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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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.

RESULTS

The proportion of P.A.S.-negative blast cells ranged from 3 to 97%. The distribution of the percentage of P.A.S.-negative lymphoblasts of patients in the series—that is, in remission at one month—and of those in remission at 3, 6, 9, and 12 months is shown in Fig. 1. The difference in the proportions of the two groups, with high and low proportions of P.A.S.-negative blast cells, remaining in remission at progressive three-monthly intervals is significant, particularly beyond six months ($P < 0.01$, Table I).

TABLE I.—Number of Cases in First Maintained Remission and Having Relapsed at Three-monthly Intervals in Weak and Strong P.A.S.-positive Groups

P.A.S. Positivity	Total in group	3 Months		6 Months		9 Months		12 Months	
		Relapsed	Remission	Relapsed	Remission	Relapsed	Remission	Relapsed	Remission
Weak ..	14	1	13	7	7	8	4	11	1
Strong ..	12	0	12	1	11	1	10	3	8
Total ..	26	1	25	8	18	9	14*	14	9*
P value from χ^2 test ..		0.5		<0.05		<0.01		<0.01	

* Three cases were withdrawn while in remission at 6 months. In the "weak" P.A.S. group more than 55% of the blast cells were P.A.S. negative, and in the "strong" P.A.S. group less than 40%. The χ^2 value was calculated from 2×2 tables with 1 degree of freedom.

The only patient in the weakly P.A.S.-positive group still in remission at 12 months relapsed at 14 months. Of the eight patients still in remission at one year in the strongly positive group, one died from encephalitis at 27 months while still in complete remission, three relapsed at 15, 24, and 32 months, and four are still in remission at 14, 20, 24, and 30 months.

FIG. 2.—Duration of survival related to P.A.S. staining of pretreatment marrow. The columns at progressive time intervals show cases surviving at these periods. X Cases still alive but not yet followed beyond these points.

TABLE II.—Number of Patients Surviving and Having Died at Six-monthly Intervals in Weak and Strong P.A.S.-positive Groups

P.A.S. Positivity	6 Months		12 Months		18 Months		24 Months	
	Dead	Alive	Dead	Alive	Dead	Alive	Dead	Alive
Weak ..	1	13	6	5	9	1	10	0
Strong ..	1	11	1	10	2	8	3	5
Total ..	2	24	7	15*	11	9*	13	5
P value from χ^2 test ..			<0.05		<0.01		<0.01	

* Eight cases are still alive but have not yet been followed for 24 months, 4 have survived for 6 months, 2 for 12 months, and 2 for 18 months.

The distribution of the percentage of P.A.S.-negative lymphoblasts of patients surviving at 6, 12, 18, and 24 months is shown in Fig. 2. The difference in the proportions of the two groups surviving at six-monthly intervals is particularly significant beyond 12 months ($P < 0.01$, Table II).

Median survival, calculated by life-table methods, is 11½ months in the group showing weak P.A.S. positivity, while that in the strong P.A.S.-positive group, in which to date only three patients have died, is 25 months.

Table III shows weak P.A.S. positivity to be significantly associated with short duration of symptoms ($P < 0.02$) and high initial lymphoblast count ($P < 0.01$).

TABLE III.—Comparison of Duration of Symptoms and Initial Peripheral Blood Blast Count in Weak and Strong P.A.S.-positive Groups

P.A.S. Positivity	Duration of Symptoms		Initial Blasts in Peripheral Blood	
	< 3 Weeks	> 3 Weeks	> 5,000/cu.mm.	< 5,000/cu.mm.
Weak ..	10	4	10	4
Strong ..	3	9	2	10
Total ..	13	13	12	14
P value from χ^2 test ..	<0.02		<0.01	

DISCUSSION

These observations suggest that the presence of a high proportion of P.A.S.-negative lymphoblasts in the bone marrow is related not only to a short length of first remission and survival but also to the associated features of high initial blast-cell count in the peripheral blood and short duration of symptoms before diagnosis (Tables I, II, and III).

The relations become more marked at the extremes of P.A.S. positivity. All the patients with more than 80% P.A.S.-negative cells had initially more than 30,000 blasts per cu. mm. in the peripheral blood. All had relapsed within one year and none had survived to 18 months. Those with less than 25% P.A.S.-negative cells had low initial blast counts even with symptoms lasting as long as 11 weeks. Only one patient had relapsed within the first year, and is the only one at present to have died before 18 months (Fig. 2).

These findings suggest that the P.A.S. reaction in acute lymphoblastic leukaemia provides a cytological feature which may be more closely related to duration of first remission and survival than is the initial peripheral blood blast count. The presence of weak P.A.S. positivity even with a low initial blast count was associated with early relapse and short survival, while both cases with strong P.A.S. positivity and a high initial blast count fared better than the median, one surviving 35 months.

The association of high initial blast count in the peripheral blood, short duration of symptoms, and a tendency to early relapse suggests a more rapid proliferation of leukaemic cells in some cases. Further evidence to suggest variations in the rate of proliferation of leukaemic cells from case to case has recently been presented (Hardisty and Norman, 1967, and Saunders *et al.*, 1967). Nagao (1966) has shown that in acute leukaemia in childhood the greater the proliferative activity of the leukaemic cells the shorter is survival.

It seems reasonable to suggest, though it has not been proved, that a high percentage of P.A.S.-negative lymphoblasts in the bone marrow indicates a high degree of proliferative activity of that particular cell line. Further work is in progress to clarify this observation.

SUMMARY

The presence of glycogen in leukaemic lymphoblasts was studied by means of the periodic-acid-Schiff (P.A.S.) reaction.

Considerable variation was found from case to case in the proportion of cells containing glycogen.

Weak P.A.S. positivity was significantly related to short first maintained remission and survival, high initial peripheral blood blast count, and short duration of symptoms at the time of diagnosis. The results suggest that P.A.S. positivity is inversely related to the rate of progression of lymphoblastic leukaemia. Further work is being carried out to elucidate this finding.

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Medical Memoranda

Spontaneous Uterine Rupture Caused by Placenta Percreta

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Placenta accreta is the abnormal adherence of the chorionic villi to the myometrium, and is associated with partial or complete absence of the decidua basalis, and in particular the stratum spongiosum (Phaneuf, 1933; Kistner *et al.*, 1952). Three degrees are recognized, according to the extent of trophoblastic penetration. Placenta accreta vera is the term applied when villi are in juxtaposition with the myometrium. In placenta increta the villi partially penetrate the myometrium. Placenta percreta indicates that the villi have invaded the full thickness of myometrium to or through the serosa of the uterus, causing incomplete or complete uterine rupture respectively.

Spontaneous rupture of the uterus due to placenta percreta is one of the most urgent obstetrical catastrophes, resulting in rapid exsanguination and high mortality in spite of prompt anti-shock therapy and massive blood transfusion. In a review Sumawong *et al.* (1966) found 30 cases of rupture caused by placenta percreta and added three cases of their own. A search of the literature has revealed only three previous reports of spontaneous rupture due to placenta accreta concomitant with placenta praevia (Bakanow, 1928; Callender and King, 1949; Malkasian and Welch, 1964). The last of these was a case of placenta praevia percreta.

This paper describes two cases of spontaneous uterine rupture due to placenta percreta, one of which was associated with placenta praevia. As pointed out by Rotton and Friedman (1957), the necessity for expeditious therapy when this condition is encountered makes imperative its clinical recognition and study.

CASE 1

A 36-year-old multipara was admitted to hospital as an emergency case on 14 July 1966 in a state of collapse. Her husband stated that she had her last menstrual period six months previously. She had been well until five hours before admission, when she experienced a continuous pain in her right shoulder while in bed. She soon developed a lancinating pain under the left costal margin and

vomited once. This was followed by progressive weakness and fainting attacks. No vaginal bleeding or discharge occurred.

Her three previous pregnancies, labours, and puerperia were uncomplicated. Her youngest child was 2½ years old. She had had no previous illnesses or operations.

General examination revealed a state of shock. Her temperature was 97.6° F. (36.4° C.), pulse barely perceptible at 136 a minute, and respiration was sighing and shallow; the blood pressure was not recordable. Gross pallor of the mucous membrane was present. On abdominal examination there was marked distension with free fluid. Generalized tenderness and guarding were elicited, and, apart from uterine enlargement consistent with a 26-week gestation, no other abnormality was detected. The foetal heart was not audible. Vaginal examination was not contributory.

Intraperitoneal haemorrhage due to rupture of the uterus, rupture of the spleen or its blood vessels, and extrauterine pregnancy, in that order, were considered in the differential diagnosis.

Investigations.—Full blood count showed a haemoglobin of 28% Haldane, and an acute post-haemorrhagic anaemia. The blood fibrinogen level was 285 mg./100 ml.

On admission resuscitation was begun with intravenous fluids, morphine hydrochloride, metaraminol tartrate (Aramine), hydrocortisone, oxygen, and compatible group B rhesus-positive blood as soon as the latter became available.

After an infusion of 2,500 ml. of blood the systolic pressure was audible at 80 mm. Hg and the pulse improved to about 110 a minute. While she was being transferred to the operating-theatre the blood pressure dropped to nil. The next two bottles of blood were simultaneously given under pressure and the necessary calcium gluconate was administered. Some improvement in the patient's condition occurred and it was decided to proceed with immediate laparotomy.

The peritoneal cavity contained about 2,000 ml. of blood and clots. The uterus was consistent with a 26-week gestation. The uterine fundus was perforated by placental tissue (see Fig.) and bleeding was occurring from that site. Total hysterectomy was rapidly performed. Both Fallopian tubes and ovaries were normal and conserved. Haemostasis was secured and the abdomen sutured in layers. The eighth litre of blood was being given at the conclusion of the operation when cardiac arrest suddenly occurred. With the endotracheal tube still in situ the lungs were ventilated and immediate external cardiac massage was performed. As this failed to maintain an adequate circulation, left anterior thoracotomy through the fourth intercostal space was performed and direct cardiac massage resulted in the return of a regular heart beat. Circulation and respiration were maintained for two and a quarter hours, when arrest of the heart again occurred. All measures at resuscitation were of no avail.