

A teenage girl with microscopic haematuria and mild proteinuria

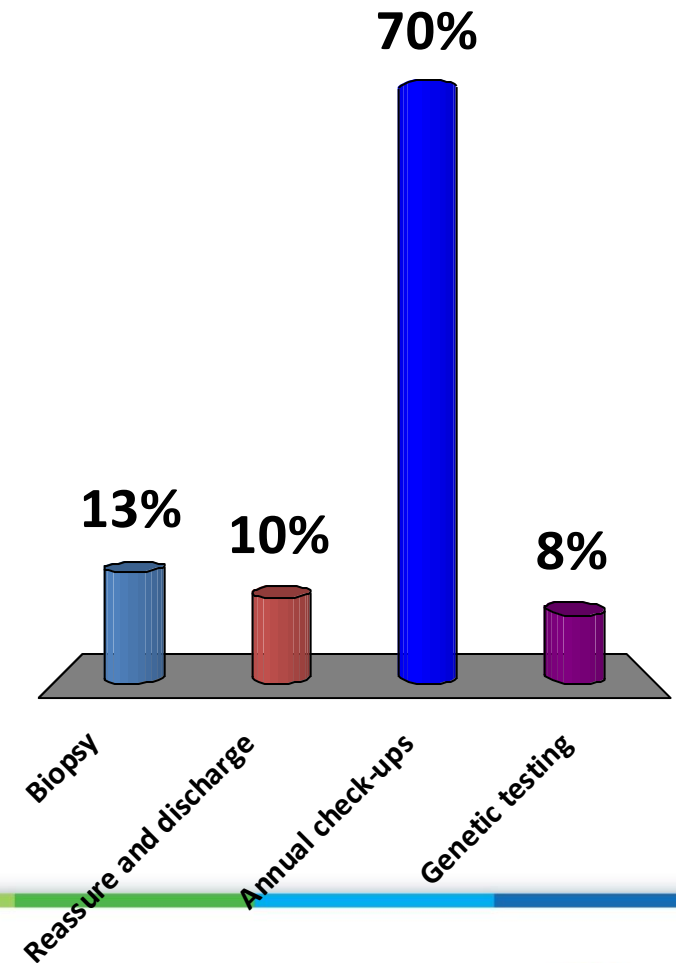
Rodney D Gilbert

12 year old girl

- Referred with microscopic haematuria
- No proteinuria
- Neither parent had haematuria
- No family history of CKD
- Normal BP
- Normal creatinine, C3, C4, ASOT and ANA

What would you do?

- A. Biopsy
- B. Reassure and discharge
- C. Annual check-ups
- D. Genetic testing

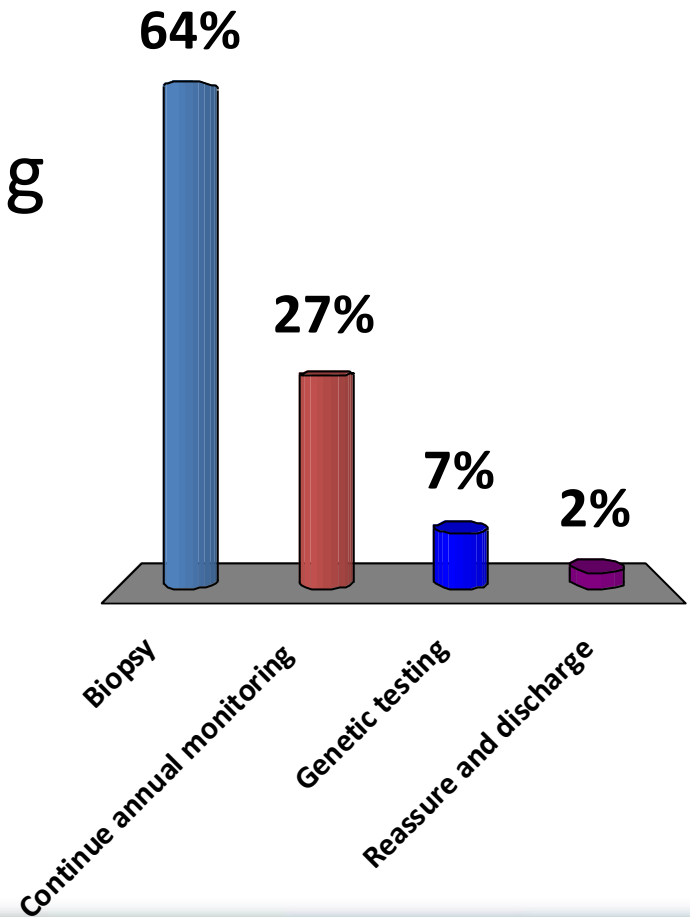


1 year later

- Mild proteinuria (UPC 33, UAC 14)
- Normal BP, creatinine
- No fever, arthralgia, rash
- Referred back
- What is the likely diagnosis?
 1. Thin basement membrane disease
 2. IgA nephropathy
 3. Alport syndrome
 4. SLE

What is the next step?

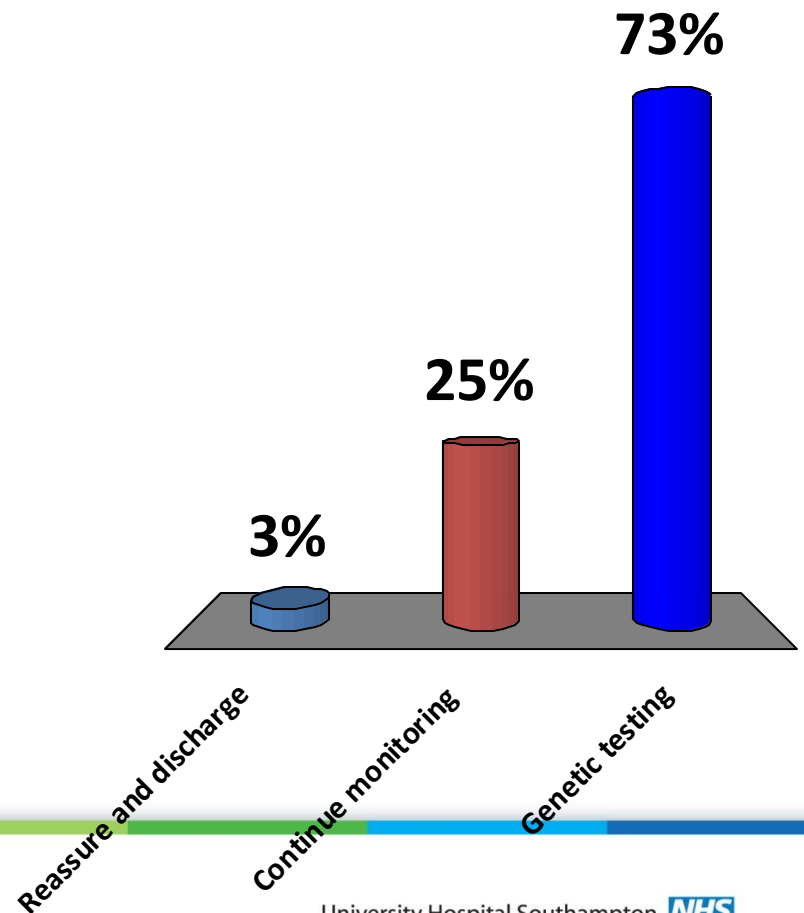
- A. Biopsy
- B. Continue annual monitoring
- C. Genetic testing
- D. Reassure and discharge



What do you do now?

**Biopsy: Normal light microscopy,
Immuno-staining negative**

- A. Reassure and discharge
- B. Continue monitoring
- C. Genetic testing



EM

- Basement membranes show heterogenous thickness and areas of rarification of the lamina densa and increased thickness of the lamina rara.

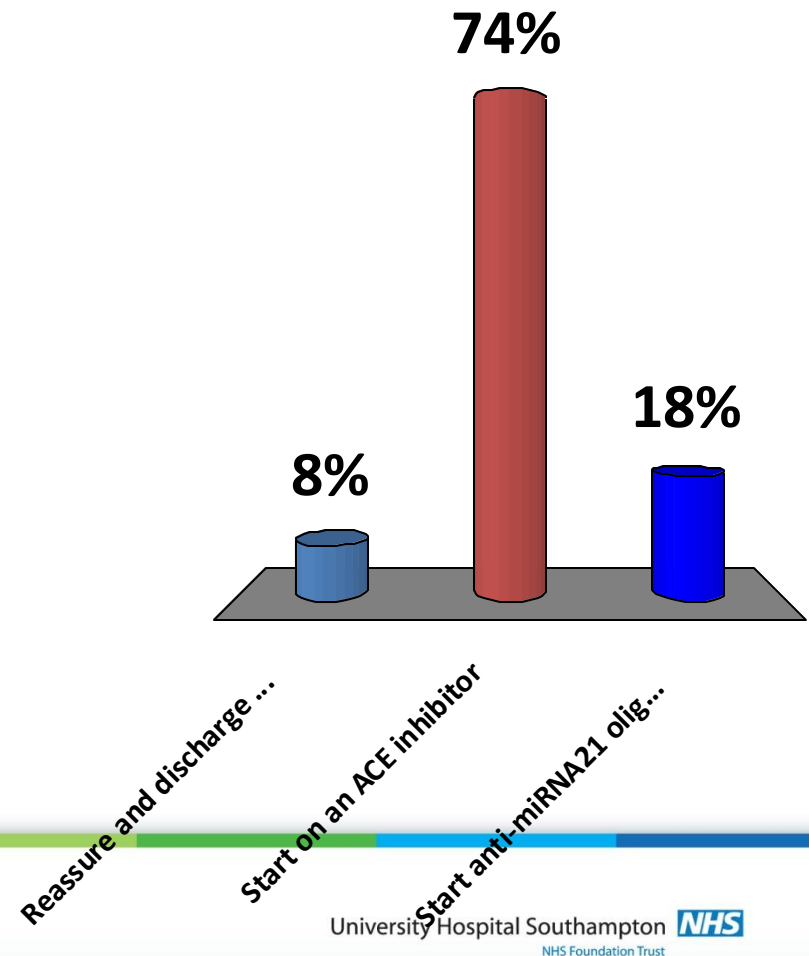
Genetics

- Mutation of *COL4A5*: c.2142delC; p.Gly716fs
- Presumed *de novo* (about 15%)

Female heterozygous X-linked Alport

What do you do now?

- A. Reassure and discharge because she is female
- B. Start on an ACE inhibitor
- C. Start anti-miRNA21 oligonucleotides



X-linked Alport syndrome in females

- Often undiagnosed
- “Affected” not “carriers”
- Twice as many affected women as men
- 15 to 30% ESRD by 60 years
 - Hypertension
 - Pregnancy
 - Other renal disease
 - Nephrotoxic drugs
- Hearing loss is common

Risk factors for ESRD

- Early onset ESRD in male relatives / severe genotype
- Deafness
- Proteinuria

Management

- RAAS blockade from onset of albuminuria
- Treat hypertension
- Avoid nephrotoxic drugs
- Healthy diet and weight
- No smoking
- Monitor hearing
- Psychological support
- Pregnancy: RAAS blockade and other complications
- Genetic counselling

Summary

- X-linked Alport syndrome is not benign in females
- It should be actively diagnosed and treated
- Comprehensive approach required