References

[1] Coffman JD, Davies WT. Vasospastic diseases; a review. *Prog Cardiovasc Dis* 1975;**18**:123-46.
[2] Raynaud AGM. On local asphyxia and symmetrical gangrene of the extremities. *Selected monographs*. No 121 (transl Bawlow T). London: New Sydenham Society, 1882.
[3] Allen EV, Brown GE. Raynaud's disease: a critical review of minimal requisites for diagnosis. *Am J Med Sci* 1932;**183**:187-200.
[4] Lewis T. Experiments relating to the peripheral mechanism involved in spasmodic arrest of the circulation in the fingers, a variety of Raynaud's disease. *Heart* 1929;**15**:7-101.
[5] Johnston ENM, Summerly R, Birnstingl M. Progress in Raynaud's phenomenon after sympathectomy. *Br Med J* 1965;i:962-4.
[6] Jarrett PEM, Morland M, Browse NL. Treatment of Raynaud's phenomenon by fibrinolytic enhancement. *Br Med J* 1978;ii:523-5.
[7] Tietjen GW, Chien S, Leroy EC, Gavras I, Gavras H, Gump FE. Blood viscosity, plasma proteins and Raynaud syndrome. *Arch Surg* 1975; **110**:1343-6.
[8] Goyle KB, Dormandy JA. Abnormal blood viscosity in Raynaud's phenomenon. *Lancet* 1976;i:1317-8.
[9] Porter JM, Snider RL, Bardana EJ, Rosch J, Eidemiller LR. The diagnosis and treatment of Raynaud's phenomenon. *Surgery* 1975;**77**:11-23.
[10] Peacock JH. The treatment of primary Raynaud's disease of the upper limb. *Lancet* 1960;ii:65-8.
[11] Coffman JD. Vasodilator drugs in peripheral vascular disease. *N Engl J Med* 1979;**300**:713-7.
[12] Tindall JP, Whalen RE, Burton E. Medical uses of intra-arterial injections of reserpine. *Arch Dermatol* 1974;**110**:233-7.
[13] O'Reilly MJG, Talpos G, Roberts VC, White JM, Cotton LT. Controlled trial of plasma exchange in treatment of Raynaud's syndrome. *Br Med J* 1979;i:113-5.
[14] Carlson LA, Eriksson I. Femoral artery infusion of prostaglandin E_1 in severe peripheral vascular disease. *Lancet* 1973;i:155-6.
[15] Carlson LA, Olsson A. Intravenous prostaglandin E_1 in severe peripheral vascular disease. *Lancet* 1976;ii:810.
[16] Szczeklik A, Nizankowski R, Skawinski S, Szczeklik J, Gluszko P, Gryglewski RJ. Successful therapy of advanced arteriosclerosis obliterans with prostacyclin. *Lancet* 1979;i:1111-4.
[17] Pardy BJ, Lewis JD, Eastcott HHG. Preliminary experience with prostaglandins E_1 and I_2 in peripheral vascular disease. *Surgery* (in press).
[18] Martin MFR, Dowd PM, Ring EFJ, Cook ED, Dieppe PA, Kirby JDT. Prostaglandin E_1 in the treatment of systemic sclerosis. *Ann Rheum Dis* 1980;**39**:44.
[19] Martin MFR, Clifford PC, Sheddon J, Baird RN, Dieppe PA. Effects of prostaglandin on objective measurements of peripheral vascular disease. *Clin Sci* 1980;**59**:23.
[20] Neilson PE, Nielson SL, Holstein P, Paulsen HL, Hansen EH, Lassen NA. Intra-arterial infusion of prostaglandin E_1 in normal subjects and patients with peripheral arterial disease. *Scan J Clin Lab Invest* 1976; **43**:633-40.
[21] Whittle BJR, Moncada S, Vane JR. Comparison of the effects of prostacyclin (PGI_2), prostaglandin E_1 and D_2 on platelet aggregation in different species. *Prostaglandins* 1978;**16**:373-88.
[22] Gosling RG, King DH, Newman DH. Ultrasonic angiology. In: Harcus AW, Adamson L, eds. *Arteries and veins*. Edinburgh: Churchill Livingstone, 1975:61-84.
[23] Darling RC, Raines JK, Brener BJ, Austen WG. Quantitative segmental pulse volume recorder: a clinical tool. *Surgery* 1972;**72**:873-7.
[24] Cosh JA, Ring EFJ. Skin temperature measurement by radiometry. *Br Med J* 1968;iv:448.
[25] Hamberg M, Samuelsson B. On the metabolism of prostaglandins E_1 and E_2 in man. *J Biol Chem* 1971;**246**:6713-5.
[26] Szeifler AJ, Cushing BA, Conway J. The relationship between pulse volume and blood flow in the finger. *Angiology* 1967;**18**:591-8.

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Breast-feeding and respiratory syncytial virus infection

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Summary and conclusions

The pattern of breast-feeding in 127 infants admitted to hospital with respiratory syncytial virus infection was compared with that in 503 age-matched controls. Thirty per cent of children with infection had been breast-fed compared with 49% of controls. The approximate relative risk of being admitted to hospital with respiratory syncytial virus infection if not breast-fed was 2·2. Several other factors were also considered, including an assessment of maternal care and home environment; the mother's age, marital state, and smoking habits; the number of siblings; and gestation. Adverse factors were all associated with an increased risk of admission with infection, but breast-feeding still appeared to provide protection after controlling for these other factors in turn.

These findings provide further support for encouraging mothers to breast-feed their infants and should prompt further studies into the immune status of mothers and into the nature of the protective factors in their breast milk.

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Introduction

Infants admitted to hospital with respiratory syncytial virus infection are less likely to have been breast-fed.[1 2] This may be because breast-feeding is protective. Nevertheless, several adverse social and environmental factors such as overcrowding, large families, and unemployment are associated with respiratory syncytial virus infection,[3] and these factors may also be linked with failure to breast-feed. It is therefore not certain whether breast-feeding itself is protective or is only a coincidental finding.

In an attempt to clarify this further we studied various epidemiological factors as well as breast-feeding in a group of children admitted to hospital with respiratory syncytial virus infection and in control children drawn from the general population.

Patients and methods

Children admitted to Tyneside hospitals with respiratory tract infections routinely have nasopharyngeal secretions and nose and throat swabs taken for viral diagnosis. The study included all infants aged 6 months and under in whom respiratory syncytial virus had been

identified from the beginning of December 1977 to the end of March 1978. For each of the infected children four controls were selected from the birth register of the appropriate area health authority matched for date of birth. They were excluded only if they had left the area before the age of 7 months. Neonatal data were obtained from birth records.

During the spring and summer of 1978 the infected and control children were visited by their health visitors, who assessed the housing and maternal care of the baby and completed detailed questionnaires on family structure, environment, and breast-feeding. The health visitors' assessments were adapted from the study by Neligan and Prudham.[4] A four-point scale was used (1=very good, 2=satisfactory, 3=unsatisfactory, 4=very unsatisfactory) to score four aspects of housing (cleanliness, sanitation, furnishing, and structure), giving a total best score of 4 and a worst of 16. Five aspects of maternal care were scored (maternal attentiveness and affectionate interest, ability to seek appropriate help with illness, preparation of feeds, clothing and bedding, and cleanliness), giving a total best score of 5 and a worst of 20.

Results

Two hundred and fifty-one children were admitted to hospital with a respiratory syncytial virus infection during the winter of 1977-8. One hundred and twenty-seven (51%) of these were aged 6 months or under, and these children were included in the study. One hundred and seventeen had a lower respiratory tract infection and 10 had an upper respiratory tract infection. Five hundred and eight controls were selected. Questionnaires were returned for all index children and 503 controls, though a few were incomplete.

The pattern of breast-feeding is shown in table I. The odds ratio or approximate relative risk[5] of being in the virus-infected group if not breast-fed was 2·2 with 95% confidence limits of 1·4 and 3·5. The frequency of other possible risk factors in the virus group and in controls is shown in table II. Relative risk did not vary significantly with social class.

When the prevalence of breast-feeding was examined controlling separately for each of the factors in table II the relative risk of admission with respiratory syncytial virus infection if not breast-fed fell slightly but remained greater than 2·0 (Woolf's test[5]). For example, the relative risk in those with good maternal care was 2·0 and in those with poor maternal care 2·2; these two relative risks did not differ significantly and the overall relative risk was 2·0 (95% confidence limits 1·3 and 3·0). A logistic discriminant analysis of breast-feeding and seven other variables with the highest relative risks in table II suggested that maternal care, a mother's smoking, and the presence of another child in the same room at night were the most useful discriminators of risk. Breast-feeding lost its significance when we tried to allow for these three other variables at the same time but retained its significance when maternal care was excluded ($p < 0.05$) and when only maternal care and breast-feeding were considered ($p < 0.05$).

The duration of breast-feeding is shown in table I. The reduced risk of admission with infection was similar whether the child was still being breast-fed at the time of admission or not. The relative risk comparing those who had stopped breast-feeding and those who were breast-fed at the time of admission was 0·9.

Sixty-seven babies admitted with infection were sufficiently ill to need at least some tube feeds or intravenous fluids to maintain a normal fluid intake, and they were looked at separately. The proportions with adverse factors in the tube-fed group and in the whole group with infection were similar (table II). Nineteen of the tube-fed group had been breast-fed and their duration of breast-feeding was similar to that in the more mildly affected infants. A comparison of only tube-fed babies with controls showed an increased relative risk of admission with respiratory syncytial virus infection of 2·3 in infants who were not breast-fed.

Discussion

Breast-feeding appears to halve the risk of admission to hospital with respiratory syncytial virus infection. Many adverse social factors are also associated with infection and all these factors tend to be associated with each other. The variation in risk with social class was too small to reach significance in the sample under study (relative risk 1·4). In contrast, the strong association with maternal care (which mirrors the earlier findings of Neligan and Prudham with regard to growth, non-verbal intelligence quotient, and school behaviour in later childhood[4]) shows that there are limitations to the epidemiological value of conventional social-class labels. In assessing maternal care the health visitors may instinctively have combined many of the factors that are important in influencing the development of respiratory syncytial virus infection. In addition, knowledge of the previous hospital admission might have influenced what was inevitably a subjective form of assessment. This would explain why maternal care was such a powerful discriminator.

Breast-feeding would also be one of the factors likely to influence the assessment of maternal care, and the consequent close association between the two explains why inclusion of maternal care in a logistic discriminant analysis causes breast-feeding to lose its significance when several factors are considered together. Of the mothers who breast-fed, 94% were assessed as providing good maternal care; this compared with 81% of mothers who did not breast-feed ($p < 0.001$). Even so, when only maternal care and breast feeding were considered breast-feeding retained its significance. We therefore consider that breast-feeding may be an independent factor influencing infection with respiratory syncytial virus.

One possible explanation for the reduced number of breast-fed babies in the group admitted to hospital might have been a greater reluctance to admit a baby who was being breast-fed if its mother was unable to come in as well. But the analysis of the more severely affected infants, who required tube-feeding and were unlikely to have been kept at home however good the circumstances, showed results similar to those for the whole

TABLE II—*Possible risk factors in infants with respiratory syncytial virus bronchiolitis compared with controls*

	No (%) of controls (n=503)	No (%) of virus-infected group (n=127)	Relative risk	No (%) of virus-infected (tube-fed) group (n=67)	Relative risk
Mother's care poor (score >10)	40 (8)	32 (25)	4·1***	16 (24)	3·8**
Single mother	20 (4)	16 (13)	3·7***	11 (16)	5·0**
Another child sleeping with baby	40 (8)	28 (22)	3·2***	15 (23)	3·3**
Gestation <36 weeks	20 (4)	13 (10)	2·7**	11 (16)	4·5**
Housing poor (score >8)	86 (17)	44 (35)	2·7***	23 (34)	2·5**
Mother smokes	206 (41)	80 (63)	2·5***	46 (68)	3·1**
Father off work	75 (15)	38 (30)	2·4***	18 (27)	2·2*
Mother <20 years	55 (11)	25 (20)	2·0*	13 (19)	2·0
One or more siblings	252 (50)	83 (65)	1·9*	42 (63)	1·7
Birth weight <10th percentile	65 (13)	27 (21)	1·7*	17 (25)	2·2*

p value by χ^2 test compared with controls: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

TABLE I—*Patterns of breast-feeding in the virus-infected group and controls*

	Controls (n=503)	Virus-infected group (n=127)	Virus-infected group *v* controls	Virus-infected (tube-fed) group (n=67)	Tube-fed infants *v* controls
No (%) breast-fed	239 (49)	38 (30)	$\chi^2 = 13.93$; $p < 0.001$	19 (28)	$\chi^2 = 9.52$; $p < 0.01$
No (%) breast-fed on admission or equivalent age	102 (20)	16 (13)	$\chi^2 = 4.25$; $p < 0.05$	10 (15)	$\chi^2 = 1.21$; NS
Mean (±SD) duration of breast-feeding (weeks)	11·9±12·5	9·4±11·8		10·4±12·4	

group, suggesting that home circumstances were not influencing admission to any great extent.

Breast-feeding certainly does not give complete protection. Work done by Toms *et al*[6] has shown that breast milk varies in its antirespiratory syncytial virus activity; only four of 16 mothers tested had high levels of IgA specific for respiratory syncytial virus and five of 17 had lymphocytes sensitised to respiratory syncytial virus in their milk. This probably relates to recent exposure of the mother to the virus.

It is interesting that infants do not need to be breast-fed at the time of exposure to infection to be protected; there appears to be a lasting effect. This may be due to the fact that lymphocytes in the colostrum or milk that are sensitised to respiratory syncytial virus colonise the infant's nasopharynx, or to stimulation of the infant's own immune response by transfer of sensitised T cells or of antigen on macrophages. Recent work has suggested that the IgE response in the respiratory tract may be important in the pathogenesis of bronchiolitis,[7] and breast milk in rats has been shown to suppress the IgE response.[8]

This demonstration that breast-feeding probably influences respiratory syncytial virus infection in infants suggests three possible approaches to the problem. Firstly, it gives another reason for encouraging mothers to breast-feed their babies. Secondly, it has prompted us to look further at the immune status of mothers and how this is reflected in their milk and in their infants: boosting mothers' immunity might increase the protection they give to their babies. Thirdly, it provides a stimulus to the investigation of the nature of the protective factors in milk, helping to increase our understanding of immunological defences against respiratory syncytial virus infection.

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References

1 Glezen WP, Denny FW. Epidemiology of acute lower respiratory disease in children. *N Engl J Med* 1973;**288**:498-505.

2 Downham MAPS, Scott R, Sims DG, Webb JKG, Gardner PS. Breast feeding protects against respiratory syncytial virus infections. *Br Med J* 1976;ii:274-6.

3 Sims DG, Downham MAPS, McQuillin J, Gardner PS. Respiratory syncytial virus infection in north-east England. *Br Med J* 1976:ii:1095-8.

4 Neligan GA, Prudham D. Family factors affecting child development. *Arch Dis Child* 1976;**51**:853-8.

5 Armitage P. *Statistical methods in medical research.* Chapter 16. Oxford and Edinburgh: Blackwell, 1971.

6 Toms GL, Pullan CR, Gardner PS, Scott M, Scott R. Anti-respiratory syncytial virus activity in human colostrum and milk. *Arch Dis Child* 1980:**55**:161-2.

7 Welliver RC, Kaul TN, Riddlesburger K, Ogra PL. Development of cell bound immunoglobulin E in respiratory epithelium during respiratory syncytial virus infection. *Pediatr Res* 1980;**14**:566.

8 Jarrett E, Hall E. Selective suppression of IgE antibody responsiveness by maternal influence. *Nature* 1979;**280**:145-7.

The neuropsychiatry of megaloblastic anaemia

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Summary and conclusions

The neuropsychiatric states of 50 patients with vitamin B_{12} deficiency and 34 patients with folate deficiency presenting with megaloblastosis in a general hospital were examined and compared. Abnormalities of the nervous system were found in two-thirds of both groups. Peripheral neuropathy was the most common condition associated with vitamin B_{12} deficiency and affective disorder with folate deficiency. The proportions of patients with organic mental change were similar in the two groups. Subacute combined degeneration of the cord was an uncommon complication and occurred only in the patients with vitamin B_{12} deficiency. There was no relation between haematological and neuropsychiatric abnormalities.

The neuropsychiatry of megaloblastic anaemia seen in this study of patients presenting to haematologists or general physicians contrasts with that reported previously, before haematological techniques for separating the two deficiencies were introduced.

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Introduction

Modern textbook accounts of the neuropsychiatry of megaloblastic anaemia are based on the many clinical reports in the first half of this century before the synthesis of folic acid in 1945 and the isolation of vitamin B_{12} in 1948, and therefore before these two deficiency states could be clearly distinguished.[1 2] No comprehensive study of the neuropsychiatry of vitamin B_{12} deficiency has been carried out since the vitamin B_{12} assay became available in the 1950s, although the effect of vitamin B_{12} deficiency on peripheral nerves,[3] mental symptoms,[4] and the effects of vitamin B_{12} malabsorption after partial gastrectomy[5] have been explored to a limited extent. Furthermore, the neuropsychiatry of vitamin B_{12} deficiency has not been compared with that of folate deficiency despite increasing reports of neuropsychiatric disorders associated with folate deficiency in the past 15 years.[6]

We undertook the present study, therefore, to obtain a more up-to-date perspective of the neuropsychiatric disorders associated with megaloblastic anaemia and to distinguish clearly vitamin B_{12} from folate deficiency with modern haematological techniques. As these deficiency states present more commonly to haematologists and general physicians than to neurologists and psychiatrists we carried out this investigation in a general medical setting.

Patients and methods

We examined and compared the neurological and psychiatric states of 84 successive patients admitted to Northwick Park Hospital with morphological and biochemical evidence of either vitamin B_{12} or folic