

Commentary

Avoiding distress when treating lacerations in a trauma unit is a commendable objective and was achieved in this study in the majority of children over the age of 4 years. However, under 4 years of age, 68% of the patients were crying. Using adrenaline and cocaine 'dripped into the wound' avoided the pain of injecting lignocaine. Their previous unreported experience excluded the use of a comparison group of patients, so it is not possible to quantify any advantage of this technique. However, the authors do not caution against the use of adrenaline on extremities supplied by end arteries, but they justify the very high dose of cocaine by claiming minimal absorption with the 'local vasoconstriction' of adrenaline.

Before requesting the hospital pharmacy to supply this solution, paediatricians should consider the potential difficulties of storing two

controlled drugs of uncertain stability unless kept at a defined temperature. Clear instructions must be issued excluding patients with a history of convulsions or cardiac disease and patients with lacerations on extremities or on mucosal or burnt surfaces.

This study suggests that the technique is not appropriate under the age of 4 years and provides no data to demonstrate that it is associated with less distress than cheaper and safer traditional infiltration with lignocaine.

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Lymphocytes bearing the T cell receptor $\gamma\delta$ in human breast milk

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Abstract

Lymphocytes bearing the T cell receptor $\gamma\delta$ (TCR- $\gamma\delta$) were searched for in human early milk lymphocyte suspensions by two colour cytofluorimetric analysis. It was found that the proportion of TCR- $\gamma\delta^+$ cells was twofold greater in colostrum than in either autologous or heterologous blood samples. Additional studies are needed to determine whether this particular subset of lymphocytes is involved in the lactation transmission of cellular immunity.

Although great strides have been made in defining the tissue distribution of, and receptor gene usage by, human lymphocytes bearing the T cell receptor $\gamma\delta$ (TCR- $\gamma\delta$),¹ their migratory behaviour and homing mechanisms are completely unknown. Human colostrum and milk contain a substantial number of immunocompetent cells,² including T lymphocytes (CD3⁺) of both helper-inducer (CD3⁺/CD4⁺) and suppressor-cytotoxic (CD3⁺/CD8⁺) phenotype.³ In vitro, colostrum T cells display certain characteristics of immunocompetence, but often possess antigenic reactivities different from those of the peripheral blood lymphocytes.⁴ It has consequently been postulated that immune system cells are compartmentalised in the mammary gland during lactation and that T lymphocytes do not accumulate randomly in colostrum, but rather are directed there by a selective homing process.⁴ With these findings in mind, we designed experiments to ascertain whether indeed TCR- $\gamma\delta^+$ cells do migrate to the mammary gland during pregnancy and lactation.

Materials and methods

Early milk samples were collected by manual expression from 15 lactating healthy mothers between days four and seven after delivery of normal term infants. The colostrum lymphocytes were separated by equilibrium density gradient centrifugation as described by Richie *et al.*³ Milk TCR- $\gamma\delta^+$ cells were phenotypically identified by an indirect immunofluorescence staining technique. The monoclonal antibodies used for staining were OKT3 (anti-CD3) (IgG_{2a}, Ortho) and anti-TCR δ 1 (IgG₁, T Cell Sciences) which binds to a δ constant region determinant of the $\gamma\delta$ heterodimer¹ and reacts with all known TCR- $\gamma\delta$ bearing cell clones and lines. Briefly, 1×10^5 cells were incubated for 30 minutes at 4°C with saturating concentrations of each antibody or with identical concentrations of isotype matched monoclonal antibodies that do not react with human cells. The cells were then washed twice and counterstained with goat antimouse F(ab')₂ subclass specific antisera conjugated with either fluorescein-isothiocyanate or phycoerythrin (Southern Biotechnology Associates). After two more washings, the monoclonal antibody bound to the cell preparations was assessed by flow cytometry (FACScan, Becton Dickinson). Data were collected from 20 000 cells per sample and analysed by a Hewlett Packard computer. Autologous and heterologous blood samples were similarly processed and the numbers of TCR- $\gamma\delta^+$ cells compared with those of the mammary secretions.

Results

As in previously published data,³ the percent-

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Lymphocytes bearing the T cell receptor $\gamma\delta$ (TCR- $\gamma\delta$) in human early milk and peripheral blood

Source of lymphocytes	No samples tested	Mean % (range) CD3 ⁺ cells	Mean % (range) TCR- $\gamma\delta$ ⁺ cells*
Milk	15	68 (55-81)	11 (6-26)†
Postpartum blood	15	72 (60-84)	5 (0-18)
Normal blood	15	72 (60-86)	6 (1-15)

*CD3⁺/TCR δ 1⁺ cells.

†p<0.01 (Wilcoxon's rank sum test) with respect to both postpartum and normal blood.

ages of milk and blood cells with a mature CD3⁺ T cell surface phenotype were similar. Two colour cytofluorographic analysis, however, showed that the proportion of TCR- $\gamma\delta$ ⁺ cells (CD3⁺/TCR δ 1⁺) was twofold greater in human early milk than in the peripheral blood (table).

Discussion

Although it is unlikely that colostrum TCR- $\gamma\delta$ ⁺ lymphocytes are merely contaminating blood borne T cells, their origin remains enigmatic. Human TCR- $\gamma\delta$ ⁺ cells populate organised lymphoid tissues (thymus, tonsil, lymph node, and spleen), as well as the gut and skin associated lymphoid systems, at similar frequencies without obvious tropism for epithelial microenvironments.¹ The recent demonstration in experimen-

tal animal models that enterally administered human milk leucocytes adhere to the gut epithelium or lie intramurally and persist in the intestine for at least 60 hours after a single breast feed, however, suggests that these cells may be involved in the host's local immune response.⁵ The problem of whether TCR- $\gamma\delta$ ⁺ cells play a part in the transfer of adoptive immunoprotection to the suckling infant remains unresolved. Now that some of the antigens these lymphocytes respond to have been defined,⁶ however, the way is open to search for the answer. Finally, because of the specificity (δ protein) of the monoclonal antibody (TCR δ 1) used in this study, the possibility that breast milk contains lymphocytes which express just one of the TCR- $\gamma\delta$ chains cannot be totally ruled out.

- 1 Groh V, Porcelli S, Fabbi M, *et al.* Human lymphocytes bearing T cell receptor $\gamma\delta$ are phenotypically diverse and evenly distributed throughout the lymphoid system. *J Exp Med* 1989;169:1277-94.
- 2 Pittard WB. Breast milk immunology. *Am J Dis Child* 1979;133:83-7.
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- 4 Oksenberg JR, Persitz E, Brautbar C. Cellular immunity in human milk. *Am J Reprod Immunol Microbiol* 1985;8:125-9.
- 5 Jain L, Vidyasagar D, Xanthou M, *et al.* In vivo distribution of human milk leucocytes after ingestion by newborn baboons. *Arch Dis Child* 1989;64:930-3.
- 6 Merckenschlager M, Beverley PC. Memory T cells. *Nature* 1989;341:392.

Intravenous immunoglobulin in virus associated haemophagocytic syndrome

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Abstract

A 1 year old boy with virus associated haemophagocytic syndrome caused by cytomegalovirus infection is described. Persistent severe thrombocytopenia responded to repeated intravenous infusions of immunoglobulin.

Virus associated haemophagocytic syndrome is known to occur in association with herpes virus infections. Although the mortality is high, complete recovery has been reported. Immunoglobulin infusions have been shown to increase platelet counts in chronic immune thrombocytopenia. This treatment was effective in a child with severe persistent thrombocytopenia complicating virus associated haemophagocytic syndrome.

Case report

A boy aged 1 year presented with a one month history of intermittent fever and rash. Two days before presentation, he developed periorbital cellulitis, epistaxis, and a petechial rash.

He was the only child of healthy, unrelated

parents. He had previously been well, had received no transfusions, and had been immunised with the full course of triple vaccine and oral polio. He was taking no medications.

On admission, he was febrile (39.1°C) with a diffuse petechial rash. There was generalised lymphadenopathy and appreciable hepatosplenomegaly. Examination of the nervous and respiratory systems was normal.

An initial peripheral blood count showed a haemoglobin concentration of 120 g/l, platelets $57 \times 10^9/l$, and a white cell count of $8.3 \times 10^9/l$, with an absolute neutrophil count of $0.08 \times 10^9/l$. Within 18 hours the haemoglobin was 83 g/l, the platelet count $4 \times 10^9/l$, and the total white count $2.7 \times 10^9/l$. Red cells were hypochromic and microcytic, and occasional reactive lymphocytes were visible. Clotting function was normal.

A bone marrow aspirate showed increased cellularity with active erythropoiesis, increased granulopoiesis, and plentiful megakaryocytes. Haemophagocytosis was present. There was no evidence of malignancy. A repeat bone marrow examination one month later was unchanged. An inguinal lymph node biopsy specimen showed reactive hyperplasia: the architecture

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