# CHAPTER IX.

## THE PROPHYLAXIS OF INFLUENZA.

Some derision has been excited amongst the laity by the prescription of rules for avoiding infection, which none but a small minority of the population can obey. The derision, although natural, is illogical, and serious mistakes in the history of preventive medicine can be attributed to the desire of physicians to provide not only a panacea, but a panacea which will be agreeable to or within the reach of the general public. We may add that not only do practically unrealisable measures excite derision, but, in those measures which might be carried out, congruity with popular notions of medical fitness (as in the leading case of Naaman the Syrian) has always been a principal factor of acceptance. In our own generation the traditionary belief in a specific pill or potion is not extinct, but it has to struggle with a more recently engendered faith in the value of laboratory methods leading to the injection of some substance beneath the skin. Like most popular beliefs these are not unwarranted— such great triumphs as the bark treatment for malaria in the past or anti-typhoid inoculation in the present are sufficient examples—but there will be found reason to suppose that half knowledge has created difficulties in the way of a clear apprehension of the prerequisites of success.

From what has been said in this report it follows that to avoid crowds, to shield the mouth and nose when coughing or sneezing, not wantonly to thrust one's face into the face of one's interlocutor, are essentially rational and appropriate methods of reducing the risk to take influenza. It even appears probable that the one form of overcrowding which in some little measure *can* be controlled by the individual is the form most potent to spread the disease. In the present state of the nation to advise the avoidance of overcrowded tenements and lodgings is, indeed, a council of perfection; it is likewise a vain quest to seek for public conveyances not grossly overcrowded ; but it is quite easy not to frequent theatres, music halls, and picture houses; it is even possible to avoid bargain sales, political meetings, and assemblies. These forms of congestion belong to the extra-domestic group which, by a process of exclusion, we have discovered to be more influential than intra-domestic conditions admittedly hard to control now.

It follows that the derided advice to avoid crowds is neither so trivial nor so absurd as has been believed. In our opinion the public ought not to be deterred from following it either by

newspaper ridicule or by the thought that in any event they cannot escape some crowding when engaged in active pursuits.

Passing to the prophylactic measures more congruent with the popular sense of fitness, we have first to consider the claims of the traditional pharmacopia and of the products of synthetic chemistry which, attested by recommendations of some medical men, have been pressed on the attention of the public.

So far as prophylaxis is concerned, in no instance has even a *prima facte* case been made out on behalf of any drug. It is surely obvious that the fact that a group of individuals to whom some prophylactic has been exhibited did not contract a disease only merits consideration when it can be shown that an essentially similar sample, submitted to the same or similar conditions of risk, but not using the prophylactic, suffered from the disease. This elementary precaution has not been observed by the bulk of adherents of specific prophylactics ; certain exceptions will be noticed below. We do not think there is any doubt that the oral administration of drugs is quite ineffective in warding off attacks of influenza.

Passing to the second approved method of defence, by means of vaccination, the following are the chief points to be had in mind.

When the *materies morbi* has been isolated, and the existence of immunising responses to inoculation with such *materies* or some derivative thereof has been observed under laboratory conditions, the antecedent probability that a method of inoculation will be useful is great. All that remains is to determine whether the extent of practical advantage conferred exceeds any risk or inconvenience attending the application of the process. The second part of the inquiry demands time and care ; the essential point is to be sure that trials on the practical scale are made *in pari materia*, inoculated differing from uninoculated solely in the matter of inoculation, or, when this is impossible, as it nearly always is, to make quantitive allowance for the disturbing influences present. The history of anti-typhoid inoculation illustrates all phases of the investigation, from the isolation of the specific microbe, through the experimental stage, up to the field inquiry. It was possible before the outbreak of the war to claim a high degree of probability in favour of the view that anti-typhoid inoculation was a prophylactic measure of the highest importance, and nothing which has since occurred casts doubt upon the validity of the arguments then used or the expediency and efficiency of the administrative actions to which they gave rise.

When the *materies morbi* is unknown in the sense that it cannot either be physically identified or cultivated *in vitro* it is evident that a truly specific " vaccine" cannot be prepared, although it may happen that a method of vaccinal prophylaxis is practically useful. This proved true in connection

with the disease known as swine fever here and hog cholera in America, the essential organism of which is ultra microscopic and incapable of cultivation *in vitro.*

The inoculation of blood from infected animals coincident!y with that of the serum of treated or recovered animals was found empirically to confer a large measure of immunity against the natural disease. In such a case the antecedent probability of success is slighter than when the vaccine is derived from a well authenticated *causa essentialis,* but, provided the field testing be carried out under the necessary conditions of stringency, the final practical result may be of equal importance. In the matter of influenza, not only do we start without the antecedent probability assured by the isolation of the essential microbe, but field testing has to be carried out under conditions of exceptional difficulty.

The bacteriological position of the subject is explored in another chapter ; here all that we need to remark is that the materials used in the preparation of vaccines consist of organisms admitted by most to be important sources of damage in the assault of influenza, and by some to be the only serious assailants. But those who admit these arguments recognise that the biological properties of the different organisms may vary from strain to strain, and some skilful bacteriologists even doubt whether the reduction of individual strains to a relatively small number of differentiated types, as has been possible for meningococci and pneumococci, is practicable. Hence there is no great *a priori* probability that if the inoculated subject do in the course of his exposure to infection encounter the micro-organism which has furnished the vaccine, such micro-organism will be of a type having immunological affinity to the source of the prophylactic.

Finally, the total failure in some instances and the partial failure in all instances of a natural attack of the disease called influenza to confer immunity against exposure to a second wave of epidemiologically similar disease is not encouraging to those who are at best imitating, *longo intervallo,* the processes of nature.

These various considerations combined to diminish any hopes of a dramatic success in the use of anti-influenza vaccines such as crowned the anti-typhoid inoculation campaign, and the consequent pessimism has been justified. The Ministry of Health assisted those willing to employ prophylactic inoculations and collected statistics which, however, have so far been scanty and unreliable. It is natural enough that during the very strenuous time of the epidemics, the pressure due to the epidemic itself being superadded to the general dislocation of war time, the statistical data provided should lack exactitude; in any event the returns were so incomplete, evidence of true comparability*

* No inferences can be drawn from a lower attack rate upon inoculated than upon uninoculated persons if the inoculations were carried out during the epidemic, without due allowance for variations of length of exposure.

in the • few instances in which a large measure of protection seemed to have been conferred upon the inoculated, so slight and untrustworthy, that we are unable to say that the arguments in favour of prophylactic inoculation as a general measure have been at all strengthened by our experience of the 1918-19 pandemic. Such evidence as we have in favour of any practical advantage points to the efficacy of vaccines derived from organisms cultivated from cases existing in the neighbourhood of the tested population. This is illustrated by the example quoted in the section of influenza in the annual report of the Chief Medical Officer. A pure Pfeiffer vaccine was used for the inoculation of employees (volunteers) in a London business house, and the inoculated escaped the disease, while their co-workers experienced a normal incidence. It appears doubtful whether any simple stock vaccine derived from a limited number of strains of micro-organisms implicated in the clinical evolution of influenza is likely to be of value. Whether vaccines derived from the special strains isolated in each community are more beneficial; if so, what geographical and population groupings might be the best units for vaccinal purposes, are questions which we cannot yet answer. It may even be that the specificity of strains is carried in nature to so fine a point that no local sub-division upon a scale practically possible would be of service. This is a problem of the future ; here we can but record the conclusion that vaccinal prophylaxis is not yet a reliable shield.*

It thus appears that neither of the methods which would fit *priori* commend themselves to the public, that of exhibiting specific drugs or that of inoculating specific vaccines is a measure which in the event of a recrudescence of the disease can be relied upon. Yet we must draw a distinction between the two in so far as the use of potent drugs, especially perhaps alcohol, may quite conceivably do serious harm while the inoculation of a vaccine, provided the operation be performed under conditions of surgical cleanliness and the source of the material above suspicion, can do no harm and may do great good.

We now come to simpler measures of prophylaxis which, chiefly on that account, need stronger credentials before they are likely to commend themselves to the public. The most important is nasal disinfection. The usual source of infection being the naso-pharynx and the toxic influence upon life of gaseous fumes painfully familiar, it was to be expected that nasal disinfection by gas would have supporters. The matter was put upon a scientific foundation by Dr. Benjamin Moore. F.R.S.. who, in conjunction with Dr. A. Gregor, carried out a number of observations upon the sterilising action of nitrogen peroxide or sulphur dioxide in high dilutions (1 in

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* *See also* pp. 64 and 195.

30,000 volumes). These observers obtained *(a)* a partial disinfection of the naso-pharynx commencing one or two hours after exposure and lasting for 8-12 hours ; (6) they believed the hydrogen-ion concentration of the nasal secretion increased, the secretion becoming acid to litmus and remaining so for some hours. When the fumes included nitrogen peroxide, starch and potassium iodide rapidly turned blue in an atmosphere which could be borne without discomfort, while, a few hours later, the nasal and bronchial secretions became orange yellow from the xantho-protein reaction with mucin.

These experimental results were a motive for epidemiological comparison of the incidence of influenza upon workers exposed to nitrous or sulphuric fumes with that on normal controls, and in a few instances there appeared to be a very much smaller incidence upon the workers exposed to gas than amongst controls. The importance of the matter led to a series of special investigations by officers of the Ministry and extensive statistics were collected at Widnes, in the Swansea Valley, and in a Metropolitan gas works. A precis of the results was included in the report of the Chief Medical Officer and the complete protocolls are appended to this report. From these it appears that the prophylactic value of such exposures as occur in the normal course of industrial life is inappreciable. These negative conclusions throw no suspicion upon the cogency of the original" experiments since there is no reason to doubt that the concentration of the fumes was often, perhaps always, less than in the conditions of those experiments, but they perhaps make it doubtful whether any method of fume disinfection suitable for wide employment is likely to be a success* ; the essential point of the experiments, viz., an attempt to heighten local resistance in the nasal-pharynx raises wider issues.

Dr. Leonard Hill, F.R.S., has recently published an important study of the relation between the condition of the nasal mucous membrane and susceptibility to eoryza. †

Dr. Hill first drew attention to the long noted relative immunity from colds of persons living under open air conditions. Dr. Hill argued that for the realisation of infection, not only must a *materies morbi* be present, but also the naso-pharyngeal tissues must in some way be rendered sensitive. He writes : " F. F. Muecke and I examined the appearance of " the nasal mucous membrane when the subject is exposed " first to outdoor conditions, and secondly, to those conditions " of heating and ventilation which are not uncommon in rooms. " Out of doors the wind moves at a much greater velocity at " head than at foot levels, owing to friction of the moving air " against the ground ; the ground, too, is warmed by the sun.

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* *See also* Parsons II., p. 58.

† The Science of Ventilation and Open Air Treatment, Pt. I., pp. 141, *et seq.* (London, 1919, published by the Medical Research Committee.)

" As a rule then, excepting such unpleasant conditions as " pertain to thawing snow, the head is cooled out of doors at a " greater rate than the feet. Cool breezes blowing round the " head, the radiant heat of the sun, and a warm ground to " stand on, are the ideal outdoor conditions. The healthy " mucous membrane of the nose, examined by aid of a " speculum, under these conditions appeared pale and taut. " If touched with a probe, it did not pit, and there is no thick " secretion upon it. Indoors in these conditions which are " unfortunately only too common, when the feet are chilled by " draught blowing over a cold floor, and the head immersed in " warm stagnant air, the nasal membrane appeared in those " examined swollen, congested, and covered with thick secre- " tion. A probe pushed into the swollen membrane formed a ' pit, showing how boggy it was, and the airway was so " diminished that I, with a deflected septum, could not breathe " through the affected nostril. Warming the feet at a fire at " once relieved the congestion and did away with the obstruc- " tion, so that the airway became free. It is the congestion " and swelling of the nasal membrane, and no doubt that of " the air sinuses opening into the nose, which largely causes " the feelings of stuffiness in the head and headache felt in crowded, overheated, places of assembly. This headache is " generally, but erroneously, attributed to the absorption of " chemical poisons supposed to be present in the stuffy " air. . . . Suppose the nasal membrane has become " swollen, congested, and covered with thick secretion in these " bad conditions, and the subjects go outside again into the " cold air, then the membrane at once becomes pale, owing to " vaso-constriction, but for some little time it remains swollen " and boggy, pitting on the touch of the probe. I believe that " these conditions of the nasal membrane have a great deal to " do with catching colds. In crowded rooms infection takes " place from mucous spray, sneezed, coughed, or spluttered out " in speaking. The inhaled bacteria will be caught by the " swollen mucous membrane covered with thick secretion. In " those who live out of doors not only is the membrane kept " taut, but the flow of arterial blood through it is rapid, for the " inhaled air has to be warmed up and moisture rapidly " evaporated from the membrane so as to saturate this air at " body temperature. Thus more lymph comes out into the " membrane from the blood vessels, and this contains pro- " tective substances. Offensive bacteria are either washed " away or destroyed, and thus kept out. On the other hand, a " membrane covered with thick secretion, and congested, offers " a medium more suitable for the bacteria to settle and grow " on, for it is boggy and stagnant, not flooded with fresh " lymph, particularly when vaso-constriction takes place on " passing from an over-hot moist atmosphere into the wintry " outside air. The ciliated cells, white corpuscles, and lymph

" may be chilled and the velocity of vital reaction reduced " when the blood vessels constrict. Colds may not always be " a question of re-infection, but of lowered resistance to the " strains of pneumococci or streptococci which people happen " to carry in their noses. Stagnant conditions of the nose and " its sinuses may exalt the virulence of organisms and so " spread infections. Epidemics may thus be started by " carriers whose humoral conditions are altered by unhealthy " enviroment. It is recognised that measles and influenza " lower the resistance to other organisms, *e.g.,* pneamococci, " tubercle bacillus; mustard gas likewise lowers the resistance " to infection, why not then the conditions set up by the " change from heated to cold atmosphere. The washing away " of bacteria by the outflow of secretion must be one of the ' most important methods of defence. T. H. C. Benians " suggests that mucin is probably the first line of anti-bacterial " defence in the nose and throat, as throughout the rest of the " alimentary canal. In most acute influenzal throat infections, " as well as other acute septic throats, the mucosa appears red, " dry, and with an absence of visible mucin. Many such " throats when tested are strongly acid to litmus. The natural " reaction is alkaline. As acidity is against the growth of " catarrhal organisms, these must escape the acid reaction " of the surface by invading the membrane. In the running " stage of a cold the secretion is often found to be sterile."

Recently Wahl, White, and Lyall* report that influenza bacilli experimentally implanted in the nares disappear in 24-72 hours, but when implanted on the throat persist and multiply for weeks. The original observations of Hill and Muecke on the changes in the nasal mucous membrane have been confirmed by Cook and Winslow, and it will appear that the general aetiological theory of Hill is in accord with the epidemiological results we have described and reconciles some anomalies of everyday experience. Thus the evidence as to the relative incidence of influenza upon indoor and out of door workers has been conflicting ; it has not been found uniformly that the outdoor workers were less affected ; omnibus conductors have been said to suffer greatly from the disease. The explanation is that the *conditions* of exposure are of paramount importance, everything depending upon the manner in which the local tissue reacts.

If a stagnant condition of the mucous membrane concomitant with a slow rate of local circulation and imperfect secretion of lymph be generated by temporary exposure to unfavourable conditions (such as arise in the course of transport workers' duty) intermittent exposure to cold may actually further reduce the local resisting power. In the end we reach the conclusion that it is not the presence in the nostrils of any specific chemical, but the realisation of the physiologically most favourable conditions, whether as a result of

* *Joum. of Infect. Diseases,* XXV., 1919, p. 419.

specific medication or otherwise, which is the true method of prophylaxis. Thus we might explain the success said to have been met with through the use of various snuffs in warding off infection. It was no specific property of the snuffs but the stimulation of the local secretion and the circulatory conditions favouring the secretion which was responsible for favourable results. Were the snuff not to produce this reaction its presence in the nasal cavity would be unavailing. It might be asked whether there is any evidence that inveterate snuff takers are less sensitive to nasal infection than others, but a moment's reflection shows that no information of value could be obtained in such a way. Persons who are addicted to this old fashioned method of using tobacco, resort to it with such frequency that it is probable that direct mechanical obstruction of the nasal passages might counterbalance any advantage which should in theory result.

The apparently great danger of spreading influenza by extra domestic crowding might be inferred from Hill's theory, since the crowded railway carriage with its humid warm atmosphere and draughty floor is precisely the condition needed to reduce the defensive power of the nasal mucous membrane to its minimum. The practical inference deducible from the results described is that attention to the hygiene of the nose may be a most useful prophylactic. Douching of the nose morning and night with a faintly antiseptic solution and occasional resort either to smelling bottle (which Dr. Hill suggests might contain sodium bisulphite) or snuff box (which may contain any of the high dried tobacco snuffs, or, if preferred, the menthol snuff sold by most chemists) are recommendable measures. The snuff or smelling bottle should be used when the subject finds that he or she cannot inspire or expire through the nose with customary ease. As remarked, the formation of a snuff habit, like that of the traditional antiquary or Scotch grandfather, would defeat the end in view, viz., to use the stimulant only when needed by the mucous membrane. We are naturally led by these considerations to the question of masks as prophylactics. From the point of view of the general population it would seem that the cogency of the arguments just recited is decisive against masks. The probability of rendering a mask, habitually and frequently worn in everyday life, a trustworthy bacterial filter is very small, of its causing sufficient obstruction to nasal respiration to disturb the physiological harmony desired, very great. None of the sensational statements in the Press that epidemics of influenza abroad have been controlled by the compulsory wearing of masks in public have been found trustworthy. In our opinion the general wearing of masks is neither expedient nor scientifically defensible.

On the other hand, when the question is of affording extra protection to the attendants upon the sick in hospital wards, the objections just adduced lose validity. It even appears desirable that such precautions be taken, since the ritual would

be intelligently carried out and its existence inculcate upon the subordinate staff a sound belief that influenza in hospital is a dangerous infective disease.

We have now reviewed the principal measures of prophylaxis which have been advocated and tested, and it seems that the simple non-mystical methods which come within the scope of personal hygiene are those which both epidemiological and physiological research sanction. It is permissible to hope that further study of the micro-biological problems presented by epidemic influenza will enable us to establish vaccine prophylaxis upon a securer foundation than it yet possesses ; the efforts of both the Ministry of Health and of the Medical Research Council are continuously directed to that end ; but the public should not suppose either that nothing of service can be attempted until the authentic *materies morbi* of influenza has been unequivocally defined or that the recognition and successful isolation of the authentic microbe would necessarily be followed by elimination of the influenza scourge. The history of all epidemic diseases is a witness to the truth that much may be done when the essential factor of a disease is undefined, and, *per contra,* that complete certainty as to biological aetiology is compatible with imperfect control of a disease. Brilliant as have been the improvements effected by the introduction of vaccinal prophylaxis for typhoid, the successes achieved by sanitarians in the 19th century, before the bacteriological era, were even greater. It is not true that without bacteriological certainty nothing important can be achieved in the direction of rational prophylaxis.