Sexual maturity.

Girls
Of the 33 girls, seven had their menarche before starting medication (mean age 12·0 years, range 9·9–14·1 years), 11 girls were prepubertal, and the remaining 15 had their menarche while on treatment (mean age 13·4 years, range 11·3–15·3 years). The normal mean age for menstruation is 13·0 years. The pubertal ratings as determined at the last visit did not deviate from the normal pattern.

Boys
In the group of 34 boys, four were in puberty before starting treatment, 14 were prepubertal, 16 entered puberty while on treatment (mean age for penis stage II 11·3 years, range 8·5–14·3 years; mean for population 12·0 years; and mean age for pubic hair stage II 13·1 years, range 11·3–14·2 years; mean for population 12·5 years).

Skeletal maturity
There was a trend for girls to show slightly earlier skeletal maturity than is normal, although the maturity scores were still within normal limits. The skeletal maturity in boys was normal.

Discussion
These results show that children with epilepsy on anticonvulsant drugs for a mean of three years (range 0·9–5·4 years) grow and mature normally. We found no significant difference from the normal timing of the menarche or of onset of puberty.

Age distribution of anginose mononucleosis

Z SPIRER, M HOLTZMAN, I MELAMED, AND I SHALIT

Department of Paediatrics, Rokach Hospital, and Department of Paediatric Immunology, Tel-Aviv University, Tel-Aviv, Israel

SUMMARY The age distribution of anginose infectious mononucleosis in children was analysed retrospectively for the years 1966–85. During that period the disease became significantly more common in children of a young age and less common in older children. This shift could not be attributed either to socioeconomic conditions or to the diagnostic methods used.

The clinical and epidemiological range of infectious mononucleosis (IMN) has been appreciated only in the past decade, since the introduction of specific serological tests. Infection during infancy and childhood is usually subclinical, whereas the classical clinical manifestations are common among adolescents and young adults. It has been reported that infection generally occurs at an earlier age in low socioeconomic groups, where overcrowding and poor hygiene prevail.

One of the clinical presentations of IMN is the anginose type. Although this is said to be more prevalent in older children and adolescents, we have

Anticonvulsant drugs, growth, and development

There was a trend towards earlier skeletal maturity in the girls, but this did not influence final height. Separate examination of children with partial seizures, those taking monotherapy, children with persistent seizures, and a small number on polytherapy, again produced no evidence of deviant growth patterns.

Some of the previously reported findings were possibly related to adverse environmental factors, high seizure frequency, or subclinical drug toxicity.

We thank Dr E H Reynolds and Dr B Neville for allowing us to study their patients.

References


Correspondence to Dr B M MacArdle, Newcomen Centre, Guy's Hospital, St Thomas' Street, London SE1 9RT.

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gained the impression that it is also common in younger children. We therefore studied retrospectively the age distribution of anginose mononucleosis in our pediatric population over the past 20 years.

Patients and methods

Hospital records of all children diagnosed with glandular fever, IMN, suspected IMN, or the mononucleosis syndrome in the department of pediatrics, Tel-Aviv Medical Center from 1966 to 1985 were searched. Cases of the anginose type of IMN were selected for further analysis according to eight criteria. (1) Temperature of greater than 38°C for 72 hours or more; (2) exudative tonsillitis present for at least 72 hours that had not responded to treatment with penicillin for at least 48 hours; (3) cervical lymphadenopathy; (4) blood smear containing more than 10% atypical lymphocytes; (5) raised liver enzyme (serum aspartate transaminase and alanine transaminase) activities; (6) positive results to serological tests (from 1966 to 1974 the Paul-Bunnell test; from 1975 to 1979 the Monospot slide test or Paul-Bunnell test; and from 1980 to 1985 specific tests for Epstein-Barr virus (virus capsid antigen IgG and IgM)); (7) negative results to serological testing for cytomegalovirus (from 1970); (8) negative results to serological testing for toxoplasma (from 1966 to 1977 a dye test and from 1978 on a fluorescence test).

Patients fulfilling all eight criteria were diagnosed as definitely having anginose IMN. As heterophil antibody tests may yield negative results in up to 60% of patients younger than 6 years old, we included in our study all patients who were negative for heterophilic antibody during 1966–79 (before specific tests for Epstein-Barr virus were performed) but who fulfilled all other criteria. All the patients included in the study during 1980–5 were positive for Epstein-Barr virus.

The significance of differences in age distribution of anginose IMN in the different periods studied were analysed with the χ² test.

Results

The number of patients diagnosed as suffering from anginose IMN from 1966 to 1985 was 1290. The ratio of female: male patients aged under 5 years was 1:2:4 and aged 5–18 years 1:1:9 (in adults during the past five years it was 1:1:6). The Table shows the distribution of cases according to age groups and calendar years. The ratio of patients aged 10 and over to those aged under 10 was 12-25:1 during

<table>
<thead>
<tr>
<th>Time of diagnosis</th>
<th>Age (years)</th>
<th>&lt;5</th>
<th>5–9</th>
<th>10–14</th>
<th>15–18</th>
<th>Total No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1966–70</td>
<td>No (%) of cases</td>
<td>3(1%</td>
<td>17(6%)</td>
<td>52(20%)</td>
<td>193(75%)</td>
<td>265</td>
</tr>
<tr>
<td></td>
<td>No seropositive</td>
<td>0</td>
<td>9</td>
<td>43</td>
<td>125</td>
<td>177</td>
</tr>
<tr>
<td>1971–5</td>
<td>No (%) of cases</td>
<td>14(4%)</td>
<td>31(10%)</td>
<td>103(33%)</td>
<td>164(53%)</td>
<td>312</td>
</tr>
<tr>
<td></td>
<td>No seropositive</td>
<td>5</td>
<td>20</td>
<td>89</td>
<td>134</td>
<td>248</td>
</tr>
<tr>
<td>1976–80</td>
<td>No (%) of cases</td>
<td>42(12%)*</td>
<td>79(23%)</td>
<td>161(47%)</td>
<td>610(18%)*</td>
<td>343</td>
</tr>
<tr>
<td></td>
<td>No seropositive</td>
<td>28</td>
<td>52</td>
<td>112</td>
<td>59</td>
<td>251</td>
</tr>
<tr>
<td>1981–5</td>
<td>No (%) of cases</td>
<td>90(24%)*</td>
<td>112(30%)</td>
<td>98(26%)</td>
<td>70(19%)*</td>
<td>370</td>
</tr>
<tr>
<td></td>
<td>No seropositive</td>
<td>90</td>
<td>112</td>
<td>98</td>
<td>70</td>
<td>370</td>
</tr>
</tbody>
</table>

*p<0.05 compared with 1971–5 and 1966–70.


Discussion

Clinically apparent IMN, including the anginose form, is most common in developed, industrialised countries and among high socioeconomic groups, in which exposure to Epstein-Barr virus occurs in the second decade of life. Most cases are diagnosed when the patients are over the age of 10, with a peak incidence in the 15–25 age group. In developing countries, tropical areas, and low socioeconomic groups exposure to Epstein-Barr virus occurs in early childhood and infections are predominantly asymptomatic or associated with mild, non-specific manifestations. Thus in both developed and developing countries and among all socioeconomic classes clinical IMN is uncommon in early childhood.

Whereas this age distribution was true for anginose IMN in our community 20 years ago, during the past decade this form of the disease has shifted noticeably towards a younger age group. About one quarter of the cases now occur in children under 5 years old, and more than half occur in those younger than 10. This is in great contrast to the distribution 20 years ago, when more than 90% of cases occurred in children over the age of 10. Moreover, our data also show a decline in anginose IMN during adolescence.

Although we are fully aware of the potential flaws of a retrospective study, and despite the differences among serological tests used in the different periods studied, we believe that our diagnostic criteria were strict enough to establish adequately the diagnosis of anginose IMN and preclude such conditions

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The table above shows the age distribution of patients diagnosed with anginose IMN over different periods from 1966 to 1985. The data is presented in a tabular format, with columns for time of diagnosis, age group, number of cases, and gender distribution. The study found that the peak incidence of IMN occurred in children aged 5-18 years, with a noticeable shift towards younger children in the past 20 years. The discussion highlights the differences in prevalence and age distribution compared to 20 years ago, indicating a shift towards younger patients.
as infection with cytomegalovirus, toxoplasmosis, streptococcal pharyngitis, infectious hepatitis, and adenovirus pharyngotonsillitis (the main differential diagnoses).

The shift in age distribution of anginose IMN in our community cannot be attributed to socioeconomic conditions as these have been constantly improving in our urban community over the past 20 years; nor can it be related to the emergence of new diagnostic tests because the changing pattern was observed before such tests were available in our medical centre.

Interestingly, Sumaya et al prospectively evaluated children with documented IMD induced by Epstein-Barr virus between 1976 and 1982 and concluded that an unexpected finding was the large number of young children less than 4 years old with this disease. They found that 45% of their patients under 4 years old had exudative tonsillopharyngitis. They also found, as we did, that the incidence in boys was more than twice that in girls. The similarity of their data, from the United States, to ours implies that the increase in the occurrence of clinical IMN in early childhood may be a worldwide rather than a local phenomenon.

References

Age distribution of anginose mononucleosis

Referral to a regional centre improves outcome in extremely low birthweight infants

R W I COOKE

Department of Child Health, University of Liverpool, Regional Neonatal Intensive Care Unit, Liverpool Maternity Hospital, Liverpool

SUMMARY Referral of extremely low birthweight infants (< 1001 g) from district hospitals in a geographically defined area to a specialist regional centre significantly improved their chances of survival.

Referral of preterm infants or of their mothers antenatal to a regional unit has been widely accepted as improving outcome, though there is little evidence to support this belief. Reports of improved survival either compare results before and after the introduction of a transfer programme, with the problem of historical controls, or contrast the outcome of infants transferred to a regional unit with that of those left behind, though such groups are not comparable. This study compares the 28 day mortality of extremely low birthweight infants in eight geographically defined areas with the rate of referral from their district hospitals to a regional perinatal centre.

Methods

Mersey regional neonatal intensive care unit is in Liverpool Maternity Hospital and with the obstetric units provides a regional perinatal referral service for Mersey region and north Wales. For the purpose of this study I divided the region into eight areas corresponding to district or area health authorities. These areas were Clwyd, Gwynedd, West Cheshire, (Chester, Warrington, Halton), East Cheshire (Crewe and Nantwich), St Helens, Liverpool, Sefton (North and South), and Wirral.

The data for the study were obtained from forms LHS 27/1 for each district for the years 1980–3 inclusive and the admissions records of the regional neonatal intensive care unit. Form LHS 27/1 is completed by each district health authority yearly and returned to the regional health authority and to the statistics department of the Department of Health and Social Security in Blackpool or, in the case of Wales, the Welsh Office in Cardiff. Information reported on the form includes the number of