with a wax crayon. Then fill to the mark with the stock standard solution and discharge into a small volume of water in a test-tube. Draw up a little water and discharge this also into the test-tube. In another tube place 5 cc of the dilute standard solution. Make both tubes up to equal volumes with water and proceed with the determination in the usual way. With the standard set at 20 a reading at 20 would, of course, mean that the crayon mark is correct.

It is, of course, necessary that the 5 cc pipette be correct, as all capillaries will reproduce whatever error it may have.

The method may be employed to calibrate any size pipette by using solutions of appropriate concentration. The volume of a single drop also may be determined: a great convenience sometimes.

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# SPECIAL ARTICLES

## PREVENTION OF EXPERIMENTAL EQUINE ENCEPHALOMYELITIS IN GUINEA PIGS BY MEANS OF VIRUS ADSORBED ON ALUMINUM HYDROXIDE

RHOADS[1] reported the prevention of experimental poliomyelitis in monkeys by the use of virus adsorbed on aluminum hydroxide, Wilstaetter's Type C.[2]

In experiments with the virus of equine encephalomyelitis[3] an attempt was made to immunize guinea pigs against the experimental disease by means of the virus so adsorbed. It was found, however, that the adsorbent, when injected subcutaneously in amounts comparable to those previously employed, produced large, nodular masses which resolved with difficulty and often became inflammatory. Inasmuch as aluminum hydroxide prepared at pH 6.6 and sterilized by heat adsorbs as much as 99 per cent. of the virus from active material, the use of less than one twentieth of the amount of the colloid hitherto employed resulted in active immunization of the test animals. Moreover, the sites of injection showed only inconsiderable, localized indurations that disappeared within 5 or 6 weeks.

The source of virus was either the brain of guinea pigs which had succumbed to the experimental disease, or tissue cultures.[4] The latter were found to be more desirable, since less protein is present and hence less adsorbent is required. Another advantage is that in tissue-culture virus concomitant infectious agents can more easily be controlled.[5]

Guinea pigs received three subcutaneous injections of one cubic centimeter each, at 7-day intervals, of the adsorbed virus. The adsorption is of such a character that none of these animals revealed signs of infection during the period of immunization. On the tenth day after the third injection, they were shown to be resistant to an intracerebral inoculation of virulent guinea pig brain material in dilutions of 1:600 to 1:1600.[6] It should be emphasized that the virus was introduced directly into the brain in the test dose, which was lethal for control animals in dilutions of $10^{-5}$ or $10^{-6}$ when given subcutaneously or intracerebrally, respectively.

Thus far 40 guinea pigs have been inoculated with the aluminum hydroxide-virus material: 16 with the Western strain of tissue-culture virus, 10 with a mixture of Eastern and Western strains of similar material; 9 with the Eastern strain of guinea pig brain virus, and 5 with a mixture of Eastern and Western strains of the brain virus. None of these animals was affected after the intracerebral injection of the homologous strains as a test for resistance. On the other hand, all the 14 control, non-immunized guinea pigs died of experimental encephalomyelitis within from 72 to 96 hours after the test inoculation.

Investigations are now under way on the possible use of this method in preventing experimental encephalomyelitis of the monkey and the horse, the length of time the adsorbed virus retains its potency (thus far determined to be at least 10 weeks), and the duration of the resistance after the immunization.

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## THE THERAPEUTIC BEHAVIOR OF LUCILIA SERICATA MEIG. LARVAE IN OSTEOMYELITIS WOUNDS

THE blowfly maggot (*Lucilia sericata* Meig.) removes by ingestion the acid-forming and bacterial-

[1] C. P. Rhoads, *Jour. Exp. Med.*, 53: 399, 1931.

[2] R. Wilstaetter and H. Kraut, *Ber. chem. Ges.*, 56: 149, 1923.

[3] We are indebted to Miss B. Howitt, of the University of California, for the Western, and to Dr. C. Ten-Broeck, of the Rockefeller Institute, for the Eastern strain of the virus.

[4] H. R. Cox, J. T. Syverton and P. K. Olitsky, *Proc. Soc. Exp. Biol. and Med.*, 30: 896, 1933; J. T. Syverton, H. R. Cox and P. K. Olitsky, SCIENCE, 78: 216, 1933.

[5] T. M. Rivers and S. M. Ward, *Jour. Exp. Med.*, 58: 635, 1933.

[6] All operations on animals were performed with the aid of ether anesthesia.

growth-promoting necrotic tissue from an osteomyelitis wound by means of the macerating activities of the powerful mouth-hooks and predigestion, or liquefaction, by the tryptase present in the excreta, as shown by Hobson[1,2,3] and Mackerras and Freney[4] in experiments with maggots upon carrion. The action of this excreted tryptase, which arises in the mid-gut, is dependent upon an alkaline reaction which is imparted to the wound by ammonia in the feces and by calcium carbonate, which is continually exuded in small quantities through the body wall.[5] The removal of the necrotic tissue and the alkalization of the wound result in a reduction of the swelling of the soft tissue, with consequent increased drainage and decreased bone destruction, in protection to the tissue cells from autolysis stimulated by an acid condition and in retardation of bacterial growth. The calcium ions liberated from the exuded calcium carbonate stimulate phagocytosis.

The characteristic healthy granulation of wounds treated with blowfly larvae is, from experimental evidence,[5] apparently due to the alkalization of the wounds.

The increased rate of growth of larvae placed in wounds in which these organisms have been employed for some time and the occasionally high mortality of young larvae placed in such wounds are both due to ammoniation of the wounds by larval activity.

Bacteriological tests of the mid- and hind-guts of maggots previously fed upon *Staphylococcus aureus*, the most common etiologic agent of osteomyelitis, are consistently negative, but histological examinations of similar guts show undissoluted bacteria to be as numerous in the rectum as in the proventriculus. Hobson[1,3] has shown that the middle segment of the mid-gut of *L. sericata* larvae has a pH value of from 3.0 to 3.5. Exposure at 30° C., the apparent minimum temperature of an osteomyelitis wound, of growths of *S. aureus* to McIlvaine's Buffer Solutions ranging through pH values of 3.0, 3.2 and 3.5 demonstrated that marked mortality occurs at the highest pH and at a pH of 3.2 complete killing was effected well within the time limit during which the food is retained in the acid region of the mid-gut. Thus are many of the pathogenic organisms removed from the wound; however, not enough of them are ingested to make this the chief factor in securing propitious results.

It is believed that a considerable portion of the destructive leucocidin liberated by the bacteria is ingested by the maggots and probably rendered inert in the acid region of the intestines by means of the direct action of the acid or by virtue of its possession of an isoelectric point close to, or at, the point of concentration of the acid.

The writer succeeded in readily developing extensive myiases in guinea pigs and in one human with *L. sericata* larvae. It was demonstrated that these maggots will readily attack normal, healthy tissue if necrotic tissue is not present, and even if it is present but not immediately accessible. It was further demonstrated, however, that these organisms do prefer necrotic tissue, provided it is exposed to their action at the time of implantation into the wound. From these findings it becomes apparent that blowfly larvae are potentially dangerous in human wounds and must, therefore, be employed with care and skill.

Brumpt[6] has suggested that the larvae of the French and Chinese strains of this fly will attack normal tissue but the American strain will not. The writer has demonstrated such not to be the case by easily and repeatedly causing experimental myiases in guinea pigs, with no necrotic tissue present, with two different American strains.

Furthermore, the author caged seven sterile *L. sericata* larvae upon perfectly intact, healthy epidermis of his fore-arm which penetrated the skin and subcutaneous tissue to a depth of 3 mm in less than forty-eight hours.

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# THE NATIONAL ACADEMY OF SCIENCES. III

*The unification of relativity theory and quantum theory:* SIR ARTHUR STANLEY EDDINGTON. The basis of unification is that *a priori* probability in quantum theory furnishes the metric in relativity theory, the metrical tensor $g_{\mu\nu}$ being identified with the energy tensor of the *a priori* probability distribution of the N particles of the system. The wave equation for a particle refers to a system in which one particle has a modified momentum distribution and the remaining N–1 particles (which are averaged) have the *a priori* distribution. The double wave function of this system is in practise replaced by a simple wave function, the physical system of N–1 particles being replaced by an ideal comparison frame which is treated as definitely known instead of as a probability distribution. The condition that this substitution is valid gives a quadratic equation for the mass associated with the simple wave function, and the two roots are the masses of the proton and electron, respectively.

[1] Hobson, *Jour. Exp. Biol.*, 8: 109, 1931.
[2] Hobson, *Biochem. Jour.*, 25: 1458, 1931.
[3] Hobson, *Jour. Exp. Biol.*, 9: 359, 1932.
[4] Mackerras and Freney, *Jour. Exp. Biol.*, 10: 237, 1933.
[5] Stewart, *Surg. Gynec. and Obst.*, 58: 155, 1934.
[6] Brumpt, *Ann. de Parasit. Hum. et Comp.*, 11: 403, 1933.