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Original Articles

THE FEDERAL CONTROL OF SERUMS, VACCINES, ETC.

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Some seven years ago Congress for the first time passed a bill,¹ the object of which was to control the purity and potency of certain remedial substances which enter into interstate traffic. This enactment, which is now a law of the land, provides for a complete system of governmental supervision over the establishments producing vaccines, viruses, serums, toxins, antitoxins and analogous products. This surveillance consists of (1) inspections; (2) licenses and (3) methods of control or check-testing in the Hygienic Laboratory, which serve to verify the care and efficiency with which the products in question are made and marketed.

The law requires that each package of virus, serum, toxin, antitoxin or other product be plainly marked with the proper name of the article contained therein; the name, address and license number of the manufacturer, and the date beyond which the contents cannot be expected beyond reasonable doubt to yield their specific results.

The law further provides a penalty of \$500 or imprisonment not exceeding one year in the discretion of the court for any violations of its provisions, and provides a still greater penalty in the power to suspend or revoke licenses for cause.

It must be clearly borne in mind that the federal supervision over the biologic products in question applies only to interstate traffic in said articles. Thus, vaccine virus prepared by the Massachusetts State Board of Health for sale, barter or exchange in Massachusetts does not come under the purview of the law, but this vaccine virus cannot cross the state border without an inspection, license and government control, as required by the law of July 1, 1902, above referred to.

THE NEED AND USES OF THE LAW

At the first inspection it was found that irresponsible persons were making and marketing biologic products without sufficient care or knowledge to insure safety and reliability. I was surprised to note the haphazard way, the antiquated methods and the lack of care with which some of the biologic products were produced before the government took a hand in these matters. Four such firms were at once refused licenses, and, not being able to produce a safe and reliable product in accordance with

modern methods, they went out of business. Several applications from other persons or firms have since been refused licenses for similar reasons. Most of the remainder were required to remodel their establishments, change the personnel or improve their methods before being licensed to engage in interstate traffic.

Since the operation of the law a marked improvement has taken place in vaccine virus; standards for measuring the strength of diphtheria and tetanus antitoxins have been established; both the diphtheria and tetanus antitoxins found on the market have a decidedly increased potency; weak serums are forbidden;² contaminated or weak serums and vaccines which have been discovered have been promptly withdrawn from the market; false or misleading labels have been changed, and in general the licensed manufacturers have reached a high state of efficiency, and have spent much money to improve their personnel and property. The law has been enforced without fear or favor.

While the law has been a material help to the practitioner and his patient, it has also been of benefit to the manufacturers in pointing out defects, correcting faults, avoiding pitfalls, improving methods and inspiring confidence in their products.

THE INSPECTIONS

The inspections are made at least once a year, and oftener when necessary, by an officer of the Public Health and Marine-Hospital Service. These inspections are not perfunctory, but comprise a very searching inquiry into the methods of manufacture, the competency of those employed to carry on the work, and into the efficiency of the material equipment. Foreign establishments desiring to do business in the United States must submit to the same inspection, and are required to have licenses similar in all respects to those required of domestic establishments. To this some foreign establishments at first demurred, but when it was found that importations of their products without a license would be impossible they submitted to the law and its regulations.

At present every confidence may be had in all biologic products made under government license. These products are now carefully standardized whenever possible by uniform methods and are cautiously tested for impurities before being placed on the market.

THE LICENSE

The license is issued by the Secretary of the Treasury to the person or firm for a specific product. Each vaccine, serum, toxin and analogous product is considered separately; general licenses authorizing the manufacture of any and all biologic products are not issued.

The fact that a serum or vaccine is granted a license does not mean that it is a valuable curative or prophylactic.

1. An Act to regulate the sale of viruses, serums, toxins and analogous products in the District of Columbia, to regulate interstate traffic in said articles, and for other purposes. Approved July 1, 1902.

2. Before the law went into effect tetanus antitoxin was quite feeble. Diphtheria antitoxin must now have at least 250 units per c.c.; no minimal number of units has yet been set for tetanus antitoxin.

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 tricresol (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.