CLCN5 & Dent Disease

What is Dent Disease?

- Dent Disease is an inherited kidney condition caused by changes in the genes CLCN5 or OCRL – CLCN5 causes type 1, and OCRL1 causes type 2.
- A change in one of these genes prevents the kidney from functioning normally, and the kidney will eventually fail.
- Affected individuals usually begin to show symptoms in childhood.
- It occurs almost exclusively in males.

What is CLCN5, and how do changes in CLCN5 affect the kidneys?

- The CLCN5 gene plays a number of roles, both in cell structure and function.
- A change in CLCN5 can result in Dent Disease Type 1.
- The change leaves kidney cells unable to reabsorb important nutrients into the bloodstream. These nutrients are excreted through urine instead.
- This results in the signs and symptoms of Dent Disease; increased urination, large proteins and excessive calcium in the urine, calcium deposits in the kidneys, and kidney stones, which cause abdominal pain and blood in the urine.
- In most affected individuals, progressive kidney problems lead to kidney failure in early to mid adulthood.

Do these changes have effects on other parts of the body?

- Type 1 may also be associated with bone disease.
    - Due to the excessive loss of calcium from the body, rickets may occur. This can present in childhood, and is associated with weakening and softening of the bones, bone pain, bowed legs and difficulty walking.

How is Dent Disease treated?

- Therapies which reduce the amount of calcium excreted may be prescribed.
- You may be recommended to have a diet high in citrate (citrus fruits, avocados, bananas etc.) which has been shown to slow down the progress of kidney dysfunction and help prevent kidney stones.
- If bone disease is present, you may be advised to take vitamin supplements and an oral phosphate therapy.
- In the event kidney failure, patients do well on dialysis and there are good outcomes with kidney transplant as the disease does not recur in the new kidney.

How is this change passed down through a family?

- Normally you have two copies of every gene – one from each parent. However, in the case of certain genes, only one copy is passed to males. CLCN5 is an example of such a gene.
- These genes are found on the X ‘sex chromosome’ – males have one X chromosome and one Y chromosome, while females have two X chromosomes.
- As a male has only one X chromosome, he will only have one copy of CLCN5.
    - If this copy is faulty, he will develop Dent Disease.
- Since a female has two X chromosomes, she will have two copies of CLCN5.
    - If one copy is faulty, she will not develop the syndrome as the other copy functions normally.
    - Females can only be carriers of the faulty CLCN5.
    - While carriers do not generally show signs or symptoms, some may have mild features of Dent Disease. Severe kidney problems are rare.
- Mothers may pass this faulty copy to their daughter, who will then also be a carrier.
- A faulty copy cannot be passed from an affected father to their son as the father only passes the unaffected Y chromosome to their son.

Should my family members be tested?

- As family members are at risk of passing on a faulty gene to any children they have, they may be offered genetic counselling when they reach adulthood.