

THE INEFFICACY OF SULFAPYRIDINE IN INFLUENZA*

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MUCH interest is now centred in the treatment of influenza. If this epidemic follows the general pattern of most others, we must expect a second and perhaps a third wave of cases; such secondary waves are usually less wide spread than the original but are more virulent and carry more complications. Before this is upon us it is well to consider the best means of treatment.

There is a common impression that sulfapyridine or sulfathiazole are of definite benefit. For any one who treats occasional cases and gives one of the drugs to all of them, such an impression is inevitable. The patient usually consults his physician on the second day of his illness, the drug is immediately given, and on the third or fourth day the temperature is normal. In the present epidemic there were but few exceptions to this course. But the sequence of events in untreated cases is not dissimilar and the exact effect of drug therapy can only be judged by comparing an untreated and a treated group. The result of such a comparison is herewith submitted.

Material.—Sixty-eight cases were treated, 42 with sulfapyridine and 26 without. They were all from the active service forces and admitted to the Department of Pensions and National Health hospital at Deer Lodge, Winnipeg. The cases all arose during a period of nine days (December 1 to December 9, 1940), and 75 per cent arose during a period of four days (December 4th to December 7th). Full bed care and treatment was started on the first day in 6 cases; on the second day in 30 cases, and on the third day in the remaining 32 cases.

DIAGNOSTIC CRITERIA

The term "influenza" is commonly used very loosely to include a multitude of minor febrile disturbances of obscure origin, usually associated with respiratory or gastro-intestinal symptoms. It is true that during non-epidemic periods isolated cases with bizarre clinical features must frequently be classed as in-

fluenza; but during epidemics there is no infectious fever that conforms so closely to a common pattern. In each epidemic the subjective symptoms and the course are almost identical in all cases occurring at or about the same time.

In an epidemic the chief confusion arises in differentiation from acute upper respiratory infection. If these two co-exist or if one follows the other (a common event), the difficulty is increased; the fact that each may be followed by acute pulmonary complications still further obscures the issue. But as a rule differentiation may be readily made in uncomplicated cases by considering the onset and the symptoms during the first two days. These may be contrasted according to the following plan.

TABLE I.

	<i>Influenza</i>	<i>Common colds</i>
<i>Onset</i>	<i>Sudden</i>	<i>Insidious</i>
Constitutional symptoms.	Marked— Headache. Fever and chills. Malaise. Prostration. Muscle pains. Anorexia. Vomiting.	Mild— Slight chilliness. Slight malaise. Slight muscular pains. Very little fever.
Local symptoms.	Mild or absent— Cough. Sore throat. Retrosternal discomfort.	Marked— Nasal discharge. Sore throat. Laryngitis. Tracheitis, etc.

Besides this contrast in onset and symptoms, influenza is nearly always accompanied by a relatively slow pulse and low leucocyte count during the first three days. In general it can be said that influenza commences as a generalized infection and may produce localized symptoms on the second or third day; in contrast, common respiratory infections are definitely localized from the beginning.

All the cases that were used for this investigation were carefully questioned to discover the exact manner of onset and the time of appearance of each symptom.

* From the Department of Pensions and National Health, Deer Lodge Hospital, Winnipeg.

The percentage of cases showing the common symptoms in the first two days are shown in the table:

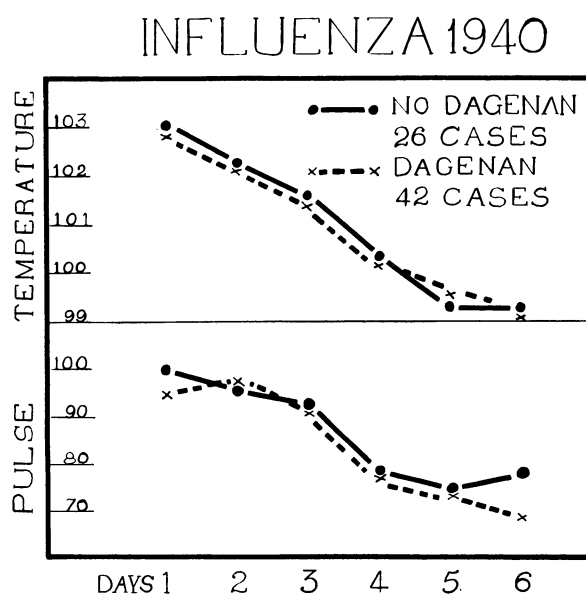
TABLE II.

	First day	Second day
Malaise.....	81 per cent	12 per cent
Headache.....	71 " "	13 " "
Cough.....	60 " "	22 " "
Chills.....	60 " "	15 " "
General pains.....	23 " "	64 " "
Sore throat.....	24 " "	24 " "
Nasal discharge.....	9 " "	21 " "

This indicates the typical general invasion of influenza and the comparative absence of upper respiratory symptoms.

Treatment.—All patients were given full bed care in hospital wards; the same staff of nurses, orderlies and doctors attended all. The treatment in the two series was symptomatic and identical except for the use of sulfapyridine. Thirty grains were given every four hours for two doses, fifteen grains every four hours for four doses and seven and a half grains four times a day thereafter till discharge.

Results.—A composite chart¹ showing the temperature and pulse was made of each group, *i.e.*, the 42 treated with sulfapyridine and the



26 treated without. A chart is reproduced here showing the two graphs superimposed. It will be seen that they are almost identical at every point.

Complications.—Can it be stated from these results that sulfapyridine or related drugs need never be given in influenza? It seems reasonable to conclude that these have no effect on the uncomplicated infection, and this has been the experience with other virus diseases (except possibly in the case of trachoma). But in the series presented there were no complications in either the treated or untreated cases and it could therefore be argued that we are still in the dark as to the influence of the drug on the incidence and course of serious complications. This is an important objection since it is pneumonia that is the chief complication in influenza. During previous pandemics it has been usually assumed that pneumonia was due to secondary invasion by streptococci or pneumococci, the soil having been prepared by the antecedent virus infection. Serious doubt is cast on this pathological assumption by the well known fact that the influenzal pneumonias completely fail to respond to chemotherapy.

Further evidence suggesting that influenzal pneumonia is *sui generis* is supplied by radiological findings. The lesion is not so dense nor so massive as is usually the case in lobar pneumonia. It is at the same time more dense, more granular and less diffuse than in bronchopneumonia. It casts a shadow which is often indistinguishable from tuberculous bronchopneumonia; when the upper lobe is involved, which is often the case, the differentiation from tuberculosis cannot be made on x-ray plates alone.

Even if we admit influenzal pneumonia to be a pure virus pneumonitis, must we insist that sulfapyridine should not be given? It can still be argued that pneumococci and streptococci may contribute in severe cases, and particularly in those that are fatal. This possibility is supported by sputum examination and post-mortem findings which disclose the presence of a variety of virulent organisms. It is quite possible that these organisms may contribute to a fatal outcome. For this reason it is justifiable to prescribe prophylactic doses of sulfapyridine or sulfathiazole in all cases of influenza. One-half gram, three or four times a day, will inhibit the growth of secondary invaders and if given for four days only, will rarely have toxic effects.

CONCLUSIONS

1. Sulfapyridine has no effect on the course of uncomplicated influenza or upon complicating virus pneumonitis.

2. Since secondary invaders may possibly contribute to a fatal outcome, the administration of prophylactic doses of one of these drugs is a wise empirical precaution in all cases.

RÉSUMÉ

Bien que la sulfapyridine ne semble pas avoir modifié le cours de la maladie chez 42 malades atteints d'influenza, par rapport à 26 cas, également atteints d'influenza, mais non soumis au Dagenan, il paraît équitable de donner quand même la sulfapyridine dans l'influenza, mais à doses prophylactiques, 0.50 gm., 4 f.p.j., afin d'éviter les complications pulmonaires dues au pneumocoque ou au staphylocoque. JEAN SAUCIER

LOBAR PNEUMONIA TREATED BY MEANS OF SULFAPYRIDINE
AND SULFATHIAZOLE*

(RESULTS IN 181 CASES)

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THE present report deals with the results of treatment in 181 cases of lobar pneumonia admitted to the Montreal General Hospital between October 1, 1939, and March 31, 1941. In 173 cases the pneumonia was due to the pneumococcus; in 6, to the staphylococcus pyogenes; in 1, to the bacillus of Friedländer; and in 1, presumably to a virus.

All cases except 4 were treated by means of one or other of the sulfonamide drugs. Thirteen patients with a pneumococcal infection died,—a mortality of 7.7 per cent. Four of the six patients with staphylococcus pyogenes pneumonia survived, although one had a serofibrinous pericarditis and another a localized empyæma. The patient with the suspected virus pneumonia recovered. The patient with Friedländer's pneumonia died.

In order to estimate properly the value of any treatment of pneumonia, data regarding age of the patient, duration of the disease before therapy, incidence of bacteriæmia, and methods of administration, are essential. These relevant facts for the pneumococcal cases are recorded in the following tables.

From the above figures it is evident that all but one death occurred in patients over 50 years of age. This observation is in conformity with the observations of other authors, who have also found a very low fatality rate in patients under 50 years of age. The one fatal case in our patients under 50 was a young man who was admitted *in extremis* and died within six hours

* From the Medical Service, the Montreal General Hospital.

TABLE I.
AGE INCIDENCE IN PNEUMOCOCCIC CASES

Age	Number of cases	Number of deaths
10-20.....	18	0
21-30.....	33	0
31-40.....	27	1
41-50.....	36	0
51-60.....	30	6
61-70.....	13	3
71-80.....	14	2
80+.....	2	1
Total.....	173	13

of the institution of chemotherapy. Although justly included from a statistical viewpoint, it cannot be regarded as indicating a failure of therapy, since, as Finland and others have shown, no therapeutic effect may be expected in any case until the drug has been administered for at least six hours, whether by the oral or the intravenous route.

Incidence by sex.—In this pneumococcal series there were 131 males and 42 females. Although the incidence of the disease is invariably higher in the male, owing probably to occupational factors, the high proportion of males in our series is, in part at least, due to the preponderance of male beds in the hospital.

Duration of the disease before therapy.—One of the chief factors which influence the effect of chemotherapy and often the outcome of the illness is the duration of the disease before therapy is begun. Table II presents these relevant facts.

At first glance it would seem that a delay in instituting treatment does not lessen its effect.