Papers and Originals

Combination Chemotherapy using L-Asparaginase, Daunorubicin, and Cytosine Arabinoside in Adults with Acute Myelogenous Leukaemia

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British Medical Journal, 1970, 4, 513-517

Summary: Cytosine arabinoside and daunorubicin used in an intensive intermittent regimen have been shown to be an effective combination for the induction of complete remissions in 14 out of 23 adult patients with acute myelogenous leukaemia. This gives an overall complete remission rate of 60%. A further patient had a good partial remission. The addition of L-asparaginase to the regimen has not increased the incidence of remission and there were more side effects in the L-asparaginase-treated group. Of the 10 patients treated with L-asparaginase in addition to cytosine arabinoside and daunorubicin, five achieved a complete remission. Of the 13 patients treated with cytosine arabinoside and daunorubicin without L-asparaginase, nine achieved a complete remission and one a good partial remission.

Introduction

The treatment of acute myelogenous leukaemia is more difficult and less successful than the treatment of acute lymphoblastic leukaemia. Complete remissions may be obtained relatively easily in almost all children with acute lymphoblastic leukaemia, whereas in only a minority of adult patients with acute myelogenous leukaemia are remissions achieved. In acute lymphoblastic leukaemia, as in some other human cancers, combination chemotherapy has proved more efficacious than single drug treatment (Henderson, 1969). The purpose of this paper is to report a series of patients with acute myelogenous leukaemia treated with intensive intermittent combination chemotherapy. The two drugs chosen were those which have hitherto proved most effective when used singly—namely, cytosine arabinoside (1-β-D-arabinofuranosylcytosine) and daunorubicin (rubidomycin, daunomycin).

The discovery of a natural supply of uracil arabinoside in extracts of sponges has given access to many new compounds of the pyrimidine nucleoside family (Bergmann and Feeney, 1951). Cytosine arabinoside has emerged as one of the most promising agents in this group. One of the largest series of acute myelogenous leukaemia treated with this single agent was reported by the Acute Leukaemia Group B (Ellison *et al.*, 1968). This study involved 16 research centres and 180 adult patients. The overall complete remission rate was 16%. Several different dose schedules were used, but even with the best regimens complete remission rates were no greater than 25%.

The best remission rates in adult patients with acute myelogenous leukaemia have been obtained with daunorubicin, which is an antibiotic in the anthracycline group obtained from *Streptomyces peucetius* (Grein *et al.*, 1963) or *S. caeruleorubidus*. It is believed to inhibit DNA synthesis by complexing with preformed DNA (Di Marco, 1968). One of the biggest series using daunorubicin as a single drug in this disease was reported by the European Co-operative Group for the Treatment of Leukaemia, with which we collaborate. Seventy-one patients were treated and 25% complete remissions were obtained (Group Coopérateur, 1969). Reports from single centres have been variable, but the average remission rates are of the same order as those reported by the European Co-operative Group. Boiron *et al.* (1969) reported a complete remission rate of 50% in adult patients with acute myelogenous leukaemia, but this response rate is considerably better than other reported series in which this drug was used alone.

Gee *et al.* (1969), using a combination of cytosine arabinoside and thioguanine in 38 adult patients with acute myelogenous leukaemia, achieved a complete remission in 15 and good partial remissions in a further four. Freireich *et al.* (1969) reported similar results with a combination of cyclophosphamide, vincristine, cytosine arabinoside, and prednisone (COAP), 53% of patients achieving complete remission. The largest published trials using combination chemotherapy have been from the Acute Leukaemia Group B (Carey, 1970). Among the 227 evaluable cases the highest complete and partial remission rates were obtained with cytosine arabinoside in combination with either thioguanine or daunorubicin. The remission rates, including partial remissions in both series, were about 50%, but the complete remission rates were somewhat lower.

The second part of our study involved the assessment of L-asparaginase treatment in combination with the cytosine arabinoside and daunorubicin regimen. This trial was conducted in the hope that the addition of asparaginase to the therapeutic regimen would help to increase the numbers of patients achieving a complete remission. It is well known that the numbers of circulating myeloblasts may be rapidly reduced by L-asparaginase therapy—for example, Beard *et al.* (1970). Nevertheless, used alone, the drug has usually proved ineffective in producing remissions, though occasional remissions have been reported (Hill *et al.*, 1969). It appears that remission rates of less than 10% occur when the enzyme is used alone in the treatment of acute myelogenous leukaemia.

Patients and Methods

During an 11-month period starting May 1969 24 patients entered St. Bartholomew's Hospital with a diagnosis of acute myelogenous leukaemia. All were admitted to the trial except one, who was excluded because daunorubicin had already been given an adequate trial in another hospital. Of the remaining 23 patients, 18 had acute myeloblastic leukaemia (A.M.L.), three had acute myelomonoblastic leukaemia

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(A.M.M.L.), and two had acute promyelocytic leukaemia (A.P.M.L.). No case was included if a remission had been achieved on a previous occasion.

There were 11 males and 12 females. The age range was from 14 to 67 years, with a mean age of 48 years. Ten had had previous chemotherapy at another hospital which proved unsuccessful. Of these 10 patients, all had had prednisolone, six had had mercaptopurine in addition, two had had busulphan in addition, and one had had cyclophosphamide combined with the prednisolone. Thirteen patients had had no previous chemotherapy.

Ten unselected patients were treated with L-asparaginase for a continuous period of up to 28 days, a dose of 30,000 i.u./m.^{2} being used in addition to the combination chemotherapy. A further 13 patients were treated with only the combination of daunorubicin and cytosine arabinoside. Patients in the L-asparaginase-treated group received the L-asparaginase for three to four days before cytotoxic chemotherapy was started. The enzyme was administered either as twice-daily injections intravenously or by continuous infusion over a 24-hour period. The combination chemotherapy consisted of repeated five-day courses of daunorubicin and cytosine arabinoside (Fig. 1). Each course consisted of daunorubicin 1·5 mg./kg. body weight by intravenous injection in a fast-flowing drip on the first day, and cytosine arabinoside 2 mg./kg. body weight by daily intravenous injection on Days 1-5 inclusively. Each course was separated by at least five days. A further course was given after this period if leukaemic cells persisted in the blood or bone marrow. Treatment was deferred in the presence of a hypoplastic marrow with few or no apparent leukaemic cells.

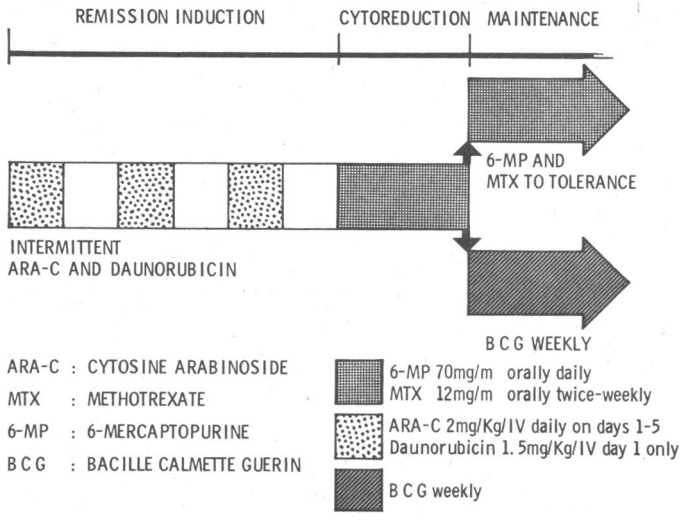
Evaluation.—Initial studies included blood and bone-marrow evaluation, blood urea and electrolytes, urine analysis, electrocardiography, radiology of the chest and abdomen, liver function tests, serum calcium, phosphate, and uric acid. Fever was investigated by culturing the blood, throat swabs, sputum, urine, and faeces. Blood counts were taken three times weekly, and bone-marrow aspirations at intervals of 10 to 14 days. Liver function tests, blood urea, and electrolytes were repeated at intervals of about 10 days. A complete

TABLE 1.—*Adult Patients with Acute Myelogenous Leukaemia Treated with* L-*Asparaginase, Cytosine Arabinoside and Daunorubicin*

Case No.	Age and Sex	Diagnosis	Previous Treatment	Status Before Trial Therapy			No. of Courses	Result	Length of Remission (Weeks)	Maintenance	Cause of Death
				Platelet Count/ mm^3.	Blood Blast Count/ mm^3.	Marrow Blast Percentage					
1	50 M.	A.M.L.	Prednisolone. Busulphan	15,000	15,000	85	2	F.	—	—	Infection (18 days)
2	52 F.	A.M.L.	Nil	16,000	9,000	66	1	C.R.	40+	Mercaptopurine. Methotrexate	—
3	54 F.	A.M.M.L.	Prednisolone. Mercaptopurine	200,000	Nil	35	1	C.R.	6	Methotrexate	—
4	43 M.	A.M.L.	Prednisolone	13,000	180	73	2	C.R.	4	Mercaptopurine. Methotrexate	—
5	62 M.	A.M.L.	Nil	150,000	18,000	96	1	F.	—	—	Uraemia. Haemorrhage (14 days)
6	63 M.	A.M.M.L.	Prednisolone. Mercaptopurine	45,000	Nil	20	2	F.	—	—	Infection (28 days)
7	38 F.	A.M.L.	Nil	100,000	80,000	95	4	C.R.	25	B.C.G.	—
8	62 M.	A.P.M.L.	Nil	15,000	8,000	97	0	F.	—	—	Coma, haemorrhage, infection
9	49 F.	A.M.L.	Nil	12,000	35,000	91	3	C.R.	40+	Mercaptopurine. Prednisolone	—
10	28 M.	A.P.M.L.	Nil	15,000	650	94	1	F.	—	—	Cerebral haemorrhage

TABLE II.—*Adult Patients with Acute Myelogenous Leukaemia Treated with Cytosine Arabinoside and Daunorubicin*

Case No.	Age and Sex	Diagnosis	Previous Treatment	Status Before Trial Therapy			No. of Courses	Result	Length of Remission (Weeks)	Maintenance	Cause of Death
				Platelet Count/ mm.^{3}	Blood Blast Count/ mm.^{3}	Marrow Blast Percentage					
11	43 F.	A.M.L.	Nil	16,000	7,500	82	2	F.	—	—	Staph. septicaemia (22 days)
12	25 F.	A.M.L.	Nil	60,000	Nil	40	3	C.R.	24+	Mercaptopurine. Methotrexate	—
13	67 M.	A.M.L.	Nil	35,000	900	98	1	F.	—	—	Renal, cardiac, and liver failure. Infection (14 days)
14	64 F.	A.M.L.	Prednisolone. Mercaptopurine	18,000	Nil	68	3	P.R.	—	Prednisolone. Cyclophosphamide	—
15	14 F.	A.M.L.	Nil	300,000	Nil	94	3	C.R.	14	Mercaptopurine. Methotrexate	—
16	32 M.	A.M.L.	Nil	55,000	1,000	92	3	C.R.	28	B.C.G.	—
17	47 F.	A.M.L.	Prednisolone	7,000	Nil	50	1	F.	—	—	Pseudomonas septicaemia (2 days)
18	42 F.	A.M.L.	Prednisolone. Mercaptopurine	55,000	60	90	2	C.R.	16+	Mercaptopurine. Methotrexate	—
19	48 M.	A.M.L.	Prednisolone. Mercaptopurine. Busulphan	21,000	Nil	40	3	C.R.	10+	B.C.G.	—
20	49 M.	A.M.M.L.	Prednisolone. Mercaptopurine	89,000	Nil	95	4	C.R.	4+	Mercaptopurine. Methotrexate	—
21	56 F.	A.M.L.	Nil	45,000	240	52	4	C.R.	3+	B.C.G.	—
22	54 F.	A.M.L.	Prednisolone. Cyclophosphamide	46,000	250	28	3	C.R.	4+	B.C.G.	—
23	58 M.	A.M.L.	Nil	18,000	110,000	93	5	C.R.	2+	B.C.G.	—



Treatment programme for acute myelogenous leukaemia in adults.

remission was established when the patient became symptom- and sign-free with a normal peripheral blood and marrow. In these patients the haemoglobin was greater than 10 g./100 ml. for females and 12 g./100 ml. for males; the W.B.C. was greater than 3,000/mm.^{3} with more than 1,500 granulocytes/mm.^{3}, and no blasts were present in the blood; the platelet count was greater than 100,000/mm.^{3}

Cytoreduction and Maintenance.—When complete remission had been achieved the patients received a cytoreduction programme, mercaptopurine and methotrexate (Fig. 1) being used. Following this the patients were randomly allocated to one of two maintenance groups. In the first group maintenance was continued with mercaptopurine and methotrexate, and in the second group patients received weekly percutaneous B.C.G. (bacillus Calmette-Guérin) vaccinations as a form of non-specific immunotherapy (Mathé *et al.*, 1969).

Results

Details of all patients in the series are given in Tables I and II.

Remission Rates

Of the 10 patients treated with L-asparaginase in addition to cytosine arabinoside and daunorubicin, five had a complete remission. Of the 13 patients treated with cytosine arabinoside and daunorubicin without L-asparaginase, nine had a complete remission, and one a good partial remission (Table III). The patient reaching partial remission had no symptoms or signs of leukaemia, and the peripheral blood was normal. The bone marrow contained a slight but patchy excess of blast cells, but was otherwise normal.

The addition of L-asparaginase to the therapeutic regimen did not increase the chances of obtaining a remission. Nevertheless, of the seven patients receiving L-asparaginase who had large numbers of blast cells in the blood, five had marked falls in the numbers of circulating blasts during the first three days of treatment—that is, before treatment with cytosine arabinoside and daunorubicin was started. Of these five patients three eventually obtained a complete remission. Nine patients received Bayer L-asparaginase and one patient received Porton L-asparaginase obtained from *Erwinia carotovora*. One patient became hypersensitive to the Bayer product, so treatment was continued with the Porton enzyme, which is antigenically different (A. P. MacLennon, personal communication, 1970).

TABLE III.—*Remission Rates After Chemotherapy*

Regimen	No. of Cases	Complete Remission	Partial Remission	Failure
Cytosine arabinoside + daunorubicin + L-asparaginase	10	5	0	5
Cytosine arabinoside + daunorubicin	13	9	1	3
Total	23	14 (60%)	1	8

With the criteria established by the Midwest Co-operative Chemotherapy Study Group (Hewlett *et al.*, 1964) the results can be expressed as follows. The 23 patients presented with extensive or extreme disease. No case was classified as having moderate disease. Fourteen patients achieved a P1 (no abnormal physical signs), S1 (no symptoms), H1 (normal blood), M1 (normal bone marrow) remission, and a further patient achieved a P1, S1, H1, M2 remission. On average between two and three courses were required before a complete remission was achieved.

Previous Treatment

The relationship between previous treatment and the remission rate is given in Table IV. There was no difference in the number of patients achieving remissions in the two groups, with and without previous chemotherapy. Complete remissions were obtained in 6 out of 10 patients who had been previously treated elsewhere and in 8 out of 13 who had not been previously treated.

TABLE IV.—*Relationship Between Previous Treatment and Remission Rate*

	Previously Treated	No Previous Treatment
Complete remission	6 (60%)	8 (61%)
Partial remission	1	0
Failure	3	5
Total	10	13

Platelet Count

The relationship between the initial platelet count and the incidence of remission is given in Table V. Ten out of the 13 patients with platelet counts over 20,000/mm.^{3} before treatment was begun went into complete remission. Only 4 of the 10 patients with initial platelet counts of less than 20,000/mm.^{3} had complete remissions, though a further patient had a good partial remission.

TABLE V.—*Relationship Between Remission Rate and Platelet Count*

Initial Platelet Count:	<20,000/mm.^{3}	>20,000/mm.^{3}
Complete Remission	4 (40%)	10 (77%)
Partial Remission	1	0
Failure	5	3

Age

The mean age of the 14 patients reaching complete remission was 44 years. The mean age of the eight failures was 53 years. The difference in ages in these two groups is not statistically significant. Of the five patients over 60 years old none had a complete remission. The oldest obtaining a complete remission was aged 58 years.

Blast Count

There was no correlation between the initial peripheral blood blast count and incidence of remission. Similarly there

was no correlation between the percentage of blasts in the bone marrow before treatment and the incidence of remission.

Side Effects and Causes of Death

All eight patients who failed to have a useful remission died within four weeks of admission to hospital. One died within 48 hours with a pseudomonas septicaemia following an infected, ulcerated, and prolapsed rectum. Another died within a few days of admission after starting the L-asparaginase but before starting the cytosine arabinoside and daunorubicin. Infection was one of the contributing factors causing death in seven of the eight patients. In patients where the organism was positively identified its origin was considered to be endogenous. Renal and liver failure was a contributing cause of death in three, but was present on admission to hospital before treatment was started. No case of liver failure was attributable to cytosine arabinoside or daunorubicin, but all patients treated for more than seven days with L-asparaginase showed a reduction in serum albumin. Gastrointestinal tract haemorrhage and ulceration occurred in several of the patients, and was present in nearly all of those going to necropsy.

Severe bone marrow depression and pancytopenia developed in all 23 patients during the course of therapy. The earliest sign of remission was a rise in the platelet count. Slight nausea and malaise usually occurred in the 24 hours following the daunorubicin. Mild nausea and occasional abdominal pain were the only symptoms following cytosine arabinoside. No cardiac complications or serious electrocardiographic changes occurred during the course of daunorubicin treatment. Some degree of alopecia occurred in most patients. Nausea, vomiting, and eventually peripheral oedema with hypoalbuminaemia were almost constant features of L-asparaginase treatment.

Remission Lengths

Only six of the patients achieving complete remission have relapsed. In this group the mean remission length was five months. As yet there is no significant difference between the group maintained with chemotherapy and the group maintained with B.C.G.

Discussion

Comparisons between trials at different centres are difficult because selection is bound to occur. Many patients die early in the disease, some before treatment is instituted. In some studies these patients have been consciously excluded. Most trials involve patients referred from other hospitals, and speed of referral becomes an important factor. The results in this paper suffer from this criticism, but no attempt has been made to exclude patients who died early during the course of treatment. A further selection was used by Gee *et al.* (1969) and Boiron *et al.* (1969). Patients were included who had already achieved one remission, and may well be said to have disease with a better outlook. No cases in relapse following remission were included in our series.

Both series included patients who had been unsuccessfully treated previously, but there were no differences in the response rates in either group. Gee *et al.* (1969) showed that about half achieved a remission whether they had been previously treated or not. They studied 38 patients with acute myelogenous leukaemia, but excluded two because they died within three or four days of starting treatment. Of the remaining 36 patients, 15 had a complete remission and a further four had a good partial remission. A low haemoglobin was the only factor responsible for these four patients being included in the partial remission group, and this may well have been due to maintenance chemotherapy. The mean dose of cytosine arabinoside used to achieve remission was 58 mg./kg. body weight. In our series the mean dose required to achieve remission was 25 mg./kg. body weight.

The action of L-asparaginase is potentiated by use of cytosine arabinoside, vincristine, and daunorubicin in the treatment of mouse leukaemia (Burchenal, 1970; Haghbin *et al.*, 1970). McElwain and Hardisty (1969) showed that combining cytosine arabinoside with L-asparaginase may be more effective than either agent used singly in the treatment of children with acute lymphoblastic leukaemia, but only nine patients were treated. Not all chemotherapeutic combinations with L-asparaginase have been shown to have a useful effect. Capizzi *et al.* (1970) showed that cells may be resistant to methotrexate when deprived of asparagine. Haghbin *et al.* (1970) showed that the therapeutic efficacy was not increased by combining vincristine and daunorubicin with L-asparaginase. Indeed the side effects were considerably greater in the group treated with L-asparaginase. In our series of adult cases of acute myelogenous leukaemia the use of L-asparaginase has not added to the remission rates obtained with cytosine arabinoside and daunorubicin alone. The patients receiving L-asparaginase in addition suffered more from side effects than those treated only with cytosine arabinoside and daunorubicin.

We feel a combination of cytosine arabinoside and daunorubicin has several advantages over other combinations (Table VI). They are the best drugs available when used singly in this disease. They have different sites of action, and cells both in and out of cycle are affected. Their side effects are different. One of the most serious side effects of cytosine arabinoside is the gastrointestinal tract toxicity, whereas cardiotoxicity is one of the most serious with daunorubicin. The doses required to achieve remission are lower than those used in other series. Both drugs are given intravenously, and this overcomes the vagaries of intestinal absorption. Intravenous use overcomes the necessity of the drug to pass through the liver and become detoxified before reaching a useful site of action. Both drugs are easy to administer, and prolonged infusions were not used. Allopurinol does not interfere with the metabolism of either drug, and this xanthine oxidase inhibitor may be used routinely to prevent the development of hyperuricaemia. The complete remission rate in this series is one of the highest so far reported in the literature. All patients with acute myelogenous leukaemia admitted to St. Bartholomew's Hospital were included in the trial if the diagnosis was confirmed and treatment instituted. A complete remission rate of 60% was obtained.

TABLE VI.—*Advantages of Cytosine Arabinoside and Daunorubicin in Adult Acute Myelogenous Leukaemia*

1. Best drugs available used single in acute myelogenous leukaemia
2. Different sites of action
3. Major serious side effects are different
4. Doses required to achieve remission are low
5. Both are given intravenously
6. Ease of administration
7. Allopurinol may be given in addition
8. Remission rates are among the highest so far published

It is of some interest that our patients were nursed in an open general medical ward. Gee *et al.* (1969) also nursed their patients in an open ward. Whether some of the early deaths could be prevented by the use of "life islands" or reverse barrier nursing wards remains to be established.

We wish to thank the family doctors and consultant physicians from many centres who referred the patients; also Dr. H. B. Allen, of F.B.A. Pharmaceuticals Limited, for supplies of Bayer asparaginase; Dr. J. Nuttall-Smith, of May & Baker Ltd., for supplies of daunorubicin; Dr. W. P. Goodyear, of Upjohn Ltd., for supplies of cytosine arabinoside; and Dr. C. E. Gordon Smith, of the Microbiological Research Establishment, Porton, for supplies of Porton asparaginase.

ADDENDUM.—Since this paper was submitted for publication a further 14 patients suffering from acute myelogenous leukaemia have been treated with daunorubicin and cytosine arabinoside. Eight had acute myeloblastic leukaemia, five had acute myelomonoblastic leukaemia, and one had acute promyelocytic leukaemia. Of these patients, nine have achieved complete remission. This brings the total number of treated patients to 37, of whom 23 achieved complete remissions (62%).

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REFERENCES

Beard, M. E. J., *et al.* (1970). *British Medical Journal*, **1**, 191.
Bergmann, W., and Feeney, R. J. (1951). *Journal of Organic Chemistry*, **16**, 981.
Boiron, M., *et al.* (1969). *Lancet*, **1**, 330.
Burchenal, J. H. (1970). *Cancer Research.* In press.
Capizzi, R. L., Summers, W. P., and Bertino, J. R. (1970). *Proceedings of the American Association for Cancer Research*, **11**, 14.
Carey, R. W. (1970). *Proceedings of the American Association for Cancer Research*, **11**, 15.
Di Marco, A. (1968). *Acta Genetical Medical et Gemellologicae*, **17**, 102.
Ellison, R. R., *et al.* (1968). *Blood*, **32**, 507.
Freireich, E. J., *et al.* (1970). *Recent Results in Cancer Research*, **30**, 85.
Gee, T. S., Yu, K. P., and Clarkson, B. D. (1969). *Cancer (Philadelphia)*, **23**, 1019.
Grein, A., Spalla, C., Di Marco, A., and Canevazzi, G. (1963). *Giornale di Microbiologia*, **11**, 109.
Groupe Coopérateur des Leucémies et Hématosarcomes (1969). *European Journal of Cancer*, **5**, 339.
Haghbin, M., *et al.* (1970). *Proceedings of the American Association for Cancer Research*, **11**, 33.
Henderson, E. S. (1969). *Seminars in Haematology*, **6**, 271.
Hewlett, J. S., *et al.* (1964). *Cancer Chemotherapy Reports*, **42**, 27.
Hill, J. M., *et al.* (1969). *Cancer Research*, **29**, 1574.
McElwain, T. J., and Hardisty, R. M. (1969). *British Medical Journal*, **4**, 596.
Mathé, G., *et al.* (1969). *Lancet*, **1**, 697.

Comparison of Coil and Kiil Dialysers

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British Medical Journal, 1970, **4**, 517-521

Summary: To assess the comparative efficiency, safety, and cost of maintenance dialysis, the treatment of 13 patients with a Kiil dialyser (representing 1,477 hospital and 735 home dialyses) was compared with that of 11 patients using a coil dialyser (898 hospital and 396 home dialyses). Kiil and coil dialysers proved equally satisfactory from a medical standpoint and equally acceptable to the patients. The capital costs of home dialysis were considerably reduced without any threat to safety or efficiency. The running costs of coil dialysers approximate to those of Kiil dialysers.

Introduction

Regular haemodialysis has been practised for 10 years and the technique has been standardized in most units (Baillod *et al.*, 1966; Shaldon, 1966; Scribner, 1967; Curtis *et al.*, 1969). About 700 countercurrent dialysers of the Kiil type were being used for intermittent haemodialysis in the United Kingdom in 1968, with dialysate supplied by various automatic proportioning systems (Kulatilake, Vickers, and Shackman, 1969). Many of these dialysis systems are very expensive, so that with current resources only a minority of the patients who could benefit will receive treatment with maintenance haemodialysis (*B.M.J.*, 1969). The high capital cost of the automatic proportioning and monitoring systems for dialysate delivery, together with the need for expert maintenance, has led us to revert to the original tank system.

Kiil type dialysers take a considerable time to prepare, so that the recent successful use of a disposable dialyser (Kulatilake *et al.*, 1969) is a considerable advance. For similar reasons the disposable coil dialyser has obvious advantages, and we have compared this with the conventional Kiil dialyser with respect to efficiency, safety, and cost. This paper describes the results of our experience in Portsmouth, which we consider could lead to a reduction in overall dialysis costs.

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Methods

Kiil/Tank System

The layout of this system is shown in Fig. 1. A list of the equipment required and the costing of individual items are shown in Table I. The 448 litres of dialysate are made in a 500-l. tank into which 12·8 l. of Ilford's concentrate (×35) are added to water softened by a Permutit D.R.2 softener. The dialysate concentration is checked by measuring its conductivity with a portable conductivity meter. A Watson-Marlow EL3N pump constantly recirculates and mixes the dialysate. The same pump also delivers dialysate to the bedside monitor. The dialysate is prepared at room temperature and de-aeration is achieved by a system very similar to that described by Parsons and Meffan (1969). The dialysate is warmed to body temperature by a Tecam Temp-unit attached to the bedside monitor. From here the dialysate goes through a flow meter and finally to the Kiil kidney. The effluent dialysate discharges into a floor-level drain. All connecting tubing is of clear plastic beverage hose of varying

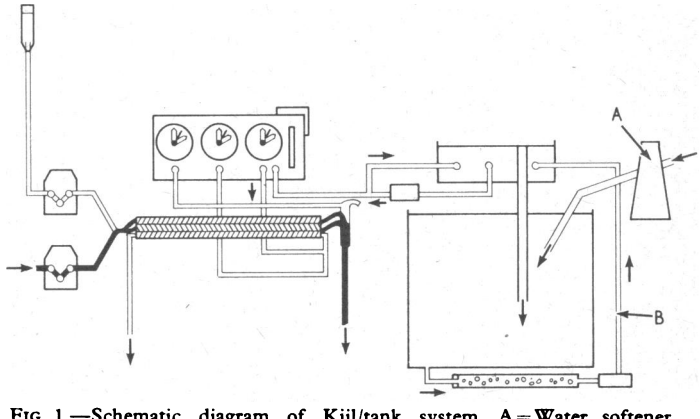

FIG. 1.—Schematic diagram of Kiil/tank system. A = Water softener. B = De-aeration circuit.