decrease in its activity leads to hyperhomocysteinaemia (Sumner et al, 1996). With vitamin B12 or folate deficiency, serum total homocysteine levels increase because methionine synthase requires both cofactors. Morrison et al (1996) reported that low concentrations of folate are associated with an increased risk of fatal coronary heart disease. Megaloblastic anaemia due to folate or B12 deficiency can be associated with thromboembolic disease (Ballas et al, 1976).

Patients with sickle cell disease typically have hyperactive bone marrow as a compensatory mechanism for chronic haemolysis. This increases the demand for folic acid and may lead to folate deficiency especially in those patients with poor dietary intake of folate-rich diets. Patients with sickle cell disease usually take 1 mg of folic acid orally every day in order to support and maintain their effective erythropoiesis and decrease the chances of developing folate deficiency that would worsen their anaemia.

We believe that treatment of patients with sickle cell disease with daily folic acid provides three benefits. First, it maintains effective erythropoiesis with a stable haemoglobin level. Second, it prevents the development of folate deficiency and the accumulation of homocysteine that may predispose to thrombotic events leading to painful episodes. Third, it prevents neural tube defects in infants whose mothers have had a previous pregnancy resulting in a fetus or an infant with such defects (MRC Vitamin Study Research Group, 1991). Treatment with folic acid costs less than 5 cents/mg/d in the Philadelphia area. It must be emphasized, however, that the serum concentration of vitamin B12 should be assessed prior to folic administration, especially in the presence of macrocytosis. Failure to do so may mask megaloblastic anaemia due to B12 deficiency by folic therapy.

Heterogeneity in the severity and frequency of sickle cell painful episodes is multifactorial. Chronic or intermittent folic acid deficiency may be one factor contributing to this heterogeneity. Fullerton et al (1965) reported that pregnant patients who had haemoglobin SC disease and megaloblastic anaemia had a higher mortality rate and more thrombotic complications than those who received adequate prenatal care with iron and folic acid. Needless to say, the role of folic acid in the prevention of vaso-occlusion in sickle cell disease needs further study. Nevertheless, folic acid supplementation for patients with sickle cell disease is harmless, cost effective, and may decrease the morbidity associated with this disease. Managed care advocates, undoubtedly, will hail such a recommendation.

**REFERENCES**


**Keywords:** thrombosis, megaloblastic anaemia, sickle cell disease, folic acid.

**ABSENCE OF HEPATITIS C VIRUS INFECTION IN NON-HODGKIN’S LYMPHOMA**

Recently it has been suggested that hepatitis C virus (HCV), which is both a hepatotropic and a lymphotropic virus (Ferri et al, 1993), is associated with non-Hodgkin’s lymphomas (NHL), especially B-cell lymphomas of low-grade malignancy (Luppi et al, 1996). Serological findings showed a HCV positivity in patients with NHL as high as 28–42% (Luppi et al, 1996; Muzzaro et al, 1996; Ferri et al, 1994). The mechanism of this association is still unknown. A possible direct oncogenic effect has been suggested because several cases of hepatocellular carcinoma in patients with HCV infection, without preceding cirrhosis, have been described (de Miti et al, 1995). However, HCV is not endowed with oncogenes or reverse transcriptase, enabling genome integration, and consequently research was focused on the possible oncogenic or proliferative effect of viral proteins.

On the other hand, Brind et al (1996) reported that HCV is an uncommon contributory factor for the development of NHL in the U.K.: none of the 63 patients with NHL screened for HCV infection were positive with the ELISA test. A possible explanation for the discrepancy between these studies is the fact that HCV is much more common in Italy than in the British population. Either there is no association between HCV and the development of NHL in the U.K., or the association is more difficult to demonstrate because of a low prevalence of HCV.

seronegative with ELISA.

Absence of Kaposi's sarcoma associated herpesvirus-like DNA sequences (KSHV) in HIV-negative multicentric Castleman's disease complicated by KSHV-positive Kaposi's sarcoma

Herpesvirus-like DNA sequences (KSHV) were first detected in Kaposi's sarcoma (Chang et al, 1994; Moore & Chang, 1995; Huang et al, 1995; Dupin et al, 1995), and have subsequently been demonstrated in body cavity based lymphomas (Cesarman et al, 1995). Recently, KSHV has also been found in multicentric Castleman's disease.