different appropriations to carry on the work, the preliminary estimates of the Federal Children's Bureau having been found to be inadequate. (Appropriations were: $1,200,000; $4,400,000; and $18,620,000. See CALIFORNIA AND WESTERN MEDICINE, October 1943, on page 226.) These appropriations indicate that Congress will be called on to grant still further deficiency allocations. How soon such call may be made is not known. The increasing number of pregnancies will determine that.

In the meantime, if physicians throughout the United States—by action of their several state and county medical societies—will acquaint their respective Congressmen with the issues involved, it may be possible to bring into being specific instructions from Congress to the Federal Children's Bureau, making it mandatory upon the Federal Children's Bureau to offer a more equitable and reasonable set-up than that which is now being carried on. Presumably, that is the only way in which a rectification of the existing deplorable edicts may be remedied. The solution of the problem depends, therefore, upon national coöperation through the State and component county medical societies.

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**General Practitioners Should Be Added to the "Advisory Board of the Federal Children's Bureau."**—On October 21, 1943, in Washington, D. C., the "Maternal and Child Health Advisory Committee" of the United States Children's Bureau held a meeting, the official minutes of which appeared in *The Journal of the American Medical Association* (November 27, on page 845). The last item, number 9, refers to a "recommendation" that "at least five general practitioners be added to the Advisory Committee."

As a matter of justice to the thousands of general practitioners who, in practice, will be called upon to carry through and do the obstetric-pediatric work, the addition of ten rather than five general practitioners, representing different sections of the country, would seem to be quite in order. Certainly, the present members of the Advisory Committee should not object. And if they did, on what grounds?

It will be interesting to note whether the Children's Bureau representatives (Miss Katherine Lenroot, chief; Dr. Martha M. Eliot, associate chief; and Dr. Edwin F. Daily, director, Division of Health Service) who were present at the last Advisory Board meeting of October 21 will have acted or so recommended when that Committee again convenes in Washington, D. C., at the meeting that has been called for December 10 to 11, 1943. The recommendation for five general practitioners was made at the October 21 meeting, but the official minutes gave no indication that action had been taken thereon up to November 23. Concerning that item and the session that since has been called, possibly more anon.

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One half of the world knows not how the other half lives.

—George Herbert, *Jacula Prudentum.* (1640).

# EDITORIAL COMMENT†

## TYPES OF TETANUS TOXIN

Hitherto unsuspected qualitative differences between different preparations of tetanus toxins are reported by Friedemann [1] and his associates of the Brooklyn Jewish Hospital.

Seven tetanus toxins were bioassayed by the Brooklyn physicians, four of which were obtained from different American firms, and one from Germany. The minimal lethal dose was determined for each toxin by five different methods: (*a*) intraventricular injection into rabbits and guinea pigs, and (*b*) intramuscular injection into rabbits, guinea pigs, and mice. From data thus obtained the calculated titers of the toxins varied from 3,200 to 20 (intraventricular) M. L. D. per c.c. for rabbits and from 64,000 to 800 (intramuscular) M. L. D. per c.c. for guinea pigs. As a wholly unsuspected finding, the relative titers of the seven toxins varied with the animal species and method of testing. If the seven products were arranged (ABCDEFG) in a descending scale of toxicity for rabbits (intraventricular test), the order would be BACEDGF for ginea pigs (intramuscular test), and CAEBG (D and F not tested) for mice (intramuscular test).

The differences became even more apparent on comparing individual toxins. In rabbits (intraventricular test) toxin D, for example, is ten times more potent than toxin G. Tested by the intramuscular route in guinea pigs, however, G is only 60 per cent stronger than D. In rabbits, D is 100 times more potent by the intraventricular than by the intramuscular route, while the corresponding ratio is but 10:1 for toxin A. In guinea pigs, C is but twice the intramuscular titer of B, while it is eight times stronger in mice.

Further differences became apparent on determining the amount of antitoxin necessary to neutralize the different toxins, antitoxin prepared by the Bureau of Laboratories, New York City Department of Health being used in all tests. In order to simulate conditions of the natural disease, an "indirect" method of titration was adopted. A constant dose of tetanal toxin (20 intraventricular M. L. D. in the guinea pig and 10 M. L. D. in the rabbit) was injected into the intraventricular space, preceded by an intravenous injection of varying amounts of antitoxin. Control "direct" titrations were also made, the same dose of toxin being mixed *in vitro* with varying amounts of antitoxin and the mixtures injected intraventricularly. The two methods gave inconsistent results. By the "indirect" test in guinea pigs, toxin A required 100 times more antitoxin per unit for its neutralization than toxin F, and 64 times more than toxin E. On "direct" test, however, toxin A required but half the amount of antitoxin necessary for the neutral-

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ization of an equal dose of toxin E. By the "indirect" method in rabbits all seven toxins were neutralized by exactly the same volume of antitoxin, while in the "direct" tests in rabbits the antitoxin requirements varied for the individual toxins.

These unsuspected results prove that, in addition to the currently recognized quantitative differences between different preparations of tetanus toxin, there are equally important qualitative differences. Whether or not these are due to different types of *Cl. tetani* has not yet been determined. The antitoxin titrations also show that there are hitherto unsuspected physiological factors that must be taken into account in antitoxin therapy.

Publication of additional data is promised for the near future.

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## SPREADING FACTOR IN SWINE INFLUENZA

In 1931, Shope [1] established that swine influenza is caused by the concerted action of two infectious agents, an ultravirus and a bacterium. While there is at present lack of evidence of a necessary bacterial component in interpandemic cases of human influenza,[2] data obtained in army camps in 1918 suggest that pandemic human influenza may possibly be of such duplex etiology. In anticipation of the next human pandemic, a simple technique for the study of virus-bacterial synergism has been developed by Bang [3] of the Rockefeller Institute, Princeton, New Jersey, based on the use of the nine-day chick embryo.

Burnet [4] and others had previously found that influenza virus placed on the chorioallantoic membrane of the chick embryo rarely gives rise to virus infection of the lungs and other underlying tissues. If the virus is injected through the chorioallantoic membrane into the amniotic fluid, however, the trachea, lungs and other underlying tissues are readily infected. Bang found that if a drop of virus filtrate is placed on this membrane, and if twenty-four to forty-eight hours later there is a superimposed infection with *H. influenza suis,* a rapidly fatal lung infection often develops. In one of his series there were but three fatalities among thirty-six control embryos infected with the virus alone and but five fatalities among an equal number infected with the bacillus alone. Among thirty-five chick embryos subjected to the combined inoculation, twenty-three (66 per cent) died. Histological studies showed that death was accompanied by a selective destruction of the embryo lung. Control tests showed that such destruction was not produced by either infectious agent acting separately.

Bacteriological studies revealed no influenza bacilli in the internal organs of the embryo. There was no demonstrable increase in the virus titer on the chorioallantoic membrane, but a high virus titer was demonstrable in the underlying amniotic fluid. The sole action of the bacteria, therefore, seemed to be due to a "spreading factor" facilitating penetration of the virus through the chorioallantoic membrane.

This interpretation of the nature of the virus-bacterium synergism is confirmed by the fact that filtered extracts of frozen, dried, or heat-killed *H. influenza suis* have the same synergic action. The filtrate retains its spreading power even after heating to 100 degrees centigrade for 30 minutes. Virus-spreading effects are also demonstrable when purified preparations of hyaluronidase are substituted for the Hemophilus filtrate. Hyaluronidase, however, does not cause a comparable increase in mortality. It seems probable that increased spread of the virus to the underlying tissues is only partly responsible for the mortality, and that other bacterial products play a rôle in chick mortality.

Bang's synergic theory and technique are of particular clinical promise, should occasion arise, to apply them to human pandemic influenza. Whether or not the Hemophilus "spreading factor" is antigenic has not yet been determined.

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MEDICAL EPONYM

### *Waldeyer's Ring*

This was described by Professor H. Wilhelm G. Waldeyer (1836-1921) of Berlin at the meeting of the Berlin Society for Internal Medicine on May 5, 1884, in a paper entitled "Ueber den lymphatischen Apparat des Pharynx [The Lymphatic Apparatus of the Pharynx]." This was reported in abstract in the *Deutsche medicinische Wochenschrift* (10:313, 1884). A portion of the translation follows:

"Since the discovery of the pharyngeal tonsil by Lacauchie, the tubal tonsil by J. von Gerlach, and the establishment of the fact that the follicles of the tongue together represent a superficially spread-out tonsillar structure (the lingual tonsil), it is now evident that a ring of lymphatic tissue surrounds the whole region of the throat and upper pharynx, the course of which may be traced as follows: beginning with the pharyngeal tonsil, it extends to the region around the orifice of the eustachian tube (the tubal tonsil), thence to the faucial tonsil and down along the margin of the glossopalatine arch to the lingual tonsil, whence it crosses to the opposite side and follows a similar path back to the pharyngeal tonsil.

"The tonsils simply represent marked accumulations of lymphatic tissue, which is nowhere absent in the above-mentioned region, being demonstrable even in all the intertonsillar spaces. The investigations of the speaker show that the lymphatic tissue also extends deeply into the nares as the center of the middle and lower turbinates and downward onto the posterior wall of the pharynx. This ring of adenoid tissue may be termed 'tonsillar ring' or the 'lymphatic ring of the throat.'"—R. W. B., in *New England Journal of Medicine.*