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INVESTIGATIONS ON THE BACTERIOLOGY OF EPIDEMIC INFLUENZA[1]

EPIDEMIC influenza has been recognized for centuries, now under one designation, now under another. According to the exigencies of the period it has had a wide or a more restricted distribution: in early times human transport carried the pestilence slowly and over limited areas; in modern times, in a world knit closely together with frequent and rapid transport, it passes quickly from continent to continent.

The source of origin of the epidemics is still under discussion, and it remains for future study to determine whether the spread takes place from a single focus or from many foci of epidemicity. History traces the outbreaks of many epidemics to regions of Eastern Russia and Turkestan; but indications are not wanting that influenza smoldered in many endemic centers preceding the pandemic of 1918. Whichever of these divergent sources of origin proves to be the true one, certain undiscovered but essential conditions must be regarded as combining to convert endemic inactivity into epidemic spread.[2, 3]

THE EPIDEMIC OF 1918

The epidemic outburst of 1918, which was of unparalleled severity, coincided with the exigencies of the Great War so that the full weight and force of modern methods of clinical and bacteriological study could not quickly be brought to bear upon the disease. In many instances also investigators were further handicapped through failure to distinguish the primary infection from the frequent secondary pneumonias of common bacterial origin, or were prejudiced in their views by the general acceptance of Pfeiffer's bacillus as the bacterial incitant of influenza.

[1] From the Laboratories of the Rockefeller Institute for Medical Research, New York, N. Y.

[2] Pearl, R., *U. S. P. H. S. Report* No. 548, 1919, xxxiv, 1744.

[3] Flexner, S., SCIENCE, l, 317.

Early in the course of the epidemic, discordant findings cast doubt on the part played by Pfeiffer's bacillus as the incitant of the disease. The doubt arose through the failure of certain competent investigators to find Pfeiffer's bacillus regularly in the blood or nasopharyngeal secretions of early cases, although, like other ordinary bacteria it was frequently found in the pneumonias that supervened on the primary infection. This organism was also reported as a secondary invader in other diseases, such as measles, whooping cough and tuberculosis, and occurred as often in normal throats as in the presence of respiratory infection. Antibodies against Pfeiffer's bacillus were not found, or could be demonstrated only with puzzling irregularity in the blood of recovered influenza patients, and serological variations among the pathogenic strains were so great that no single type could be identified as common to the majority of cases, although the rapid spread and common character of the epidemic would postulate a single incitant. Finally, vaccines containing Pfeiffer's bacillus and other ordinary bacteria cannot be said materially to have affected the incidence of influenza among those vaccinated. Apparently a certain protection against the secondary pneumonias could be effected by their use.[4]

Similarly, studies of other common bacteria (such as *Micrococcus catarrhalis,* or organisms of the streptococcus or pneumococcus groups) frequently found in the nasopharyngeal secretions or pathological exudates of influenza victims, failed to discover the primary infectious agent in the epidemic disease.

DEFINITION OF EPIDEMIC INFLUENZA

The other factor contributing to the confusion that existed during the early period of the epidemic was a frequent failure to recognize influenza as a specific primary disease, and to relegate the various bacterial pneumonias that developed in influenza-injured lungs to the rôle of secondary infections. Unless this distinction was clearly recognized, and the influenzal incitant sought only in the early hours of the disease, before it was masked and perhaps completely supplanted by associated organisms, little hope could be entertained of its recovery.

It is therefore important to define epidemic influenza in its early stages, before secondary infections obscure its specific characters. Our investigations were based on the uncomplicated disease within 36 hours after onset. Uncomplicated epidemic influenza is usually a mild affection. On the fringes of an epidemic it is not always easy to make an assured diagnosis from other indefinite ailments of the upper respiratory tract. In the midst of an epidemic, however, when many similar cases may be seen, its manifestations are more obvious and uniform. The onset is usually sudden with a chill, or chilly sensations, and fever. Headache, frontal or general, develops, with pains in the back, joints and extremities. In the severer cases the prostration that accompanies these symptoms forces the patient to bed. The eyes become inflamed and sensitive to light. The face is suffused; the throat edematous and raw, a thin irritating secretion flows from the nose, and the progress of the infection is denoted by hoarseness and a dry and distressing bronchial cough. Examination of the chest, however, reveals no certain signs of lung involvement. Other organs are not usually obviously affected. Pulse and respiration are only slightly accelerated. The temperature remains fairly constant, between 101.5 to 103° F. for two to four days and then, after a profuse perspiration, it falls rapidly to normal with the onset of convalescence.

A peculiar feature of the disease is an early drop in the circulating white blood cells to less than 5,000 cells per cubic millimeter. This diminution may persist through the acute stages of influenza and into convalescence. The mononuclear cells are particularly affected, but convalescence may witness a compensatory rise above the normal.

The duration of uncomplicated influenza is usually one to three days; in the severer cases four to six days. When symptoms persist beyond this period a secondary pneumonia or some other sequel is to be suspected.

Variants of the typical disease have been observed, with signs and symptoms referable to the gastro-intestinal tract, the nervous system and the heart. Mild and abortive cases

[4] Park, W. H., *Jour. Immun.*, 1921, vi, 103; McCoy, G. W., *Jour. Amer. Med. Assn.*, 1919, lxxiii, 401.

also occur—cases that may be missed but that probably are capable of spreading the infection. These patients may experience the typical syndrome and show the characteristic changes in the blood picture, but are not so severely stricken as to be driven from their daily tasks. The presence of the influenzal injury is indicated, nevertheless, in an incidence of complications out of proportion to the apparent innocence of the primary ailment.

The striking features of an epidemic, the features that give influenza its evil reputation, are the rapid spread, coupled with a high incidence of infection; so that more than half a population may be attacked in the first wave; the frequent occurrence of severe and fatal secondary pulmonary infections to which influenza makes its victims liable; and the recurrence of successive waves of diminishing extent and severity until, in the course of three or four years, the epidemic dies out.

EXPERIMENTAL INOCULATIONS

In September, 1918, when it was decided to undertake an etiological investigation of epidemic influenza in the laboratories of the Rockefeller Institute it was thought fruitless to attack the problem by the common cultural methods of bacteriology. Animal transmission experiments were considered first with a view to initiating an experimental infection of an influenzal character. Among the characteristic signs of the human infection, the typical changes in the blood picture seemed to promise a measurable diagnostic criterion. It also appeared probable that some pathological basis might be found for the striking defect in resistance to secondary infections which so often opened the way to pneumonias of bacterial origin.

The first experiments were undertaken with the unfiltered nasopharyngeal secretions of patients with uncomplicated epidemic influenza, as diagnosed from the train of symptoms and signs narrated above. These nasopharyngeal secretions, obtained by a saline lavage of the nose and throat, of course contained an extensive bacterial flora. It was expected, however, that in favorable instances ordinary bacteria might be suppressed by animal passage and that the specific effects of an extraordinary microorganism might thereby be revealed.

In a short series of experiments, monkeys (*Macacus rhesus*) were found to be unsuitable, because of their scarcity and the frequent presence of pulmonary infections (especially tuberculosis) in the stock. These preliminary experiments served, however, to orient us in methods of inoculation. Injections of influenzal nasopharyngeal secretions into the nose and throat, the conjunctivæ, the circulation and under the skin produced no distinctive effects. On the other hand, when the injections were made intratracheally into the lungs, the animals showed a subsequent decrease in the white cells of the blood, a change affecting chiefly the mononuclear cells. But this suggestive sign could not be correlated with local lesions in the lungs because of the frequence of pathological conditions due to other causes. Our results were essentially different from those obtained by Bradford, Bashford and Wilson[5] who obtained broncho-pneumonia and nephritis under similar experimental conditions. Nor could we cultivate from the monkey's lungs or from the nasopharyngeal material the "globoid bodies" described by them or by Gibson, Bowman and Connor.[6] The rabbit was then chosen as the experimental animal.

Inoculations through the trachea into the lungs of normal adult rabbits of the nasopharyngeal washings of patients in the early hours of influenza were found to be followed by characteristic effects. On the first or second day after injection the rabbits appeared ill, with ruffled fur, conjunctivitis, and, usually, a degree or two of fever. The constant feature was a definite and often striking numerical depression of the circulating white blood corpuscles, affecting chiefly the mononuclear cells, which often fell below 2,000 and sometimes below 1,000 per cubic millimeter. In the natural course of events these signs endured for two or three days and the animal then returned to normal. If the rabbit was killed at the height of the attack—for in the absence of secondary infection by ordinary bacteria none died—an unusual pathological picture was discovered in the lungs. The respiratory organs alone were visibly affected. The lungs were distended by

[5] Bradford, J. R., Bashford, G. P., and Wilson, J. A., *Quart. Jour. Med.*, 1918, xii, 259.

[6] Gibson, H. G., Bowman, F. B., and Connor, J. I., *Brit. Med. Jour.*, March 22, 1919, 331.

an exudation of fluid (edema) into the interalveolar walls and by a large emphysematous space due to their rupture. On surface view and on cut section they were mottled with numerous large and small hemorrhages in the substance of the lung. Macroscopically, besides the edema, ruptures and hemorrhages, a scanty cellular exudate of mononuclear and, to a less extent, of polynuclear cells was found. The bronchii and bronchioles also were often filled with serous fluid and showed necrosis and exfoliation of their epithelium. Thus, while the lung structure was severely injured and disorganized in certain areas, there was a complete absence of the fibrinous and cellular consolidation of the lungs which characterizes pneumonias of ordinary bacterial origin. In many instances no ordinary bacteria could be recovered from the lesions either in stained impression films or by erobic or anerobic methods of cultivation. We concluded that the clinical and pathological effects induced by the intratracheal injection of the influenzal washings were independent of the presence of commonly recognized microorganisms.

By the intratracheal injection of a saline suspension of ground lung tissue from a previously affected rabbit, the typical syndrome just described could be induced successively in a series of animals. In one instance 15 successive passages were obtained before the experiment was discontinued. Because of the persistence of these characteristic effects, in spite of the repeated dilution of the original material between passages, we were led to believe that we were dealing with a self-perpetuating agent; a living virus or microorganism.

It was soon found that the elements of this virus were of such minute proportions that they readily passed through earthenware filters impervious to ordinary bacteria. In this way it could be separated from other microorganisms in the nasopharyngeal secretions or in affected rabbits' lungs. The filtered material produced the typical train of clinical and pathological effects in rabbits and so proved that ordinary bacteria were not involved in the process. The microorganism was a filter-passer.

Now although very few filter-passing microorganisms have been identified, the group, in general, has certain well-known characters which this virus was found to share. For example, although it was readily killed by heat at 56° C., it was resistant to drying or freezing, and could withstand the action of 50 per cent. glycerol for periods up to nine months. When animal tissues containing it were contaminated by molds or bacteria the virus still survived.

Another noteworthy effect of this active agent early claimed our attention. When unfiltered nasopharyngeal secretions from influenza patients were intratracheally injected in rabbits, other microbic residents of the upper respiratory tract were likewise deposited in the animal's lungs. Ordinarily such bacteria do not produce lesions under these conditions, but are overpowered by the active protective mechanisms of the body. But in the presence of the primary injury caused by the influenzal agent these bacteria were sometimes able to multiply and cause severe pneumonias. We have already referred to the frequency of such a train of events in human cases, and the similarity of these accidental infections in the experimental animals led to a series of experiments to put this significant sequence of events to further test.

Thus it was found that a decrease in pulmonary resistance to such common bacteria as the pneumococcus, streptococcus, and *Bacillus pfeifferi* was a characteristic result of infection with the filterable virus. In some experiments, after the lungs had been damaged by the influenzal agent, the other organisms were injected into the trachea, since this is the route they are supposed to follow in man. In other experiments, as a severer test, small doses were injected into the circulating blood. Uniformly the common bacteria invaded the injured lungs and there induced a typical pneumonia. To the normal lungs of control animals the same doses of these microorganisms were harmless.

One more effect of the influenzal agent may be mentioned here before passing on to its identification. Rabbits allowed to recover from a primary infection with the virus were found to be immune to a subsequent inoculation.

In all, thirteen specimens of the active agent were recovered from the nasopharyngeal secretions of influenza patients in the first 36 hours of the disease. Five strains were obtained in 1918-1919, two during the recurrence of 1920 and six in 1922. During the same

periods, three similar transmission experiments failed. On the other hand the active agent was not obtained from 12 influenza patients, the onset of whose illness had occurred more than 36 hours previously, nor from 17 persons free from influenza during the epidemic and inter-epidemic periods.

ARTIFICIAL CULTIVATION

In the beginning of this investigation, while the first animal transmission experiments were in progress, attempts were made to isolate the active agent in artificial cultures. For this purpose ordinary methods of cultivation were discarded in favor of the particular methods which Dr. Noguchi had developed in the course of his successful cultivation experiments with various highly parasitic treponemata, and with the filterable "globoid bodies" of poliomyelitis. These methods, in turn, were based on the earlier experiments of Dr. Theobald Smith. The Smith-Noguchi culture medium consists of sterile ascitic fluid or diluted serum, to which is added a small fragment of fresh, sterile, tissue —usually rabbit kidney. The peculiar attributes of the tissue fragment are not completely understood, but it seems to combine special nutritive or growth-promoting properties with a reducing activity which establishes anerobic conditions in the depth of the tube. The choice of this medium for the cultivation of the active agent of the transmission experiments proved to be a fortunate one.

In November, 1918, certain extremely minute but characteristic bodies were observed in strictly anerobic cultures of the filtered nasopharyngeal secretions of an influenza patient in the early hours of the disease. They approached the globoid bodies of poliomyelitis in size, but were somewhat longer in one axis than in the other. They stained with difficulty with the usual basic dyes and decolorized by Gram's method. That was about all that the sparse growths of the initial cultures revealed. Soon, however, other cultures were obtained, both from the filtered nasopharyngeal secretions of other influenza patients and from the whole or filtered lung tissue suspensions of rabbits which had been typically affected by these secretions, as has been described. As these minute microorganisms were carried through successive generations of culture, they became better adapted to artificial cultivation and multiplied more luxuriantly, so that the cultures could be used in animal experiments with unequivocal results. These experiments proved beyond question the identity of the active agent obtained from influenza cases and the bodies obtained in culture. Both were derived from the same sources. Both were filterable. Both produced identical clinical and pathological effects in rabbits, and from the pulmonary lesions produced by either, further animal passages, or cultures, could be obtained. Both, protected by bits of affected lung tissues, withstood 50 per cent. glycerol for periods of months. Both had that curious property of damaging the lung in such a way as to lower its resistance to secondary invasion with ordinary bacteria. It was from this character that the microorganism, objectively, received its name. We called it *Bacterium pneumosintes*—a bacterium that injures the lung. Finally, conclusive evidence of the identity of the virus and *Bacterium pneumosintes* was furnished by a series of experiments which showed that a previous infection with either one of these pathogenic agents rendered an animal immune to attack by the other.

IMMUNITY

In many infectious diseases, the immunity conferred by an attack is associated with the appearance in the blood of specific principles, or antibodies, which can be demonstrated by serological tests. Our efforts were therefore directed toward the observation of antibodies in the blood of experimentally infected rabbits, and of influenza patients, from which the strains of *Bacterium pneumosintes* ultimately had been derived. But it was found that cultures of *Bacterium pneumosintes* in the Smith-Noguchi medium were unsuitable for serological experiments. The sparse growth of the earlier generations was mixed with protein precipitate that interfered with agglutination and precipitation reactions and had antigenic properties that precluded its use. It was therefore necessary to devise special methods of cultivation, and before these methods were available the first opportunity was lost to test for antibodies in the blood of influenza patients and of affected rabbits.

We found later that if the Smith-Noguchi medium was enclosed in a collodion sac, sur-

rounded by distilled water or physiological salt solution, anerobic conditions were shortly established throughout the system and the nutritive and growth-promoting substance of the medium diffused through the membrane in sufficient quantities to support a luxuriant growth in the surrounding liquid. The protein-precipitate that collected around the tissue fragment was retained within the sac.

When it was possible to cultivate *Bacterium pneumosintes* by this method in quantities sufficient for use, rabbits were repeatedly injected intravenously with small doses of live cultures, or of heat-killed organisms. After a suitable interval, their blood serum was found to possess specific antibodies against *Bacterium pneumosintes* which could be demonstrated by agglutination, precipitation, complement fixation and phagocytic tests. A significant feature of the immunological experiments and also of these serological tests was the fact that all the strains tested had similar antigenic properties and reacted identically with the specific antibodies produced by any one of them. This is what would be expected if they were all derived from a common source.

The development of immunity in experimental animals as a result of previous infection, and the appearance of serum antibodies after intravenous inoculation of living or killed cultures led us to infer that the mechanism of protection against *Bacterium pneumosintes* does not differ from that which comes into play in the case of infections with erobic pathogenic bacteria. Two important deductions, both susceptible of experimental proof, may be drawn from this conclusion.

One has already been mentioned—that the immunity conferred by an attack might be associated with the appearance of specific protective principles in the blood. The other is that these specific antibodies might be developed as a result of prophylactic subcutaneous injections of heat-killed organisms.

But in the absence of recent cases of influenza, or of fresh, pathogenic strains of *Bacterium pneumosintes*—(for the strains obtained in 1918-1919 and 1920 had become saprophytic from long cultivation) we were for some time unable to test these hypotheses. The opportunity was finally afforded by a recurrence of epidemic influenza in New York City in January and February, 1922.

With material obtained from a number of early cases of influenza in this outbreak we repeated all of the essential steps of the former investigation, so that this series of experiments served to check and confirm the results of the earlier work. In brief, from the nasopharyngeal washings of eight patients in the early hours of uncomplicated influenza, the pathogenic agent was transmitted to animals in six instances. One of the two failures may possibly be attributed to the fact that the nasopharyngeal secretions stood for 24 hours at room temperature before injection. From these animals or their successors, three new strains of *Bacterium pneumosintes* were isolated, and a fourth strain was recovered by direct cultivation from a ninth patient whose filtered secretions were not injected into rabbits.

Since the clinical and pathological effects produced in rabbits by the new strains of the active agent appeared to us to be identical with those observed during the former epidemic waves, it is not necessary to describe them again in detail. The new strains of *Bacterium pneumosintes,* when isolated in artificial cultures, also had properties identical with those of the old strains obtained in 1918-1919 and 1920.

For example, they had the same morphology and cultural characters. They were filterable. They resisted the action of 50 per cent. glycerol. They were typically pathogenic for rabbits and reduced the resistance of the pulmonary tissues to secondary invasion with common bacteria. The new strains were specifically agglutinated by immune serum made with the old strains, and *vice versa.* Rabbits immunized by intratracheal injection of the old strains were subsequently resistant to the new.

In the earlier transmission experiments *Bacterium pneumosintes* had not been identified with certainty in microscopic sections of affected rabbits' lungs, but during these recent studies, by special methods of staining, we demonstrated the presence of minute bodies, morphologically identical with *Bacterium pneumosintes,* in the pulmonary lesions of six rabbits injected with

the active agent from 1922 cases of influenza. From three of these animals pure cultures of the organism were subsequently obtained.

With the 1922 strains of *Bacterium pneumosintes* we were now able to carry out the tests for specific antibodies in the blood of recovered influenza patients, and also the study of prophylactic vaccination which had long been postponed. In the first experiments specimens of serum from 19 persons who had recovered from influenza from 10 days to five months previously and from 22 other persons who gave no history of influenza since 1920 were studied in agglutination tests. The method used was one recently developed in the laboratory of the Rockefeller Institute, by Dr. Northrop and Dr. De Kruif[7] that increases the sensitiveness of the reaction without impairing its specificity. In the control tests no agglutinins or precipitins were found in the serum of 22 persons who had never had influenza or had not been recently attacked. We concluded that the blood of normal persons does not contain demonstrable antibodies against *Bacterium pneumosintes*. On the other hand, the serum specimens from 17 of 19 persons who had influenza during the recurrence of 1922 specifically agglutinated both old (1919) and new (1922) strains of *Bacterium pneumosintes,* and in 12 of 15 sera tested precipitins were also discovered.

One of the persons chosen as a control subsequently had clinical influenza. It was interesting to find that his blood serum, previously negative, contained agglutinins for *Bacterium pneumosintes* when tested on the tenth and eighty-ninth days after recovery. In other instances demonstrable agglutinins persisted in the blood for at least five months following an attack of influenza.

The second series of experiments that were made possible by the acquisition of new and pathogenic strains of *Bacterium pneumosintes* dealt with the immunizing effects in rabbits of subcutaneous injections of appropriate doses of the heat-killed organisms. When a number of rabbits had been prepared by three injections of the killed bacteria the protective effects of the vaccination were demonstrated in two ways. By serological examination it was found that 11 among 15 vaccinated animals had developed specific agglutinins against *Bacterium pneumosintes*. Their resistance was then tested to doses of the living organisms which were pathogenic for normal, unvaccinated animals. In all but two instances the protection was complete. Not only did the vaccinated rabbits fail to show the characteristic signs of infection with *Bacterium pneumosintes* but, with the two exceptions noted above, they were normally resistant to secondary infection with a pneumococcus, a streptococcus, or *Bacillus pfeifferi*. Incidentally, it was observed that the doses of vaccine were well borne and did not even temporarily reduce the rabbits' resistance to other infections. These experiments therefore pointed the way to a similar series of observations in man.

At the invitation of Lieutenant Colonel Charles F. Craig, a number of officers and enlisted men at the Army Medical School in Washington, D. C., volunteered to submit to vaccination with *Bacterium pneumosintes*. They were accordingly given three subcutaneous injections of killed culture in a manner similar to that employed with antityphoid vaccine. The doses chosen did not cause any severe local or general reactions, the subjective effects being somewhat milder than those experienced after antityphoid vaccination. But on the tenth or eleventh day after the final injection the blood serum of seven among nine men examined contained specific agglutinins for *Bacterium pneumosintes,* thus indicating the formation of protective antibodies as a result of the injection of vaccine.

On the basis of these observations the vaccine is being offered to much larger groups of men in the United States Army. It is not possible, of course, to determine the protective effects of these injections directly. In the event of a recurrence of epidemic influenza in the near future, however, the efficacy of vaccination with *Bacterium pneumosintes* as a preventive measure may be put to test. Meanwhile methods are at hand for the production of large amounts of vaccine if its widespread use should be indicated.

Before summarizing briefly the results of these experimental studies of the nasopharyngeal secretions of influenza patients mention may be made of the fact that *Bacterium pneumosintes* is not the only anerobic, filter-passing, Gram-negative microorganism to be found in the human respiratory tract. From the naso-

[7] Northrop, J. H., and De Kruif, P. H., *Jour. Gen. Physiol.*, 1922, iv, 639, 655.

pharyngeal secretions of one influenza patient, and of a considerable number of other persons, normal or suffering from various mild respiratory infections, other filterable organisms, not *Bacterium pneumosintes* and not pathogenic for rabbits, have recently been cultivated. What the importance of these microorganisms may be, or whether they have any pathogenic significance, remains to be determined. They indicate, however, that the cultural methods recently employed in these studies may lead to the isolation of a group or groups of hitherto undescribed bacterial inhabitants of the upper respiratory tract and so they point to interesting opportunities in this field of bacteriology.

CONCLUSIONS

In conclusion, we have isolated from the nasopharyngeal secretions of influenza patients in the early hours of the epidemic disease a hitherto undiscovered organism, *Bacterium pneumosintes,* filterable, anerobic, resistant and pathogenic for rabbits, in which it induces a typical infection comparable with epidemic influenza in man. The significant features of this experimental infection are the incidence of a leucocytic depression chiefly affecting the mononuclear cells, and the production of a characteristic lesion in the lungs associated with a defect in their resistance to secondary invasion with common pathogenic bacteria.

All our strains of *Bacterium pneumosintes* have similar antigenic properties, indicating a common source. Animals subjected to a primary infection, or injected with living or killed organisms are immune to subsequent injection. The killed bacteria induce specific antibody formation even when injected subcutaneously in doses well tolerated by man. The blood serum of recovered influenza patients contains agglutinins for *Bacterium pneumosintes,* whereas that of normal persons does not.

On the basis of these experimental observations, reported in detail in *The Journal of Experimental Medicine,*[8] and especially in view of the source of the cultures, their clinical and pathological effects in rabbits, their antigenic identity, and the presence of specific agglutinins in the blood serum of recently recovered influenza patients, it might seem justifiable to claim *Bacterium pneumosintes* to be the bacterial incitant of epidemic influenza. At present, as already stated in an earlier report, such a course does not seem desirable. Apparently we are at the threshold of knowledge of a group or class of minute microorganisms which the anerobic Smith-Noguchi technique and more recently developed methods of cultivation have thrown open to exploitation. It has seemed wiser, therefore, merely to report the experimental facts, and to defer decision of the precise relation which *Bacterium pneumosintes* bears to epidemic influenza until further experience is obtained.

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[8] Olitsky, P. K., and Gates, F. L., *Jour. Exper. Med.,* 1921, xxxiii, 125, 361, 373 and 713; *ibid.,* 1921, xxxiv, 1; *ibid.,* 1922, xxxv, 1, 553 and 813; *ibid.,* 1922, xxxvi, 685. Papers XI and XII in press.

GARDEN FOR THE PROPAGATION OF TROPICAL AND SUBTROPICAL PLANTS

UNDER a revocable license, which it is believed insures a sufficiently long tenure to secure useful results, Secretary Weeks has just turned over to Secretary Wallace the Chapman Field air station of 850 acres, located on Biscayne Bay, 12 miles south of Miami, Florida. This tract has a coast line of 1⅘ miles and is composed of about 195 acres of pine land and rock reef and 655 acres of low land and mangroves, more or less subject to overflow during the high waters. Of this latter, 80 acres have been filled above high water level and will be made available for use as soon as the salt has been washed out of it.

The striking feature of this tract of land is that it is located in one of the warmest spots on the whole peninsula of Florida, which means that it is less liable to cool winter temperatures than almost any other spot in continental United States. Vegetation which is strictly tropical, such as that of the mango, coconut palm, and West Indian avocado can be grown here in perfect safety. It is not commonly understood that in such a station can be propagated to advantage a wide range of those valuable food and otherwise useful plants upon