THE OUTLOOK FOR THE
CONTROL OF INFLUENZA

by

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School of Public Health, University of Michigan
and Director of the Commission on Influenza,
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MR. CROSS: Good evening! This is Milton Cross acting as spokes-
man and interviewer for Lederle Laboratories, a Unit of
American Cyanamid Company. Once again we bring to
the members of the medical and allied professions a discus-
sion on one of the important problems now of interest to
the doctors, dentists, public health workers, and health
department officials of America. It is basically an account
of our never-ending search for better health.

Our topic tonight is “The Outlook for the Control of In-
fluenza,” and our guest is Dr. Thomas Francis, Jr., Pro-
fessor of Epidemiology, School of Public Health, University
of Michigan, and Director of the Commission on In-
fluenza, Army Epidemiological Board. . . . Dr. Francis,
I would say that no discussion of influenza can start with-
out some mention of the terrible epidemic that swept
through this country in 1918. I remember it vividly. . . .

DR. FRANCIS: I don’t think anyone who lived through that period
can ever forget it, Mr. Cross. The fact that it occurred
during the last war cut it even more deeply into our memo-
ries . . . for it was catastrophe piled on catastrophe.
MR. CROSS: Yes... and I think it has had the effect of making most people think that there is some real connection between war and influenza.

DR. FRANCIS: In war or in peace, influenza is a threat. Despite the truly great advances in medical knowledge, respiratory diseases continue to constitute the major cause of illness in the temperate climates of the world. In this category influenza is of major importance. Obviously, the reason for this is that it sweeps in epidemic proportions through wide geographic areas plus the fact that it appears at times, in a highly virulent form with high mortality.

MR. CROSS: Just how deadly was the epidemic we have been talking about... the one that struck in 1918?

DR. FRANCIS: The epidemic in the autumn of 1918 spread through the population of the entire world in a few months. It affected uncounted numbers and it resulted in an estimated 20 million deaths.

MR. CROSS: Twenty million deaths! Why, Doctor, that's two and a half times as many as were killed in all the armies during the four years of World War I!

DR. FRANCIS: It's a gruesome fact... but a true one, Mr. Cross. Few episodes in the recorded history of mankind have been so devastating. It would be sad enough if influenza death on a large scale had been confined to this period... but they have continued. Epidemics arise explosively... they extend rapidly... they attack from 10 to 30 per cent of the population! Invariably, these epidemics result in an increased number of deaths... deaths not only from respiratory diseases, mind you... but among those suffering from other diseases as well... and you can't forecast the potential danger in any epidemic. For instance, the epidemic of 1918 produced a mortality rate 600 per hundred thousand above the expected level. In the wave that hit during 1928 and higher th...
1928 and 1929, the rate was 65 per hundred thousand higher than was expected.

MR. CROSS: What about the epidemic that we had last winter, Dr. Francis?

DR. FRANCIS: Well, that was considered a rather mild outbreak ... and yet the deaths were 50 per hundred thousand greater than normal. It is so difficult to estimate the seriousness of any epidemic. Morbidity figures are not accurate ... because, in addition to the typical cases ... there is almost an equal number who have such negligible symptoms as to escape notice ... but these cases are infected ... and they can transmit the virus of influenza to others!

MR. CROSS: That, I think, brings us directly to the question of just what is influenza? How can it be recognized and treated?

DR. FRANCIS: Influenza is ordinarily a disease of three to five days' duration. After an incubation period of scarcely more than 24 hours, the onset of the illness itself is abrupt. Chills, fever, aches, and prostration occur out of all proportion to the signs of respiratory infections. Convalescence is slow. This is due to the weakness which persists well beyond the period of immediate recovery. When, however, fever continues or rises a second time ... it usually indicates that more dangerous pulmonary complications have set in. These are the features which make influenza hazardous.

MR. CROSS: What causes the disease in the first place, Dr. Francis?

DR. FRANCIS: The search for the true cause of influenza has been one of the great "treasure-hunts" of medical research. Since the time of Koch and Pasteur extensive efforts have been made to identify the causative agent of this disease.

MR. CROSS: With any success?
DR. FRANCIS: Well, as far back as 1891, Pfeiffer described a bacillus which he called the influenza bacillus. It seemed then that the goal had been reached... the treasure found... but through the succeeding years it became apparent that the influenza bacillus did not furnish the solution, for even in 1918 investigators could not establish an exclusive relationship between Pfeiffer's bacillus and the disease itself.

MR. CROSS: That sounds like a blind alley...

DR. FRANCIS: Well, no... you couldn't call it that, exactly. In 1931 Shope demonstrated that a disease of swine... the so-called "hog-flu"... was caused by a filterable virus acting in conjunction with a bacterium similar to Pfeiffer's bacillus. Another great step forward was made two years later when it was demonstrated by British workers, that secretions from the respiratory tracts of human influenza patients contained a virus which could transmit the disease to ferrets. Coincident with this was the discovery that in the blood of a large proportion of the adult population there were antibodies indicating that they had previously been infected with the virus.

MR. CROSS: Did the presence of these antibodies in the blood produce any type of immunity, Dr. Francis?

DR. FRANCIS: No... it was found that even if antibodies were present it was possible for man to be reinfeächted by the same virus. A sharp rise in antibodies followed this second attack... and thus, proof was obtained that permanent immunity is not derived from one attack of the disease.

MR. CROSS: How does this fact affect the search for a method of immunizing against influenza, Dr. Francis?

DR. FRANCIS: Before I answer that directly, Mr. Cross... there is some additional information that should be mentioned.

Every second year what is now termed virus we have been ever, there were o disease but which caused by this vir able, finally, to iso influenza "B"... experimentally a e sense, however, more types.

MR. CROSS: That has r a lem, I should judg

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MR. CROSS: Both after i

DR. FRANCIS: Yes, after "A" is immune to versa. Moreover, animals immune cutaneously... tions the virus do... but, rather, and distinctly e resist infection. I shown that the in creases the power inactivate the vir see what it mean
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Every second year from 1932 to 1940-41, epidemics of what is now termed influenza "A" were produced by the virus we have been talking about. In 1936 and 1940, however, there were outbreaks of what looked like the same disease but which yielded no evidence that they were caused by this virus. From the 1940 epidemic we were able, finally, to isolate a new virus ... now referred to as influenza "B" ... which produced both clinically and experimentally a disease similar to influenza "A." In one sense, however, ... that of immunity, they represent two different diseases. There may eventually prove to be even more types.

MR. CROSS: That has rather a complicating effect on the problem, I should judge....

DR. FRANCIS: Yes ... but the prospects for effective immunization are not so gloomy as this sounds. In the first place, it is quite clear that both in man and in animals, there is a period of unknown duration after recovery in which the individual is immune to reinfection....

MR. CROSS: Both after influenza "A" and influenza "B"?

DR. FRANCIS: Yes, after both. The individual recovered from "A" is immune to "A" but not necessarily to "B", and vice versa. Moreover, we have discovered that we can make animals immune to influenza by injecting the virus subcutaneously ... that is, under the skin. Under these conditions the virus does not cause the characteristic infection ... but, rather, it induces the production of antibodies and distinctly enhances the ability of the animals to resist infection. Now ... in man ... it has been clearly shown that the injection of the virus under the skin also increases the power of secretions from the nose to combat and inactivate the virus. All right ... let's add this all up and see what it means. We know that the virus ... under nat-
ural conditions... enters the body by means of the respiration tract... through the mouth and nose. If we increase the ability of the secretions of the respiratory tract to power the virus... and we can do that by injecting the virus under the skin... then it seems very likely that we may have a very potent weapon against influenza.

Mr. Cross: Well, then, Dr. Francis... what net progress has been made? Can this method of virus-injection produce a real, lasting immunization?

Dr. Francis: In the past several years, Mr. Cross, there have been a number of studies by different investigators aimed at answering just the questions you ask. They are trying to determine whether subcutaneous vaccination can protect human subjects against epidemic influenza. Just a year ago, members of the Commission on Influenza of the Army Epidemiological Board undertook another investigation. A concentrated vaccine was prepared from virus developed in hen's eggs. Influenza virus of both types "A" and "B" were included.

Mr. Cross: This work was done by the Army, you say?

Dr. Francis: Yes... in cooperation with other agencies. The subjects selected for the investigation were 12,500 men in the ASTP units at eight universities in different parts of the country and a group of five medical and dental schools. These various groups were studied by members of the Influenza Commission from the Rockefeller Foundation, Cornell Medical School, Minnesota and California Departments of Health, the University of Iowa Medical School and my associates at the University of Michigan School of Public Health. The subjects were divided into two groups. One half received the vaccine; the other half... the controls... received an injection of simple physiological salt solution.
Mr. Cross: I see. Then, actually, the subjects themselves did not know if they were or were not getting vaccine.

Dr. Francis: That's correct. In a sense, we were quite lucky because shortly after this study had been instituted, an epidemic of influenza "A" was detected in the Middle West and it spread rapidly throughout the country. Thus, it was possible to compare rather accurately the incidence of the disease in the two groups.

Mr. Cross: What were the results, Dr. Francis... did they justify the use of the vaccine?

Dr. Francis: Well, among the 6,263 vaccinated men only 2.2 per cent developed influenza...

Mr. Cross: And in the control group?

Dr. Francis: In the control group... 6,211 subjects... the number who came down with influenza came to 7.1 per cent.

Mr. Cross: 7.1 per cent as against 2.2 per cent. More than three times as many. That sounds quite encouraging.

Dr. Francis: Yes... it was most encouraging, Mr. Cross. In most places 3 to 4 times as many became sick among the controls as among the vaccinated. In certain units influenza was 5 to 6 times more frequent among the controls than among those who had been vaccinated. There is reason to believe that the benefit was even greater than these figures indicate.

Mr. Cross: Would you say, then, that vaccination can prevent influenza, Dr. Francis?

Dr. Francis: I would say that the evidence is clear cut: vaccination probably, will eventually prevent influenza in most cases. How long the effect lasts, and numerous other factors...
are not fully known. Other procedures which may increase the effect of vaccination still remain to be studied... but at last... the possibility that influenza can be controlled by preventive measures has been demonstrated.

**MR. CROSS:** Well, it would seem that this will represent a major medical triumph.

**DR. FRANCIS:** I certainly agree. Together with our new drugs... the sulfa drugs and penicillin for the treatment of bacterial complications... and the possibility of sterilizing the air in rooms occupied by influenza patients, there is a new outlook upon the conquest of influenza. Perhaps... soon... we will be able to say that one of the last of the unconquered scourges can be conquered!

**MR. CROSS:** Thank you, Dr. Francis!

"THE DOCTORS TALK IT OVER" has brought you a discussion by Dr. Thomas Francis, Jr. on "The Outlook for the Control of Influenza." Copies of Dr. Francis' remarks are available to our professional listeners and may be obtained by addressing a request to Lederle Laboratories, Inc. 30 Rockefeller Plaza New York 20 New York.

This is Milton Cross saying good evening and inviting you to join us again next week for an informal discussion of medical problem of the day as "THE DOCTORS TALK IT OVER."