War Section.[1]

President—Surgeon Rear-Admiral Sir ROBERT HILL, K.C.M.G., C.B., C.V.O., R.N.

The Biology of Epidemic Influenza, illustrated by Naval Experience.[2]

By SHELDON F. DUDLEY, O.B.E., M.D., Surgeon-Commander, R.N.

WITHOUT going deeply into the question as to whether *Bacillus influenzæ* was the cause of 1918-19 pandemic, I will at once say my own experience points to Pfeiffer-like bacilli being the cause, or at any rate a very important factor in the ætiology of influenza outbreaks. During 1918, 1919, 1920 and this year I was able to demonstrate *Bacillus influenzæ* in practically all cases examined during the febrile period. The only cases in which I failed to do so were the spring cases of 1918, when I was using an unsatisfactory technique. Besides technical difficulties with culture media which are very real, as I know to my cost, there is another explanation which may possibly account for the reported absence of *Bacillus influenzæ* in certain of the epidemic cases. There are many contributory factors on which the magnitude of epidemics depends, in addition to a specific germ and a specific susceptibility of the population. It is reasonable to suppose these non-specific factors favour the dispersal of many other micro-organisms as well as the virus of influenza. Also, influenza is a disease that undoubtedly renders its victims more prone to invasion by other pathogenic bacteria that happen to be in the environment at the same time. It is quite possible that, in some cases, after a period of association with the influenza germ, some of these secondary organisms increase their infectivity and acquire the power of causing local outbreaks unassociated with the specific cause of the main pandemic. Thus small epidemics are produced within the main pandemic and are unlikely to be differentiated from it, especially when one considers the indefinite symptomatology of a disease like influenza, the diagnosis of which has often to be made by the process of excluding other diseases, together with the fact that influenza happens to be epidemic at the time. These reasons, and the fact that *Bacillus influenzæ* can often be cultivated from the discharges of patients in which bacilli are invisible in stained preparations, are sufficient to my mind to account for most cases of its reported absence. In those infections which possess a more definite symptomatology—as for example, gonorrhœa or meningitis—we do not deny to the gonococcus or meningococcus an ætiological significance in the many cases in which we fail to find them. But while I think *Bacillus influenzæ* is the

[1] At a meeting of the Section, held May 9, 1921.

[2] I have been requested by the London Hospital authorities to acknowledge that this paper is largely based on the essay which was awarded half the Liddle Prize, Professor J. MacIntosh taking the other half.

most likely cause of the late pandemic, I admit it is very far indeed from being the proved cause.

Though I may have demonstrated the constant association of *Bacillus influenzæ* with those epidemic cases that came under my own observation and explained, to my own satisfaction, its reported absence elsewhere, yet there is another fact that requires just as much elucidation—namely, the remarkable prevalence of influenza bacilli in the nasopharynges of healthy sailors. Since 1918 up to the present year I have swabbed at intervals batches of men who exhibited no signs of influenza, and as far as I knew had not recently been in contact with influenza patients. In all 266 men, chiefly venereal convalescents, with apparently normal throats were examined. The percentage of men in each batch harbouring influenza bacilli was roughly the same, about 50 per cent., and this figure showed no obvious relation to influenza prevalence, nor did a previous history of influenza seem to have much influence on the likelihood of a positive result in individual cases.

This tremendous prevalence of so-called influenza bacilli in apparently healthy men requires as much explanation as their reported absence in certain clinical cases. At first sight it would appear that *Bacillus influenzæ* cannot be the cause of the epidemic; because if it is present as a harmless saprophyte in the throats of half the population, its association with clinical influenza might well be incidental. But whatever the cause of influenza may be, in a pandemic of the size we have lately witnessed, the germ is certain to exist in a host of carriers as well as in the epidemic cases, and from this point of view, a high carrier-rate substantiates rather than weakens any claim *Bacillus influenzæ* has of being the specific cause of the pandemic. However, the fact remains that the majority of these carriers seem to be harmless, and this at first sight appears difficult of explanation.

Now let us consider what are the characters usually employed to identify the organism known as *Bacillus influenzæ*? They are its characteristic colonies on certain changed blood media, its absence of growth on ordinary agar, absence of, or feeble growth, on blood smeared agar and its Gram-negative and morphological characters. Suppose, for the sake of argument, we were dependent on two or three culture media only, and the morphology, for classification of the Gram-negative intestinal bacilli; under these restrictions we should only have two or three varieties, which would include the dozens of harmless and noxious species that we know exist. For this reason it is not unlikely that the organism called *Bacillus influenzæ* is not a single organism but a group. Variations in serological reactions and the morphology of different strains are evidence in support of this view. Though even these detectable variations may be considered hyperspecific, yet the changes in bacterial protoplasm correlated with variations in infectivity and virulence are in many cases still further beyond the reach of laboratory technique; and it is on these variations that epidemics depend for their magnitude and malignancy. All workers with vaccines know that while two organisms may be identical from the systematic botanist's standpoint, yet one may prove to have much better antigenic qualities than the other. Without pressing the subject further it may well be that the explanation of the considerable number of influenza bacillus carriers is, that only certain varieties of *Bacillus influenzæ* can cause symptoms of disease.

Before proceeding with some other attempts to solve the carrier problem it may be advisable to consider virulence and infectivity from the biological standpoint. Is virulence really a useful asset to a parasite? If a parasite

produces so much toxin and destruction of function as to immobilize or destroy its host it is limiting its own chance of dispersal or survival beyond that single host. Very sick men or corpses have little opportunity of spreading their parasites as compared with those people whose parasites do them no injury, and permit them for long periods of time to wander about among their fellows. Virulence, once the number of susceptible hosts has diminished to a certain point, must be a handicap in the struggle for existence, as the parasite possessing virulence shows an imperfect adaptation to its environment, which is the biological hallmark of a successful species. A non-sporing pathogenic bacterium that destroys its host commits suicide. The destruction of the human race by supervirulent microbes has often been predicted, but these are some of the reasons why this catastrophe has not occurred long ago and is unlikely to occur in the future. Pathogenic organisms are not the successes of the bacterial world—how many more *Bacilli coli communes* are alive to-day than typhoid bacilli?

Infectivity is an attribute that differs from virulence, for it is obvious the more infectious a parasite is, that is the greater the ease with which it establishes itself and breeds in fresh hosts, other factors remaining the same, the more it will succeed as a species. Therefore, once an epidemic is started the more infective strains will tend to be selected for survival. If this view is correct, the question at once arises as to why the whole population does not become infected? In the case of the influenza-like organisms I believe this does happen; seeing that, in my experience, at any instant of time during the last two years a sample of the population produced 50 per cent. of carriers, it is not improbable that if the whole population could have been repeatedly examined, nearly 100 per cent. would have been found at one time or another, for longer or shorter periods, to harbour influenza bacilli.

To understand this last point of view we must turn to the parasite's host, as infection depends on the degree of his susceptibility as much as on the infectivity and mass of the invading parasite. A man infected with an organism reacts against it, and after the usual struggle which may, or may not, be indicated by symptoms of disease, either the man or the organism is generally destroyed, but a third course is possible, and parasite and host may adapt themselves to each other and live in harmony, the result being a chronic carrier. When a man has destroyed or adapted himself to a parasite, certain changes take place that give him for a longer or shorter time various degrees of acquired immunity. In the non-virulent strains of an organism the reaction of the host will not be so intense, and hence non-virulent organisms have a better chance of complete adaptation or anyhow of surviving in their hosts for greater lengths of time. This theory, if correct, would account for the harmlessness of most carriers. However, virulent carriers do exist, and, perchance, the mutual adaptation that takes place in such cases is more on the part of the host. The infected individual learns to tolerate the exeretions and ferments of an organism still pathogenic to the general population.

The ease with which an epidemic can spread in a population depends, among other things, on the degree of infectivity of the specific germ and the density, that is the number per unit area, of people susceptible to that degree of infectivity. The epidemic weeds out these susceptible persons until a point is reached when their density is too small to permit further dispersal of the germ. The epidemic in that locality then dies out; meanwhile the wave of infection passes on, and the infectivity of the specific germ increases, until

later the same type of germ, but with an increased infectivity, is reintroduced to the localities that had been previously visited, and a second epidemic wave is formed. The victims of the second outbreak being mainly those who, while possessing sufficient resistance to withstand the infectivity of the early specific germs, could not resist the increased infectivity subsequently evolved.

The explanation of the number of harmless carriers of *Bacillus influenzæ* can now be summarized. An organism of the required infectivity having arisen, an epidemic begins, and spreads rapidly through a highly susceptible population, but as the susceptibility decreases the more infectious strains of parasite are selected for survival, and later the more virulent strains are eliminated by natural selection, until finally the organism succeeds in adapting itself to its environment by the evolution of highly infective but innocuous strains which produce a multitude of so-called "carriers" of the original pathogenic ancestors.

I also believe that the late cerebro-spinal meningitis outbreaks illustrated these principles. The disease itself, after a preliminary increase in virulence, undoubtedly became less virulent as time passed, and the drop in mortality from 80 per cent. to 30 per cent. is more than one can attribute to improved antisera. In a paper[1] on cerebro-spinal fever, Dr. Dorgan reported that the carrier rate in a certain garrison actually increased as the number of meningitis cases diminished. An apparent paradox, which is simply explained if it was the case that harmless strains of meningococci were succeeding in adapting themselves to their environment, as the virulent strains were being eliminated by natural selection.

It should be noted that at the commencement of epidemics there is often a preliminary rise of virulence, and it is probable, seeing how virulence often goes with great power of multiplication of parasites in the host's tissues, infectivity and virulence are characters that often increase together. The handicap of virulence is not felt so long as susceptible hosts are sufficiently numerous. Also, the increased mass of infection per individual in severe illnesses may counteract to some extent the immobility and partial isolation severe infections generally cause. The application of biological first principles may also throw some light on the origin of epidemics. Personally I think species of bacteria are much more flexible than most text-books would have us believe. I may have conveyed the idea that increase of infectivity takes place by means of the continuous selection of small variations in the same direction; but modern botanical teaching would suggest that sudden large steps, that is mutations in virulence and infectivity are just as likely, if not more likely, to occur. One objection to the survival of mutations of asexual bacteria is that if only one or two bacilli should acquire fresh characters their offspring would be swamped by the non-mutated bacilli. In nature, however, it is easy to imagine situations in which the mutation of a single bacterium could survive. For example, a cell in the respiratory tract is invaded by a bacillus which mutates while isolated in that cell. Later the owner of the cell sprays it, together with the mutated offspring of the bacillus which it contains, into the nasal passages of another individual. The latter is now infected with a "new disease," and may possibly become the first case of a world pandemic. Should the strain of bacillus arising as a mutation only differ from its non-mutated ancestors in the characters of virulence or

[1] *Lancet*, 1919, ii, p. 97.

infectivity, the "new disease" it causes will in other respects resemble the "old one" it arose from. In this way, perhaps, epidemic influenza may have arisen as a mutation of sporadic influenza.

In case these biological ideas seem out of place when applied to bacteriology, it is well to remember the latter science is only a small branch of botany. Again, a great part of a clinical bacteriologist's time is spent in isolating pathogenic organisms from the numerous harmless bacteria resembling them. Consider, for instance, these different groups—the streptococci, the Gram-negative diplococci, the intestinal bacilli, and the diphtheroids. If we have any faith in evolution we must allow that each of these groups probably had a common ancestor in the past, and from what is known of the mutation of higher plants, it may be that the origin of many species of bacteria is far more recent than is usually presumed.

There is no time to consider the claims of organisms other than *Bacillus influenzæ* to be the specific cause of the pandemic. The remarks already made apply equally well whatever the true germ of influenza may be, for it is almost certain a disease possessing the characters of epidemic influenza will be associated with many carriers. Here I use the term "carrier" in its most literal sense, and include all ambulant and missed cases, the latter consisting of many so-called colds, chills and catarrhs, as well as the man who, though being really ill, forces himself to go about his usual occupation. The number of almost trivial cases of the disease is an especial character of influenza, and doctors, I think, are prone to forget this. Personally, when the word influenza flashes into my field of consciousness, I first visualize purple patients spitting blood and streptococci; the thousands of people with no more than a degree or so of temperature and a headache, keep well away in the background, yet it was they who formed the vast majority of the epidemic cases which were not in most instances seen by the medical profession at all. In Switzerland it was estimated that only one-third of the epidemic cases were seen or notified by a medical man.

The cause of the great variation in individuals and also in groups of cases at different times or in different places is probably three-fold. First, variations of the primary organism; secondly, variable susceptibility of individuals; and, thirdly, and probably most important, different combinations of the bacterial flora causing the illness. This now brings us to the so-called secondary infections.

In times now passing it was customary to try to fix the blame for the different combinations of body changes that constitute a disease on a single organ; for example, pneumonia was a disease of the lungs. At the present time we often merely substitute for the single organ a single kind of bacteria, then pneumonia becomes a pneumococcal infection, when in many more instances than is generally recognized, pneumonia and other diseases are due to a combination of parasites rather than to any single species. The most familiar example of this is "consumption," in which the secondary invaders, when once established, do a greater amount of harm than the tubercle bacillus itself. So with influenza, whatever the primary parasite may be, it depresses the resistance of the patient so that any pathogenic organisms in the environment seem able to infect with increased virulence, the result being a complex disease in which the secondary invader may play the more important part. I will illustrate a compound infection by means of a rather uncommon case from my own experience. A man was admitted to H.M. Hospital Ship *Agadir* during the height of the epidemic; he was suffering

from the broncho-pneumonia prevalent at the time. His sputum contained *Bacillus influenzæ* and hæmolytic streptococci, while a blood culture revealed similar streptococci and typhoid bacilli. Here was a man with three definite infections, and possibly a fourth, if we consider his illness primarily due to the epidemic and refuse to admit *Bacillus influenzæ* is the specific cause.

Among the secondary infections the streptococci and pneumococci attracted most attention because of their association with the severe pulmonary cases; but secondary invaders were just as common in the uncomplicated cases, which are better designated as cases without definite pulmonary symptoms. Among these latter cases the commonest organisms in my experience found in association with influenza bacilli were Gram-negative diplococci and pneumococci. In the early spring cases of 1918 the predominant secondary organisms I found were Gram-negative diplococci, and similar organisms were common in a small outbreak this year (1921) at Portsmouth. In the former cases I failed to demonstrate *Bacillus influenzæ*, a fact I attribute to the use of an unsatisfactory culture medium—namely, blood smeared agar. In this year's cases *Bacillus influenzæ* was recovered from fifteen out of sixteen influenza patients, using Fildes pepsinized blood media.[1] These two groups of cases were clinically very similar, as I can vouch for personally, as I was in charge of their treatment as well as of the bacteriological examinations in both instances.

There is another point worthy of more emphasis than is generally attached to it. The pulmonary complications of influenza are usually present from the onset of the illness, this suggesting that the so-called secondary infections are not really secondary in time but are contracted simultaneously with the primary specific infection. Such observations introduce the interesting possibility that influenza is always a compound infection of *Bacillus influenzæ* plus some other organism, either moiety of the combination increasing the virulence of the other. Animal experiments have been published which indicate that admixture of *Bacillus influenzæ* with small and otherwise innocuous doses of other organisms greatly increase the former's virulence, and vice versa, small doses of *Bacillus influenzæ* increase the toxicity of other organisms.

The inhibition of the normal blood cellular response to those infections which are usually accompanied by a leucocytosis may be part of the mechanism by which the influenza virus lowers the resistance of its victims to other parasites. In normal times it is rare to get white blood counts of under 10,000 per cubic millimetre in lung conditions due to the pneumococcus or streptococcus. Yet among thirty-seven pulmonary influenza patients, whose leucocytes were counted, only eight had more than 10,000 per cubic millimetre and in no less than fifteen of these patients there was a leucopenia (white count less than 5,000 per cubic millimetre). It is the absence however of a leucocytosis in so many cases with inflamed lungs rather than any marked leucopenia, which is the striking feature of these leucocyte counts. Thus it may be that *Bacillus influenzæ* is unable to become pathogenic without assistance from other micro-organisms. The influenza virus, by lowering the resistance of the patient, permits other parasites to invade the tissues, and perhaps, in return for this service the secondary invaders provide some product essential to the influenza germ. *In vitro*, influenza bacilli sometimes form compound colonies on culture media and they are said to grow in association with staphylococci on media they are unable to survive on alone. The compound

[1] *Brit. Journ. Experi. Path.*, 1921, ii, p. 16.

nature of the infection in most cases of influenza explains the pleomorphism of the disease among both individuals and batches of patients. For example, so marked is the difference in the symptoms of pulmonary cases infected with pneumococci or streptococci that one could nearly always guess the infection before any bacteriological examination had been made. At Scapa Flow the pneumococcus was the predominant cause of inflamed lungs at the time streptococcus was working its ravages in the South of England, though hæmolytic streptococci became more prevalent at Scapa as the autumn to winter epidemic proceeded. Biologists are yearly adding more and more facts bearing on the widespread importance and significance of mutualism and symbiosis in organic nature, and there are undoubtedly mutual relations between the parasites of man and man himself, of which we have not as yet more than the haziest indication.

I now propose to refer to a few ships of the Royal Navy and see how far the epidemic as it affected them bears out the principles I have just enunciated. In the Grand Fleet just over 10,000 men were reported sick in the spring wave of the epidemic while in the autumn only about 5,000 were attacked by influenza. At first sight this looks like a lowering of the infectivity of the germ but I hope to show the lesser incidence in the autumn was chiefly due to an increased resistance of the personnel of the fleet combined with improved quarantine regulations. The case-mortality in the two waves was respectively 0·03 per cent. and 2·8 per cent. which is nearly a hundredfold increase of killing power; yet though I may be accused of straining a fact to fit a theory, I believe this increase was more likely to be due to prevailing secondary infections than to any increase of virulence in the primary specific cause of influenza.

Turning to an individual ship I will first take H.M.S. *Revenge*. This ship suffered from two definite outbreaks and her experience is a model of what happened in many other ships. In her the first wave lasted about twenty days, 207 men—17 per cent. of the ship's complement—were officially reported as sick. The autumn wave lasted about the same time, 20 per cent. of the ship's company being returned sick. This makes a total official attack-rate for the two outbreaks of 37 per cent. Surgeon-Commander Burniston, the senior medical officer of the *Revenge* (whom I must thank for giving me this information) states in his official report that quite half as many again were ill without going off duty, so the official attack-rate is much below the real attack-rate and 50 per cent. is much nearer the real number attacked in the combined outbreaks.

I will now take two examples from ships that escaped the first wave of the epidemic. First H.M.S. *Newcastle:* Surgeon-Commander Page published an account of this outbreak from which I have taken these notes. During the first fortnight of October, 1918, 51 per cent. of the ship's company of 450 men were attacked by an illness consisting of three or four days fever, headache and backache. Dr. Page writes: "There was a complete absence of any malignant symptoms or complications." All cases returned to duty within a few days. The examination of stained films of sputum were said to reveal "numerous Gram-negative bacilli resembling Pfeiffer's bacillus," also Gram-negative cocci were noted in some of the films. This outbreak started seven days out at sea and ran its course far from land in the South Atlantic. The extreme mildness, but high infectivity, of the illness is a point worthy of careful attention.

The second example of a ship to be infected in the autumn only is H.M.S.

*

Africa. Of her complement of 779 men, 75 per cent. were struck down with a serious illness. Surgeon-Commander Alderson who kindly let me abstract this information from his official journal, tells me that, as far as he had time to observe, many cases were pulmonary in type from the onset and their expectoration was blood-stained. Fifty-one men died, a 9 per cent. case-mortality or nearly 7 per cent. of the ship's complement. Some samples of sputa were sent ashore for examination, but apparently only stained films were made, and a "Gram-positive diplococcus" was reported to be the predominant organism seen. There was no mention of influenza-like bacilli, but this is no evidence of its absence if cultures on suitable media were not made at the time direct from the cases.

The above three ships are type examples and there were many ships of each type. The *Revenge* is the two-wave type generally seen in home waters. The *Newcastle* is the highly infective but very mild type, while H.M.S. *Africa* is the super-virulent and infective type of ship. The last two were commoner in foreign waters.

Roughly generalizing, it may be said that in the spring in an early wave of the epidemic the attack-rate was 25 per cent., with a further 25 per cent. when the wave of the epidemic returned in the autumn. These two attack-rates combined make 50 per cent. which, it is most important to notice, is the same as the attack-rate of the ships which escaped the early wave and only got attacked when there had been time for an increase of the specific organism's infectivity. The conclusions I draw from these morbidity-rates are that a ship's company, and possibly the population as a whole, consist of a quarter highly susceptible to influenza who succumb, leaving three-quarters unaffected; but when the parasite has gained sufficient infectivity in its travels and returns, it attacks a further but different quarter, the quarter originally attacked with few exceptions having gained sufficient immunity to resist a second attack even after the infectivity has increased. Half the population remains free from attack in both waves because it possesses a natural immunity sufficient to resist the degree of infectivity the organism has acquired at the time of a subsequent invasion. The total morbidity for a locality is roughly the same when passed over by a late wave of the epidemic whether or not it has received the doubtful benefit of recent earlier visitations.

The main differences between the *Newcastle* and *Africa* outbreaks are that in the former the disease was mild, the mortality *nil*, and influenza-like bacilli predominated in the sputa; whereas in the latter the illness was severe, with 9 per cent. of deaths, and Gram-positive cocci were in evidence in the sputa. This difference is most simply explained by supposing that in the *Newcastle* epidemic *Bacillus influenzæ* was the primary infection, either alone, or combined with a mild secondary bacterium such as *Micrococcus catarrhalis*, while in the case of H.M.S. *Africa* the primary agent was combined with a virulent organism, which was responsible for the great increase of malignancy. The *Newcastle* experience seems to show there was, if anything, a decrease in the virulence of the influenza virus when unassociated with dangerous secondary invaders, as the occurrence of 240 cases with no complications at all was exceptional in home waters, even during the spring; but though the virulence in this case showed no increase, the infectivity was double that seen in ships during the spring.

A point of great importance in the rate of spread of epidemics is the amount, extent, and rapidity of migration and mixing that is taking place among the peoples of the world. At no time in the world's history was the

value of these factors so high as during the period of the late pandemic, and it may well be that the rapid transference of strains of organisms, from individual to individual, and from place to place and back again, gave both the primary and secondary infections those changes of environment necessary to produce the alterations in the characters of virulence and infectivity that undoubtedly took place.

The outbreak at Sierra Leone in West Africa may illustrate one way the epidemic travelled. H.M.S. *Mantua* left England in August, 1918; two days out influenza appeared on board. She touched at Sierra Leone on the 15th and coaled with coolie labour. She then had had over 200 cases of influenza. By August 25, that is ten days later, the influenza epidemic was so bad ashore that there was insufficient coolie labour to coal ships on their way to England. So H.M.S. *Africa* and *Britannia* lent parties of men to help coal these ships. In this way it is presumed the *Africa* got infected. Anyhow most of the first influenza patients were men who had formed part of the coaling parties. We may suppose the white men in H.M.S. *Mantua*, or some other ship, infected the black coolies, who passed the infection back, via the colliers, to the white sailors of H.M.S *.Africa;* and it is not improbable that this passage through a different variety of man may have increased the virulence of the infecting germs and account for the malignancy of the disease in H.M.S. *Africa*. The *Africa* now returns to England bearing a cargo of bacterial strains of increased virulence and infectivity for use in the autumn wave of the pandemic. Besides migration, the rate of spread in any area is a function of the density of susceptible persons and the mass of infection, which depends on the number of cases and carriers, in that area. The density of susceptible persons in a ship must be very great as compared with an assemblage of susceptible persons on shore. If, for example, we contrast the sleeping accommodation in a ship with that of a big institution, we find that in the ship hammock hooks are less than 2 ft. apart, whereas institution bed centres are rarely less than 8 ft. apart. Even when head to toe slinging is insisted on in a ship the men's heads must often be within 3 ft. of each other. Now the volume of spray from a mouth at 3 ft. is nearly twenty times that at 8 ft. Therefore how much more readily will the man sleeping in a battleship's mess-deck get a requisite dose of infectious material than the man sleeping in an institution ashore? Again we also hear of many men in a ship not ill enough to go off duty, and, thus being immobilized, wandering about among their fellows.

When we consider these points, and at the same time realize that a modern battleship, with its tiers of lumbered decks, its cramped accommodation, and its crew of often over 1,000 men, covers an area of less than one-fiftieth of a square mile, I do not think it possible to doubt the infective material must become so dense and diffused as to saturate the ship. That is to say, everyone on board receives a dose of the specific agent sufficient to cause influenza, unless he happens to be highly immune at that time to the strain of organism responsible for the epidemic. In a ship, the density of susceptible persons, the mass of infection, and the local migration are all so great that any diminution in one or more of these factors that may be produced by the use of sprays and gargles, by early isolation of cases and disinfection, is scarcely likely to diminish the rate of spread in a ship, once influenza has obtained a footing on board. And I think naval experience, where all these preventive measures have been vigorously employed, justifies this pessimism, as I have been unable to learn of any definite cases in which they did any good. In ships the outbreaks lasted ten days to three weeks; ashore the wave took

about three months to pass over a locality. The longer wave period ashore was probably due to the lesser density of susceptible persons and infective sources, more time being required for the infection to hunt out all the susceptible individuals within its reach.

I mentioned above that the attack-rate for the whole fleet, as distinct from single ships, in the second wave was only half that in the first; a fact probably due to the escape of whole ships, rather than diminished incidence in ships thoroughly infected during the autumn. Improved quarantine regulations may have made the transference of the virus from ship to ship more difficult. Perhaps an immunizing effect of the earlier wave may have decreased the susceptibility of the fleet as a whole, but the figures from individual ships suggest that the number of susceptible individuals was the same at the time of both outbreaks.

Naval experience indicates that a previous attack of influenza confers some immunity. According to Sir Robert Hill's figures, the attack-rate in the autumn among those who were victims of the spring epidemic was 1·8 per cent., as against 5·6 per cent. of those to escape the early outbreak. But these figures also indicate how far this immunity was from being absolute, even after a period as short as six months.

It may be of interest to turn now to ships that were infected this year (1921). Between January 17 and February 15, H.M.S. *Fisgard* returned eighty-two cases of influenza, which was 7 per cent. of the ship's company. Between January 13 and February 7, H.M.S. *Royal Sovereign* returned sixty-one cases, or 6 per cent. of 1,050 men. It should be admitted that many of these cases were little more than "feverish colds" but were mixed up with undoubted cases of clinical influenza, and fifteen out of sixteen examined harboured *Bacillus influenzæ*. These two ships were among the most heavily infected at Portsmouth this year, yet a 7 per cent. incidence was far below the average attack-rate of ships who had influenza outbreaks in 1918-19. Those who believe the specific cause of this 1921 outbreak was the same as that of 1918 can explain these figures as follows. Only 7 per cent. got influenza because the remaining 93 per cent. were always immune to the disease or had acquired immunity in 1918. But when we turn to the 7 per cent. to be attacked this year it is found that about half of them admitted a previous attack of influenza during the last three years. These may be considered to be hypersusceptible individuals on whom a previous attack had conferred no lasting immunity. The other half, who gave no previous history of influenza, and had come unscathed through the 1918-19 epidemic, may have succumbed this year because their natural immunity had decreased since 1918, or because they had been isolated from infection in 1918. Perhaps however the strain of influenza of 1921 is entirely different to the 1918 strains and requires different specific antibodies to resist it. Personally I prefer the first explanation, and I think if we contrast the condition of the world with regard to influenza at the beginning of 1918 and 1921 we can roughly state it to be something like this: In 1918 about 50 per cent. of the population were susceptible to influenza and 50 per cent. immune to ordinary doses of the virus. In 1921 the population consists of 90 per cent. immune to ordinary doses of influenza germs, 5 per cent. of a hypersusceptible class who will get influenza whenever exposed to infection, and 5 per cent. ordinary susceptible subjects who escaped previous infection.

I have not considered the influence of food, fatigue, race or weather on the epidemic, as the part they played cannot have been of great importance seeing

the way in which the epidemic attacked without distinction rich and poor, black and white, lazy and energetic, in all kinds of climates, weathers, and seasons. The more important points these naval outbreaks seem to indicate better than figures obtainable ashore are that the second wave of the epidemic must be attributed to an enhanced infectivity of the parasite, rather than to an increased immigration of susceptible hosts into a locality, though I believe the latter theory is the more popular view. The marked variation in virulence is almost entirely a function of the prevalent secondary infections, a point so well brought out by the contrast of the illness in H.M.S. *Newcastle* and *Africa*, when both these ships had been infected with autumn strains of influenza. In the report on influenza issued by the Ministry of Health there are some very interesting statistics and graphs of the incidence of influenza in merchantmen.[1] The writers tentatively suggest these curves indicate a three-phase epidemic in ships, analogous to the three-wave epidemic seen ashore, but running its course in days instead of months. But in H.M. ships, where the same crew remained unchanged all through the whole epidemic of 1918-19, though the period of the waves was a tenth to a sixth of the wave-periods ashore, yet the lapse of time between the spring and autumn waves in ships was if anything longer than that usual ashore. This interval was twenty-seven weeks in the *Revenge* and twenty weeks in the *Royal Sovereign*, as compared with sixteen weeks in London; I therefore think the three-phase outbreaks in the merchant ship graphs must have been coincidental, though there may be indications of a similar phenomenon in some of the graphs I have of the naval outbreaks.

I have purposely left out all consideration of the third epidemic wave in the Navy, not because I think it vitiates the conclusions I have come to above, but because I was unable to obtain enough figures relating to it and was unable to find any ship to show three definite waves comparable to the two waves as typified above in H.M.S. *Revenge*.

From the preventive medicine point of view I think we have learnt the following lessons in the Navy: First, that gargles, sprays, disinfection, and isolation can have little effect in checking influenza in the crowded conditions that exist in warships. But there is evidence to show the disease can be kept from spreading from ship to ship and from shore to ship if really strict isolation is enforced. But the quarantine must be absolute. It is altogether useless to allow a favoured few to go ashore such as certain officers, mess-stewards, post-men, and duty boat's crews. In the Royal Navy it is quite possible completely to isolate a ship; boats from other ships and shore establishments can bring stores and mails alongside, and these can be hoisted in without any contact between the ship's crew and the men in the boat. Only in this way can the disease when it has once broken out in a ship be prevented from spreading to the rest of the fleet or even infecting a whole country. If men are on leave in an epidemic area, it is better to let them stop there rather than to return to infect their ship and, perchance, the whole fleet. As regards other methods I think Sir William Leishman's figures for the Army prove the value of pro-phylactic vaccination. It probably diminished incidence threefold and mortality twentyfold. Even should the vaccine not contain the specific antigen of influenza, it contains the antigens of the lethal pulmonary infections and for this reason alone vaccine is worth using.

[1] Reports on Public Health and Medical Subjects. No. 4: Report on the Pandemic of Influenza, 1918-19 (Ministry of Health) 1920, pp. 57-65.

At the first sign of an epidemic compulsory vaccination should be enforced and usually there should be plenty of time. For if we had known in 1918 what we know now, we should have had a month's warning that it was time to vaccinate the fleet, as the epidemic was well under weigh in China and America in March and did not appear in the fleet until April. As in the case with most prophylactic measures, vaccination if used at all, must be thorough. Every soul in the Navy must be vaccinated and not allowed ashore until it is done. "Conscientious objectors," protecting themselves at the expense of society, should not be allowed ashore till the epidemic is over. If vaccination were practised in this way there is hope it would lead to such a diminution in incidence, virulence, and rate of spread, that even if a vaccinated ship became infected, all cases could be treated efficiently on board, without overtaxing the medical arangements or interfering with the efficiency of the ship as a fighting unit; and by this means the only other satisfactory preventive measure could be more easily enforced, namely, absolute isolation.

In conclusion I must apologize if I seem to have made rather sweeping assertions on somewhat flimsy evidence. I can only say that the subject was rather large to do justice to in the time, and that this paper is condensed from a much longer essay.

DISCUSSION.

The PRESIDENT (Sir Robert Hill) said that he was struck with the similarity between the epidemic of 1918-19 and that of 1889-90. Cases in both epidemics began in the same way—a sharp onset, collapse for twenty-four to forty-eight hours and a rapid recovery. The epidemic of 1889-90 was followed in the late autumn by a broncho-pneumonia which killed old people and young children. But in the serious return wave of the 1918-19 epidemic boys and senior officers (men in their fifties) seemed to escape better than men in their thirties. This was very noticeable in the crews of destroyers, where there was considerable mortality amongst men in their late twenties and thirties. The development of severity in an influenza epidemic had its parallel in measles. The first cases of measles in a school were generally mild, but the outbreak became more virulent until 30 to 40 per cent. might be affected.

Surgeon Rear-Admiral P. W. BASSETT-SMITH said that Surgeon-Commander Dudley, in his most interesting and thoughtful paper, had reached a high plane of ætiological and epidemiological speculation. He (Admiral Bassett-Smith) thought there was some doubt about the mutability of the species mentioned and the organism which was primarily the cause of the disease, but there was no doubt that this primary virus gave rise to a condition in the lungs, namely, a blood-stained œdematous fluid, which was a most favourable medium for the growth of such pathogenic organisms as the pneumococci and streptococci so frequently found in certain phases of the epidemic. With regard to immunity—judging from the figures which he was able to work out—there appeared to be a certain amount of protection conferred on those who had suffered in the spring epidemic against the autumn epidemic, but much further statistical evidence was required on this point. Referring to vaccines, in which he was particularly interested, he emphasized the importance of early and thorough immunization of ships' companies, &c., and the fact that practically all investigators in Australia, New Zealand, France and Great Britain, recognized that vaccination at least reduced the mortality. He quoted the following interesting report of Surgeon-Commander Sutton, R.N., as an instance of the prophylactic value of vaccine in the Royal Navy: "The staff here consists of four medical officers. Two of these were taken ill on October 19. The other two were both inoculated at once and, though very much overworked and exposed to infection, we both escaped. Also four of the staff of twelve nurses here had been taken ill before the inoculations started. All were inoculated, and there were no more cases among them. All the sick berth staff, consist-

ing of eight men, were inoculated, and they all escaped. This is in itself a testimonial to its great value. When the inoculations were started the epidemic was at its height. The severest cases were coming from small mine-sweeping vessels ; it was quite common for the whole of the small ship's company (consisting of about five men) of one of these vessels to be taken ill in one day with the influenza, so that a relief crew had to be sent. All the ship's companies of these vessels, consisting of over 138 men, were done at once. The influenza at once stopped in these ships, and only two cases of a mild nature occurred among them.

RESULTS.

	Number	Cases
Inoculated	1,368	2·8 per cent.
Not inoculated	2,801	13·4 per cent."

Dr. BERNARD MYERS said that the influenza epidemics had affected the members of the New Zealand Expeditionary Force fairly severely. A certain number had suffered from the " heliotrope variety " with practically uniformly fatal results. On one transport with 1,150 officers and other ranks which had arrived in England early in 1918, influenza had been evidently contracted at Freetown and about 900 cases with eighty-three deaths had resulted. It appeared that the commander of one of the British warships there had called a conference on board his ship of all captains of transports. On shore influenza was apparently taking distinct toll of the natives and there had been a certain number of severe cases with deaths on the warship. The captain of the New Zealand Expeditionary Force transport sat next to the captain of the warship. The former did not suffer from influenza subsequently although he felt rather " off colour " for the few days following. There had been absolutely no contact between shore and transport although some provisions were apparently delivered to the ship's side. Influenza had begun when the ship was about four days out and increased quickly in violence until practically all of the soldiers were more or less affected. The symptoms were overwhelming, and in fatal cases the victims lived only two to three days after the appearance of actual symptoms. In 1917 a mixed catarrhal vaccine had been first made for them by Dr. Eyre and Dr. Lowe. It contained *Bacillus influenzæ*, pneumobacillus, pneumococcus, catarrhalis, and *Streptococcus hæmolyticus*. Two inoculations had been made at ten days' interval. There was no question of the distinct utility of this vaccine. They had arranged for practically our entire forces in France, Egypt, and the United Kingdom to be inoculated. It had certainly helped to decrease the case incidence and mortality. Every man, before embarking on a transport, had been inoculated, and upon proceeding on board ship had been passed through the inhalation chamber (zinc sulphate). An endeavour had been made to arrange hammocks so that spray infection would be minimized. Plenty of fresh air had been provided and men encouraged to report sick at once, when immediate isolation and disinfection were carried out. By the above-mentioned means influenza almost disappeared from the New Zealand Expeditionary Force transports.

Squadron Leader H. E. WHITTINGHAM, R.A.F., M.S., said that Surgeon-Commander Dudley's paper had presented the Section with a full and yet concise account of the recent influenza epidemic as it had occurred in the Royal Navy. The published reports of work done in influenza in the Army and Royal Air Force all bore testimony to one outstanding fact, namely, that various competent observers, working in different places often with different technique, obtained very similar results. In some waves of the epidemic the number of cases from which the *Bacillus influenzæ* was isolated had been small, in others large. And not only that, but the predominant, so-called " secondary infecting " organisms in each epidemic had been found to be the same by most workers. Moreover, workers using one and the same media throughout the various epidemics had obtained a very different number of positive influenza cultures according to the epidemic investigated. This would point to the fact that the high percentage of *Bacillus influenzæ* " carriers " now to be found could not be entirely accounted for by the improvement in technique, as Surgeon-Commander Dudley had put it. The high percentage of *Bacillus influenzæ* " carriers " rendered it very difficult to diagnose

bacteriologically a case of influenza, even with fairly typical clinical signs. Some help might be obtained from the blood picture. In the Royal Air Force extensive blood pictures had been made during the various epidemics. From these, three distinct types of blood pictures had been elucidated: *Type I*, influenza uncomplicated; *Type II*, pneumonic form of influenza; *Type III*, lethargic form of influenza. In Type I there was a leucopenia accompanied by a relative lymphocytosis. On the third to fifth day of disease a moderate degree of leucocytosis set in with a relative neutrophilia. This was the blood picture seen in simple *Bacillus influenzæ* infection. Type II presented a distinct leucocytosis from the onset with a relative neutrophilia. This was well seen in so-called "secondary infections"—i.e., cases where the *Bacillus influenzæ* was not the predominant organism. Type III showed an initial leucopenia which daily became more pronounced until death occurred, usually in three to five days. Here there was apparently a failure of the defensive powers of the body. Generally speaking, a leucocytosis was a good sign, a persistent leucopenia a serious sign. Hence the advisability of giving vaccine treatment to try to produce a leucocytic reaction. Incomplete recoveries and the oncoming of a relapse could often be diagnosed from the blood picture, even when the clinical signs were slight or absent. The mutability of the influenza bacillus had been discussed at some length, but little had been attributed to the atmospheric conditions in bringing about these changes. That they had an effect was suggested by the occurrence in spring epidemics of laryngitis and pharyngitis, in summer of diarrhœa and other intestinal symptoms, and accompanying the humidity of autumn pneumonic symptoms. Their knowledge of the action of the endocrine glands in microbic infections was in its infancy. Such action might account for the 1918 epidemic chiefly affecting young adults. It was known that adrenalin given before the administration of certain vaccines, sera, and other organic compounds prevented the occurrence of rigors and other untoward symptoms.