HAEMOPHILIA AND OTHER COAGULATION DEFECTS AMONGST BOYS RESIDENT AT LORD MAYOR TRELOAR COLLEGE

Summer Term 1974 and Autumn Term 1974

The number of boys suffering from these defects, registered with the College for the above two terms, are shown in Table I.

Although the total figures for each term appear to be approximately the same there was a marked change in the population between the Summer and Autumn Terms. Fourteen boys suffering from haemophilia left the College at the end of the Summer Term and were replaced by another nine boys.with this defect at the commencement of the Autumn Term. In addition, one boy categorised under the miscellaneous group, namely [redacted] (53), who was a spastic and only a potential haemophiliac with a factor VIII level of more than 7%, left at the end of the Summer Term. His place was taken in the Autumn Term by [redacted] (107), suffering from radial aplasia with thrombasthenia and thrombocytopenia. He is, therefore, shown on Table I for the Autumn Term 1974 as a miscellaneous case.

HAEMOPHILIA

During the Summer Term, five boys were included in the Prophylactic Trial. Day to day records of bleeds and transfusions for the remaining 37 boys are shown in Figure A. During the Autumn Term only 3 boys were selected for the Prophylactic Trial. Day to day bleeds for these 3 boys and the remaining 36 are shown in Figure B. An analysis of the figures for bleeds and transfusions for all these boys are in Tables II, III and IV. In Table II the figures for the boys suffering from haemophilia, excluding those on the Prophylactic Trial and those with inhibitors, are analysed independently and it is quite remarkable how closely the figures for each term resemble each other, in spite of a change of approximately 38% of the population between the Summer and Autumn Terms.

At the request of Dr. Katherine Dormandy, one of these boys, [redacted] (10), received a prophylactic dose of factor VIII every other day when undertaking his G.C.E. examinations, and it is for this reason that he was excluded from the Prophylactic Trial:during the period he received this prophylaxis he suffered only one minor bleed.

It will be seen from Table II that the mean frequency of bleeding episodes for each of these terms for this group of boys, was approximately that of previous terms, namely, Summer Term - 7.3 and Autumn Term - 7.1 per 100 days. The figure for the Autumn Term is remarkably low considering that there were nine new boys, (Case Nos. 94,96,97,98,100,102,103,104,106) five of whom appear to be relatively severe clinically. However, one of the new boys, [redacted] (94), who has a basic factor level of about 2% suffered from no haemorrhagic episodes during his first term. The total number of mild cases, i.e. those bleeding less than 3.5 bleeds per 100 days remain approximately the same for each term (Summer Term: 9, Autumn Term: 7). Table III shows an analysis for all cases of haemophilia including those involved in the Prophylactic Trial but excluding those with inhibitors. The influence on the figures of including these additional severe cases is apparent.

In Table IV is an analysis of the boys included in the Prophylactic Trial and the figures for bleeds and transfusions given are those for the whole term and not just for the period that they were receiving prophylactic transfusions. Furthermore, it is not known what prophylactic dose any of these boys was receiving. It will also be noted that the three boys in the trial during the Autumn Term received prophylactic transfusions over a very short period of time. It is,however, remarkable how closely the analysis figures for each term resemble each other.

HAEMOPHILIA ASSOCIATED WITH FACTOR VIII INHIBITORS

Details for this group of boys for the two terms are shown in Table V. It will be noted that [redacted] (62), has been excluded from this table during the

Autumn Term 1974. This boy is a bit of a mystery. During the Christmas holiday a weak factor VIII inhibitor was detected at Oxford and it was for this reason that he was included in this table for the Summer Term. However, he responds well to replacement therapy and frequent tests for an inhibitor have been equivocal. Those tests that have been positive have only shown little more than a trace of what appears to be an antigoagulant. He has, therefore, been treated normally throughout the Autumn Term with replacement therapy as if no inhibitor were present.

It will be seen from Table V that boys in this group have been receiving more replacement therapy than formally. Furthermore, this practice does not appear to have raised their inhibitor level to any marked degree, with the exception of [redacted] (74) whose antibody titre rose to more than 100 Biggs' units after receiving five transfusions for haemarthrosis of the knee. In spite of this, his condition improved but unfortunately, he fell and again injured this knee. This accident produced a very severe haemarthrosis and because of the high antibody titre he was transferred to the Nuffield Orthopaedic Centre (N.O.C.) on 26.11.74 for further treatment and remained there for the rest of the term.

It will also be seen from Table V that [redacted] (45) was given nine therapeutic transfusions during the term and his inhibitor was continuously monitored. The rise in antibody never exceeded 18 Biggs' units and fifteen days later it had fallen to 4 Biggs' units. He responded well clinically to transfusions although the maximum post transfusion rise of factor VIII level never exceeded 4%.

CHRISTMAS DISEASE

Details of the boys suffering from factor IX deficiency are shown in Table VI. It will be seen that there are now eight boys at the College suffering from Christmas Disease, four of whom entered at the commencement of the Autumn Term 1974 (Case Nos. 95,99,101,105). Two of the new boys (95 and 99) appear to be relatively severe and this accounts for the rise in the mean number of bleeds per 100 days for this group of boys. However, investigations on these new boys are still far from complete. One new boy, [redacted] (105), suffered no bleeds during his first term.

MISCELLANEOUS CASES

[redacted] (107) suffers from radial aplasia. His f.VIII and f.IX levels eppear to be normal but his thrombocyte count on two occasions barely exceeded 30,000 per cmm. Aggregometer tests also appear to indicate a delay in aggregation but this needs to be confirmed. He suffered from no haemorrhagic episodes during the term nor does he show any signs of anaemia.

HAEMATURIA

Only one boy suffered with haematuria during the Summer Term 1974, namely [redacted] (6). He returned bleeding from the Easter holiday and under treatment of Prednisone. This treatment, however, appeared to have no effect as he continued to bleed for four days. He was then transfused with cryoprecipitate and his bleeding ceased within 48 hours without further complications.

There were no cases of haematuria during the Autumn Term.

HEPATITIS

Two boys with inhibitors (Case Nos.45 and 69) and eight of the haemophiliacs (Case Nos. 43,27,54,56,57, 85,88, and 97) developed hepatitis during the Autumn Term. With the exception of 69, 97 and 45, all cases were extremely mild, icterus being absent and bilirubin levels were only very slightly raised above 1mg. All, however, had some symptoms. The remaining three cases69,97 and 45 were more severely affected: all three boys were jaundiced with significantly raised bilirubin levels. All ten boys had markedly raised S.G.P.T. and S.G.O.T. levels. One thing common to all cases was a batch of Hemofil with which they were treated. Furthermore, Case 69

had received no other replacement therapy with the exception of this batch of Hemofil.

This outbreak is being further investigated by the Public Health Laboratory Service in conjunction with Dr. Peter Kirk who has spent a great deal of time and trouble with these investigations. It is hoped that a full report concerning this outbreak will eventually be published. No boy at the school, other than those suffering from coagulation disorders, has suffered from jaundice

REPLACEMENT THERAPY

The total number of transfusions given during the two terms is shown in Table VII. It is quite remarkable how closely the figures approximate to each other, especially so when there was such a marked change in the population of the boys at the commencement of the Autumn Term. Furthermore, the mean number of transfusions per day remains at approximately 10% of the total number of boys under observation and this figure holds true for all the boys suffering from haemophilia with the exception of those with an inhibitor. (See Tables II and III).

There is, however, one major difference between the Summer and Autumn Terms, namely that during the Summer Term 1974, 60 transfusions out of 442 were given at the College but during the Autumn Term, 178 out of 457 were administered there. It will be seen, therefore, that the number of transfusions given at the College has almost tripled. This is largely due to the fact that there now three medical officers available to afford treatment, i.e. the Research Fellow; Dr. Peter Kirk, S.H.O. in Haemophilia, and Dr. John McHardy, who was appointed as Medical Officer of the College and took up his appointment in September 1974. There is no doubt that the increase of treatment at the College has proved to be beneficial for the boys

Haemophilia - The total number of therapeutic transfusions administered to boys suffering from haemophilia, including those with inhibitors, are shown on Tables II, III and IV. It will be seen that the response to treatment has continued to improve: approximately 1.3 - 1.4 transfusions per bleed being required. There is no doubt, therefore, that the potency of the cryoglobulin received from Southampton has been maintained at a relatively high level. The mean figure per donor unit now being approximately 80 units of factor VIII.

Christmas Disease - In Table VI it will be seen that the number of therapeutic transfusions per bleed for both terms remains, as usual, between 1.2 and 1.3 per bleed. Practically all cases were treated with factor IX concentrate (intermediate potency) supplied by Dr. Bidwell. Fifty-nine transfusions were given during the two terms, forty-seven of them being given at the College. The response to treatment with this material (administering approximately 30 units per kg.) was as expected.

BOYS TREATED AS IN-PATIENTS IN HOSPITAL

(Boys sent to Lord Mayor Treloar Hospital for orthopaedic treatment are not included if hospitalised for less than four days)

GROA (16) - This boy developed a very severe bleed into the right ileo psoas on the 21.6.74. There was marked contraction with flexion of the right thigh and loss of sensation down the medial surface of the thigh and leg. He was, therefore, transferred to Lord Mayor Treloar Hospital under the care of Mr. F. J. Moynihan, where he remained until the end of term when it is understood he was transferred to the Nuffield Orthopaedic Centre, Oxford.

GROA (27) - This boy was admitted to Lord Mayor Treloar Hospital under the care of Mr. F. J. Moynihan, for treatment of a severe haemarthrosis of the right knee following a fall. He remained in hospital for eight days when he was able to return to the College and attend classes in a wheelchair for another week.

GROA (45) - This boy fractured the neck of his femur during the Easter holidays and remained in the Nuffield Orthopaedic Centre throughout the whole of the Summer Term.

GROA (73) - Admitted to the Nuffield Orthopaedic Centre towards the end of the summer holiday for an operation to correct equinus deformity of both legs due to contracture of the calf muscles. He had been on the waiting list for this operation for more than two years. He did not return to school for the whole of the Autumn Term but he has now returned and is walking well, the treatment having been completely successful.

GROA (74) - See 'Inhibitor' section, page (1).

GROA (54) - This boy was transferred to the Churchill Hospital Oxford Haemophilia Centre on the 23.10.74 for observation ? appendicitis. However, he was found to be suffering from acute hepatitis and returned to the College nine days later.

RESEARCH PROGRAMME

Prophylactic Trial - This trial is now complete and a report is being prepared.

A new research programme to cover the next three years has been formulated and acceptance of this programme is awaited from the National Fund for Research into Crippling Diseases; some preliminary work has,however, already been carried out. Certain other projects are being continued, namely :

(a) Hepatitis - In view of the recent outbreak the Public Health Laboratory Service, The Virus Reference Laboratory, Colindale, have agreed to the further continuance of this project.

(b) Arthritis in Haemophilia - This work is being continued in conjunction with the M.R.C. Rheumatoid Unit at Taplow and the M.R.C. Haemophilia Research Unit at Oxford.

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Research Fellow in Haemophilia

SGR/RCS
JANUARY 1975

TABLE 1

	Summer 1974	Autumn 1974
Haemophilia	42	39
Haemophilia with Inhibitors	5	5
Christmas Disease	4	8
Miscellaneous	1	1
TOTAL	52	53

TABLE 11

Haemophiliacs (Excluding those on Prophylaxis and those with Inhibitors)

	Summer 1974	Autumn 1974
No. of Cases	37	36
Days	2965	3245
Bleeds	215	230
Transfusions	304 (31)	308 (95)
Mean Bleeds/100 days	7.3	7.1
Mean Transfusions/Bleed	1.4	1.3
Mean Transfusions/Day	3.6	3.4

This Table excludes 7 Prophylactic transfusions given to one of these boys at the College.
() = Transfusions given at College.

TABLE III

All Haemophiliacs (Excluding those with Inhibitors)

	Summer 1974	Autumn 1974
No. of Cases	42	39
Days	3370	3521
Bleeds	269	268
Therapeutic transfusions	375(37)	358 (109)
Bleeds/100 days	8.0	7.6
Transfusions/bleed	1.4	1.3
Transfusions/day	4.5	3.9

() = Transfusions given at College.

TABLE IV

Haemophiliacs on Prophylactic Trial

NAME	DAYS Summer '74	DAYS Autumn '74.	BLEEDS Summer '74	BLEEDS Autumn '74.	THERAPEUTIC TRANSFUSIONS	Summer '74	Autumn '74.	PROPHYLACTIC TRANSFUSIONS Summer '74.	Autumn '74.
GRO-A	69(42)	Absent	10	Absent	LMTH	11	Absent	5	Absent
					College	1	-	-	-
GRO-A	84(68)	92(23)	21	13	LMTH	26	12	7	3(9)*
					College	2	4	2	11
					Elsewhere	1	1	-	-
GRO-A	84(70)	92(37)	10	12	LMTH	11	12	9	4
					College	2	2	-	1
GRO-A	84(66)	92(44)	9	13	LMTH	12	11	9	5
					College	1	8	-	1
GRO-A	84(65)	Absent	4	Absent	LMTH	4	Absent	8	Absent
					College	-	-	1	-
TOTALS	405(311)	276(104)	54	38	LMTH	64	35	38	12(9)*
					College	6	14	3	13
					Elsewhere	1	1	-	-

	Summer '74.	Autumn '74.
Bleeds/100 days	13.3	13.8
Transfusions/100 days	17.5	18.1
Transfusions/Bleed	1.31	1.32

() = Days on Prophylaxis.

()* = Prophylaxis prior to physiotherapy before admission to trial.

TABLE V

Haemophilia with factor VIII Inhibitors

NAME	NO.	BLEEDS		TRANSFUSIONS		DAYS	
		Summer 1974	Autumn '74	Summer'74	Autumn'74	Summer	Autumn
GRO-A	92	4	5	-	-	84	92
GRO-A	69	1	5	-	3(2)	84	92
GRO-A	74	3	2	1(1)	5	84	76
GRO-A	62	6	-	4	-	84	-
GRO-A	45	Absent	7	Absent	9(7)	-	92
GRO-A	63	6	4	1(1)	-	84	92
TOTALS		20	23	6(2)	17(9)	420	444
Mean Bleeds/100 days.		4.8	5.2				

() = Transfusions given at College.

TABLE VI

Christmas Disease

NAME	NO.	BLEEDS		Therapeutic Transfusions.		Prophylactic Transfusions.		Days	
		Summer'74.	Autumn '74.	Summer 1974.	Autumn 1974.	Summer 1974.	Autumn 1974.	Summer.	Autumn.
GRO-A	95	Absent	7	Absent	7(7)		3(3)		92
GRO-A	60	3	7	4(4)	8(5)			84	92
GRO-A	61	3	4	4(3)	4(2)		1(1)	84	92
GRO-A	99	Absent	9	Absent	12(8)				92
GRO-A	101	Absent	2	Absent	2(2)				92
GRO-A	89	4	6	5(4)	9(8)			84	92
GRO-A	105	Absent	-	Absent	-				92
GRO-A	80	-	-		-			84	92
TOTALS		10	35	13(11)	42(32)		4(4)	336	736

Bleeds/100 days 3.0 4.76
Transfusion/Bleed 1.3 1.20

() = Transfusions given at College.

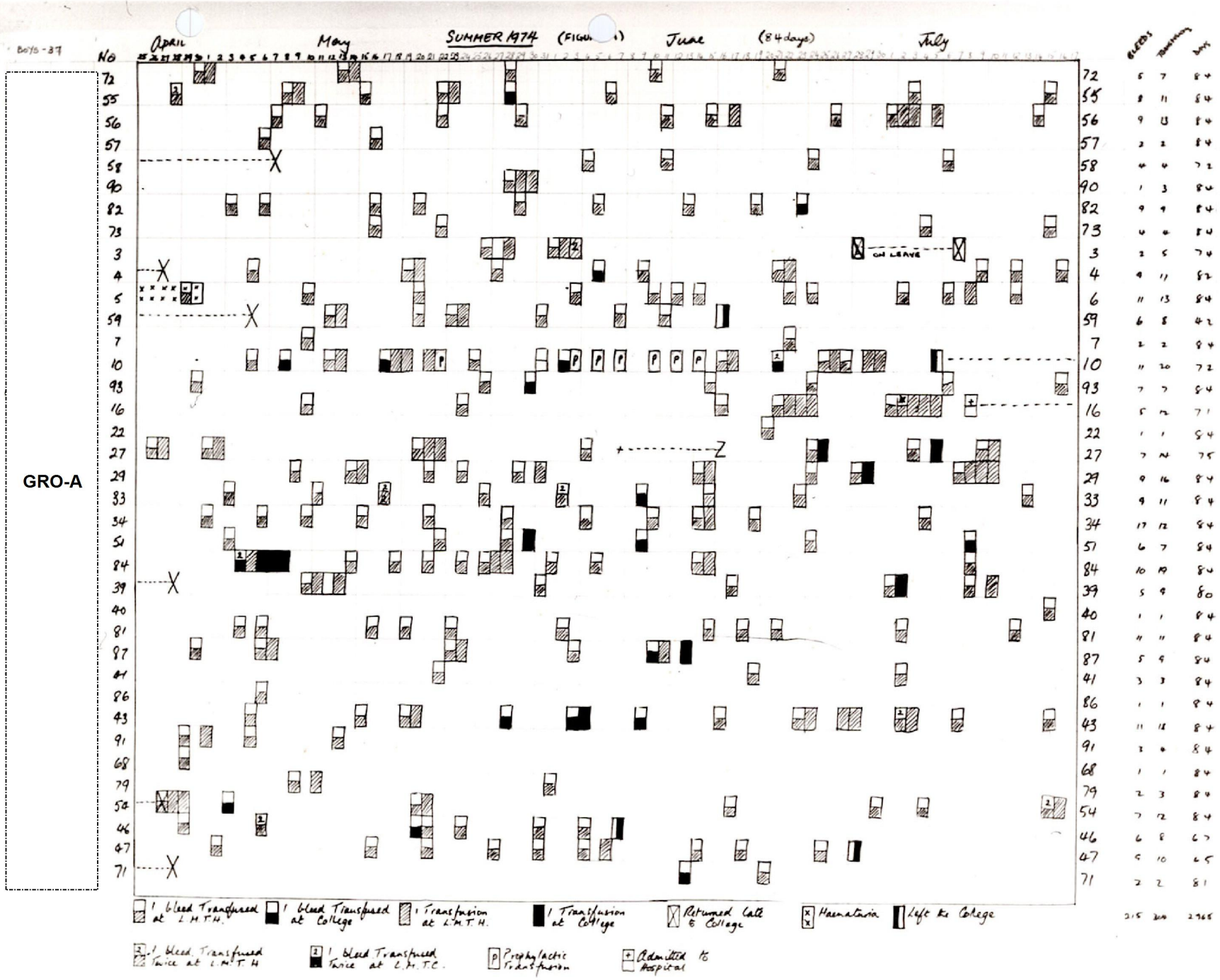
TABLE VII

REPLACEMENT THERAPY

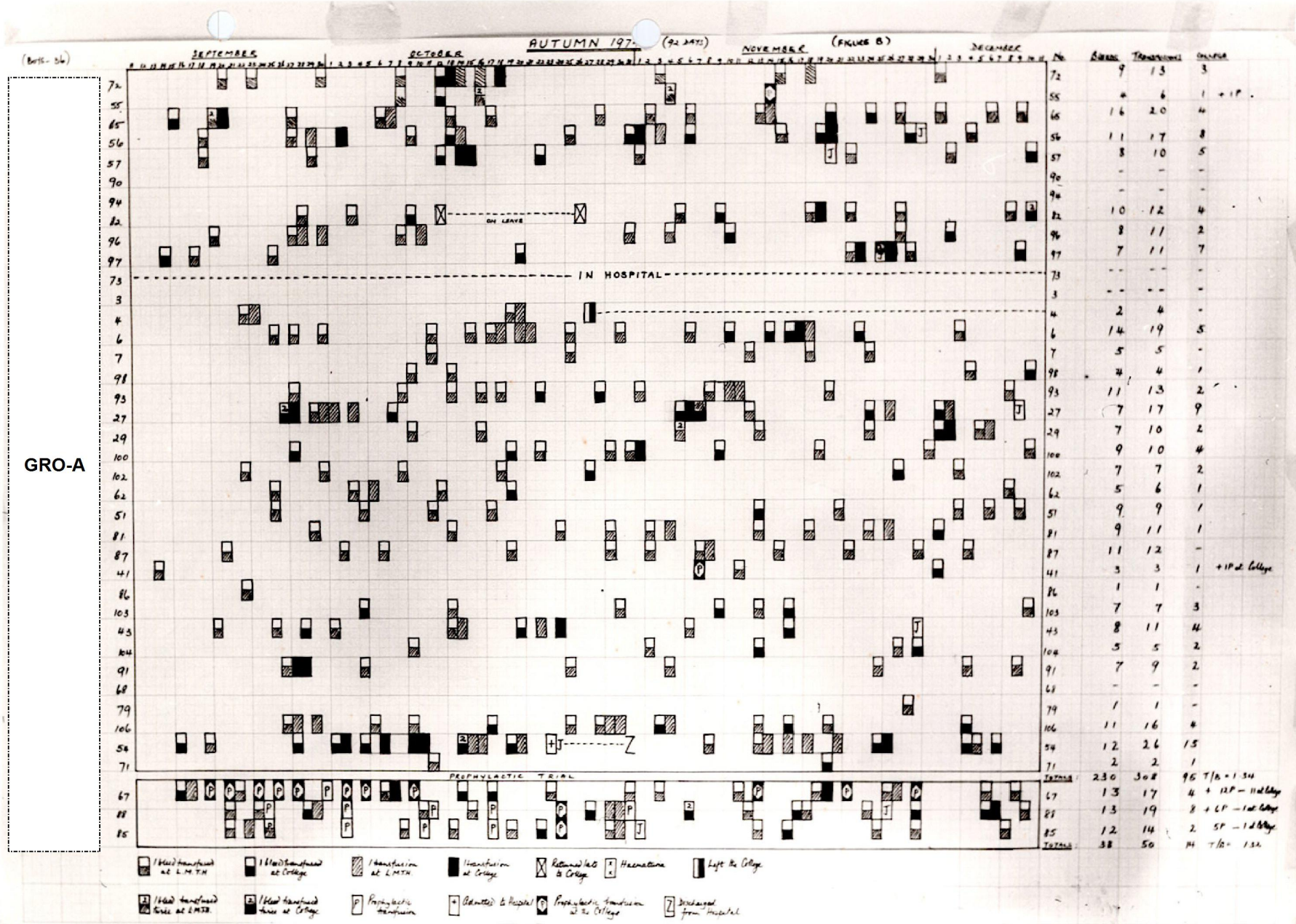
DISEASE	NO. OF PATIENTS	THERAPEUTIC			PROPHYLACTIC		
		LMTH	COLLEGE	ELSEWHERE	LMTH	COLLEGE	TOTALS
			Summer Term 1974				
Haemophilia, excluding those on Prophylactic Trial	37	273	31	-	-	7	311
Haemophilia with Inhibitors	5	4	2	-	-	-	6
Christmas Disease	4	2	11	-	-	-	13
Haemophiliacs in Prophylactic Trial	5	64	6	1	38	3	112
TOTALS	51	343	50	1	38	10	442
			Autumn Term 1974				
Haemophilia, excluding those on Prophylactic Trial	36	213	95	-	-	2	310
Haemophilia with Inhibitors	5	8	9	-	-	-	17
Christmas Disease	8	10	32	-	-	4	46
Haemophiliacs in Prophylactic Trial	3	35	14	1	12	22	84
TOTALS	52	266	150	1	12	28	457

Total transfusions/day — Summer Term 1974 : 5.3 — Autumn Term 1974 : 5.0

Total transfusions/day excluding those on Prophylactic Trial — 3.9 — 4.1



GRO-A



GRO-A