may be used to connect the patient to a static cylinder and so enable him to get about within a restricted area with less distress. The Polymask is unsuitable for portable oxygen because, unless there is a high flow of oxygen, the lack of a non-return valve allows CO_2 to accumulate within the mask, and this in itself increases the ventilatory requirements of the patient both at rest and on exercise (Cotes, 1962). Suitable masks that avoid this are available from Siebe Gorman Ltd. and other firms.

Most patients receiving long-term oxygen therapy in the home suffer from chronic respiratory disease and have been in hospital previously. Because of this it should be possible for the hospital staff to assess patients before discharge with a view to advising general practitioners of the possible value of oxygen and the best method of administration. In chronic respiratory disease oxygen at rest is unlikely to provide worth-while benefit unless the patient is breathless at rest because of severe anoxia. It is very probable that this type of patient will have chronic hypercapnia also (arterial P_{CO_2} 50 mm. Hg or more) and, if so, oxygen should be provided by a mask that delivers a concentration of not more than 30%. Even then very careful supervision is required during an exacerbation of the illness if an attempt is made to treat the patient at home. If the patient is capable of limited exercise which causes distressing breathlessness or if he would like to be more active, consideration should be given to the provision of oxygen during exercise by one of the methods described. For those with chronic hypercapnia the provision of 30% oxygen will increase effort tolerance, though not to the same degree as concentrations of 50–60% (Cotes, 1963). For those without hypercapnia or severe anoxia oxygen therapy may still be worth while for the relief of effort dyspnoea, but the success of this largely depends on the provision of efficient portable apparatus.

Summary

Current practice in the use of oxygen in the home in Dundee is described. Forty-three per cent. of the general practitioners had prescribed it at least once over a period of 14 months. Twenty-two patients were receiving oxygen at home during the period of study in January and February 1965, and nearly all were seriously disabled by chronic respiratory disease.

Oxygen was used both at rest and after exertion for the relief of dyspnoea and was delivered by Polymask at a flow rate of 2 or 4 l./min. from a static cylinder. Arterial blood gas measurements showed that 12 of the 22 patients suffered from hypercapnia (arterial P_{CO_2} 50 mm. Hg or more) while breathing room air at rest. The dangers of delivering oxygen by Polymask in this type of patient are discussed and illustrated by the rapid deterioration of one patient who fell asleep with his mask on. It is suggested that a patient with chronic hypercapnia should be provided with a mask that delivers not more than 30% oxygen.

For the relief of effort dyspnoea oxygen should be used during rather than after exertion, but the success of this again depends on the correct choice of equipment and method of administration.

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Cyclophosphamide in the Treatment of Systemic Lupus Erythematosus

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Steroids have played an important part in the treatment of systemic lupus erythematosus (S.L.E.). Recently, however, cytotoxic drugs have been used in a variety of autoimmune diseases, of which S.L.E. is one form. Dameshek and Schwartz (1960) used mercaptopurine and 6-thioguanine with considerable benefit in eight patients suffering from S.L.E. Later, Schwartz and Dameshek (1962) used the same drugs on 14 patients with autoimmune haemolytic anaemia, good results being obtained in nine of them. Taylor (1963) reported on a patient with autoimmune haemolytic anaemia who failed to respond to steroids but who responded to repeated courses of various alkylating agents and finally was stabilized on cyclophosphamide (Endoxana). Hill and Scott (1964) obtained early good results with a course of cyclophosphamide in a patient with systemic lupus who had failed to respond to steroids. Finally, Mackay *et al.* (1964) used mercaptopurine and azathioprine (Imuran), a derivative of mercaptopurine, with success in three patients with active chronic hepatitis and two with lupoid hepatitis.

From the foregoing it was thought that an ankylating agent like cyclophosphamide, which produces very few serious side-effects as opposed to steroids, may be of value in the management of S.L.E. Since 1963 all newly diagnosed cases of S.L.E. admitted to the unit have been treated with cyclophosphamide.

So far 15 patients have been treated with this cytotoxic agent but only nine have been followed up long enough for assessment (for periods varying from 3 to 27 months). Below we discuss the response of these nine patients to this form of therapy.

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Method

The initial diagnosis of S.L.E. was made on clinical grounds and confirmed in all nine patients by a positive L.E. phenomenon (method based on that of Zinkham and Conley (1956) as described by Dacie and Lewis (1963)). All of them had the classical "butterfly" rash on the face. In addition to a clinical examination, the following investigations were made before starting treatment with cyclophosphamide: full peripheral blood counts, the L.E. phenomenon, erythrocyte sedimentation rate, rheumatoid factor, blood Kahn test, Coombs test, serum bilirubin, serum glutamic oxalic transaminase, serum glutamic pyruvic transaminase, blood urea, serum protein electrophoresis, urine analysis, and bile pigments in the urine. Renal biopsies, chest *x*-ray examinations, and electrocardiography were also carried out and repeated when indicated.

An initial loading dose of cyclophosphamide was given intravenously at a dosage of 20 mg./kg. body weight, with a maximal single dose of 1 g. for adult patients. To allow any depression of the white-cell count to return to normal no further cyclophosphamide was given for the next two weeks. Thereafter 200 mg. of cyclophosphamide was given intravenously three times a week for the next 10 weeks. During this period clinical reassessment and all investigations were repeated 2, 6, and 12 weeks after the beginning of treatment with cyclophosphamide. At the end of 12 weeks the patients were discharged to a follow-up clinic, where they continued to receive 400 mg. of cyclophosphamide intravenously weekly for an indefinite period.

Results

Three of the nine patients (Cases 1, 2, and 3) made a very good therapeutic response to cyclophosphamide (Table I). These cases are reported in detail below. Cases 4, 5, and 6 responded moderately well. Case 4 had a combination of steroids and cyclophosphamide, and had just completed six months of therapy. Cases 5 and 6 defaulted after completing three months of treatment, but had a moderately good response during the period of observation. The remaining three patients (Cases 7, 8, and 9) failed to respond to cyclophosphamide. Case 7 had severe stomatitis and ulcers in the mouth before cyclophosphamide was given, but after its administration the ulcers became worse, severe alopecia and leucopenia occurred, and she became psychotic; she improved after cyclophosphamide was stopped and steroids were given. Case 8 presented with a nephrotic syndrome, which became worse after the administration of cyclophosphamide; she too improved on stopping the drug and on receiving steroids. Case 9 presented with S.L.E. and hepatitis and failed to respond to cyclophosphamide initially, and later to steroids also; he ultimately died from liver failure.

Clinical Response

Fever.—Six of the nine patients had high fever initially, and in all six the fever abated two weeks after the institution of cyclophosphamide therapy.

Arthralgia.—This was present in seven patients initially. At the 12th week of therapy arthralgia had disappeared in four and was much less in the other three. Frank arthritis was present in two patients before treatment. At the 12th week of treatment it had completely cleared up in one patient and was much improved in the other.

Rash.—The typical facial rash was present in all nine patients before therapy. By the 12th week the rash had disappeared in six and was fading in one. It failed to clear up in two patients, who did not respond to cyclophosphamide as a whole.

Effusions.—Pleural effusions and ascites were present in three patients before therapy: in one the effusion and ascites cleared up completely; in the other two there was no improvement, and both failed to respond to cyclophosphamide as a whole.

Hepato-splenomegaly.—Hepatomegaly was present before therapy in six patients, and had disappeared in three of them by the 12th week of therapy. Similarly, the spleen was enlarged in three patients before therapy but was not palpable in two of them at the 12th week of therapy.

Laboratory Results (see Table II)

L.E. Phenomenon.—L.E. cells were present in all nine patients before therapy. At the end of 12 weeks the L.E. phenomenon had become negative in three, and since then another two have also become negative. Two other patients who were still positive at the end of 12 weeks defaulted soon after. Both had shown

TABLE I.—*Therapeutic Response to Cyclophosphamide in S.L.E.*

Case No.	Race	Age	Sex	Mode of Presentation	Treatment	Duration of Cycloph. (Months)	Response to Cycloph.
1	Chinese	19	M	Nephritis. Hypertension. Intestinal obstruction	Steroids initially, later cyclophosphamide alone	18	Very good
2	,,	15	F	Arthritis. Raynaud's phenomenon	Cyclophosphamide	20	,, ,,
3	,,	32	F	Purpura. Menorrhagia	,,	15	,, ,,
4	Malay	18	F	Fever. Joint pains	Steroids plus cyclophosphamide	6	Good
5	,,	24	F	,, ,, ,,	Cyclophosphamide	3	,,
6	,,	18	F	Joint pains. Haemolytic anaemia	,,	3	,,
7	Chinese	37	F	,, ,, Nephrotic syndrome. Oral ulcers	Cyclophosphamide, later steroids only	3	Poor
8	,,	14	F	Nephrotic syndrome	,, ,,	4	,,
9	,,	42	M	Joint pains. Ascites	,, ,,	2	,,

TABLE II.—*Laboratory Results*

Case No.	E.S.R. (in mm.)		L.E. Cells		Rheumatoid Factor		Serum Albumin (g./100 ml.)		Serum Gamma-globulin (g./100 ml.)	
	Before Cycloph.	After 12/52	Before Cycloph.	After 12/52	Before Cycloph.	After 12/52	Before Cycloph.	After 12/52	Before Cycloph.	After 12/52
1	84	65	+	−	−	−	2·5	2·1	0·4	0·8
2	68	42	+ +	+ (few)*	+	+*	2·8	4·5	3·9	1·4
3	86	62	+	−	+	−	3·9	3·8	3·0	2·4
4	99	42	+ +	+ (few)*	+	+*	3·3	3·6	1·7	1·0
5	44	35	+ +	+ (few)	−	−	4·6	5·3	2·2	1·4
6	121	65	+	+	+	+	3·8	4·7	3·7	2·0
7	43	35	+	+	−	−	2·9	3·3	2·3	1·6
8	29	40	+	−	+	+	2·4	2·6	3·1	3·3
9	Abandoned cyclophosphamide in 8th week of therapy because of poor response									

* Negative since then after further treatment with cyclophosphamide.

a moderately good response to the drug, and it is most probable that they too would have become negative if they had persisted with treatment.

E.S.R.—At the end of 12 weeks the E.S.R. in the six patients who responded to the drug fell quite definitely. In the remaining three, who in general did not respond to the drug, the E.S.R. was not affected.

R.A. Factor.—This was positive in five patients before therapy. At the end of 12 weeks it became negative in one patient, and since then it has become negative in two others. The remaining two had a positive R.A. factor at the end of 12 weeks, but no follow-up was possible because they defaulted.

Serum Proteins.—The serum albumin was below 3 g. in four patients. At the end of 12 weeks there was a rise in serum albumin in three of these. The gamma-globulins were elevated before therapy in seven patients. At the end of 12 weeks there was a definite fall in six of them.

Case 1

A 19-year-old male Chinese labourer was admitted to hospital on 9 March 1963 with symptoms and signs of incomplete intestinal obstruction. His blood-pressure was 150/100 mm. Hg, and urine examination revealed heavy albuminuria, W.B.C. 15 to 20 per field, and granular casts. Blood urea was 110 mg./100 ml.

Pyelonephritis with incomplete intestinal obstruction was thought to be the most likely diagnosis. He responded to bed-rest and conservative therapy, and was discharged with a normal blood-pressure and blood urea. On 3 May he was readmitted with incomplete intestinal obstruction, but this time with an erythematous rash on the face, stiffness of the small joints of the hands, and slight swelling of both ankle-joints; the diagnosis of S.L.E. became evident. L.E. cells were found in the blood and he was started on prednisolone, and later discharged on a maintenance dose of 5 mg. t.d.s. In July, August, and September he was readmitted three times because of repeated episodes of incomplete intestinal obstruction while he was still on steroids. In September his blood urea was 181 mg./100 ml., and his blood-pressure rose to 170/120. He developed generalized fits, which were controlled by methyldopa and sedatives. On 24 October he was started on cyclophosphamide because of his poor response to steroids. A week later steroids were gradually withdrawn. His response to cyclophosphamide was very good. Fever, facial rash, joint pains, and hypertension vanished and the L.E. phenomenon became negative. The E.S.R. fell. For the past two years he has been given 400 mg. of cyclophosphamide a week intravenously, and at the time of writing was well, with normal blood urea and blood-pressure, and a negative L.E. phenomenon.

Case 2

A 15-year-old Chinese girl was first seen on 7 August 1963 with a history of multiple joint swellings for four years and a facial rash for two months. On examination she had the typical butterfly rash on the face, together with swelling of the metacarpophalangeal and interphalangeal joints of both hands and soft-tissue swellings around both knees. Flexion of both knees was moderately limited.

On investigation the L.E. phenomenon was positive; the E.S.R. was 68 mm. (first hour, Westergren); gamma-globulins were 3.9 g./100 ml. Cyclophosphamide was administered, and at the end of 12 weeks the rash and joint pains had disappeared. Slight swelling of both knee-joints was still present with limited flexion. The L.E. phenomenon was weakly positive, the E.S.R. was 42 mm., and the gamma-globulins were 1.4 g./100 ml. After 21 months of therapy she was quite well, with almost a full range of joint movements and a negative L.E. phenomenon.

Case 3

A 32-year-old Chinese woman was admitted on 30 January 1964 with a history of arthralgic pains for four years, and menorrhagia and spontaneous bruising for four months. On examination she had a slight but typical facial rash and bruises on the limbs; the Hess test was positive. Investigations revealed a positive L.E.-cell phenomenon, E.S.R. 86 mm., R.A. factor positive, and gamma-globulins 3 g./100 ml. Platelets were 45,000/c.mm., and bleeding-time was six minutes. Cyclophosphamide was given alone, and at the end of 12 weeks the joint pains and bleeding tendency had gone, the E.S.R. was 60 mm., and the L.E. phenomenon was negative. Gamma-globulins were reduced to 2.4 g./100 ml. and platelets had risen to 140,000/c.mm. After 17 months of therapy she was quite well and the L.E. phenomenon was negative.

Discussion

There is no doubt that with a patient acutely ill from S.L.E. the treatment of choice is still the use of steroids. However, although this treatment can be life-saving it may have to be withdrawn later because of its known complications. High dosage and prolonged steroid therapy can cause most undesirable side-effects. It is in such instances that cyclophosphamide will be useful.

Initially we used cyclophosphamide alone except in Case 1, as we were investigating its therapeutic values. In our experience the patients presenting with serious complications should be given the benefit of steroid therapy first. Cyclophosphamide, introduced later in combination, will certainly lower the steroid requirements. In those not acutely ill cyclophosphamide may be used alone with practically no side-effects (Cases 2 and 3). Rarely cyclophosphamide may be effective where steroids have failed (Case 1).

The only serious complications of cyclophosphamide therapy occurred in the three patients who did not respond to the drug, and took the form of severe alopecia, severe leucopenia, and aggravation of mucosal ulcerations in one patient. The other six patients had only transient mild leucopenia.

Summary

Nine patients with systemic lupus erythematosus were treated with cyclophosphamide. The therapeutic response to the drug was very good in three and moderately good in another three. The remaining three, however, failed to respond to cyclophosphamide.

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