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organisms includes one assessment¹ of chloramphenicol. The flora from two nurseries were compared, one using kanamycin and penicillin for the empirical treatment of babies with suspected sepsis and the other using chloramphenicol. In the nursery which routinely used chloramphenicol 43% of *E. coli* strains were resistant to >20 µg/ml of chloramphenicol whereas in the other nursery only 13% were resistant.

In our study stool surveillance was not predictive of the sensitivity of gram-negative pathogens, a lack of relationship noted in another intensive care nursery setting.² The suppressive effect of systemic antibiotics on neonatal gastrointestinal flora that we found has also been recorded by Bennet et al.³

Our study raises serious concern about the liberal use of chloramphenicol in an intensive care nursery. The widespread introduction of any antimicrobial agent into such a setting should be accompanied by careful surveillance, though surveillance cultures of colonising flora seems to be of doubtful value.

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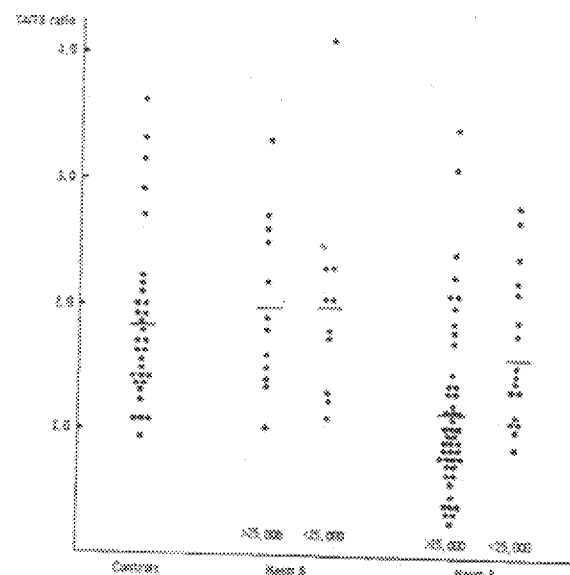
CHARLES G. PROBER
PERCY RAUCHGOT
ROBERT M. BANNATTINE
ROSE CHEUNG
FRANCIS GOOD
ELIZABETH HARDING
STUART MACLEOD

Divisions of Infectious Diseases
and Clinical Pharmacology
and Department of Bacteriology,
Hospital for Sick Children,
and University of Toronto,
Toronto, Ontario, Canada M5G 1X8

PLASMA FRACTIONATION METHODS AND T-CELL SUBSETS IN HAEMOPHILIA

SIR.—Abnormalities of T-lymphocyte subset distribution, characterised by low helper/suppressor (T4/T8), ratios are common in US haemophiliacs treated with commercial factor VIII concentrates. However, patients with acquired immunodeficiency syndrome (AIDS) represent a very small proportion of those exposed to factor VIII.^{1,2} In the UK more than half the factor VIII used is derived from commercial donors in the United States³ and public attention has focused on the possibility that imported concentrates might carry greater risks than similar products made in the UK from volunteer donor plasma. The evidence from Scotland (May 28, p 1226) and Australia (July 2, p 50) for low T4/T8 ratios in patients treated exclusively with locally produced blood products argues against this possibility. US patients treated with cryoprecipitate from volunteer donors have been reported to have normal T4/T8 ratios, but the validity of this finding has been questioned⁴ and others have found abnormal results.⁵

We have studied 64 patients with haemophilia A (mean age 32, range 4–80) treated with both commercial and NHS factor VIII concentrates, 23 patients with haemophilia B (mean age 34, range 3–61) treated with NHS factor IX concentrate alone, and 31 untransfused healthy male controls (mean age 31, range 23–44). Only 1 patient had clinical features of AIDS; a patient with haemophilia A had unexplained lymphadenopathy. The patients were subdivided into those who had received more or less than 25 000 units of concentrate in 1982, a figure which approximates to average annual usage per patient in the UK.⁶ Amounts used in 1982 reflected the intensity of treatment in previous years. T lymphocytes were typed by flow cytometry on an 'EPICS V' cell sorter.



T lymphocyte helper/suppressor ratios in haemophiliacs and controls.

Horizontal bars indicate mean values.

21 of the 47 patients with haemophilia A in the high exposure group, but only 1 of the 17 in the low exposure group, had T4/T8 ratios below the lowest control value (figure). All the patients with haemophilia B had normal ratios. Differences between the high exposure haemophilia A group and the controls and between the high and low exposure haemophilia A groups were significant (Mann Whitney test, $p < 0.0001$ and < 0.005 , respectively). There were no significant differences between the factor IX treated patients and controls.

The observed differences between factor VIII and IX treated patients seem more likely to be causally related to differences in fractionation methods than to differences in donor plasma sources, since small numbers of US patients treated with commercial factor IX concentrates have also been found to have normal T4/T8 ratios.¹² NHS factor VIII concentrate is prepared by aluminium hydroxide absorption of cryoprecipitate, whereas factor IX is fractionated from cryosupernatant using DEAE cellulose. Comparative examination of fractionation intermediates and procedures may be a more profitable approach to resolution of the problem of transfusion-induced immunological abnormalities than attention to donor pool sources. Our observations also suggest that low T4/T8 ratios may have simple biochemical causes and should not necessarily be regarded as being predictive of AIDS.

Haemophilia Centre
and Department of Immunology,
Royal Free Hospital,
London NW3 2QG

CHRISTINE A. LEE
G. JANOSY
J. ASHLEY
P. B. A. KERNOFF

STATISTICS, T-LYMPHOCYTE SUBPOPULATIONS, AND HAEMOPHILIA

SIR.—The paper by Dr Luben and colleagues (March 5, p 503) reporting abnormal distributions of T-lymphocyte subpopulations in children and adolescents with haemophilia was interesting and, with other reports,^{1,2} suggests that acquired immunodeficiency

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