lar size, these authors were able to identify a lactase band in the brush-border membranes of three patients with congenital lactase deficiency. Technical problems probably prevented demonstration of the enzyme in the fourth patient. This residual enzyme was in the same position as that found for normal intestine, indicating that it may be very similar or identical to the normal enzyme. Hence, patients with congenital deficiency appear to retain some enzyme that is qualitatively indistinguishable from normal lactase; this observation suggests that congenital deficiency may be caused by a regulatory defect, and brings into question the hypothesis that the congenital and acquired maladies are substantively different. Perhaps the regulatory system may simply be set at different quantitative levels in the two conditions. Since manufacture of the enzyme continues at low levels under such circumstances, it may be feasible to devise a method to alter regulation, thereby unleashing the structural gene to synthesize normal levels of enzyme. Unfortunately, no simple method has yet been found that will effectively induce lactase in man, although long-term feeding of lactose for five to 10 weeks does induce the enzyme in post-weanling rats.[12]

The technic used by Freiburghaus et al. is one of the most powerful tools for the separation of proteins and enzymes, but a discrete alteration in the structure of lactase might not change the size or charge characteristics of the protein, so that the altered lactase could migrate exactly like the normal enzyme in acrylamide electrophoresis. Further characterization of the defect in acquired and congenital lactase deficiency will depend on final isolation of human brush border lactase, something that has eluded investigators because of the lability of this enzyme when it is subjected to purification procedures. Once the enzyme is purified, specific antibodies to it could be raised in animals injected with the protein, and could then be used to probe regions of the large lactase molecule (molecular weight of 280,000 daltons) other than the active enzyme site. In this manner, it should eventually be possible to determine precisely whether the lactase protein is qualitatively altered in lactose malabsorption states.

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INFLUENZA — 1918, A REVISIT?

THE recent recommendation by the President of the United States that a vaccine containing swine-influenza virus be promptly prepared for mass immunization in the early fall of 1976 was stimulated by the experience at Fort Dix, New Jersey, where, within the last two months, this agent was identified as the cause of disease that led to one death. Transmission from person to person was documented. This fact alone would not have provoked a strong reaction were it not for the suspicion that this was the agent that had probably been responsible for the pandemic of 1918. The basis for this hypothesis was the demonstration many years later that people who either were well or had survived an episode of influenza in 1918 had neutralizing antibody for the virus known to be responsible for large outbreaks of influenza in swine. It was suggested that, if this were the case, the agent that had been involved in the tremendous tragedy early in this century, although it had never been identified, either had been present initially in pigs and had been transmitted to human beings or had first found a reservoir in these animals after the pandemic. It is of considerable interest that sporadic cases of influenza due to the porcine strain had been noted, but there was no evidence of person-to-person transmission. An even greater stimulus to the proposal for mass protection against this agent is the fear that the experiences of the pandemic of 1918 might be repeated in 1976-1977.

The influenza pandemic of 1918 occurred in three waves. The first appeared in the winter and spring of 1917-1918. Because it was especially prominent in Spain it was called "Spanish flu." There were sporadic outbreaks in many installations of the United States Army in the spring, first at Camp Funston in Georgia. All areas of the world, with the exception of two islands, St. Helena and Mauritius, were involved. This wave was characterized by high morbidity (50 per cent of the world's population were affected) but very low fatality rates. The disease spread widely among military units in Europe. It was labeled "Flanders grippe" when it involved British soldiers; in the Chinese in the French army it was called "Chungking fever" and in the German troops, "Blitzkatarrh." The second wave, which started at Fort Devens in Ayer, Massachusetts, on September 12, 1918, involved almost the entire world over a very short time, the only areas spared being Australia and a few remote islands. Its epidemiologic behavior was most unusual. Although person-to-person spread occurred in local areas, the disease appeared on the same day in widely separated parts of the world on the one hand, but, on the other, took days to weeks

to spread relatively short distances. It was detected in Boston and Bombay on the same day, but took three weeks before it reached New York City, despite the fact that there was considerable travel between the two cities. It was present for the first time in Joliet, Illinois four weeks after it was identified in Chicago, the distance between these areas being only 61 km (38 miles). None of the people who had been infected in the first wave contracted illness in the second one. However, among those who had not had influenza during the previous winter and spring, the impact of the disease was almost unbelievable. It has been estimated that about 500 million people were involved during a period of probably about six to eight weeks. This number does not indicate the true extent of the pandemic, because reporting of cases from remote and underdeveloped areas of the world was nonexistent. Its tragic impact is underscored by the reported fatality rates. It is estimated that there were about 20 million deaths. The number of fatalities at the height of the outbreak in Boston were 175, in New York City 600 to 700, and in Philadelphia 1,700 per day. Two per cent of all the men in the United States Army had the disease; one of every 67 died. The impact of this pandemic was as great as that of the plague in London, which killed about 2 per cent of the population per month, and of yellow fever in Philadelphia, which accounted for 2.5 per cent fatalities per month. At its height, influenza, complicated by pneumonia, was responsible for death in 2 per cent of the population per month. A third wave of influenza, occurring in the spring of 1919, was featured, however, by very low morbidity and fatality rates.

It is evident that it is impossible to predict that, because swine-influenza virus has been responsible for a few cases of disease in the winter of 1976, it will cause an outbreak in 1976-1977. It can be argued that the possibility that such an outbreak will occur is high, or alternatively that it is low. In addition, there is no proof that, if this virus causes the next wave of influenza, it will, in fact, involve most of the world or, even if it does, that it will produce the tragic consequences experienced in 1918. The evidence that the agent that caused the problem earlier in this century is the one now present in pigs is only circumstantial. In addition, there is the possibility that, because it has persisted in these animals for almost 40 years, it has altered its antigenic structure and degree of invasiveness, and it may therefore not behave in the way it did 58 years ago. It is also possible that the next outbreak of influenza will be due to an entirely different viral type. These speculations may suggest that there is no cause for the alarm provoked by the recent experience at Fort Dix. However, it must be emphasized that there is also the possibility that the swine virus is, in fact, the same agent or is closely related to the one that caused the early pandemic, and that, once widely seeded in populations, it will produce the devastation it did in 1918. These too are speculations for which there is little or no supporting evidence at the moment.

Those who have questioned the need for immunization against the swine-influenza virus this year have advanced cogent arguments that demand attention. First of all, the possibility that we will have the same experience as in 1918 is unpredictable. Secondly, it has been suggested that, because one of the most important causes of death in 1918 was secondary bacterial pneumonia, and because there are now available a large number of potent and effective antimicrobial drugs, fatality rates should be considerably lower. It has also been pointed out that the toxicity of swine-influenza viral vaccine may produce uncomfortable, if not dangerous, reactions. However, much of the experience of 1918 tends to question the validity of these points. Whether or not the next outbreak of influenza will be of the same magnitude as the one that occurred in the early part of the century cannot be determined; it may be just as severe. The risk of death may not be strikingly reduced by the availability of antibiotic agents. Study of the pathological material derived from patients who died during 1918 indicates clearly that a large number of the pneumonias were indeed caused by secondary bacterial invasion. However, the clinical course was so dramatically short that, if effective agents had been available, diagnosis and institution of therapy could not have been carried out rapidly enough to have an important impact on survival. Any physician active during 1918 will recall that many patients who died of a bacterial pneumonia first sickened in the morning of one day and were dead before the dawn of the next. In a large number of cases, the fatal pneumonic process was produced by the virus alone. In many others, the pulmonary disease represented a double infection, viral plus bacterial, the path for intrusion of the bacteria into the lungs having been prepared by the virus. It is doubtful if, even with the most modern methods of diagnosis and treatment, death rates will be very sharply altered when the rapidity of the process, the time required for physicians to get to patients and the period of therapy necessary for a beneficial effect to appear are considered. In addition, a number of the deaths during 1918 resulted from myocarditis and acute encephalitis, disorders for which there is no effective form of management. If postencephalitic Parkinsonism was a consequence of influenzal viral infection, there is the possibility that the present almost complete disappearance of this syndrome will be reversed, if a pandemic of the proportion and intensity of the one in 1918 develops again. Whether a vaccine containing swine-influenza virus will produce severe reactions is unknown but cannot be denied. Only experience, possibly obtained from small field trials carried out before mass immunization is performed, will answer this question.

Not the smallest problem associated with an outbreak of influenza of the magnitude of the one in 1918 is the tremendous load of work imposed on physicians and allied health personnel, and the almost impossible task of seeing and caring for the huge number of people stricken almost simultaneously. The economic impact of such a pandemic, in terms of time lost from work and cost of medical care (physicians, nurses, hospitalization and drugs), would be tremendous, and would unquestionably exceed by far the 135 million dollars requested for the program of immunization. In addition, the social consequences of such widespread disease in relation to disruption of public and other services because of the incapacity of the large number of persons required to provide them might be overwhelming.

It is very clear that neither those who support strongly the recommendation for mass immunization against swine in-

fluenza nor those who have a qualified, if not negative, reaction to it, are in a position at present to demand acceptance of their particular view. On the basis of the recorded experiences of 1918, the circumstantial evidence that the swine-influenza virus may be the agent that caused the pandemic, I have taken the stand that it is probably safest to carry out mass prophylaxis later this year, when enough vaccine has become available to immunize the bulk of the population. The suggestion that it might be well to wait until there is evidence of disease due to this virus in other parts of the world is open to serious question. In the first place, it may well be, as it was in 1918, that a new pandemic will start in the United States. Moreover, even if the disease first appears in other parts of the globe, there may not be sufficient time to prepare enough of the immunizing agent to protect a sufficiently large segment of our population. In addition, it must be emphasized that experiences with the epidemiology of influenza over many years, but especially during the second wave of infection in 1918, point out very clearly that the disease may appear in widely separated areas of the world almost, if not, simultaneously. So, as in the early part of the century, influenza may again become a problem in as far distant cities as Bombay and Boston on the same day.

Two other questions require consideration. Who should be immunized? Should swine-influenza virus vaccine be monovalent? Although it has been proposed that the entire population of the United States be immunized, there is adequate evidence that young children, with the possible exception of those under one year of age, do not require such protection. Experience in 1918 and in subsequent epidemics and pandemics has indicated that influenza is a mild disease in youngsters under the age of 13 and that, in many cases, the infection is clinically inapparent and detected only when serial studies of levels of specific antibody are carried out. The premise that only those who account for excess mortality rates during outbreaks of influenza — persons with chronic heart (especially mitral stenosis) and pulmonary disease, people over the age of 50 years and pregnant women — may not be tenable for disease due to the porcine virus. Not only such patients but also a very large number of young (20 to 30 years of age), otherwise healthy persons sickened and died in 1918. This fact suggests that the "mass" to be immunized should include all persons older than 12 years. The possibility that pregnancy will increase the risk of potentially serious reactions to swine-influenza virus vaccine cannot be denied. However, it must be weighed against the increased frequency of maternal and fetal death observed in 1918 as well as in epidemics of the disease that have occurred since then.

It is probably best to include the swine-influenza virus in a vaccine containing other Type A and B strains known to have recently been involved in outbreaks of the disease. This precaution is necessary for two reasons: the next epidemic may not be caused by the porcine virus; and it is possible, although not very likely, that more than one viral type will be involved, and that both swine and human agents will produce infection in a given area simultaneously.

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THOU SHALT BE VACCINATED

WHAT does J.Q. (for Queasy) Healthsumer do when the President, flanked by Albert Sabin, Jonas Salk, and a host of co-experts, proclaims, "Thou shalt be vaccinated against the flu"? J.Q.H.'s response is predictable: he joins the legion of vaccinees — i.e., if he can get the vaccine in time.

On March 25, 1976, when the newspapers announced this new "war" on a given disease, details of how the decision was made were meager, and some readers had strong misgivings. Were, in fact, the viral experts summoned to Washington and told to support what a public-relations wizard had dreamed up as an election-year gimmick? And had the scientists had any chance to discuss the host of problems that might make the "war" resemble our campaign in Cambodia? As recently as April 6 this year, the *New York Times* editorialized on the doubts that linger in the minds of many.[1]

In the preceding editorial, however, Dr. Louis Weinstein, a senior statesman in infectious disease and unencumbered by political pressure and presidential prestige, reassures us by supporting pan-vaccination — except for children and those sensitive to egg white. The management of pregnant women poses a tough choice: in them, a reaction to vaccination may have more serious consequences, but in them, as well, the disease itself may be more serious.

In addition, fears that the medical scientists merely served the President as window dressing appear unwarranted. Indeed, at an earlier meeting in January plans had been laid for the containment of any viral epidemics that might threaten. Contrary to the impressions given by the rather skimpy news accounts at the time of the March 25 announcement, the decision was neither a response to an ultimatum nor a pro forma affair. All the questions mentioned by Dr. Weinstein, and others as well, were apparently well debated and not swept under the rug for political reasons.

Two basic, essentially philosophic aspects of the decision to engage in preventive war against the swine-influenza virus warrant recognition. Firstly, whatever the competence and involvement of the scientists present when the decision to vaccinate for swine influenza was made, and whatever the prestige of the individuals or groups that have lined up behind the plan, decisions of this type unavoidably are made under circumstances in which the principles of Pascal's Wager[2] predominate over those of objective decision analysis. What scientist can assure the President that a viral flu epidemic will not rage in 1976-77, or which expert can suggest an alternative and reasonably effective prophylactic measure? Under such circumstances, only one decision is practically and emotionally possible. If the vaccine is given and nothing happens — or even if there are a number of flu cases — no one will be blamed, and the decision makers may well be praised. But if vaccination is not recommended and an epidemic ensues.... What can anyone — expert or non-expert, President or J.Q.H. — do but hedge?

Secondly, is not the entire performance somewhat ironic in the light of our well publicized dedication to the principle of informed consent? Any physician is now well indoctrinated that, if he is inclined to vaccinate a given patient on