Papers Presented to Local Branches

OINTMENT BASES.*

DR. EUGEN UNNA.

It gives me great pleasure to address you on a subject which I hope will be of interest to you. I intend to give, in the form of a critical comparative review, a short summary of the ointment bases which have been in general use up to the present time.

As you know, up to the middle of the nineteenth century, fats of animals and plants were used for the preparation of ointments. Among these fats, mutton-fat and lard played the most important roles. Lard has always been preferred. While, like lard, mutton-fat is a mixture of the glycerides of palmitin, stearin and oleic acid, in lard the percentage of oleic acid is much higher and for this reason its consistency is softer and it is blander.

The disadvantages of both fats are that they cannot be kept long without becoming rancid and they cannot be mixed, to any marked degree, with alcohol, water, hydrocarbons, and glycerin. Yet this miscibility is the first desideratum of a perfect ointment base. In the middle of the seventies two mineral bases were placed on the market: petrolatum and paraffin. Both products are obtained in the processes of manufacturing petroleum. At that time, with these new bases it seemed possible entirely to replace the animal fats. Only the fact that it is possible to preserve lard by benzoating it enabled that fat to hold its place among the ointment bases. I may mention here that German dermatologists did not aupreciate the benzoated lard for the following reasons: First, the stability was not complete; and secondly, the addition of benzoin resulted, particularly on tender skins, in disagreeable irritations.

When Hebra, the father of dermatology, about forty years ago, raised this science to the position of a special branch of medicine, it happened fortunately, that just at that time two new ointment bases, petrolatum and paraffin, found their way into the medical profession. These mineral fats which, owing to their stability and harmlessness, soon obtained an important position in the technic of ointments, are hydrocarbons of the alipathic series. By petrolatum or "vaseline" we understand, as you know, a solution of isoparaffins in liquid hydrocarbons of various combinations. Its melting point does not differ much from the melting point of lard, but in comparison with the latter it is extremely greasy and difficult to remove from parts to which it has been applied. These shortcomings, though, are equalized by a decided advantage; petrolatum can be kept

*Read at the June meeting of the New York Branch of the American Pharmaceutical Association.

indefinitely. This could not be said of lard, even if the latter was benzoated. This advantage of petrolatum being evident, how about its innocuous effects on the skin, as well as on admixed medicaments?

Petrolatum is generally believed to be stable and immutable. Nevertheless there exist in petrolatum, as you know, several oxidation products such as vasogen, vasoliment, and vaselinum adustum, which show that deterioration of the fat could be possible. Some time ago I investigated with my colleague, Golodetz, different kinds of petrolatum. The idea was to find why certain organic oxidation products after having been mixed with petrolatum lost their activity. We succeeded, partly by using the old sulphuric acid reaction, partly by means of osmic acid, to prove the existence of certain reducing bodies, which according to my opinion, must have a similar constitution to oleic acid. While we may consider petrolatum stable for practical use, we must keep in mind that it often contains reducing bodies, which undoubtedly are able to destroy the action of oxidizing medicaments.

Paraffin is entirely free from this drawback. Petrolatum is a residuum, paraffin a distillate, and is therefore purer. I do not need to discuss here the different kinds of paraffin, because I know that you are absolutely familiar with this subject; their main properties are generally the same. Paraffin ointment really is an ointment base which fulfills all demands for blandness and stability.

The advantage mentioned obtained for petrolatum and paraffin first place amongst the ointment bases whilst lard, and even benzoated lard, lost the greater part of its importance. But these ointment bases are not yet the ideal ones. A most important property is still lacking in them to a great extent, that is, miscibility with water and other liquids. Experiments which I have made with the just-mentioned bases have shown that none of them would combine with more than 30 per cent of water.

When in 1885 the adeps lanæ or lanolin was put on the market, this above-stated disadvantage seemed to have been overcome. To avoid misunderstanding I wish to define the terms "wool-fat" and adeps lanæ" of the Pharmacopœia. The Pharmacopœia of the United States calls adeps lanæ a purified wool-fat. This termination leads us to think that the difference between these substances is just about the same as the difference between crude zinc oxide and the purified zinc oxide. That that is not the case was shown by the thorough investigations which P. G. Unna made about the ingredients of wool-fat and of the so-called purified adeps lanæ or "lanolin." I quote from his report of these investigations the following: "At that time we were entirely in the dark as to the difference between wool-fat and the purified wool-fat, 'lanolin.' We know now, though, what we have to understand under the term 'purified wool-fat.' It is a mixture of the above-mentioned alcohols and fat acids, partly in the free state, partly combined as ethers; it contains outside of this 5 to 8 per cent of natural potassium soaps. When compared to the other fats it is characterized by the following properties; it contains isocholesterin, oxycholesterin, lanocerin acid and lanopalmin acid, whilst glycerin is entirely lacking.

"Lanolin, therefore, is only a part of the natural wool-fat; it contains all the ingredients of the latter, but their quantity is entirely different, for during the

process of cleaning wool-fat, the greatest part of all three cholesterins and a large percentage of the lanocerin wax is lost."

We will see that through the method of cleansing used for the adeps lanæ of the Pharmacopœia, we lose its most important constituent. Now it is just on account of this constituent that adeps lanæ has been accepted by the Pharmacopœia. I will prove that the acception of the wool-fat in the purified state was a mistake in the Pharmacopœia. After Hartmann, in 1860, and Schulze, in 1872, had proved that the fat of sheeps' wool contained cholesterin and isocholesterin, O. Braun discovered the peculiar property in this same fat, of taking up, in a physical way, large quantities of water. Liebreich claimed, in 1886, that the latter property was brought about by the former. Yes; he even went so far as to say that the absorbing quality was a reaction for "cholesterin fats." It is also due to the authority of Liebrich that this opinion, based upon poor experiments, soon found its way into the most important medical text books. For years it was considered as a fact without receiving the slightest opposition. This was very feasible, for Liebreich gave for his opinion an explanation which at that time seemed credible enough, but nevertheless was based upon great errors.

The next fault that Liebreich had made was, that he started with the wrong opinion; that is, that the capacity for absorbing water belonged to the cholesterin ethers.

In order to prove this, he used Liebermann's cholesterol reaction, by which free cholesterin, but not its ethers, is shown. Without taking notice of this fact, he simply claimed that this reaction could be used for cholesterin fats. He says: "Cholesterin fats, in which not a trace of free cholesterin could possibly be present, were shown with extreme sharpness by the cholesterol reaction." Taking this second error as a fact, Liebreich examined the human skin, which, as you know, contains cholesterin, on the cholesterol reaction. He showed the presence of free cholesterin, but he himself believed that he had shown his cholesterin fats, to which, according to his opinion, belonged the capacity of absorbing water. He even went so far that he claimed the human skin, showing the cholesterol reaction also must contain "lanolin" (adeps lanæ).

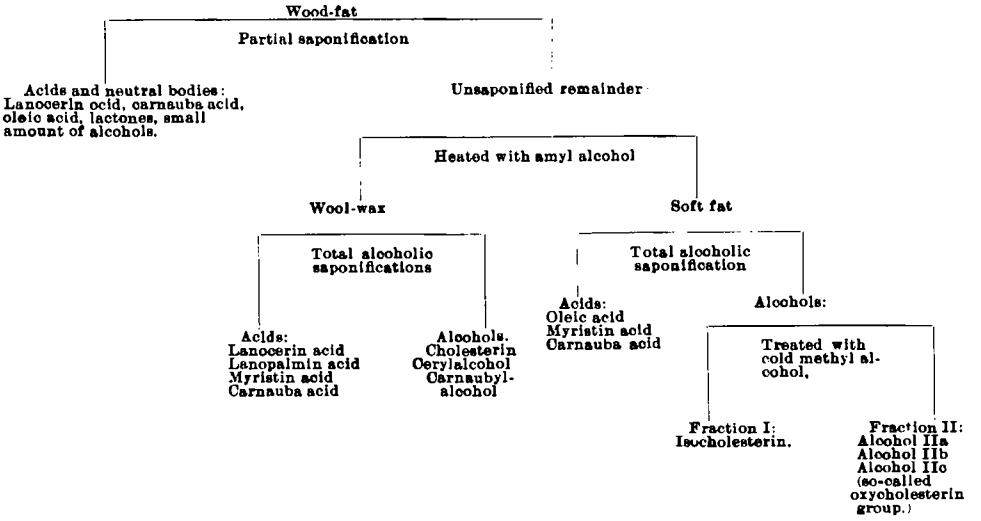
We are indebted to the Russian chemist, Lifschuetz, for having discovered, after twelve years of work, in wool-fat the body to which only belongs the power of absorbing water. Thus he enabled P. G. Unna finally to correct the errors of Liebreich, which have been accepted by the pharmacopœias of all nations, up to the present day, as facts. Lifschuetz first isolated the cholesterin ethers of Liebreich and proved that no noteworthy power of absorbing water belonged to them. Then he discovered his well known acetic-sulphuric acid reaction on the spectrum of which he clearly could determine the relative absorbing power for water.

He arrived further at the very logical conclusion: "If a reaction shows by its intensity the relative capactity for water, it must necessarily be also a reaction for the very body to which belongs this capacity of absorbing water." In this way he succeeded partly by saponification, partly by alcoholic extraction and fractional distillation, in isolating a body from the wool-fat, which he called alcohol II. *c*, and which forms a group of free alcohols of iso and oxycholesterin. To this

group then belongs the water-absorbing power of wool-fat, but it is only contained to a small percentage (about 0.5 per cent) in the crude fat.

The adeps lanæ of the Pharmacopœia contains this important body in a still smaller percentage, as by the peculiar process of purification, just this body is almost lost. P. G. Unna, to whom we are indebted for the thorough investigation of the new body of the oxycholesterin group, discovered by Lifschuetz, eucerin wax, and the new ointment base prepared from it, eucerin, the composition of which we shall consider later, has shown by his experiments that the commercial adeps lanæ has a capacity for from 30 to 200 per cent. of water, while eucerin wax combines with 700 per cent. The principal difference in the composition of the adeps lanæ of the Pharmacopœia and the eucerin, or, if I may say so, the improved adeps lanæ, is the following: In the adeps lanæ of the Pharmacopœia the good properties of the oxycholesterin group are sadly influenced by the presence of the high molecular acids and alcohols. In the new ointment base, eucerin, we find the only important constituent of adeps lanæ free from all drawbacks ready to display its action unrestricted. By the addition of 5 per cent. of this eucerin wax we are able to combine any fat with an amount of water up to 300 per cent. and even more.

Allow me to demonstrate to you in the following the composition of the crude wool-fat, of the adeps lanæ of the Pharmacopæia, and the isolation of its most important constituent, the eucerin wax:



Let us now consider the properties of adeps lanæ. Crude wool-fat has a disagreeable odor which even adheres to the purified adeps lanæ. It cannot be kept any length of time without becoming rancid. The absorbing power for water is changing with the degree of the so-called purification, for, as I said before, the more wool-fat is purified, the smaller becomes its absorbing power for water. Extreme purification is liable to give you an adeps lanæ which will not absorb any appreciable amount of water.

Another and probably the most objectionable feature is its pitch-like tenacity.

This tenacity and also its proneness to rancidity are due to the presence of the just-mentioned acids and alcohols.

You know yourselves how difficult it is for the pharmacist to prepare ointments with adeps lanæ. In order to show you its disadvantages as a medicinal agent, I have to explain first the value of an absorbing capacity for water in therapeutics.

Cooling ointments or cold creams are of great importance to the dermatologist. The cooling effect is brought about by the water which is incorporated into the fat. As you know, this cooling effect is dependent on a physical phenomenon. Water has the property of evaporating. For this purpose it needs heat. This heat it abstracts from the surrounding surface, in this case from the human skin, which is cooled thereby. It is clear, therefore, that the larger amount of water present and the quicker its evaporation, the greater must be the cooling effect.

Adeps lanæ does not take up water readily. The suspended water it gives up slowly on account of the tenacity of the fat. In other words, the cooling effect is thereby decidedly minimized. In eucerin the result is just the reverse, owing to its great affinity for water and its lack of tenacity. Here we have the full benefit of evaporation of the water contained in the ointment, and the long-ventilated question as to a suitable basis for cold cream has found its happy solution in the discovery of this substance.

But in this combination of wax alcohols with mineral fats we will find another very important property. That is, the facility with which the ointments prepared with it can be rubbed into the skin. The reason therefore seems to be of a physical nature and due to the hydrophilia of the oxycholesterin group. When I speak about the concentrated eucerin-mercury ointment, I shall have an opportunity to give you a striking example of this property.

Now we have to ask: "What have modern therapeutics and cosmetics to demand of a perfect cold cream?"

First. It must have a great absorbing power for water; secondly, its fat basis must be unchangeable; and finally, its consistence has to be soft, but not greasy or even sticky. All these properties we find separated in the ointment bases known hitherto, but nowhere combined. Adeps lanæ has a rather great absorbing power for water, but its action is only slightly apparent. It is of great tenacity and stickiness, and its fat basis cannot be kept long. Petrolatum and paraffin, although they may be kept long, are lacking in an absorbing power for water, and therefore cannot be used for the preparation of cold creams. Lard has the advantage of great softness and blandness, but it does not have the important keeping qualities and the capacity for water.

The compilers of the Pharmacopœia in constructing the formula for cold cream had to ignore the other properties and took into consideration only the softness. They prescribed a mixture of white wax, spermaceti, and oil of almonds, and so succeeded in preparing an ointment base of great softness and blandness. But, as the ability to take up water was lacking, the percentage of oil of almonds had to be increased to such an extent that the keeping qualities

became diminished. The result was, that the cold cream of one Pharmacopœia did not contain more than 19 per cent. of water, while in the cold cream of another Pharmacopœia was combined only 25 per cent.

This has been the situation up to the present day. It was clear that the problem of the cold creams was solved at once when we became able to incorporate with any stable and harmless ointment base a body which gave to it the lacking properties of softness and absorbing power for water. This body is eucerin wax, discovered by Lifschuetz. Only 5 grams of this wax melted together with 95 grams of petrolatum or paraffin ointment form an ointment base of extraordinary softness, which can be kept indefinitely and which may be combined with water up to 500 per cent. Such a great amount of water is desirable, of course, only in special cases. There has therefore been recommended as the cold cream of the next edition of the German Pharmacopœia, a paraffin ointment which contains 5 per cent. of eucerin wax and 60 per cent. of water, that is to say, more than three times as much as unguentum aquæ rosæ.

We had the same difficulties for years and years with unguentum glycerini, and the successful solution of this problem is also due to the discovery of the new wax alcohols. In spite of the complicated formulas which came into use in the course of years, it was not possible to prepare an ointment base which could be combined with more than 40 per cent. of glycerin. However, a combination of petrolatum with 5 per cent. of the oxycholesterin alcohols will take up 400 per cent. of glycerin.

As the time which I am allowed to speak is necessarily limited, I cannot go through the development of the formula for unguentum glycerini of the Pharmacopœia. Therefore, I refer to the thorough investigations of unguentum glycerini cum eucerino by P. G. Unna and P. Unna, in which the question of the unguentum glycerini seems finally to be settled. The formula which has been recommended for the German Pharmacopœia consists of a mixture of 20 grams of anhydrous eucerin and 20 per cent. of glycerin.

I may mention here that we have to understand under eucerin wax the group of free alcohols of the iso- and oxycholesterin group. Five grams of this wax together with 95 grams of petrolatum give the anhydrous eucerin, which forms by the addition of a certain quantity of water the eucerinum cum aqua.

I am now going to speak about one of our most important ointment combinations, mercury ointment. The pharmacopœias of all nations have always shown the highest interest in this universal medicament for syphillis. At all times it was the principal idea to prepare an ointment which contained the mercury as concentrated as possible. Let us consider next the formula given by the last edition of the German Pharmacopœia. There we find a very complicated formula which seems to have been brought about with the intention of facilitating the disintegration of the metallic mercury; 40 grams of lard, 25 grams of suet, 5 grams of adeps lanæ, and 1 gram of peanut oil are mixed with so many grams of mercury that an ointment containing 30 per cent. of mercury is formed. I do not need to emphasize that besides the small percentage of mercury

we have here a combination of all the drawbacks of the ointment bases previously mentioned. The formula of the United States Pharmacopœia had already proved a progress. It contains 50 per cent. of mercury, is less complicated, and denotes an effort to increase the keeping properties of the lard by benzoating it. Nevertheless, this ointment also becomes rancid. This disadvantage ought to be strictly avoided, however, as this particular ointment, in mercury inunctions is absorbed by the human skin more readily than any other preparation.

All these disadvantages have been avoided at the Eppendorfer Krankenhaus, the governmental hospital of Hamburg, by introducing a preparation of the following composition: 135 grams of mercury and 30 grams of anhydrous eucerin were mixed with the subsequent addition of 6 grams of water. The result was an ointment containing 79 per cent. of mercury. By diluting with eucerinum cum aqua, an ointment could easily be obtained, the amount of mercury in which corresponded to the formulas of the United States or German pharmacopœias. The disintegration of the mercury in this formula is very simple and can be done with great rapidity. But, besides that, we find here another new property. While inunctions made with the mercury ointment of the Pharmacopœia took about twentyfive to thirty minutes, experiments which have been made with the eucerin ointment in German hospitals have shown that five to six minutes were sufficient to make the mercury disappear in the skin.

In conclusion, allow me to summarize once more the main properties of the mentioned ointment bases in the form of a table:

	Odor	Consistence	Stability	Capacity for Liquids
Lard	existing	very soft	becomes rancid	very small
Suet	existing	rather soft	becomes rancid	very small
Petrolatum	none	soft	can be kept	small
Paraffin ointment	none	soft	can be kept	small
Adeps lanæ	existing	greasy and sticky	becomes rancid	up to 200 per cent.
Eucerin	none	very soft	can be kept	up to 500 per cent.

It is not the object of this address to give a review of the practical uses of the ointment bases in therapeutics. I have spoken thoroughly about this matter in an address given before the Royal Society of Medicine in London. Therefore, should you be interested, I take the liberty of referring you to that address.

It seems to me by the analysis of adeps lanæ and the discovery and isolation of the very important group of wax alcohols, that we have entered a new stage of ointment technic. It is difficult to say to which of the above named ointment bases will be accorded the position of greatest efficacy. The most suitable would be lard on account of its soft consistence. This can only be possible if we should succeed in increasing its keeping properties indefinitely by adding a body which in contrast to benzoin is harmless and which is, on the other hand, of such a character that the ointment base prepared by it does not lose its harmlessness, in spite of the addition of medicaments of any kind.

As long as that is not possible we will have to prefer the stable mineral fats, whether they are called petrolatum, paraffin, or otherwise. Adeps lanæ loses its

importance utterly, since we are able to isolate its most precious constituent, free from all the drawbacks of the crude fat. Eucerin wax, finally, is not an ointment base at all, but the long-sought-for body, by means of which we are able to render any stable fat into an ideal ointment base.

THE PRODUCTION OF VACCINE.*

W. F. ELGIN, M. D.

I shall discuss the question of vaccination tonight largely from the laboratory side, leaving for the gentlemen who follow me, its practical application. But to make a connected story for the benefit of those present who may not be familiar with the subject, I shall call attention to a few historical facts in reference to smallpox, the ravages of the disease, and the earlier methods employed to secure protection.

It is thought by some that the great plague of Athens referred to in the History of the Peloponnesian War, was smallpox. It was probably unknown in China prior to the twelfth century, B. C., but is said to have prevailed in India at a much earlier date.

Rhazes, an Arabian physician who died in 932, A. D., seems to have been the first to give a succinct account of the disease.

According to some authorities, the disease was probably unknown in Europe prior to the sixth century; others claim a much more remote antiquity. Smallpox appears to have been introduced into Mexico by the Spaniards in 1520, and is said to have destroyed 3,500,000 people; in some places whole tribes were wiped out.

In 1707, smallpox was introduced into Iceland, where it apparently had never existed before. Eighteen thousand out of 50,000 died of the disease.

From the fifteenth to the seventeenth century, it was practically universally present in most of the large cities over the known world. The epidemology resembled measles of the present day. No class of society was exempt. The king on his throne and the peasant in his hut were equally liable to the contagion. The question asked in the industrial world was "Have you had your smallpox?" just as today we ask "Have you been vaccinated?"

There was a high smallpox death rate in all large cities at that time. Dr. Farr estimated deaths from variola in the eighteenth century at about 4000 per million. Sir Lyon Playfair's estimate for all England was 3000 deaths per million, and it is calculated that about one-twelfth of the total mortality from all causes was due to smallpox. Smallpox was preëminently a disease of childhood. In Berlin from 1758-74 6000 deaths were reported, and only about 45 over 15 years of age, or one in 147 deaths.

Facts of this character could be presented almost without number, showing

*Report of a lecture delivered to the Philadelphia Branch, May 7, 1912.