

Thesis:-

The Literature of the Creosote Treatment  
of Pulmonary Tuberculosis; with an  
Account of Three Cases in which large  
Doses were Escribed.

by  
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*Introduction:-*

*Historical Sketch:-*

\* Bishop Berkeley wrote upon Jar Water, & knew nothing about Creosote.  
 This should be made clear, as the good bishop can hardly have known how  
 to have "killed with overpraise" a remedy which did not even come to life  
 till 200 years after his day!

For a considerable number of years Creosote has been highly esteemed in the treatment of Pulmonary Tuberculosis; so much so, indeed, as to draw from Professor Dujardin - Beaumetz of Paris the statement that Creosote is recognised as the most efficient agent we possess for the treatment of tuberculosis." (1)

The derivation of the word creosote (κρεας, flesh, & ωγειν to preserve) naturally takes us back to its discoverer Reichenbach, who first used the term in 1832, owing to its property of preserving animal substances from decay (2) It has been urged, & I think, rightly, that it would have been more in accordance with etymological accuracy had the former B. P. designation of Creosote been adhered to (3).

Addison is stated to have used the drug (4). But its popularity in the early days of its history was shortlived, for we find according to Colliotson, that Bishop Berkeley killed it by overpraise, just as Pope killed Berkeley when he said, -

"Manners with candour are to Benson given,  
 To Berkeley every virtue under heaven." (5)

Chemistry:—

For the succeeding forty years we find the use of creosote in tuberculosis seldom mentioned.

It is to Bouchard & Gimbert in France, in 1877, that we owe the revival of the use of creosote.

Sommerbrodt aroused a fresh German interest in the matter in 1887, by claiming it as a specific (6).

Since the publication of the observations of these gentlemen creosote has continued to receive widespread attention & consideration.

It must be admitted that there has not been complete harmony in praise of the drug; & this may be accounted for by the inconstant nature of pulmonary tuberculosis & the use of impure preparations of creosote.

It will be well to devote a brief space to the chemistry of creosote. In reply to the question "what is creosote?" we naturally turn for an authoritative answer to the British Pharmacopoeia. In the 1898 edition we find creosote (creosotum) described as "a mixture of guaiacol, cresol & other phenols, obtained by the distillation of wood tar."

"The Characters & tests are: a colourless or yellowish highly refractive liquid, having a

strong empyreumatic odour & acid taste. It is faintly acid to litmus. It is dissolved by a 150 parts of water at ordinary temperatures & is more soluble in hot water. It is freely soluble in alcohol (90%), ether, chloroform, glycerine & glacial acetic acid. Specific gravity w/ below 1.079. It distils between  $392^{\circ}\text{F}$  ( $200^{\circ}\text{C}$ ) &  $428^{\circ}\text{F}$  ( $220^{\circ}\text{C}$ ). A 1% solution in alcohol (90%) or a half percent solution in water, with a drop of test solution of ferric chloride, yields a green coloration rapidly changing to a reddish-brown. It rotates the plane of a ray of polarized light to the left. Dropped on white filtering paper & exposed to a temperature of  $212^{\circ}\text{F}$  ( $100^{\circ}\text{C}$ ) it leaves no translucent stain (absence of less volatile liquids). It is miscible with equal parts of collodion without gelatinisation, & when shaken with five times its bulk of solution of ammonia its volume should not be diminished materially (distinction from phenol) Dose 1 to 5 minims. " (7)

It will be seen that the particular kind of wood tar employed is not mentioned; to ascertain that "beechwood" is meant we have to refer to Martindale, who says "that

There are two kinds of genuine creosote to be met with in commerce - one from pine wood, which is anhydrous & mixes perfectly with oil of turpentine, consisting chiefly of creosol; & the other principally from beech wood, which contains guaiacol & is more soluble in water. The latter is now made official." (8). The variety mentioned is derived from oak wood tar, but I can hardly credit that such a form of creosote should be recognized by the B. P., that is, if we may rely on Béhal & Choay's analysis (13) by which we understand it to contain only 14% of guaiacol. The U. S. P (9) is more explicit than our own, giving a preference to the wood tar derived from the beech, *Fagus Sylvatica*.

The B. P. content itself with mentioning that the constituents are guaiacol, creosol & other phenols. To learn the definite proportions of the constituents we have to go further afield. But unfortunately the authorities who have devoted attention to this matter are not in agreement. Thus, according to Squire (10) "the two chief constituents of creosote are guaiacol & creosol, the first of which predominates



in some specimens the second in others. Beechwood creosote contains most guaiacol; formerly, it was stated to contain more than 60 p.c., but when the demand for creosote & its salts arose, the proportion in commercial creosote dropped to 20 p.c. It can now be obtained containing 50 p.c. Hare (11) is of opinion that creosote contains 60% of guaiacol & 40 of cresol, not cresol. According to the Codex Supp. a good creosote (12) should contain about 20% of guaiacol with 40% of cresol & 40% of monatomic phenols, which latter should contain about 15% of cresylols.

A. Béhal & Choay (13) as a result of analysis made by them, state that beechwood creosote consists of 39 parts of monophenols; 19.72 of guaiacol; & 39.98 of cresylol & its homologues.

On the question of Solubility, again, we find varying reports. Thus according to Ferris, beechwood creosote is soluble about 1 in 110 of water, & 'English' creosote about 1 in 350; while the B. P. states that it is soluble in 150.

Glycerine has been added to the B. P. list of solvents; by this agent we can distinguish

between "beechwood" creosote & "English, Norway, or pinewood" creosote, the former being soluble & the latter insoluble in glycerine. (3)

The B. P. describes creosote as colourless or yellowish. This is apparently in complete contradiction to Stare ("), who says that creosote is of a reddish-amber hue. To remove the difficulty we must turn to the Reference-Book of Practical Therapeutics (15) where we learn that "the colour deepens on exposure to light, & as obtained in the market it is of a reddish-amber tint."

The B. P. of 1898 states that the plane of a ray of polarised light is turned to the left, while in the 1885 B. P. it is said to turn to the right.

The specific gravity is higher in the 1898 B. P. (1.079) than it is in the 1885 edition (1.071).

We have it on the authority of H. A. Griffen of New York (15) that many unprincipled chemists adulterate creosote with, or even substitute for it, carbolic acid; but by means of the B. P. ammonia test already given (on page 3) we can readily in any given specimen ascertain whether such is the case.

Bearing all these facts in mind it appears <sup>that</sup> regrettable, the B. P. which has lately been

Physiological action:-

issued should not have dealt more thoroughly and definitely with creosote. It distinctly savours of recommending a proprietary article when we have to specify a certain maker's name in prescribing, & yet many careful physicians feel compelled to adopt this course. I have ascertained from leading dispensing chemists that it is still the rule to qualify creosote by the word "beechwood", the necessity for this evidently arising from the vagueness of the B. P. description of creosote.

Creosote like Carbolic acid has the power of destroying minute forms of vegetable life & of rapidly arresting fermentation. (16) Walker (32), accepting Poppe's experiments with guaiacol as equally applicable to creosote, believes that on its ingestion into the stomach no more than 15 m to 20 m can be absorbed; but R. Seifert (45) traverses this statement, quoting Eschle's experiments on himself which proved that at least 100 m could be absorbed by the alimentary tract. Eschle further showed that creosote is passed off in the urine partly in combination with sulphuric acid, & partly with glycuronic acid. It exercises on the

Poisoning & its Treatment

wine remarkable keeping properties (16), the wine keeping for 14 days without change in patients taking creosote. Besides the bowels & kidneys, it is said to be given off by the skin & lungs, especially when given in large doses. (57) Personally I have not been able to detect any odour of creosote in the breath or urine of a patient taking it; to develop the odour in the urine, recourse must be had to distillation with sulphuric acid (strong) (53)

In many cases the wine is described as changed in colour; for instance Jamfield (60) found the wine turned to a dark or even porter colour. Revillet (29) noticed that the wine became blackish or black-green. Lamplough in a portion of his cases (59) noted a change to a dark olive or brownish tint. As far as my observations go no such change takes place. But in any case no importance need be attached to the discoloration for no bad symptoms have been noted accompanying it (59) (60).

Poisoning has occurred in a few cases but only in doses which were very large, the symptoms observed in such cases are dizziness, headache, dimness of vision, contracted pupils,

Literature of Creosote:

depressed heart action, a tendency to stupor, convulsions & coma. Trismus & cyanosis have also been observed. The treatment for such a condition is the administration of an antidote, the best being a soluble sulphate. (15)

As already stated Bouchard & Gimbert gave the first real impetus to the modern use of creosote. (18). They published in 1877 an exhaustive analysis of 93 cases of pulmonary tuberculosis treated with creosote (19)

They found (1) a lessening of the cough & expectoration in one or two weeks; (2) in three weeks a diminution of the fever with an increase in the appetite and strength; (3) at the same time frequently the night sweats vanished, & the disease appeared arrested; (4) a few weeks later, improvement of the physical signs indicative of fibrosis appeared, this sometimes occurring with almost incredible rapidity.

Professor Sommerbrodt (20) was the chief means of arousing a fresh German interest in creosote, he appears to have continued very active for many years in advocating its claims. After treating 5,000 cases with it he came to the conclusion that it was a specific by unfitting



the lung tissue for the growth of the bacillus. He quotes Dr. Guttman's observations that this organism can scarcely be cultivated in sterilised serum containing  $\frac{1}{4000}$  of its volume of creosote, & is incapable of development in slightly stronger solution. While Guttman, however, believes that it is impossible to keep the proportion of creosote in the blood as great as 1 to 4,000, which would mean the constant presence in the blood of 20 grains of the drug, in which case the bacilli would probably cease to develop, Sommerbrod thinks that it is quite possible, & that it can be done by gradually increasing doses till 20 to 25 grains are daily given for months [But the question naturally arises whether the 20 grs daily by the mouth is absorbed into the blood].

Sommerbrod (21) in 1891 reaffirms his confidence in creosote both for incipient & advanced cases. He advocates giving the patient as much as he can tolerate; in this way only can full benefit be derived. In 1892 (22) we find the same authority interesting himself in the use of creosote in the Prussian Army; Dr. von Coler, the physician-general informed him that it was already in use in the army & from the reports received from the sanitary officers it would be more widely used.

Sommerbrodt (23) urged the early use of creosote stating that the earlier it was employed the better the results were. He advocated creosote in Cape does.

Prof. Beverley Robinson (24) reported very favorably on beechwood creosote after using it in 143 cases. He found it most valuable in the early stage; he thought the beneficial effects were brought about by inducing the growth of fibrous tissue in the lungs, & by its aiding the general nutrition rather than as a bacillicide.

D. C. F. Collins (25) of St Luke's Hospital found in a 150 cases of phthisis treated with creosote no digestive disturbances, nor any renal (even where kidney disease existed) & the results were better than any other treatment.

Of its value in consolidation without cavity D. Austin Flint (26) speaks highly.

Andreesen (27) came to the conclusion that creosote had no specific action in phthisis, but that it did good by its action on the gastro-intestinal tract.

D. W. H. Flint (28) prescribed creosote in various ways: by mouth & by rectum & also as an inhalation, & considered milk an excellent

vehicle. He advocated its administration in a maximum dose, which he found to be usually, from 10 to 15 mgs daily.

The administration of creosote by the rectum was advocated by Dr. Reville (29). He noticed that absorption took place at once & that the patient perceived the characteristic taste, and that the urine became blackish or black-green.

Seifert & Holscher (30) were led to believe that difference of opinion with regard to the action of creosote arose from its varying composition.

According to Dr. Kinnicutt (31) benefit only resulted from continued & prolonged use of the drug.

Severe symptoms of poisoning were noticed in a case recorded by Dr. W. Freudenthal (32). The patient, a lady, who took the fairly large dose of 2.4 grams, twice daily, on one occasion took two doses in a short time; she became unconscious & remained so for eight or nine hours; the eyes were closed, the breathing was stertorous, loud coarse râles could be heard at a distance, the jaws were tightly clenched, the lips were cyanotic, & the pupils were contracted & insensible to light; all reflex movement was abolished & the urine was passed unconsciously. The pulse was 128 & the respiration 30. The kidneys were not affected. Stimulants

were given & recovery ensued, & afterwards even large doses were taken without harm.

7. Guindal<sup>(34)</sup> gives us the result of his experience of the use of creosote in tuberculosis in children. He made experiments on guinea-pigs & rabbit, which led him to the following conclusions: (1) The injection of creosote (however prepared) by the rectum in children is undesirable when any gastro-intestinal disturbance is present. (2) The experiments on guinea-pigs show that the administration by the rectum is an effective means of preventing invasion by tubercle or of lessening its virulence. (3) Administration by the mouth is inadequate for this purpose, inasmuch as it is impossible in that way to introduce a sufficient amount of the remedy to produce a therapeutic effect. If the mucous membrane of the rectum is in a sound condition even large doses do not cause irritation.

No diminution of the bacilli has been noticed by A. Albu<sup>(35)</sup> as a result of the creosote treatment; he found no lessening of the virulence in the bacilli when laboratory experiments were carried out, thus showing that no specific influence existed. He considers it a most useful remedy in phthisis, acting in most patients as an

effective expectorant; in many cases as a stomachic  
in many cases again as a tonic; but it does not cure  
the disease.

Among our own great authorities on diseases of  
the lungs, we find Douglas Powell (36) expressing a  
favourable opinion of creosote & its emperers. He  
regards the idea of destroying the tubercle bacillus  
by any internally <sup>administered</sup> antiseptic as happily abandoned.  
But he favours the view that "they have an indirect  
germicidal function in that they diminish suppura-  
tion in the walls of the cavities & about tubercular  
centres, which started in the first instance by  
tuberculosis, tends to be perpetuated by the action  
of pyogenic organisms, & thus render adjacent  
tissues more susceptible to fresh bacillary attack.  
Remedies of the creosote class are only of use in the  
afebrile period of the disease."

F. Simon (37) considers that, though the constitu-  
tional treatment of tuberculosis by large doses  
of creosote cannot claim in any way a specific  
effect, yet it can be positively stated that as  
a symptomatic treatment it exceeds any other form  
at present known. The drug can be well tolerated  
if absolutely pure.

R. Frey (38) sums up his opinion of the

hypodermic method by saying that although it is not the ideal remedy for tuberculosis, & although it will not succeed in every case, yet his own experience encourages him to hope that in many cases in which all other means prove useless, subcutaneous injections of creosote are capable of bringing about not only material improvement but relative cure.

after a careful consideration of his own experience & that of others J. J. Whittaker (39) arrived at the following conclusions:

1. When pure, creosote is harmless.
2. It has no direct action on the tubercle bacilli.
3. Tuberculosis pulmonum is chiefly a secondary infection by a streptococcus.
4. Creosote has no direct action on this streptococcus, hence none whatever on hectic fever.
5. It destroys lower organisms especially those which produce fermentation, without affecting the process of digestion.
6. Hence the virtue of creosote, which is undeniable in most cases, is chiefly if not wholly due to its influence upon nutrition.

Dunsey Geo (40) agrees with Professor Jaccoud, who is a warm advocate of the creosote

treatment & believes that creosote exerts a curative influence on the tubercular process in the lungs by promoting sclerotic changes. It diminishes expectoration, lessens its purulency, & removes any factor it may possess; it reduces the extent of the catarrhal lesions, & so reduces the area of the pulmonary changes. It lessens the tendency to haemoptysis. It cleans the tongue & promotes appetite & the capacity of taking food by its stimulating action on the stomach. Geo advocates the use of beechwood creosote.

W. Kingston Lyffe (41) conducted some experiments on guinea-pigs with the sputa of tubercular patients; the conclusions he arrived at were different from those of Albu. It is worth while recording with some fulness his methods & results as they were thorough & scientific. The observations were taken with the object of showing whether the benefit derived from the use of creosote in phthisis is due to any interference with the virulence of the organism, or simply to the fact that the drug by its antiseptic qualities stops fermentation in the stomach & consequently improves digestion & aids assimilation. at the Victoria Hospital, where the observations were

made, creosote was administered in three ways: as an inhalation; by the mouth & by means of the creosote chamber. The latter is a room eight or nine feet square; the patient, with his eyes protected by glasses & his nostrils plugged, is placed in it and a few ounces of commercial creosote are heated in an iron dish over a spirit lamp; the fumes rapidly come off till the room is filled with vapour, which the patient breathes; he is kept in it for an hour. Observations on the bacilli showed that their number bore little or no relation to the condition of the patient's health, & that no distinction could be drawn, either from their number or their morphology, between the bacilli from those cases treated by creosote & those taking other drugs. The plan adopted was to inject the sputum into the leg of a guinea-pig. If a guinea-pig is thus inoculated with the bacillus, it appears to invariably occur that in a few days the popliteal glands are ~~affected~~ affected, then the inguinal & finally the lumbar; after fifteen days the spleen & liver are diseased & in a month or five weeks the animal dies with implication of the lung. It is therefore possible to gauge the virulence of



the injection by the extent of the mischief done. Thus if at the end of fifteen days, when the liver, spleen & glands should be affected, only the glands are the seat of the disease, it is fair to say that the virulence of the sputum is less than normal....

In the next series of cases the patient took creosote by the mouth, & here the results were strictly more encouraging. The dose varied from 2 to 12 minims three daily. Taking first the cases treated with 2-drop doses, in one case a guinea-pig inoculated before the commencement of the treatment died in eighteen days, whereas, when the patient was taking 2-drop doses of creosote, the guinea-pig inoculated did not die for seven weeks. In another case the animal inoculated with the untreated sputum was killed within fifteen days, & was found to have tubercle in all its organs; while another inoculated at the end of two months' treatment, & killed also on the fifteenth day, showed tuberculosis of the glands but no affection of the internal organs. With large doses of creosote the effect was more striking. Thus, inoculation with the untreated sputum caused death on the twentieth day, with the usual post-mortem appearances. After two months' treatment with 6 minims of creosote three

times a day, one guinea-pig inoculated lived for nine weeks; another was killed on the fifteenth day, with tubercle in the lumber glands but not in the viscera; the glands were inflamed but not caseating; the bacilli were few, small & thin, not empyrating into colonies, & an attempt to cultivate them did not succeed. Inoculations were then made from patients taking up to 12 minims three daily. The longest time that any guinea-pig lived was three months after inoculation from a patient taking 10 minims at a dose; while another inoculated from a patient taking twelve minims, lived a shorter time. If the animal lived long enough, it always died of tuberculosis.

The observations may be summed up as follows: In the first series of cases, those that were taking creosote as an inhalation in addition to other drugs, no effect on the violence of the disease was noted. In the second series where the drug was given by the mouth in doses varying from 2 to 12 minims three times a day, though when the smaller doses were given the diminution was slight, yet when the larger amounts were reached it was extremely marked. In the third series, though the animal lived longer than in the other

case, it is impossible to dogmatise from so small a number. Fourthly, creosote injected under the skin in tuberculous guinea-pigs had a markedly restraining effect, provided that the disease was not too far advanced. Repeated attempts were made to grow the bacilli in serum from animals inoculated with tuberculous sputum from patients taking creosote in large doses, either by the mouth or by means of the creosote chamber.

Dr. John R. Conway of New York (42) upholds the doctrine of the specific curative action of creosote in tuberculosis in large doses. He has used it in nearly four hundred cases, including not only the pulmonary form, but tubercular disease of the peritoneum, the joints, the bones, the glands, & the larynx. He lays great stress on the method of administration & on the quality of the creosote. He prescribes capsules containing from 2 to 4 minims with cod liver oil.

J. Weiss (43) has on the contrary arrived at the conclusion that creosote is not a direct specific against tuberculosis, but that it influences the disease indirectly by lessening secretion & acting as a stomachic. He considered it the best remedy for the symptomatic treatment of phthisis.

Dr. Arthur Foxwell (6), although acquainted with the opinions of Bouchard, Gimbert, & Sommerbrodt, confesses to failure in the use of creosote. In his own experience he has found creosote act as a gastric irritant in any quantity beyond a daily dose of 6 minims, & he has never traced any change in the pulmonary & constitutional condition of his patients in its use in such small amount. But he has never thoroughly tried the drug as, when pushed, he has found it so disagreeable — It would be interesting to ascertain the kind of creosote used & the method of its administration, as his lack of success may have largely depended on these factors.

According to F. R. Walters (82), creosote and guaiacol, in addition to their action as antipyretics, diminish secretion from pulmonary cavities & appear to have a marked inhibitory influence over the spread of tuberculosis. Hudson supposed that creosote acted on the toxins produced by the bacillus. When creosote is used it is important to notice that it is beechwood & not coal-tar or junewood creosote. He quotes Poppi's experiments with guaiacol (which are probably applicable to creosote) which show that not more than 15 to 20 m's are absorbed per diem in the alimentary canal, so

that bigger doses are of no advantage when given by the mouth; & where more is required it must be administered by the skin .... If the kidneys are unimpaired the drug must be cautiously administered. He has used the hypodermic method with considerable success; enormous doses have been reached when gradually increased, such as nearly 8 ozs. of a 1 in 15 solution. For this purpose he used sterilised almond oil.

R. Seibert (45) fails to accept the results of Professor Poppi's experiments, quoting Eschle's on himself. Eschle showed that quinaed was excreted by the kidneys partly in combination with sulphuric acid & partly with glycuronic acid. At least 100 minims were absorbed daily in these experiments of Eschle.

Harris & Beale (46) state, in their book on the treatment of pulmonary consumption, that they have obtained results which were not all they would wish. That this opinion was not final will, at least so far as Dr. Beale is concerned, appear later on.

Ransome (47) discussing the results of the use of creosote at the Manchester Hospital for Consumption, says that on the whole they confirmed the results from other institutions, & he is in-

claimed to attribute most value to the results derived from the outdoor department. In many of these cases there was certainly a distinct improvement; & there were several cases of undoubted arrest & apparent cure. These results of Dr. Ransome are of importance owing to the class of patients in which he met with success. He admits however that these patients had spent some time in hospital; & had subsequently changed their residence in obedience to the advice usually given to such patients.

Daremburg (48) protests against what he calls "Ces orgies créosotiques" & thinks that larger doses than 1 gramme per diem are dangerous, likely to provoke digestive troubles, fatal hæmoptisis and fresh deposits in the lungs or distant organs, [But results such as these must surely be rare; at least they are so far as I have been able to discover.]

Discussing the method of administering creosote by subcutaneous injections the 1897 Yearbook of Treatment (49) states that abroad, they have been largely used, the drug being dissolved in liquid vaseline or almond oil. Beginning with modest doses, it has been pushed to half-an-ounce at a single injection, with the idea of so thoroughly creosoting the whole body as to render it no longer a good feeding ground for the

bacilli. It is amazing, it goes on to say, that greater disasters have not happened. There is no evidence whatever that the subcutaneous method offers any advantage over those usually employed, & the pain & danger are obvious.

H. A. Griffen of New York (16) takes the view that Creosote has no specific action whatever on tubercularis, & that while it is beyond doubt beneficial in a large number of cases, its favourable effects are due only to its action as an expectorant & as a stomachic; the latter being practically important because of the gastric disturbance in fermentation so often present in the phthisical."

Ringer (51) says that "Creosote in full doses is strongly recommended in phthisis, especially in non-febrile or only slightly febrile cases. It is said to diminish expectoration, improve appetite & increase weight. The pure beechwood creosote is to be prescribed & the dosage should be pushed to the extent of 5 drops or more for a dose, thrice daily after meals."

J. K. Crook (52) reports 45 cases of pulmonary tuberculosis treated with large doses of creosote. Of these 5 were apparently cured - that is, there was a complete disappearance of the symptoms & physical signs of phthisis; 5 showed marked improvement & 8 received some benefit; 13 showed no influence at all from

The treatment 7 & 8 died. The remainder were not treated long enough to enable the author to draw any positive results. Of the 15 cases that were cured, 2 were in the second stage & 3 in the first stage; of the 5 that were benefited 2 were in the first & 3 in the second. Crook believes that creosote is a remedy capable of arresting certain cases of tuberculosis.

Dr. Clifford Seale (53) in a paper read before the Harveian Society spoke eulogistically of beechwood creosote in large doses in pulmonary tuberculosis. He began with 5 minims dissolved in cod-liver oil, the same amount of creosote being added to the dose every other day until 160 to 180 minims a day were reached. The results achieved were highly satisfactory. The fall of temperature, gain of weight & general subsidence of the symptoms were in many cases surprising, & seemed to be more definite & lasting than the degree of improvement commonly observed as the result of hygienic treatment only.

At the same meeting Dr. St. Clair Thomson (53) related how at Falkenstein he had found creosote, after a long trial, had been completely abandoned along with tuberculin & all other specific remedies. Small doses were occasionally given but merely for their effect on the digestive system.



Continuing the discussion Dr. Stamford G. Fellee (63) inquired whether Dr. Beale used creosote of any particular manufacture, as he had found the results vary greatly with different specimens of the drug, which in a large proportion of cases was not tolerated by the stomach.

A. J. Garland (Omaru, New Zealand) (64) says that creosote can be used with great advantage, & quotes one of the many successful cases he has had, illustrative of this statement.

G. H. Hicks (Wymeswold, Leicestershire) (65) has, in a few very advanced cases of pulmonary tuberculosis, found creosote to have a retarding effect.

As an example of extreme tolerance of beechwood creosote Chas. Graham of Carlisle (66) reports that a patient of his, by gradually increasing the dose, reached 340 minims in the 24 hours.

Harvey Campbell (67), commenting on this case, says that he has found little difficulty in getting patients to tolerate drachm doses three or four times a day. In fact he states that, to obtain the full therapeutic effect, not less than one drachm three daily should be given. All the secretions, more especially the expectoration, become impregnated, thus showing that the

drug is eliminated by the very organ we wish to act upon.

D. Edmond Chaumier, of Lyons, (58) describes creosote as a "marvellous" remedy. He points out that hygienic surroundings are of great value in assisting the good effects of the drug. For really successful treatment large doses are required, & the best means of administering creosote by the mouth are pills, and solution in cod-liver oil. The limit of tolerance is easily reached in some cases. He takes it as proved by Hagem & Renault that dyspepsia & inflammation of the stomach occurring in phthisical patients are due to creosote & guaiacol; this is of course a very serious drawback in a disease where the maintenance of the digestive power is so important. It has often happened, he goes on to say, that just as the patient is beginning to really benefit by creosote he has to stop it on account of gastric derangement.

An experience of the use of large doses of beechwood creosote in 100 consecutive cases of pulmonary tuberculosis, in the City of London Hospital, enables Charles Lamplough (59) to speak highly of its value. Of these 100 cases, 62 had disease of both lungs, 18 had signs of cavitation, many were of an acute type,

3 had diarrhoea, & 4 were suffering from albuminuria, when the treatment was commenced. Where the diagnosis was doubtful no creosote was given until the tubercle bacillus was found in the sputum. In most cases beneficial results were recorded as evidenced by increased weight, improvement in physical signs; & in those suffering from albuminuria disappearance of that symptom. No circumscribed inflammatory patches in the alimentary canal were noted in the only post-mortem made. In concluding his very able article Launplough suggests the following points as worthy of consideration and further investigation:

1. The best beechwood creosote can be given in amounts varying from 120 to 240 minims daily in cases of pulmonary tuberculosis.
2. The drug is best administered in cod-liver oil or in spirituous solution, & in some cases the "Creosote Chamber" or oro-nasal inhaler may be ordered with advantage.
3. The dose should be small at first, but it can be rapidly increased to 40 minims three times daily for an adult. In 3 cases doses of 30 minims three times a day were well-tolerated by children.
4. Large doses rarely cause any gastric disturbance.

on the contrary, the appetite is frequently increased, symptoms of dyspepsia disappear, & cod-liver oil is more easily assimilated. The cough, expectoration and night sweats are diminished & the physical signs improved.

5. Owing to its disinfectant action on the alimentary canal the drug probably diminishes the risk of tubercular enteritis by auto-infection when patients swallow their sputa, but owing to increased peristalsis, which is created by creosote, it is usually contra-indicated in cases where ulceration is already advanced.

6. The drug does not tend to cause haemoptysis but rather to prevent its recurrence.

7. Creosote does not tend to irritate the normal mucous membrane of the genito-urinary tract.

8. Owing to its extremely small cost pure creosote can be given to a much larger number of patients than the carbonates of creosote & guaiacol, which respectively cost four times & twelve times as much as the older drug.

That creosote still occupies watchful attention in France we have evidence of in M. Davine of Paris (61), who has spent considerable <sup>time</sup> in finding out the mode of action of creosote.

He thinks the favourable action of creosote to be due, firstly, to its bactericidal action on the microbes which accompany the bacillus of Koch, such as streptococci, pneumobacilli & the like; secondly, to its stimulating action on nutrition, so that phagocytes which prey on the bacillus of Koch are increased in number; and thirdly, to its action on the toxins secreted by the bacillus. The patients to whose cases M. Savine referred were those suffering from pulmonary phthisis of the first & second degrees but were not cachectic. In some of the cases, commencing with 40 minims by the mouth, in milk, oil or emulsion, he gradually increased up to 300 minims in the 24 hours.

Hale White (62) states that creosote has been much employed for phthisis, & many authors claim considerable success. The doses must be gradually pushed till 30 or 60 minims are taken at a time. It should be given immediately after meals. The taste may be concealed by putting it in a few drops of rum, but it is best given in capsules."

Percy Kidd (63) remarks that "creosote along with some other drugs has gone through successive stages of hasty and exaggerated laudation; half-hearted approbation and contemptuous neglect."

*Nodes of Administration of Creosote:-*

Osler (4) speaking of creosote says that it is "an old remedy, strongly recommended by Addison, & the reports of Jaccoud, Fraentzel & many others show that it has a positive value in the disease."

According to Dr. Hector Mackenzie, while few are prepared to state that creosote has any specific action, most will admit that it has very valuable properties in the treatment of tuberculosis.

The purest beechwood creosote should be employed. (64)

Whitla (16) refers to creosote as the best of all remedies in ordinary phthisis.

It will serve a useful purpose at this point if some attention be devoted to the modes of administration of creosote.

It is interesting to note that every possible way in which creosote can be exhibited has been tried. Out of the host of formulae recommended the idiosyncrasy of any particular patient may easily be met.

Creosote has been given by the mouth; as an inhalation; by means of tracheal, rectal, hypodermic or intrapulmonary injection; & by inunction. The "intensive" method (16) is a combination of the hypodermic, rectal, inunction and

inhalation methods.

It will be well to notice that oxide of silver is an incompatible, an explosive mixture being formed when this substance is combined with creosote in the pilular form, unless it is previously mixed with some inert powder (16). Martindale (65) observes that calcined magnesia and slaked lime, sometimes recommended as excipients, form compounds with creosote perfectly insoluble & indigestible.

There are four kinds of creosote in the market:

1. Beechwood creosote, made from 'Rhenish beech tar' (66)
2. Oakwood creosote (3).
3. Pinewood, English or Norway's creosote (3), made from 'Stockholm tar' (67).
4. Commercial or coal-tar creosote (67).

The majority of those who have met with success in the use of creosote emphasize the necessity of prescribing the "beechwood" variety. The "coal-tar" product, being a powerful irritant, is unsuitable for internal administration; medicinally it is only used for burning in the creosote chamber (68).

We now come to the dosage & formula that have been recommended. In the B. P. we find three forms: 1. Creosote, dose 1 to 5 minims



2. *Mistura Creosoti* 1 minim in 10z

A nearly colourless mixture, consisting of creosote & spirit of juniper, of each 16 mins., syrup 1oz., & distilled water 15 ozs

Dose  $\frac{1}{2}$  to 1oz.

3. *Unguentum Creosoti* 1 in 10.

A white ointment, prepared by melting together 1 oz. creosote, 4 ozs. hard paraffin, & 5 ozs. white soft paraffin, & stirring till cold.

It is impossible to get creosote taken by itself owing to its acid taste & peculiar odour, it would, too, injure the coats of the stomach being irritant in a concentrated form. The B. P. mixture is an elegant preparation, containing juniper & syrup as flavouring agents. Where for any reason, it is desirable to vary the method of administration it may be given by injection, using the ordinary B. P. ointment, or

4. A modification of Valentine Gilbert's ointment (49) :-

$\mathcal{R}$  Creosoti  $\mathfrak{z}\text{ss}$

Lanolin

Adipis Prepar

Ol Olive  $\bar{a}\bar{a}$   $\mathfrak{z}\text{j}$ . or in

5. Suppository (49).

6. A very easy way of giving the drug is in capsules (69), a plan which most authorities speak highly of.

7. Very little difficulty will be found in getting adults to take <sup>the</sup> drug in the form of pills:-

(A) Pilula Cresoti (Squire) (60)

Cresote 12 minims

Curd soap in powder 6 grs

Refuonce in powder 30 grs

Mix & divide into twelve pills.

(B) Pilula Cresoti (Martindale) (65)

Cresote 2 dractms

Curd Soap in powder 120 grs

Put the cresote in a 1-ounce wide mouth stoppered bottle, add the soap & mix well. Then digest in a water bath till they combine. Each two grains of the mass will contain, as nearly as possible, 2 minims of cresote.

8. The firm of Oppenheimer, Son & Co make the taking of cresote a very trivial task indeed by enclosing the drug in their palatinoids and bi-palatinoids. Other drugs may be combined with the cresote:-

(a) In Palatinoid in combination with camphor & capsaicin; or Eucalyptol; or Menthol; or

Eucalyptol & Eodofon.

(3) In Bipalatinoids along with Hypophosphites; or Sodii Bicarb, P. Zingib. & Menthol; or Ferrous Carbonate; or Menthol; or Gaston's Syrup; or Calomel.

Creosote in the form of pills, capsules, or palatinoids, or bipalatinoids should be taken soon after meals to ensure thorough dilution.

9. The "Journal des Praticiens" recommends the following formula for the administration of Creosote, the prescription being put up in cachets (70):-

℞ Creosote }  
Benzoin } of each 15 grains

Powdered Charcoal  $1\frac{1}{2}$  grains

Triturate the creosote & the benzoin for a moment together & add by degrees the charcoal. This mass is then to be divided into 5 or 10 cachets, each one of which will then contain a proper dose. It is claimed this prescription is very well borne by the stomach.

10. Various kinds of mixtures have been recommended:-

(a) One of the simplest & best is the form employed by Clifford Beale (53) & Lamplough (59) of giving pure beechwood creosote dissolved in

Cod liver oil, beginning with 3 to 5 minims, the same amount being added to the previous dose every alternate day until a maximum of 160 or 180 minims a day is reached.

(4) Oppenheimer, Son & Co keep mixtures which prove acceptable in many cases.

They combine Creosote with Cream of Malt.

.. Cream of Malt & Cod Liver Oil.

.. Cream of Malt, Cod Liver Oil & Hypophosphites.

(4) Creosote may be given in olive oil (8)

(8) If the patient be unable to take creosote in cod liver oil, a trial may be given to the following (59):-

℞ Creosote ℥v  
℥i Gent. Cojāā ℥xx  
Sp. Vini Rect }  
℞ Sol. Glycerin. Liq. ℥ss  
aq ad ℥i

℞. To be taken three times a day.

Five minims of creosote may be added every other day to each dose till a maximum of 40 minims three times a day is reached.

(E) an excellent alternative to the foregoing is called "Wine of Creosote" (40):-

Creosote ℥i  
 ℞ Gentian ℥ij  
 Brandy ℥ij  
 Malaga wine ℥x

From 2 to 4 tablespoonfuls are given daily, each mixed with a glass of water.

(F) Ransome (47) suggests milk as a vehicle, & it is to be given an hour after food.

(G) When milk does not agree with the patient Dr. W.C. Glasgow uses California port wine & dilutes freely with water (71)

(H) Ransome recommends this prescription:-(47)

℞ Creosoti ℥i to ℥i  
 Syr. Tolutani ℥i  
 muc. Hafacanth ℥ijss  
 Aq. vel Aq. Camph. ad ℥ss

(I) Some put forward a mixture called "Gutte Creosoti" (40):-

℞ Creosote 16 minims  
 mucilage of Acacia 60 minims  
 Syr. of Orange 1 oz  
 Water to 2 oz.

Mix the creosote with mucilage & add

the other ingredients. One or two teaspoonfuls for a dose in an ounce of milk.

(K) Squie, in addition, gives a list of several useful formulae :-

Élixir Créosoté (Fr) (10) :-

Creosote 15

Rum 95

(L) Éosote (Creosote Valerianate) (10) :-

A fluid distilling at 240°C. has been recommended as a substitute for Creosote on account of its freedom from corrosive & toxic properties. Commencing dose 3 grains, increasing to 6 or 9 grains three times a day.

(M) Tannosol (Creosote Tannate) (10). - A brown powder soluble in water.

(N) Douglas Powell (36) in prescribing creosote with cod liver oil adds essence of peppermint:-

Beechwood Creosote 3 to 6 minims

Essence of Peppermint 1 minim

Cod Liver oil 2 fl ℥

A fourth part three or four times a day; or 3 drops of cognac or rum, & 1½ oz of Glycerine, may replace the oil in the formula

(E) S. Solis-Cohen (72) has found this prescription useful:-

℞ Creosoti (beechwood) ℥ XXX or LXXX

℥r. Cardamomi ℥ iv

Glycerini ℥ ii

Alcoholis q. s. ad ℥ iv

Sig. ℥ ii in water after food.

Note, to the glycerine add the creosote, then the tincture of cardamomo & alcohol. The smaller dose of creosote is used at first, & the quantity gradually increased until 5 drops, four times a day is reached.

11. The hypodermic injection of Creosote, in sterilised almond oil, 1 in 15, has been successfully used by F. R. Walters (32).

12. Yet another way of giving creosote is by inhalation:-

(A) Dry, on an oro-nasal or "ozonic" inhaler (8)

(B) Moist inhalation may be carried out by using:-

Vapor Creosoti (8):-

Creosote 80 minims.

Liq. Carbamate of Magnesium 30℥

Water 1 ounce.

A teaspoonful in a pint of water at a 140° F.

(Y) The most thorough way of using inhalation is by means of the "Creosote chamber" (G.), which is a room eight or nine feet square; the patient with his eyes protected by glasses, his nostrils plugged, is placed in it & a few ounces of commercial creosote are heated in an iron dish over a spirit lamp; the fumes rapidly come off till the room is filled with vapour, which the patient breathes; he is kept in it an hour.

Remarks. Of all these methods the one I am most favourably disposed to is the mixture of cod liver oil & creosote; it has decided advantages: ease of dispensing, readiness with which it may be taken by most patients, the cod-liver oil being such a useful food in tuberculosis, & its cheapness making it accessible to the poorer classes.

Where the question of cost is no object, palatinoids, bipalatinoid & capsules will no doubt prove most acceptable, their tastelessness appealing to the fastidious.

Subcutaneous injections are painful & sometimes dangerous & will never become popular. Intra-pulmonary injections present too obvious risks in the way of hæmoptysis to ever be generally employed.



Clinical Cases:-

With regard to dosage, though encouraging results have been obtained with the smaller range of dose, yet I think a good deal remains to be said in favour of large doses. That large quantities may be taken with benefit has been proved by Beale (53), Campbell (57), Lamplough (59) & others. The biggest daily quantities are those recorded by Graham (56) where a patient of his took as much as 340 minims for a considerable period; & by M. Savine (61) who managed to get a number of his patients to take 300 minims in the 24 hours.

Inhalation by means of the oro-nasal or "Jonie" inhaler is a very generally adopted method. Though some have advocated the claims of the "Creosote chamber", Dr. Chaplin (62) has failed to find any good effect from its use in phthisis.

I will now proceed to briefly describe & discuss three cases in which I watched the administration of gradually increasing doses of beechwood creosote, given in the form of capsules. The patients were inmates of the Victoria Hospital for Consumption at Craigleith, an institution where the "open-air" treatment is in operation. It is to the kindness of Dr.

R. W. Philip that I owe the privilege of having these cases for observation.

Case I. Elizabeth Dall, 18 years of age, had been complaining for some months before I saw her of pain in the right side of the chest & bad cough. She had had an attack of hemoptysis three months previously.

The Sputum, scanty in amount, was several times examined for tubercle bacilli without success. The physical signs, however, gave little room to doubt as to the diagnosis:

There was dulness over both apices in front, more marked on the right side; bronchial breathing could be detected on both sides, and pectoriloquy was present on the right side. Posteriorly there was marked dulness over both scapular regions with bronchial breathing; expiration was somewhat prolonged in the left axilla, & over the left base distinct cogwheel breathing could be made out. The temperature was normal or subnormal.

This patient commencing with 3 minims of creosote reached 30 minims three times a day after food, in a period of three weeks, by increasing the dose every other day. During this

fine gradual improvement took place in both  
 lungs, as shown by the dulness clearing up, the breath-  
 ing becoming stronger & the accompaniments fewer. The  
 appetite remained good, there being no gastric dis-  
 turbance. A few patches of eczema, which appeared  
 on the nose, left ear & left hand, disappeared with-  
 out any special attention. The breath was free  
 from the odour of the drug. The urine though daily  
 examined presented no change in colour, smell, reac-  
 tion, or specific gravity & was non-albuminous; to  
 get the odour of creosote distillation with strong  
 sulphuric acid was necessary.

Some loss of weight occurring at the end of  
 three weeks, it was thought best to discontinue the  
 drug.

Case II. James Scott, 35 years of age, had  
 no serious illness until 8 years ago when he  
 had a severe hæmoptysis; this was the first of  
 five similar attacks. He had when I first  
 saw him in December 1898 a short frequent  
 cough & a considerable amount of expectoration  
 tinged with blood. Tubercle bacilli were present  
 in the sputum.

Pulmonary tuberculosis was further evidenced  
 by the presence of: Dulness on percussion and

bronchial breathing at both apices in front; abundant moist crackles & pleurisy at the right apex; cogwheel breathing below & to the outside of the left nipple. Posteriorly, marked dullness existed in the interscapular region and bronchial breathing over the same area. A slight amount of pyrexia was present.

Creosote was given in 5 minim doses three times a day after meals; the dose being gradually increased every other day until 40 minims were reached. There was no gastric disturbance.

The physical signs in the chest showed distinct improvement, such as lessening of the accompaniments & better entry of air. The odour of creosote was only on rare occasions perceptible in the breath. The urine presented no abnormal features, as far as ordinary tests are concerned, although tested daily; it was only by employing distillation with strong sulphuric acid that the odour of creosote could be detected. At the end of a month as the patient was not gaining in weight the creosote was stopped.

Case III. Wm. Dickson, aged 16 yrs, had been ailing for four months before I saw him. He had a slight cough with a small amount of

expectoration; and in the latter there were numerous tubercle bacilli. There was no history of haemoptysis. Physical examination revealed: Dulness at both apices; cracked pot sound in second left interspace in the parasternal line; moist accompaniments; pectoriloquy under the left clavicle. On the right side expiration was somewhat prolonged & there was copious wheezing over the same area. Posteriorly extensive areas of dulness existed in the scapular & inter-scapular regions and over the left base. The breath sounds were bronchial in type but feeble over the scapular area, & very feeble over the left base; there were accompaniments over the area of dulness described. The temperature was normal or subnormal.

In this case, starting with 5 minims, creosote was given in gradually increased doses up to 45 minims three daily. This patient took the drug for five weeks. The condition of the lungs underwent considerable improvement as shown by the gradual disappearance of crepitations & freer entry of air. The chest measurement showed an increase. No odour of creosote was present at any time in the breath. There was never any symptom of gastro-intestinal disturbance.

on the contrary the appetite steadily improved.

The urine was perfectly normal to ordinary tests, there being no change in colour, reaction or specific gravity, nor was there any albumen present; distillation with strong sulphuric acid had to be used to develop the odour of creosote.

Remarks. The excellent hygienic conditions in which these patients were placed would no doubt largely discount the results of any line of medicinal treatment that might be adopted. The number is too small & the period of trial too short to generalise very much; still they are in my opinion worth recording for they prove:

1. The feasibility of large doses of creosote being taken without disturbance of the alimentary tract.

2. Although cavities were present in the three cases, & in two there was a history of hæmoptysis, no hæmorrhage from the lungs was induced by the drug.

3. The urine remained unaltered, & the kidneys were therefore unaffected. To develop the odour of the drug distillation with strong sulphuric acid had to be employed.

4. The breath & expectoration of these patients being free from the odour of the drug shows that

Conclusion :-



large doses may be exhibited without the lungs eliminating any of the creosote taken.

I must confess that I should like to have seen the effects of administering creosote in cod-liver oil in these cases. I consider this combination an excellent one & I shall certainly give it a decided trial when the opportunity is presented in the future. Had this formula been used there would most probably have been a gain to record all round in the weight, instead of a loss in Case I & a stationary condition in Case II.

An impartial perusal of the literature of creosote in the treatment of pulmonary tuberculosis, & a consideration of the cases I have briefly outlined warrant the following conclusions:-

The preponderating weight of evidence is distinctly in favour of creosote.

The kind of creosote mostly recommended is the pure beechwood (24, 40, 32, etc)

Darvemberg's charges re "Creosotic Oozes" terminating in digestive troubles, hæmoptysis & extension of the disease to other organs meet with denial in very many quarters (47, 59 &c.).

Percy Kidd's statement (63) of creosote being heated

with "contemptuous neglect" does not apply to Edinburgh, where to my own knowledge many authorities, such as Byron Bramwell, John Lyllie, & Peter McBride, speak highly of the value of creosote.

The cause of failure in many cases, e.g., Arthur Foxwell (19), Thomson (53) & Felce (63), very probably arises from impure preparations being used.

As to the mode of action of creosote various theories have been promulgated: (a) Sommerbrodt (20) regarded it as a specific by unfitting the lung tissue for the growth of the bacillus. (b) Kingston Tyffe (41) as the result of numerous experiments came to the conclusion that though the bacilli were not lessened in number, their virulence was decidedly diminished. Douglas Powell (73) makes the remark that the bacillus would cheerfully withstand doses far beyond the tolerance of the host. (c) Bumez Yeo (40) finds himself in line with Professor Jaccoud who considers that creosote acts by inducing sclerotic changes in the lungs. (d) Hudeod (74) believes that creosote acts on the toxic produced by the tubercle bacillus. (e) It may act, according to Douglas Powell (36) by destroying pyogenic organisms which accompany the bacillus. (f) Albu (35) Whittaker (39) & others consider that benefit chiefly results by creosote acting as an intestinal antiseptic

& thus favourably influencing nutrition. (g) M. Savine of Paris (61) regards creosote as acting in a combination of three ways already stated: (d)(e)(f).

Whatever the exact mode of action may be most observers nowadays are in agreement at any rate on one point - the favourable influence creosote exerts as an expectorant & on digestion; in the latter case by preventing the fermentative changes in the stomach so common in the phthisical.

The power of creosote to produce dyspepsia & inflammation of the stomach urged by Hagen and Renault (75) receives contradiction from Lamplough (57)

no bad effect on the kidneys need follow its use according to C. F. Collins (25); on the other hand benefit in diseased conditions may accrue (59).

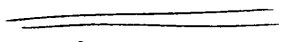
The cheapness of creosote places it in the reach of a large number who could not afford the more expensive derivatives, the carbonates of Guaiacal (Dustal) & Creosote (Creotal); this is a point which specially appeals to me, having for many years been engaged in a large works' practice where pulmonary tuberculosis was common & the means of the people limited.

Although the temperature has been noticed to fall during its use by various authorities (32)

References: -

Creosote is mostly advocated in the afebrile or slightly febrile period of the disease (36).

Finally, I may say that I believe we have in creosote one of the most powerful remedies for good in pulmonary tuberculosis; & it will continue to hold its position pending the discovery of a reliable tuberculicid.



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