

lactic agent; in fact, it may have little or no therapeutic value. Thus, firms are licensed to sell normal horse serum or normal goat serum, provided they are honestly labeled and free from impurities. Further, antistreptococcic serum, antityphoid serum and other antisera of weak and doubtful efficiency and substances in the experimental stage are sometimes licensed. The law provides for the license of biologic products "applicable to the prevention and cure of diseases of man."

It is evidently the province of the medical profession to determine for itself whether a certain substance has therapeutic value or not. The chief concern of the government is to protect the practitioner against sophistications, impurities, faults or mislabeling.

LABORATORY CONTROL

Samples are purchased on the open market by officers of the Public Health and Marine-Hospital Service in all parts of the country and sent to the Hygienic Laboratory in Washington for examination as to potency and purity. Inspectors also obtain samples directly from the manufacturer, which are similarly examined. These examinations are constantly in progress. If any fault is found with a sample the manufacturer is required by the Surgeon-General to withdraw all of that particular product from the market. Antidiphtheric serum, antitetanic serum and vaccine virus are examined for potency and purity; all other serums and vaccines for purity only. All serums are tested to determine whether they contain an excessive amount of preservative.³

These examinations require a certain amount of technical proficiency which has been developed as a specialty in the division of pathology and bacteriology of the Hygienic Laboratory. In these examinations special attention is given to Section 2 of the law, which provides "that no person shall falsely label or mark any package or container of any virus, serum, toxin, antitoxin or product aforesaid; nor alter any label or mark on any package or container of any virus, serum, toxin, antitoxin or product aforesaid so as to falsify such label or mark."

LICENSED MANUFACTURERS

During the past year fifteen establishments were re-inspected and relicensed, and four additional establishments were inspected and licensed. A list showing the establishments which received licenses and the products for which licenses were granted appeared in *THE JOURNAL* of Sept. 18, 1909, p. 961.

GOVERNMENT GUARANTEE

The government does not guarantee that each vaccine point or each package of antitoxin will produce its full therapeutic effect and be free from all danger. This would be impracticable with the extent and variety of the business in biologic products now carried on in this country and abroad. It would be ideal if the government could guarantee the purity and potency of each package, but to do so would require more than supervision—it would almost mean government ownership.

Certain states and municipalities have found it convenient and economical to produce their own vaccine virus and diphtheria and tetanus antitoxins. The federal government has not gone farther than a legal surveillance, although it might some day be found desirable for the government to make these products for use in the medical services and territorial and insular possessions.

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3. Chloroform or trichresol (0.4 per cent.) are the preservatives commonly used.

VACCINE VIRUS

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Vaccine virus is the specific principle in the material obtained from the skin eruption of calves¹ having a disease known as vaccinia. The eruption begins as a papule, which develops into a vesicle, and later a pustule. For the purpose of propagating vaccine virus the material is usually taken from the vesicles when fully developed. This may be somewhere between the fifth and the eighth day after the animal has been vaccinated.

The material should be taken only from typical, unbroken vesicles, and is usually obtained by scraping with a curette. This material scraped from the skin eruption is called vaccine "pulp." The fluid which exudes after the pulp is taken is called vaccine "lymph." Both the pulp and the lymph are mixtures containing epithelial cells, serum, blood, leucocytes, products of inflammation, debris, bacteria, etc., in varying proportions.

The use of the pulp for the purpose of vaccination is of comparatively recent origin. Formerly the lymph was used extensively in a dried state on ivory points, constituting the so-called "dry points."

The specific principle of vaccinia is unknown. The organism, whatever it is, exists chiefly in the epidermal lesions, and the pulp, therefore, contains a more potent and concentrated virus than the lymph. Further, the pulp may be purified with glycerin or other substances, whereas the lymph dried on points is not amenable to such treatment. The pulp is mixed with glycerin in the proportion of about 50 to 60 per cent by weight. The glycerin acts as a preservative for the vaccine virus, but is an antiseptic for the frail non-spore-bearing bacteria. The germicidal action of the glycerin depends largely on the time and temperature at which the glycerinated pulp is kept. At ordinary temperatures the germicidal action of glycerin is feeble, and probably depends on its affinity for water.

Other antiseptic substances have been used for the purpose of purifying vaccine virus, viz., phenol (carbolic acid), potassium cyanid, chloroform, chlorbutanol (chlorotone), etc., but with less success in practice.

It is evidently impossible to obtain vaccine virus free from the bacteria of the skin. Practically all the vaccine virus on the market contains a certain number of harmless bacteria, such as the hay bacillus, common molds and spores which exist everywhere and are exceedingly difficult to destroy. It is evidently impracticable to use strong antiseptic methods on the skin of the vaccinated animal, for such substances would destroy the viability of the vaccine virus itself. In the propagation of vaccine virus, therefore, cleanliness and asepsis are the watchwords.

The dry points usually contain a larger number of bacteria than the ripened² glycerinated virus and are, therefore, less desirable. The new federal regulations forbid interstate traffic in the old-style dry points after Jan. 1, 1910.

In imitation of the old-style dry point, which is a very convenient method of vaccination, manufacturers have placed a small drop of glycerinated virus on ivory or glass points hermetically sealed in paraffin or glass. These are safe and satisfactory. In some instances

1. For obvious reasons vaccine virus of direct human origin is now little used in the United States.

2. Glycerinated vaccine virus is said to be "green" before the glycerin has had a chance to be effective. At ice-box temperatures this usually takes thirty days; then the virus is said to be ripe.

gummy substances, such as serum, dextrose, etc., are used to encourage the adhesion of the virus to the point. The glycerin may first be largely extracted from the ripened glycerinated virus by pressing it between blotting papers.

All vaccine virus is tested according to modern bacteriologic methods for streptococci, tetanus spores and other virulent bacteria. These tests include animal inoculations. The tests made by the manufacturer must be satisfactory before the virus is placed on the market and permanent records are required of each lot. Special tests are made to determine the absence of foot-and-mouth or tetanus infection.

The calves are kept in quarantine under observation for seven days before being vaccinated. Only healthy calves free from diseases of the skin are used for this purpose. The calves are killed or otherwise rendered insensible to pain before the virus is removed. The practice of renting calves for the purpose of propagating vaccine virus is no longer countenanced by the federal regulations. The animals must be autopsied as soon as practicable after the removal of the virus in order to determine the presence of lesions indicating other infections than cowpox (vaccinia). The federal regulations further require that the vaccine virus taken from an animal showing indications of complicating infections must be destroyed.

All establishments manufacturing vaccine virus for use in interstate traffic are required to operate under government supervision, which has been described in my article on "The Federal Control of Serums, Vaccines, Etc." (see p. 249, this issue).

Reports received by the Surgeon-General from health officers and others all over the country indicate that since the operation of the law the vaccine virus has been much more satisfactory than before.

WHY VACCINE VIRUS SHOULD BE IN THE PHARMACOPEIA

Vaccine virus was the first and it is the oldest and best specific preventive known. It is a drug in the broadest sense of that term, and as such is handled by every pharmacist. One of the first advantages in admitting vaccine virus into the Pharmacopeia would be to establish for it an official and legal name. This would help avoid much confusion now existing on account of the bacterial vaccines and other substances called "vaccines" used in the prevention and cure of disease. For almost a hundred years vaccination was a specific term limited to the introduction of the virus of vaccinia into the skin for the prevention of smallpox. In recent years the term "vaccination" has been used in a generic sense to include the introduction of many different substances, in many different ways and for many different purposes. To establish a definite and accurate nomenclature is one of the important functions of the Pharmacopeia.

Furthermore, a certain amount of confusion would be avoided and increased definiteness would be given to the various forms in which vaccine virus is marketed by adopting such titles as "virus vaccinium glycerinatum" and "virus vaccinium siccum," etc.

To include vaccine virus in the Pharmacopeia would be one of the best means of calling the attention of all pharmacists to the fact that it must be kept in a cool, dry place, etc. Much of the vaccine virus on the market is inert because not properly handled in the trade. Hence, concise, authoritative directions in the Pharmacopeia would have an educational value and would help prevent smallpox and save life.

The objection that vaccine virus is an indefinite substance, the "active principle" of which is not known, is no longer valid, for the Pharmacopeia contains many such substances, including the ferments, against which similar objection holds.

The objection that vaccine virus can not be "assayed" by the average druggist also lacks force when we recall that the potency and purity of vaccine virus in interstate traffic is cared for by the federal government under the law of July 1, 1902, which relieves the pharmacist of this responsibility. Further, other substances, such as serum antidiathericum, the testing of which requires special training and special laboratories, have been admitted into the Pharmacopeia.

The Pharmacopeia should briefly state the essential requirements of the law above mentioned concerning false labeling or marking of any package or container of vaccine virus; requiring further that each package of vaccine virus must be plainly marked with the proper name of the article, the name, address and license number of the manufacturer, and the date beyond which the contents can not be expected, beyond reasonable doubt, to give specific results. Such information in the hands of every druggist will serve an educational purpose and also help the federal authorities in the rigid enforcement of the law.

The Pharmacopeia should briefly state the method of preparing vaccine virus and specify the difference between glycerinated preparations and dry points and the other forms found on the market. As a precedent, it might be stated that the Belgian Pharmacopeia (third edition, 1906, page 194) has introduced vaccine virus under the title of "vaccinum," and the Swiss Pharmacopeia (fourth edition, 1907, page 512) has introduced vaccine virus as "vaccinum," synonyms: "Kuhpockenimpfstoff," "vaccine," "vaccin jennérien," "vaccino jennèriano."

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ANTIDIPHTHERITIC SERUM AND ANTIDIPHTHERITIC GLOBULIN SOLUTIONS*

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Until recently the only means we had of giving diphtheria antitoxin was in the whole serum of the horse in which it had originated. The accumulated knowledge obtained in the investigations of a number of workers allowed the development of a practical method for eliminating a portion of the non-antitoxic serum substances while retaining the antitoxin. Because of this, besides the whole serum, we have at present on the American market two globulin preparations containing diphtheria antitoxin. As these are rapidly displacing the whole serum, I will give a brief description of them.

GLOBULIN PREPARATIONS

The Gibson process of purification and concentration is based on the fact that antitoxin is associated with the globulins soluble in saturated sodium chlorid solution. This purification appeared to be considerable, as

* Read in the Section on Pharmacology and Therapeutics of the American Medical Association, at the Sixtieth Annual Session, held at Atlantic City, June, 1909.