NOTE ON THE VALUE OF GUAIACOL APPLIED EXTERNALLY AS AN ANTIPYRETIC.

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IN THE MEDICAL NEWS for January 27, 1894, Dr. Da Costa publishes some interesting clinical remarks on the use of guaiacol externally in reducing high temperatures in typhoid fever and other febrile diseases. Following the observations of Sciolla, Bard, Lannois and others, concerning the powerful antipyretic action of guaiacol applied in this manner, Dr. Da Costa states that he was induced to try its effect in the "systemic fevers." The guaiacol was applied with a camel's-hair brush, and then rubbed in for fifteen minutes with the hand, or covered immediately with an impermeable bandage. Thirty to sixty drops at a time were applied, thirty being about the average dose. A very marked effect on the temperature was noticed, a fall of several degrees occurring through two to three to four hours. The effect was so marked in cases where large quantities were used that Da Costa advises small doses in the beginning—not more than twenty minims, for instance, is advised as an initial dose in a temperature of 103°. During the fall in temperature no ill

[1] Liébeault: Thérapeutique Suggestive, p. 109. Paris, 1891.

effects were noted on the pulse or the respiration. In one case, after the temperature had reached its lowest point, there were chills on three occasions, but in the other cases no particular reference was made to excessive sweating or to chills. Dr. Da Costa suggests the possible value of this method of treatment in cases of typhoid fever, in which, for one reason or another, baths are inadvisable.

On the appearance of Dr. Da Costa's note we proceeded to test the action of guaiacol in various cases in Professor Osler's wards at the Johns Hopkins Hospital, with results which are perhaps of sufficient interest to note. Guaiacol has been used in all in eight cases. The skin, generally of the abdomen, was washed carefully with soap and water, and dried. The guaiacol was then painted on with a camel's-hair brush and immediately covered with an impermeable dressing, or else rubbed in for fifteen minutes with the hand, the area being afterward covered with a similar dressing. The results, in brief, are as follows:

CASE I.—*Acute pneumonia; fall of 3½° in temperature, with profuse sweating in two hours and a half after the application of guaiacol, gtt. xx; chilliness between three and four hours after the application, with rapid return of fever.*

The patient was a male, eighteen years of age, at the fourth day of the disease (January 30, 1894). The temperature, at 8 A.M., was 102.8°; at 10 A.M., 103°; at 12 M., 104.2°; at 2 P.M., 103.6°; at 4 P.M., 102.8°; at 6 P.M, 99.8°; at 8 P.M., 103.4°; at 10 P.M., 103.6°; at 12 midnight, 104°. At 3.30 P.M., guaiacol, gtt. xx, was rubbed into the abdomen. Between 4 and 6 o'clock there was profuse sweating;

between 6 and 8 o'clock chilliness. The pulse fell from 92 to 72 at 6 P.M.; at 8 P.M. it was 112. The crisis occurred on the following day.

CASE II.—*Typhoid fever; applications of guaiacol, gtt. xxx (1 c.c.), followed by falls in temperature varying from 3° to 4.5°; profuse sweating; chills or chilly sensations with the reaction.*

The patient was a woman, twenty-four years old. On the ninth day of a mild attack of typhoid fever, the temperature being at about 103°, twenty drops of guaiacol were applied to the outer side of the thigh, without previously washing the skin; no effect was noted. On the two ensuing days six applications of guaiacol, each of thirty drops (1 c.c), were made; the skin was washed and the guaiacol rubbed in with the hand. The falls of temperature varied between 3° and 4½°, the lowest point being reached in from two to four hours. In all instances, shortly after the lowest point was reached there were either chilly sensations or a distinct chill, with a rapid rise of temperature. An example of one of these falls after the application is as follows:

On February 1st, the temperature at 4 A.M. was 102°; at 6 A.M., 103.2°; at 8 A.M., 99.8°; at 10 A.M., 100.4°; at 11 A.M., 103.4°. Thirty drops of guaiacol were applied at 6 A.M.; profuse sweating followed between 6 and 8 o'clock; at 10 A.M. there was a chill. The patient was much relieved by the applications, and expressed a desire that they should be continued. The profuse sweating and the chills or chilliness following the applications had had, however, a visibly weakening effect, and the applications were discontinued. Tub-baths and cold sponge-baths were renewed, and there was an uninterrupted recovery.

CASE III.—*Pneumonia; application of guaiacol, ʒss (2 c.c.), followed by a fall of only, 0.8°; further application of gtt xx followed by a fall of 0.2°.*

A male, aged fifty-four, had acute pneumonia. On February 3d, the third day, the temperature at 8 P.M. was 102°; at 10 P.M., 101°; at 12, midnight, 100.2°; at 2 A.M., 101°; at 4 A.M., 101.2°; at 6 A.M., 102.4°. Guaiacol, ʒss, was applied at 10 P.M.

At 1.30 P.M., on the following day, guaiacol, gtt. xx, was applied, when the temperature was 103°, with no visible effect. Several counts of the leukocytes, before and after the application of the guaiacol, showed no particular change.

CASE IV.—*Typhoid fever; application of guaiacol,* ʒj (*3.75 c.c.*), *followed by a fall of temperature of about five degrees in three and a half hours; profuse sweating; chill, with rapid rise of temperature, in about four hours.*

The patient was a woman, nineteen years of age. On February 6th, in the third week of the disease, the temperature at 4 P.M. was 103.8°; at 6 P.M., 103.5°; at 8 P.M., 103 4°; at 9 P.M., 102.3°; at 10 P.M., 99.8°; at 12 midnight, 97.6°; at 2 A.M., 104.2°; at 4 A.M., 103.2°. Guaiacol, ʒj (3.75 c.c.), was applied at 8.30 P.M.; this was followed by profuse sweating between 9 and 12 o'clock, and a chill between 12 and 2. The dose in this case was (accidentally) larger than those used previously, and the effect was correspondingly more marked. The chill was quite severe.

CASE V.—*Pulmonary tuberculosis; five applications of guaiacol,* ♏xxx; *falls in temperature varying from* 1.2° *to* 5.8°, *occurring in from one to two and a half hours, with profuse sweating and chilliness.*

The patient was a man, thirty-three years of age, with bilateral pulmonary tuberculosis, with excavations. The fever was remittent, with evening exacerbations. The applications in this case were on each occasion thirty minims (2 c.c.) The sweating was so profuse, and the patient complained so bitterly of weakness and exhaustion after the

applications, that they were omitted. An example of a moderate fall is the following:

On February 15th the temperature at 2 P.M. was 101°; at 2 45 P.M, 102.2°; at 3.45 P.M, 100.8°; at 4.45 P.M., 99.8°; at 6 P.M., 101°; at 8 P.M., 102°. Guaiacol, ℥xxx, was applied at 2.30 P.M.; there was profuse sweating during the fall in temperature, and chilliness later on.

CASE VI.—*Pulmonary tuberculosis; applications of guaiacol, gtt. xx and ʒss respectively ineffectual; fall of 4 8° in three hours after ʒj (3.75 c.c.); chill in about four hours, with rapid return of fever.*

The patient was a colored woman, thirty years of age, with evidences of infiltration at both apices. She had had a steady, continuous fever, varying for three days from 100.6° to 103.4°.

On February 10th, guaiacol, gtt. xx, was applied at 5.30 P.M.; this was followed by a slight chill at 10 P.M.; there was no effect on the temperature.

On February 19th, guaiacol, ʒss (2 c.c.), was applied at 9.20 A.M., the temperature being about 101°, without any effect.

On February 19th, the temperature at 2 P.M. was 102 2°; at 3.50 P.M., 102.8°; at 4.50 P.M., 103°; at 5 50 P.M, 98.8°; at 6.50 P.M., 98°, at 8 P.M., 98°; at 9.30 P.M., 103.6°; at 10.30 P.M, 103°. Guaiacol, ʒj (3.75), was applied at 3.50, followed by sweating and a slight chill between 8 and 9.30 o'clock. This patient was a colored woman, with thick skin, hence, possibly, the inefficacy of smaller doses.

CASE VII.—*Acute rheumatism; application of ℥xxx (2 c.c.) of guaiacol followed by a fall of 3.4° in four hours, with profuse sweating.*

The patient was a woman, thirty-two years of age, with acute rheumatism. On February 19th the temperature at 2 P.M. was 101°; at 3.50 P.M., 101.4°; at 4.50 P.M., 100.4°; at 5 50 P.M., 99.6°; at 6.50

P.M., 99.2°; at 8 P.M., 98°; at 10 P.M., 101°. Guaiacol, ♏xxx, was applied at 3.50 o'clock; there was profuse sweating during the fall in temperature.

CASE VIII.—*Typhoid fever; fall of temperature of six degrees in three and a half hours after the application of 2 c.c. (℥ss) of guaiacol; profuse sweating; chill lasting an hour, with a return of the temperature in two hours to a point higher than before the application.*

The patient was a man, twenty-one years of age. On February 3d, the ninth day of the disease, the temperature at 8 P.M. was 104.5°; at 10 P.M., 103.5°; at 12 midnight, 103.8°; at 1 A.M., 104°; at 2 A.M., 103°; at 3 A.M., 100°; at 4 A.M., 98°; at 5 A.M., 103.2°; at 6 A.M., 105°; at 7 A.M., 104.6°. Guaiacol, 2 c.c., was applied at 1 A.M.; profuse sweating began at 1.45 A.M.; a chill, lasting an hour, occurred between three and four hours after the application.

In almost all of these eight cases the cutaneous application of guaiacol was followed by a marked fall in temperature. In Case II the first application of only twenty drops had no effect. The dose, however, was very small and was applied to the outer side of the thigh without previous preparation of the part. In Case III the results, with twenty drops and with half a dram, were either negative or very slight. This was a case of pneumonia in a fat man. In Case VII twenty drops and half a dram were followed by slight effect, while a dram (3.75 c.c.) showed a marked result. This case was that of a colored woman, in whom the skin was possibly thicker than in the other patients. The lowest point of the temperature was reached generally in from two to four hours, the average time being between three and four hours. In almost all of the

cases there was very profuse sweating, of which in one instance the patient complained bitterly. In the majority of the cases after the lowest point in the temperature was reached there was a rather rapid rise, associated in almost all instances with chilly sensations, in several instances with severe shaking chills, the temperature within two hours generally reaching a point as high or higher than at the time of the application. In none of the instances was there any marked effect upon the pulse or respiration During the fall of temperature there was generally some slowing of the pulse; in the cases in which there were marked chilly sensations with the reaction, the pulse was somewhat quickened. In none of our cases were there symptoms of collapse. The urine showed no marked changes. The breath shortly after the application of guaiacol gave a distinct odor of the drug.

Hence, while the antipyretic action of guaiacol was certainly very striking in these cases, the profuse sweating, the marked chills, in some instances even with small doses, and the decidedly weakening effect which was noted in those cases in which it was frequently repeated, have led us to take a somewhat less hopeful view of its possible value than Dr. Da Costa's experience would suggest; and these conclusions would on the whole seem to agree with those which have been reached by the majority of observers who have recently experimented with this drug. Sciolla (quoted by Stolzenburg, *Berliner klin. Wochenschr.*, 1894, No. 5) used guaiacol in a variety of different febrile affections. He applied the drug with a camel's hair brush to different parts of the

body, covering it immediately with a protective dressing. The doses used varied between 2 c.c. and 10 c.c.

In all cases there was a fall in temperature lasting between three and four hours, amounting to several degrees C. This fall was generally associated with profuse sweating. After six or eight hours there generally occurred a rapid rise in temperature associated with a chill or chilly sensations. Shortly after the application of guaiacol the characteristic taste was noticed.

Sciolla determined that the drug was excreted in the urine and in the respiration in from five to six hours without deleterious effects. He concluded that, used in this manner, guaiacol is a prompt and harmless antipyretic.

Bard (*Lyon Medical*, June 4, 1893) used the drug by this method in cases of tuberculosis, erysipelas, and pneumonia. At first he used doses of 3 c.c., but soon diminished the doses to 2 c.c. or 1 c.c., or even 0.5 c.c. He noted the profuse sweating in almost all of the cases, and frequently the following chills. He believes that the drug, applied in this manner, may be of value in some cases of tuberculosis, though he recommends special care in the dose with weak patients.

Lannois (*Lyon Médical*, August 6, 1893) obtained exactly similar results in a number of observations. He notes, however, that in some instances the local effects upon the skin may be unpleasant. In one case, for instance, in which the drug was applied on an area on which tincture of iodin had been recently painted, there was marked exfoliation of the skin, while in another, in which the sweating

was profuse, the skin over the seat of application was raised in quite large bullæ.

Stolzenburg (*Berliner klinische Wochenschrift*, 1894, No. 5) made an extensive series of observations in Senator's clinic with similar results, excepting that he notes the falls in temperature as lasting rather longer—between five and eight hours. At the time when the lowest point was reached there was, in a majority of instances, chilliness, or a definite chill, with a rise in temperature to a point even higher than before. There was almost always profuse sweating. In weak patients he has seen symptoms of collapse. While in most instances no ill effects on the respiration and pulse were noticed, the patients often complained of the weakening effect of the sweating. In a few instances a dark color of the urine was noted, similar to that seen in carbolic-acid poisoning. In his conclusions Stolzenburg states that the initial dose should not be above 2 c.c., and that it should probably never be above 4 c.c. on account of the danger of collapse. On account of the weakening sweats and chills, with the reactive fever, he concludes that the continued use of guaiacol is not to be recommended.

It will be noted that all observers agree as to the efficacy of guaiacol applied externally. Its employment has been so far limited to the fever of infectious diseases of various sorts, but in all it has been efficacious. There can be no doubt also that it is *absorbed* directly through the skin. Lannois (*loc. cit.*) tested in three cases the inhalation of guaiacol in considerable quantities for a considerable time, but without effect. Stolzenburg (*loc. cit.*) tried similar

experiments with Curschmann's mask. More recently Linossier and Lannois (*Comp. rend. hebd. de la Soc. de Biol.*, February 9, 1894) have shown that while a small amount was actually absorbed by inhalation, as proved by its appearance later in the urine, this quantity was insufficient to affect the temperature. Its *elimination* has been shown by Sciolla and Lannois to take place by the urine and the respiration. The early appearance of the taste suggests that it appears in the saliva. The elimination, according to Sciolla (*loc. cit.*), is accomplished in from five to six hours. Lannois and Linossier have shown that in most instances traces appear in the urine a quarter of an hour after the beginning of the application. The part to which the guaiacol is applied would appear to have some influence upon the rapidity and thoroughness of the action. This would be suggested by the result in Case II of our series, in which the first application on the external part of the thigh showed no result, while afterward doses but slightly larger applied to the abdomen were so efficacious.

There is, of course, no difference in the effect of guaiacol absorbed through the skin from that which follows its introduction into the system in other manner. Lannois, for instance, showed that its action in enemata was exactly the same, the effects appearing in almost the same time. In one instance we have made a similar experiment, the patient being the same colored woman who figures in Case VI in the earlier part of this note.

On March 4th the temperature at 8 A.M. was 100.7°; at 12 M., 100 2°; at 4 P.M., 99.8°; at 5 P.M., (?); at 6.30 P.M., 100.8°; at 7.30 P.M., 98.8°;

at 8.30 P.M., 97°; at 9.30 P.M, 95.2°; at 10.30 P.M., 96 8°; at 11.30, 97.2°; at 12.30, 97.3°; at 4 A.M., 104.2°; at 5.30 P.M. guaiacol, 2 c.c., was given by enema. At about 12.30 there were well marked chilly sensations; there was, however, no very marked sweating. The urine after the application showed a well-marked, smoky, greenish-brown color.

Interesting as may be these results concerning the antipyretic action of guaiacol, there is really little that is new, excepting in so far as they prove the readiness of its absorption through the skin. Exactly similar effects have been shown from the hypodermatic and rectal use of creosote, of which drug guaiacol forms the most important part.

Lépine, who used creosote hypodermatically (*Semaine Médicale*, 1890, No. 20, page 221), noted marked sweating after the injections.

Gimbert (*Gaz. hebd.*, Paris, 1891) also noted similar results from the subcutaneous introduction of creosote—*i. e.*, the sweating, the fall of temperature, the chill with reactive rise in temperature.

Revillet (*Semaine Médicale*, 1891, page 266) used creosote by enemata in doses of from 2 c.c. to 4 c.c. He noted the almost immediate taste of the drug in the mouth, the elimination by the respiration, by the urine, by the saliva, the well-marked antipyretic action, with the profuse sweating, and the subsequent disagreeable chilly sensations. Though the creosote was free from carbolic acid, he noted in one instance, two hours after a dose of 3 c.c., a well-marked dark color in the urine. The exact similarity of all these results with those formerly obtained by the administration of carbolic acid may be noted.

Lannois (*Lyon Méd.*, 1882, No. 30), for instance, in speaking of the results of the treatment of typhoid fever by carbolic acid, notes the same train of symptoms—the fall in temperature with profuse sweating, the reactive chill and rise in temperature, the discoloration of the urine. This similarity is, of course, not remarkable when one considers the close chemic relation between guaiacol and carbolic acid.

In *conclusion*, then, from the few experiments which we have made here, and from a consideration of the results obtained by other observers, we are perhaps justified in asserting that guaiacol applied to the skin is readily absorbed into the economy; that its application is followed in most instances of fever by a gradual reduction in temperature, which reaches its lowest point generally between three and four hours after the application; that this fall of temperature is almost always associated with disagreeably profuse sweating; at a variable period, usually a short time after the lowest point is reached, the temperature rises rapidly, generally in association with marked chilly sensations, if not with an actual chill; that a dose of more than 2 cc. is rarely advisable; that exactly similar results are produced by the absorption of guaiacol through any other channel (the rectum, or the subcutaneous tissues); that the antipyretic action is exactly similar to that which has been previously observed to follow a corresponding use of creosote and carbolic acid; that owing to the disagreeable effects of the immediate application of guaiacol (sweating and chilliness) and the weakening effects of the continued use, its employment as an antipyretic, as in the case of carbolic acid and creosote, will probably have but a limited application.

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