easily be seen how difficult it is to obtain a sterile preparation of iodoform, and it is no wonder we are looking forward to a preparation which will take its place.

The preparation which I should recommend to the profession for consideration is iodocrol or carvacrol iodid. Carvacrol is an isomer of thymol, differing only in relative position of the hydroxyl groups in the nucleus. It is manufactured in the following manner: Two grams of carvacrol and thirty-eight grams of potassium iodid are dissolved in 40 c.c. of a 10 per cent. aqueous solution of sodium hydrate. To this a solution of chlorinated soda is gradually added under continuous stirring until no more of a precipitate is found. During the reaction the mixture is kept cool by placing the vessel in cold water. The precipitate is collected on a filter and first washed with water to which a very small quantity of alkali has been added, and then with pure water. It is then allowed to dry at the temperature of the room. The product is a bulky, grayish yellow or buff-colored amorphous powder having a faint aromatic odor. It is soluble in ether, chloroform, benzin, carbon disulphid, volatile and fixed oils. From its solution in ether and chloroform it is precipitated on the addition of alcohol, becoming paler in color. This purified product did not show signs of shrinkage until above 170 degrees C., and at 200 degrees C. had become tarry and black, but not liquefied. It combines the antiseptic properties of carvacrol with those of iodine and possesses the advantage over iodoform in being odorless or nearly so, and in being five times as bulky.

Experiments have been made to grow staphylococci and streptococci on carvacrol iodid, but with negative results, thus proving it to be a true antiseptic. It may be used as a dusting powder, either pure or diluted with boracic acid. In the treatment of the nose and throat it is best used in a solution of almond oil or olive oil. It has been used as a dressing for wounds to a great extent in Milwaukee in the National Home of Volunteer Soldiers. It is also manufactured into gauze. It may be used with great benefit in almost all surgical dressings; eczema, pruritus, chancres, chancreoids, etc.

In conclusion, I would say that this preparation has so many advantages over iodoform, especially so of being a true antiseptic, that I sincerely recommend it to the profession and hope it will be given a fair trial.

A NOTE ON TWO NEW CREOSOTE COMPOUNDS: CREOSOTE VALERIANATE AND GUAIACOL VALERIANATE.

Presented to the Section on Materia Medica, Pharmacy and Therapeutics, at the Forty-eighth Annual Meeting of the American Medical Association at Philadelphia, Pa., June 1-4, 1897.

BY FRANK WOODBURY, M.D.
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In these days of new remedies of ephemeral usefulness and evanescent reputation, it is refreshing to take up, for brief consideration, a drug with an established record of more than half a century. We recall the fact that while experimenting with tar from beech-wood, Reichenbach, in 1832, first obtained a fluid substance, which, on account of its possessing pre-eminently the power of preventing putrefaction in organic substances, he termed "creosote," or "flesh preserver." That expert chemist also fully recognized

the fact that the new chemie agent was not a simple, but a very complex, substance, being composed principally of hydrocarbons of the aromatic group. It also contains a variable quantity of water. According to a recent authority, Marasse, it contains phenol, cresol, phlorol, guaiacol and creosol; also methylcreosol and the methylic ethers of guaiacol, phlorol, etc. By fractional distillation, Hofmann separated the dimethylic ethers of pyrogallol, of methyl-pyrogallol and of propyl-pyrogallol from that portion of the creosote which passes over at a temperature above 220 degrees. Hofmann discovered a new body, which he named coerulignol, possessing powerful toxic properties and which should be carefully removed from creosote that is designed to be used for medicinal purposes. Its presence may be detected by treating an alcoholic solution of creosote by a test solution of barium hydrate. If coerulignol is present the solution will turn blue or show a bluish tinge. Benzin may be substituted for alcohol with the same result. The United States Pharmacopeia has adopted this as one of the tests indicating the suitability of a specimen of creosote for medicinal use.

I have referred to the early studies of creosote by its discoverer, Reichenbach, in order to bring into marked prominence the fact that it was first obtained from tar from the beech wood, and the early experiments made upon this agent, not only chemically but also physiologically and clinically, were made with the form of creosote which is still considered the best for medical use and which is now used almost exclusively in therapeutics. An analogous substance obtained from coal-tar is simply a mixture of phenol and cresylol of variable composition, or in other words an impure carbolic acid. These differ, chemically, principally in the following characters: Creosote from wood-tar added to an equal quantity of glycerin is precipitated upon the addition of water; added to collodion it does not coagulate it; and when treated with nitric acid and heat, by Clarke's method, yields oxalic acid. The so-called creosote from coal-tar is not precipitated by water from its gelatin solution; it does coagulate collodion, and yields picric acid when treated with nitric acid. There are corresponding and equally well marked differences between the two compounds in their physiologic action, the most important being the comparative innocuousness of pure wood-tar creosote, which can be taken in large doses, not only without toxic symptoms, but with decided therapeutic results, 500 drops daily having been taken without ill effect.

It has unfortunately occurred that, for many years, the coal-tar extractive was frequently dispensed for creosote, and the latter consequently fell into disrepute for a time on account of the accidents and untoward results from its use. Creosote, according to Dr. H. C. Wood, is also liable to be adulterated with eupion. In the latest edition of the "United States Dispensatory," by Professors Wood, Remington and Sadtler, the statement is made that "Commercial creosote almost always contains carbolic and cresylic acids from coal-tar, and indeed, much of what is sold for creosote is nothing more than impure carbolic acid." I can not, however, agree with these distinguished authorities in the statement contained in the sentence immediately following the above, which says, referring to carbolic acid, that "this acid strongly resembles creosote, and this resemblance probably extends also to their therapeutic effects, so that the

substitution is less to be regretted than might otherwise be the case." This I regard as a most misleading and dangerous teaching. A patient may take as much as 600 drops of creosote, as in Dr. Freudenthal's case (*Medical Record*, 1892), and recover practically without the use of any remedies; but would this case have resulted so favorably had the same quantity of carbolic acid been swallowed instead of creosote?

The principal constituent of creosote is guaiacol, the methyl ether of pyrocatechin, which is present in the proportion of 60 to 80 per cent. in the best specimens. Guaiacol in a pure state is crystalline, but as commonly met with is an oily-looking fluid with a peculiar pungent, smoky odor. It can be obtained, however, in an absolutely pure condition from a commercial sample, by cooling with a mixture of ice and salt and then separating the crystals which have formed, as stated by S. Winghoffer (*Pharmaceutische Zeitung*, Berlin, 1894).

On account of the liability to adulteration in commercial guaiacol and its variable composition, various compounds have been introduced into the practice of medicine as substitutes for creosote and guaiacol. Among the more prominent of these are the carbonate of guaiacol, guaiacol salol, benzyl-guaiacol or benzosol, cinnamyl-guaiacol or styracol, guaiacol phosphite, guaiacol biniodid, and most recently the guaiacol valerianate. These various compounds are administered with the view of their undergoing decomposition in the intestinal tract and yielding guaiacol at the point where it can be most readily absorbed into the blood vessels. In this way the administration of chemically pure guaiacol is accomplished more surely than by any other method. Moreover, these compounds, generally speaking, are more agreeable to the palate than the guaiacol itself.

Physiologic action.—Locally, guaiacol acts, like solutions of carbolic acid, to produce limited surface anesthesia. Dr. Newcomb of New York, at the recent meeting of the American Laryngologic Association, recommended a 5 per cent. solution in olive oil as a substitute for cocain for nasal operations. I have used the guaiacol valerianate for this purpose both in full strength and diluted, and found it to produce, after slight sensation of heat, decided anesthetic effects which are slower in appearing than after the application of cocain, and which are not followed by secondary hyperemia. The antiseptic power of guaiacol is also of great value in throat and nose operations. We know of the frequency of the presence of virulent bacilli in the nasal chambers of apparently healthy individuals, and the routine use of detergent remedies followed by a decided antiseptic, such as guaiacol in oily solution, or the more agreeable valerianate of guaiacol, is now almost necessary in the conduct of our hospital and private work. I should have stated that the valerianate has a strong odor of valerian which almost masks the guaiacol, and produces a combination suggestive of walnuts. Guaiacol valerianate is a local anesthetic to the skin when applied in full strength. The temperature-reducing power of guaiacol, discovered by Sciolla¹ in 1894, is one of the most remarkable observations in the whole realm of pharmacology. This is not likely to occur in persons of good health with a normal temperature, but it is very marked in conditions of pyrexia. Caporali² has found that the external applications of guaiacol not

only relieve pain and reduce abnormal temperature, but also increase the utilization of albuminoids by the organism and the absorption of fat, and diminish oxidation.

Administered internally, guaiacol and creosote both exert a powerful antiseptic action on the contents of the alimentary canal. The temperature reduction appears to be due to a special action of guaiacol upon the peripheral end-organs of the nerves in the skin and mucuous membranes. Upon the heart and blood vessels there are no obvious effects from moderate doses of creosote or guaiacol. In larger doses it acts as a cardiac depressant, producing diaphoresis from relaxation of the blood vessels, also giddiness and a tendency to fainting or collapse, convulsions or coma, but these disagreeable effects are more likely to occur from commercial creosote or guaiacol than from a chemically pure article. In escaping from the blood by the bronchial mucous membrane and urinary organs, guaiacol exerts a local stimulant and antiseptic action.

From the very brief review of the physiologic action of guaiacol, I turn to the therapeutic use, confining my remarks to the guaiacol valerianate and creosote valerianate, which were recently introduced by Dr. Gustav Wendt of Berlin, and which I have used, to some extent, for the past three months in private and dispensary practice. I will simply summarize some of the results of the use of these agents. Both of them are liquid and have a characteristic odor, the guaiacol valerianate being more agreeable to patients than the creosote compound.

In painful affections of the skin, attended by hyperemia such as inflamed acne, or abscess in the external auditory canal, pin-boils, etc., applications of pure guaiacol valerianate relieved pain, and checked further pus formation. In chilblains this agent promptly relieved the annoying symptoms. Small compresses wet with guaiacol and applied over the painful spots of Valleix, afforded almost immediate relief in neuralgia.

In an acute erythema of the face, apparently erysipelatous, but possibly the result of rhus-poisoning, a single application of this agent for ten minutes, followed by applications of zinc ointment containing creosote (one drachm to the ounce), afforded immediate relief and prompt disappearance of the inflammation. In the cases of children, however, or where larger areas are involved, the antithermic effect should be borne in mind, and not more than 25 to 30 drops applied at one time.

I have already alluded to the use of guaiacol valerianate in the treatment of affections of the nose. In acute rhinitis it should be diluted with three or more parts of oil of sweet almonds, or liquid albolene, and in this form it acts as a protective as well as an analgesic and antiseptic application. In chronic rhinitis, especially the purulent form, as well as in some varieties of atrophic rhinitis, it is used in full strength with advantage, as many of these cases are kept up by the presence of virulent micro-organisms, the action of which is inhibited by the guaiacol. In ulcerated conditions, even of supposed tubercular origin, a few applications of pure guaiacol or creosote valerianate materially promotes the healing process, at the same time relieving pain. This observation also applies to the larynx. I have not yet employed it in lupus, but it might be of service here for its local anesthetic effects, prior to scraping and the application of lactic

¹ *Cronica di Clin. Med. di Geneva* for 1892, Vol. p. 171.

² *Riforma Medica*, Naples, No. 175, 1894.

acid and the subsequent use of a 20 per cent. guaiacol spray as recommended by Dr. P. Watson Williams.³ In tuberculosis of the air-passages, external applications of pure guaiacol have been recommended by Prof. J. Solis-Cohen, and for this purpose the valerianate would have an especial advantage. Internally guaiacol valerianate is given either in milk, in dilute alcohol, or better, in the form of capsules. It checks bronchorrhea and reduces the number of tubercle bacilli in the sputum, at the same time that it tends to prevent re-infection from the intestinal tract. It is well borne in moderate doses, 10 to 30 minims daily, or one to three capsules, each containing 2 grains, or $3\frac{1}{2}$ minims, three times a day.

In the treatment of gastric catarrh, chronic gastritis with gastrectasia, and other conditions associated with, or producing fermentation of the contents of the stomach, I have used creosote valerianate in preference to the guaiacol as I believe it to exert stronger antiseptic action. It also overcomes nausea and in connection with lavage, favors the return to healthy condition of the mucous membrane and the re-establishment of appetite and normal digestion.

Fifty years ago, Dr. Fahnestock⁴ used pure creosote as an application to erysipelas, with remarkable success. I have already referred to the use of guaiacol valerianate as a local application for erythema and would suggest its use as a topical agent in erysipelas, and also in smallpox.

In cases of pulmonary phthisis the remedy has been well borne, but I have had it under observation too brief a time to report decided results. Very favorable results, however, have been observed by Dr. Rieck of Bassum, Germany,⁵ who reports increase of appetite and powers of digestion, and of physical strength under its use. In cases of the initial stage of tuberculosis of the lungs, this improvement was quite marked, with a decided diminution of the cough; the expectoration not only became more free, but it also decreased steadily in quantity. The night sweats disappeared. His report was based on the study of twenty-three cases (sixteen of catarrh of the apices and seven of developed tuberculosis), which were markedly benefited.

I have found the guaiacol valerianate of decided value in the treatment of the so-called catarrhal state which is sometimes considered as the pre-tubercular stage of phthisis pulmonalis. It seems especially suited, when properly diluted with some bland oil, for intra-tracheal injection in cases of advanced phthisis, with or without ulceration in the larynx, or cavity in the lung. Inhalations of creosote in combination with oil of peppermint is claimed by Dr. Carasso, to cause a disappearance of the tubercle bacilli from the sputum, and he reports good results clinically after nearly ten years experience with it. Certainly, the form of aerial medication is worthy of extended trial, and guaiacol valerianate would be preferable to creosote for this purpose. I am of the opinion that we have in guaiacol the best remedy known at present to counteract the pernicious activity of the tubercle bacillus, and I may repeat the words of Dr. Jacobi: "No one treatment of all forms of tuberculosis ever satisfied me to the same degree as has that of guaiacol." When introduced into the stomach, the guaiacol valerianate is decomposed and the effects

of pure guaiacol, with the sedative action of valerianic acid, are simultaneously obtained, which may be expected to have a favorable effect on the nervous manifestations of the disease, reducing cough and restlessness. In pneumonia, Malderasco used applications of guaiacol to the thorax posteriorly, over the affected area of the lung, with reduction of temperature and a diminished mortality.

For further and more detailed information, I may refer those interested to reports from the medical clinic of the Royal Charity Hospital of Berlin, by Dr. Grawitz, and Dr. Rieck already referred to, which have appeared in the *Deutsche Medizinal. Zeitung* and the *Therapeutische Monatsheft* for 1896.

DISCUSSION.

A visitor stated that he had examined several specimens of creosote last year and had not found them to contain any guaiacol whatever.

Dr. WOODBURY said that this confirms the statement in the Dispensatory that commercial creosote is often merely impure carbolic acid.

MEDICAL BOTANY.

Presented to the Section on Materia Medica, Pharmacy and Therapeutics, at the Forty-eighth Annual Meeting of the American Medical Association, held at Philadelphia, Pa., June 1-4, 1897.

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Prior to emergence from its nameless barbaric state, the human race was undoubtedly versed in botany of a strictly practical kind. All omnivorous and vegetable feeding creatures distinguish between wholesome and poisonous plants. Even the butterfly selects the right species on which to deposit its eggs, often from among others that to our eyes are almost identical with it. As our race has advanced in civilization, owing its progress to a more and more rigid division of labor, with the attendant and ever increasing specialization by which each piece of the great machine does its work more perfectly, yet more and more completely loses its direct touch with all but a few of the other parts, most men have lost much of what was at first common to all; and this is, perhaps, quite as true of a knowledge of plants as of anything else. As we go from the higher to the more primitive civilization of the present time, we approach by successive steps toward what was at one time characteristic of the entire human race. The country boy has names for most of the plants that the city boy passes by perhaps with a vague notion that they have no names, and he knows abundant uses for many of them. Many is the time that I have hunted sweet cicely and pipsissewa, wintergreen and sarsaparilla in the Connecticut woods; and hoarhound and boneset, yarrow and wormwood are still to be found in the kitchen or the attic of most New England farmhouses. In less favored parts of the globe, where the farmer is a peasant, and the peasant often little better than a clodhopper, this sort of knowledge is even more extensive and widespread.

It is said that the mongoose, when bitten by a cobra, runs at once into the jungle and seeks out a plant which it recognizes and eats as an antidote. Whatever the actual knowledge and its value may be, it is certain that every primitive community believes in the healing virtues of many plants and makes use of them for these supposed virtues; and this sort of knowledge was undoubtedly the first that came after

³ Medical Annual, London, 1897.

⁴ American Journal of the Medical Sciences, 1848.

⁵ Deutsche Medizinal. Zeitung, Berlin, Dec. 24, 1896.