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# High incidence of subacute sclerosing panencephalitis in South India

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SUMMARY

During 1983–7 a clinical diagnosis of subacute sclerosing panencephalitis (SSPE) was confirmed by the detection of measles virus haemagglutination inhibiting antibody in the cerebrospinal fluid (CSF) in 81 subjects resident in Tamilnadu. The antibody titre (reciprocol of the end-point dilution) in the CSF ranged from 2 to 32 and in the sera from 8 to 2048. The CSF : serum ratios of titres were 1 : 4–1 : 64 in 80 cases and 1 : 128 in one case. The median age at onset of SSPE was 10 years and 97% of cases were diagnosed at stage 2 and beyond. Based on the geographic distribution of 72 cases in an estimated population of 8·4 million, the annual incidence of SSPE was calculated to be 2·14 per million population, or 4·3 cases per million children below 20 years. Assuming that only 10% of all cases would have reached the level of laboratory diagnosis, the incidence may be as high as 21 cases per million population.

## INTRODUCTION

The complications, early sequelae and mortality of measles are higher in India than in industrialized nations [1–3]. It was for this reason that we recommended routine immunization against measles in India more than 15 years ago [4]. However the importance of measles as a public health problem was not appreciated by health planners and it was only as late as 1986 that measles immunization was included in the Expanded Programme on Immunization. Subacute sclerosing panencephalitis (SSPE) is a late sequel of measles virus infection. Prior to the extensive use of measles vaccine in industrialized nations the annual incidence of SSPE was reported to be 0·06–1 case per million population [5–7]. The majority of SSPE cases occur in those below 20 years of age [8]. Using this age group as the

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denominator instead of the whole population, the incidence has been calculated at 1–5 cases per million population under 20 years of age [9–10]. As shown in this paper, our recent experience indicates that the risk of SSPE is several times higher in children in our country than has been reported elsewhere.

## SUBJECTS AND METHODS

A diagnosis of SSPE was suspected in a previously well child or young adult who presented with dementia and/or myoclonus. Electroencephalography as well as cytological and biochemical analysis of the cerebrospinal fluid (CSF) were done on all patients. The disease was staged according to Jabbour [11] and the diagnosis confirmed by the detection of measles virus antibody in the CSF. Since late 1983, neurologists from Madras and Vellore have been submitting serum and CSF samples from patients with suspected SSPE for measles virus antibody testing. The CSF and blood were collected on the same day from each patient. If the CSF was contaminated with blood the specimen was rejected and a fresh specimen was requested and received. The presence of measles virus antibody was tested by the haemagglutination inhibition technique (HI) as previously described [12] and the titre expressed as the reciprocal of the final dilution found to be positive. A questionnaire was sent to the referring physician requesting clinical and other laboratory data on each case. For the purpose of this study we have analysed information only from patients who were resident within the state of Tamilnadu. We have assumed that the population of this state is uniformly distributed and the number of people below the age of 20 years represent 50% of the total population [13].

## RESULTS

During the 4 years of 1983–7, a clinical diagnosis of SSPE was confirmed in 81 subjects by the demonstration of measles virus HI antibody in their CSF; 14 cases were diagnosed in 1983–4, 23 in 1985, 20 in 1986 and 24 in 1987. Their places of residence were plotted on a map and 72 (90%) were found to reside in the catchment area shown in Fig. 1. This area comprised parts of North Arcot, Chengalpattu and South Arcot districts as well as the urban areas of Madras, Pondicherry and Vellore. We have estimated the area of this catchment to be approximately 11000 sq. kms and that 75%, 29% and 12% of Chengalpattu, North Arcot and South Arcot districts respectively lie within this catchment area. The population of the three districts are 3·46, 4·34 and 4·14 million respectively [14]. Assuming that the distribution of population within each district is uniform, there are 2·6, 1·26 and 0·497 million people from respective districts within the catchment area. If we add the population of Madras (3·3 million), Pondicherry (0·5 million) and Vellore (0·25 million) to this, approximately 8·4 million people are estimated to reside in the catchment area. Since 50% of the population is below 20 years of age, there are approximately 4·2 million people in this age group. In other words, in a period of 4 years there were 72 cases of SSPE in 8·4 million total population, or in 4·2 million under 20 years of age. The annual incidence of SSPE may therefore be calculated to be 2·14 cases per million total population or 4·3

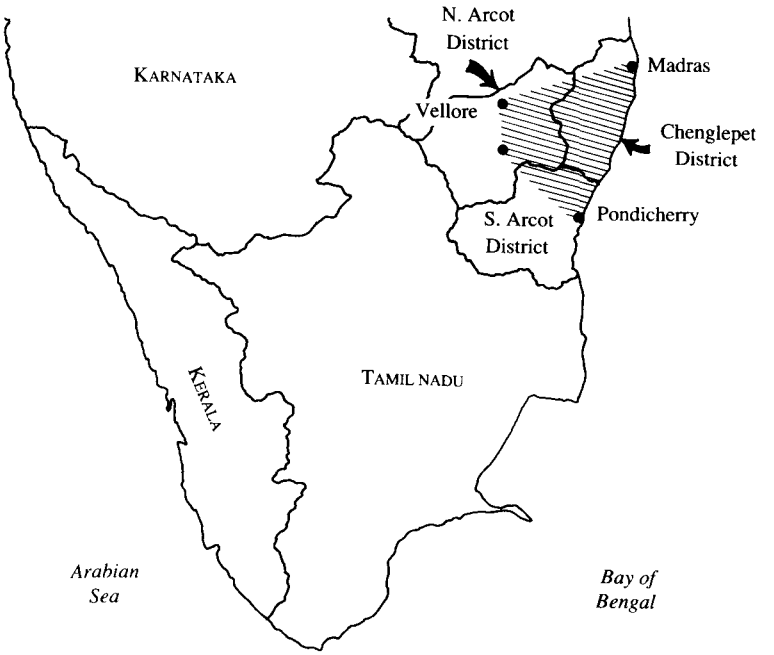


Fig. 1. Map of south India showing the catchment area in which the patients with SSPE were resident. The area includes parts of North Arcot, South Arcot and Chenglepet Districts as well as the urban areas of Madras, Pondicherry and Vellore.

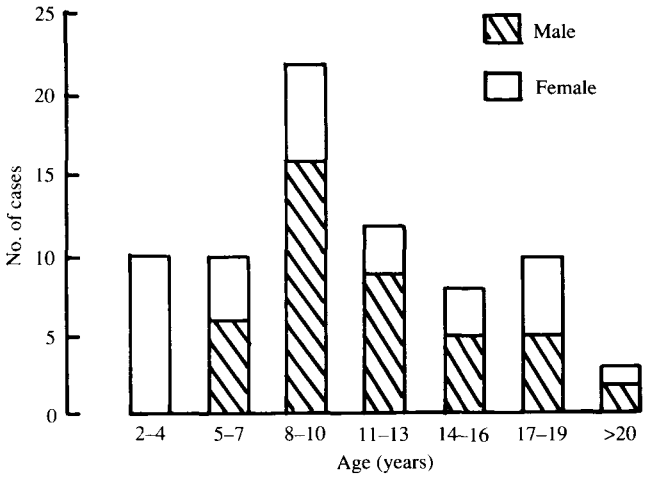


Fig. 2. Age at which SSPE was first diagnosed in 75 cases (53 males and 22 females).

Table 1. *Age at which measles occurred in patients with SSPE* ($n = 58$)

| Age at which measles occurred (yrs) | < 1 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|
| Number of patients with SSPE | 3 | 31 | 8 | 2 | 7 | 1 | 6 |

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cases per million below 20 years of age. All cases of SSPE occurring in this region do not come to our attention and we have no way of directly assessing the actual proportion of cases which were investigated and confirmed. Therefore the incidence must be higher than the rates mentioned above, as will be discussed later.

In our group of cases, the interval between onset of symptoms and hospitalization was short, ranging from 10 days to 6 months, with a mean of 8 weeks. The distribution of cases by age and sex is shown in Fig. 2. The male:female ratio was 2·3:1. The median age of onset was 10 years. Only three patients were above the age of 20 years and the oldest patient was 31 years. A history of measles was obtained in 58 cases; in 34 (60%) measles had occurred during the first 2 years of life, as shown in Table 1.

The clinical details for staging the disease at the time of diagnosis was available in 55 cases. In 53 (97%) SSPE was diagnosed at stage 2 or above. Myoclonic seizures were noted in 44 (80%) and generalized seizures in 10 (18%). Gross dementia was seen in 23 (42%). Ophthalmic involvement (chorioretinitis or optic atrophy) was observed in five (9%).

The CSF glucose and protein levels were normal and no pleocytosis was seen. The measles HI titres in the CSF ranged from 2 to 32 and in the sera from 8–2048. The CSF:serum ratios ranged from 1:4 to 1:128; in the majority (60/72) it was either 1:16 or 1:32. In only one case it was 1:128 with CSF and serum titres of 16 and 2048.

## DISCUSSION

We have diagnosed SSPE on the basis of the typical clinical features and the presence of measles virus antibody in the CSF. Measles antibody titres in children following infection as well as in mothers and in their infants, are lower in India than in developed countries [12]. The relatively low csf titres in our cases are in keeping with this observation. Moreover, antibody levels obtained by the HI method in the CSF of patients with SSPE are lower than those obtained by the complement fixation test or enzyme linked immunosorbant assay. However the HI antibody is more specific [15].

Among the diseases of the central nervous system suspected of being caused by viruses and in whom a laboratory diagnosis is requested by submitting specimens to us, SSPE is the third most frequent diagnosis after paralytic poliomyelitis and encephalitis. Annually we receive CSF specimens from 40–50 suspected cases of SSPE. This suggests that SSPE occurs more often than would be expected if the incidence was the same here as in the West.

There are three major differences in the epidemiology of measles virus infection in our population as compared to that in the West. First, in the United States of America when the SSPE rate was only 0·25 per million population, 25% of the population was below 20 years of age [16]. For practical purposes it can be assumed that all cases of SSPE occur in this age group. Therefore in a population of a million of whom 250000 are at risk 0·25 cases of SSPE would occur in a year. In India 50% of the population are below 20 years of age and if SSPE were to occur at the same rates as it did in the USA, we should expect an incidence twice

that of the U.S.A. Secondly, measles occurs earlier in life in India than in the pre-immunization era in the West. In developed countries 50% of those with SSPE as compared to 20% of those who are not affected, give a history of measles prior to their second birthday [17]. This suggests that measles in the very young is more likely to result in SSPE than in older children. In India 50% of all children have had measles by the age of 2 years and in our group of cases 60% had had measles by this early age. A larger proportion of children in our community are therefore at risk for SSPE. Finally, we have found that 20–40% of our children have a subclinical infection with measles virus [1]. Therefore the 17 (23%) patients with no history of measles infection may have had a subclinical measles virus infection. We suspect that early subclinical measles may also be an added risk factor for the sequel of SSPE. Taking all these factors into consideration we would expect a higher incidence of SSPE in our community than in the West.

It is most unlikely that we have seen a majority of the cases of SSPE occurring in the catchment area. In our region, children with severe, life-threatening or chronic illnesses are not always brought to the attention of physicians or paediatricians. Even when paediatricians are consulted they often fail to diagnose SSPE. All the cases in our series were first diagnosed by a consultant neurologist and a majority of cases would not have reached a specialist familiar with the diagnosis. We are unable to determine accurately the proportion of cases of SSPE that reached the level of laboratory confirmation. In Karachi, Pakistan (population 4 million), 38 cases of SSPE were diagnosed in the neurology institute during 1974–85. Based on the known incidence of motor neurone disease, and the numbers of cases of the same disease and of SSPE seen in the Institute, an incidence of 12·7 cases of SSPE per million total population was derived [18]. Thus only 6·4% of cases of SSPE were diagnosed neurologically. In this study also, only a proportion of all cases occurring in the community would have reached us. Perhaps as few as 10% of cases were diagnosed and this could mean that the true incidence may have been as high as 21 per million total population or 43 per million population below the age of 20 years. We feel that this is not an unreasonable estimate because a comparable incidence of 40 cases of SSPE per million total population has been previously reported from Tyre [19].

The higher incidence of SSPE in developing countries than in developed ones is due to an increased proportion of the total population below 2 years of age (a reflection of the high birth rate), a higher proportion of measles cases in the very young, more frequent subclinical measles virus infection and perhaps other host factors. SSPE is invariably fatal. It is also preventable by measles vaccination [20]. In order to prevent this tragic, fatal and not so rare complication of measles we emphasise the immediate necessity of achieving a high measles vaccine coverage.

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