

## **Burkitt's lymphoma: A cancer of the immune system.**

**Sometimes called small cleaved cell lymphoma, Burkitt's lymphoma is humanity's fastest growing tumor and is capable of doubling in just 24 hours.**

Burkitt's lymphoma is a rare form of Non-Hodgkin Lymphoma that affects thousands of people in the world. This is a cancer that can spread very rapidly. It is humanity's most aggressive tumor. It can double in size in just 24 hours.

Burkitt's lymphoma accounts for as many as 40% of all childhood non Hodgkin lymphoma patients worldwide. It also accounts for as many as 40% of all Non Hodgkin lymphomas in HIV/AIDS patients. It also can affect adults and in the US more than 50% of all Burkitt's lymphoma patients each year are adults.

There are three classifications for Burkitt's lymphoma. Immunodeficiency Burkitt's is basically related to transplant patients and HIV/AIDS patients. Endemic Burkitt's which is associated to equatorial Africa and the Sporadic form of Burkitt's that is "sporadic" or it just doesn't fall in to the other two classifications.

Currently, the exact trigger for Burkitt's is not known. DNA mutations are at the root, but what triggers these mutations to cause the cancer is not understood. With the progress being made in DNA studies, researchers believe that they are getting closer to an answer.

Burkitt's lymphoma is often misdiagnosed as an infection or some other ailment, perhaps because it is so rare. Not very many people have ever heard of this cancer and this includes physicians. The symptoms (listed below) also indicate other more common ailments, and chances are that a person presenting these symptoms probably does not have Burkitt's lymphoma. For a person who does have Burkitt's, however, early diagnosis is very important.

The symptoms of Burkitt's lymphoma are quite broad but may include some of the following.

1. Swollen stomach
2. Swollen lymph node in the neck, groin or elsewhere that swells rapidly.
3. Testicular swelling.
4. Weight loss.
5. Back Pain.
6. Night sweats

Although very aggressive, Burkitt's lymphoma has high cure rates especially with children, but it is cancer, and survival should never be taken for granted, because Burkitt's can become resistant to chemotherapy. The treatment for Burkitt's is also very brutal, where the chemotherapy regimens are some of the most powerful in the world.

## **The meaning of "Aggressive" in the context of Burkitt's lymphoma**

*Dr. Ian Magrath, International Network for Cancer Treatment and Research*

BL is often described as "aggressive" because the tumor can increase in size very rapidly due to its potential doubling time of close to a 24 hours under optimal nutrient conditions (it is one of a handful of extremely rapidly progressive tumors). The doubling time varies according to the tissue that the tumor cells reside in as well being different in tumors in different individuals, so that some tumors are more aggressive than others. Occasional cases, e.g., of tonsillar BL, may remain apparently localized for long periods, although such cases are very rare indeed and one should always assume that a tumor diagnosed as BL is likely to have the ability to grow very rapidly. Because BL often infiltrates tissues (i.e., insinuates itself between cells) rather than growing as a lump, patients may sometimes conceal more tumor in their bodies than is immediately apparent, this can change rapidly, even in the course of only a few days. Thus, even when a patient appears to have only a small amount of tumor, it is safer to consider the detection of BL as signifying a potential medical emergency. It is important to rapidly establish a firm diagnosis, and to determine the extent of disease (which is relevant to the choice of treatment regimens) as quickly as possible, so that treatment can be initiated within a few days of reaching the hospital where the patient will be cared for. Since BL is a rare disease, most non-specialists see few, if any, cases in a lifetime, and may not be aware of the need for urgency. In situations where it is difficult to access medical assistance, such as in equatorial Africa, patients may die before they receive medical attention, or be moribund on arrival at a tertiary care facility.

*Find more information at the following website:*

[www.burkittslymphomasociety.com](http://www.burkittslymphomasociety.com)

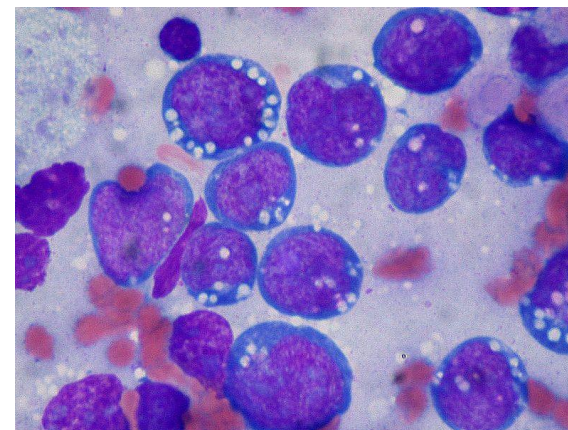


# Diagnosis – the Pathology of Burkitt Lymphoma

*Dr. Ian Magrath, International Network for Cancer Treatment and Research*

The usual method of diagnosing BL is to remove a piece of tumor, fix it in formalin (i.e., harden it), cut it into very thin sections that can be placed on glass slides, stain the cells with special dyes and look at them under the microscope at various degrees of magnification. When magnified markedly in this way, BL cells generally have a highly characteristic appearance (morphology), being round cells of intermediate size with a large central nucleus containing multiple nucleoli (2-5 areas where there is a lighter, rounded area within the nucleus). When stained by standard hematological dyes used to show up the morphological differences in various cell types, the cytoplasm is dark blue and contains many lipid vacuoles. Although, as cell populations go, BL cells are similar in size and shape, there are some tumors in which the cells are more variable than usual in that they contain a mixture of cell sizes, and may begin to resemble a related tumor called diffuse large B cell lymphoma (DLBCL). In some cases, it may be impossible to be certain, using standard microscopic and staining techniques, whether the tumor is a DLBCL or a BL and even highly experienced pathologists may disagree on the diagnosis. The pattern of protein expression by the cell (it's immunophenotype), however, can be determined with the aid of monoclonal antibodies, which are carefully layered over the tissue on the slide, incubated then washed and looked at under the microscope. Because these proteins relate to the degree of differentiation of the cells, they are usually referred to as "cluster of differentiation" (CD) proteins. BL and DLBCL tend to have somewhat different patterns, but there is no absolute distinction between the two using immunohistochemistry alone. Both BL and DLBCL characteristically expresses B cell markers such as CD20 and CD79, as well as immunoglobulin – most often of the IgM class. BCL6 protein, which is involved in the creation of germinal centers is also expressed on both tumors, as is Ki67, a protein associated with rapid cell division. Ki-67 is expressed to a much higher level on BL cells than on DLBCL, - almost all cells express it, but some DLBCL express high levels of Ki67; sometimes more than 90%. BL nearly always expresses CD10, a molecule expressed on immature B cells (including B cell acute lymphoblastic leukemia cells) as well as the cells of the germinal follicle. CD10 is not characteristic of DLBCL, however, although some 10% or so of cases may express it. BCL2, a protein which protects against apoptosis is the converse, frequently expressed by DLBCL (and sometimes genetically rearranged at the *BCL2* locus), and uncommonly by BL.

Thus, a typical BL Immunophenotype would be CD79a, CD20, CD10, BCL6 and Ki67, a typical DLBCL CD79a, CD20, and BCL6. Cells which have a more advanced degree of differentiation, and may resemble plasma blasts, tend not to express Ki67, but often express MUM-1 and CD138. For long, pathologists have recognized that some B cell lymphomas have a morphology that is not typical of either BL or DLBCL. These have been called variously, Burkitt-like lymphomas or atypical BL. The latter terminology is probably quite accurate because at the level of the gene expression pattern, these tumors are indistinguishable from BL. Thus, the morphology of BL is not well circumscribed. In fact some tumors which appear on morphology and immunohistochemistry to be typical DLBCL prove to have a gene expression pattern typical of BL (see below). Clearly, morphology, and Immunophenotyping by immunohistochemistry, although the most widely used methods of diagnosis, are not 100% perfect. Fortunately, DLBCL particularly in young people (up to the age of about 30 years) is nearly always of the germinal center cell subtype of this kind of tumor, and treatment with standard BL therapy is known to be very effective. In fact in children and adolescents, this would be the treatment of choice for DLBCL. Thus, it is not critically important to distinguish between these two morphologies in young people. In older individuals, BL tends to be less common, and it not as certain that DLBCL in this age group responds well to "BL therapy" since such tumors are treated by medical oncologists rather than pediatric oncologists who generally use different treatment regimens. In addition to study of the morphological and immunophenotypic characteristics of the cells, the chromosomal translocations present in the majority of BLs can be detected by a method known as *fluorescent in situ hybridization*. Briefly, the tumor cells are attached to glass slides and stained with *probes* consisting of DNA derived from a part or all of each of the genes involved in the translocations to which different colored fluorescent dyes have been attached (e.g., red for one gene and green for the other). Under appropriate conditions, the probes will bind (stick) to the genes present in the tumor cells. In normal cells, separated spots of each color can be seen, since the genes are on different chromosomes. In cells bearing a translocation the different colored spots are brought close to each other, or "fused" by the translocations. Two "fusions" can be seen – one for each of the chromosomes involved in the translocation, as well as separated spots of different colors where the probes have bound to the normal chromosomes (cells bear two copies of each chromosome, only one of which is involved in the translocation). BL cells may also be identified by a method known as molecular profiling, in which the pattern of expression of a large number of genes is examined. BL has been shown to have a distinct pattern, which differs markedly from the vast majority of cells diagnosed histologically as DLBCL. At present, this method is only carried out in research laboratories. The number of genes required to identify BL can, of course, be reduced to a minimum once the major differences between BL and related tumors such as DLBCL have been identified. Molecular or genomic profiling has shown that the majority of morphologically atypical BLs and a small number of DLBCL have a molecular profile typical of BL. For now, the gene expression pattern is considered to be the final arbiter of the type of lymphoma. However, this method remains a research tool for the time being.



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