for the unusually long stalks, repeated twisting of which would cause haemorrhage into the polyp and this, together with secondary inflammation, facilitates the passage of adenomatous epithelium through the muscularis mucosae into the submucosa. The haemosiderin-laden macrophages are the consequence of haemorrhage.

The recognition of pseudo-carcinomatous invasion is important in the differential diagnosis of benign and malignant polyps of the large bowel. Failure to distinguish it from carcinoma may lead to wrong treatment and false reports of the incidence and prognosis of cancer of the colon and rectum.

Reference

Muto, T., Bussey, H. J. R., and Morson, B. C. (1973). Pseudo-carcinomatous invasion in adenomatous polyps of the colon and rectum. *J. clin. Path.*, **26**, 25.

False Polycythaemia

SYLVIA W. DAVIES, EVELINE GLYNNE-JONES, AND E. PATRICIA LEWIS (*Area Department of Pathology, Exeter*) Fifty-five patients were referred for investigation because they were suspected clinically of having either polycythaemia rubra vera or secondary erythraemia. Thirty had an increase in the red cell mass; 15 had polycythaemia rubra vera with enlargement of the spleen and abnormal haemopoiesis; 15 had secondary erythraemia which was due to hypoxia or renal disease; haemopoiesis was normal and in several there was increased erythropoietic activity of the plasma.

Twenty-five patients who were plethoric with high values for the blood haemoglobin and the packed cell volume had no abnormalities of the peripheral blood or bone marrow and there was no increase in the red cell mass above normal. The common feature to all was a decrease in the plasma volume. Twenty-one were hypertensive; the plasma volume was lowest in those who were receiving treatment.

These cases are presented in order to demonstrate that blood volume studies are essential in patients with plethora in order to differentiate the state of reduced plasma volume from polycythaemia rubra vera or secondary erythraemia.

SYMPOSIUM ON INFECTIOUS MONONUCLEOSIS

Virological Aspects

JOAN M. EDWARDS (*Virus Reference Laboratory, Central Public Health Laboratory, Colindale*) The Epstein-Barr (EB) virus, first isolated from Burkitt lymphoma, is a member of the herpesvirus group which are large ether-sensitive DNA viruses with an icosahedral core and an outer membrane. Eight proteins have been identified in the EB virus which has a density of 1·2 to 1·3, a molecular weight of 100×10^8d, and a DNA density of 1·72.

It is a cell-associated virus which cannot be grown in the usual tissue cultures nor has animal passage been achieved. However, progress has been made in the study of the relationship of the virus to infectious mononucleosis. It has been shown that leucocytes from individuals without EB antibody do not form continuous lymphoblastoid cell lines spontaneously on culture. Those from subjects who have at some time been infected with EB virus may do so. Leucocytes from EB antibody-negative individuals when exposed to various EB virus-containing cell line concentrates or to throat washing or swabs from cases of infectious mononucleosis will form continuous lymphoblastoid cell lines.

Antibodies arising at the time of development of infectious mononucleosis have been identified by complement fixation, gel diffusion, neutralization tests, and in an antigen-antibody complex blocking test using ferritin-tagged antibody. Several different immunofluorescence tests have been developed to detect and differentiate antibodies to early antigen, to membrane antigen, and to viral capsid antigen in various Burkitt lymphoma cell lines.

Diagnostic problems arise in infectious mononucleosis due to the inability to isolate virus by a routine laboratory technique and the persistence of most of the antibodies long after infection. The heterophil antibody test and the immunofluorescence test for the presence of specific EBV IgM are the most informative in the diagnosis of current infection.

Immunopathology

R. L. CARTER (*Chester Beatty Research Institute, London*) The best documented immune responses in infectious mononucleosis are those mediated by antibody. The antibodies encountered in this disease are (1) heterophil antibodies used in diagnostic serology, (2) antibodies directed against EB virus, and (3) auto-, iso-, and other heteroantibodies including anti-i, lymphocytotoxins, Wassermann antibody, rheumatoid factors, and anti-smooth muscle antibodies. When properly tested, the heterophil antibodies are unusually specific for infectious mononucleosis. They are predominantly or exclusively IgM and show little or no gammaM → gammaG conversion. The distinctive infectious mononucleosis sheep cell agglutinins have been induced in volunteers with sheep erythrocytes, and in Squirrel monkeys inoculated with EB 3 cells. Little is known of the immunochemistry of the relevant antigenic determinants. Most of the auto-, iso-, and other heteroantibodies that appear transiently during the acute phase of IM are also IgM or IgM/IgG complexes. Anti-i is the main cause of haemolysis in infectious mononucleosis. The other antibodies described have no known clinical significance though autoimmune antibodies may perhaps contribute to liver damage and the rare complications of thrombocytopenia and agranulocytosis. There is no certain evidence of immune complex disease in infectious mononucleosis.

Serum IgM levels are strikingly raised during the acute phase of infectious mononucleosis and they may remain elevated for months after apparent cure. The cells responsible for IgM synthesis are not yet clear: the circulating atypical lymphocytes are probably not involved but lymphoid cells in the bone marrow and lymph nodes may be. Plasma cells are not conspicuous in these tissues and, in the nodes, the main feature is hyperplasia of the (thymus-dependent) paracortex with many pyroninophilic blast cells.

The paracortical blast cells are almost certainly identical with the atypical lymphocytes in the blood, and it is probable that the circulating cells are T lymphocytes (based mainly on their capacity to form rosettes with sheep erythrocytes). Consequently, information is now urgently needed about cellular immune responses in infectious mononucleosis, in which T cells are implicated.

The circulating atypical lymphocytes appear to be antigenically different from normal blood lymphocytes, as shown in mixed lymphocyte tests and, more problematically, in continuous cultures. Cultured infectious mononucleosis leucocytes acquire (EBV-associated) neoantigens on their membranes and also a capacity to grow progressively as heterotransplants in animals. These and several

other characteristics of long-cultured infectious mononucleosis leucocytes are thought to be attributable to the presence of EB virus; they do not, on their own, indicate that infectious mononucleosis is a disease with an inherent neoplastic potential.

EB Virus and Other Diseases

B. G. ACHONG (*University of Bristol, Bristol*) EB virus is very closely associated with two human neoplasms—Burkitt's lymphoma and nasopharyngeal carcinoma—and a very large body of evidence has accumulated supporting the view that the virus does indeed play a causative role in these two malignancies.

Thus 100% of patients with Burkitt's lymphoma or nasopharyngeal cancer have antibodies to EB virus VCA; the EB viral genome is present in all Burkitt tumours and in the malignant epithelial cells of nasopharyngeal carcinoma, and in the case of Burkitt's lymphoma is expressed *in vivo* by the production of viral-determined membrane antigen in the tumour cells; the virus confers the power of unlimited proliferation in culture on normal human peripheral lymphocytes and satisfies the criteria established for transformation of normal cells *in vitro* by known oncogenic animal viruses including induction of cellular DNA synthesis, production of neo-antigens analogous to membrane transplantation antigens and nuclear T antigens, and the ability of the transformed cells to grow on heterotransplantation to laboratory animals to form invasive, metastasizing, fatal tumours; the ability of the viral genome to be activated by BUDR; the extremely close parallels between the biological behaviour of EB virus and that of known oncogenic animal herpes viruses and finally recent experiments describing the development of malignant lymphomas in South American primates following inoculation of the virus have demonstrated the oncogenic capacity of EB virus *in vivo*.