of these, 9 out of 14 very chronic joints cleared up after one treatment. Of the 284 joints injected, 68 (24%) became painless with full movement and normal function; in 102 (36%) objective signs were ameliorated, deformity and swelling reduced, and movement increased; 114 (40%) showed temporary subjective alleviation. One case was worse after injection. Details are summarised in the table.

RESULTS IN JOINTS INJECTED

Disease	Became painless with full movement and normal function	Objective signs ameliorated, deformity and swelling reduced, movement increased	Subjective alleviation	Total
Osteo-arthritis ..	18	38	37	93
Active infective or focal arthritis ..	38	33	42	113
Rheumatoid arthritis	5	14	7	26
Mixed arthritis ..	3	5	20	28
Arthritis associated with spondylitis adolescens ..	0	11	2	13
Others, mainly traumatic	4	1	6	11
Total	68 (23·8%)	102 (35·9%)	114 (40·3%)	284

(Worse after injection: 1)

The best results are obtained in quiescent disease with a normal sedimentation-rate. Failure is usually due to too active infection or an unsuccessful attempt to reach the joint. Fingers, knees and wrists give the best results. Hip-joints require repeat injections from time to time. No sepsis or other surgical accident occurred.

SUMMARY

A series of 280 painful and swollen rheumatic joints have been treated by the intra-articular injection of 1% acid potassium phosphate in isotonic solution. One injection was usually sufficient.

Lasting improvement was obtained in three-fifths of the cases and temporary relief in all the remainder but one, which was made worse by the injection.

VACCINES AND CHEMOTHERAPY IN PNEUMOCOCCAL LOBAR PNEUMONIA

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DURING 1941–42 I studied a series of 441 cases of pneumococcal lobar pneumonia in patients over 15 years of age; the results are included in a joint publication from the Glasgow Fever Hospitals which is in course of preparation. An analysis of 380 of these cases to which only a sulphonamide drug was administered has confirmed the importance, as prognostic factors, of the age of the patient, the type of the infecting pneumococcus and the presence of bacteræmia at the time of starting treatment (Anderson 1943). The continuing high fatality-rate in type II infections (in my cases 14·4%)—which in Glasgow account for about a third of the city's pneumonia—suggests that there is still need to study treatment in an attempt to improve the results.

The use of combined chemotherapy and serum therapy has been studied both in this country and in America. Anderson and Cairns (1940) in the treatment of type II infections in Glasgow with combined chemotherapy and serum therapy reported a fatality-rate of 5·0%; this compared favourably with a rate of 12·5% in cases receiving sulphapyridine alone. Plummer et al. (1941) in a series of 607 cases of all types, in America, had a fatality-rate of 11·1% in those who received chemotherapy alone, compared with a rate of 14·6% in those who received combined chemotherapy and serum therapy. This slight difference persisted throughout closer analyses not only in respect of the age of the patient but also in regard to the presence of bacteræmia. Such figures scarcely afford a sound basis for the continuation of this method of treatment.

Vaccines alone have been used in the treatment of lobar pneumonia in many parts of the world as well as in this country (Wynn 1936). Although the few advocates were quite emphatic in their approval, most of them omitted any analysis of such factors as the type of the infecting pneumococcus and the presence or absence of bacteræmia—so essential in establishing the value of any therapeutic procedure in pneumonia. The treatment of an acute infection by the administration of a vaccine has not been proved of value in any other disease and there is consequently no support by analogy for its use in pneumococcal pneumonia. However, Barach (1931) demonstrated the presence of specific protective substances in the serum of patients suffering from pneumonia 4 days after the administration of pneumococcus vaccine and showed that they were produced as a result of the vaccine injected. Increasing the immunity by means of type specific pneumococcus vaccine in addition to the administration of a sulphonamide drug might thus improve the results, especially as MacLean, Rogers and Fleming (1939) had noted that the combination of chemotherapy and vaccine therapy was extremely advantageous in the treatment of experimental pneumococcal infections in mice. No results of the treatment of pneumococcal lobar pneumonia by combined chemotherapy and vaccine therapy have been published in this country.

METHOD

During the period of trial two methods of treatment were used.

The first group (control group) received sulphapyridine only, in a dosage of 2 grammes followed by 1 g. every four hours for 6–7 days. The others (vaccine group) received the same dose of sulphapyridine and in addition three doses, each of 1 c.cm., of type specific pneumococcus vaccine containing 50,000,000 organisms per c.cm. The injections were made intramuscularly over 3 consecutive days; the first two doses were of stock vaccine and the third dose was autogenous.

It was decided to allocate the cases alternately to the two treatment groups and, in view of the importance of the type of the infecting pneumococcus, to run alternating series in each of types I, II, III and group IV infections; there were 61 cases in each group.

Though it is always difficult, in grouping cases, to distribute evenly the main factors of prognostic significance, the following figures show that this method of selection gave a fairly even distribution. The number of cases in each group caused by infections due to types I, II, III and group IV was 17, 22, 5 and 17 respectively; the incidence of bacteræmia in the vaccine group was 27% and in the control group 25%; finally in the vaccine group 48% of the patients were over 40 years of age and in the control group 49% were over this age.

RESULTS

An analysis of the two treatment groups was made in respect of the final outcome of the disease (recovery or death), duration of the primary pyrexia and the occurrence of complications of pneumonia.

1. *Results of therapy as gauged by the fatality-rate.*—From table I the fatality-rate in the vaccine group and

TABLE I—CASES AND DEATHS IN VACCINE AND CONTROL GROUPS

Organism	Vaccine group		Control group	
	Cases	Deaths	Cases	Deaths
Type I ..	17	0	17	2
,, II ..	22	1	22	3
,, III ..	5	0	5	1
Group IV ..	17	1	17	1
All types ..	61	2	61	7

in the control group was found to be 3·3 and 11·5% respectively. If deaths within the first 24 hours after admission to hospital are excluded the respective figures are 1·7% and 8·5%. The percentage difference (6·8)

has a standard error of ±7·8 so that it is not statistically significant. Moreover, 3 of the cases in the control group (infections due to types II, III and VII) were extremely ill on admission to hospital and only survived for 3, 1½ and 3 days. Recovery in such ill patients was not expected and even had vaccine been administered to such cases it is very doubtful if it could have influenced the ultimate issue. Excluding these 3 cases there is little to choose between the two forms of therapy. It is clear that the fatality-rate is now so low that it cannot be of value in a small series of cases as a criterion of assessment.

2. *Results of therapy as gauged by duration of primary pyrexia.*—Table II shows that there was very little

TABLE II—DURATION OF PRIMARY PYREXIA; RECOVERIES ONLY

Pyrexia (hr.)	Vaccine group	Control group
48	28	23
96	22	24
144	1	1
Over 144 (no effect)	6	4
Afebrile	2	2

difference between the vaccine and the control groups in respect of the duration of pyrexia. The cases were also analysed according to whether treatment began during the first 3 days of illness or after the third day, but no apparent advantage was gained by the early administration of the vaccine: 25 (92%) of those treated during this period and 25 (83%) of those treated after the third day of illness were afebrile 96 hours after therapy commenced.

3. *Results of therapy gauged by the incidence of complications.*—The complications include delayed resolution (in which there was both clinical and radiological evidence of consolidation 3 weeks after the onset of the illness), sterile pleural effusion and empyema. In the vaccine group 12 cases of delayed resolution, 3 cases of sterile pleural effusion and 1 case of empyema were encountered; in the control group the respective figures were 12, 1 and 1. Such complications developed even when the vaccine was administered during the first 3 days of illness.

DISCUSSION

The series of cases investigated is small but a careful comparison with a control group of cases which were alike in respect of the three chief prognostic factors—the age of the patient, the type of the infecting pneumococcus and the presence of bacteræmia—showed that the results of therapy were essentially similar in respect of the final outcome (recovery or death), the duration of primary pyrexia and the occurrence of complications.

If the comparison were to depend solely upon an analysis in respect of recovery or death then it is clear that no definite conclusions could be reached from this small series. It might even be argued that, since the object of administering vaccines is to induce a greater production of antibody than would be found in a case receiving only a sulphonamide drug, it might be of little benefit to those patients who are critically ill on admission to hospital because the antibody response does not occur for several days. Similarly the period of primary pyrexia is not likely to be shortened by the administration of vaccines. On the other hand, if vaccine therapy were to enhance sulphonamide therapy in man then one might expect a more rapid resolution of the consolidated lung. The occurrence of delayed resolution in 12 patients (20%) is therefore of some significance.

The process of resolution must depend either upon the presence of specific immune substances or upon the natural or inherent powers of resistance. The failure of combined chemotherapy and vaccine therapy to reduce the incidence of delayed resolution would suggest that the inherent powers of resistance are of more importance in restoring the lung to normal.

Nearly all deaths in the larger series occurred in patients over 40 years of age—most of them in patients with bacteræmia when treatment began. There are grounds for believing that natural resistance is poorer in those persons who have passed middle life. The relative failure of chemotherapy in the aged and the apparent inability of immune sera and vaccines to overcome this relative inefficacy would tend to substantiate Anderson's (1943) view that in man "chemotherapy achieves its effect by a host-response different from that of specific serotherapy."

SUMMARY

The sulphonamide drugs have caused a considerable fall in the fatality-rate of lobar pneumonia, but a high fatality-rate persists among the type II infections, so common in Glasgow.

Two adjuvants to chemotherapy—serum therapy and vaccine therapy—have been tried.

In a controlled series of 122 cases, half of which received combined chemotherapy and vaccine therapy, the addition of vaccine did not significantly affect the final outcome of the disease, shorten the duration of the primary pyrexia or reduce the occurrence of complications—in particular of delayed resolution.

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NICOTINIC ACID AND RIBOFLAVIN IN BEEF EXTRACTS AND CORNED BEEF

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IN 1908 THE LANCET reported the findings of a special commission on the Origin, Manufacture and Uses of Extract of Meat. The conclusions arrived at, which have remained substantially unchallenged, were that such extracts were of negligible food value but were useful as flavouring agents and for promotion of appetite. In this latter function, Pavlov showed them to be the most powerful exciters of gastric secretion among the great variety of materials which he investigated. They were thus to be classified as dietary adjuvants rather than foodstuffs sensu stricto. A reinvestigation of this subject from a vitamin standpoint has now been carried out with a view to determining the contribution which beef products can make to the diet in respect of nicotinic acid and riboflavin.

Nicotinic acid was estimated by the method of Kodicek (1940) modified in certain instances by the replacement of the 0·4 ml. of *p*-aminoacetophenone reagent by 1 ml. of 10% procaine ('Novocain') in 10% HCl, a change which produces a more intense colour (and therefore gives greater sensitivity) and also provides a more stable colour which may be measured at any time from 5 to 25 minutes after the procaine addition.

TABLE I—NICOTINIC ACID AND RIBOFLAVIN CONTENT OF MEAT EXTRACTS, MEAT JUICE AND A YEAST EXTRACT

Material		Nicotinic acid μg/g.	Riboflavin μg/g.
Meat extract	A	900	23·35
	B	1025	25·8
	C	410	15·6
	D	560	18·3
	E	375	Not measured
Meat juice	F (concentrated)	615	15·4
	G ,, ,,	345	Not measured
'Marmite' yeast extract ..		655	,, ,,

Colour measurements were made in the 'Spekker' absorptiometer using Ilford filter No. 602 (spectrum blue). Riboflavin was estimated by the microbiological method of Barton-Wright and Booth (1943).