these lymphoblasts with neuraminidase (Chapel, 1973; Mehrishi and Zeiller, 1974) did not increase the number of cells with markers and failed to show masked determinants.

It is noteworthy that four out of the five patients with detectable Ig on the surface of their lymphoblasts were investigated at presentation before treatment. Further studies are planned to investigate if these lymphoblasts with surface Ig persist during the course of the disease. The findings in one patient (case 11) suggest that they do. Apart from this observation there was no correlation between the presence or absence of markers with the prognostic assessment at diagnosis, based on leucocyte count, percentage blasts, and presence or absence of mediastinal enlargement on chest x-ray picture.

Nevertheless, important information can be obtained by characterizing surface markers on A.L.L. lymphoblasts. Such an approach may be clinically important in the early classification of cases of A.L.L. since there is some evidence that cases of T-cell origin have an exceptionally poor prognosis (Borella and Sen, 1973; Catovsky *et al.*, 1974 b). The important observation that some A.L.L. lymphoblasts express B-cell markers, together with other recent findings (Haegert *et al.*, 1974 b), suggest that A.L.L. is a disease of heterogeneous origin divisible into at least four groups—those without surface markers, those with T- or B-cell markers, and those cases expressing combined T- and B-cell determinants (Haegert *et al.*, 1974 b).

J. L. Smith was supported by the Leukaemia Research Fund, D. G. Haegert by a fellowship from the Medical Research Council of Canada.

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MEDICAL MEMORANDA

Successful Thymus Graft for T-cell Deficiency in a 6-year-old Boy

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British Medical Journal, 1975, **1**, 314-315

Thymus transplantation in patients with DiGeorge's syndrome (August *et al.*, 1968; Cleveland *et al.*, 1968) has been shown to produce rapid and dramatic reconstitution of cell-mediated immunity. Temporary reconstitution of cell-mediated immunity (Levy *et al.*, 1971) but not of humoral immunity (Amman *et al.*, 1973) has been achieved in vari-

ous immunodeficiency diseases. We report the successful grafting of a fetal thymus into a 6-year-old boy with T-lymphocyte deficiency proved on three occasions before the operation.

Case Report

A 6-year-old Caucasian boy was admitted to hospital with a history of repeated respiratory infections. He was regularly off school three days out of four and was almost continuously on antibiotics. He was an adopted child and had a half-brother aged 7 years, also adopted by the same family. They had the same mother but different fathers.

The patient had normal facies and none of the features of DiGeorge's syndrome. He was apparently well until the age of 1 year, when he began to have feverish illnesses with coughs, diagnosed as bronchitis, which responded to antibiotics. Various antibiotics had been prescribed over a relatively short period. His doctor had tried on one or two occasions to leave him without antibiotics but he became rapidly worse and eventually had to be given antibiotics. He showed no eczema and sneezing was not a feature though wheezing was common. At one stage he developed severe allergy to streptomycin. He received quadruple immunization, oral polio vaccine, and, later, measles vaccination. His mumps and chickenpox were no worse illnesses than those of his brother and he had not had measles. He had frequent attacks of pneumonia and clearly had a much higher tendency to infections than did his brother.

INVESTIGATIONS

Methods and Materials

Lymphocyte transformation to phytohaemagglutinin (PHA) was done according to the standardized method of Yamamura (1973) and to candida immunogen by the standardized method of

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Foroozanfar *et al.* (1974). For the one-way mixed lymphocyte reaction the stimulator cells were freshly separated lymphocytes from the same donor throughout blocked with mitomycin C and thereafter well washed. A total of 200 000 stimulator cells were added to 200 000 of the patient's cells and the rest of the test was performed as for candida immunogen.

Throughout all the tests shown in tables I and II both the patient's fresh plasma and a known male compatible plasma were used at 20% (for PHA at 10%) strength in the culture medium. Results are given as the transformation index (T.I.) calculated as C.P.M. of stimulated cells/C.P.M. of unstimulated cells.

TABLE I—*T-cell Function before and after Thymus Grafting as Shown by Transformation Indices (See Text)*

	Before	After
PHA (normal range 27-255)	4.5-29	70-260
Candida immunogen (normal range 2.5-84)	1.1-1.2	3-5
Allogeneic cells (normal >2.5)	<1-<1	27-31

TABLE II—*T-cell Function before and after Thymus Grafting as Shown by Numbers of Non-Ig-bearing Lymphocytes per mm³ of Peripheral Blood*

	Before	After
Total No. (normal 676-2667)	2100	2000
No. forming sheep R.B.C. rosettes (normal 600-2300)	<20	1200

Immunoglobulin levels were measured by a modified Mancini method (Hobbs, 1970).

Phagocytosis was assessed both by a candida killing test (Foroozanfar and Yamamura, unpublished) with and without the patient's fresh plasma and by a nitroblue tetrazolium test.

Fetal thymus 6578 was kindly supplied fresh from the Royal Marsden Hospital's fetal tissue bank (Dr. S. Lawler). It was from a male fetus of HL-A types HL-A 2, W 19, W 14, and W 18 (three loci being distinct from those of the patient).

Results

Humoral Immunity.—Serum immunoglobulin levels on three occasions ranged as follows (normal values in parentheses): IgG 4.4-8.4 g (5-16 g), IgA 0.5-1.8 g (0.65-2 g), and IgM 0.55-0.75 g (0.4-1.6 g)/l. and IgE 115-400 units (55-640 units)/ml. Surface-marker studies using fluorescent antisera showed normal numbers of B-lymphocytes in his peripheral blood: IgG 240 (103-369)/mm³, IgA 280 (15-590)/mm³, IgM 115 (40-301)/mm³. Complement studies of fresh plasma showed normal levels of C3 and C4 with no appreciable conversion.

Phagocytosis.—The total W.B.C. was 5600-8000/mm³, with neutrophils 2200-2520/mm³ and monocytes 152-240/mm³, showing normal morphology and normal content of myeloperoxidase. The patient's white cells attacked standard *Candida albicans* in either his own plasma (30% kill) or normal plasma (40% kill), the results being clearly within the normal range (20-40% kill). The nitroblue tetrazolium test gave normal results. Thus no defect was detected intrinsic to the phagocytes or to the patient's plasma.

T-cell Immunity (tables I and II).—The total lymphocyte count was 2460-3050/mm³. The results of lymphocyte transformation tests showed on all occasions severe T-cell deficiency. There was no delayed hypersensitivity reaction to a candida skin test. His peripheral blood lymphocytes showed less than 1% of cells forming spontaneous rosettes when tested once against sheep red blood cells. These results show defective T-cell with normal B-cell function.

TREATMENT AND PROGRESS

The patient received a 20-week-old male fetal thymus by implantation in the rectus abdominis sheath. The second day after the

operation the lymphocyte transformation to PHA, candida immunogen, and allogeneic cells became normal and has remained normal (table I). Two months after the operation he received a smallpox vaccination and had a normal primary response. The vaccination was necessary because he was going to travel through India and the Far East. Antivaccinal γ -globulin and other supportive measures were made available at the time.

Eight months postoperatively he had had no further recurrent infections, repeated administration of antibiotics was not necessary, and he was attending school normally. No peripheral blood cells sensitive to cytotoxic antisera against W 19, W 14, and W 18 (the three types confined to the thymus graft) were detected. His immunoglobulin levels and W.B.C. had remained normal.

Comment

The immediate appearance of cell-mediated immunity in this patient may well be compared with case reports presented by other workers (August *et al.*, 1968; Cleveland *et al.*, 1968) in which thymus grafting was performed in children with DiGeorge's syndrome. Rapid normalization of cell-mediated immunity in these cases and ours argues strongly in favour of a humoral factor (thymic hormone?) released from the graft effecting a final "polishing" of non-Ig-bearing lymphocytes (presumably immature T-cells) already circulating.

Our findings differ from those of Amman *et al.* (1973), in which reconstitution of cell-mediated immunity in a patient suffering from severe combined immune deficiency did not appear until nine months after thymus transplantation and the donor-type lymphoid population appeared in the peripheral blood of the recipient. We have been unable to detect cells of graft origin. Our patient did not have any stigmata of chronic mucocutaneous candidiasis as did the patient of Levy *et al.* (1971) and one of the two patients described by Aiuti *et al.* (1974).

It is not clear what to call this boy's defect. It appeared to be confined to T-cells and was almost certainly congenital. Such children, dying earlier from measles, might have been said to suffer from a syndrome similar to that reported by Nezelof *et al.* (1964), but clearly our case and the two Italian girls reported by Aiuti *et al.* had precursor T-cells capable of rapid conversion to competent T-cells after thymus grafting. The simpler classification of immune deficiency used by Hobbs (1974) would categorize this boy as having a qualitative defect of T-lymphocytes (dyslymphocytosis) and act as a sound practical guide to treatment.

We therefore believe that immunological functions were successfully reconstituted in this child having defective cell-mediated immunity, and until the purified thymic hormone becomes available implanting fetal thymus remains the treatment of choice.

We are indebted to the staff of the fetal tissue bank of the Royal Marsden Hospital and to those who supply it, for without these facilities the therapy would not be available. We also thank Dr. K. Hugh-Jones, under whose care the patient was admitted.

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