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A STUDY OF THE EFFECTIVENESS OF INFLUENZA VACCINATION IN AN INDUSTRIAL POPULATION

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In November 1960, influenza vaccination was offered to an industrial population. Some 2,500 volunteers indicated that they wished to take advantage of it. Due to the nature of the reactions experienced by vaccinated personnel, this number fell to 1,850.

This study compares the sickness absence of vaccinated and non-vaccinated groups due to influenza, bronchitis, and other respiratory causes, during the ensuing winter months. The vaccinated group appeared to derive a moderate degree of immunity, particularly in the age group over 45 years, but some effort should be made to minimize the reaction caused by the vaccine.

The problem of increased sickness absence in an industrial population during the winter months, due largely to the increased incidence of influenza, upper respiratory tract infection, and bronchitis, is well known. The prevention of such illness appeals to the industrial medical officer and even more to management which, as a result of such increased absence, may have to face disruption of production programmes for two to three months of the year. The economic loss is by no means as great as the suffering and hardship, if these can be equated, caused by such illnesses to employees and their families.

The prevention of influenza and its complications by a suitable vaccine is long overdue. As a favourable impression had been gained when influenza vaccination with a commercial vaccine was offered to about 200 employees at the Springfields Works, Preston, of the United Kingdom Atomic Energy Authority, in 1959, it was decided in the autumn of the following year to offer vaccination at the same works on a wider scale, using a proprietary influenza virus polyvalent vaccine.

This was prepared from the following strains: A/Asian/Formosa, B/England/59, containing 12,000 haemagglutination units per millilitre; it was not an oil-adjuvant vaccine.

Methods

Some 2,500 individuals indicated that they wished to avail themselves of the opportunity to have vaccination. The vaccination was spread over a period of about one month. Normally 1 ml. was given to each individual in a single dose, but in cases where there was a history of previous allergic response to any form of injection, a small test dose was given of 0·1 ml. followed by 0·9 ml. after 30 minutes' interval. Where there was a doubtful history of asthma, hay fever, or other generalized allergy, a dose of 0·5 ml. was given on two separate occasions to the individual, but those actively suffering from such conditions were excluded.

Reactions

At the time of the inoculation immediate reaction was rare, each individual being encouraged to rest for 10 minutes after vaccination, before returning to work. However, some hours later a reaction occurred in about 50% of those vaccinated. This varied from a local condition affecting the arm around the site of injection, to a general systemic effect with malaise, headache, and aching of the limbs and a rise of temperature ranging up to 102°F. (38·9°C.).

Reaction persisted into the following day, and it was some 24 hours after the time of vaccination before the symptoms began to abate; they were usually clear after 36 hours. It was manifest that for those engaged in manual work the reaction tended to be such that they could not continue with this type of job without serious inconvenience some hours after, and about 10 to 15% of those vaccinated were unable to do a normal day's work on the following day. The reaction produced by the vaccine quickly became known, and eventually only 1,850

individuals were immunized out of the 2,500 original applicants. It is clear that the vaccine in its present form has many disadvantages for use in an industrial population where continuity of work is required.

Diagnosis and Classification

From routine records details were abstracted of the sickness experienced by the volunteers and by a control group, both in respect of absence due to influenza and to other respiratory causes. This study compares such certified sickness absence of the male employees during the winter of 1960-61. The diagnosis was normally obtained from records maintained for all employees and was based on medical certificates issued by the patients' general practitioners. Although the accuracy of the diagnosis obtained in this way has sometimes been doubted (Norman and Spratling, 1956), it has been suggested that less than 2% of total spells of absence cannot be ascribed to three-figure code numbers, using the basic certificate supplemented by the knowledge of their medical departments.

Almost all sickness absence episodes are placed satisfactorily in the three digit codes of the International Standard Classification, with something like one-third of 1% remaining with an ill-defined or absent diagnosis; of the latter, few are absences of other than one day only. On the other hand it is recognized (Cruickshank, 1959) that a clinical diagnosis of influenza often includes other febrile diseases of the upper respiratory tract, and for this reason the analysis has not been confined to this one condition. An over-diagnosis of influenza should, therefore, lead to a reduction in the episodes attributed to upper respiratory tract infections and vice versa. The subsequent Tables are constructed so that, in general, influenza can be assessed between the two groups, either alone or in other combinations. Furthermore, in a trial of this size, errors of classification are likely to be equally split between the groups. A doctor, without knowledge of the patients' groups, used the individual medical record and history in an attempt to classify the bronchitic episodes into acute and chronic spells. The inclusion or exclusion of bronchitis from the acute episodes did not materially affect the pattern disclosed by the trial.

In the text, the diagnoses given imply classification under the International Statistical Classification numbers (Table 1).

TABLE 1

Diagnosis	Code No.
Influenza	480-482
Acute upper respiratory tract infections	470-475 and 788·8
Acute bronchitis	500
Chronic bronchitis	501-502
All other respiratory conditions	510-527·2 and 783

A control group was selected randomly from males engaged on similar work in the same Works. The selection of controls was not carried out by staff from the establishment concerned. Elsewhere, a pack of punched cards was raised to cover the range of identity numbers assigned to the individual members, and by means of nominal rolls the identity numbers of females and all unassigned numbers were obtained; these were then withdrawn from the pack and discarded. The pack then consisted of a numbered card for each currently employed male. The medical department provided the identity numbers of those inoculated, and their related cards were removed from the pack, thus ensuring that no vaccinated male remained in those available for random selection for the control group. These potential control group cards were randomized using a standard pack of Rand random punched cards (a million random digits with a hundred thousand normal deviates) and the requisite number taken as a control group. The two groups of cards were then taken to the factory concerned, and details of age, length of service, grade, etc. for the vaccinated and controls were obtained from the medical records and incorporated into their respective packs.

The vaccine was offered to all employees equally. These included a small proportion of females. The employees may be divided into the weekly paid employees, most of whom are engaged on what is loosely termed "process work", and the monthly paid supervisory and administrative staff. It is perhaps of interest to point out that there were 1,235 industrial and 333 non-industrial workers in the vaccinated group; the comparable figures for the control group were 1,218 and 339.

Both vaccinated and control groups were confined to males who, at December 31, 1960, had reached the age of 16 but were under 65. Although some females were vaccinated, their numbers were too small to justify analysis. No staff were included

TABLE 2

Age (years)	Vaccinated Group	Control Group
16-	145	157
25-	403	388
35-	482	464
45-	404	402
55+	134	146
Totals	1,568	1,557

TABLE 3

NUMBERS IN EMPLOYMENT IN EACH GROUP AT DECEMBER 31, 1959

Age (years)	Vaccinated Group	Control Group
15-24	87	97
25-34	310	299
35-44	395	394
45-54	346	341
55-64	126	137
Totals	1,264	1,268

who commenced employment after November 7, 1960 (when the first vaccination session was held), and men in either group whose service terminated before March 31, 1961 have been excluded. For this reason the total numbers in each group were similar though not exactly equal. All sickness absence figures given are based on a seven-day week. Table 2 gives age distribution of the staff involved.

Assessment of Comparability of Groups

Since volunteer groups may not be typical of the population from which they are drawn, and without evidence of equality it is unwise to compare vaccinated with other groups, it was decided to assess the similarity of vaccinated and control groups by reviewing sickness absence experience of the two groups for respiratory episodes completed before the vaccination dates. However, not all those vaccinated, nor all controls, were at risk for the whole of this preliminary review, and those not in employment at December 31, 1959, were excluded from this particular assessment. The age distribution of those considered is given in Table 3 and the results based on all respiratory episodes completed between January 1 and October 31, 1960, are shown in Table 4.

Although the two groups are well matched and appear suitable for comparison, statistical analysis of data in this form is difficult because the distribution of absences is skew, with few long-term absences and many short ones; and, additionally, any person may have more than one absence in the period under consideration. A more usual way of applying a statistical test is to contrast the percentages of persons having no sickness, and this is done in Table 5, using the same basic data as that in Table 4. From the results it is concluded that the difference between the respiratory experiences of the two groups is not significant, *i.e.* any differences are such that they are likely to have arisen by chance.

TABLE 5

COMPARISON OF PREVIOUS RESPIRATORY DISEASE IN THE TWO GROUPS
NUMBERS OF PERSONS EXPERIENCING RESPIRATORY SICKNESS

	Vaccinated Group	Control Group
Number at risk	1,264	1,268
Number with no absences	1,069 (84·57%)	1,059 (83·52%)
Number with one absence	165	177
Number with two absences	26	22
Number with three absences	3	10
Number with four absences	1	—
Percentage of those at risk with sickness	15·43	16·48

Standard error of the difference of these percentages—1·5—not significant.

A breakdown of the episodes by month of onset further confirms that the two groups are adequately matched as seen in Fig. 1.

Main Investigation and Results

It was concluded from Table 5 that in the absence of a significant difference between the groups, there was sufficient justification to proceed with a post-vaccination review, but as the vaccinations were spread over November 1960, it was considered unrealistic to assess the sickness absence of the two

TABLE 4

COMPARISON OF PREVIOUS RESPIRATORY EPISODES IN TWO GROUPS
(EPISODES COMPLETED BETWEEN JANUARY 1 AND OCTOBER 31, 1960)
(NUMBERS AT RISK AS IN TABLE 3)

	Episodes		Total Days Lost		Days Lost per 100 at Risk		No. Episodes per 100 at Risk		Average Length of Episode (days)	
	V.G.	C.G.	V.G.	C.G.	V.G.	C.G.	V.G.	C.G.	V.G.	C.G.
Influenza	77	86	1,188	1,311	94·0	103·4	6·1	6·8	15·4	15·2
Acute U.R.T.I.*	97	99	1,169	1,298	92·5	102·4	7·7	7·8	12·1	13·1
Subtotal	174	185	2,357	2,609	186·5	205·8	13·8	14·6	13·5	14·1
Bronchitis	36	43	992	1,110	78·5	87·5	2·8	3·4	27·6	25·8
All other respiratory disease	20	23	399	362	31·6	28·5	1·6	1·8	20·0	15·7
Total	230	251	3,748	4,081	296·5	321·8	18·2	19·8	16·3	16·3

V.G.: Vaccinated group; C.G.: Control group.
*Upper respiratory tract infection.

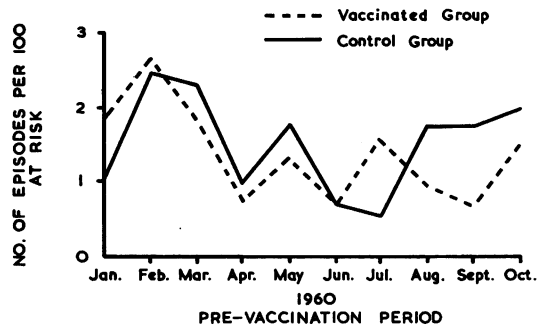

FIG. 1.—Number of episodes per 100 at risk—influenza and acute upper respiratory tract infection only. Males aged 16 to 64 years.

groups during this month. The review, therefore, included all respiratory episodes arising between December 1, 1960 and March 31, 1961, by which date the incidence of new influenza cases had diminished greatly. All certified sickness absence is included regardless of duration; in the vaccinated group nine episodes, and in the control group 12 episodes, were of less than four days' duration. The results are shown in Table 6 with some aspects expressed graphically in Figs. 2 and 3.

It appears that the vaccine may have only a limited value in certain age-groups and that there is no effect on the length of absence once sickness has occurred. As data in this form are not readily susceptible to significance tests Table 7 has been prepared.

The numbers shown in some of the totals may not be the sum of the sub-divisions. For example, there were 54 persons (vaccinated group, 45 to 64 years) who suffered from influenza, 10 from acute U.R.T.I., and four from acute bronchitis, but the sub-total shows 67 persons, not 68. This is because one person had sickness on two occasions with diagnoses which fell once into one category and once into another, so that only 67 separate persons were involved.

Of major importance is the length of time over which the vaccine would be likely to afford an appreciable measure of protection. A breakdown of episodes by certain diagnoses and by month of onset is given in Table 8.

TABLE 6

COMPARISON OF EPISODES IN THE TWO GROUPS AFTER THE VACCINATION
(EPISODES COMMENCING DURING THE PERIOD DECEMBER 1, 1960 TO MARCH 31, 1961)
(NUMBERS AT RISK AS IN TABLE 2)

	Episodes		Total Days Lost		Days Lost per 100 at Risk			No. of Episodes per 100 at Risk		Average Length of Episode (days)	
	V.G.	C.G.	V.G.	C.G.	V.G.	C.G.	C.G.:V.G. (%)	V.G.	C.G.	V.G.	C.G.
A. Aged 16 to 44 years											
Influenza	109	125	1,403	1,559	136·2	154·5	113·4	10·6	12·4	12·9	12·5
Acute U.R.T.I.*	36	56	458	571	44·5	56·6	127·2	3·5	5·6	12·7	10·2
Acute bronchitis	10	14	148	256	14·4	25·4	176·4	1·0	1·4	14·8	18·3
Subtotal	155	195	2,009	2,386	195·1	236·5	121·3	15·1	19·4	13·0	12·2
Chronic bronchitis	1	1	22	11	2·1	1·1	52·4	0·1	0·1	22·0	11·0
All other respiratory	12	3	148	26	14·4	2·6	18·1	1·2	0·3	12·3	8·7
Total respiratory	168	199	2,179	2,423	211·6	240·2	113·5	16·4	19·8	13·0	12·2
B. Aged 45 to 64 years											
Influenza	54	82	1,098	1,648	204·1	300·7	147·3	10·0	15·0	20·3	20·1
Acute U.R.T.I.	10	24	164	274	30·5	50·0	166·7	1·9	4·4	16·4	11·4
Acute bronchitis	4	11	51	259	9·5	47·3	497·9	0·7	2·0	12·8	23·5
Subtotal	68	117	1,313	2,181	244·1	398·0	163·0	12·6	21·4	19·3	18·6
Chronic bronchitis	6	11	303	250	56·3	45·6	81·0	1·1	2·0	50·5	22·7
All other respiratory	3	4	60	111	11·2	20·3	181·3	0·6	0·7	20·0	27·8
Total respiratory	77	132	1,676	2,542	311·6	463·9	148·9	14·3	24·1	21·8	19·3
C. All Ages											
Influenza	163	207	2,501	3,207	159·5	206·0	129·2	10·4	13·3	15·3	15·5
Acute U.R.T.I.	46	80	622	845	39·7	54·3	136·8	2·9	5·1	13·5	10·6
Acute bronchitis	14	25	199	515	12·7	33·1	260·6	0·9	1·6	14·2	20·6
Subtotal	223	312	3,322	4,567	211·9	293·4	138·4	14·2	20·0	14·9	14·6
Chronic bronchitis	7	12	325	261	20·7	16·8	81·2	0·4	0·8	46·4	21·8
All other respiratory	15	7	208	137	13·3	8·8	66·2	1·0	0·4	13·9	19·6
Total	245	331	3,855	4,965	245·9	319·0	129·7	15·6	21·2	15·7	15·0

V.G.: Vaccinated group; C.G.: Control group.
*Upper respiratory tract infection.

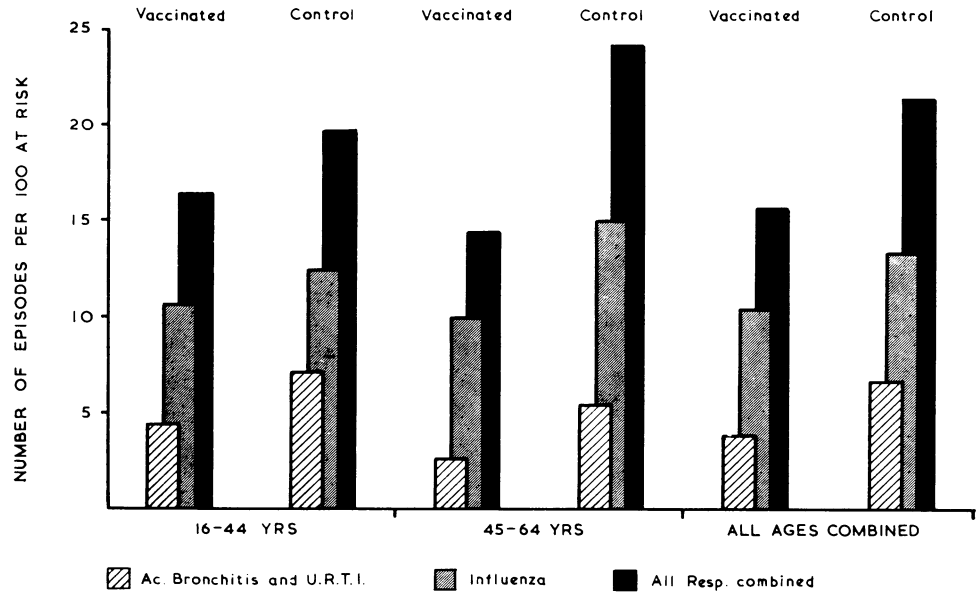

FIG. 2.—Number of episodes per 100 at risk.

TABLE 7

NUMBER OF PERSONS (AS OPPOSED TO EPISODES) HAVING HAD ONE OR MORE EPISODES OF DIAGNOSIS SPECIFIED (BASED ON THE DATA USED IN TABLE 6)

	Vaccinated Group		Control Group		Standard Error of Difference in Percentages
	No. Sick	No. Sick As % of Total At Risk	No. Sick	No. Sick As % of Total At Risk	
A. Aged 16 to 44 years					
Influenza	108	10·5	123	12·2	1·4
Acute U.R.T.I.*	34	3·3	50	5·0	0·9
Acute bronchitis	10	1·0	14	1·4	
Subtotal	149	14·5	184	18·2	1·6 +
Chronic bronchitis	1	0·1	1	0·1	
All other respiratory	12	1·2	3	0·3	
Total	158	15·3	188	18·6	1·7
B. Aged 45 to 64 years					
Influenza	54	10·0	80	14·6	2·0 +
Acute U.R.T.I.	10	1·9	21	3·8	
Acute bronchitis	4	0·7	11	2·0	
Subtotal	67	12·5	109	19·9	2·2 +
Chronic bronchitis	5	0·9	9	1·6	
All other respiratory	3	0·6	3	0·5	
Total	74	13·8	121	22·1	2·3 +
C. All ages					
Influenza	162	10·3	204	13·1	1·1 +
Acute U.R.T.I.	44	2·8	71	4·6	0·7 +
Acute bronchitis	14	0·9	25	1·6	
Subtotal	216	13·8	293	18·8	1·3 +
Chronic bronchitis	6	0·4	12	0·8	
All other respiratory	15	1·0	6	0·4	
Total	232	14·8	310	19·9	1·3 +

+Significant, *i.e.* differences unlikely to have occurred by chance. *U.R.T.I.: Upper respiratory tract infection.
N.B. Where the number of episodes does not reach 50 in one group or other, standard errors have not been calculated.

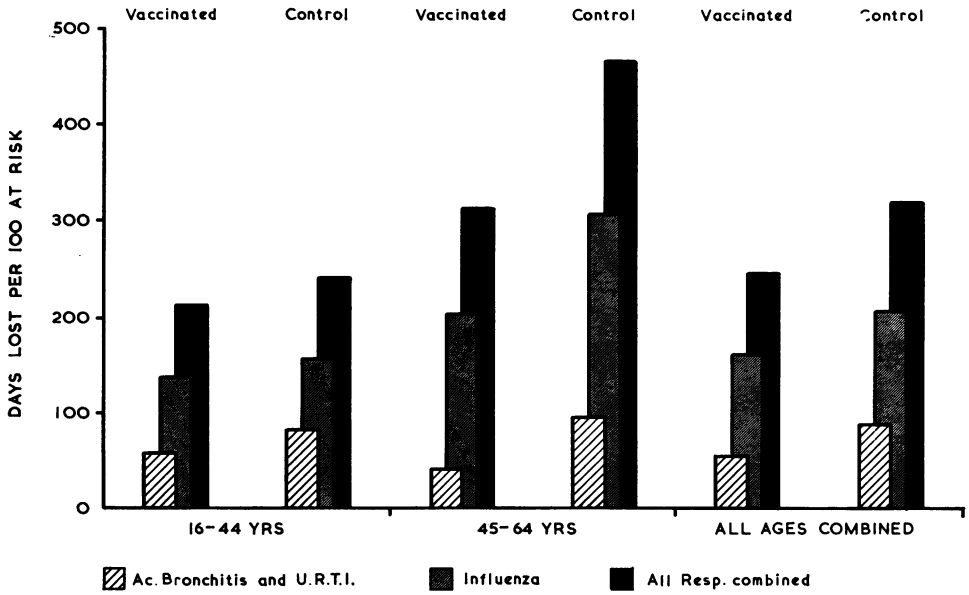

FIG. 3.—Days lost per 100 at risk.

TABLE 8

RESPIRATORY SICKNESS BY MONTH OF ONSET

	Month	Vaccinated Group		Control Group		Ratio of C.G. to V.G. per 100 at Risk (%)
		Episodes	No. of Episodes per 100 At Risk	Episodes	No. of Episodes per 100 At Risk	
A. Aged 16 to 44 years						
Influenza and acute U.R.T.I. only	Dec.	18	1·7	28	2·8	164·7
	Jan.	77	7·5	115	11·4	152·0
	Feb.	30	2·9	24	2·4	82·8
	Mar.	20	1·9	14	1·4	73·7
Subtotal		145	14·0	181	18·0	127·0
All respiratory episodes	Dec.	22	2·1	36	3·6	171·4
	Jan.	86	8·3	123	12·2	147·0
	Feb.	34	3·3	26	2·6	78·8
	Mar.	26	2·5	14	1·4	56·0
Total		168	16·2	199	19·8	120·9
B. Aged 45 to 64 years						
Influenza and acute U.R.T.I. only	Dec.	7	1·3	14	2·6	200·0
	Jan.	35	6·5	75	13·7	210·8
	Feb.	16	3·0	14	2·6	86·7
	Mar.	6	1·1	3	0·5	45·5
Subtotal		64	11·9	106	19·4	162·2
All respiratory episodes	Dec.	9	1·7	23	4·2	247·1
	Jan.	41	7·6	83	15·1	198·7
	Feb.	17	3·2	22	4·0	125·0
	Mar.	10	1·9	4	0·7	36·8
Total		77	14·4	132	24·0	168·5

V.G.: Vaccinated group; C.G.: Control group; U.R.T.I.: Upper respiratory tract infection.

Fig. 4 presents similar data in a graphic form.

Discussion

It is evident from the results of this investigation that the vaccine used afforded some protection against influenza and acute upper respiratory tract infections.

In the early months of 1961, A/Asian influenza was epidemic in this part of the country, and the impression was gained at the time that total sickness absence was less than at other works in the neighbourhood.

Having analysed the results, the percentage of improvement found, of about 30% for those vaccinated, was far below that hoped for (*Brit. med. J.*, 1960), and on this basis it would be hard to recommend that it be used for routine annual administration, unless a marked increase in protective effect could be achieved (Hawkins, Hatch, and McDonald, 1956).

There was a marked difference in its effect in the younger and older people. Below the age of 45, the incidence of influenza experienced by the Control Group was only 13% higher than that experienced by the Vaccinated Group; above the age of 45 this figure rose to 47%, and there is no doubt that the 45 to 64 years age group derived far greater benefit from the vaccine, both for influenza and upper respiratory tract infections. The reason for this is not clear, and although the numbers in this age-group were smaller than in the younger group, we feel that this did not affect the trend. It had been suggested that the vaccine might afford some protection against acute upper respiratory tract infection, and that this was so is borne out by the results.

Of particular interest was the distribution of episodes by month of sickness onset, as shown in Table 8. The vaccinated group enjoyed a considerable advantage over the control group in December and January; in February the pattern was changing and in March the control group achieved more favourable results. By the end of March the number

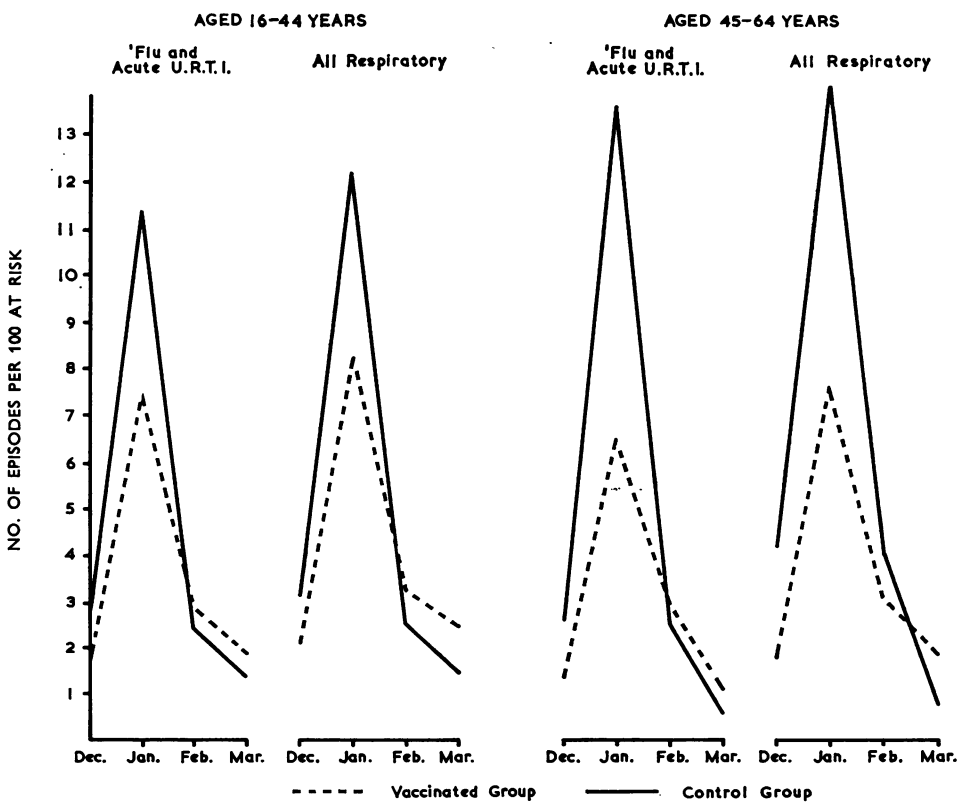

FIG. 4.—Number of episodes per 100 at risk, by month of onset of sickness.

of new cases had dropped considerably and were at too low a level for confident significance tests. It may be that the poor results in the vaccinated group in this month are attributable to chance variations. It had been hoped to obtain a six to nine months' protection against influenza by a single vaccination, but from the results shown it appears that the maximum period of protection is not more than three months. This short duration of immunity indicates that a booster dose is required to give protection throughout the winter.

Once sickness had occurred the length of sickness absence was roughly the same in both the vaccinated and the control group, and there was no evidence that the vaccine reduced the severity of influenza and other diseases in those who were absent from work.

It was unfortunate that at the time and in contrast to other workers (Cope, 1960) such severe reactions to the vaccine were experienced. This undoubtedly threw the immunization campaign out of its stride; some 700 people who had indicated that they would like to be immunized against influenza defected once the reactions became known. From the lay point of view this caused concern, especially as several poliomyelitis immunization campaigns had been completed in this works, where thousands were immunized and, of course, with no after-effect. Had the reaction been confined to a pain in the arm for a few hours, this could easily have been overcome, but the fact that a considerable proportion were unable to perform their work later in the day on which they were vaccinated and on the following day in a satisfactory manner did cause a big problem; it is felt that with the vaccine in its present form future immunization would not be possible where continuity of work is expected, and it is also probably fair to say that it would only be acceptable to the more keen volunteers.

The expense incurred and the effort required to organize a programme of this type are considerable, bearing in mind the relatively high cost of the vaccine and the individual length of time spent away from the job, *i.e.* 20 minutes.

Conclusions

The vaccine used was of some value in diminishing the incidence of influenza and other acute upper respiratory tract infections, particularly in the over 45 age-group.

Once sickness occurred the vaccine had no effect on the length of absence from work.

With the vaccine used reactions were such as to be unacceptable for a population where manual work was to be performed during the 36 hours after administration, and because of this it would not be acceptable to other than the most keen volunteers if offered annually.

The impression was gained that there was little reaction amongst volunteers with a history suggestive of previous allergic conditions, provided the dose was suitably divided.

The duration of protection given by the vaccine when administered in a single dose is relatively short lived, probably not exceeding three months.

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