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.

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^{4–6} 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

- Montouris GD, Fenichel GM, William McLain L. The pregnant epileptic. A review and recommendations. *Arch Neurol* 1979;**36**:601–3.
- Hiilesmaa VK, Teramo K, Granstrom ML, Bardy AH. Foetal head growth retardation associated with maternal antiepileptic drugs. *Lancet* 1981;ii:165–7.
- Harvey W, Sandy J, Robinson P, Monro P. Anticonvulsant drugs decrease resistance of cartilage to vascular invasion. *J Dent Res* 1986;**64**:497.
- Round JM. Growth development and biochemical changes during puberty in a population of epileptic children. In: Dam M, Gram L, Penry JK, eds. *Advances in epileptology, XII International Symposium*. New York: Raven Press, 1981:461–7.
- Robinson PB, Harris M, Harvey W. Abnormal skeletal and dental growth in epileptic children. *Br Dent J* 1983;**154**:9–13.
- McGowan MEL. Final adult height of patients with epilepsy. *Dev Med Child Neurol* 1983;**25**:591–4.

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

Received 12 December 1986

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,¹ 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.² Although this is said to be more prevalent in older children and adolescents, we have

gained the impression that it is also common in younger children. We therefore studied retrospectively the age distribution of anginose mononucleosis in our paediatric 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 paediatrics, 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 heterophilic antibody tests may yield negative results in up to 60% of patients younger than 6 years old³ 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 χ^2 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 Age of patients, time of diagnosis, and numbers positive for Epstein-Barr virus

<i>Time of diagnosis</i>		<i>Age (years)</i>				
		<5	5-9	10-14	15-18	<i>Total No</i>
1966-70	No (%) of cases	3(1)	17(6)	52(20)	193(73)	265
	No seropositive	0	9	43	125	177
1971-5	No (%) of cases	14(4)	31(10)	103(33)	164(53)	312
	No seropositive	5	20	89	134	248
1976-80	No (%) of cases	42(12)*	79(23)	161(47)	61(18)*	343
	No seropositive	28	52	112	59	251
1981-5	No (%) of cases	90(24)*	112(30)	98(26)	70(19)*	370
	No seropositive	90	112	98	70	370

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

1966–70, 5.93:1 during 1971–5, 1.83:1 during 1976–80, and 0.83:1 during 1981–5.

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.⁴ 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.⁵ 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

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 1982⁶ 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

- Sumaya CV. Primary Epstein-Barr virus infections in children. *Pediatrics* 1977;22:231-65.
- Christie AB. *Infectious diseases: epidemiology and clinical practice*. 2nd ed. Edinburgh: Churchill Livingstone, 1974: 964-82.
- Timar L, Budia J, Koller M. A prospective study of infectious mononucleosis in childhood. Symptoms, serology, Epstein-Barr-virus specific leukocyte migration inhibition. *Infection* 1982;10:139-43.
- Nye FJ. Social class and infectious mononucleosis. *J Hyg (Lond)* 1979;71:145.
- Henle G, Henle W. Observations on childhood infections with the Epstein-Barr virus. *J Infect Dis* 1970;121:303.
- Sumaya CV, Ench Y. Epstein-Barr virus infectious mononucleosis in children. I. Clinical and general laboratory findings. *Pediatrics* 1985;75:1003-10.

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 antenatally 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.¹ 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 Macclesfield), 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