Psychiatric Illness after Hysterectomy

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It has often been reported that patients with gynaecological complaints are particularly prone to be psychologically unstable and more liable than other women to postoperative psychiatric sequelae.

Snaith and Ridley (1948) stated that 46% of their gynaecological patients had "psychologically unstable constitutions." Rogers (1950) claimed that half of the women who presented themselves for gynaecological treatment had no gross gynaecological disorder, and described their illness as "a psychic conflict sailing under a gynaecological flag." Cohen *et al.* (1953) found gynaecological operations to be seven times commoner in patients suffering from hysteria than in control subjects. Benson *et al.* (1959) claimed that 33% of subjects with atypical pelvic pain showed indications of psychosomatic disease.

It is perhaps surprising therefore that few studies by gynaecologists mention psychiatric sequelae after hysterectomy. Melody (1962), in his series of 267 patients, found 11 who developed depressive symptoms in the first three months post-operatively; but Howkins and Williams (1963), in their series of 1,000 patients, mentioned only two who developed psychiatric illnesses.

Psychiatrists, on the other hand, particularly in the United States, have published many studies on the incidence of psychiatric sequelae after hysterectomy and the possible factors involved in their development. Lindemann (1941), in a study of only 40 women who had undergone surgical operations, found that those who had had a pelvic operation were more likely to have postoperative depressive symptoms than those who had had a cholecystectomy. Stengel *et al.* (1958) reported on a series of 80 patients with severe postoperative mental disorder, of whom seven had had a hysterectomy, and found that, though the incidence of mental disorder was no higher after gynaecological operations generally than after other abdominal operations, there was a significantly higher incidence of psychosis after hysterectomy. Ackner (1960) reported that 30% of his series of 50 patients had emotional complaints six months after hysterectomy. Others (Patterson *et al.*, 1960; Patterson and Craig, 1963) have reported that, although admission to a psychiatric ward was commoner in women who had had a previous hysterectomy than in the general population, no direct relation between the operation and referral could be established in the majority of cases. Also, Bragg (1965), in a survey of 3,000 postoperative patients followed up for an average period of 10 years, found that only 43 had been subsequently admitted to a psychiatric hospital: there was no significant difference in subsequent admission between the hysterectomy and the cholecystectomy patients.

The problem of identifying those liable to develop psychiatric sequelae after hysterectomy has also received considerable attention. The patient's attitude to her uterus and its significance for her in her "own self image of womanliness" was stressed by Kroger (1957), Drellich and Bieber (1958), and Hollender (1960). A more objective observation was made by Lindemann (1941), Ackner (1960), and Melody (1962), who stated that many of those who experienced emotional disturbance postoperatively had had psychiatric symptoms preoperatively.

Miller (1946) claimed that 33% of hysterectomies were carried out in the absence of pathological findings, and inferred

that some were performed because of the complaints of emotionally disturbed patients. He was followed by other workers who made similar observations. These papers were criticized by D'Esopo (1962), who stated that even when there was no significant finding, as in dysfunctional bleeding, hysterectomy was still the operation of choice, and advocated that psychiatric advice be sought only in the small proportion of patients with atypical pelvic pain. Ackner (1960), on the other hand, found a higher proportion of subsequent emotional disorder in those with organic disease at operation as compared with those with "functional uterine disturbance."

Most of these papers dealt with small numbers and reported percentages and tendencies without submitting the data to statistical analysis. Also, the criteria used for determining psychiatric sequelae ranged from mental hospital admission to "emotional instability," thus allowing no comparison of data.

The present study was designed to examine the incidence of psychiatric breakdown after hysterectomy, and to submit the findings to statistical analysis. Referral to a psychiatrist was used as a criterion of breakdown because it was a more objective measure than "emotional instability," and included the large number of people now being treated at psychiatric outpatient departments. The incidence of psychiatric referral after hysterectomy was compared with that after another operation performed in middle life, cholecystectomy, and also with the expected rate of psychiatric referral in the general population. The hysterectomy patients were divided into two groups according to pelvic pathological findings, and these groups were compared with regard to incidence of referral. The effect of marital state, as being a crude indication of sexual adjustment, was examined for its value in predicting psychiatric referral after hysterectomy.

Method

The 729 women who had undergone a hysterectomy in the two general hospitals in the city of Dundee during the period 1 January 1960 to 31 December 1964, and were normally resident in Dundee at the time of operation, were included in the study.

All women who had had a cholecystectomy in two of the three surgical wards in the city over the same period, and were residing in the city at the time of the operation, were used as a control group. One patient was excluded because she was found to have ovarian carcinoma and had had a bilateral oophorectomy at the same time, leaving 280 in the study.

Any psychiatric records of the gynaecological and surgical patients were then searched for in the files of the Dundee Psychiatric Services—the name, date of birth, address, and confirmatory evidence of previous operation being used as means of identification. The records were searched up to 31 December 1966, so that patients were followed up for a minimum of two and a maximum of seven (mean four and a half) years. As all patients referred to a psychiatrist in Dundee are recorded centrally, it was felt that almost complete coverage was achieved.

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The gynaecological case notes and pathological reports were examined in all the 729 hysterectomy patients for details of pathological findings, marital state, and nulliparity at the time of operation.

χ^2 tests of significance were used mainly in the analysis, as being appropriate to proportionate data. All were of one degree of freedom. Yates's correction was used for small cell entries.

Incidence of Psychiatric Referral after Hysterectomy and Cholecystectomy

A significantly higher proportion of hysterectomy patients than of cholecystectomy patients were referred to a psychiatrist after the operation (Table I). This was particularly evident in those who had not been referred to a psychiatrist previously (Table I).

TABLE I.—Patients Referred to Psychiatrist After Operation

	Hysterectomy (N=729)	Cholecystectomy (N=280)	χ^2	P
Total psychiatric referral post-operatively	53 (7%)	9 (3%)	5.1	<0.025
Psychiatric referral for first time postoperatively	36 (5%)	3 (1%)	6.95	<0.01

Because not all of the women were followed up for the same length of time, the total number of referrals per woman-years at risk was calculated for the six years before and the six years after operation in both groups of patients. If a patient was referred more than once in any year this was counted as a single referral, and referral of the patient while still convalescent in hospital was regarded as referral at operation. A comparison was then made between the incidence of referral in both groups before operation and similarly after operation

FIG. 1.—Comparison of total number of psychiatric referrals per woman-years at risk for hysterectomy and cholecystectomy patients.

(Fig. 1). There was no significant difference in the psychiatric referral rate before operation. In the six years after operation there was a significantly higher incidence in the hysterectomy patients, giving a $\chi^2=6.6$ ($P<0.01$).

As may be seen from Fig. 1, the incidence of psychiatric referral after hysterectomy reached a peak two years after the operation. However, 43 patients (81%) claimed to have become nervously unwell within the first year postoperatively, 28 immediately after operation, and 15 within a few months, during which time they had initially felt better (Fig. 2).

The incidence of psychiatric referral occurring for the first time within the two years after hysterectomy and cholecystectomy was then compared with the incidence of psychiatric referral within the female population of the City of Dundee over a similar period of time. As there was no significant variation from year to year in the number of patients so referred after operation, the numbers were pooled over the whole study for each operation group. This incidence was compared with an expected first referral rate over a two-year period calculated from the incidence of first referrals to the psychiatric service from within the City of Dundee in the years 1961 and 1962. The female population figures were obtained from the 1961 census (Registrar General, 1962).

FIG. 2.—Time lapse between operation and onset of psychiatric symptoms and psychiatric referral in hysterectomy patients.

Since it was clear that the age distribution in the operation patients and the psychiatric control groups differed substantially, all three groups were separated into decades by age. On the basis of the observed incidence in each decade in the control group, an expected frequency was calculated for each decade in the hysterectomy and cholecystectomy groups. The expected numbers were then combined to give a total expected number of first referrals in both groups and compared with the observed number of first referrals in the same groups.

The expected incidence of first referral within two years after hysterectomy was 9.04 (1.2%), compared with an observed incidence of 23 (3.2%) ($P<0.005$). There was no significant difference between the expected incidence of 3.12 (1.1%) and the observed incidence of 3 (1.1%) in the cholecystectomy patients (Table II).

It has been inferred that removal of the ovaries, producing a premature menopause, may be associated with a higher incidence of psychiatric sequelae (Lewis and Jackson, 1940).

TABLE II.—Comparison of Incidence of Psychiatric Referral for First Time Within 2 Years after Hysterectomy and Cholecystectomy

Age	Female Population of Dundee			Hysterectomy Patients			Cholecystectomy Patients		
	N	No. of Psychiatric Referrals For 1st Time in 1961-62	%	N	No. of 1st Referrals Within 2 years		N	No. of 1st Referrals Within 2 years	
					Expected	Observed		Expected	Observed
25-34	12,009	154	1.28	117	1.5	4	23	0.28	—
35-44	12,024	174	1.44	332	4.78	9	40	0.58	1
45-54	12,896	126	0.98	201	1.96	7	67	0.66	2
55-64	11,768	92	0.78	45	0.36	2	70	0.54	—
65-79	10,772	142	1.32	34	0.44	1	80	1.06	—
Total	59,469	688	1.2	729	9.04 (1.2%)	23 (3.2%)	280	3.12 (1.1%)	3 (1.1%)

$\chi^2 = 21.83$, $P < 0.005$

N.S.

In the present series 140 women had a premature menopause, induced by bilateral salpingo-oophorectomy. Only eight had a subsequent psychiatric referral—all for the first time. This was not significantly different from the incidence of psychiatric referral among those women who did not have an induced menopause. It would appear, therefore, that a premature menopause was not associated with a higher incidence of psychiatric illness.

Gynaecological Diagnosis and Psychiatric Referral

In assessing gynaecological diagnosis the patients were placed in two groups according to the pathological reports. Group 1 included those who had pelvic carcinoma, carcinoma-in-situ, or other significant disease of the pelvic organs such as fibroids, adenomyosis, ovarian tumours, or endometrial changes associated with anaemia ($Hb < 75\%$). Group 2 included those in whom no physical signs or pathological abnormality had been demonstrated, or where simple endometrial changes were shown pathologically but *without* anaemia—for example, "hyper-oestrinism," "hormonal imbalance," "some gland infolding." There were 570 patients in group 1 (significant disease) and 159 in group 2 (no significant disease).

The incidence of psychiatric referral after operation was found to be significantly different in the two groups: 32 (6%) patients in group 1 and 21 (13%) patients in group 2 ($P < 0.005$). This was largely accounted for by the fact that approximately half of all patients who had had a previous psychiatric referral were re-referred after hysterectomy, and the incidence of previous psychiatric referral was five times greater in group 2 than in group 1 ($P < 0.005$) (Table III).

TABLE III.—All Hysterectomy Patients—Comparison of Incidence of Psychiatric Referral with Pathological Findings

	Group 1 (N=570)	Group 2 (N=159)	χ^2	P
Total postoperative psychiatric referrals	32 (6%)	21 (13%)	9.53	<0.005
Psychiatric referral for first time postoperatively	26 (5%)	10 (6%)	N.S.	
Those with preoperative and postoperative referral	6 (1%)	11 (7%)	16.31	<0.005
Preoperative psychiatric referral	14 (2%)	16 (10%)	16.38	<0.005

While examining the gynaecological and other general hospital case records of the patients it became apparent that there was a much higher total "psychiatric morbidity" than was indicated by referral alone. "Morbidity" here was defined as comprising all those with a psychiatric referral plus those who had been given a psychiatric diagnosis by another physician or surgeon, or had been treated with an antidepressant drug, tranquilizer, or sedative. Those who were merely stated to be "nervous," "anxious," or "hypochondriacal" were not included.

The figures for psychiatric morbidity (Table IV) follow closely the figures for psychiatric referral (Table III). However, two points emerge. Firstly, the subsequent psychiatric morbidity can be seen to be twice as great as subsequent referral, rising to 25% of all patients in group 2. Secondly, the difference between groups 1 and 2 with respect to psychiatric mor-

TABLE IV.—All Hysterectomy Patients—Comparison of Incidence of Psychiatric Morbidity with Pathological Findings

	Group 1 (N=570)	Group 2 (N=159)	χ^2	P
Total psychiatric morbidity postoperatively	49 (9%)	39 (25%)	29.83	<0.005
Psychiatric morbidity recorded for first time postoperatively	42 (7%)	22 (14%)	5.71	<0.025
Psychiatric morbidity before and after operation	7 (1%)	17 (11%)	31.11	<0.005
Preoperative psychiatric morbidity	22 (4%)	25 (16%)	27.05	<0.005

bidity occurring for the first time after operation is statistically significant ($P < 0.025$), being twice as high in group 2 patients

Marital State and Psychiatric Referral

The incidence of divorce among the hysterectomy patients was not significantly different from the incidence among the female population of Dundee (1961 Census). With the procedure adopted above for Table II, an expected number of 10.68 (1.5%) divorced women was calculated; this compares with the observed number of 11 (1.5%).

However, when those patients with a psychiatric referral postoperatively were compared with those without subsequent referral a different pattern emerged.

Though the Census returns gave figures only for divorce it was possible here to identify 31 patients who were divorced, had been divorced but remarried, or were currently separated from their husbands. All these patients were grouped together under the heading "marital disruption."

The incidence of both divorce and marital disruption was seven times greater in those patients referred to a psychiatrist after operation as compared with those not referred in the follow-up years ($P < 0.005$) (Table V).

TABLE V.—Marital Disruption—Comparison of Hysterectomy Patients Who Had Postoperative Psychiatric Referral with Those Not Subsequently Referred

Marital State	Patients Without Subsequent Referral (N=676)	Patients With Subsequent Referral (N=53)	χ^2	P
Divorced	7 (1%)	4 (7%)	7.94	<0.005
Marital disruption	20 (3%)	11 (21%)	34.07	<0.005

Divorce is known to occur more often among psychiatric patients (Ødegard, 1953), but the incidence of divorce and marital disruption among the patients referred to a psychiatrist after hysterectomy was also significantly higher than the expected incidence based on the figures for the total number of female referrals to the Dundee Psychiatric Services in 1962 (Table VI).

TABLE VI.—Comparison of Expected and Observed Incidence of Marital Disruption Among Those Referred to a Psychiatrist After Hysterectomy

Marital State	Patients Referred to Psychiatrist After Hysterectomy (N=53)			
	Expected No.	Observed No.	χ^2	P
Divorced	1.15 (2%)	4 (7%)	4.91	<0.05
Marital disruption	4.43 (8%)	11 (21%)	9.08	<0.005

Eleven (35%) of those women with marital disruption at operation were subsequently referred to a psychiatrist, compared with 39 (6%) of those who had a stable marital history ($P < 0.005$). The incidence of psychiatric referral occurring before operation and for the first time after operation was also significantly higher among those with marital disruption ($P < 0.005$) (Table VII).

TABLE VII.—Incidence of Psychiatric Referral Among Those with Marital Disruption Compared with Those with Stable Marital Histories

	Stable Marital History (N=626)	Marital Disruption (N=31)	χ^2	P
Total psychiatric referral postoperatively	39 (6%)	11 (35%)	31.89	<0.005
Psychiatric referral for first time postoperatively	29 (5%)	6 (19%)	9.42	<0.005
Preoperative psychiatric referral	22 (4%)	5 (16%)	8.99	<0.005

All those women who had a history of marital disruption and a previous psychiatric history were subsequently re-referred, whereas only 50% of those with a previous psychiatric history and stable marriage were re-referred.

It would appear then that marital disruption is associated with a six times greater incidence of psychiatric referral after hysterectomy than is a stable marital history. Also in those women already predisposed by reason of previous breakdown it increases still further the chance of re-referral.

There were only 72 (10%) spinsters among the hysterectomy patients. Three were referred to a psychiatrist after operation. Two had been previously referred. All had significant disease. When compared with married women there was no significant difference for psychiatric referral.

Mention has been made of the tendency for those who wanted more children to have a psychiatric breakdown after hysterectomy (Ackner, 1960). In the present study a comparison was made between those women who were stably married and parous and those also stably married but nulliparous. There were 69 nulliparous women, of whom 4 (6%) were subsequently referred to a psychiatrist, and 557 parous women, of whom 35 (6%) were referred. Nulliparity appeared to have no special effect on psychiatric referral.

Of the women who were referred postoperatively 41 were still married or cohabiting. Nine of the "husbands" showed disturbed behaviour after the hysterectomy, including impotence, suicide, irritability, promiscuity, and taunting the wife with being "only half a woman" or "no use." Eight of their wives had given histories of difficult sexual or marital circumstances before the hysterectomy. In only one instance was there an apparently satisfactory marital history previously, and here the wife lost her sexual libido postoperatively.

Psychiatric Diagnosis and Symptoms

Of the 53 patients referred to a psychiatrist after hysterectomy 45 (85%) were suffering from depression (manic-depressive reaction, depressive and neurotic-depressive reaction). The others were diagnosed as suffering from psychoneurosis (3), paranoid states (2), psychosis with cerebral arteriosclerosis (1), psychosis resulting from brain tumour (1), manic-depressive reaction, manic (1).

It was interesting that 35 (66%) of these patients had also been referred to at least one other outpatient department between the hysterectomy and referral to a psychiatrist. The most common symptoms were "nervousness" (14), recurrence of somatic complaints (12), "depression" (12), "exhaustion" (9), and insomnia (3). Fifteen (28%) patients were admitted to a general hospital, having taken an overdose of drugs while depressed in spirits.

Discussion and Conclusions

Stengel *et al.* (1958) suggested that the higher incidence of psychiatric referral after hysterectomy which they reported might have been due to the older age of the hysterectomy patients in their series, who were therefore exposed to stress at a "particularly vulnerable age." In the present study the hysterectomy patients had a mean age of 44 years compared with a mean age of 55 in the cholecystectomy patients, and yet the incidence of psychiatric referral remained higher among the hysterectomy patients.

Most other follow-up studies have been concerned with psychiatric sequelae during the first six months after hysterectomy (Ackner, 1960; Hollender, 1960; Melody, 1962). In the present study the peak period for psychiatric referral was the second year after hysterectomy. There was no such peak after cholecystectomy (Fig. 1). This would suggest that hyster-

ectomy may be followed by psychological effects, the impact of which is not felt until long after the patient has recovered from the surgical operation.

Three factors were found to be significantly linked with an increased chance of psychiatric referral after hysterectomy. These were the absence of pelvic disease, psychiatric referral before operation, and a history of marital disruption. Of the 570 patients with pelvic disorder 32 (6%) were subsequently referred to a psychiatrist, compared with 21 (13%) of the 159 patients who had no pelvic disorder. This incidence was twice as high ($P < 0.005$, Table III). Of the 699 patients who had had no previous psychiatric referral 36 (5%) were subsequently referred to a psychiatrist; whereas 17 (57%) of the 30 patients who had been referred to a psychiatrist before hysterectomy were re-referred after the operation ($\chi^2 = 133.29$, $P < 0.005$). This indicates that those who had had a previous psychiatric illness were more than 10 times as likely to have a further illness after hysterectomy. Of the 626 patients with stable marital histories 39 (6%) were subsequently referred to a psychiatrist, compared with 11 (35%) of the 31 patients with a history of marital disruption. This was a six times greater incidence ($P < 0.005$, Table VII).

It is suggested, therefore, that there are certain patients on whom a hysterectomy should be performed only after much thought and perhaps only after psychiatric assessment. This would be the case where the patient complained of menorrhagia or pelvic pain, and where there was no anaemia or significant finding either on pelvic examination or on curettage, especially if the patient had had a previous psychiatric referral or had a history of marital disruption.

After hysterectomy most of the women were followed up at the gynaecological clinic for a period of six weeks, but it was found that few of the patients in this series who were subsequently referred to a psychiatrist had admitted at this time to having nervous symptoms. Some had even stated that they felt better during the period immediately after the operation. This study showed, however, that depression should be looked on as one of the major postoperative complications of hysterectomy, and a longer period of follow-up would appear to be necessary in order to exclude psychiatric sequelae. It is suggested that this might be best carried out by the general practitioner, as the period might have to extend over two years after hysterectomy. Those women who have had a previous psychiatric referral or a history of marital disruption should be followed up with special care after operation.

As somatic symptoms are often features of a depressive illness, attention should be paid to both physical and emotional complaints, particularly exhaustion, the recurrence of somatic symptoms, nervousness, and depression. In all such cases the patient should be specifically questioned about depression of mood and other depressive symptoms, and a psychiatric opinion sought if necessary.

Summary

It was found that 7% of 729 women who had had a hysterectomy were referred to a psychiatrist within a mean period of four and a half years after the operation. This rate was two and a half times higher than the incidence of psychiatric referral after cholecystectomy, and almost three times higher than the expected incidence among women of similar age in the general population. Eighty per cent. of the psychiatric referrals occurred within two years of hysterectomy. The most frequent psychiatric symptom was depression.

The incidence of psychiatric referral after hysterectomy was more than twice as high among patients without significant pelvic pathology as among those with significant pathology. Fifty-seven per cent. of all patients with a previous psychiatric history were re-referred after the operation. Thirty-five per cent. of all women who were separated or divorced at the

time of operation were referred to a psychiatrist after hysterectomy.

Conclusions were drawn for preoperative assessment and for follow-up after hysterectomy.

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REFERENCES

- Ackner, B. (1960). *Advanc. psychosom. Med.* (Basel), 1, 248.
 Benson, R. C., Hanson, K. H., and Matarazzo, J. D. (1959). *Amer. J. Obstet. Gynec.*, 77, 806.
 Bragg, R. L. (1965). *Amer. J. publ. Hlth*, 55, 1403.
 Cohen, M. E., Robins, E., Purtell, J. J., and Altmann, M. W. (1953). *J. Amer. med. Ass.*, 151, 977.

- D'Esopo, D. A. (1962). *Amer. J. Obstet. Gynec.*, 83, 113.
 Drellich, M. G., and Bieber, I. (1958). *J. nerv. ment. Dis.*, 126, 322.
 Hollender, M. H. (1960). *Amer. J. Obstet. Gynec.*, 79, 498.
 Howkins, J., and Williams, D. (1963). *J. Obstet. Gynaec. Brit. Cwlth*, 70, 20.
 Kroger, W. S. (1957). *West. J. Surg.*, 65, 317.
 Lewis, A. J., and Jackson, J. (1940). *J. Neurol. Psychiat.*, 3, 101.
 Lindemann, E. (1941). *Amer. J. Psychiat.*, 98, 132.
 Melody, G. F. (1962). *Amer. J. Obstet. Gynec.*, 83, 410.
 Miller, N. F. (1946). *Amer. J. Obstet. Gynec.*, 51, 804.
 Ødegard, Ø. (1953). *J. ment. Sci.*, 99, 778.
 Patterson, R. M., and Craig, J. B. (1963). *Amer. J. Obstet. Gynec.*, 85, 104.
 Patterson, R. M., Craig, J. B., Dinitz, S., Lefton, M., and Pasamanick, B. (1960). *Obstet. and Gynec.*, 15, 209.
 Registrar General (1962). *Preliminary Report on 16th Census of Scotland, 1961*. H.M.S.O., London.
 Rogers, F. S. (1950). *Amer. J. Obstet. Gynec.*, 59, 321.
 Snaith, L., and Ridley, B. (1948). *Brit. med. J.*, 2, 418.
 Stengel, E., Zeidyn, B. B., and Rayner, E. H. (1958). *J. ment. Sci.*, 104, 389.

Preliminary Communications

Duration of Remissions in Lymphoblastic Leukaemia of Childhood

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The presence and distribution of glycogen in blood cells can be studied by means of the periodic-acid-Schiff (P.A.S.) reaction. Interest has been shown in the frequent occurrence of quantitative changes in disease states, particularly lymphoproliferative disorders (Astaldi and Verga, 1957; Quaglino and Hayhoe, 1959; Bjornberg, 1963). A wide variation, both in proportion of cells containing glycogen and in the quantity of glycogen in individual cells, has been demonstrated in the primitive cells of lymphoblastic leukaemia (Hayhoe *et al.*, 1964). The question arises whether any special significance is attributable to this variation.

During a recent evaluation of the effect of cyclic maintenance therapy on the duration of first remission in acute leukaemia of childhood (Willoughby and Laurie, 1968) it was noticed that strong P.A.S. positivity appeared to be related to longer first remissions. The present study was undertaken to investigate this point further.

MATERIAL AND METHODS

Studies were made of 26 patients diagnosed on cytological and cytochemical grounds as suffering from lymphoblastic leukaemia (Hayhoe *et al.*, 1964). All subsequently achieved remission. Marrow smears taken before the beginning of treatment were stained by the P.A.S. reaction and the percentage of P.A.S.-negative lymphoblasts was obtained from a count of 500 such cells. The 26 patients could readily be divided into a group with less than 40% P.A.S.-negative blast cells and a group with less than 55% P.A.S.-negative blast cells—strong and weak P.A.S. respectively. Duration of first maintained remission and survival were compared in each group.

The length of the first remission was measured as the number of completed calendar months from the beginning of treatment.

The criteria of maintained remission and the standard cyclic drug regimen used during the period of remission are described elsewhere (Willoughby and Laurie, 1968). The length of remission and survival in acute leukaemia has been shown to be less the shorter the duration of initial symptoms and the higher the initial blast count in the peripheral blood (Acute Leukaemia Group B, 1963; Zuelzer, 1964). The incidence of these two features was therefore also compared in each group. Symptoms of less than three weeks were thought to be of short duration and a peripheral blood blast count greater than 5,000/cu. mm. was thought to be high (Acute Leukaemia Group B, 1963).

Three patients were removed from the series at six months, while still in remission, after modifications to the maintenance regimen. Five of the lymphoblastic cases from the previously reported series were excluded because of lack of a satisfactory marrow preparation before treatment. Chemotherapeutic agents have been shown to lower the P.A.S. positivity of leukaemic lymphoblasts (Quaglino and Hayhoe, 1959).

FIG. 1.—Duration of remission related to P.A.S. staining of pretreatment marrow. The columns at progressive time intervals show the cases remaining in their first remission at these periods. X Cases withdrawn at 6 months while in remission.