

# Ask the Expert

**Kjell Tullus, Manish Sinha & Rachel Lennon**

# Case 1

- 8 year old boy with abdominal pain
- Urine dip shows +++ blood
- Repeat test 2 weeks later when he is well shows ++ blood
- Has investigations
  - FBC, renal profile normal
  - Urine culture no growth
  - Urine microscopy confirms haematuria
  - Urine Ca:cr ratio and urine protein:creatinine ratio normal
  - US scan of kidneys normal

Do I need to do anything else?



**Manchester University**  
NHS Foundation Trust



The University of Manchester

# Persistent microscopic haematuria

Rachel Lennon

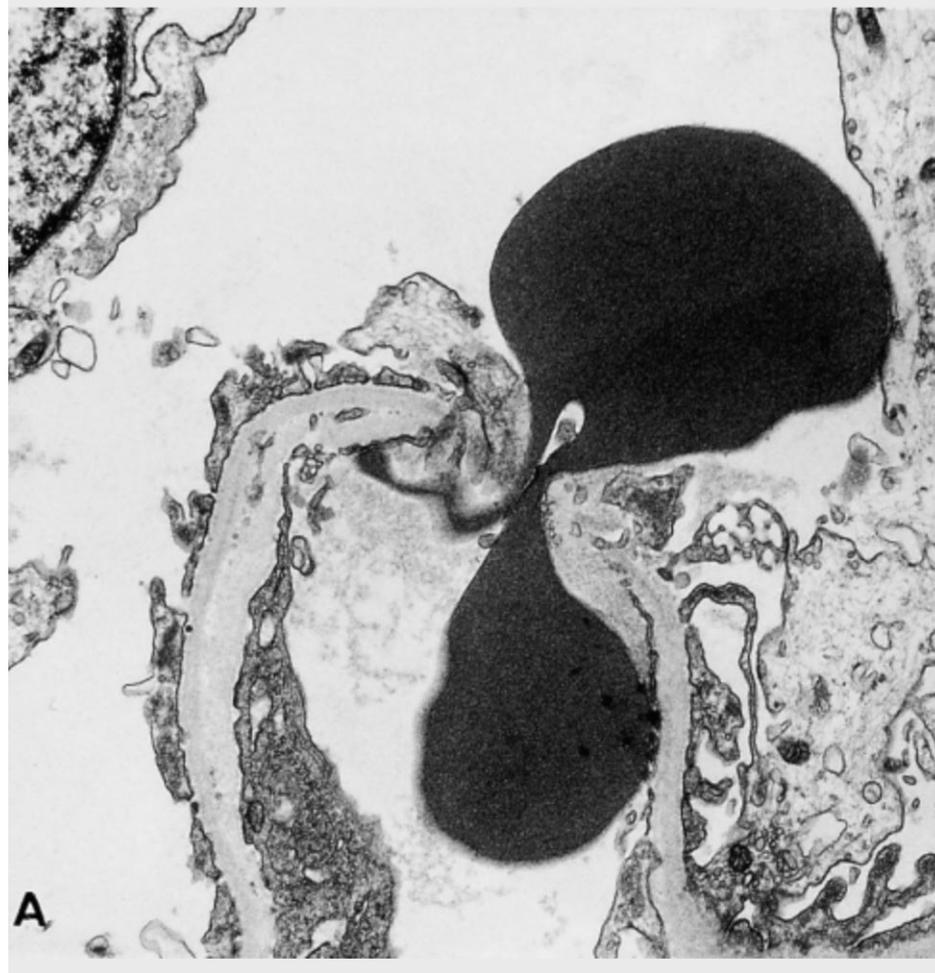
*Professor of Nephrology & Consultant Paediatric Nephrologist,  
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**Nephrology Study day 4<sup>th</sup> June 2019**

# Causes of haematuria in children

- Glomerular
  - Glomerulonephritis
    - C3 deposition
    - IgA disease (Henoch-Schönlein Purpura)
  - **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

# Red cell traversing the barrier



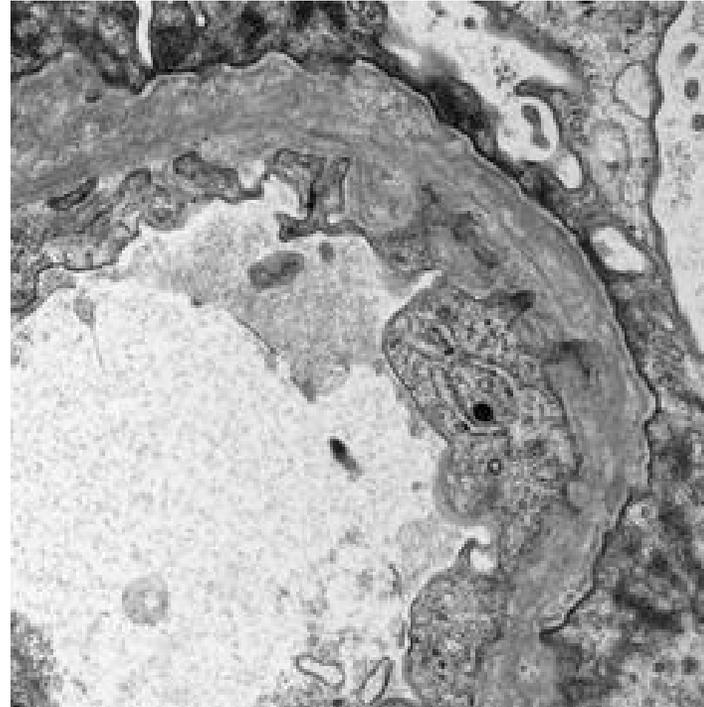
Collar JE, Ladva S, Cairns T and Cattell V:  
Red cell traverse through thin glomerular basement membranes *Kidney International* 2001

# Familial haematuria- genetics

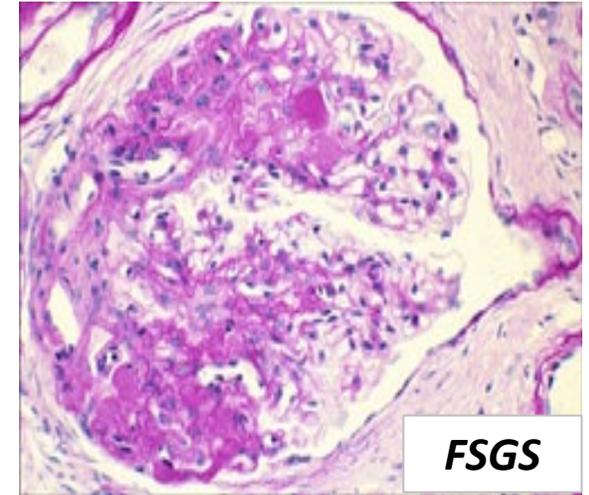
- Alport syndrome
  - *COL4A3,4,5,6*
- Thin basement membrane nephropathy
  - *COL4A3,4*
- Epstein/Fechtner/Sebastian/May-Hegglin
  - Macrothrombocytopenia
  - *MYH9*
- Glomerulopathy with fibronectin deposits
  - *FN1*
- C3/CFHR5 glomerulonephritis
  - *CFHR5*
- More...

# Alport syndrome

- Macro/microscopic haematuria
- Rare: 1-5000-1:10000
- 1-2% of ESRD
- Mutations
  - *COL4A3,A4*- autosomal recessive
  - *COL4A5*- X-linked
  - Heterozygous mutation
- Impaired collagen IV assembly
  - kidney, inner ear and eye



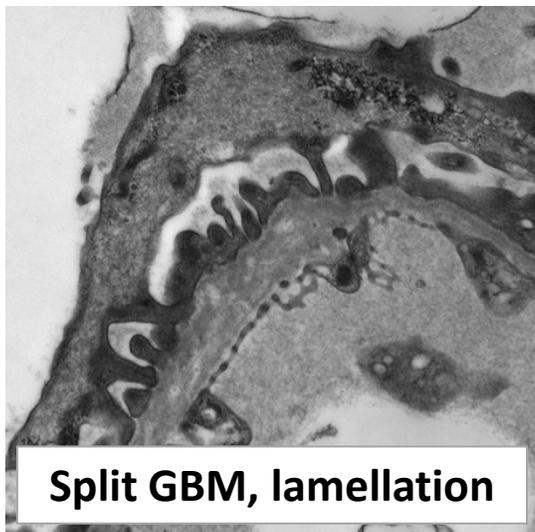
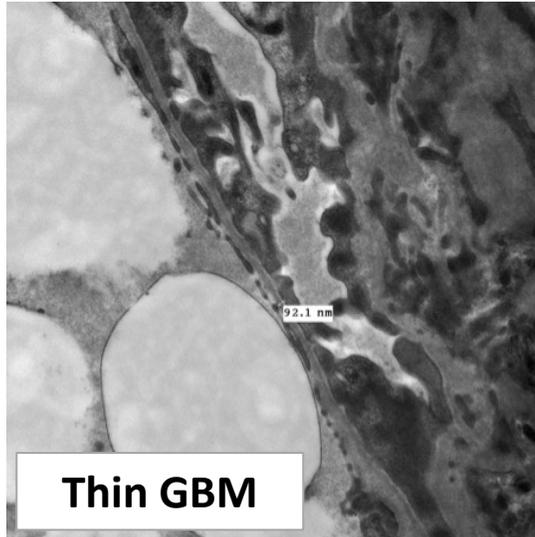
*Irregular GBM, basket weave, lamellation*



## ***COL4A3* Gene Variants and Diabetic Kidney Disease in MODY**

Yiting Wang,<sup>1</sup> Junlin Zhang,<sup>1</sup> Yingwang Zhao,<sup>1</sup> Shanshan Wang,<sup>1</sup> Jie Zhang,<sup>2</sup> Qianqian Han,<sup>1</sup> Rui Zhang,<sup>1</sup> Ruikun Guo,<sup>1</sup> Hanyu Li,<sup>1</sup> Li Li,<sup>1</sup> Tingli Wang,<sup>1</sup> Xi Tang,<sup>1</sup> Changzheng He,<sup>3</sup> Geer Teng,<sup>4</sup> Weiyue Gu,<sup>5</sup> and Fang Liu <sup>1</sup>

# Basement membrane vulnerability



- Alport syndrome
- Microscopic haematuria
- 1% population?
- Heterozygous *COL4A3/4/5*
- **Thin basement membranes**
- Variable progression
  - Genetic modifiers
- Environment
  - Blood pressure

## Management

### Lifelong surveillance

Reduce proteinuria

Hydrostatic pressure

Renal survival: 15 years

New agents

Bardoxalone?

# Case 2

- 13 year old girl
  - BMI 95<sup>th</sup> centile
  - BP 142/80mmHg
  - U&Es normal, TFT normal
  - US kidneys normal
- 
- Does she require further investigations?
  - Does she require anti-hypertensive treatment?

# Case 3

- 8 year old boy incidentally found to have ++ protein on dipstick
- No haematuria, BP normal
- First am urine protein:creatinine ratio 102mg/mmol
- U&Es normal, plasma albumin 34g/l
  
- What further tests (if any) are required?
- Does he need a kidney biopsy?
- Would you start an ACEi without need for biopsy?