areas, there is commonly a prolonged bodily reaction of this kind which produces a conscious restless anxious exhaustion.

What, then, can be done to eliminate this collision of exciting and inhibiting reflexes and the resultant pathologic nervous state? What technical advances are at hand to apply to these physiologic data to make of the traffic light a more efficient biotechnical device?

Inventors have sensed this problem, and there are now in the United States Patent Office patented devices by Altman,[4] Degner,[5] Olafson[6] and Schubert[7] to improve the traffic light. From a physiologic point of view, the last is probably the best. It is constructed as follows: A circular glass panel, illuminated from the rear, is divided into sectors, the upper green, the lower red, and two small intermediate sectors at each side yellow. A hand, similar to a clock's hand, revolves slowly around the circular panel in a clockwise direction, as shown in the accompanying illustration. The driver may see at a glance how much green or red remains on the panel and by noting the speed of the revolving hand he may respond to the stimulus more rationally. Two stimuli now evolve into a flowing continuum of stimulation rather than a rapid succession of colliding antagonistic patterns. The signal itself, being more graphic, is more easily defined consciously and therefore becomes a more efficient physiologic stimulus.

Traffic lights of this kind are to be seen in operation, though far too rarely. It is altogether fitting that the land of Pavlov's birth should be an early employer of such a device. In the summer of 1934 I saw such a signal in operation at the southern end of the Red Square in Moscow. Another was to be seen in the Bahnhofstrasse in Zurich, Switzerland, in 1937. Perhaps there are many others, but at best there are far too few. The universal adoption of a traffic signal of this or similar type would undoubtedly bring a real measure of relief to the motoring public, for, as Pavlov states, "this conflict and this balancing are not too easy for the nervous system."

SUMMARY

Lewis Mumford has pointed out that in the employing of machines we have too often forgotten their biologic effects in our constant search for mechanical perfection. He envisions a new period in technical history, the biotechnic era, when the machine will be restudied and redesigned on a physiologic basis—oriented toward the culture of life. The ubiquitous traffic light is examined in the light of this criticism and, although its mechanical efficiency is unquestioned, it is found to be bad physiologically—bad for us who have to live with it. The adoption of another form of traffic signal, less exhausting to the nervous system, is desirable.

726 Carew Tower.

4. Altman, V.: U. S. Patent Office No. 1,751,969, March 25, 1930.
5. Degner, G. C., and others: U. S. Patent Office No. 1,522,617, Jan. 13, 1925.
6. Olafson, A. O.: U. S. Patent Office No. 1,719,020, July 2, 1929; No. 1,749,390, March 4, 1930.
7. Schubert, P.: U. S. Patent Office No. 1,847,903, March 1, 1932.

The Incubus of Galen.—It was in this century that such scientists as Copernicus, Vesalius (1514-1564) and Paracelsus (1493-1541) lived and worked. There was still much medievalism in the beliefs of these men; but they were endeavoring to do, and did, considerable independent thinking. In the domain of medicine all thinkers were struggling to get rid of the incubus of Galen.—Hurd-Mead, Kate Campbell: A History of Women in Medicine, Haddam, Conn., the Haddam Press, 1938.

COLD VACCINES

AN EVALUATION BASED ON A CONTROLLED STUDY

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Our reasons for adding to the already voluminous literature on the use of vaccines for the prevention of colds are, first, that few studies of these vaccines have been adequately controlled and, second, that in spite of their questionable value cold vaccines are administered to hundreds of thousands of persons throughout the country each year. Physicians in private practice have little or no opportunity to evaluate such preparations and so are apt to base their opinions as to value on the reports of individual patients. On the other hand, organizations such as college and industrial health services, which are charged with the prevention of illness among large groups of persons, have a special interest in colds and have made various attempts to evaluate vaccines and other preventive measures. If vaccines are effective in a considerable proportion of cases and are harmless, they should be used extensively; if not, doctors and patients should cease wasting their time and money on them.

The study here reported extended over a period of three years and included work with one vaccine administered subcutaneously and two administered orally. Until recently all cold vaccines were injected either subcutaneously or intramuscularly, but during the past few years several vaccines for oral use have been developed and are already being widely utilized.

TECHNIC OF STUDY

The subjects were all students of the University of Minnesota who volunteered to participate in the study because they were particularly susceptible to colds. When they reported for their first vaccine treatment, the records of their physical examination were inspected and they were questioned concerning the symptoms which usually accompanied their colds. This procedure was followed in order to exclude from the study persons whose difficulties seemed to be due primarily to chronic sinusitis or allergic rhinitis. At the same time a record was made of each student's recent history of acute infections of the upper part of the respiratory tract, with particular attention to the number and the severity of colds experienced during the previous year and the amount of time lost from school on account of them.

Experimental and Control Groups.—At the beginning of each year of the study students were assigned at random and without selection to a control or to an experimental group. The students in the control groups were treated in exactly the same manner as those in the experimental groups but received placebos instead of vaccine. All students thought that they were receiving vaccine and so had an unprejudiced attitude toward the study. Even the physicians who saw the students at the health service when they contracted colds during the period of the study had no information as to which group they represented.

From the Students' Health Service and the Department of Preventive Medicine and Public Health of the University of Minnesota.
Read before the Section on Preventive and Industrial Medicine and Public Health at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

Reporting of Colds.—The students in all groups were instructed to report to the health service whenever a cold developed and to keep a record of each cold of more than twenty-four hours' duration. A report was obtained from each student monthly during the first year of the study and quarterly during the second and third years. The physicians who cared for the students who reported to the health service with colds made notations on their records concerning the severity and the type of the cold in each case. These records were checked later against the reports which were made by the students.

There might be some objection to the use of subjective as well as objective criteria as a basis for the determination of results, but our experience in the study of colds over a number of years indicates that the appearance of the nasal and nasopharyngeal mucous membranes is not so dependable a criterion on which to base the diagnosis of a cold as is the patient's report of his symptoms.

Loss of Time.—At the beginning of the study each student was instructed to keep a record of the number of days which he lost from school because of colds. These reports were collected quarterly and were checked by the conferences which the doctors in charge of the study had with the students.

At the end of each year reports as to the incidence of colds and the time lost from school were summarized according to experimental and control groups.

SUBCUTANEOUS ADMINISTRATION OF VACCINE

No attempt will be made to review the many reports [1] on subcutaneous vaccination against colds. Some of the more uncritical workers have been enthusiastic about the value of these vaccines, but the better controlled studies indicate that little of value can be expected from their use.

Vaccine Utilized.—The vaccine selected for this study was standardized according to the milligrams of nitrogen per cubic centimeter, as follows: pneumococci 0.015 mg., streptococci 0.015 mg., Bacillus influenzae 0.01 mg., Micrococcus catarrhalis 0.0025 mg. and staphylococci 0.0075 mg. It was prepared by the so-called Kreuger method; that is, the organisms were destroyed mechanically instead of by heat. This method of preparation is supposed to provide a vaccine which is a superior antigen because the bacterial proteins have not been changed by heat. The evidence that the method is of practical value is not conclusive, but this vaccine was chosen for study because it has all the merits of heat-killed vaccines and possibly more.

1. These include:
von Sholly, A. I., and Park, W. H.: Report on the Prophylactic Vaccination of 1,536 Persons Against Acute Respiratory Diseases, J. Immunol. **6**: 103-122 (Jan.) 1921.
Ferguson, F. R.; Davey, A. F. C., and Topley, W. W. C.: The Value of Mixed Vaccines in the Prevention of the Common Cold, J. Hyg. **26**: 98-109 (March) 1927.
Lempriere, L. R.: Catarrhal Vaccines in Public Schools, Brit. M. J. **1**: 973 (May) 1929.
Ward, R. V.: Three Years' Experience with Vaccination Against the Common Cold, Canad. M. A. J. **25**: 408-412 (Oct.) 1931.
Brown, W. E.: Vaccine in the Prevention of the Common Cold, Am. J. Hyg. **15**: 36 (Jan.) 1932.
Stoltenberg, L.: Combating of Catarrhal Hospital Infections with Anticatarrhal Vaccines: Experiences in Children's Department of the University Hospital, Oslo, Acta paediat. **12**: 169-180 (No. 4) 1932.
Dochez, A. R.; Mills, K. C., and Kneeland, Yale, Jr.: Disease of the Upper Respiratory Tract; Problems Connected with the Etiology and Prophylaxis, J. A. M. A. **101**: 1441-1444 (Nov. 4) 1933.
Kneeland, Yale, Jr.: Protection Afforded by Vaccination Against Secondary Invaders During Colds in Infancy, J. Exper. Med. **60**: 655-660 (Nov.) 1934.
Gyllenswärd, Curt: Anticatarrhal Vaccination in Homes for Children Under School Age, Acta paediat. (supp. 1) **17**: 78-90, 1935.

Dosage of Vaccine.—The vaccine was administered hypodermically to the experimental group as follows: 0.5 cc. twice a week for three weeks and then 0.5 cc. every two weeks throughout the fall, winter and spring. The control group received injections of physiologic solution of sodium chloride administered in the same way, at the same intervals and throughout the same period. Our experience indicates that it is extremely important in such a study to treat the control group and the experimental group in exactly the same manner and not to use for control a group of persons who receive no treatment whatever.

Results.—Table 1 presents a summary of the results reported by the students who received the bacterial vaccine subcutaneously and by the corresponding control group during the years 1935-1936 and 1936-1937.

TABLE 1.—*Results of Bacterial Vaccine Administered Subcutaneously*

	Vaccinated Group			Control Group		
	1935-36	1936-37	Total	1935-36	1936-37	Total
Subjects who completed study	156	116	272	107	169	276
Percentage	94.0	89.0	92.0	87.0	88.0	87.0
Number of colds per person during previous year*						
(*a*) Average	6.0	5.6	5.9 ±0.14	5.4	5.7	5.6 ±0.09
(*b*) Median	**5.6**	**5.1**	**5.4**	**5.0**	**5.3**	**5.2**
Number of colds per person during year of study						
(*a*) Average	1.8	1.3	1.6 ±0.05	2.4	1.8	2.1 ±0.06
(*b*) Median	**2.3**	**1.7**	**2.0**	**2.8**	**2.0**	**2.4**
Differences between experimental and control groups						
(*a*) Average	−0.6	−0.5	−0.5±0.08			
(*b*) Median	**−0.5**	**−0.3**	**−0.4**			
Percentage differences						
(*a*) Average	−22	−27	−25			
(*b*) Median	**−18**	**−15**	**−17**			
Number of days per person lost from school						
(*a*) Average	1.0	1.3	1.1	1.1	1.0	1.0
(*b*) Median	**0.7**	**0.8**	**0.7**	**0.7**	**0.7**	**0.7**
Subjects who had no colds during year of study, percentage	18.0	23.0	20.0	8.0	13.0	11.0

* Reported from memory.

The results have been tabulated so that comparisons can be made for each year separately as well as for the total experimental period.

Two hundred and seventy-two students in the vaccinated group and 226 in the control group completed the study, representing 92 per cent and 87 per cent, respectively, of the number who began it. These are high percentages in view of the fact that a considerable number of university students drop out of school during the course of the year for scholastic or other reasons.

The uniformity of the average number of colds which the students in the several groups reported that they had had during the year prior to the study indicates that the groups were well equated so far as susceptibility to colds is concerned.

During the two years of the study the experimental group reported an average of 1.6 colds a person yearly. This represents a reduction of 73 per cent from the average of 5.9 colds per person which the same students reported for the year prior to the study. Such a reduction would seem to be definite evidence of the value

of the vaccine. However, when we turn to the summary of the reports from the control group we find almost as great a reduction; namely, from an average of 5.6 colds per person for the year prior to the study to 2.1 colds per person yearly during the period of the study. This is a reduction of 63 per cent and is as much as has been reported by most writers who recommend the vaccine.

TABLE 2.—*Subcutaneous Vaccination in Relation to Frequency of Colds*

	Less Than Six Colds in Previous Year*		Six or More Colds Previous Year*	
	Vaccinated Group	Control Group	Vaccinated Group	Control Group
Number of subjects	158	178	114	98
Average number of colds per person during previous year*	4.1 ± 0.05	4.0 ± 0.04	8.4 ± 0.24	8.3 ± 0.35
Average number of colds during year of study	1.6 ± 0.06	2.0 ± 0.07	1.6 ± 0.08	2.2 ± 0.11
Difference between experimental and control groups	0.4 ± 0.09	.....	0.6 ± 0.14	
Percentage	—20.0		—27.0	

* Reported from memory.

The difference between the average number of colds per student in the experimental and in the control groups during the two years of the study is 0.5 ± 0.08 colds per person yearly. This difference in favor of the vaccinated group, although statistically significant, is too small to be of practical importance. A similar comparison of the median number of colds reported by the experimental and by the control groups gives even less evidence of value of the vaccine.

The average and the median number of days lost per person from colds is essentially the same for the vaccinated and the control groups. The proportion of subjects who reported no colds whatever during the period of study was 11 per cent for the control group and 20 per cent for the vaccinated group. If this group is excluded from our computations, we find that the average number of colds per person among those who had any colds was 2.5 for the vaccinated group and 2.7 for the control group. In other words, the margin of benefit in the vaccinated group is represented entirely by the difference of 9 per cent in the number who had no colds whatever.

TABLE 3.—*Results with Same Subjects in Different Groups*

Year	Number of Subjects	Treatment Group	Average Number of Colds per Person
First	25	Control	2.6
Second	25	Subcutaneous vaccination	1.9
First	30	Subcutaneous vaccination	1.9
Second	30	Control	1.7

TABLE 4.—*Cutaneous Sensitivity and Results of Vaccination*

	Average Number of Colds Yearly	
	Positive Cutaneous Test with Vaccine	Negative Cutaneous Test with Vaccine
Subcutaneous vaccination group	1.4 (114 cases)	1.7 (140 cases)
Control group	2.0 (130 cases)	2.1 (127 cases)

In an effort to determine whether the reduction in colds was occurring in any particular group an analysis was made of the results among students who reported six or more colds as compared to those among students who reported less than six colds during the previous year. Table 2, which presents this analysis, shows no significant differences between the groups.

A few students participated in this study during both the years in which it was conducted. Twenty-five of these were in the control group the first year and in the vaccinated group the second year, thinking, of course, that they were receiving the same vaccine the two years. Table 3 shows that this group reported an average of 2.6 colds during the year in which they were in the control group and 1.9 colds during the year in which they were in the vaccinated group. On the other hand, thirty students who were in the vaccinated group the first year and in the control group the second year also reported somewhat fewer colds during the second than during the first year (table 3).

TABLE 5.—*Results with Polyvalent Vaccine Administered Orally*

	Vaccinated Group			Control Group		
	1936-37	1937-38	Total	1936-37	1937-38	Total
Subjects who completed study	162	201	363	169	203	372
Percentage	83	80	82	87	81	84
Number of colds per person during previous year*						
(*a*) Average	5.6	5.6	5.6	5.7	5.2	5.4
(*b*) Median	**4.9**	**5.6**	**5.3**	**5.3**	**5.2**	**5.2**
Number of colds per person during year of study						
(*a*) Average	1.9	1.7	1.8	1.8	1.6	1.7
(*b*) Median	**2.2**	**2.0**	**2.1**	**2.0**	**2.0**	**2.0**
Difference between experimental and control groups						
(*a*) Average	+0.1	+0.1	+0.1			
(*b*) Median	+0.2	0	+0.1			
Number of days per person lost from school						
(*a*) Average	1.3	0.5	0.8	1.0	0.4	0.7
(*b*) Median	**0.7**	**0.6**	**0.7**	**0.7**	**0.6**	**0.7**
Subjects who had no colds during year of study, percentage	11	14	13	13	14	14

* Reported from memory.

Thinking that the students benefited might be those who were sensitive to some of the organisms in the vaccine, we made an intracutaneous test with the vaccine on all subjects at the beginning of the study. The results, as shown in table 4, do not indicate that this procedure is useful in identifying the persons who may expect benefit from the vaccine.

ORALLY ADMINISTERED VACCINE

Rockwell, Van Kirk and Powell[2] have reported several studies which suggest that vaccines containing organisms of the respiratory group administered by mouth may be useful for the prevention of colds. Their studies contain control groups, but the subjects in these groups apparently received no treatment whatever. If this inference is correct, the results which this group reports cannot be accepted as comparable to the results reported by the experimental groups.

2. Rockwell, G. E.; Van Kirk, H. C., and Powell, H. M.: Oral Immunization to Colds, J. Immunol. **28**: 475-483 (June) 1935; Further Studies on Oral Immunization to Colds, J. Lab. & Clin. Med. **22**: 912-917 (June) 1937.

Through the courtesy of the producers, two types of cold vaccines for oral administration were studied. One of these is available commercially and widely used throughout the country; the other has been prepared and used more or less experimentally by Dr. E. C. Rosenow of the Mayo Clinic.

Polyvalent Vaccine for Oral Administration.[3]—This vaccine, containing 25 billion pneumococci, 5 billion Haemophilus influenzae, 15 billion streptococci and 5 billion M. catarrhalis, was used during the winters of 1936-1937 and 1937-1938. During the first year in which the orally administered vaccine was used a control group was receiving sterile saline solution hypodermically. This group, it was decided, could justifiably serve as a control for the orally administered vaccine. During the second year of the use of this vaccine a special group to serve as a control was set up. The subjects in this group were given lactose-filled capsules which were indistinguishable from the capsules containing the vaccine. They were prescribed with exactly the same instructions as the capsules containing the vaccine.

TABLE 6.—*Results with Streptococcus Vaccine Administered Orally*

	1937-1938	
	Vaccinated Group	Control Group
Subjects who completed study	154	203
Percentage	77	81
Number of colds per person during previous year*		
(*a*) Average	4.8	5.6
(*b*) Median	**4.7**	**5.2**
Number of colds per person during year of study		
(*a*) Average	1.5	1.6
(*b*) Median	**1.9**	**1.6**
Difference between experimental and control groups		
(*a*) Average	—0.1	
(*b*) Median	**—0.3**	
Number of days per person lost from school		
(*a*) Average	0.9	0.4
(*b*) Median	**0.7**	**0.6**
Subjects who had no colds during year of study, percentage	14	14

* Reported from memory.

The directions for taking this vaccine were as follows: "The capsules must be taken on a resting and empty stomach. Take one capsule with a drink of cold water one hour before breakfast. One capsule must be taken each morning for seven consecutive mornings and then two capsules weekly throughout the season."

Each student was given a supply of capsules sufficient to last eight weeks, at the end of which time he returned to the health service for a new supply. This enabled the physicians in charge of the study to check on the actual use of the capsules by the students.

Results.—The method of reporting results was the same as that which has been described for the vaccine given subcutaneously. The tabulation of the reports (table 5) shows a reduction for the vaccinated group of approximately 70 per cent in the average number of colds per person for the year of the study as compared to the previous year. This is approximately the same reduction that was reported by Rockwell and his associates. However, when we turn to our control group we find just as much reduction as was reported by the vaccinated group. In other words, this study shows that in the average or the median number of colds per person yearly, in the number of days lost from school and in the proportion of students who had no colds during the period of the study, there is no evidence of any benefit whatever from the vaccine.

TABLE 7.—*Symptoms Attributed to Vaccine* *

	Polyvalent Oral Vaccine	Control Group	Streptococcus Vaccine
Gastrointestinal upset	4	1	1
Diarrhea	1	..	1
Abdominal pain	1	..	..
Nausea	..	..	1
Tired feeling	1	..	..
Headache and groggy feeling	1	..	..
Pain in chest	..	..	1
Irritation in nose	..	1	..
Nasal discharge	..	..	1
Sneezing	1	..	2
Sneezing and headache	1	..	..
Dry feeling in mouth	1	..	..

* 1938 only.

Streptococcus Vaccine.—Dr. E. C. Rosenow,[4] who has been experimenting with several types of vaccines, supplied us with a streptococcus cold vaccine which he had prepared for use by mouth. The streptococci in this vaccine were isolated from the nasopharynx or sputum of patients with common colds. The final concentration of the vaccine contained 20 billion organisms per cubic centimeter. It is put up in a corn syrup vehicle. The first dose was 5 drops daily, taken preferably from a half to one hour before breakfast. This dose was increased by 5 drops daily up to 20 drops; then 20 drops was taken once or twice weekly throughout the winter.

During the year in which this vaccine was studied a control group was taking lactose-filled capsules. This group, it seemed, could serve satisfactorily as a control for both orally administered vaccines and was so used.

TABLE 8.—*Complications*

	Influenza	Tonsillitis; Pharyngitis	Pneumonia	Other Complications, Such as Bronchitis, Sinusitis, Otitis Media	Total	Patients Hospitalized
Subcutaneously administered vaccine	3	5	0	4	12	8
Control group	3	5	0	3	11	11
Polyvalent oral vaccine	2	8	1	19	30	9
Control group	5	13	0	16	34	9
Streptococcus vaccine*	1	14	0	17	32	8

* Approximately half as many subjects as in the other groups.

The results reported with this streptococcus vaccine (table 6) parallel exactly the results reported by the control group.

Untoward Symptoms.—Table 7 shows a summary of the symptoms which the students attributed to the orally administered vaccines during 1937-1938. It will be noted that although relatively few students reported any such symptoms there is a distinct differentiation between the groups in this regard.

3. The firm which developed this vaccine was interested in its further evaluation and supplied us with the vaccine used in this study.

4. Rosenow, E. C., and Heilman, F. R.: Streptococcal Vaccines in the Prevention and Treatment of Respiratory Infections, Am. J. Clin. Path. **8**: 17 (Jan.) 1938.

COMPLICATIONS

It has been stated frequently that, even though bacterial vaccines may have little or no value for the prevention of colds, they probably reduce the frequency and the seriousness of complications. Table 8 presents a summary of what might be considered complications from acute colds as these were recorded on the health service records of the several groups of students. Since some of the subjects lived at home, this report is not complete. On the other hand, it would seem that by groups the data should be relatively comparable. The larger number of complications reported by both groups which received "oral vaccine" and by the control groups during the last year of the study indicates that the acute infections of the upper part of the respiratory tract were more severe and of a different type during the last year than during the earlier years of the study. The number of cases involved in the several groups is too small to justify the drawing of conclusions, but certainly this table presents no evidence that the vaccines reduced the complications among these particular students.

CONDITION OF NOSE AND THROAT AND FREQUENCY OF COLDS

Every student included in this study had had a nose and throat examination by an otolaryngologist of the health service staff, in most instances within two months of the beginning of the study. Table 9, which presents a summary of the reports in accordance with the recorded condition of the nose and throat, gives no support to the impression that students with nasal obstruction or infected tonsils are unusually susceptible to colds.

TABLE 9.—*Condition of Nose and Throat and Frequency of Colds*

	Average Number of Colds Yearly in Several Groups During Period of Study		
	Normal Nose and Throat	Nasal Obstruction	Hypertrophied or Infected Tonsils
Subcutaneously administered vaccine	1.5	1.8	1.5
Control group	1.9	1.9	2.2
Polyvalent oral vaccine	1.9	1.5	1.7
Control group	1.7	1.7	1.7
Streptococcus vaccine	1.6	1.6	1.5

COMMENT

These studies were so planned that the reports of results would be made without prejudice on the part of either the patient or the physician. Tabulations were made for each year separately without the persons who made the tabulations having the summaries of the previous years at hand. The students were not under such constant supervision or subject to such accurate checks of absences due to illness as are certain groups of industrial employees. On the other hand, these students made intelligent, cooperative and conscientious subjects. Hence it would seem that the results here presented are sufficiently dependable and sufficiently well controlled to serve as a basis for conclusions.

Statistical analysis of the results reported for the subcutaneously administered vaccine shows that the differences reported are statistically significant and indicates that this vaccine has a definite biologic effect. However, in a group such as this, selected on the basis only of susceptibility to colds, the beneficial effect is too small to be of practical value. On the other hand, further studies to determine how, why and for what persons the vaccine is of value are clearly indicated. If such studies should make it possible to select for vaccination the persons most likely to be benefited, it is possible that the average effectiveness of the vaccine could be greatly improved.

During the winter of 1936-1937 Drs. T. B. Magath and Joseph Berkson [5] of the Mayo Clinic conducted a study of oral vaccination [6] very similar to the one here reported. The subjects of their study consisted of doctors, nurses, stenographers, clerks, technicians and other employees of the Mayo Clinic. The experimental and the control groups were carefully equated and treated in a like manner. As in our study, the control group received lactose-filled capsules which they thought contained vaccine. All subjects kept accurate records of their colds, on which they reported each month.

A tabulation of these results shows an average of approximately 18 per cent less colds per person in the vaccinated group than in the control group. Just why Magath and Berkson obtained this evidence of slight benefit from the orally administered vaccine when our study shows none, it is difficult to say. The benefit may have been due, at least in part, to the differences in the ages and in the average susceptibility to colds of the subjects or to differences in the methods of collecting reports. For practical purposes, however, the results which they obtained and those which we are reporting are not at variance. In fact, the results with the orally administered vaccine are almost identical with those which we obtained with the subcutaneously administered vaccine. With this the average number of colds per person was 25 per cent less for the vaccinated group than for the control group, but who would advocate either the expense or the inconvenience of taking cold vaccines throughout the fall, winter and spring in order to reduce by 25 per cent the probable number of colds that one might have during the year?

SUMMARY AND CONCLUSIONS

In a carefully controlled study of the value of three different vaccines which are recommended for the prevention of colds the subjects were cold-susceptible students of the University of Minnesota.

A "control group" was observed during each year of the study. Such groups were chosen at random from the students who applied for cold prevention treatment; the members were treated in exactly the same manner as those of the vaccinated group, and they believed throughout the period of the experiment that they were receiving vaccine. Sterile physiologic solution of sodium chloride was administered hypodermically as a control for the subcutaneously administered vaccine and lactose filled capsules as a control for the vaccines administered orally.

One of the most significant aspects of this study is the great reduction in the number of colds which the members of the control groups reported during the experimental period as compared to the number that the same students reported for the previous year. In fact, these results were as good as many of those reported in uncontrolled studies which recommend the use of cold vaccines.

The group which received vaccine subcutaneously experienced an average of 25 per cent less colds per

5. Personal communication to the authors.
6. The vaccine which they studied was the same polyvalent oral vaccine that was used in this study.

person than did the control group. This difference occurred during both years of the study and is statistically significant. Practically, however, it is of little or no importance, because a reduction of 25 per cent in the average number of colds in a group of individuals is not sufficiently great to justify the time and expense involved in carrying out the intensive vaccination procedure which was utilized.

The group which received the polyvalent vaccine administered orally experienced just as many colds as the control group during both years of the study.

The results reported by the students who took Rosenow's streptococcus vaccine parallel exactly those reported for the control group.

Although the data are not entirely conclusive, there is no evidence in this study either that vaccines reduce the complications of colds or that the condition of the nose and throat is related to the frequency of colds in a cold-susceptible group.

ABSTRACT OF DISCUSSION

DR. W. A. SAWYER, Rochester, N. Y.: The investigation of the authors is proof of how easy it is to jump to conclusions and make deductions on too little evidence. I have been guilty of concluding that because a patient reported no colds after taking a vaccine it was probably the result of the vaccine. Again and again one hears doctors say that they believe vaccines against colds are about 50 to 70 per cent effective. Such statements are based on evidence of very few cases, and almost always without a control study. Dr. Diehl and his co-workers have exercised much care in eliminating any personal psychology. What the individual feels or imagines has had too great an influence. In 1930-1931 in Rochester subcutaneous cold vaccines were given to a small group, with the result that 42 per cent reported no colds or mild colds. In all the work I have advised vaccines only to those who are highly susceptible. This 42 per cent looked encouraging. In 1931-1932, 45 per cent reported no colds or mild colds, again a figure giving some hope. In 1932-1933 the same percentage was obtained, 45. In 1933-1934 it was only 40 per cent. From such figures I think any one might assume that vaccines have been of some real value, particularly when given to persons who have previously had numerous colds. At least the percentages are rather consistent in these four different groups. Likewise, the percentages of those not helped were consistent, being 13, 15, 18 and 16. In 1934-1935 vaccines were given to 115 cold-susceptible employees, with the result that 57.4 per cent reported no colds or mild colds. This looked even more encouraging; however, this time there was a control group, but not to the extent that Dr. Diehl and his co-workers had. This control group did not receive anything to prevent colds, not even a placebo. Records were carefully kept of their colds and 46.8 per cent of them reported no colds or mild colds. This gives a slight margin of value to the vaccine, but not sufficient to warrant its general use. You see how different the picture looks with a control. This control group rated higher than any of the groups in any of the previous years. All of this looks rather encouraging, if one does not question what might have happened if they had not taken anything. We owe a debt of gratitude to Dr. Diehl and his co-workers for their valuable investigation.

DR. L. D. BRISTOL, New York: Throughout industry we have been attempting to appraise the value of these cold vaccines for some time, but, as Dr. Sawyer has indicated, it is often difficult to set up a controlled experiment of this sort in industry. Last fall I reported 20,000 instances of vaccinations against the common cold among six of our operating companies in the Bell system, covering an experience of from five to seventeen years. This was not a controlled experiment in any sense of the word but simply a study of what appeared to be the results; from that study we arrived at practically the same conclusions as Dr. Diehl and his co-authors have presented here; in other words, no apparent reduction in the incidence of colds. The only way in which my study differed, slightly, from the authors' results was in finding some evidence of a reduced length of disability from work and some less severity and complications of colds among those who had received these vaccines. Such groups as the authors' in our universities are the ones to give the results of such scientifically controlled experiments. Their study goes a long way toward determining the real value of these cold vaccines.

DR. J. E. NELSON, Seattle: How do you account for the lower number of colds in the vaccinated and the controlled groups during the study than what they reported in the previous years?

DR. ROBERT K. CUTTER, Berkeley, Calif.: All reputable biologic laboratories welcome controlled studies of their products. Clinicians are often optimists and to control their overenthusiasm we urge the use of a placebo and the product to be tested, labeled only by numbers, the "key" held by a notary until the study is complete. It is unfortunate that Dr. Diehl and his co-workers used the Krueger antigen rather than the standard bacterial vaccines used in most other studies of cold vaccines, particularly as Dr. Singer-Brook reported at the American Academy of Pediatrics last week that in a study of whooping cough immunizing products the Krueger antigen group showed no greater immunity than the control group, while the group immunized with phase one vaccine, which is a true bacterial vaccine, showed definite immunity. This certainly does not prove that bacterial vaccine injections would prevent colds but it does indicate that a study involving Krueger's antigen does not evaluate the usual bacterial vaccines. I hope that Dr. Diehl and his co-workers will have an opportunity to study the worth of unmodified bacterial vaccines by injection in the future.

DR. H. S. DIEHL, Minneapolis: The results, I admit, were distinctly disappointing. We had hoped to find among these vaccines a specific preventive measure to reduce the incidence of colds. Dr. Sawyer's experience in connection with employees of the Eastman Kodak Company is enlightening and critical and, as he points out, shows again the necessity of having a control group before one is justified in drawing conclusions in a study of this sort. Individual opinions, as these studies show, mean nothing. During the course of this study several physicians have written or called us to say "I have a patient who was a student at the university last year and took your cold vaccine and got such splendid results that he wants to continue it. Will you be good enough to tell me what vaccine you are using?" And we would look it up and find in many instances that the person in question got the sterile saline solution or the lactose capsules. In answer to the question as to how we explain the smaller number of colds during the year of the study than during the previous year, this, I think, is merely evidence that none of our memories are accurate as to the number of colds we had a year ago. Furthermore, during the year of the study we gave each student a definition as to what to consider a cold. These were that "You are to record the condition as a cold only if the symptoms last twenty-four hours or longer. If you have a little coryza for half a day and it is gone, do not consider that a cold. These probably are the reasons for the fewer colds during each experimental period than during that previous year. These differences appear for the control groups as well as for the vaccinated groups. As to the use of heat-killed vaccine, we have no evidence that the heat-killed vaccine might not be better than the Krueger type vaccine, prepared without the use of heat. On the other hand, we assumed that if we were to use the heat-killed vaccine there might be some suggestion that the so-called undenatured antigen would be better, while if we used this mechanically killed and undenatured antigen the results would be applicable to the heat-killed vaccine as well. If this study did not accomplish anything else, it demonstrated the importance of treating "control" groups in exactly the same manner as experimental groups. In such preventive or therapeutic studies it is not sufficient to use for control purposes groups which are merely observed. They must be treated in exactly the same manner as the experimental group if the results are to have significance.