

blood culture 16 days after completing a course of chloramphenicol. He also responded to co-trimoxazole in four days and had no further relapse. Both these patients may have been reinfected, but far more probably they were genuine cases of relapse.

There were no serious complications such as haemorrhage, perforation, or circulatory collapse in any patient in either group. Nor were there any severe side effects. Minor side effects were equally common in both groups, the only notable difference being a significantly greater incidence of weakness in the control group (19 patients) compared with the trial group (5 patients).

Discussion

All patients in both groups in our series responded to specific therapy, thus confirming the results of Akinkugbe *et al.* (1968), Farid *et al.* (1970), and Kamat (1970). In contrast, two out of 23 patients in Geddes *et al.* (1971) series and 8 out of 103 in Scragg and Rubidge's (1971) series treated with co-trimoxazole failed to respond. Farid's (1971) observations on the dosage in Scragg and Rubidge's series that underweight and undernourished children who were given co-trimoxazole on a body-weight basis might have received less than a therapeutic dose is very pertinent and may explain Scragg and Rubidge's poor results with the drug. This also confirms our earlier experience (Sardesai, 1971) when we did not encounter a single failure in 40 patients treated with co-trimoxazole.

In this trial the response of toxæmia to treatment occurred significantly earlier in the trial (co-trimoxazole) group compared with the control (chloramphenicol) group. Before the end of the third day 78.1% of toxæmic patients in the trial group became non-toxæmic compared with only 50% in the control group. At the end of six days only 3.1% of patients in the trial group remained toxæmic as compared to 16.6% in the control group. These results are similar to almost all previous workers (Kamat, 1969; Kamat, 1970; Farid *et al.*, 1970; Geddes *et al.*, 1971; Scragg and Rubidge, 1971).

Two patients in our control group relapsed but none in the trial group did so. Kamat (1970), and Farid *et al.* (1970) did not encounter any relapse in patients treated with co-trimoxazole. In Geddes *et al.* (1971) series there were two relapses out of 23 patients and in Scragg and Rubidge's series a staggering relapse rate of 12.6% in patients treated with co-trimoxazole.

Our overall results are similar to those in the very large series of Kamat (1970) in that co-trimoxazole seemed superior to chloramphenicol in relieving toxæmia but equal to it when judged by the duration of fever. In our series, however, co-trimoxazole also seemed to be superior to chloramphenicol when judged by the incidence of relapse. The comparatively poorer results with co-trimoxazole in the series of Geddes *et al.* (1971) and Scragg and Rubidge (1971) are difficult to explain. It seems that various factors such as differences in strains of *Salm. typhi*, ethnic differences, and possibly differences in herd immunity to typhoid may be responsible for the apparent contradictions. Clearly, however, in our part of India co-trimoxazole is superior to chloramphenicol in the treatment of typhoid fever.

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Association between Previous Tuberculous Infection and Cerebral Glioma

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Summary

An increased incidence of previous infection with tuberculosis has been found in a series of patients with cerebral gliomas, and it is suggested that such an association may be due to defective immunity acting as a common aetiological factor.

Introduction

When it was noticed that three patients with cerebral gliomas, seen consecutively, had associated disease a survey of further patients with gliomas was conducted (Finn *et al.*, 1972). This showed that about a quarter had a history or significant radio-

logical evidence of previous tuberculous infection compared with a tenth of a series of 56 controls. Consequently, the larger study was carried out.

Patients and Methods

For the purpose of this investigation previous tuberculous infection was defined as either a previous history of clinical tuberculosis or the presence on chest radiography of healed apical fibrotic lesions, with or without extensive calcification, often involving the hilar regions.

Altogether, 100 case records of patients, each with a histologically-proved glioma, were studied. Eight had to be rejected because of inadequate information. The ages of the remaining 92 patients ranged from the mid-20s to over 80 years.

As controls we examined in detail the previous histories and chest radiographs of 100 patients admitted consecutively to two general medical units. In view of the decline in tuberculous infection over recent years we limited selection to patients aged 50 years or over, with the exception of three under the age of 50 who were known to have had tuberculosis in the past.

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Results

Of the 92 patients with gliomas 20 (21.7%) had evidence of previous infection with tuberculosis as defined by the criteria above. Of the 100 controls only seven had suffered such previous infection (7%). Previous tuberculosis was, therefore, significantly more common in the glioma cases ($\chi^2 = 8.613$, $P < 0.01$).

Discussion

By using the above criteria of previous tuberculous infection the data suggest that such infection is three times as common in patients with gliomas than in a random control series. This association could be explained on the basis of a common predisposing factor.

Possibly the malignancy arose as a result of increased or heightened immunological activity over a long period stimulated by and directed against the tubercle bacillus. There was, however, no clinical evidence to suggest a close temporal relation between the two conditions.

It may be that the opposite view is more tenable, that the gliomas arise—as did the tuberculosis before—in an environment favourable because of impaired immunity. The possibility that some cancers may arise where defects in immunological surveillance exist has been discussed (*Lancet*, 1971; Walder *et al.*, 1971). Evidence for this has been well documented (Burnet, 1972). Firstly, cancer is more likely to arise during those

periods of life when immune responsiveness is impaired—the perinatal period and old age. Secondly, there is a high risk of malignancy, particularly of intracerebral lymphomas, after immunosuppression in transplant recipients, and, thirdly, neoplasms are a common complication in certain immune deficiency states of genetic origin.

In this study it may be that patients with normal immune responses dealt rapidly with the primary infection of tuberculosis leaving no evidence of significant disease other than perhaps a healed primary focus. Those with impaired responses may have had more difficulty in dealing with the tubercle bacillus, prolonged infection being the result.

If this association between tuberculosis and cerebral gliomas is confirmed by other workers it would provide further evidence for an immunological role in the pathogenesis of neoplasia, and would call for more detailed immunological studies in patients with gliomas and tuberculosis.

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Subtypes of Hepatitis B Antigen in Blood Donors and Post-transfusion Hepatitis: Clinical and Epidemiological Aspects

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Summary

Subtyping of hepatitis B antigen (HBA) in blood donors revealed subtype *ad* in 56% while patients with icteric post-transfusion hepatitis from the same centre showed subtype *ay* in the majority of the cases (75%). Donors with subtype *ad* in serum were mostly asymptomatic long-term carriers of the antigen with normal liver function (83%), while 70% of donors with subtype *ay* in serum had signs of acute or chronic liver disease. Healthy long-term carriers of HBA seem to present little risk of transmitting hepatitis irrespective of subtype. It is, however, possible that these differences in blood donors with subtype *ad* and patients with post-transfusion hepatitis with subtype *ay* might reflect epidemiological circumstances rather than biological differences in the two viral strains.

Introduction

The first evidence concerning heterogeneity of hepatitis B antigen (HBA) was given by Levene and Blumberg (1969), who on the basis of spur formation in gel diffusion postulated three determinants on HBA called *a*, *b*, and *c*. Subsequently this was confirmed by Le Bouvier (1971), who apart from a common antigenic determinant *a* found another two determinants designated *d* and *y*. These determinants seemed to be mutually exclusive, since hepatitis cases associated with HBA had either subtype *ay* or subtype *ad* in serum but never both. Furthermore, all cases of hepatitis B with a common source of infection carried either *ad* or *ay*. Thus it was presumed that *d* and *y* were two different specific strains of hepatitis B virus (Kim and Tilles 1971; Le Bouvier 1971; Mosley *et al.*, 1972).

Other subspecificities of HBA have been described (Bancroft *et al.*, 1972; Magnius and Espmark, 1972) but further research is needed to resolve the character and significance of these antigenic determinants.

In a previous report on blood donors (Iwarson *et al.*, 1972) the relation between the occurrence of HBA in serum and actual signs of liver disease was described. This report presents further work on the significance of two different subtypes of HBA in serum of blood donors and includes a study of HBA subtypes in post-transfusion hepatitis cases from the same centre.

Subjects

Blood Donors.—Donors at the Blood Centre, Sahlgren's Hospital, have been tested for HBA since January 1970. The

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