a few facts about the ebv

dr. t.j. bugeja. m.d.

INTRODUCTION: The EBV as it is now known is none else than the Epstein-Barr Virus. The name was derived from those of the two groups of workers who independently observed the virus under the electron microscope for the first time.

The story dates back to 1958 when Dr. Denis Burkitt described the chief characteristics of Burkitt's lymphoma as it is now known. Very significant was the observation that this was mostly confined to the lower, hotter areas of Africa where mosquitos were common so that a mosquito-borne virus was tentatively held as the causative agent. Subsequently the examination under the electron microscope of suspension cultures of biopsy material from these lymphomas revealed the herpes-type virus now known as the EBV. With the development of an indirect immunofluorescence test for the detection of antibody to this virus it was not only discovered that antibody was present in the sera of many African and American children but that high EBV antibody titres were seen in patients with nascpharyngeal carcinoma, Hodgkin's disease, sarcoid, S.L.E. and infectious mononucleosis. In the latter heterophile antibody can be detected temporarily usually in the first 10 days of the illness. On the other hand this EBV antibody was found to persist indefinitely.

Soon evidence was available that EBV infection is worldwide and is even found among Eskimos and Indian tribes. It appeared that as soon as maternal EBV antibody disappeared from the child's blood, infection with the virus is liable to occur. Whilst in the developing countries and amongst children in poor socio-economic levels infection occurs early in life from orphanages, day nurseries and big families it tends to appear later in more civilised parts of the world. In the child it is thought that EBV infection causes a mild atypical form of infectious mononucleosis (IM) which confers long lasting immunity to further infection. In the adult the picture is more typical of IM. These ideas were strengthened by the fact that a mononucleosis due to EBV occurs following transfusion of EBV antibody-free persons with EBV positive blood.

The EBV is known to be cell bound and not easily released from infected cells. This might explain the low contagiousness of infectious mononucleosis. It also implies that intimate and prolonged oral contact is required to transfer these infected cells to the new host. Though these ideas are consistent with epidemiologic evidence EBV isolation from the saliva or the throat has not as yet been accomplished. In the new host heterophile, antibodies may appear in titres of 1 in 40 or more and may transiently increase. As already mentioned EBV antibody is more permanent and a titre of 1 in 160 is suggestive of recent infection. It does not matter which is detectable first and neither has any relation to the clinical severity of the disease. In children not uncommonly one finds no heterophile antibodies in the presence of EBV antibodies; these are liable to show a milder form of infectious mononucleosis with less marked changes in the blood and hepatic function. The hospital stay in these cases would also be a short one. However, in all these cases where clinical and haematological pictures are those of infectious mononucleosis and heterophile antibodies are present, cytomegalic virus mononucleosis comes into the differential diagnosis. In fact this virus is held responsible for half these cases. These usually lack a sore throat and enlarged lymphnodes but have definite hepatosplenomegaly; fever may last anything between 2 and 3 weeks and the average age is higher than similar cases due to infectious mononucleosis. They are the "typhoidal variety" described years ago by Tidy.

Plenty of evidence derived using the election microscope and various antibody techniques is very suggestive of the EBV as the causal factor. There is still the possibility of its being a passenger virus multiplying in tumour-tissue. In addition malaria is thought to be an important co-factor in the production of lymphomas in Africa and New Guinea as the incidence is so much higher in holoendemic areas.

In nasopharyngeal cancer not only are antibodies detected in large titres but cultures cells derived from nasopharyngeal cancer also are known to contain the EBV. It is notwithstanding all this still possible that the EBV exists in the lymphoid elements in the tumour rather than the tumour cells themselves.

Antibodies to the EBV have been looked for in patients with Hodgkin's disease and figures where compared to a control group. The results were the following:

GROUPS	EBVA present	Titres = $\frac{1}{160}$
Hodgkin's	95%	47%
Control	89%	17%

An inverse relationship was also observed between the frequency of lymphocytes in the malignant lesions and the level of anti-EBV antibodies. Similar observations have been made in patients with sarcoidosis — especially the chronic and inactive forms of the disease and systemic lupus erythematosus. In the latter it is conjectured that the viruses may participate in the immune complexes that deposit in the kidney and skin.

DISCUSSION: Three questions arise out of necessity from what has gone before: Can the EBV be isolated from the throat or saliva and can infection be forstalled by the production and use

of an EBV vaccine. It is simply a matter of time before these things are done. The third is a more fundamental and perhaps more significant point and this is the relationship of the EBV to cancer, if any!

The experimental observation that tissue culture cells which underwent virus-induced malignant transformation can lose all signs of the abortive infection without changing their malignant potential points to the possibility that in humans too chronic viral infections might lead to the development of neoplastic cells which years later develop into infiltrative neoplasms. Thus if all trace of infection has ebbed from the neoplastic cells, the virus-induced tumours would be indistinguishable from neoplasms occurring "spontaneously" or as a result of carcinogens. With these ideas in mind it has been suggested that whilst infectious mononucleosis is a primary infection with EBV in an immunologically competent host, the chronic disease syndromes may be delayed host responses to EBV infection in immunologically incompetent hosts. The facts may be integrated with the theories in this discussion, as shown in Figure I (Bugeja Jan. 1972).

CONCLUSION: The existence of the EBV has been firmly established. Its relationship to infectious mononucleosis is real but that to Hodgkin's and Burkitt's lymphomas, systemic lupus, sarcoid and nasopharyngeal cancer is not definite yet. Further research will establish whether nasopharyngeal isolation of the EBV and a vaccine against infection by it are practical possibilities or not.

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