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Immunosuppression and lymphomagenesis

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Individuals who are immunosuppressed are at an increased risk for developing aggressive, primarily B cell, lymphoproliferative disorders/lymphomas (LPDs). There are four clinical settings recognized by the WHO classification which are associated with development of LPDs: (1) primary immune disorders, (2) HIV infection, (3) iatrogenic immunosuppression following solid organ or allogeneic bone marrow transplantation and (4) methotrexate therapy, usually for an autoimmune disorder. The diagnosis of LPDs is often problematic and the prognosis of the patients difficult to predict. In some instances these immunodeficiency-related LPDs are clearly neoplastic, however, other cases, such as the major-

ity of those arising in the post-transplant setting, are difficult to classify due to their polymorphic appearance. Thus, the accurate diagnosis of these lesions usually requires not only morphologic examination, but also the use of immunophenotypic and genotypic techniques as well as correlation with viral content. The majority of these LPDs are Epstein Barr virus (EBV)-related. Thus, in situations where immunocompetence can be re-established these EBV-driven proliferations may regress without additional therapy. However, the development of genetic structural alterations in the setting of EBV-related lymphoid proliferation may result in malignant transformation.