Plette; Standardization of Digitalis, H. C. Colson, Jr.; Some Color Changes in Solutions Containing Citro-chloride of Iron, W. R. White; The Microchemistry of the Alkaloids of *Datura stramonium*, Chas. O. Lee.

Officers of the Section for the ensuing year were then elected as follows: *Chairman*, W. W. Stockberger; *First Vice-Chairman*, E. V. Howell; *Second Vice-Chairman*, W. F. Gidley; *Secretary*, H. C. Fuller.

A vote of thanks was given the retiring officers of the Section for their work during the year, after which the Section adjourned.

W. W. STOCKBERGER,
Secretary.

BIOLOGICAL PRODUCTS FROM THE POINT OF VIEW OF THE PHARMACIST.*

BY L. E. SAYRE.

Pharmacy, like medicine, is extending its boundaries. In the period of a few generations it has passed from the crude drug, through elegant pharmacy—the "Elixir Period"—through the organic-synthetic period, and now has fully entered the biologic period. I shall take the liberty of using the term "biological" in its broadest sense.

It is needless to say, perhaps, that the medical profession regards biological products as constituting one of the most important groups of drugs with which the physician has to deal; this is the language of the volume, endorsed by the American Medical Association, entitled *Useful Drugs*.

The literature relating to this class of agents is extensive and of such a character as to invite the attention of the pharmacist, yet there is a lamentable ignorance of their production, application and of the valuable findings in this field of research. Taking the pharmacist as a class, they are satisfied to know how to cater to the business created by the physician and the manufacturer—to know how to "stock up" in a fair assortment, how to preserve and how to sell them. Since the varieties have become so numerous, this stocking up requires knowledge and judgment, it is true, because there is more or less of an individuality in products. Yet the criticism still remains. We know less than we should, and if we would keep abreast, as pharmacists, with the development of medical practice, it is incumbent that we should be as familiar with this part of our materia medica as with other portions. The physiological action of these agents should be known, and, with the relation that some of them have to specific infectious diseases, we should be acquainted. The potency and safety tests employed in their standardization are likewise important. We should at least be as familiar as the detail man who periodically visits the physician. Above all, we should know enough to have confidence in what we dispense as public servants.

This criticism is not made in the spirit of faultfinding; the writer can be censured as well—he, too, has not taken full advantage of the opportunities so available to meet the responsibility. It would be unfair to assume that many druggists would not make the same confession.

* Read before Scientific Section, A. Ph. A., Indianapolis meeting, 1917.

About 16 years ago (1901) the writer, as chairman of a special committee of this Association, reported on the advisability of admitting diphtheria antitoxin into the Pharmacopoeia. This report will be found in the published proceedings of that year. The decennial convention, which had met at Washington the year previous, had, by a ruling, practically prohibited the introduction of any remedial agent into that national standard that could not be standardized by any other than biological methods; now, in addition to recognizing several of the products, the Pharmacopoeia has introduced many valuable biological and clinical tests and reagents; this fact is incidentally mentioned to mark the development along the lines of medical practice. Our colleges, with much difficulty, are trying to meet the obligation this development demands. A few of our colleges have optional courses in bacteriology, but very few indeed lead to the study of these microscopical flora with a view to bringing about an appreciation of their functional processes and their application in different departments of science, departments closely connected with pharmacy. Sanitary science should engage the attention of the pharmacist. In sanitary water analysis there is employed the gas-forming bacteria. Many other of their physiological activities, such as pigment formation, toxin and ptomaine elaboration, are indirectly, at least, applicable to pharmacy. However much he may disclaim an interest, the pharmacist's point of view should be tinctured with some concern for those who are in training to meet future demands of our vocation. Pharmacists should urge that more optional courses in this subject be introduced along the line indicated, and as soon as possible have these courses changed from optional to required. Our representative educators should urge that our reorganized standard curriculum as published in the *Pharmaceutical Syllabus*, should at least acknowledge the value of this subject, if they would give our young pharmacists a chance for education in order to meet the demand of the times. The *Syllabus*, 2nd edition, makes no mention whatever of an outline for biological study, or a study of biological products. In connection with materia medica, occurs the paragraph: "Animal Drugs," in which are mentioned antitoxin and vaccines; no other reference than this to biological products or the study of biology, or bacteriology, is made. We have had presented at previous meetings of this Association brief outlines of biological study which might well form a basis of an outline to be adopted by the Syllabus Committee.

Our pharmaceutical literature, it is true, in periodicals and volumes, has contributed much information, the manufacturing houses have been exceedingly profuse in publications of valuable data, but these do not supply a systematic course which the writer feels should be prescribed for the pharmacy student of today.

These articles too often take for granted more knowledge than the reader possesses, they try to be elementary, but they often puzzle and bewilder the reader by slipping in words, undefined, that appear meaningless. It should be said, however, to their credit, that some of the manufacturing houses have issued primer-like compends, which, as far as they go, are quite satisfactory. It might be well to have some of these reprinted in our JOURNAL.

It must be admitted, of course, that the principal concern of the pharmacist is in the distribution or dispensing of these products. In so doing he regards storage, selection of stock and familiarity with certain talking points as important.

This service of dispensing, one of our largest manufacturers tells me, is now given by the majority (or the "cream") of the drug trade. Several contributions have been made, by pharmacists of experience, on the handling of biological products; one of these, worthy of mention, was presented by H. H. Whyte.[1] In his allusion to the cold storage of them, he refers to the advantage of the special refrigerator, which is furnished in different sizes, now coming into common use. He also refers to the rapid deterioration of the specially susceptible vaccine virus, quoting Dr. Elgin's tabulation, which, in substance is as follows:

If kept at the following temperatures it becomes inert: 140° F. in 5 minutes; at 98° F. (body temperature), in 3 or 4 days; at 70° F. is weakened in three weeks.

It remains active: At 50° F. from 3 to 6 months; at 10° F. for 4 years.

Another significant paragraph from this paper I am persuaded to quote:

"Without doubt a well-organized biological department is about the most desirable attribute of a well organized pharmacy. The work in itself is interesting—if properly conducted it is profitable and adds prestige to any store, and, above all, there is a satisfaction and gratification in knowing that you are aiding in saving life. The service which you render can put you in closer touch with the physicians and customers more than anything else that you can do and justifies your standing as a professional man in your community."

The A. M. A. list of approved *Useful Drugs* (including practically the same number as the U. S. P.) introduces the same by the following statement:

"There being no established standard for the various other products, they are not examined for their therapeutical value in the laboratory, but are tested for the amount of preservative and freedom from bacterial antitoxin contaminations."

As there is no recognized standard for, nor official recognition of, the various other products, a letter was addressed to a few of the manufacturing houses, asking the question which of the products, in their opinion, should be standardized, and officially recognized in the next revision of the U. S. Pharmacopoeia. As a result a flood of good literature was sent the writer, accompanied with the following suggestions:

From Dr. F. E. Stewart, who has contributed many papers to this Association upon biological products, comes the suggestion:

The Typho-bacterin is just as important an immunizing agent as diphtheria antitoxin, or small pox vaccine, and should be incorporated in the next revision of the Pharmacopoeia.

From A. W. Lescohier, the value of whose suggestions every one would appreciate, I am sure, is the following:

The products which occur to me as being worthy of inclusion in the next U. S. P. and which are not mentioned, are: Antirabic Vaccine, Luetin, Toxin Antitoxin Mixtures (overneutralized), Diphtheria Toxin, for Shick Test,[2] Pollen Extracts.

As far as antirabic vaccine is concerned, it is practically impossible to establish a definite standard because of lack of uniformity in the manufacturing methods used by different laboratories.

For instance, one way of its preparation is by the Cumming method, used in the Pasteur Department of the University of Michigan. We are confident that it surpasses in efficiency and

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[1] *Bull. Phila. Coll. of Pharm.*, Dec. 16, 1916.

[2] Schick Test.—The soluble toxic substance obtained by growing pure cultures of the *Bact. diphtheriae* in beef bouillon is used by intradermal injections to determine susceptibility to diphtheria; a positive reaction in persons exposed to infection indicates that a prophylactic injection of antidiphtheric serum should be given.

safety other methods of antirabic vaccination. However, most laboratories still make this vaccine from attenuated cord, and the methods employed in the different places is subject to considerable variation. This being the case, it is obvious that it would hardly be practical at the present time, to outline any standard method for preparing the vaccine.

Luetin is another product which cannot be standardized in the ordinary sense of the term. The control of the activity of this product must depend upon the use of good cultures, and rigid adherence to manufacturing formula.

The other products mentioned are of more definite character.

The toxin antitoxin mixture could be prepared on a definite basis. For instance, an amount of toxin comparable to 7 minimum lethal doses for a 250 Gm. guinea pig, overneutralized by the addition of 10 units of antitoxin.

Diphtheria toxin for the Schick test, supplied by various laboratories is presumably of uniform activity, $^1/_{50}$ of a minimum lethal dose of toxin contained in 0.2 Cc.

Pollen extracts can also be standardized on the weight of pollen which they represent. In fact, most laboratories have adopted this method of standardization, first suggested by Noon. The strength of the products is expressed in units, a unit representing one millionth of the extract of one gramme of the pollen.

Summarizing what has been said or intimated in this paper, the pharmacist—especially the pharmacist of the future—if he is to be abreast of the demands of his vocation—of necessity will be familiar with this developing part of materia medica.

The point of view now taken by our representative pharmacists and of the revisers of our Pharmacopoeia, to say nothing of the medical practitioner, is forcing the acceptance of this view upon the members of the profession as a whole. Quite a number of the agents of this group are classified as belonging to preventive medicine and most of them may be classified as Defensive Medicines.

Quoting Dr. George Crile:

The injection of live or dead bacteria or of foreign protein substance into the blood stream of the body supplies the exciting factor which calls out the activity of chemical defenses through the excitation of chemical ceptors. On this important fact is based the practice of serum therapy and of vaccination, by which diphtheria, typhoid, smallpox, tetanus and other like diseases are conquered.

The point of view of the pharmacist, as well as the physician, must differ in this defensive therapy, from that which has characterized the other portions of our materia medica. This new point of view cannot be acquired, nor its demands met by the pharmacist, simply by catering to the demands of the trade. To meet the responsibilities of the pharmacist, there is much more required than that which obtains from merely stocking up and selling the products.

ABSTRACT OF DISCUSSION.

F. E. STEWART: I want to say something this morning on the subject of so-called Bacteriological Infection, but it is impossible to talk intelligently or for very much edification of the audience on such a very broad subject as this in a short time. The subject of bacteriological products includes a very wide field. It might be taken up from very many points of view—many practical points of view—in fact. One point of view, as an example is that of the storing of biologicals. Sometime ago I read a paper before the Seaboard Medical Association at Norfolk, and the President of the Virginia Board of Health said, "I wish you would bear this message to the pharmacists of this country; if they don't take more care in the preservation of biological products, we, as members of the boards of health, will establish facilities for that purpose, and take the business away from them."

Then again we might discuss the thing from the point of view of the knowledge that the pharmacist should have in regard to biological products from other points of view. For instance, the question of post action of tetanus is one that is constantly coming up. It was only about

a year ago I think that there were three cases of post action of tetanus in New Jersey which I had occasion to investigate. I found that the pharmacist and physician both knew very little on the subject. They read from the text books published long ago information that no longer is considered reliable, and based their arguments on those points that they found in the text books; but if they had known that the Bureau of Hygiene at Washington has investigated the subject and found that they cannot infect a person—that is they cannot infect healthy tissues—by mixing tetanus germs with vaccine and injecting it into the healthy tissue, unless there is also pus infection, they would have had a very different view of the entire subject and been saved a great deal of trouble. As I said before, there are so many points from which this subject can be discussed that we might talk a long time and still be taking up points of exceeding value and interest to the Association.

JACOB DINER: More than five or six years ago, I presented a paper on vaccine before this section, wherein I endeavored to point out to the pharmacist that he must interest himself in the newer methods of treating disease. It is the pharmacist's duty to be conversant with the remedial agents, their origin, composition, and mode of acquisition. While he, in a manner, does familiarize himself with the chemical and medical drugs which he handles, there has been a woeful lack of interest in the matter of allied remedial agents, particularly vaccines, and antitoxins. There are many pharmacists who do not know the difference between vaccine and antitoxin; and I might say in all fairness that there are a number of physicians who do not know the difference. Pharmacists shou'd have more knowledge relative to biological products, not only that they may intelligently handle them but to discuss the subject with physicians. There is no excuse for the prevailing lack of information, as the opportunities for acquiring it is not only afforded by text-books but also through related articles in the journals.

W. M. BOWMAN: I want to call attention to one thing in biologicals. That is the point of scientific honesty. I think that when it comes to the handling of biologicals—the sale of biologicals to physicians—you will find that point something which can very well be borne in mind. In the sale of biologicals to physicians you are coming in contact, seventy-five percent of the time, not with the ultra scientific man, but with the man who doesn't know very much about biological products. The main thing in handling biologicals from the pharmacist's point of view is to thoroughly know the products; and one cannot know these only through a thorough study of the whole subject. And above all, whatever information is supplied should be backed by a knowledge of facts; when these are communicated it may occasionally result in loss of business, if the product is not adapted for the intended or contemplated use, but this is the correct proceeding, that is what I call scientific honesty.

BIOLOGICAL ASSAY METHOD OF THE U. S. P. IX.*

BY PAUL S. PITTENGER.

The history of standardization may well be divided into five important steps.

The *first step* was made by Dr. Lyman Spalding, who, in 1817, submitted to the Medical Society of the County of New York City the project for the formation of a National Pharmacopoeia, the adoption of which resulted in the publication of the first National Pharmacopoeia in 1820.

The *second important step* was the organization of the American Pharmaceutical Association in 1852 to improve and regulate the drug market.

The *third important step* consisted in the adoption of the Purity Rubric and of assay processes for galenical preparations by the Pharmacopoeial Convention of 1890.

The *fourth important step* consisted in the securing of legislation known as the

* Read before Scientific Section, A. Ph. A., Indianapolis meeting, 1917.