as accepted by Osler may serve to minimize the confusion which has arisen relative to the causative organism in the disease. Leichtenstern has divided influenza into three types: first, epidemic influenza vera, caused by Pfeiffer's bacillus; second, endemic-epidemic influenza-vera, which often occurs for several years in succession after a pandemic, caused by Pfeiffer's bacillus; and third, endemic influenza nostras, a pseudo-influenza or catarrhal fever, commonly called grip, caused by various organisms alone or in combination.

The importance of knowing the causative organism is more appreciated during these days when vaccines and sera are of so much importance in the prevention and treatment of so many diseases. The opportunities given in our army camps for studying the disease under controlled conditions will doubtless throw considerable light not only upon the epidemiology of the disease but also upon the organisms concerned in producing such epidemics as the present one.

REFERENCES.

1. KEEGAN. Jour. Am. Med. Assn. 1918. *71*: 1051.
2. OSLER. Principles and Practice of Medicine. Eighth edition.
3. WEAVER. Jour. Am. Med. Assn. 1918. *70*: 26.
4. MATHERS. Jour. Am. Med. Assn. 1917. *68*: 678.
5. PFEIFFER. Ztschr. F. Hyg. u. Infektionskr. 1893. *13*: 357.
6. DAVIS. Jour. Am. Med. Assn. 1915. *64*: 1814.
7. WILLIAMS. Bull. Dept. of Health, N. Y. Feb. 1916.
8. CLAPPS and MOODY. Jour. Am. Med. Assn. 1916. *67*: 1349.
9. HEWLETT and ALBERTY. Jour. Am. Med. Assn. 1918. *71*: 1056.

◈

THE USE OF INFLUENZA VACCINE IN THE PRESENT EPIDEMIC.

TIMOTHY LEARY, M. D.,
Professor of Pathology and Bacteriology, Tufts College Medical School, Boston, Mass.

THREE strains of influenza bacilli obtained from cases during the present epidemic have been used in the manufacture of vaccine. Strain "Carney" came from a culture from the nose of a nurse at the Carney Hospital. It was present in association with a white staphylococcus in abundant growth, in contrast to the picture obtained in most nose and throat cultures, which do not usually show the influenza bacillus. Strain "Navy" was procured from Lieutenant Keegan at the Chelsea Naval Hospital. Strain "Devens" was obtained from Major Spooner through Doctor Allen.

The technic used in the preparation of vaccine follows: 1½ per cent agar has been prepared from meat infusion (beef hearts) without glucose, and made 1 per cent acid to plenolphthalein. This is autoclaved for forty-five minutes at fifteen pounds pressure after tubing. Three to five drops of human blood are added to each tube. Blood is collected from the median basilic vein—15 to 40 cc. Poorest growth occurs when the blood is added to agar at 60° C. or below. Most abundant growth appears in tubes to which blood is added, with the agar at 80° to 90° C. The greater heat leads to a brown discoloration of the blood. Colonies on red agar (60° C.) are small, translucent and discrete, and produce a fine frosting on the surface. The growth on brown agar (80° to 90° C.)

is heavier, tends to be confluent, and more opaque.

Experience seems to indicate that organisms grown on red blood agar retain their virulence in higher degree, and furnish a more efficient vaccine. Brown blood agar furnishes a more abundant crop.

After the addition of blood the agar is slanted, cooled and incubated twenty-four hours in order to control its sterility.

We have prepared in this way up to 4,000 tubes of blood-agar per day.

Seed for planting is grown on selected red tubes. Heavy seeding of tubes used for vaccine is obtained by mixing the growth on the surface of seed tubes with the water of condensation, and transferring with a loop large amounts of the emulsion to the whole of the surface of fresh tubes.

Cultivation is carried out for fifteen to eighteen hours at 37° C.

After careful inspection of growths, with a hand lens, and the discarding of all doubtful tubes, 2 cc. of saline solution are added to each tube. The growth is scraped from the surface and emulsified by means of a platinum loop and shaking. The saline suspensions are collected in small flasks and filtered through sterile gauze, to remove fragments of agar. The suspensions are then exposed to 56° C. for twenty-five minutes in a water bath. The killed suspensions are then pooled in a large bottle and added to .5 per cent carbolized saline in a proportion varying from 1 to 10 to 1 to 20, depending upon opacity. Since we have been able to obtain Three Cresols, the suspensions have been diluted directly in saline solution, containing .4 per cent Three Cresols, and have not been exposed to heat. The dosage is essentially 400,000,000 per half cubic centimeter.

We have bottled vaccine in 10 cc., 30 cc., 50 cc., and 100 cc. amber bottles, closed with test tube caps or closed nursing bottle nipples.

Sterility of vaccine is controlled by transfer of 1 cc. from each of ten bottles of each lot to blood agar, and to 25 cc. 1 per cent glucose bouillon in fermentation tubes. If controls are not satisfactory at first, storage of the vaccine will usually result in sterile controls within a few days.

Dosage.—The prophylactic dosage has been .5 per cent cc., 1 cc. and 1.5 cc. in three doses at twenty-four hour intervals. The therapeutic dosage has been .5 cc. every twelve hours. It is probable that all of these doses are too small, notably the therapeutic dose. Many men are obtaining best results with 1.5 to 2 cc. at twelve to twenty-four hour intervals.

Prophylactic Use.—The prophylactic use of vaccine will not furnish as high protection as does typhoid prophylaxis, probably because the exposure is greater and infection more readily produced. The percentage of complete protection appears to be high, and there is marked amelioration of symptoms in those who do come down, and pneumonias appear in very few cases.

Therapeutic Use.—The therapeutic use of vaccines is followed by the best results when large doses are exhibited early in the disease. It should be possible to abort a large percentage of the cases, and prevent the development of pneumonia. After pneumonia has developed, many clinicians report excellent results under large doses of vaccine. The disease is a local disease, usually limited to the respiratory tract. Blood cultures are constantly negative during life or after death. If the pneumococci or streptococci which occur in symbiosis with the influenza bacillus in the lung processes were important factors, one would expect to find them present in blood cultures at some time in the course of the disease. For

Continued on page 768.

primarily upon the intestinal flora and the resistance of the intestinal wall; but the conditions with which Puntoni worked were so extreme that they do not appear of special interest from a practical standpoint.

2. On the other hand we find that the odors from moist feces do have a real, although slight and transitory, influence upon the growth curve of guinea pigs. For the first week of exposure, animals breathing such gases gain in weight less rapidly than normal controls. Later they become accustomed to the odors and grow as rapidly as the controls, indeed tending to catch up with them in weight by the end of the second week. The difference between these results and those reported by Delépine may most probably be explained by the fact that gases of putrefaction must have been in much lower concentration in his experiments, although the number of animals used by him was in any case perhaps too small to reveal such slight differences as we have found. Our results may probably be considered to be analogous to those reported by the New York State Commission on Ventilation in regard to the effect of stale air upon the appetite of human beings.

3. Finally it may be concluded that the effect of putrefactive odors upon resistance to disease remains unproven (unless they are present in such extreme concentration as to be directly toxic, as in Puntoni's experiments). It does appear, however, that such gases may exert a real but transitory effect upon the appetite for food in human beings, and upon the growth curve of guinea pigs, an effect which in each case tends to disappear as the subjects become accustomed to the odors in question.

THE USE OF INFLUENZA VACCINE IN THE PRESENT EPIDEMIC.

By Timothy Leary, M. D.

Continued from page 754.

these reasons the objections which are made to the use of vaccines in the treatment of septicemias do not hold in the pneumonias of the present epidemic.

Each injection of vaccine should be made into a new muscle group. It is the belief of the writer that the muscles are important producers of immune substances. In no other way is it possible to explain the rarity of bacterial infection of muscles, even when the viscera, blood and lymphatic systems show deep infections. In a local disease, limited as this is to the respiratory system, it should be possible theoretically to awaken the muscle groups to an activity, which they do not exhibit in response to an infection in which the organisms are localized in one part of the body.

Vaccine treatment is not recommended in moribund cases with massive pneumonias and cyanosis. Unlike antitoxins, vaccines require reacting ability on the part of the patient.