

On the characters of the expectoration in cases of fetid bronchitis and gangrene of the lung / by Arthur Gamgee, M.D.

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ON THE

CHARACTERS OF THE EXPECTORATION

IN CASES OF

FETID BRONCHITIS

AND

GANGRENE OF THE LUNG.

BY

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EDWARD BRONCHITIS

AND

GAUGERINE OF THE LUNG

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REPRINTED FROM THE EDINBURGH MEDICAL JOURNAL, MARCH 1865.

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ON THE
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NOTWITHSTANDING the impetus which the study of pathological chemistry has of late years received both in our own country and on the continent of Europe, the labours of those who have devoted themselves to its advancement have told us little of the properties of the majority of the animal secretions and excretions in a state of disease. As a result of those labours we possess merely a tolerably complete account of the condition of the urine in disease, and a necessarily much less accurate and complete account of the diseased conditions of the blood.

That the other secretions and excretions deserve the minute attention of the physician, is a matter upon which we can have little doubt; that we may ultimately derive information of an accurate and useful character from a careful examination of the saliva, sweat, sputum, and feces, is, I venture to say, almost certain. In publishing the observations which I lately made in two cases of fetid bronchitis and gangrene of the lung, I am guided very much by the fact that the chemistry of the sputum has hitherto been almost entirely neglected, and that the facts with which we are accurately acquainted are so scanty that any little accession to our knowledge of the subject must be not altogether uninteresting.

Before proceeding to the narration of the cases which form the basis of this communication, I would remark that the point of practical importance which I wish to elucidate more particularly is one concerning the semeiological value of the presence of butyric acid in the expectoration.

In the *Medical Times and Gazette* for May 1857 (page 479), was published the substance of a clinical lecture on fetid bronchitis, delivered by Professor Laycock in the Royal Infirmary of this city. The paper was entitled "Substance of a Clinical Lecture on Fetid Bronchitis, with Discovery of Butyric Acid in the Sputum." This lecture was based upon three cases of chest disease, which had been

observed by Dr Laycock, in all of which the expectoration was characterized by great fetor, and which were looked upon by Dr Laycock as examples of that most unsatisfactorily studied disease, fetid bronchitis. The sputum of one of these cases was, at Dr Laycock's request, subjected to chemical investigation by the late Professor Gregory. The odour was, it is stated, found to be due to the presence of methylamine with butyric and acetic acids. In his comments on this case, Dr Laycock remarked that it would formerly have been regarded as an example of pulmonary gangrene, but it resembled in the leading symptoms the class of cases known as fetid bronchitis. He remarked that in fetid bronchitis the odour is not that of putrid flesh, but very characteristic of butyric acid, and the new odorous compounds, the butyrates of ethyl, now used to flavour confectionary. To this discovery of butyric acid in the sputum Dr Laycock attached considerable importance, concluding "that the production in the lungs of the peculiar compound to which the odour of the sputa was due might be referred to some change in the ganglia of the pneumogastric and the sympathetic in connexion with the pulmonary mucous surfaces, of an asthenic character."

Were the presence of butyric acid in the sputum really a distinguishing sign between bronchitis attended with fetid expectoration, and that infinitely more formidable disease gangrene of the lung, too much value could not be attached to the observations of Dr Laycock; for the physician would thereby have acquired a most valuable diagnostic sign, guiding him in his treatment, and especially in his prognosis of a class of cases which, of rare occurrence, are often involved in doubt and obscurity.

During the winter session 1863-64, I was asked by Dr Laycock to examine the sputa of a case of fetid bronchitis. The patient, I was informed, expectorated large quantities of sputum, which, always fetid, assumed at certain periods a somewhat ethereal odour. The sputum which I had the opportunity of examining possessed an intensely fetid odour, or rather it possessed two odours, of which one—rotten cabbage like—was far more repulsive than the other, which was sour.

On distilling the secretion, which had an alkaline reaction, an intensely fetid distillate was obtained, of alkaline reaction, and possessing, in a concentrated form, the odour of the original expectoration. On acidifying the fluid and redistilling it, the distillate retained exactly the odour of the original sputum. When heated with caustic potash and again distilled, it passed over unchanged. By these processes I obtained a perfectly neutral fluid, having exactly the odour of the sputum. What was the nature of the peculiarly fetid substance upon which the odour of the sputum depended? Was it methylamine or a compound of butyric acid? Certainly not, for had it been the former (to which I may say it did not present the slightest resemblance), it would, when subjected to distillation with sulphuric acid, not have passed over; and had it

been a compound of butyric acid, the distillation with sulphuric acid must undoubtedly have decomposed it, and caused the appearance of butyric acid.

The fetid substance was most probably a sulphur compound, for the fluid which distilled was subjected to analysis, and found to contain unoxidized sulphur. That it was not a substance readily prone to decomposition was proved by its being unchanged by distillation with acids and alkalies, and by the fact that it was kept in a stoppered bottle for some months, and possessed at last all the freshness of its original fetor. Having so far investigated the characters of the peculiar fetid substance, I directed my attention to the discovery of compounds of butyric acid. On adding dilute sulphuric acid to that portion of the sputum which remained in the retort after the fetid substance had been distilled off, and applying heat, a fluid distilled, which had an acid reaction, and the odour of butyric acid. The resemblance was perceived by several chemical friends, perfectly competent to form an opinion on this point. The fluid thus obtained was neutralized with carbonate of soda, and cautiously evaporated to dryness. The residue was placed in a small retort, acidified with sulphuric acid and heated, when a fluid was obtained still more closely resembling in smell pure butyric acid. I repeated the process of purification, then neutralized the fluid with chalk, and obtained, on evaporation, a solid substance having the physical appearance of butyrate of lime, and which, when examined under the microscope, was found to consist of crystals resembling exactly in character crystals of pure butyrate of lime with which they were compared. The sputum was in this way shown to contain butyric acid in a state of combination, in addition to the peculiarly fetid organic substance upon which the odour has been shown to have depended.

Having satisfied myself of the presence of butyric acid in the above case, I determined, when opportunities occurred, to examine the expectoration in other cases of chest affection, and more especially cases characterized by fetid expectoration. During the summer recess a most interesting case of gangrene of the lung occurred in Ward VII. of the Royal Infirmary, under the care of Dr Haldane. Through that gentleman's kindness I had the opportunity of investigating with considerable care this case, of which the following is a detailed account:—

T. T., æt. 67, a widower, residing in Leith, was admitted into the Royal Infirmary on the 23d of August 1864.

Until six weeks before the date of his admission the patient had enjoyed the most perfect health. Of originally strong constitution and temperate habits, he had been able to pursue his duties as a labourer in the works of the Shotts Iron Company for twenty years, without a single day's absence.

At the period already alluded to the patient quite suddenly commenced to suffer from swelling of the legs and feet, which compelled

him to stop at home. A week later he was seized quite suddenly with intense pain in the lateral thoracic regions on both sides, and simultaneously a cough made its appearance. The cough after some days increased, and was accompanied by excessively profuse expectoration of a black colour and horrible fetor.

On the 1st of September, the sputum of this patient was sent me for analysis. It was of a greyish colour, and possessed a very fetid odour, reminding me very strongly of the sputum of the case just narrated; it also possessed a very decidedly sour odour. Its reaction was acid. When placed in water it was found to float very readily. When distilled, there passed into the receiver a fluid possessed both of the fetid and sour smells of the original sputum. On neutralizing this fluid with carbonate of soda, and re-distilling it, I obtained the more fetid of the two smells, quite free from the sour odour. On now acidifying with sulphuric acid, and again distilling, I obtained a distillate of neutral reaction, possessed of the peculiar fetor of the original sputum, and destitute of acid odour. It was almost identical in smell with the fluid obtained from the sputum of Dr Laycock's case, and its chemical deportment was the same. I found in this, as in the former case, that the stinking distillate contained unoxidized sulphur.¹

The original distillate from which the fetid substance had been separated, and which had been neutralized with carbonate of soda, was now acidified with sulphuric acid and distilled; as a result, a distillate was obtained which had an acid reaction, and possessed strongly the odour of butyric acid. It was found not to reduce the salts of silver, and not to be coloured red by perchloride of iron, proving that it contained neither formic nor acetic acids. Another portion of the sputum was evaporated to dryness, treated with an alcoholic solution of oxalic acid, and the solution thus obtained filtered. Oxide of lead was added to the fluid, which was again filtered, treated with sulphuretted hydrogen, heated to drive off the excess of gas, and then boiled with oxide of zinc. On filtering and evaporating the solution, a yellowish residue was obtained, which was found to contain, especially at its edges, numerous very characteristic crystals of lactate of zinc, showing that lactic acid must have existed in the expectoration.

On the 3d of September I again examined the expectoration of this patient. The total quantity of expectoration in twenty-four hours amounted to 1018 grains. This was of acid reaction, and was distilled to dryness in the water bath. The distillate was extremely fetid and decidedly acid. The total amount of free acid in the distillate was determined by means of a standard solution of caustic soda. Assuming all the free acid to have been butyric acid, the quantity present in the sputum was .067 gramme (= .10338 grain). The fetid substance was found to possess the same characters as when

¹ Precautions had been taken to ascertain that the fluid contained no traces of sulphuretted hydrogen.

first analyzed. Besides the free butyric acid, the residue in the retort contained this acid in combination with bases, for, on acidifying the residue with sulphuric acid, an additional quantity of acid distillate was obtained. In order to separate it completely the process was conducted in a chloride of zinc bath.

The residue in the retort was dissolved in alcohol and filtered. The filtrate was treated with neutral acetate of lead, and the fluid filtered from the abundant white precipitate which fell. A current of sulphuretted hydrogen was passed through it, and after being heated and filtered, it was tested with Fehling's solution and found to contain considerable quantities of glucose.

On the 5th of September, I again examined the sputum. The quantity which the patient expectorated in twenty-three hours amounted to 245·2 grammes (8·64 ounces). It was of acid reaction. When examined microscopically it was found to contain mucus and pus cells and epithelium. Without detailing the lengthened examination which I made of it, the results may be stated as follows:—It contained water, free butyric acid, butyric acid in combination with bases, the peculiar fetid compound which I have described, a little fat, albumen, mucin, some glucose, undetermined organic matters, and salts.

Water and volatile constituents amounted in 100 parts to	88·412
Substances soluble in ether297
" " alcohol	3·29
Mucin and albumen	5·66
Salts	1·015
Undetermined organic matter, and loss	1·326
	<hr/>
	100·000

signs underwent a modification. On the 15th of September, a certain degree of dulness was found over the lower right back; and on the left side, in a line with the lower angle of the scapula, and between it and the spine, the breath sound became intensely tubular—almost cavernous. The voice sound had the characters of true pectoriloquy. On causing the patient to cough, distinct gurgling was heard. During the period intervening from the date of the last analysis I continued to examine the sputa, both microscopically and chemically. On suspending and agitating in water some of the substance expectorated on the 12th of September, I noticed a considerable number of fibrinous bodies, which presented the appearance of casts of the bronchial tubes. I, at first, supposed them to be portions of expectorated lung tissue,—a supposition which, however, was proved to be erroneous by Dr Haldane, who unhesitatingly pronounced them to have the characters of fibrinous bronchial casts. I found that they possessed one very remarkable character: iodine colouring them of a purple colour;—the reaction produced by iodine alone resembling the reaction obtained under the most favourable circumstances, by acting with iodine and sulphuric acid, on organs affected with amyloid degeneration. The very central portions of the casts possessed this peculiar property of being coloured purple by iodine.

The patient continued to sink rapidly, and ultimately died on the 27th of September.

The body was examined on the succeeding day by Dr Stewart, who has kindly given me the following notes of the sectio:¹—

“The body was much emaciated. The pericardium contained a small amount of clear fluid. The heart was soft, and the tissues appeared somewhat fatty. The valves were natural. The right pleura was slightly adherent at the apex and the base; the left pleura was adherent throughout, loosely in front, and more firmly behind. Near the lower border, posteriorly, there was a collection of fetid pus about three inches long by two broad, of a depth which could not be ascertained. This communicated with a large gangrenous abscess situated in the lower lobe of the lung. This abscess contained numerous shreds of broken-down tissue, and a large quantity of very fetid pus. On its inner surface there projected numerous knobs and processes like the columnæ carneæ of the heart. These consisted of bronchial tubes and vessels, whose walls were thickened and inflamed, and cavities occluded by fibrinous coagula in different stages of transformation. Many of the arteries and veins in the neighbourhood of the abscess contained purulent looking matter, and in one of the main branches of the pulmonary artery there was a firm old coagulum with processes passing into different branches; close to the coagulum was a large bronchial

¹ Before the post-mortem examination was commenced, I specially requested Dr Stewart to search for bronchial casts, and to notice the mode in which they reacted with iodine.

gland suppurating. The upper part of the lung was œdematous, as was also the right lung. There was a solid, nearly pneumonic, condition of the lower lobe of the right lung; many of its bronchi contained casts. The liver, spleen, and intestines were natural; some of the renal tubes contained exudation, and there was a good deal of fat in the epithelial cells. The renal arteries were more atheromatous than any others examined. The other organs were natural. The brain was not examined. Some of the superficial veins, particularly the right cephalic, contained firm old clots. On examining microscopically some of the bronchial casts from the right lung, numerous mucus corpuscles and epithelial cells were observed, and amongst them there were many groups of cells and amorphous masses which assumed, on the addition of iodine, a purple colour. This fact had been observed during life by Dr Arthur Gamgee, and confirmed by Dr Haldane. The margin of the left lung was emphysematous. That lung also contained one mass of cheesy tubercle about the size of a plumstone. There was no recent tubercle, nor any trace of it, at either apex."

The case which I have just described possesses, it appears to me, many points of the greatest interest. The physical signs possessed, undoubtedly, no remarkable complexity; they pointed conclusively to the existence, at first, of extensive consolidation of one of the lungs, and subsequently to the undoubted existence of a cavity. The odour of the sputum and the breath, and the increasing prostration, left little doubt that this cavity was gangrenous. But what was the origin of this state? was the case one originally of simple pneumonia, terminating (as so few cases do) in abscess of the lung, or was it one of phthisis pulmonalis running its course rapidly? It is my impression that neither of these suppositions is the correct one. The post-mortem examination revealed, it is true, a small mass of cheesy tubercle in the more affected lung, but this was unaccompanied by recent tubercular infiltration. It disclosed, however, a most important pathological condition,—the existence of a firm and old clot in one of the main branches of the pulmonary artery. The hypothesis which, it appears to me, explains better than any other the history of the case, is that the obstruction of the pulmonary artery was of the nature of an embolism, and was the primary cause of all the pathological conditions which followed. Experimentally it has been shown, that by introducing foreign bodies into the large veins going to the heart, embolism of the pulmonary artery is induced, and as a result, often at least, inflammation of the lungs; and clinical records supply us with cases in which, all the circumstances favourable to the occurrence of embolism existing, the pulmonary artery has been occluded, and as a result gangrene of the lung has followed.¹ The very sudden occurrence of the disease in a man of very vigorous constitution bears out the supposition as to the embolic nature of the case.

¹ See Trousseau, *Clinique de l'Hôtel Dieu*, vol. i. p. 579.

Amongst the minor points of interest is the remarkable reaction which the fibrinous casts, found in the sputum during life, and in the bronchi after death, presented when treated with iodine—a reaction which had not, I believe, previously been noticed in the case of any animal product. It appeared to me that possibly the protein substance of which the casts were composed might, under the influence of putrefaction, and in the presence of butyric acid, have become so altered as to give with iodine a purple reaction; and I accordingly performed a series of experiments, which consisted in causing coagulated egg albumen and blood fibrin to putrefy at the temperature of the body, and then testing with iodine. In some cases I mixed butyric acid with the albumen or fibrin before causing them to putrefy, and in one experiment I placed coagulated albumen in the putrid fluid obtained from a macerating tub. On testing with iodine, I never observed, however, the purple reaction which was produced by the action of iodine on the casts.

The chief points of interest are connected with the chemical history of the case of gangrene of the lung which I have related, and which proves, I think, in the most conclusive manner, how little characteristic of the disease, fetid bronchitis, is the occurrence of butyric acid, and teaches us how careful we should be before looking upon the occurrence of butyric acid as a manifestation of a vitiated condition of the nervous system. No case could have occurred where the nervous system participated less in the morbid phenomena, or appeared so little to have influenced their production. In all probability a mechanical cause induced the gangrene of the lung, which followed almost as a natural consequence upon it, and amongst other results of putrefaction, a considerable quantity of butyric acid occurred in the sputum. For besides being produced in the decomposition of saccharine matters, and as a further stage of the lactic acid fermentation, butyric acid is developed during the imperfect oxidation of albuminoid matters, and during their putrefaction, especially under such favourable circumstances as to temperature, moisture, etc., as exist in a gangrenous lung.

But besides explaining in this way the occurrence of a large quantity of butyric acid in the sputum, I have to direct attention to a most important fact which I have recently made out, viz., that butyric acid, or one of the homologous volatile fatty acids, is present in the sputum of almost all, if not all, cases of chest disease; in other words, that the sputum always, or nearly always, contains a volatile acid.

On taking the most odourless expectoration of a case of simple acute, or chronic bronchitis, or the mucous expectoration of early phthisis, or the muco-purulent expectoration of the advanced disease, acidifying with sulphuric acid and boiling the fluid, vapours are evolved which have an acid reaction to test paper, and possess in a

marked manner the odour of one of the volatile fatty acids—generally of butyric acid. If the process be carefully carried on in a retort, and the distillate be neutralized with an alkali, evaporated to dryness and then acidulated, a fluid is obtained possessing in a marked manner the odour of the fatty acid occurring in the sputum—the odour being the best available test which we can employ in the detection of small quantities of these acids; being as characteristic as it is delicate.

On examining the sputum of a patient recovering from acute bronchitis, I discovered that the acid which was evolved, after acidifying and boiling, had very much the odour of caprylic acid. The muco-purulent sputum of a case of phthisis yielded an acid vapour which had at first the odour of formic acid. On boiling the fluid farther, a butyric-acid odour was evolved. The acids which I think occur in the sputum are butyric acid, propionic acid, formic acid, acetic acid, and possibly caprylic acid. The occurrence of these acids in the sputum is not a matter for surprise. The researches of Scherer, Gorup-Besanez, and Schottin, have proved the existence of most of these in the muscular juice, milk, etc., which most probably derive them preformed from the blood. Formed by the oxidation of various fatty matters, they are probably constantly present in small quantities in the blood, where they are partly consumed, and partly separated by the various excretory organs, and, like other volatile substances, especially by the lungs. When the air passages contain fluid it is only natural that they should be dissolved by the fluid, and thus find their way into the sputa. It will be a subject for future inquiry whether the quantity of the volatile acids in the sputum is not greatest in those cases where the function of the lungs is so much impaired as to interfere materially with the oxidation of the blood.

The above observations answer, it appears to me, in a satisfactory manner, the questions which I purposed solving in this communication;—they show that the occurrence of butyric acid in the sputa cannot at present be proved to have any semeiological value; and that its presence is in no way characteristic of fetid bronchitis.

In reference to fetid bronchitis, it appears to me that the facts which have been collected with regard to it are scarcely of such a nature as to warrant our admitting a disease bearing this name into our nosologies. Like all other excretions, that of the air passages is occasionally liable to exhale a disagreeable odour. This sometimes occurs in acute and chronic bronchitis. No distinct and uniform series of phenomena have, however, been shown to characterize those cases of bronchitis in which the expectoration is fetid. We should, I think, avoid a needless and unphilosophical complication of our nosologies were we to speak of a bronchitis accompanied by fetid expectoration, instead of a disease *sui generis* “fetid bronchitis.”

