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Spread of rotavirus within families: a community based study

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Abstract

The spread of rotavirus infection was studied over four weeks in a sample of 28 families exposed to a child with rotavirus infection. The results showed a high incidence of intrafamilial infection, with 46% of members of these families developing rotavirus infections compared with none in another series of 18 families. Children in the families with an index case were more frequently affected than adults: 75% of the children developed rotavirus infection but only 33% of the adults. Children tended to suffer the infection in a more severe form.

Intrafamily contact is clearly important in transmitting rotavirus infection, and preventive measures should aim at reducing the likelihood of such cross infection.

Introduction

There have been several studies of the prevalence of rotavirus infection in child populations.¹ Typically between 50% and 80% of children admitted to hospital with vomiting and diarrhoea during winter are found to have rotavirus infection. The spread of infection in nurseries,² hospitals,³ nursing homes,⁴ and day care centres⁵ and among medical personnel⁶ has been described. Relatively little is known, however, about the transmission of the disease within the community, although it

is commonly thought that most of the spread of infection is intrafamilial.⁷⁻⁹

We describe here a study of the spread of rotavirus infection in a series of families exposed to a child with a rotavirus infection and a series of comparison families. The aims of the study were threefold: (a) to estimate the likelihood that family members would develop rotavirus infection after exposure to an infected family member; (b) to document the frequency with which asymptomatic rotavirus infection occurs in adults and in children; and (c) to estimate the relative contributions of intrafamilial and interfamilial rates of infection, through a comparison of rates of infection in the series of families exposed to rotavirus and the corresponding rates in the comparison series.

Methods

The subjects for the study comprised the family members of 47 children aged under 5 years who presented to their family doctors with vomiting or diarrhoea. Only those children from families who had been without symptoms of vomiting or diarrhoea for at least four weeks before the child's attendance at the family doctor were included in the study.

DATA COLLECTION

Once the children had entered the study families were given the following series of assessments. Firstly, all the families were visited by a medically trained investigator (KG), who explained the objectives of the study and enlisted the family's cooperation. Of the 47 families who entered the study all but one agreed to participate. Secondly, at the initial interview a faecal sample was collected from the presenting child and from any other member of the family who had symptoms of gastrointestinal illness. Blood for serological examination was obtained from all members. Thirdly, all family members were given a diary record in which they were asked to record daily symptoms of rotavirus infection.¹ The symptoms examined were: vomiting, diarrhoea, respiratory symptoms, fever, and malaise. Fourthly, during the four week study the families were telephoned or visited every day, or both; any member who developed gastrointestinal symptoms was visited on the same day and faecal samples were collected. Finally, at the end of the four weeks the family was revisited and a further blood sample obtained.

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LABORATORY METHODS

Faecal samples were tested for the presence of rotavirus antigen with Enzygnost enzyme linked immunoabsorbent assays. Faecal samples from the reference child were also tested for the presence of rotavirus antigen by immunoelectrophoresis.¹⁰ Serum rotavirus antibody titres were tested by complement fixation with a microtitre method based on that of Bradstreet and Taylor.¹¹

DEFINITIONS

On the basis of the initial faecal sample from the reference child, the 46 families participating in the study were classified into two series. The index series comprised the 28 families whose child had rotavirus detected in the faeces on the basis of immunoelectrophoresis or enzyme linked assay, or both. In the remaining 18 families (the control series) the child did not have rotavirus detected in the faeces.

For this study we counted children aged over 12 as adults. The two series of families were similar in family size, age of children, and number of adults in the family (table I).

TABLE I—Characteristics of families with (index) and without (control) in child with rotavirus infection. The reference children have been excluded

	Index families (n = 28) (No ("n"))	Control families (n = 18) (No ("n"))
No of children:		
0	12 (43)	9 (50)
1	12 (43)	4 (22)
2	1 (4)	4 (22)
≥ 3	3 (11)	1 (6)
Ages of children (years):		
≤ 4	12 (50)	8 (53)
5-8	10 (42)	4 (27)
9-12	2 (8)	3 (20)
No of adults:		
1	3 (11)	0 (0)
2	24 (86)	17 (94)
≥ 3	1 (4)	1 (6)

Each family member in the two series was classified as follows: (a) those who showed a fourfold rise in complement fixation antibody titres with or without detectable rotavirus antigen between the initial and final assessments and who also reported symptoms of gastrointestinal illness were classified as rotavirus positive and symptomatic; (b) those who showed evidence of a fourfold increase in complement fixation antibody titres but reported no symptoms were classified as rotavirus positive and asymptomatic; and (c) those who failed to show a fourfold increase in complement fixation antibody titres or the presence of rotavirus antigen were classified as having no infection.

Results

Table II shows the rotavirus status of the subjects, excluding the referred child, at the end of the four week study period. Within the 18 control families (38 adults and 15 children) no one developed any evidence of rotavirus infection. In the index series of 28 families (54 adults and 24 children), however, there was an overall infection rate of 46%. A χ^2 test applied to these differences showed them to be highly significant ($\chi^2 = 33.94$; $p < 0.001$).

Within the index families there was clear evidence of differential

TABLE II—Incidence of infection among family members (excluding the reference children) at the end of four weeks

	Children (≤ 12 years)		Adults (> 12 years)	
	Index families	Control families	Index families	Control families
No rotavirus infection	6	15	36	38
Asymptomatic infection	2	0	4	0
Symptomatic infection	16	0	14	0
Total	24	15	54	38

resistance to infection depending on age. Seventy five per cent of children developed evidence of rotavirus infection, whereas 33% of adults were affected ($\chi^2 = 11.53$; $p < 0.001$). The mean onset of symptoms in children was 4.9 days after the onset of symptoms in the reference child, in contrast to a mean of 6.4 days for adults.

TABLE III—Symptoms that occurred in 18 adults and 18 children infected with rotavirus and their mean duration

	Mean duration of symptoms (days)	
	Children (≤ 12 years)	Adults (> 12 years)
Vomiting	1.28	0.22
Diarrhoea	2.28	1.17
Respiratory	5.06	1.33
Fever	0.44	0.28
Malaise	3.33	1.72
Total	12.39	4.72

Finally, the children seemed to suffer the disease in a more severe form. Table II shows that four out of 18 adults with rotavirus infections were asymptomatic but only two out of 18 children. Because of the small numbers, however, this difference failed to reach statistical significance. Table III shows the number of days over which adults and children had various symptoms. Children had many more symptom days (12.4) than adults (4.7). ($t = 1.94$; $p < 0.05$ one tail test.)

Discussion

Our findings suggest that the primary mechanism in the spread of rotavirus infection is through intrafamilial contacts. Of 78 adults and children exposed to a child suffering from rotavirus infection 36 developed the disease in the subsequent four weeks. In contrast, within a comparison series of 53 adults and children exposed to a child who had vomiting and diarrhoea which was not due to detectable rotavirus infection none developed the condition. The model of infection which emerges is one in which there is a low probability that any family member will contract the condition but once one member becomes infected there is a relatively high probability of cross infection.

Children are more susceptible to intrafamily infection than adults. Of the 24 children in the index families 18 developed the condition, whereas only 18 of the 54 adults were infected. This difference may be due to two factors. Firstly, children are generally more susceptible to rotavirus¹; secondly, children within a family may have more physical contact with each other, which, together with their longer rotavirus excretion rates, increases the likelihood of cross infection.¹² Not only were children more susceptible to infection; they also tended to suffer the disease in a more severe form, having more symptomatic illness, a longer duration of symptoms, and a greater number of symptoms. These findings and previous evidence⁸ all suggest that rotavirus infection in children is associated with more severe symptoms than in adults.

The practical impact of this study is that it shows the important role of intrafamily contact in the transmission of rotavirus infection. The primary emphasis in the prevention of this condition should be on reducing the likelihood that other family members will be infected.

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Serum folate concentrations during pregnancy in women with epilepsy: relation to antiepileptic drug concentrations, number of seizures, and fetal outcome

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Abstract

Serum folate concentrations, blood counts, and anti-epileptic drug concentrations were measured during 133 pregnancies of 125 women with epilepsy. There was an inverse correlation between serum folate concentrations and concentrations of phenytoin and phenobarbitone. The number of epileptic seizures during pregnancy showed no association with serum folate concentrations. No cases of maternal tissue folate deficiency or fetal damage attributable to low maternal serum folate were observed. Maternal serum folate concentrations for infants with structural birth defects, "fetal hydantoin syndrome," or perinatal death were similar to those for healthy babies. A low dose (100 to 1000 µg daily) of folate supplement appeared sufficient for pregnant women with epilepsy despite the antifolate action of antiepileptic medication.

Monitoring folate concentrations in pregnant women with high serum concentrations of phenytoin or phenobarbitone is recommended.

Introduction

Folic acid is required for synthesis of DNA and is essential for the normal development of the human fetus.¹ A deficiency of

folate has been suspected of causing damage to the fetus, particularly if operative in the early weeks of pregnancy.² Treatment with antiepileptic drugs may result in lowered serum folate concentrations^{3,4} and even in megaloblastic anaemia.² Epileptic women taking antiepileptic drugs may reasonably be expected to be at particular risk of folate deficiency during their pregnancies¹; systematic investigations on this are, however, lacking.

We undertook a prospective study of epileptic women during pregnancy, with serial measurements of both folate and antiepileptic drug concentrations.

Patients and methods

A total of 139 epileptic women were followed up during 150 pregnancies. Eighty eight women had grand mal (tonic and clonic convulsive) seizures, 16 had psychomotor (temporal lobe) seizures, 19 both grand mal and psychomotor, 10 focal motor or sensory, and six other or unclassified. The patients recorded their seizures on a calendar, which was checked at each visit. Of the 150 mothers, 137 took combined vitamin tablets with an average daily content of 500 µg (range 100 to 1000 µg) of folic acid from the sixth to the 16th week of pregnancy until parturition; 143 received oral iron supplementation. Of the 150 pregnancies, 17 were excluded because of inadequate fast (see below) or failures in obtaining the blood samples. Subsequently, 133 singleton pregnancies in 125 women remained for analysis. Of the 133, 60 mothers had entered the study by the end of the 16th week of pregnancy.

Serum and red cell folate was radioassayed by a competitive protein binding method^{5,6} at Medix Laboratories, Kauniainen, Finland. Values of serum folate above 4.0 nmol/l (1.8 ng/ml) (2.5 percentile) were considered normal. Haemoglobin concentrations and mean cell volume were measured with a Coulter S counter. Serum phenytoin and phenobarbitone concentrations were measured by gas chromatography⁷ and carbamazepine concentrations by spectrophotometry.⁸ Venous blood for folate and drug assessments was drawn between 1300 and 1500 hours, after a five to eight hour fast following breakfast and the last drug dose. There is evidence that antiepileptic drugs do not interfere with the radioassay of folate.⁹

Serum folate and haemoglobin concentration, mean cell volume, and serum concentrations of antiepileptic drugs were examined

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