humphries MJ:
The Importance of Podocyte Adhesion for a Healthy Glomerulus. *Frontiers 2014*

Red cell traversing the barrier



Collar JE, Ladva S, Cairns T and Cattell V:
Red cell traverse through thin glomerular basement membranes *Kidney International 2001*

Familial haematuria- genetics

- Alport syndrome
  - *COL4A3,4,5,6*
- Thin basement membrane nephropathy
  - *COL4A3,4*
- Epstein/Fechtner/Sebastian/May-Hegglin
  - Macrothrombocytopenia
  - *MYH9*
- Glomerulopathy with fibronectin deposits
  - *FN1*
- C3/CFHR5 glomerulonephritis
  - *CFHR5*
- More…

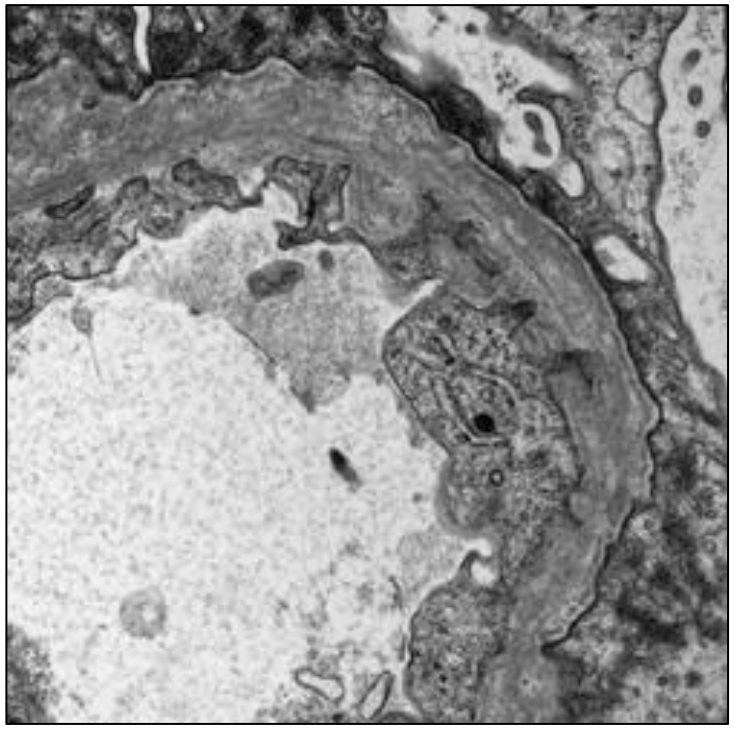
Alport Syndrome

- Cecil Alport 1927
- 'Hereditary nephritis', hearing loss, lenticonus

- Rare: 1-5000-1:10000
- 1-2% of ESRD

- Mutations
  - *COL4A3,A4*- autosomal recessive
  - *COL4A5*- X-linked

- Impaired collagen IV assembly
  - kidney, inner ear and eye



Irregular GBM, basket weave, Lamellation

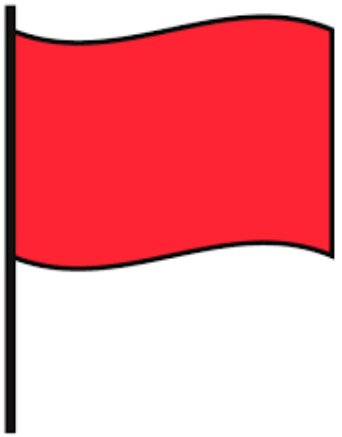
Collagen network required to maintain long term GBM integrity

Heterozygous mutations in *COL4A3/A4*

http://www.kidney-international.org clinical investigation

see commentary on page 1081

Rare hereditary COL4A3/COL4A4 va
be mistaken for familial focal segm
glomerulosclerosis



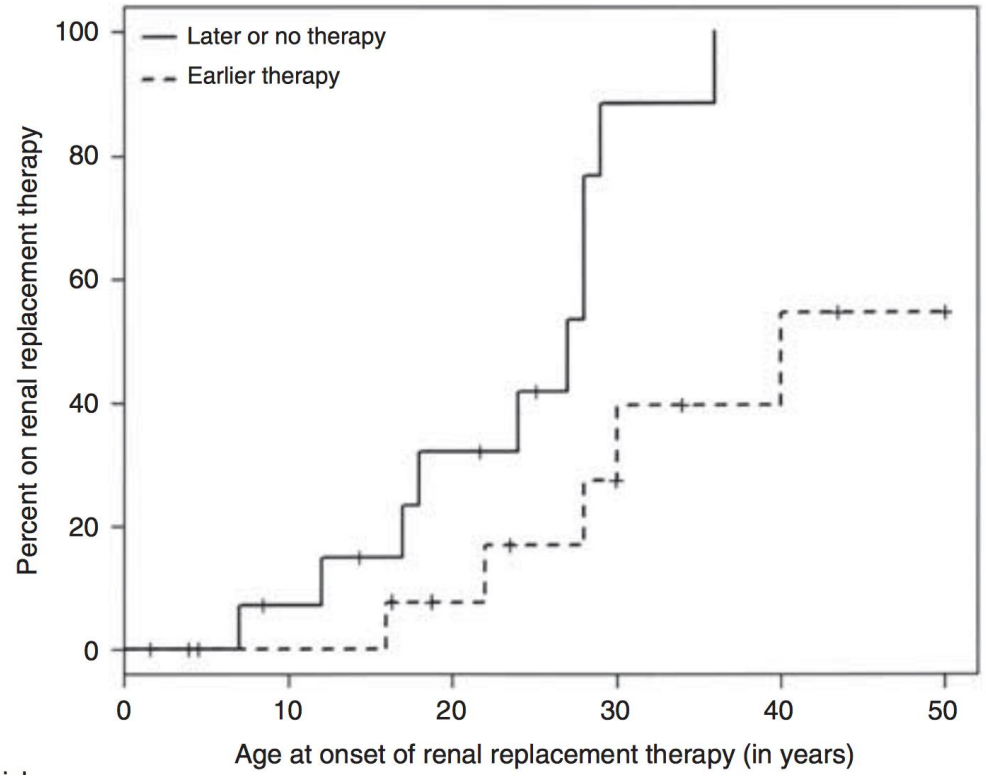
Andrew F. Malone[1,2], Paul J. Phelan[1,2], Gentzon Hall[1,2], Umran Cetinc
Andrea S. Alonso[1,4], Ruiji Jiang[1,4], Thomas B. Lindsey[1], Guanghong W
Stephen R. Smith[2], Nicholas J.A. Webb[5], Philip A. Kalra[6], Adebowale
Shaw[8],
Peter J. Conlon[9], J. Charles Jennette[10], David N. Howell[11], Michelle P.
and
Rasheed A. Gbadegesin[1,4]

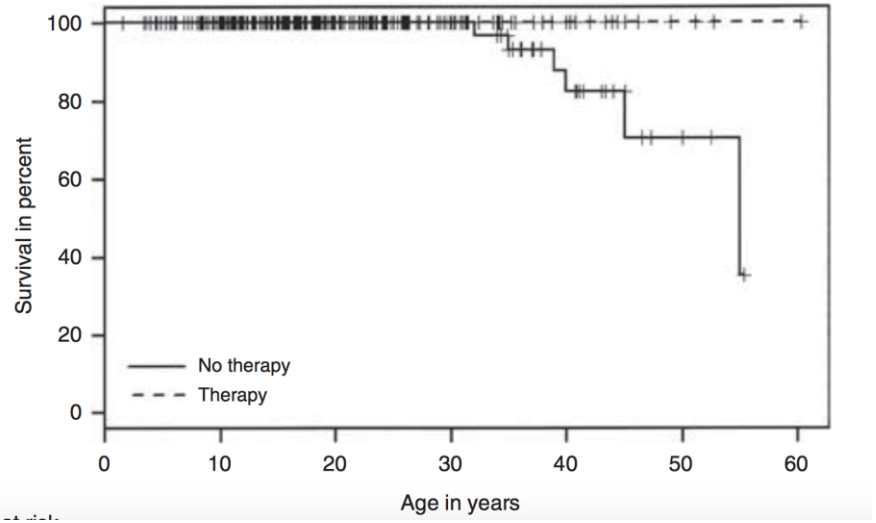
Blood pressure

- **Lifelong surveillance**

Intervention

Early angiotensin-converting enzyme inhibition in Alport syndrome delays renal failure and improves life expectancy





Oliver Gross *et al* Kidney International 2012

Intervention

- RAAS blockade:
  - ACE inhibition/Angiotensin receptor blockade
    - *Savige J, Gregory M, Gross O, Kashtan C, Ding J, Flinter F. Expert guidelines for the management of Alport syndrome and thin basement membrane nephropathy. J Am Soc Nephrol 2013;24(3):364-75.*
- Current trials
  - Anti-miR 21: Fibrosis
- Future trials

Summary

- Causes of haematuria
- Microscopic haematuria is **not benign**
- Importance of genetic testing
- Patient registry
- Lifelong surveillance: BP and urinalysis
- Use of RAAS inhibitors for persistent proteinuria