The microscopic structure of hemlock bark is illustrated by reproductions of micro-photographs.

The chief pharmaceutical uses of the bark are described and selection of the bark for particular purposes is discussed.

Comparative prices of whole and rossed bark are given. It is suggested that the very slight increased cost of the bark in the rossed condition imposes but a negligible burden upon those who heretofore have employed only the whole bark.

Tentative standards for hemlock bark for pharmaceutical purposes are suggested.

BOTANICAL DEPARTMENT,
H. K. MULFORD COMPANY,
PHILADELPHIA, PA.

THE PROPHYLACTIC AND THERAPEUTIC VALUE OF VACCINES.*

BY G. W. McCOY.[1]

In discussing the prophylactic value of vaccines I take it for granted that there is no need to take time to consider smallpox vaccine and antirabic vaccine. These two agents, to which indeed alone the name "vaccine" ought to be restricted, are on so well established a basis as to put them beyond the stage where it is necessary to advance evidence to prove their worth.

Coming to killed bacterial suspensions to which the names "bacterial vaccines" or "bacterins" are applied and discussing first the prophylactic uses of the preparations we must first consider the scientific basis for them. It has long been known that a mild attack of certain infectious diseases would prevent the development later of severe attacks of the same disease. It was but a step from this to the prevention of the disease by the injection of the bacteria which are responsible for the infection. The killed germs are generally employed though there are some examples of the use of living cultures.

As a basis of vaccination of this sort we must know first what is really the cause of the disease and then know whether the causative organism is capable of inducing a change in the condition of the animal body that will prevent the securing of a foothold by the invading germs or at least render the invasion relatively harmless. There are some organisms which are known to cause disease, yet the preparation of a vaccine from them will fail to protect against infection. A good example of this is tuberculosis; we have known the cause of tuberculosis for about 40 years and it is an organism that is relatively easily cultivated, but no one has yet been able to devise any effective preventive vaccine though the subject has enlisted the efforts of the best minds engaged in the study of immunity.

What, then, are the diseases we can effectively vaccinate against? The number is regrettably small; the best example, and at the same time the one on which the evidence is most satisfactory, is typhoid fever. I will not burden you with figures, but will simply state that, based on apparently trustworthy data,

* Read before Scientific Section, A. Ph. A., City of Washington meeting, 1920. This and two other papers are part of a symposium. The titles of the other papers are: "Biological Assay—Its Scope and Limitations" by H. C. Hamilton and "Vaccines and Immune Serums—Have they Come to Stay?" by F. E. Stewart.

[1] Director, Hygienic Laboratory, Washington, D. C.

typhoid fever has been eliminated from armies almost entirely by systematic vaccinations, and the same holds true for those closely related diseases, the paratyphoid fevers.

Leaving this generally recognized success and passing to other members of the group of intestinal infections, such evidence as we have is wholly favorable to the view that Asiatic cholera and tropical dysentery may be controlled by means of bacterial vaccines, but it is too early to speak with much assurance on this point.

During the past eighteen months we have heard much about the use of vaccines in the prevention of, or at least the mitigation of, the complications of respiratory infections, particularly influenza; it is perhaps a good indication of the want of large success in this line that the subject is still in a debatable stage. The first trouble we encounter here is that we do not know with any degree of certainty as to just what organism is the cause of epidemic influenza. We have given a great deal of attention to this subject at the Hygienic Laboratory since the epidemic appeared in the autumn of 1918 and have investigated many alleged successful uses of influenza vaccine, but when the evidence is summed up we must admit that the results have not been encouraging. The sources of error in observations of this sort are many and I want to draw your attention to just one—a very common one. We are told that in a given group of persons exposed in about the same way one-third were vaccinated, none of whom got the disease, while among the unvaccinated two-thirds there were many cases; possibly all, or in any event a large percentage of the two-thirds contracting the disease. This sounds very encouraging—at least it did to me the first time I heard it. But when we make a personal investigation and learn that vaccinations were done only after most of those who became sick had been stricken, the experience is seen in a different light. We now realize that those who were vaccinated and escaped were the part of the population that would have escaped in any event.

In order to eliminate such sources of error the Public Health Service conducted observations by vaccinating half of the persons in groups that had not been exposed. In such of these groups as later became infected it was found that influenza and pneumonia took impartially the vaccinated and unvaccinated. In other words, under conditions as nearly ideal as we could make them the vaccines available failed to prove of service. Possibly in time a more scientifically devised or a more skilfully prepared vaccine against influenza and its complications may be available, but at present the outlook is not particularly encouraging.

We have been much interested in the subject of vaccination against pneumonia not due to influenza and here the outlook is more encouraging. Considerable work in the Army, and some little civil experience, indicates that a considerable degree of protection is afforded by the use of a vaccine made of various kinds of bacteria that are associated with the kind of pneumonia which, in normal times, claims so many victims. This is in many respects different from the pneumonia that follows influenza.

Much has been done in the way of attempts to produce a vaccine that could be given in a single dose and at the same time give the killed bacteria in large enough dose to give reasonable assurance of conferring any immunity that is to be had. At one time it seemed likely that vaccines suspended in oil offered the solution of the problem but a considerable volume of experimental data rather points

in the direction of much decreased effectiveness of the oil vaccines compared with those in ordinary use.

From what I have said you will be prepared to hear me express a somewhat conservative, probably even skeptical, opinion of vaccines against "colds." In the very nature of the thing it is very hard to secure trustworthy evidence about these preparations; so few people have been vaccinated, there are no accurate reports on the occurrence of colds among the vaccinated and non-vaccinated, and, on the whole, our basis for any opinion is slender. As we know next to nothing about the essential cause of colds we clearly have no rational basis for vaccine prophylaxis, and, as I have indicated, no good empirical indications.

The consideration of the *therapeutic* side of my subject will occupy but little time. While prophylactic vaccination is directed chiefly against diseases that prevail in epidemic form curative vaccination is practiced chiefly against the more purely personal infections and especially those of a chronic nature.

At the start it should be made plain that there are two kinds of therapeutic vaccines—the "stock" and the "autogenous" varieties. The former are made from standard cultures and usually by large manufacturing plants, while the latter are prepared for each individual patient from growths derived from that patient. The latter are usually prepared by the physician or by a specialist in this line of work. Each class has some advantages; I do not pretend to be able to hazard an opinion as to the respective merits of the two.

Now, what are the conditions in which vaccines may be used in a curative way with prospect of success? Judging by reports of men of large experience, in some forms of acne, in boils, in chronic pus infections and in some other long standing conditions we may expect benefit from vaccines.

In certain acute conditions, notably typhoid fever and pneumonia, modified vaccines given intravenously sometimes appear to work an almost marvelous benefit. There is some reason for believing that this action is not due to the fact that a preparation of the causative organism has been used, but rather because a foreign element has been introduced. This so-called foreign protein reaction is attracting much attention in recent years but is not yet on a basis that justifies any definite statements.

There are not wanting those who assert that the greatest value that resides in vaccines in treatment is the psychological one. The use of a medicine hypodermically has about it, so say these skeptics, something that makes so marked an impression on the patient that it is reflected in an actual or believed improvement. They also rather broadly intimate that some physicians are not averse to encouraging this, to the benefit of everybody concerned, including, I hope, the pharmacist.

It has always seemed to me a rather significant fact that in many of the best hospitals, and particularly in the Government hospitals, vaccines for treatment find almost no sphere for use. You may draw your own conclusions from this.

Finally let me say that vaccines have one advantage over many other remedial agents—they are relatively harmless.

I should be remiss if I did not embrace the opportunity presented by appearing before this group to urge that as dispensers of medicine you should use every endeavor to assure your patients that the goods you sell are as efficient as it is

possible to have them, and in this respect your chief concern should be that biological products should be kept cool—actual contact with ice is all but imperative with the most useful and important of the whole list—smallpox vaccine.

BIOLOGIC ASSAYING: ITS SCOPE AND LIMITATIONS.*

BY HERBERT C. HAMILTON.

To many of you this subject of biologic standardization may seem hackneyed and time-worn. Among my earliest recollections in connection with this subject was a controversy between the representatives of two pharmaceutical manufacturing firms as to whether it is possible to make the test quantitative, neither party questioning its truly qualitative character when properly applied.

Now, however, the question seems to have advanced a point. It is apparently doubful in some minds whether it is even qualitative. It was stated recently that "If you would know the effect of a drug on a human it must be tested on a human; this cannot be deduced with any degree of certainty by its action on one of the lower animals."

Is there any excuse for continuing an apparently profitless discussion? There is more than an excuse, there is a reason and a vital one. To each of us, either for himself or for some one near and dear to him, it is a vital question since few of us are fortunate enough to escape the physician and the druggist.

If you respond that most of the drugs we use are standardized chemically or are so harmless that they need no standardization, it is really a strong point for biologic standardization for why should any powerful agent be left to chance if a method can be applied by which a uniform product results?

Is there any less reason why the physician and the patient should be able to purchase standardized digitalis, ergot or antitoxin than for us to be able to buy standardized solutions of strychnine or morphine?

But some will say that standardization of digitalis does not insure potency when you buy it some months or years afterwards. But it does insure the marketing of a uniform product from a drug which is highly variable.

Digitalis grows under many varying conditions of climate, season and soil, sometimes cultivated, sometimes not. The time of gathering, the method and efficiency of the drying, the extraction, all may influence the activity of the final extract. Should this be left to chance if it is possible to make it a certainty?

But, you may reply by the question "How much certainty is there when the basis of the test is only that the drug will kill a dog, cat, pig, frog or gold fish?" That question, however, is really beside the point. The question of killing is unimportant; it is the amount that kills and the character of the death. If two tinctures of digitalis are tested on cats or frogs and one is found to kill with one-half the dose required for the other, which would the physician choose? Or, if two tinctures are tested on frogs and one stops the heart in systole while the other, although equally toxic, consistently leaves the heart in diastole and when tested on the laid-bare heart does not slow the rhythm, one must conclude that there is little digitalis in the solution. The latter may contain some digitalis activity

* Read before Scientific Section, A. Ph. A., City of Washington meeting, 1920.