Webinars for patients

Sickle Cell Disease

Topic on Focus

EuroBloodNet

Polyuria and enuresis: kidney damage in sickle cell disease

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Conflicts of interest

Advisory boards, steering and data monitoring committees

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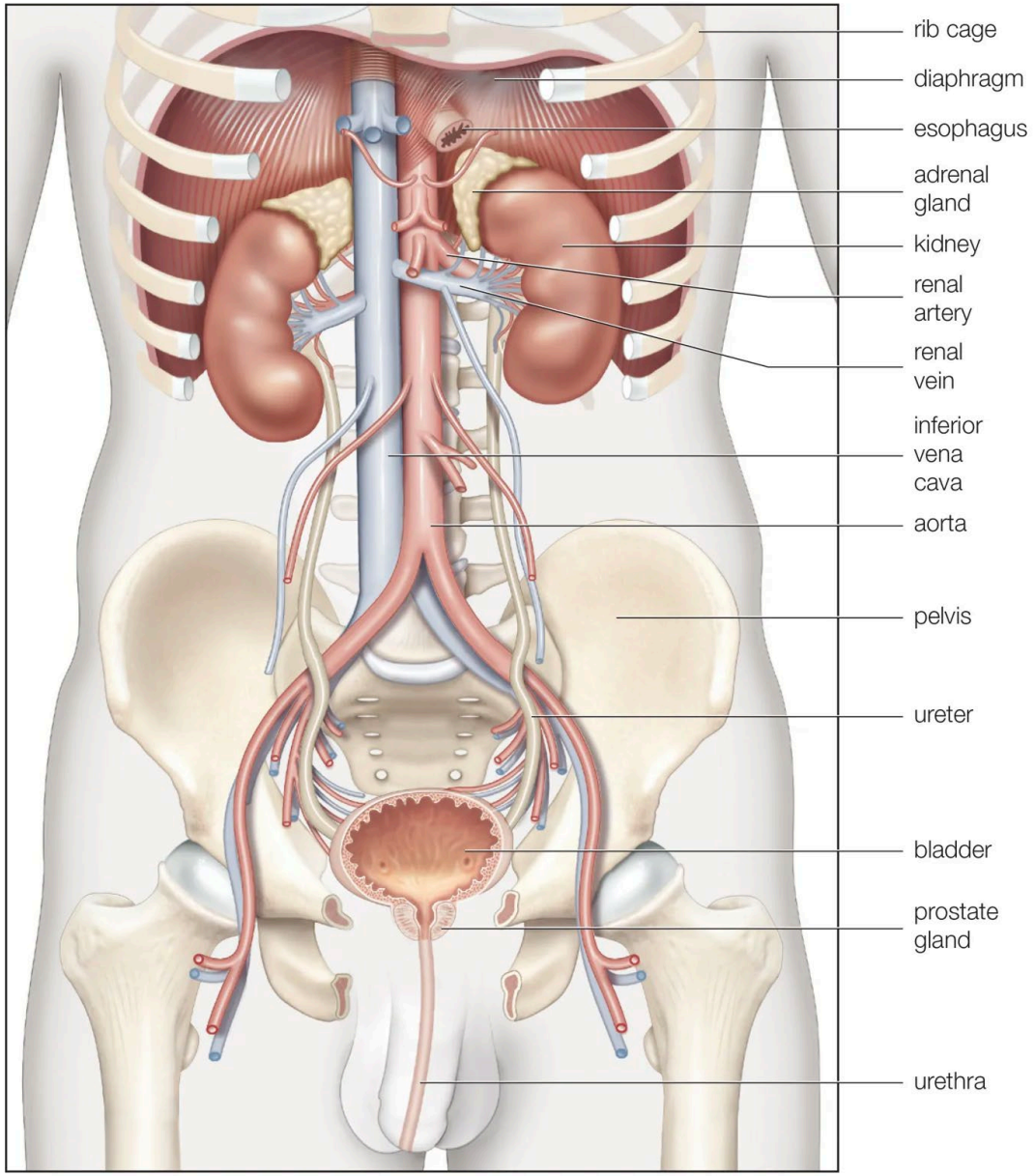
AstraZeneca

Kidneys

- **Functions of kidneys**
  - **Filter blood and remove toxins and waste products**
  - **Produce urine**
  - **Produce hormones which control blood pressure**
  - **Produce erythropoietin which drives production of red blood cells**

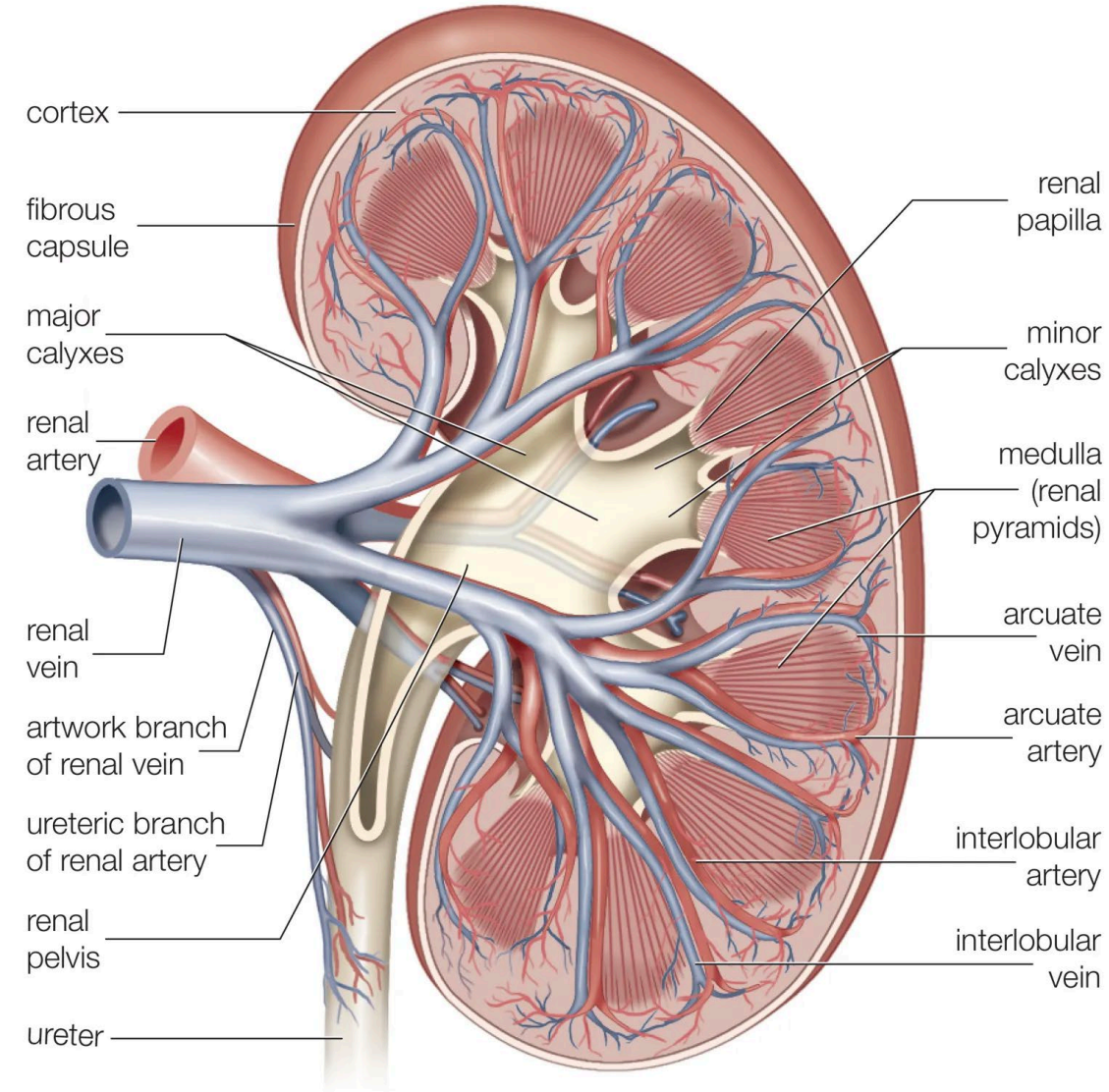
Kidneys



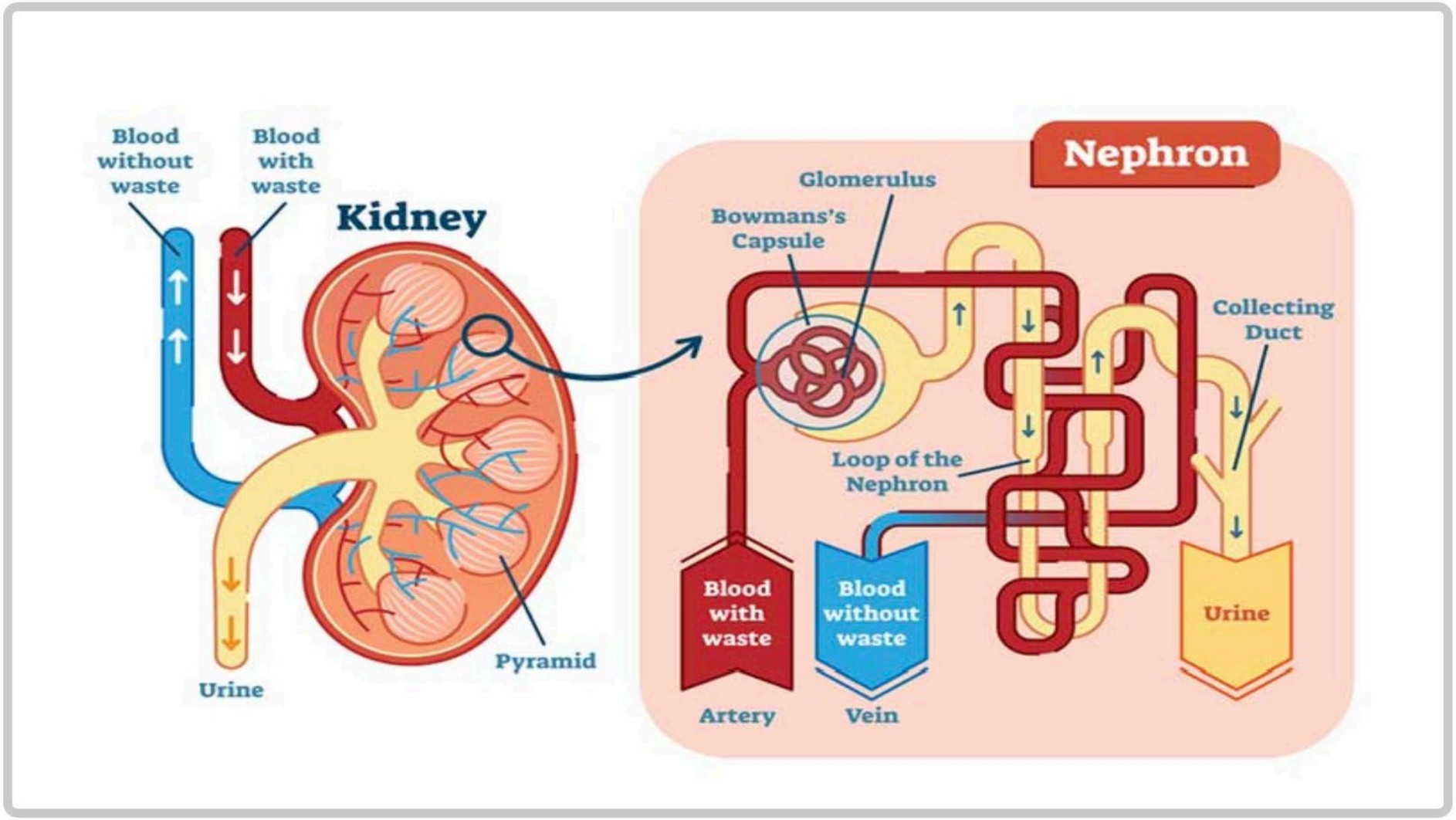
Normal kidney function

- Blood goes into kidneys through large artery, which branches into lots of much smaller arteries
- Smaller arteries go to lots of tiny filters
  - Each filter is called a glomerulus
- Filter separates cells from plasma
  - Plasma goes through thin tubes into the middle (medulla) of the kidney
  - Harmful chemicals and waste products removed from plasma to form urine
  - Clean plasma returns to blood
  - Urine passes to bladder through small tubes called ureters

Kidney



Normal kidney function



Kidneys Are Often Damaged in Sickle Cell Disease

- Conditions in kidney promote sickling
  - Low oxygen levels
  - Acidic environment
  - High concentration of chemicals causing red cell dehydration
- Rigid sickle cells damage blood vessels in kidneys
  - Damages tissue in the kidneys, reducing function
- Anaemia, inflammation, abnormal clotting may all contribute to kidney damage
- Some drugs may damage kidneys

Kidney problems in sickle cell disease

- **Kidney failure**
  - **Sickling gradually infarcts kidney tissue, reducing ability to filter blood**
  - **About 30% adults develop renal failure as they get older**
- **Blood in urine (haematuria)**
  - **Sometimes damaged kidneys bleed into urine**
  - **Usually stops without need for treatment**
  - **Occasionally blood clots form and block passage of urine**

Kidney problems in sickle cell disease

- **Leaky kidneys**
  - **Kidneys should acts as a filter, and keep proteins in the blood, and let waste products go into urine**
  - **Damage to kidneys results in proteins leaking into urine**
    - **Particular albumin (main protein in plasma)**
  - **Small amounts albumin present in urine of many children with sickle cell disease**
  - **This increases with age, and becomes a problem in about 20% adults**

Kidneys in sickle cell disease

- **Other kidney problems in sickle cell disease**
  - **Increased urine production**
    - **Volume of blood going throught the kidneys is increased**
    - **Increased volume of urine produced - polyuria**
    - **Starts to occur in first year of life**
  - **Not certain why this occurs**
    - **Maybe effects of anemia**
    - **Decreased sensitivity to some hormones**

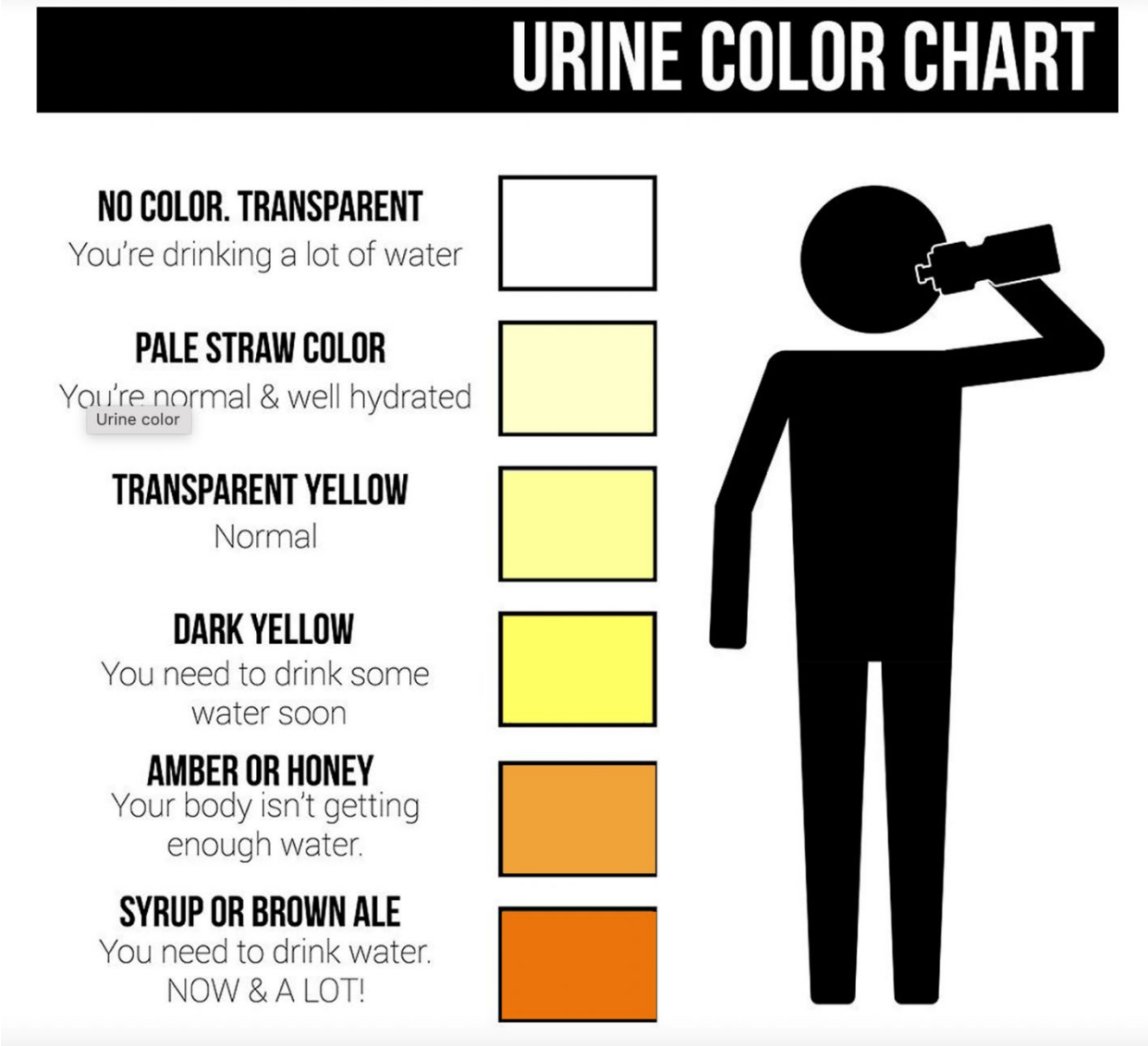
Kidneys in sickle cell disease

- Dilute urine containing lots of water
  - Normally, dehydration causes kidney to keep more water in the body, making urine more concentrated
    - Impaired in sickle cell disease
  - Normally at night small volume of concentrated urine produced
    - Also impaired in sickle cell disease
  - Problems occur because of
    - Damage to kidney reduces ability to make concentrated urine
    - Reduced sensitivity to hormone which makes urine more concentrated
      - Vasopressin or ADH
  - In sickle cell disease
    - Larger volumes of dilute urine produced
    - Increased risk of dehydration if not drinking enough
    - Increased urine production at night

Polyuria in sickle cell disease

- **Polyuria: producing excessive amounts of urine**
  - More than 3 litres per day in adults
- **Many different causes, apart from sickle cell disease**
  - Drinking excessive water
  - Alcohol and caffeine
  - Medicines, including diuretics
  - Diabetes
- **Maximum urine concentration**
  - Adults – 1200 mOsm/kg
  - Adults with sickle cell disease – 450 mOsm/kg
  - Chinchillas – 7600 mOsm/kg

Urine in sickle cell disease



Urine colour more difficult
To interpret in sickle cell disease, as urine usually darker due to jaundice caused
by high bilirubin levels

Consequences of polyuria in sickle cell disease

- Increased risk of dehydration, particularly if
  - Very hot rooms or weather
  - Diarrhoea or vomiting
  - Water or other drinks not easily available
  - Sedation from drugs, such as opiates, making drinking difficult
- Dehydration increases tendency of red cells to sickle, possibly triggering acute painful episodes
- Increased amount of urine particularly at night

Drinking in sickle cell disease

- As for everyone, need to replace lost water
- Little evidence on exactly how much water people with sickle cell disease should drink
  - In normal conditions should not need much more than other adults
    - About 3 litres per day
  - Need to increase fluid more than normal when increased fluid losses
    - Hot weather with excessive sweating
    - Diarrhoea or vomiting
- Should avoid prolonged periods of time without drinking
- Possible benefit associated with increasing fluids above normal needs, although very uncertain and potentially dangerous

Intravenous fluids in sickle cell disease

- Intravenous fluids often given when people unwell in hospital with sickle cell disease
- Very little evidence on how useful iv fluids are
- Important if:
  - Very dehydrated
  - Unable to drink
  - Significant diarrhoea and vomiting
- Oral fluids better if possible
- Disadvantages of intravenous fluids
  - Damage to veins
  - Risk of too much fluid or abnormal electrolytes

Enuresis

- Enuresis – involuntary urination
  - Nocturnal enuresis – wetting at night
  - Daytime enuresis – wetting during day
  - Primary enuresis – children who have never learnt to be dry
  - Secondary enuresis – children who were dry but then start wetting

Nocturnal Enuresis

- **Nocturnal enuresis**
  - Bed wetting occuring, after the age of 5 years, at least twice per week for at least 3 months
- **In general population**
  - Tends to run in families
  - More common in boys than girls
    - Age 5: 7% males, 3% females
    - Age 10: 3% males, 2% females
    - Age 18: 1% males, very rare in females
  - Increased in sickle cell disease, diabetes, constipation, obstructive breathing during sleep

Nocturnal Enuresis in Sickle Cell Disease

- Nocturnal enuresis is more common in sickle cell disease
  - 5 years old: 30 – 50%
  - 10 years old: 15 - 20%
  - 15 years old: 10 - 15%
  - 20 years old: 5 - 10%
- Reasons for increased nocturnal enuresis in sickle cell disease
  - Higher urine output during the night
  - Encouragement to drink water during night
  - Bladder instability
  - Obstructive breathing during sleep

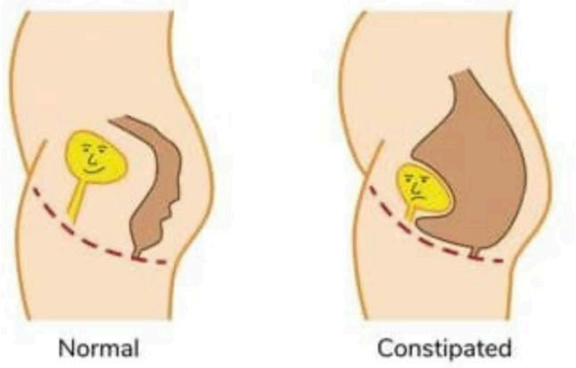
Nocturnal Enuresis in Sickle Cell Disease

—Problems associated with nocturnal enuresis

- Disrupts sleep
- Cost of and time spent washing sheets frequently
- Associated with anxiety and depression
- Difficulties with sleepovers and school trips

Managing nocturnal Enuresis in Sickle Cell Disease

- **Basic measures**
  - Protective sheets
  - Limited role of nappies and pull-ups, particularly in older children
    - Concern that this delays recovery from enuresis
  - Testing for urine infection
- **Drinking**
  - Stop drinking water and fluids about 1 hour before bed time
  - Avoid drinking water during the night
  - Possibly sip water if mouth very dry
- **Treating constipation**
  - Constipation increases problems with enuresis
    - Faeces in bowel compress bladder in pelvis
  - Treat constipation with diet, laxatives etc



Managing nocturnal Enuresis in Sickle Cell Disease

–Treating obstructive breathing at night

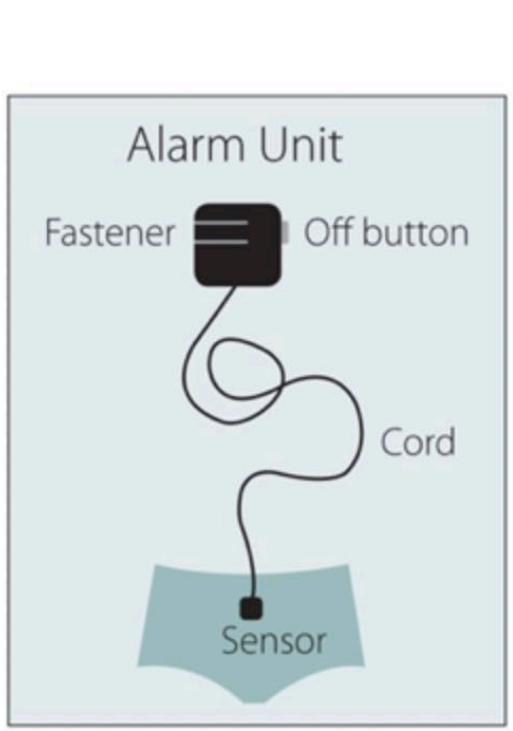
- History of loud and persistent snoring
- Sometimes associated with very deep sleep
- Potential benefit from overnight oxygen
- Tonsillectomy if tonsils enlarged or inflamed

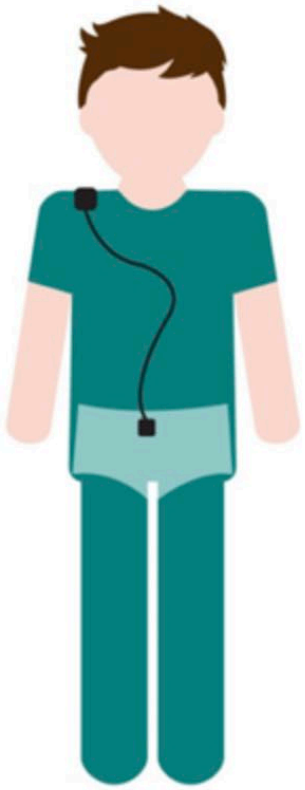
Managing nocturnal Enuresis in Sickle Cell Disease

Waking during night

- Parent wakes child and takes them to toilet (lifting)
- Enuresis alarm – detects wetness and makes noise
  - often too late
  - child sleeps through alarm
- Child sets alarm for fixed time during night
- Child learns to wake up when bladder full and goes to toilet
  - Nocturia
  - Reported by 80% patients with sickle cell disease

Enuresis alarms





Alarm unit fastens onto outside of pajama top at shoulder

Cord runs under pajama top from alarm unit to sensor

Sensor clips to underpants

Reducing amount of urine made at night

- Avoid drinking at night
- Desmopressin
  - Desmotabs or Desmomelts
  - Hormone which acts on kidneys to reduce amount of urine produced
  - Potentially fewer episodes of enuresis
  - Continue for up to 3 months, but stop after 4 weeks if no response

Bladder instability

- Bladder contracts unpredictably in some children, causing enuresis
- May also be associated with day time wetting or urgency
- Some drugs increase bladder stability and improve enuresis
  - Oxybutinin
  - Tolterodine
  - Imipramine

Support

- Referral to bladder clinic
  - Usually if child still wet most nights age >7 years
  - Scan of bladder may be helpful to make sure bladder fully empties
  - Detailed advice about alarms, drugs
- Psychology
  - Able to explore possible causes related to stress, anxiety, family events
  - Help support child and family with stress associated with enuresis
- Patient information and websites
  - eric.org.uk

Support

More information

Tips for using a bedwetting alarm

Tips for getting the most out of your alarm and increasing your child's chance of success.

Read more

George's experience

A teenager's experience of bedwetting including tips for managing this condition from George's point of view.

Read more

Bladder health

Advice and tips for keeping your child's bladder healthy and working properly.

Read more

Summary

- Enuresis common in sickle cell disease
- Investigation and treatment if persistent age > 7 years
- Resolves in most cases as children learn to wake up and pass urine during night
  - 80% patients with sickle cell disease report nocturia
- Benefits from not drinking at night, avoiding constipation