University of Michigan Health System
The Department of Internal Medicine
Division of Nephrology

INFORMATION SHEET

GLOMERULAR DISEASES CLINIC

Alport Syndrome and Thin Basement Membrane Disease

Alport syndrome and Thin Basement Membrane Disease are inherited diseases of the filter part of the kidneys. Alport Syndrome is caused by large or particularly severe mutations in the genes which code for **collagen**, a protein that helps build the part of the kidney filters (glomeruli) that is called the **basement membrane**. The basement membrane is the "wall" part of the filter, and collagen is the bricks and cement that holds the wall together. When the basement membrane is weakened, the filters can become damaged and leaky, spilling blood and protein.

The diagnosis of Alport Syndrome is usually made by urine and blood tests, along with skin or kidney biopsy. These tests help determine how much the kidneys are affected, and look for specific signs of Alport Syndrome, as well as make sure there are no other causes of kidney disease. Since collagen helps build parts of the eye and ear, these also can be affected in Alport Syndrome. Hearing and eye exams are needed once the diagnosis of Alport Syndrome is made.

The severity of the disease depends on the particular mutation and how much it affects the building of the basement membrane. There are three different collagen proteins that can be involved in Alport Syndrome: COL4A3, COL4A4, and COL4A5. Mutations in COL4A3 and COL4A4 cause disease in both men and women with equal severity. Mutations in COL4A5, which is on the X chromosome, usually cause more severe disease in men. Some women, especially with the X chromosome form, have only a small amount of blood in their urine and never develop any serious kidney damage. Other people, especially men with the X-linked form, develop kidney failure and deafness in their early teens.

It is possible to have genetic testing to determine what kind of mutation an affected person carries. This may allow a better idea early on whether the kidneys are more likely to develop severe damage, and how rapidly this might occur. Right now the interpretation of these tests is somewhat difficult. But with more information being gathered, it is possible that genetic testing may become important in all patients with Alport Syndrome. Talking with a genetic counselor or a doctor specializing in Alport Syndrome can be a good idea before deciding on whether genetic testing would be helpful.

Thin Basement Membrane Disease (TBMD) is caused by less severe mutations in the same collagen proteins. Most often it occurs when the person affected has inherited only one copy of the gene with a mutation, and has another normal copy to help balance this out. Like Alport Syndrome, TBMD shows up with a small amount of blood in the urine found on routine exam. While TBMD does not cause severe kidney problems in most people, it really is just a mild form of Alport Syndrome. Since it is sometimes difficult early on to distinguish between the two, a presumed diagnosis of TBMD should be followed through the years with routine check ups. If high blood pressure or abnormal urine protein develops in a person with TBMD, further evaluation is needed.

For more information, the Alport Syndrome Foundation is at

https://www.alportsyndrome.org/index.html