

Ask the Expert

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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

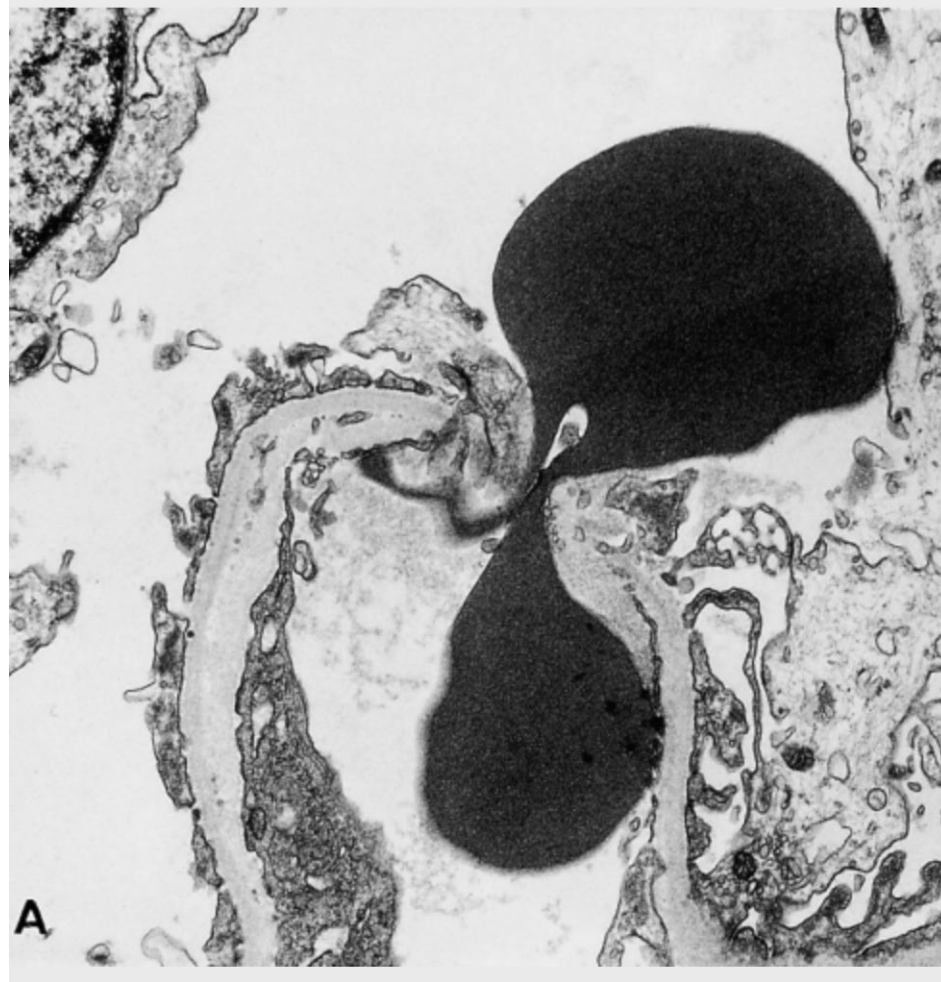
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Nephrology Study day 4th June 2019

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



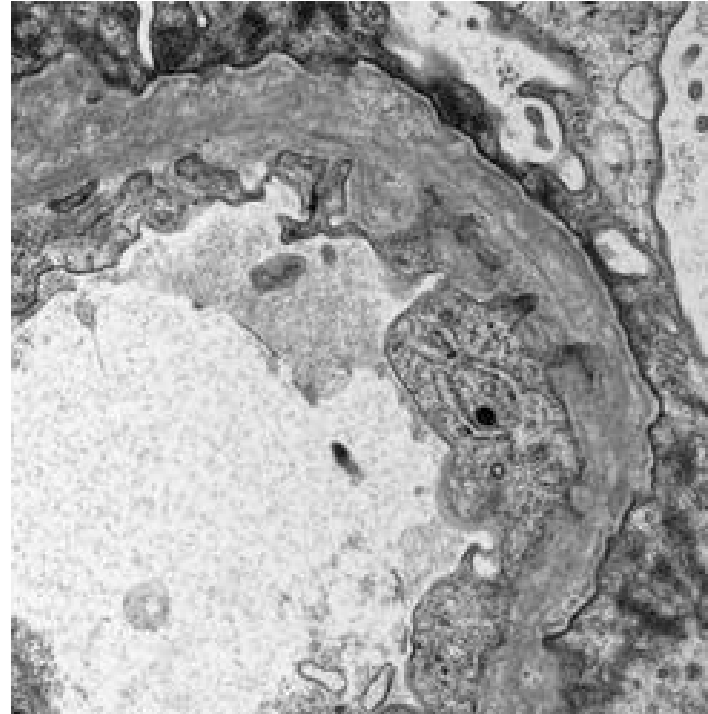
Collar JE, Ladva S, Cairns T and Cattell V:
Red cell traverse through thin glomerular basement membranes *Kidney International* 2001

Familial haematuria- genetics

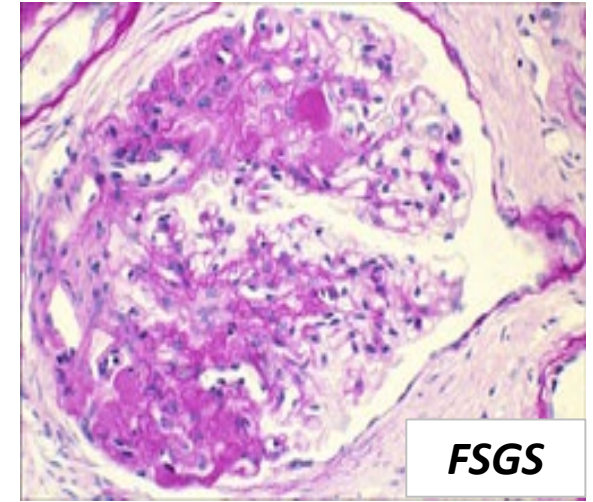
- Alport syndrome
 - *COL4A3,4,5,6*
- Thin basement membrane nephropathy
 - *COL4A3,4*
- Epstein/Fechtner/Sebastian/May-Hegglin
 - Macrothrombocytopenia
 - *MYH9*
- Glomerulopathy with fibronectin deposits
 - *FN1*
- C3/CFHR5 glomerulonephritis
 - *CFHR5*
- More...

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



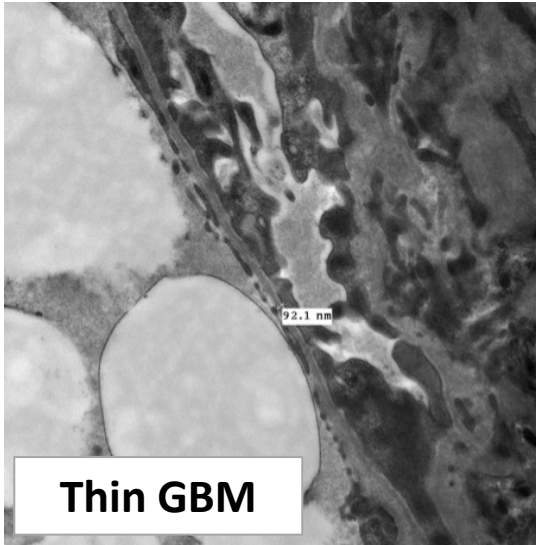
Irregular GBM, basket weave, lamellation



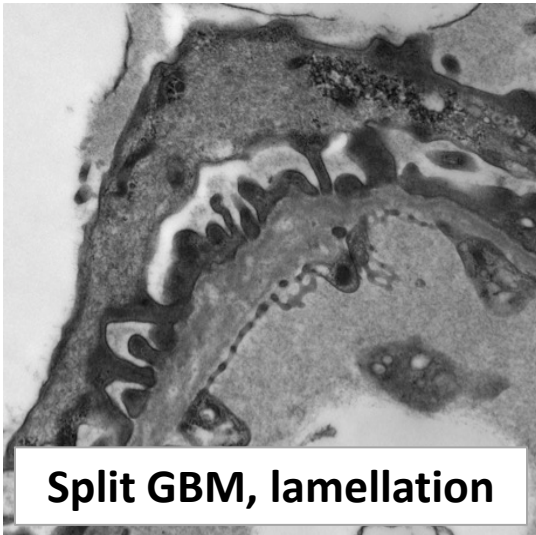
***COL4A3* Gene Variants and Diabetic Kidney Disease in MODY**

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

Basement membrane vulnerability



Thin GBM



Split GBM, lamellation

- 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 95th centile
 - BP 142/80mmHg
 - U&Es normal, TFT normal
 - US kidneys normal
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- 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
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- What further tests (if any) are required?
 - Does he need a kidney biopsy?
 - Would you start an ACEi without need for biopsy?