Definition:

X-Linked Agammaglobulinaemia (XLA) was first described in 1952 by Dr. Ogden Bruton and is sometimes known as Bruton's Agammaglobulinaemia or Congenital Agammaglobulinaemia. It was one of the first immunodeficiency diseases to be identified. XLA is an inherited immunodeficiency disease in which patients lack the ability to produce antibodies, proteins that make up the gamma globulin or immunoglobulin fraction of blood plasma.

Antibodies are an integral part of the body's defence mechanism against certain micro organisms (e.g. bacteria, viruses); they are important in the recovery from infections, and also protect against getting certain infections more than once.
Antibodies are produced by specialized cells in the body called plasma cells. The development of plasma cells proceeds in an orderly fashion from stem cells located in the bone marrow, to B-lymphocytes. On contact with a foreign substance called an antigen (such as a micro organism) B-lymphocytes mature into the plasma cells that produce and secrete antibodies. Patients with XLA have mutations in a gene that is necessary for the normal development of B-lymphocytes.
This gene, discovered in 1993, is named BTK, or Bruton's Tyrosine Kinase, in honour of the discoverer of the disorder, Dr Bruton. As the name of the disorder suggests, the BTK gene is located on the X chromosome.

CLINICAL PRESENTATION:

As they lack antibodies, patients with X-Linked Agammaglobulinaemia (XLA) are prone to develop infections. The infections frequently occur at or near the surfaces of mucus membranes, such as the middle ear, sinuses and lungs, but in some instances can also involve the bloodstream or internal organs. They also may have recurrent gastrointestinal tract infections that can cause diarrhoea (gastroenteritis). In patients without antibodies, any of these infections may also penetrate the mucosal surface, invade the bloodstream and spread to other organs deep within the body, such as the bones, joints or brain. Infections in XLA patients are usually caused by micro organisms that are killed or inactivated very effectively by antibodies in normal people. The most common bacteria that cause infection are pneumococci, streptococcus, staphylococcus and Haemophilus influenzae. Some specific kinds of viruses may also cause serious infections in these patients.

DIAGNOSIS:

When a patient is suspected of having X-Linked Agammaglobulinaemia (XLA), the diagnosis is established by several tests. In XLA all of the immunoglobulins (IgG, IgM, and IgA) are markedly reduced or absent in the blood. The most characteristic laboratory feature of XLA is the absence of B-lymphocytes in the blood. This is the most reliable test, since it is not influenced by age, previous immunizations, or the IgG that the baby received across the placenta from the mother. Finally, it is now possible to test the BTK gene itself for errors or mutations.

INHERITANCE:

X- Linked Agammaglobulinaemia (XLA) is a genetic disease and as such can be inherited or passed on in a family. It is inherited as an X-linked recessive trait. This is why boys are affected and females are the carriers. Now that the precise gene that causes XLA has been identified, it is possible to test the female siblings (sisters) of a patient with XLA, and other female relatives such as the child's maternal aunts, to determine if they are carriers of the disease. Carriers of XLA usually have no symptoms, but have a 50% chance of transmitting the disease to each of their sons.

TREATMENT:

At the present time, there is no way to cure patients who have XLA. At this time the defective gene cannot be repaired or replaced. However, patients with XLA can be given some of the antibodies that they can not make. The antibodies are supplied in the form of gamma globulins (or immunoglobulins) and can be given directly into the blood stream "intravenously" or just under the skin "subcutaneously". Gamma globulin is extracted from a large pool of human plasma consisting mostly of IgG and containing all the important antibodies present in the normal population. Recurrent or chronic infections of the mucus membranes, such as sinusitis or pneumonia, can occur in some patients with XLA despite the use of gamma globulin. In these patients, it may be necessary to use long courses of antibiotics or other therapies.
Finally patients with XLA should not receive any live viral vaccines, such as live polio, or the measles, mumps, rubella (MMR) vaccine. Although uncommon, it is possible that live vaccines (particularly the oral polio vaccine) in Agammaglobulinaemia patients can transmit the diseases that they were designed to prevent.

EXPECTATIONS:

Most X-Linked Agammaglobulinaemia (XLA) patients who are receiving gamma globulin on a regular basis will be able to lead relatively normal lives. They do not need to be isolated or limited in their activities. Infections may require some extra attention from time to time, but children with XLA can participate in all regular school and extracurricular activities, and adults can have productive careers and families. A full active lifestyle is to be encouraged and expected!

These booklets are designed to offer medical professionals, patients and their families' basic information about these rare disorders of the immune system.
For further information please contact your immunologist, paediatrician, physician or the National IDF Health Coordinator

Other booklets available:

Living with PID
What is IVIG Therapy
Recurrent infections
Common Variable Immune deficiency (CVID)
Genetic Testing & PID
Chronic Granulomatous disorder (CGD)
Selective IgA Deficiency

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Immune Deficiencies Foundation
Asia Pacific Alliance

The Immune Deficiency Foundation Asia-Pacific Alliance, IDFAPA.

An alliance of not-for -profit PID Patient support groups across the Asia Pacific Region.

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Living with Primary Immune Deficiency Disorders

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