

HANDLING BIOLOGICAL PRODUCTS IN THE DRUG STORE.*

BY ROBERT P. FISCHELIS.

Biological products are playing such an important role in the materia medica of the present day that the pharmacist should be alive to the possibilities afforded him of making his establishment known to physicians as one at which these products may be obtained in first-class condition at any time, together with general information as to their administration and use.

As pointed out by Mr. W. L. Cliffe, in a paper presented to the Philadelphia Branch of the American Pharmaceutical Association in 1912, the pharmacist logically and naturally is the recognized distributor of bacteriological products, because the time that would elapse in procuring them direct from the maker every time they are needed by the physician would bring about serious inconvenience. Most pharmacists handle bacteriological products nowadays, although a great many confine themselves to keeping a few packages of vaccine virus and diphtheria antitoxin on hand, because they have not yet learned the possibilities of financial remuneration connected with making their establishments headquarters for all kinds of bacteriological products.

In order to take up biological products as a side line, the pharmacist should know something of their nature, manufacture, keeping qualities and administration and be able to assist the physician in the selection of the proper serum or bacterin that may be required. Further, he should select the products of a reliable house so that he may have the confidence necessary to enable him to recommend these products to physicians. The pharmacist must also bear in mind that no matter how excellent a product may be when he receives it from the manufacturer, his (the pharmacist's) reputation depends on the condition in which the product leaves the drug store. The question of proper storage, therefore, is a very vital one.

It is a well-known fact that bacteriological products depend for their activity upon highly complex and delicate protein compounds and must in consequence be subject to deterioration. Such changes may be chemical, resulting from the gradual degeneration of the active chemical constituents, as in the case of antitoxins. On the other hand, the active constituent may be a living microorganism and deterioration of the product containing it may be due to an effort at continued growth, with resultant exhaustion of the food supply, or to the accumulation of metabolic products—naturally, one of these processes is somewhat dependent upon the other, and together they weaken and destroy the life of the active constituent more or less rapidly in a length of time depending upon the conditions under which the product is kept. A typical example of this class is smallpox vaccine virus. The studies of prominent bacteriologists reveal that cold is the most important factor known at present for the preservation of biological materia medica.

Elgin studied the rate of deterioration of vaccine virus when exposed to various temperatures: He found that at 37°C. (98°F.) the vaccine is dead within three or four days; at 21°C. (70°F.) it will live for from one to three weeks; at 10°C. (50°F.) it is still active after three to six months; while at 12°C. (10°F.) it will retain its activity for more than four years, perhaps indefinitely. This work has been confirmed by others. It is thus plainly seen that even at ordinary refrigerator temperature, vaccine virus retains its activity for only a few months, and, owing

* Read at the meeting of the Pennsylvania Pharmaceutical Association, June 20, 1916.

to variability in the virus obtained at different seasons, etc., the dating on the finished tubes or points is usually only from six weeks to two months from the date of preparation.

As said above, the substance in antitoxic or antibacterial serums which gives them their specific value is subject to deterioration, and it has been found that upon keeping serums for a considerable time they lose strength. Light and heat are the most potent agencies in bringing about this change. It is customary to protect all biological products from light by putting them up in dark glass containers. Actual experience and actual scientific experiment have demonstrated the value of cold for the preservation of the specific activity of serums, and it has been found by scientists who have studied the rate of deterioration of various serums that some antitoxins deteriorate a great deal under the ordinary conditions of the market, while others suffer very little change. They all, however, point out the fact that loss in potency does not result in the formation of any harmful substance.

On account of this deterioration, it is customary for manufacturers of antitoxins to place in their packages an excess of units of strength, sufficient to make up for the average maximum loss in potency during a time, the limit of which is noted on the package.

The rate of deterioration under the conditions of the market as estimated by Kinyoun and Hitchens is such that an excess of 24 percent in units should be added, if the serum is to remain on the market for twelve months.

Anderson thinks that $33\frac{1}{3}$ percent for two years is sufficient, and American manufacturers follow this rule pretty closely. In other words, a package of diphtheria antitoxin said by the manufacturer to contain ten thousand units at the time it is placed on the market will actually contain sufficient excess to allow for $33\frac{1}{3}$ percent deterioration during two years' exposure to the average conditions of the market.

If the pharmacist is keeping his biological products under the best conditions, the deterioration will be much less than $33\frac{1}{3}$ percent, and even though the patient receives it at the end of two years, he will get much more than ten thousand units, and since the therapeutic result depends directly upon the number of units administered, the result will be proportionately better.

It may be assumed that tetanus antitoxin and the antibacterial serums deteriorate, if not in the same ratio, at least similarly with regard to cold. Therefore, the value of refrigeration as an indispensable aid in serum therapy is clearly demonstrated.

From what is already known of the rate of deterioration of antitoxins when kept at a low temperature, we may deduce that cold affects bacterial vaccines (bacterins) much as it does serums, that is, it has a preservative influence. No extensive experiments to determine the degree of deterioration in bacterial vaccines have yet been completed. Information regarding the danger of deterioration of bacteriological products has been freely circulated, and pharmacists should be well acquainted with the facts in the case. Yet there are some who disregard not only the facts placed before them in current pharmaceutical literature, but the directions explicitly given in the United States Pharmacopœia.

The Ninth Revision of the Pharmacopœia will recognize, besides diphtheria antitoxin, which was recognized in the Eighth Revision, tetanus antitoxin and vaccine virus. The following directions are given for the preservation of antitoxin: "It must be kept in sealed glass containers in a dark place, at a temperature between 4.5° and $15^{\circ}\text{C}.$ "

The directions for the preservation of vaccine virus are: "Preserve it at a

temperature between 4.5° and 15°C.; protect it from light." In each case, the Pharmacopœia also states that the serum or vaccine must bear the "name, address and license number of the manufacturer and the date beyond which the product cannot be expected to yield its specific results."

Since the foregoing facts are known and the directions of the Pharmacopœia are so specific, it behooves pharmacists to regulate their facilities for storing biological products accordingly, and the apothecary who does not keep his stock of antitoxins, bacterins and vaccine virus in a refrigerator or cold store room is as far behind the times as the surgeon who prepares his scalpel for an operation by sharpening it upon his boot.

Since the Committee on Papers and Queries of this Association published its annual list of queries, it has been my privilege to visit the establishments of several Philadelphia pharmacists which are provided with biological refrigerators, and by their courtesy I am permitted to discuss some of the methods in vogue in taking care of biological business in the retail store, in answer to Query No. 9.

The majority of the stores visited were equipped with a Mulford Biological Refrigerator, which is specially constructed of enameled steel to meet the needs of storing these products. It consist essentially of two properly insulated chambers, the upper one being used for ice and the lower one being divided into eight separate compartments arranged in the form of drawers, thus permitting storage of each kind of bacteriological products exclusively in one or more of the compartments. A fairly good sized piece of ice will maintain a temperature below 40°F. in this refrigerator very easily, and this temperature comes well within the pharmacopœial requirements.

In several of the stores visited, no further attempts at systematizing the stock of these products in the refrigerator are made than to see that as each order comes in, the product is put away under its proper classification. At periodic intervals, someone goes over the entire stock and takes note of the expiration dates on the packages and sorts out those which have reached the time limit and prepares to exchange or return them for credit. While this method is fairly satisfactory for a store which does not do a very large business in biological products and is so situated that any desired package can be obtained at very short notice by sending to the manufacturing house, it is not satisfactory for stores which are located at some distance from the source of supply.

In the Farrow Pharmacy, Twenty-ninth Street and Columbia Avenue, Philadelphia, a scheme is followed by which the stock on hand is kept account of as well as of the dates of expiration, with very little trouble. Pieces of plain white cardboard are ruled as shown below, and placed in each compartment of the refrigerator.

Name	A	B	C	D	E
Acne Serobacterin	7- 8-16				
Influenza Serobacterin	8-16-16	8-16-16	8-16-16	8-16-16	
	9- 7-16				
Neisser Serobacterin	9-20-16	9-20-16			
	9-20-16	9-20-16			
	10- 7-16		10- 7-16		

In the column at the extreme left, the name of the antitoxin, bacterin or whatever it may be is written with pencil. In the column immediately adjoining, A, the expiration date of the package is written. If two or more packages of the same product are in stock, two or more expiration dates are written in this column. The

card, therefore, not only serves as a memorandum of expiration dates, but also becomes an inventory of the particular compartment to which it refers. Each time a package is removed, its date of expiration is erased from the card, so that, if properly kept, one need simply glance at the card to see how many packages of each product are on hand and how soon they must be exchanged.

The columns headed *B*, *C*, *D* and *E* are used to record expiration dates of different sizes of the product recorded on the same line in column *A*.

The most complete system of storing and keeping track of biological products that I have seen in any retail drug store in Philadelphia is that followed in Peacock's Pharmacy at Broad Street and Erie Avenue.

This store is known to physicians as headquarters for biological products, and with the many new preparations that constantly appear, the ordinary biological refrigerator is taxed for space, but Mr. and Mrs. Peacock and their assistants have mastered the problem of storing a maximum amount of biological products in a minimum of space.

Instead of laying packages of the various products in the compartments promiscuously, the ordinary packages with square ends are stood on end, in alphabetical or numerical order, with the date up, in rows separated by neat cardboard partitions. Four-syringe packages of bacterins, because of lack of room elsewhere, are placed on specially adjusted narrow shelves arranged between the wall of the refrigerator and the wall of the drawer. The space here is just wide enough to store these packages comfortably.

Larger packages, such as antitoxin, etc., are laid in the compartments in the usual manner, but all of one kind and make of preparation are kept together. The compartments are lettered *A*, *B*, *C*, *D*, etc., and an alphabetical card index, showing, opposite the name of each product, the letter of the drawer in which it can be found, is now being prepared so that anyone will be able to find any biological product in stock, although it is very easy to do this at present with the alphabetical arrangement referred to above.

A novel method for keeping track of expiration dates is also in use at the Peacock Pharmacy. A five-cent Wanamaker Diary is kept on the desk near the refrigerator. On or about the first of the year the name of every package in the refrigerator is written on the page of the diary which corresponds to the expiration date of the preparation, providing, of course, that this date comes within the ensuing year. Each additional package bought during the year is entered the same way, provided its expiration date comes within the year for which the diary holds good. Of course, any preparations expiring later than this particular year will be recorded in the diary for the following year, if they are not already sold by the first of January following. Once this record is made, the man in charge has no trouble in keeping fresh stock on hand. Each day or two he will consult the diary for three or four days in advance, to see which packages will then be out-dated, and then he looks into the refrigerator to see if they have been sold, crossing their names off the list if the latter is the case, and taking out those packages which remain, preparatory to exchanging them for new stock. All told, this requires less than fifteen minutes a day, on the average, and as a result, the words "We have it, but the date expired yesterday" are strangers at Peacock's Pharmacy.

Biological business, like any other side-line in the drug store, must be handled in an efficient, business-like manner if proper returns are desired.

It is a clean, ethical and necessary line and its proper handling brings prestige as well as financial returns to the retail druggist who is willing to give it a little time and attention.

Manufacturing houses supplying biological products are very liberal with explanatory literature, follow-up letters and post cards for physicians, which advertise both the products and the store at which they may be had.

If it is true that the use of biological remedies has to some extent curtailed prescription writing, that is all the more reason why the retail druggist should show his physician friends that he is just as able to intelligently fill orders for these products as he is to fill prescriptions, and that he not only has the latest information on how to keep biological products in condition for instant demand, but that he puts this information to practical use for the benefit of the physician and his patients.

CHOLERA MIXTURE; AN IMPROVED FORMULA.*

BY OTTO RAUBENHEIMER, PHAR. D.

The sale of diarrhœa mixtures or so-called "cholera drops" has become a necessity, especially during the summer months. For this reason the National Formulary, one of our legal standards according to the Pure Food and Drugs Act and the State Laws, provides five different formulas, two of which, namely Squibb's Diarrhœa Mixture and Sun Cholera Mixture, will be retained in the 4th edition of the N. F., now in print and official from September 1, 1916.

The "Sun Mixture" is without doubt the most important, and its history is given in another paper. However, owing to its high opium content, namely 20 volume percent of tincture of opium, it cannot be sold to the public without a physician's prescription, according to the Federal as well as the State Laws.

What is the pharmacist to do under these restrictions? Various suggestions have been made, so as to sell cholera mixture to the suffering public.

1. To reduce the quantity of tincture of opium, so that one fluidounce contains *not more than 2 grains of opium or one-fourth of a grain of morphine.*

2. To replace the 20 percent of tincture of opium by such astringents as tincture of cinnamon or kino or gambir.

3. My own suggestion is to modify the formula in such a way as to contain 50 percent of paregoric. Here is my formula:

IMPROVED SUN CHOLERA MIXTURE.

Spirit of Peppermint	2 volumes
Spirit of Camphor	1 volume
Tincture of Capsicum	1 volume
Tincture of Rhubarb	1 volume
Camph. Tincture of Opium	5 volumes

Dose: 1 to 2 teaspoonfuls in a wineglass of water as required.

Why do I advocate the use of paregoric? Because from personal experience I am convinced of its beneficial use in cramps, pains and diarrhœa. Elixir Paregoricum has most certainly stood the test of time, both as a household remedy, as well as a pharmacopœial preparation, having been originated about 1700 by Dr. Le Mort, Professor Chemistry at the University of Leyden, Holland.

These "Improved Cholera Drops" contain merely a trace of opium, namely 0.2 percent, or 0.02 percent of anhydrous morphine. It seems hardly possible that the "opium habit" could be contracted from this mixture, as its taste is not any too inviting.

As another argument in favor of this preparation, I beg to state that I have sold these cholera drops for over a year with perfect satisfaction to my customers.

* Read before annual meeting of New York Pharmaceutical Association.