Section of General Practice

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DISCUSSION ON THE COMMON COLD

Dr. R. E. Hope Simpson (Cirencester):

When we have been baffled by a problem for a sufficient time, when we have assaulted it with this theory and that hypothesis and it remains unsolved to plague us both intellectually and physically, it may be that the time has come to imitate Joshua, to draw our forces a little way off, to march round and round our problem considering it from every angle. Inferences may then suddenly become so plain to us that we blow loudly on the trumpets of a new idea and down tumble the impregnable walls. Some such feeling has animated our approach to the problem of the common cold, a fortified city that has so far successfully resisted the most determined and persistent frontal attacks. I shall consider one aspect from my own vantage point.

For many years we studied the broad picture of respiratory disease as presented to us in general practice. In particular it seemed important not to assume that colds were infectious unless the facts proved them to be so and I shall quote certain features of the epidemiology of colds which are inexplicable by a theory of simple transmission.

J. J. van Loghem collected records from nearly 8,000 volunteers in various parts of Holland. He analysed them separately for seven different regions of Holland and found nearly the same incidence in each region, and that the secular curves of morbidity of each had approximately the same troughs and peaks. It is as if one started measles in seven different parts of a country simultaneously, then selected susceptible volunteers at random from the seven different regions, and when the epidemic was over one found that the measles amongst the volunteers gave identical curves of prevalence and incidence in each region. Such a thing would be an incredibly unlikely coincidence, yet this actually happened with colds and has since been confirmed by Frost and Gover and again by Tucher in the United States. Some other powerful agency must be in operation besides case-to-case transmission, if such indeed does occur.

Rarity and commonness in diseases are interesting characteristics worthy of close attention. A common disease presents the difficulty that its very abundance may make it almost impossible to decide whether case-to-case transmission occurs or not. Colds may be so abundant that the appearance of transmission is simulated by chance alone.

A second characteristic, in addition to the extreme abundance of colds, is their seasonal tide. The five-year average of cases of respiratory disease presenting in each calendar month in the practice gives a curve with its peak in the winter months and its nadir in the summer. The thirty-five-year average each month for the air temperature when inverted shows a broad parallelism with the respiratory disease curve.

This parallelism with the temperature did not hold for cases of sore throat. It seemed that a big group of respiratory illnesses, the commonest diseases with which we have to deal, followed a seasonal trend running to abundance in the cold weather, and that another symptomatically distinct respiratory group did not. This crude epidemiological observation merited a closer scrutiny. We therefore enrolled some 350 volunteers, about 80 families, who keep a daily record of certain respiratory symptoms.

Incidence.—We had two main objectives, firstly to discover in detail the true incidence, and secondly to see how closely colds paralleled the changes in seasonal temperature. Here again we tried to shed our preconceptions. We did not in the first place record colds, separate illnesses, as units or episodes but we recorded the daily morbidity in case colds were not episodes of illness like measles. We hoped that the facts if adequately and accurately elicited would speak for themselves. We did not know what other mode of illness there might be. Perhaps a state of chronic morbidity with the morbid process increasing in severity every now and then so that its toxicity rose above the threshold of symptom production and then again sank below it, or perhaps a latent virus infection prompted to periodic activity by extraneous agencies in the manner of herpes simplex virus, or again, perhaps the normal bacterial flora prompted to unwonted activity by the advent of viruses passing continuously from person to person. Whatever the possibilities we had no right, in view of the quite different epidemiological picture presented by colds, to carry over to this enquiry conceptions based on the epidemiology of diseases like measles and typhoid fever. If we can be sure of anything, we can be sure of this, that in colds we have to deal with a mode of illness totally different from those.

Each of us probably suffers from measles for two of the 3,500 weeks of his life. How long do we suffer from colds? Our figures for 1954 and 1955 suggest that we probably suffer from a cold for 700 weeks of our life—one-fifth of our days. During each of these years the average for man, woman and child was seven episodes of respiratory illness averaging ten days each—seventy days per annum.

Though this may be a minor disease it is not a minor mode of illness.

Seasonal link.—How closely are colds associated with cold?

The secular curve of morbidity from colds amongst our volunteers was compared continuously on a comparable scale with the inversion of the temperature taken a foot deep in the earth. This gives a good picture of the seasonal temperature damping out the effects of brief erratic changes in the air temperature (Fig. 1). The concordance between the two curves is remarkable. It seems that the temperature has only to drop 1° F. for the morbidity from colds to rise by about 1%.

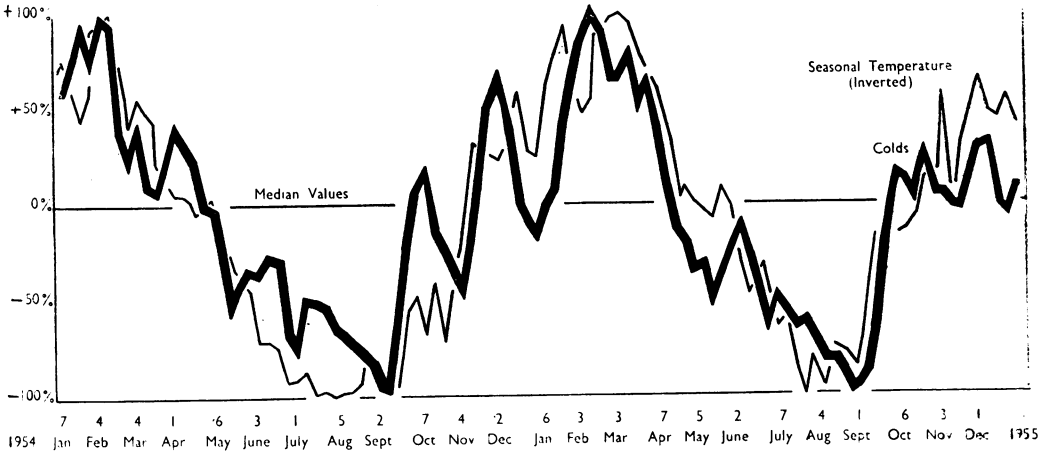

FIG. 1.—*Morbidity from colds with seasonal temperature* 1954 *and* 1955. Thick line—percentage of volunteers showing symptoms. Thin line—earth temperature (inverted).

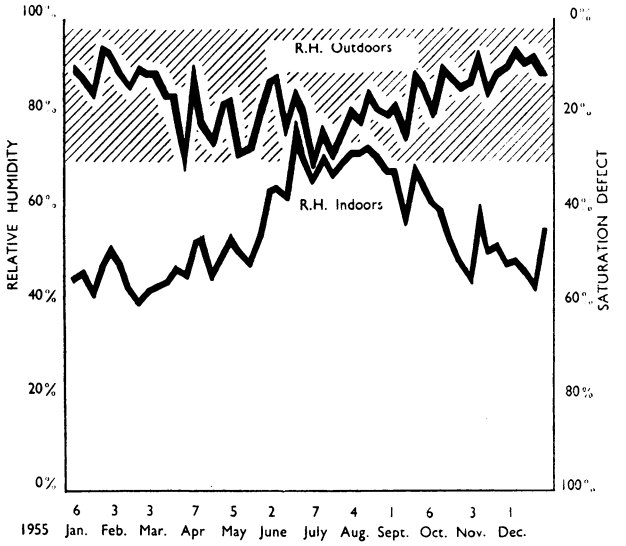

FIG. 2.—*Relative humidity outdoors and indoors* 1955. Top curve—relative humidity at 10.0 a.m. outdoors. Lower curve—relative humidity at 3.0 p.m. indoors. Shaded area shows the usual range of natural outdoor relative humidity.

It is, of course, possible that the drop in seasonal temperature itself directly causes the increased morbidity, but one finds difficulty in accepting this solution of the problem. The effect may be secondary, mediated through another agency acting directly on the human organism, an agency the effect of which varies in intensity with the seasonal temperature change. This seems the more likely because most of us spend much of our time, especially in winter, in temperatures far removed from those of the outside air, and yet it is in winter particularly that we must seek the baleful agency. In the search for this agency our suspicions were aroused by the humidity of the indoor atmosphere, or, to be more precise, by the converse of

the humidity, the evaporating power or dryness of the air. Here is an agency acting directly on the respiratory apparatus in the most intimate fashion imaginable.

Direct evaporimetry is tricky, but it is fairly easy to obtain a measure of the drying effect of the air from the saturation deficit and the temperature. The saturation deficit tells us in percentages how much more water vapour the atmosphere can accommodate, and the temperature allows us to envisage the avidity of the air for water. The usual range of humidity of the outdoor air in our part of the world is from 70% to 98% with an average of about 80%. This has a deficit of from 30% to 2%. For a brief period in summer the air indoors reaches this "natural" state of humidity (Fig. 2). For most of the year, however, the air indoors is considerably drier than the outdoor air.

The difference in humidity between the atmosphere indoors and outdoors gives a curve over the year that approximates very closely to that of the morbidity from colds, in fact we may say that the increase of colds and the increase of dryness due to artificial heating run closely parallel (Fig. 3).

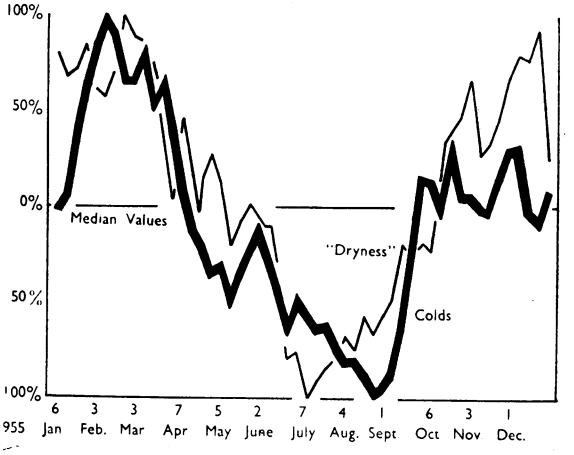

FIG. 3.—*Colds and indoor dryness* 1955. Thick line—morbidity from colds. Thin line—difference between relative humidity outdoors and indoors.

Our respiratory apparatus requires that the air shall be fully saturated with water vapour if it is not to suffer severe damage. Lassen discovered this tragically when poliomyelitis hit Denmark and produced the great crop of cases of bulbar palsy. They found themselves faced with numerous patients unable to breathe and only two iron lungs in the country. Lassen rapidly improvised methods of positive-pressure respiration with anæsthetic apparatus. He found that unless the gases were fully saturated the patients developed respiratory infections. Here is clear evidence of the importance of an adequate content of water-vapour, and we know that there is an apparatus in the human nose and upper respiratory passages for saturating incoming air. This humidifying apparatus, it is reasonable to suppose, is designed to meet the exigencies of the "natural" variations in humidity, but the conditions indoors depart widely from anything that we meet outdoors, especially in winter. Moreover, the effect is enhanced enormously by the temperature. For each 10° rise in temperature we get a

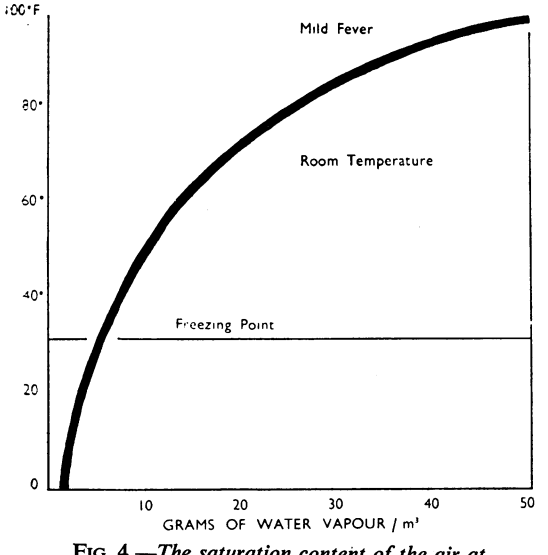

FIG. 4.—*The saturation content of the air at different temperatures.*

proportionately increasing capacity of the air to store water, coupled with an enhanced molecular activity, so that the thirst of the air develops enormously as one proceeds up the scale (Fig. 4).

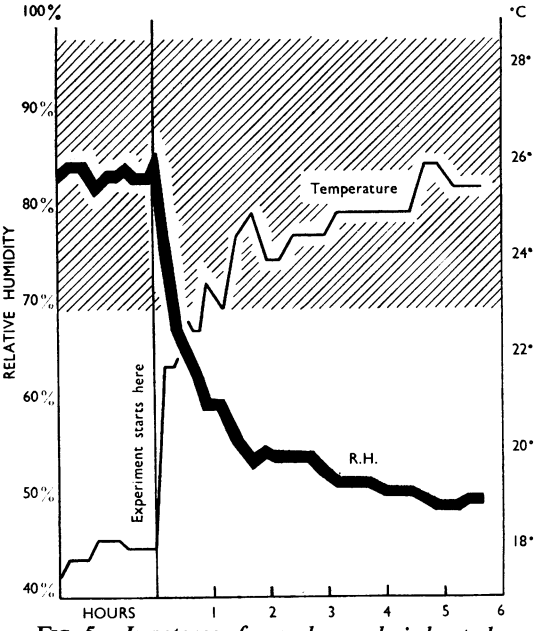

FIG. 5.—*Impotence of open door and window to keep the room moist after switching on a one-bar electric fire.* Thick line—relative humidity. Thin line—temperature. The relative humidity drops rapidly below the natural (shaded) level.

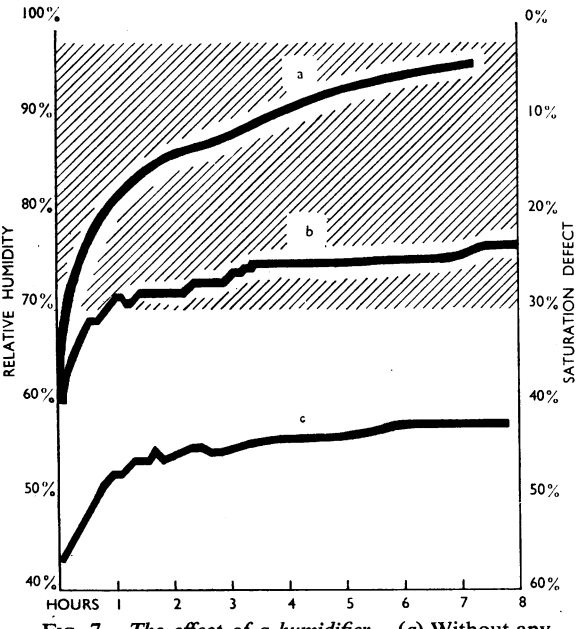

FIG. 7.—*The effect of a humidifier.* (*a*) Without any artificial heat (room temperature 20° C.). (*b*) With a single-bar electric fire (room temperature 25° C.). (*c*) With a double-bar electric fire (room temperature 30° C.). Shaded area represents "natural" relative humidity.

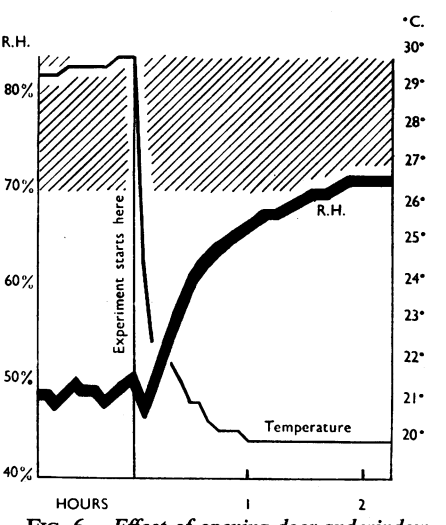

FIG. 6.—*Effect of opening door and window in a dry hot room without a source of artificial heat.* Thick line—relative humidity. Thin line—temperature. The humidity rapidly rises to a natural level (shaded area).

The bronchial tree is lined with ciliated epithelium continuously in action wafting a stream of mucus in spiral fashion towards the mouth. Upon this mucus stream fall all the particles of dust, the airborne bacteria, and viruses. They are washed upwards until they reach the mouth and are swallowed. Dry air can so thicken the mucus that it impedes the action of the underlying cilia. Over long periods of time this might lead to areas of irritation and damage to the underlying cells and certainly would impair the cleansing mechanism of the respiratory tract. Bacteria and viruses might find themselves in regions unaccustomed to their presence, locally non-immune, so that they might set up temporary inflammatory processes. Osmotic changes in the cells might also lead to trouble.

Opening the windows of the room does not put all this right. When the room is moist and cool to a degree equivalent to the outside air and the electric fire is switched on, the atmosphere rapidly becomes warm and dry and in almost no time the humidity is far below the outdoor level (Fig. 5). Switch off the fire and open the door and window and the air soon becomes moist (Fig. 6). Even with a humidifier

continuously working it is difficult to bring the air into the region of natural humidity whilst an electric fire is switched on (Fig. 7).

Summary.—The common cold is a mode of illness that attacks with a frequency far outstripping that of any other disease. The incidence is so closely correlated with seasonal temperature that a drop of 1° F. is associated with an increase of 1% in morbidity. We found that the drying and warming of the air by the artificial heating in our houses provided a most suggestive association with the morbidity from colds.

It is difficult to design an experiment to settle the importance of this factor, but we were fortunate enough to obtain a record which contributes to the subject. A cheese factory in Wales was recently provided with a room kept at a temperature of about 57° F. and a humidity of 80%. It was feared that the workers in this room might suffer from the high humidity and cold atmosphere. In fact over a period of twelve months their morbidity rate was less than half that of the other workers in the factory.

Dr. A. T. Roden (London):

Clinical Assessment of the Common Cold

While engaged in a study of the records of the Common Cold Research Unit at Harvard Hospital, Salisbury, I became interested in the question—What criteria does the clinical observer use in making his assessments?—and as a corollary to that—How consistently does he apply them?

The volunteers who come to this Unit live, usually in pairs, in isolation accommodation. Clinical observations are recorded daily. For my present purpose I have abstracted from the records the following signs and symptoms—nasal discharge, nasal obstruction, sore throat, cough and pyrexia.

Table I shows such an abstract from the record of an individual volunteer. The days

TABLE I.—MILD COLD

	Days 1	2	3	4 ↓ 5	6	7	8	9
Clear discharge ..					+	+	±	±
Purulent discharge						+	±	
Extra handkerchiefs					9	30	15	1
Nasal obstruction						±	±	
Sore throat ..				±	±			
Cough								
Fever								

TABLE II.—MODERATE COLD

	Days 1	2	3	4 ↓ 5	6	7	8	9
Clear discharge ..			±		+	+	+	+
Purulent discharge					+	+	+	+
Extra handkerchiefs	1	1		1	8	11	7	6
Nasal obstruction						+		±
Sore throat ..					+			
Cough								±
Fever						±		

begin and end at noon. The first four days were a preliminary period of observation during which the volunteer was free from symptoms. At the end of the fourth day infective material—from the nasal secretions of a person suffering from a common cold—was administered by intranasal instillation. Within twenty-four hours—or to be more precise about eighteen hours—after administration the volunteer felt a slight soreness of the throat. The next day there was an increase of nasal discharge, at first clear but, by the following day, muco-purulent. At the height of the nasal discharge there was slight nasal obstruction. No cough. No pyrexia. The assessment—mild cold.

Here is an example of a minor respiratory illness of which the predominant clinical manifestation is an increase of nasal exudate. Now, in my reading of the medical literature, I have yet to come across any adequate description of the quantity of the nasal discharges either in health or in disease. I may not have carried my reading far enough. But if I am right this is a very surprising omission. Because a rough quantitative estimate can be based on quite simple observations and would, presumably, have been made by many clinicians if it were thought to have a diagnostic value.

The extra handkerchiefs used were of paper. They are called "extra" because each volunteer is allowed one as a normal daily ration. The symbol + against nasal discharge indicates that the quantity on the handkerchief was such that it could not be used again without unpleasantness. The symbol ± indicates a perceptible quantity but such that the handkerchief could have been used again.

Table II shows another individual record. Again there is the same preliminary period of observation during which there was a little insignificant nasal discharge. On the second day after administration of infective material—coryza and sore throat. At the height of the coryza, transient slight pyrexia—in this instance about 99·6° F. Later some slight cough. The assessment—moderate cold.

The assessment is interesting. The degree of coryza just exceeds the minimum amount

in category 4 of our arbitrary scale (*see* below) with 8 extra handkerchiefs on one day and 11 on the next. In Table I the volunteer with the mild cold used 9 extra handkerchiefs on one day and 30 on the next. So the severity of the cold has been judged not by the degree of coryza alone but by the combination with other symptoms and by the general misery of the patient.

The following is a summary of observations on a total of 407 volunteers, of whom 198 were given positive control material—that is material from persons suffering from a cold and, therefore, presumably infective—and 209 were given negative control material—that is some inert fluid. I have not brought into this summary any volunteers given culture materials under test for the presence of virus.

All the assessments were made by one clinical observer and all his observations on positive and negative control groups have been included. The volunteers were allocated at random to their groups and neither they nor the observer were aware of the nature of the material used until the assessments had been recorded. This is a normal experimental precaution against bias.

In Tables III to VI the degree of coryza—using coryza as a synonym for increased nasal discharge—is represented on the following arbitrary scale:

0 = None or ± only.
1 = + on one day only.
2 = + on two days or more.
3 = + with at least 8 extra handkerchiefs on one day only.
4 = + with at least 8 extra handkerchiefs on two days or more.

Table III shows the correlation between the degree of coryza on the arbitrary scale and

TABLE III.—CORRELATION OF CORYZA WITH OTHER SYMPTOMS

		Other symptoms		
		− or ±	+	%+
Degree of coryza	0	263	17	6·1
	1	26	4	13·3
	2	25	20	44·4
	3	3	9	75·0
	4	3	37	92·5
	Total	320	87	21·4

the presence of one or more of the other symptoms and signs which I have mentioned. This correlation may be taken as evidence that both the coryza and the other symptoms have a common causation.

The figures from the second and third columns of Table III are set out thus: 263 in the category 0−, 17 in the category 0+ and so on, in relation to the clinical assessments.

Table IV shows our ten categories and the assessments—no cold (−), doubtful cold (±),

TABLE IV.—RELATION OF ASSESSMENTS TO SYMPTOMS

		Assessments					
		−	±	m	M	S	Total
Degrees of symptoms	0−	254	9	—	—	—	263
	0+	11	5	1	—	—	17
	1−	20	5	1	—	—	26
	1+	1	3	—	—	—	4
	2−	8	10	7	—	—	25
	2+	—	7	9	4	—	20
	3−	—	—	3	—	—	3
	3+	—	—	6	3	—	9
	4−	—	—	3	—	—	3
	4+	—	—	13	19	5	37
	Total	294	39	43	26	5	407

mild (m), moderate (M) or severe (S) cold. It will be observed that in categories 0 and 1 only 2 out of a large number reach an assessment of mild cold. In categories 3 and 4 all are assessed as colds. Between, in category 2, there lies an ambiguous zone. In each category it will be seen that the presence of other symptoms influences the assessment.

Tables V and VI show the degree of coryza and the assessments in relation to the experimental procedure.

TABLE V.—NEGATIVE CONTROLS

		Assessments			No. of cases
		−	±	+	
Degree of coryza	0	176	7	—	183
	1	10	2	—	12
	2	5	8	1	14
	3	—	—	—	—
	4	—	—	—	—
	Total	191	17	1	209

TABLE VI.—POSITIVE CONTROLS

		Assessments			No. of cases
		−	±	+	
Degree of coryza	0	89	7	1	97
	1	11	6	1	18
	2	3	9	19	31
	3	—	—	12	12
	4	—	—	40	40
	Total	103	22	73	198

Table V—the negative control group—shows that in no instance did the degree of coryza rise above the ambiguous zone. One volunteer out of 209 managed to achieve assessment as a mild cold.

Table VI—the positive control group—shows the degree of coryza observed and the assessments made of definite colds in 73 out of 198 volunteers.

I have used these data to illustrate two aspects of the rationale of clinical judgments.

First by an examination of the primary observations to ascertain the degree of consistency of the assessments.

Second to test the validity of the clinical concept against some factor—in this instance the nature of the experimental procedure—which is independent of the clinician's judgment.

Dr. J. Morrison Ritchie (Birkenhead):

In 1930, when the Birkenhead Municipal Laboratory was opened, a female clerk of the M.O.H. Department who had been a martyr to colds for years was very persistent in demanding treatment. On the understanding that she would have an injection once a week during the following winter no matter what happened, I made her an autogenous vaccine from her sputum.

She went through the winter without a cold, the first time for years. At the end of the following summer (1931) she and several others asked for a vaccine. They all had a winter without colds, although some had the prodromal stages. We then had, for years, a procession of corporation staff, much against my will, but it soon seemed that our only failures were where actual damage had occurred to mucous membrane. The theory was evolved that the function of the virus might be essentially to depress resistance, so giving the normal (though heterogeneous) nasopharyngeal flora a more or less free hand—in other words, the virus is a kind of starting handle.

When the Birkenhead Laboratory was taken over by the Public Health Laboratory Service, permission was obtained from Professor Wilson for a controlled experiment, and a series on approximately 200 volunteers was carried out during the winter of 1955–6, in conjunction with the factory at Port Sunlight. Of these, allowing for wastage, 109 were given autogenous vaccines prepared from their saliva, while 75 got saline injections only. Apart from prodromal stages, i.e. a clear running nose for a couple of days (presumed to be the virus activity which was relatively unaffected), the percentage of full colds was six times as high in the controls as among the vaccinees who were able to carry on throughout the winter. I gave the vaccines, while assessment was carried out by Port Sunlight's staff, who did not know who were controls.

This was very encouraging, but naturally autogenous vaccines on a large scale are not practicable, so the idea was tried of tackling the problem from the opposite angle, i.e. instead of boosting the patient's resistance, to depress the activity of the bacteria at the appropriate time. Without going into details, the proposal was to do a series of sensitivity tests on the saliva of volunteers and card the results, this being done before the cold season began. Then, when each reported the beginning of a cold, the works Medical Centre

would issue the appropriate antibiotic tablets. In short, the idea now was to balance the depression of the patient's resistance by a corresponding temporary depression in the activity of the bacteria. The minimal dose of four tablets spread over two days was used to avoid interference with the patient's normal flora or the production of insensitive organisms.

For this later investigation, altogether just over 1,000 volunteers were available, in half a dozen works, a large office staff, and a school, all assessment being done by the Medical Centres concerned. Inert tablets were used as controls. The Birkenhead Police also co-operated, using the Laboratory as Medical Centre, and they became a day-to-day check on the investigation, without controls, being for this reason excluded from the investigation itself. This check was very useful, as it was found that in a few cases four tablets gave a rather short course and five or six would abort the condition. Once more the clear running stage for twenty-four to forty-eight hours was regarded as prodromal, due to the virus, but it was strange how many people used the phrase "turned off like a tap" after that period.

There were 22/581 colds among those receiving antibiotic tablets on the first day, as against 87/338 among those receiving inert control tablets—3·8% as against 25·7%, a drop to one-seventh. In the adult industrial population, the proportion was one to nine, and this drop was evident in all the units of the investigation.

Application of the Findings

(1) *In industry.*—Where a works has a Medical Centre, the antibiotic method is simple and consists of: (*a*) Preliminary sensitivity tests by a laboratory, results being carded and filed in the Medical Centre. (*b*) Substitution of the appropriate antibiotic tablets for whatever palliative has been used in the individual works concerned. (*c*) Taking care not to overdo the antibiotic, and that the approval of the patient's own doctor is obtained.

(2) *In practice.*—A. The antibiotic method is less easy to carry out because:

(*a*) Patients are not likely to report at a surgery on the first day, and, while the antibiotics will work even if given later, the whole idea is to forestall the attack by the patient's flora, and where that has begun the treatment is naturally at a disadvantage.

(*b*) Antibiotics should not be issued casually, nor should they be freely available to all and sundry.

An interesting point is that a number of practitioners have been treating some early influenzas with systemic antibiotics on purely empirical grounds, and some have expressed the opinion that complications have been markedly fewer. Initially severe cases have recovered more rapidly, albeit toxic, with this treatment than less severe cases which have trailed on with malaise and complications where antibiotics have not been used. This has been on purely experimental lines, but, if one assumes that the theory of the starting handle may apply to influenza also, fits into the picture.

B. Autogenous vaccines, however, if properly made, could be used a great deal more than they are. It must be emphasized that none but autogenous vaccines are likely to be of service, as the nasopharyngeal organisms of the general population are very heterogeneous. With the simple technique we used, these are easily made in the laboratory. The weekly dosage—0·1, 0·3, 0·5, 0·5 ml., &c., of a 500 million per ml. suspension—is a nuisance, but the real chronic cold sufferer will put up with anything that he hopes will help, and these are the cases which show most benefit. Several of our volunteers, after having two winters' injections, have been persuaded to try going the next winter without injections and have remained free, suggesting a build-up of immunity.

Disadvantages

(1) *Autogenous vaccines.*—I know of no drawbacks apart from the tedium of weekly injections. A slight redness at site of inoculation was seen in some cases, but gave no trouble and subsided readily without treatment.

(2) *Antibiotic tablets.*—The only trouble was the incidence of "strawberry" tongue. This seems to be a form of idiosyncrasy as most volunteers were unaffected. It might persist for some time, although the cold itself had cleared up in forty-eight hours or less. The makers of the tablets say that the cause is not yet clear. An interesting point is that the school in our series had no trouble of this kind, which suggested a balanced vitamin diet, though the manufacturers have found no connexion with vitamins but favour the glucose angle. The condition was usually mild, having little more than nuisance value except in a very few cases. Possibly reduction in dosage to less than the 15 mg. per tablet might be the answer. When this difficulty has been eliminated the way may be clear to the control of the common cold in industrial establishments.

See also Ritchie, J. M. (1958) *Lancet*, i, 615, 618.