logically disturbed environment? In a world where there are too many children should women be forced to endure this tyranny of unwanted pregnancies? If the answer is no, we must plan accordingly.

In Britain this means making contraceptive advice freely available under the National Health Service and offering tubal ligation to women who have had the desired number of children. This would help to free women from the tyranny of unwanted pregnancies and also make them more independent and able to choose freely how they will use their training and skills, especially after their desired number of children have been born. The world outside the home needs the skill and productivity of trained workers, and women, as well as men, need the satisfaction of education to their maximum potential ability and the opportunity to exercise their skills in a wider sphere than the immediate family.

To quote Huxley again: "The progress of medical science, besides accomplishing control of disease, must also improve the quality of life by providing greater fulfilment for more human beings. Fulfilment in this sense involves physical, mental and spiritual well-being."

To achieve this the world needs a Fifth Freedom—freedom from the tyranny of civilized man's excessive fertility.

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Depot Injections in Treatment of Hay-fever and Pollen Asthma*

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Brit. med. J., 1965, 2, 1148-1152

The injection of pollen extracts in the form of mineral-oil emulsion was introduced by Loveless in 1947. Since then it has been extensively employed in the United States, particularly by Brown (1958, 1959, 1961), who has consistently claimed good results with few systemic reactions. Other American workers (Feinberg *et al.*, 1960; Arbesman and Reisman, 1964; Sobel, 1961, 1962; Mechaneck, 1963) have claimed less good results and a higher proportion of systemic reactions. Side-effects, including general reactions, sterile abscesses, and delayed skin reactions, are referred to in an editorial of the *Journal of Allergy* (1961). The obvious advantage for both patient and doctor is that injections of pollen emulsion are limited to one, two, or three, compared with 20-40 of the conventional aqueous injections. In each type of treatment the course of injections should be repeated annually for at least three years.

Preliminary reports from this country (Frankland, Macaulay, and Evans, 1963; Frankland, Macaulay, Evans, and Edwards, 1964) suggested that emulsion therapy in hay-fever and pollen-asthma sufferers warranted further trial. In Europe depot-emulsion therapy has been little used (Dal Bo, 1964). All the indications from published reports suggested that a large-scale combined trial should be carried out. This has now been undertaken in a number of centres, a commercially made grass-pollen emulsion being used. The investigation was made during 1963 and 1964. During the first year attention was paid mainly to the incidence and variety of side-effects, while in the second year comparison was made between the effect of treatment with emulsions and aqueous extracts and also between three schemes of dosage of emulsion therapy with a view to determining the optimum safe dose. The objectives were therefore to determine whether the "depot" treatment was in the first place safe and in the second place effective.

Selection of Patients.—All patients suffered from hay-fever or pollen asthma, or a combination of the two, as judged by the seasonal nature of their symptoms and the presence of positive skin reactions with grass-pollen extracts. Patients with perennial rhinorrhoea or asthma, even if they were sensitive to grass pollen, were excluded, but it is probable that some patients were sensitive in some degree to other air-borne seasonal allergens, such as tree pollens, or certain mould spores.

Patients treated in 1963 had in the majority of cases been treated with aqueous pollen in previous years; but in 1964, out of 379 patients given emulsion therapy 294 had received only palliative treatment with antihistamine or bronchodilator drugs in the past; 85 had been desensitized with aqueous extracts in previous years. None had received previous "depot" therapy.

Methods and Materials

The pollen emulsion was made with the mineral oil Drakeol, with Arlacel A as the emulsifying agent, in a ratio of 65:35. It was packed in a disposable syringe which contained inert emulsion separated by a flange from active emulsion containing the grass pollen. The preliminary injection was given during February, March, and early April, and in no case was the second or third injection given after the second week of May. Injections were given subcutaneously into the upper arm: the skin was drawn upwards before insertion of the needle; the inactive "shield" (0.7 ml.) was first injected, then the needle was advanced 2-3 mm. so that the active material (0.3 ml.) contained in the second compartment of the syringe could be injected into the centre of the inert emulsion. After withdrawal of the needle the skin was allowed to return to its normal position, thus making a valve which prevented leakage down the needle track. An antihistamine preparation (a combination of pyrobutamine 15 mg., phenylpyramine 25 mg., and cyclopentamine hydrochloride 12.5 mg. (Co-pyronil) (1963)) or chlorpheniramine (Piriton) 4 mg. (1964) was given orally 30

* The following members of a subcommittee of the British Allergy Society took part in this trial: Dr. R. M. Boveri, Dr. R. G. Evans, Dr. A. W. Frankland, Dr. E. W. Jarratt, Dr. S. Z. Kalinowski, Dr. J. M. Kerr, Dr. D. B. Macaulay, Dr. Monica McAllen, Dr. R. S. Bruce Pearson (Chairman), Dr. J. Pepys, Dr. H. Royle, Dr. J. M. Sheriff, Dr. E. C. Tees

minutes before injection and repeated four hours later. Two spare doses of antihistamine and one tablet of isoprenaline (20 mg.) were also given to each patient with written instructions to take in the event of severe local or systemic reactions.

Results

Comparison Between Desensitization with Aqueous and Depot Pollen

Frankland and Augustin (1954) showed that desensitization with aqueous pollen extract produced 80% good or excellent results compared with 40% in those treated with placebo injections of phenol saline. The difficulties encountered in attempting to assess the effect of treatment in hay-fever have been fully discussed at a Conference on Evaluation of Hay-fever Therapy (1964).

In this trial we compared the effect of standard desensitization by repeated injections of aqueous pollen extract up to a maximum strength of 9,000 Noon units¹ with the effect of two injections of emulsified pollen extract of 750 and 7,500 Noon units during 1964. The patients, from two hospitals, were placed in one of the two groups by random selection; the two groups were comparable for age and sex. In one centre all the patients treated were included in these two groups, whereas in the second centre the patients were placed in four groups receiving (1) aqueous pollen extract, (2) emulsified extract in a single dose of 750 units, (3) in two doses of 750 and 7,500 units, and (4) in three doses of 750, 7,500, and a second dose of 7,500 units: patients from groups (1) and (3) only were therefore compared on this occasion.

The effect of treatment was assessed in each case by the following methods: (1) a general assessment made by the treating physician and the patient, taking all the other parameters, objective and subjective, into consideration at the end of the season concerning whether the effect was "satisfactory" or "unsatisfactory"; (2) comparison with the previous season's symptoms; (3) grouping of the symptoms as "none," "slight," "moderate," or "severe." These assessments were made with the help of a symptom chart given to each patient, who was asked to fill in for each 24-hour period whether he had symptoms of (a) hay-fever, (b) asthma, and whether these were slight, moderate, or severe. Finally, these charts were used as a means of computing a score for each patient from 20 May to 19 July, inclusive, a period considered to cover the grass-pollen season in this country. Three points were given for each day with severe, two for moderate, and one for slight symptoms. It will be appreciated that the fewer points scored the more effective was the treatment.

Table I shows assessment of the two groups as regards hay-fever. It will be seen that those patients receiving depot pollen were considered to have 87.8% satisfactory results, compared with 63.2% for those on standard aqueous injections. The difference between the two groups is statistically highly significant ($0.001 > P$).

In Table II the average numbers of points scored for the patients in the two groups are compared, and, though less striking, the difference is still statistically significant ($0.02 > P > 0.01$). It will be noted that approximately 10% were virtually symptom-free (less than 7 points) in each group.

Highly significant differences were also shown in favour of the depot therapy when the two groups were assessed by comparison with the previous year's symptoms, 83.5% being better and 5.9% worse on depot therapy, compared with 60.7% better and 18.8% worse on aqueous ($0.01 > P > 0.001$); and also on the basis of severity of symptoms, 80.6% having no or slight

symptoms on depot therapy, compared with 53.6% on aqueous solution ($0.001 > P$).

Comparison as regards asthma showed a similar trend, but the numbers in each group (25) were small and the differences did not achieve a significant level: nevertheless 21 (84%) receiving depot therapy claimed to have been better than in the previous year, compared with 14 (56%) of those on aqueous therapy.

TABLE I.—Comparison Between Treatment of Hay-fever with Depot Pollen (750, 7,500 Units) and Aqueous Injection (9,000 U.) (1964)

	No.	Satisfactory	Unsatisfactory	Defaulted
Aqueous ..	68	43 (63.2%)	25 (36.8%)	1
Depot ..	67	58 (87.8%)	8 (12.2%)	1

Difference between the two groups highly significant at $0.001 > P$.

TABLE II.—Comparison Between Treatment of Hay-fever with Depot Pollen (750, 7,500 Units) and Aqueous Injection (9,000 U.) (1964)

Treatment	No. of Patients	Points	Average	Inadequate Information Provided	Patients with Less than 7 Points
Aqueous ..	60	2,807	46.8	8	6
Depot ..	61	2,137	35.0	6	7

Six patients received aqueous treatment in 1963 in each group. The remainder had received only palliative treatment in previous years.
Difference between groups significant at $0.02 > P > 0.01$.

Comparison Between Three Dosage Schemes of Pollen Emulsion

Six centres co-operated in this part of the trial, including one of those which had taken part in comparing the effects of emulsion therapy with multiple aqueous desensitization.

All cases were originally placed in one of three groups by random selection, a modification of Fisher and Yates's tables (1957) being used. Group 1 received 750 units of depot pollen only; Group 2, 750 units followed after one month by 7,500 units; and Group 3, 750 units, 7,500 units, followed one month later by a second injection of 7,500 units. All injections were given subcutaneously.

Unfortunately a number of unforeseen difficulties arose which interfered with this procedure: this became apparent when it was seen that Group 1 contained 107 patients, Group 2 had 127, and Group 3 had 88. Explanations for the excessive number of patients in Group 2 are, first, that doctors did not like to proceed with the third injection if a systemic reaction followed the second, and, secondly, that holidays were not long enough to allow three injections to be given to school attenders. Group 3 therefore included an appreciably smaller number of patients below the age of 20 (15) than Group 1 (40) and Group 2 (37). A separate statistical analysis was therefore made for those over 20 years of age in each of the three groups, and for groups 1 and 2 as a whole. These comparisons appear to give a trustworthy indication of the relative merits of the three treatments, and the conclusions below are based on them.

Table III shows the comparison between the general response of hay-fever sufferers to the courses of treatment. There is a significant difference in favour of Groups 2 and 3 compared with Group 1, though the additional injection of 7,500 units in Group 3 seems to have given no extra benefit over the two injections in Group 2. The cases are subdivided in each group to show comparative figures for those given only palliative treatment in the previous year and those who received aqueous desensitization: those who had previously received aqueous injections appear to have done somewhat less well than those who had palliative treatment only.

Similar results are given in Table IV, showing the comparison with the previous season. It will be noted that those whose symptoms were classed as "the same" must be regarded as failures if they had had palliative treatment alone in 1963,

¹ Fifty-two patients completed the course, seven received 3,000–6,000 units, five less than 3,000 units, and in four the final dose was unknown.

but are likely, at least in the majority of cases, to have responded well if they had received aqueous treatment.

TABLE III.—*Effect of Treatment of Hay-fever with Three Different Doses of Depot Pollen (1964)*

Treatment in 1964	Treatment in 1963	Total No. of Cases	Satisfactory	Unsatisfactory	Defaulted
1 injection: 750 U.	Palliative Aqueous		41	31	7
			13	12	3
		107	54 (55.6%)	43 (44.4%)	10
2 injections: 750 U. 7,500 U.	Palliative Aqueous		71	18	6
			22	10	0
		127	93 (76.8%)	28 (23.2%)	6
3 injections: 750 U. 7,500 U. 7,500 U.	Palliative Aqueous		43	13	5
			16	9	2
		88	59 (72.8%)	22 (27.2%)	7

Comparison of Groups 1, 2, and 3 (over 20 years of age), $0.02 > P > 0.01$.
Comparison of Groups 1 and 2 (all ages), $0.001 > P$.

TABLE IV.—*Symptoms of Hay-fever after Three Different Doses of Depot Pollen (1964) Compared with those in 1963 after Palliative or Aqueous Injection Treatment*

Treatment in 1964	Treatment in 1963	Better	Same	Worse	Defaulted
1 injection: 750 Noon units	Palliative Aqueous injections	41 (57%)	17 (23.6%)	14 (19.4%)	7
		7 (28%)	10 (40%)	8 (32%)	3
	Total:	48 (49.5%)	27 (27.8%)	22 (22.7%)	10
2 injections: 750 Noon units 7,500 Noon units	Palliative Aqueous injections	72 (80.8%)	13 (14.6%)	4 (4.6%)	6
		20 (62.5%)	6 (18.7%)	6 (18.7%)	0
	Total:	92 (76.0%)	19 (15.7%)	10 (8.3%)	6
3 injections: 750 Noon units 7,500 Noon units 7,500 Noon units	Palliative Aqueous injections	45 (80.4%)	9 (16.1%)	2 (3.5%)	5
		13 (52%)	4 (16%)	8 (32%)	2
	Total:	58 (71.6%)	13 (16.1%)	10 (12.3%)	7

Comparison of Groups 1, 2, and 3 (over 20 years of age), $0.01 > P > 0.001$.
Comparison of Groups 1 and 2 (all ages), $0.001 > P$.

Assessment on a points basis, though following the previous trend, failed to show a significant statistical difference between the three groups (Table V). Groups 2 and 3 had a higher percentage of patients with less than 7 points. It will be noted that a relatively high proportion of cases in Groups 1 and 2 failed to provide the information required.

Comparison as regards symptoms of asthma show a similar result, the average number of points for 37 patients in Group 1 being 20.4; for 38 patients in Group 2, 15.7; and for 31 in Group 3, 18.0. On general assessment the results for asthma are shown in Table VI.

TABLE V.—*Comparison of Results of Treatment Between Three Doses of Depot Pollen (1964) in Hay-fever*

	Patients Assessed	Average Points	No. with Less than 7 Points	Inadequate Information Provided
Group 1 ..	84	49.4	4	23
" 2 ..	111	42.7	15	16
" 3 ..	81	44.3	9	7

Comparison of Groups 1, 2, and 3 (over 20 years of age), $P > 0.20$.
Comparison between Groups 1 and 2 (all ages), $0.05 > P > 0.02$.

TABLE VI.—*Comparison of Results of Treatment Between Three Doses of Depot Pollen in Asthma*

	No.	Satisfactory	Unsatisfactory	Incomplete
Group 1 ..	46	31 (61.5%)	15 (38.5%)	7
" 2 ..	49	41 (83.6%)	8 (16.4%)	2
" 3 ..	39	23 (67.6%)	11 (32.4%)	4

Comparison of Groups 1, 2, and 3 (over 20 years of age), $0.20 > P > 0.10$.
Comparison between Group 1 and Group 2 (all ages), $0.10 > P > 0.05$.

Side-effects Following Emulsion Treatment

In 1963 712 patients were treated at 10 different centres with two injections of depot pollen containing 750 Noon units and 7,500 Noon units by subcutaneous injection at intervals of one month. Each patient was given a form with spaces to indicate the presence and duration of (1) local swelling at the site of reaction, (2) hay-fever, (3) asthma, (4) generalized urticaria, or (5) anaphylactic shock following the injection.

Similar information was obtained in 1964 for the 397 patients given injections of depot pollen and also for the 68 treated with aqueous extract. These results are shown in Table VII. The figures include all those patients with hay-fever only, hay-fever and asthma, and asthma only who provided information after each injection, and also 17 patients given 750 + 750 units (who were excluded from the assessment of results of treatment) and 23 patients who reported on the effects of injections but failed to mention the result of treatment.

TABLE VII.—*Reactions following Depot Pollen, 1963 and 1964, and Aqueous Extracts, 1964*

	No. of Patients	Anaphylactic or Severe General Reactions	Local Reactions	Hay-fever	Asthma	Generalized Urticaria	Nil
<i>Depot Pollen, 1963</i>							
750 + 7,500 U.	712	2 (0.3%)	466 (65.4%)	141 (19.6%)	128 (17.9%)	18 (2.5%)	155 (21.7%)
<i>Depot Pollen, 1964</i>							
1st injection, 750 U.	397	1 (0.3%)	195 (49.1%)	52 (13.1%)	31 (7.8%)	5 (1.3%)	—
2nd injection, 7,500 U.	284	5 (1.8%)	165 (58.1%)	61 (21.4%)	39 (13.3%)	29 (10.2%)	—
3rd injection, 7,500 U.	97	0	52 (53.6%)	14 (14.4%)	14 (14.4%)	4 (4%)	—
	397	6 (1.5%)	273 (68.8%)	95 (23.9%)	67 (16.6%)	36 (9.1%)	76 (19.1%)
<i>Aqueous Pollen, 1964</i>							
Max. 9,000 U.	68	3 (4.4%)	14 (20.6%)	7 (10.3%)	13 (19.1%)	15 (22%)	31 (45.6%)

The number of reactions following depot pollen injections in 1964 have been separately analysed for the first injection of 750 units, the second of 7,500 units, and the third also of 7,500 units. In addition the total number of patients giving reactions of each type on one or more occasions was estimated, and can be compared with the figures for 1963.

Table VII shows that two anaphylactic general reactions were recorded in 712 patients in 1963, and six of 397 patients in 1964, making a total of eight anaphylactic reactions in 1,109 patients. The only general reaction to follow an injection of 750 units was probably not anaphylactic. A girl of 18 had what appears to have been an epileptic fit 15 minutes after the injection. She had no urticaria, respiratory distress, or rhinorrhoea, and it seems likely that the fit was only indirectly related to the injection. A second injection of 750 units was given a month later with no effect. The remaining anaphylactic reactions all followed injections of 7,500 units—an incidence of 0.7%. Where information was supplied these reactions all took place two to four hours after the injection; in addition to evidence of shock, symptoms included loss of consciousness (1), severe asthma (7), urticaria (5), and oedema of the glottis (1). In none of these cases did the initial injection of 750 units give rise to any untoward response which might have acted as a warning that the injection of a larger dose would cause trouble. All cases recovered after the injection of adrenaline or after taking isoprenaline.

Comparison of the total figures for 1963 and 1964 shows roughly similar results. Approximately 20% of patients had no reactions at all in each year. A large number (65–70%) had transient local reactions which persisted from one to three days at the site of injection: hay-fever and/or asthma, usually

reported during the evening of the day of injection, were recorded in 15–24% ; these were in most cases mild, and in none gave rise to any anxiety. The proportion of cases with generalized urticaria was much higher (9.1%) in 1964 than in 1963 (2.5%), and this sometimes recurred over two to three weeks. No explanation for this discrepancy can be offered.

In addition to these side-effects persistent nodular or cystic lesions at the site of injection were reported in eight cases. Seven nodules which persisted for six months or more were recorded. At least four were more than 2.5 cm. in diameter. One sterile abscess was recorded: a small nodule at the site of injection was found six months after injection ; this caused no symptoms at the time. However, after two further injections of depot pollen the following year the nodule enlarged to the size of a tennis ball. Aspiration withdrew thin pus, sterile on culture and containing no eosinophils. The lesion subsequently broke down to form a large ulcer with indurated edges, which is now slowly healing. A biopsy of another of these lesions was reported as showing "foreign-body reaction of the sarcoid type with oil globules, giant cells, and epithelioid cells." It is probable that a greater number of nodules persisted for six months or more than were reported by patients to their physicians.

It will be noticed that following injections of aqueous extract three (4.4%) patients had anaphylactic general reactions. One of these had three anaphylactic reactions after successive doses of pollen. Though local reactions lasting 24 hours or more were appreciably fewer, hay-fever (10.3%) and asthma (19.1%) occurred with some frequency and generalized urticaria was present in 22%. On the other hand, 45.6% had no reactions, compared with 20% with depot pollen. This difference was mainly due to the increased number of local reactions with the latter.

Discussion

Comparison between the results of treatment of hay-fever with conventional aqueous injections up to a maximum dose of 9,000 Noon units and treatment with two doses of depot pollen (750 and 7,500 Noon units) showed a statistically significant difference in favour of the latter. It should be pointed out that the maximum dose usually aimed at in standard courses of desensitization in this country is approximately twice that employed here (20,000 Noon units). The lower dose of aqueous extract was selected in order to provide a fairer comparison with the depot pollen. Frankland and Augustin (1954), giving the larger dose of aqueous pollen (20,000 Noon units), reported 27% to be free of symptoms. The lower figures (10%) in this series could be explained by the smaller maximum dose, but it must be pointed out that 1964 was a year with exceptionally high atmospheric pollen counts, and a lower proportion of good results might be expected.

Comparison between three groups receiving depot pollen showed that treatment with two injections (750 and 7,500 units) was statistically more effective in all respects studied than with a single dose of 750 units. There was, however, no advantage in repeating the dose of 7,500 units. Patients with asthma also did better with depot pollen than with repeated injections of aqueous extract ; they also responded more favourably to two doses of depot pollen (750 and 7,500 units) than to a single injection of 750 units or to three doses (750, 7,500 and 7,500 units). Nevertheless the treatment with two depot injections could not be regarded as more than moderately successful, as shown particularly in Tables II and V.

Depot injections of pollen emulsion administered subcutaneously in doses of 750 and 7,500 units caused side-effects in a relatively high proportion of cases: in the great majority of patients these were not troublesome. General reactions of anaphylactic type occurred in 7 of 996 patients (0.7%) after the larger dose. These reactions all developed two to four hours after the injection had been given and responded to

treatment with injection of adrenaline and antihistamine drugs or, in some cases, to isoprenaline and antihistamine tablets only. Local reactions at the site of depot injection were common but were rarely severe, and late local reactions (cysts or granulomatous conditions) occurred in eight patients, including one with a sterile abscess. Asthma, hay-fever, and general urticaria occurred with some frequency after several hours, in a mild form. Patients treated with conventional aqueous injections also gave similar reactions. Local reactions lasting more than 24 hours were fewer, but three (4.4%) patients of a series of 68 had anaphylactic reactions.

Nearly all patients liked the depot method of treatment, and those who had previously been treated by the conventional multiple injections with aqueous extract greatly preferred the former. Even severe local or systemic reactions did not discourage them. Nevertheless, doctors should be careful not to be persuaded too easily by the convenience of the method for themselves and their patients without taking into full consideration the risks associated with side-effects. The presence of sterile abscesses and ulcers at the site of injection is undoubtedly a serious though infrequent hazard, which it is hoped may be minimized by changes in the nature of administration. General anaphylactic reactions do not seem to occur more often, and in this series they were less frequent than after conventional injections. The reactions usually take place after several hours, at a time when the patient has returned home or to his work, when it may not be easy to obtain the immediate services of a doctor to give adrenaline or intravenous antihistamine: after aqueous injections such reactions usually take place within half an hour, during which time the patient should still be under observation and treatment more readily available. In the present state of our knowledge it is probably wise not to give depot pollen to patients who have had severe general reactions after multiple aqueous injections of pollen ; nor should it be given in the presence of severe flexural eczema. It is evident, too, that there is no point in using hyposensitization methods such as the injection of depot pollen for treatment of hay-fever in patients whose symptoms are readily controlled by antihistamine drugs.

There is no doubt that a maximum dose of 7,500 Noon units is more effective than one of 750 Noon units, and it is possible that a larger final dose would produce a higher proportion of symptom-free patients. It is clear, however, that any attempt to increase the dose should be limited to those who have had no or minimal side-effects after a dose of 7,500 units.

In conclusion, the method of depot injections if used judiciously appears to offer certain advantages over multiple injections of aqueous pollen but has not yet reached a stage when it can be recommended without qualification.

Summary

Pollen emulsion containing 750 and 7,500 Noon units was given to 1,109 patients. Severe general reactions occurred in 0.7%. Three patients out of 68 (4.4%) had similar reactions after receiving multiple aqueous injections.

Comparison between patients treated with two injections of depot pollen (750 and 7,500 Noon units) and those who received multiple injections of aqueous pollen (maximum dose 9,000 Noon units) showed that the former had fewer symptoms of hay-fever and asthma.

Comparison between a single dose of 750 Noon units (Group 1), two doses of 750 and 7,500 Noon units (Group 2), and three doses of 750, 7,500, and 7,500 (Group 3) showed that patients in Group 2 responded more favourably than those in Group 1, but that those in Group 3 fared no better than those in Group 2.

We are grateful for statistical assistance and advice provided by Dr. Ian Sutherland, Medical Research Council, Statistical

Research Unit. We are also grateful to Dr. F. H. Milner, Bencard Allergy Division, Beecham Research Laboratories Ltd., for supplying both the depot pollen and aqueous extracts for the purpose of this trial.

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Idiopathic Pulmonary Haemosiderosis and the Goodpasture Syndrome

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Brit. med. J., 1965, 2, 1152–1155

Idiopathic pulmonary haemosiderosis (I.P.H.) is a distinct clinical and pathological syndrome characterized by haemoptysis, iron-deficiency anaemia, diffuse pulmonary shadowing, haemosiderin-laden macrophages in the sputum, and brown induration of the lungs. Until recently this condition was regarded as an uncommon disease, practically confined to childhood; it is now being recognized with increasing frequency in adults, and Soergel and Sommers (1962), in a comprehensive study of the literature, reviewed 112 cases, including four new patients of their own. Twenty-one of these patients were 16 years or older when the disease was first diagnosed. Spreccace (1963) reported six patients, and Canfield *et al.* (1963) three patients, all of whom were 18 years of age or older; two of Spreccace's patients and all of Canfield's had, in addition, glomerular lesions in the kidneys, and hence represented a clinical variant of I.P.H. known as the Goodpasture (1919) syndrome. This syndrome, rare in children, is found predominantly in young adult males.

We now report a further three adult patients, two of whom are examples of the Goodpasture syndrome; the third patient has uncomplicated I.P.H.

Case 1

A 30-year-old man, with a past history of four to five years' underground gold-mining at Kalgoorlie and one to two months in the asbestos mine, Wittenoom Gorge, was admitted to Sir Charles Gairdner Hospital (formerly Perth Chest Hospital), Western Australia, in June 1962 with haemoptysis, anaemia, and a chest radiograph which showed diffuse bilateral "ground-glass" mottling, most pronounced in the right mid-zone. His only relevant past history was a previous admission to Kalgoorlie District Hospital in 1957 with a diagnosis of pneumonia. At that time he was found to be very anaemic and was transfused with 4 pints (2.3 litres) of blood. Thereafter he returned to work and was well until mid-May 1962 apart from a harsh smoker's cough and occasional blood-streaked mucoid sputum.

On examination he appeared fit but pale, with a chest expansion of 2½ in. (6.3 cm.). There were no other abnormal physical signs, such as heart murmurs, finger-clubbing, splenomegaly, petechiae, or purpura. The Hess test was negative. A chest radiograph on 5 July (Fig. 1) showed that there had already been some clearing

of the "ground-glass" mottling seen on the pre-admission chest radiograph. Mantoux was negative to 1/1,000. Sputum was negative for acid-fast bacilli, but showed many haemosiderin-laden macrophages. E.C.G. was normal. Bronchoscopy was normal apart from a small quantity of blood clot in the right main bronchus. Vital capacity, forced expiratory volume, and ventilation equivalent were all normal. Blood examination showed an iron-deficiency anaemia with a haemoglobin of 8.8 g./100 ml., M.C.H.C. 29%, white-cell count 7,400/c.mm. (polymorphs 52%, eosinophils 6%), and an E.S.R. of 1 mm. in one hour (Westergren). Bone-marrow was normal. There was no evidence of loss of blood from any system other than the lung. Rectal examination and proctoscopy, barium-meal examination, and stool tests for occult blood were all negative. Urine microscopy showed no red cells or haemosiderin; there was no evidence of intestinal malabsorption. Serum iron was 29 µg./100 ml. (normal males, 80–170 µg./100 ml.), total iron-binding capacity 180 µg./100 ml. (normal males, 240–390 µg./100 ml.), and saturation 11% (normal males, 25–65%).

FIG. 1.—Case 1. Radiograph taken on 5 July 1962.

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