ANTIPYRETIC EFFECTS OF EXTERNAL APPLICATIONS OF GUAIACOL.

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AMONG the latest and most efficient antipyretics external applications of guaiacol deserve an important place. It seems that Dr. Sciolla¹ was the first to whom the idea occurred of employing guaiacol in this way. His observations attracted considerable attention, especially in France, and further communications have appeared from Drs. Bard,² Guinard,³ Robillard,⁴ Solis-Cohen,⁵ Lépine,⁶ Stolzenburg,⁷ Da Costa,⁸ Linossier and Lannois,⁹ and others. From these observations there is no doubt that guaiacol has energetic properties as an antipyretic.

The following remarks are based upon 114 personal trials of the drug made upon 13 cases (febrile phthisis 9, acute pneumonia 2, healthy persons 2). Eight observations were made on normal temperatures: in the remaining 106 the temperature ranged from 99° to 103°. Pure guaiacol was used sixty-eight times; creasote (containing about 90 per cent. of guaiacol) forty-six times. The liquid drug was rubbed into the axilla at 5 or 6 P.M., the quantity usually employed being 3j, but in a few instances only 3ss was used.

The temperature was reduced in 104 instances. There was no reduction in ten instances, but in five of these the temperature was normal at the time of application. The action of guaiacol was distinctly more energetic than that of creasote. With guaiacol the temperature fell 6° twice (in the same case), from 5° to 6° eight times, from 4° to 5° nine times, and from 3° to 4° thirteen times. With creasote the temperature fell once 5.2°, once 3.2°, and from 2° to 3° nine times. The lowest point to which the temperature fell was 96° three times, 96° to 97° ten times, 97° to 98° thirty-two times. The lower temperatures were obtained in every instance by guaiacol. The fall usually began at once, but occasionally there was a slight rise of temperature for the first hour, after which the fall was abrupt. The shortest time occupied in reaching the minimum temperature was one hour, the longest time was five hours, and the average time was about three hours. As a rule, after reaching the minimum, the temperature rose again abruptly to a point sometimes above, and sometimes below, what it was previously to the application. In two cases of phthisis the mean daily temperature was persistently reduced, and in one of these the temperature became practically normal under the continued use of the drug.

In addition to the fall of temperature other phenomena were pretty constantly observed. A short time after the application the skin of the part began to smart and burn, sometimes only very slightly, while in some few so severely that it was compared to burning with a hot iron. The smarting almost invariably passed off in the course of an hour, but when the application had been repeated for several nights in succession it sometimes caused mild superficial inflammation followed by slight desquamation of the cuticle. Inflammatory trouble was, however, quite exceptional; it more often occurred with creasote than guaiacol, and quickly subsided on suspending the application for two or three nights.

Marked general sweating was almost invariable; it was often copious, and occasionally so profuse as to saturate the bed clothes. The sweating was not always proportionate to the fall of temperature, although this was the rule; on six occasions there was a marked fall in temperature with very little if any sweating; on one occasion the temperature did not fall at all (but rose 1.8°) and yet there was sweating; while on three occasions (normal temperature) there was neither fall of temperature nor sweating.

When the temperature fell below normal, there were symptoms of collapse, but only once to a serious extent. In these cases there was always very profuse sweating, an indescribable sense of sinking, and occasionally a feeling of nausea. Apart from the actual danger of collapse, the symptoms are extremely distressing to the patient, and under

such circumstances the applications should either be discontinued or repeated with much smaller doses.

The abrupt rise of temperature after its reduction has already been referred to. When the fall was considerable, and especially when the minimum reached was below normal, this abrupt rebound of fever was very commonly associated with shivering, and sometimes with a decided rigor. In every instance it was found that the temperature was rising rapidly during the rigor. This symptom cannot therefore be regarded as a sign of collapse, but probably is the result of nervous shock brought about by sudden invasion of fever, such as we are familiar with at the outset of all acute specific diseases which begin abruptly.

The frequency both of the pulse and respirations was reduced as the temperature fell, but not to an extent greater than would be accounted for by the diminished fever.

The quantity of urine secreted was greatly increased, with a corresponding fall in specific gravity, and both an absolute and a relative diminution of solid constituents. As the fever returned, the urine gradually recovered its previous character. Lannois and Linossier state that after the external application of 2 grammes of guaiacol, elimination of the drug by the kidney began in a quarter of an hour, reaching its maximum from one and a-half to four hours, then decreasing rapidly for six or seven hours, till at the end of twenty-four hours only a trace was observed in the urine. They state that not less than 55.5 per cent. of the amount applied may be eliminated in the urine. This shows that the drug really enters and passes through the system.

I do not propose in the present communication to deal with the therapeutic uses of external applications of guaiacol in any detail, but the observations above recorded suggest the following considerations:

1. That used in this way guaiacol is a valuable addition to our list of trustworthy antipyretics; and though the tendency of recent experience is greatly to restrict the usefulness of this class of remedies, yet whenever the employment of an antipyretic is indicated guaiacol offers advantages which deserve attention.

2. That, by virtue of its diaphoretic effects, it may possibly be of value as an eliminant in adynamic conditions arising from the retention within the system of toxic substances.

3. That, by reason of its antimicrobial properties and the large amount of the drug which can in this way be introduced into the system, it is likely to be of service as an internal antiseptic, especially in the treatment of phthisis.

It should be pointed out that for therapeutic purposes smaller quantities of the drug are desirable than those employed in this investigation. Probably $\pi 20$ to $\pi 30$ would be generally sufficient. For continued use smaller doses would be desirable than when used to meet a temporary and urgent indication.

What is the explanation of the antipyretic effect of guaiacol applied externally? At present no certain answer can be given to this question. To some extent it turns upon the answer to another question: does guaiacol so applied enter the system, and, if so, does it enter it in any considerable proportion? Bard and Guinard say that it does not appear in the urine, and is not absorbed, and accordingly attribute the effects to a reflex action on the nerve centres through the peripheral nerve endings. They further say that exactly analogous results were obtained in rabbits, when a liquid preparation of mustard was substituted for guaiacol. It seems hard to believe that this view is correct, otherwise how is it that creasote, which is so much more irritating than guaiacol, has such a much feebler antipyretic effect? Also, the purer the preparation of guaiacol the less is the local irritation, and yet the greater is its antipyretic effect.

If the observations of Lannois, already quoted, on the large elimination of the drug in the urine are to be trusted, it seems far more reasonable to suppose that this action of guaiacol is due to its internal effects after absorption. Moreover, we find that everything that facilitates absorption increases the effect of the drug—*ceteris paribus*. Whether the drug acts directly upon the central nervous heat centres or whether it acts upon them indirectly by some neutralising effect on the fever-producing toxins there is as yet no evidence to show.

It is impossible to disregard altogether the antipyretic

effect of the sweating which so generally attends these applications of guaiacol. But since there is no regular relation between the intensity of sweating and the fall in temperature, and since sweating is occasionally absent though the temperature falls, it seems clear that we must look elsewhere for a complete solution of the problem.

REFERENCES.

¹ *Medical Week*, vol. i, p. 179, 1893. ² *Lyon Méd.*, June, 1893. ³ *Bulletin Gén. de Thérap.*, vol. xl, 1893, p. 339. ⁴ *L'Union Méd.*, July 11th, 1893. ⁵ *Philadelph. Med. News*, September 30th, 1893. ⁶ *Medical Week*, vol. i, 1893, p. 505. ⁷ *Berlin. klin. Woch.*, No. 5, 1894. ⁸ *Nashville J. of Med. and Surg.*, March, 1894. ⁹ *BRITISH MEDICAL JOURNAL* EPITOME, February 17th, 1894, par. 135.

INCOMPETENCE OF THE PULMONARY ARTERY.

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CARDIOGRAPHERS are agreed that diseased conditions of the orifice of the pulmonary artery developed after birth are uncommon. This applies, not only to lesions that narrow the mouth of the vessel, but particularly to those that allow of regurgitation of blood into the right ventricle. Constantin Paul maintains that incompetency of the valves of the pulmonary artery is of all cardiac lesions the rarest. Few authors have written much about reflux through these valves. Huchard and Walshe make no mention of it. Sansom in his classic work gives an interesting summary of the bibliography of the subject, and states that "a murmur of diastolic rhythm having its origin at the orifice of the pulmonary artery is very rare." As a small contribution to the literature of this interesting affection I give in detail the following case:

S. S., aged 60, married, was admitted into the Newcastle Infirmary August 26th, 1890, complaining of shortness of breath and swelling of feet and legs. She has had a comfortable home, but has had to work hard. There is nothing of importance in the family history. She had typhus (?) fever at the age of 9 years. There is no history of rheumatic fever. Patient considers that her illness dates from four years ago, when she caught a severe cold. This was followed by shortness of breath, which has never since entirely left her. She is badly nourished, is sallow and cyanosed. Urine has a specific gravity of 1014, is alkaline, and contains albumen. Tongue moist and coated; bowels are regular. Pulse 76, is rather incompressible; the artery feels hard. The movements of the chest are restrained. There is an increased area of cardiac dullness; it extends from the nipple line to $1\frac{1}{2}$ inch beyond the right border of the sternum. The apex beat is diffused; it is displaced downwards and outwards to the left 2 inches below the nipple. Over the apex a systolic murmur is heard, followed by a loud ringing and accentuated second sound. Down the middle of the sternum and to the left of it a systolic murmur is heard, louder and more grating in character than a similar murmur which can be heard over the aortic area. Along the left border of the sternum a diastolic murmur of fairly long duration is detected. The veins of the neck are extremely distended, and are seen to collapse during deep inspiration. Pressure upwards, with the hand driven firmly but gently under the right costal arch, increases the venous distension in the neck. Under this procedure the jugular veins would almost immediately pass from the size of a penholder to that of one's little finger. There is œdema of feet.

Under rest in bed and treatment patient regained health to such an extent that she was able to return to her duties as an office cleaner. She left the infirmary on October 1st, 1890.

On March 10th of the following year she was readmitted, complaining of a recurrence of her old symptoms, which again subsided under treatment. She left the infirmary, but returned on June 26th, the dyspnoea having become aggravated, cyanosis being more marked, and emaciation more advanced. There was little or no cough. It is noted that there is very extensive pulsation over the cardiac area, and that it affects principally the right side of the heart. The superficial veins in the neck are widely distended. Over the aortic area there is a systolic murmur, followed by a well-marked second sound. Over the xiphoid cartilage is heard a double murmur, whilst over the seat of the pulmonary artery there is a well-marked systolic murmur, followed by a prolonged diastolic. There is a soft mitral systolic at the apex; here the second sound is healthy. Small crepitation, with diminished respiratory murmur, is detected at the base of the left lung, back and front. Pulse varies from 90 to 100; it is small and jerky; the radial arteries are hard and tortuous. Urine, specific gravity 1016, acid and albuminous. Liver dullness is slightly enlarged. By degrees the dullness in the left chest increased, and with it the dyspnoea passed into orthopnoea. The patient is only able to sleep resting on her knees and elbows. The symptoms gradually increased in severity; fluid began to accumulate, too, in the abdomen.

On August 6th we tapped the left chest, drawing off 52 ounces of serum. This gave great relief to her breathing. Patient could now lie in the recumbent position, and she slept comfortably. Gradually, however, the fluid reaccumulated in the pleural cavity; the breathing again became difficult, but nothing would induce her to have the chest tapped. The pulse became irregular, and the quantity of urine diminished to 10 ounces daily. As the illness drew to its close she became rather rambling and delirious, but never acutely so. A very profuse epistaxis

came on on August 18th—over a pint of blood being lost before the bleeding was restrained. Two days subsequently there was again epistaxis. Her pulse now rose to 140, and within forty-eight hours of the second epistaxis she died completely exhausted.

Post mortem a considerable quantity of fluid was found in the left pleural cavity. Beyond being compressed, the left lung presented nothing abnormal. The right lung was congested and œdematous. The heart was enlarged to almost twice its normal size, the enlargement affecting particularly the right side. A branch of the left coronary artery in the interventricular groove was atheromatous, and a portion of it was seen to be firmly plugged by a white fibrinous thrombus. The aortic valve was competent, and its segments were healthy seen from above. The pulmonary artery was incompetent. The myocardium appeared to be healthy except at the apex, where the wall was very thin. Lying firmly attached to it internally was an old laminated greyish-white clot. The aorta was slightly dilated. The pulmonary artery was widely dilated; it was from one-fourth to one-third as wide again as it ought to be. The aortic valves seen from below were quite healthy. Those of the pulmonary artery, when again tested with water, did not fall closely together, but allowed the liquid to escape. On closer examination the defect was observed to be due to the presence of thickened patches on two of the segments, which had caused them to shrivel. Mitral and tricuspid valves were healthy. A fairly deep ulcer, the size of a threepenny piece, was found at the beginning of the descending aorta. On the surface of the liver was a large patch of thickened capsule, the size of a five-shilling piece; it had all the characters of cicatricial tissue (? specific). The liver on section was nutmeggy. The kidneys were enlarged; in the left was a cyst, the size of a small nut, with gelatinous contents. Both kidneys were irregular in shape, and granular. The capsule was adherent, and the cortex was diminished. The other abdominal viscera were healthy.

Apart from congenital heart disease, lesions of the orifice of the pulmonary artery are extremely rare. Now and again they are met with in the course of ulcerative endocarditis. Under most circumstances the diagnosis of pulmonary insufficiency is a matter of difficulty. In the case reported it was suspected on the grounds that the diastolic murmur was located over the pulmonary artery, and conveyed down the left side of the sternum to the apex of the right ventricle; that the second sound heard over the aortic area was healthy and quite distinct; that the pulse was hard and incompressible, and not the collapsing pulse of aortic regurgitation. There was just some doubt, however, in my own mind in regard to making the diagnosis of pulmonary regurgitation absolute, and it arose from the possibility of there being some cardiac adhesions which might have given a twist to the heart in its long axis, thus altering the positions of the orifices of the large vessels arising from the base of the heart relative to their normally corresponding points on the surface.

It is noted in my case that the pulmonary artery was widely dilated. Hope, in his *Diseases of the Heart*, reports a similar case. There was no stenosis of the orifice, a point of some interest when viewed in the light of a strong statement by Dr. Michel Peter of Paris. In the brief paragraph devoted to lesions of the pulmonary artery in his *Maladies du Cœur* he says "we have seen *à propos* of lesions of the aortic orifice that the most common lesion was insufficiency, and that stenosis indicated a stage further advanced in the evolution of chronic endocarditis. It seems, on the contrary, that insufficiency of the pulmonary orifice is only an exaggerated product of the lesion which has caused narrowing of this orifice." As a clinical and anatomical entity Peter says stenosis of the pulmonary artery is well known, but there are very few examples of insufficiency without stenosis. I am using the word "stenosis" here in the sense of very distinct narrowing, such as would cause obstruction to the onward flow of the blood. With this meaning attached to the word there was in the above case no stenosis. The diastolic murmur was well heard over the seat of the pulmonary artery and down the left of the sternum, a circumstance I again allude to, for it must be admitted that during the course of many cases of chronic endocarditis there must occur pulmonary regurgitation so slight as not to give rise to murmur. In fact, this is one of the points that Duroziez lays considerable stress upon, and which he regards as one of the reasons why pulmonary incompetence is not recognised during life. It is the absence of a diastolic murmur. As this remark applies more or less to all forms of valvular disease, we cannot assign to it the importance claimed for it by Duroziez. Bramwell, whilst admitting the rarity of pulmonary incompetence, gives an excellent summary of the symptomatology of the disease. My own case fully confirms what he says of the seat and convection of the diastolic murmur, and of the effect of the lesion upon the right side of the heart and the venous system. The right ventricle was dilated and hyper-