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CLINICAL LECTURE

ON

Dyspnœa, especially on the Dyspnœa of Asthma and Bronchitis,

AND THE EFFECTS OF NITRITES UPON IT.

BY

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GENTLEMEN,—In the study of disease in the wards of the Infirmary your attention is very frequently drawn to the occurrence of dyspnœa, or difficulty in breathing. You have seen that it presents itself in various forms and degrees, in various conditions of the patient, and in connexion with many diseases. We have together studied several of its forms and varieties. We have seen it associated with disease of the heart, with morbid changes in the larger air passages, with pain in the thorax, and with diseases of the lungs; and it has been our endeavour to distinguish in each case any peculiarities in the phenomena which accompany it. We have seen, for instance, in cardiac disease, that it is associated with evidence of valvular lesions, or of dilatation of the heart, or of disease of the large blood-vessels; that it is frequently paroxysmal, the paroxysms being induced by physical exertion or mental excitement, although even in the interval between each exacerbation it does not altogether depart; and that pain

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in the region of the heart or extending into the shoulders and arms is often one of its superadded miseries. In disease of the larger air passages, such as œdema or spasm of the glottis, constriction of the trachea, or paralysis of the vocal cords, we have several times observed that the great difficulty in respiration seems to occur during inspiration, which is laboured and prolonged, while the expiration is relatively brief and without effort. In thoracic pain of pleuritic or neuralgic origin, the attitude of the patient, and especially the modifications in posture and movement adopted by him, are almost sufficient to characterise the dyspnœa apart from the readily discoverable conditions by which the pain is induced. In asthma, the opportunities for investigating the phenomena have not been altogether favourable, as our cases have presented the peculiarity, which so frequently occurs in this disease, that the dyspnœa has made its appearance only during the night or early morning. Most of you, however, are familiar with the circumstances that in asthma the dyspnœa is characterized by loud wheezing sounds and great prolongation of expiration, that it is paroxysmal in its manifestation, leaving the patient free or nearly so from all symptoms of breathlessness in the intervals, and that no structural alterations have as yet been discovered to account for the intense distress which marks each paroxysm. On the other hand, examples of the dyspnœa of bronchitis have been abundantly presented to you for consideration. You have seen that it is associated sometimes with acute, sometimes with chronic, inflammation of the bronchial tubes, that it very frequently occurs in patients suffering from emphysema, that it is often paroxysmal, and that it is accompanied with pain or uneasiness over the front of the chest, with a sputum that may be tenacious or frothy and watery, and with such auscultatory phenomena as rhonchi and sibilations, crepitations, and prolonged expiration.

While the dyspnœa in each of these conditions would supply abundant material for full and elaborate discussion, my intention to-day is to consider with you in further detail some of the phenomena presented by it in bronchitis and asthma only. I make this selection because our attention has been given in a more special manner during the last few weeks to a consideration of the breathlessness of these two diseases. I group them together because the dyspnœa frequently presents in them many points of similarity, and when it does so I believe that a large element in its production is an element operating in both diseases.

It is in pure (or nervous) asthma that dyspnœa assumes the most intense degree possible in disease of the respiratory apparatus. When the paroxysm occurs at night, the patient may go to bed feeling quite well, but is awakened from sleep by a feeling of suffocation. He sits up in bed in various constrained positions, or he is impelled to leave his bed altogether and walk about, resting now and again to recover strength. He struggles violently for breath; inspiration and expiration succeed each other rapidly for a short time; then expiration becomes brief, the chest seems to become rigid in full expiration, violent respiratory efforts are made, with but little change in the volume of the thorax, and the extraordinary muscles of respiration are brought into play with very inadequate results. After this state of distress has lasted for some time, it may be for hours, relief is obtained, and the patient returns to bed and usually soon falls asleep; but on many occasions this sleep may in a short time be again interrupted by a recurrence of the paroxysm. The great difficulty in asthma seems to be to expel air from the chest, and the expiratory muscles are strained to the utmost in the effort to accomplish this. If the condition of the patient during the period of dyspnœa be further examined, several other phenomena

of significance are observed. The normal relationship between inspiration and expiration is found to be reversed, and in place of inspiration being longer than expiration, the latter seems sometimes to be two or three times as long as inspiration. The contrast with dyspnœa produced by constriction of the glottis or trachea, where inspiration is greatly lengthened in its duration, is therefore a very pronounced one. The diaphragm, further, is unduly low, the chest is expanded, and the percussion note is markedly resonant; while on auscultating the chest, not only is confirmation obtained of the great prolongation of expiration, but every variety of dry râle is heard, snoring, creaking, and whistling sounds displacing each other in different parts of the chest.

Now, what is the cause of this intense dyspnœa? No anatomical lesions, as I have stated, have been found that are sufficient to account for it. It was explained by Willis, and subsequently by Cullen, Romberg, Salter, and others, as due to a spasmodic affection of the muscles and nerves of respiration, and especially of the muscles in the bronchi; and this explanation was generally coincided in for more than half a century. It has not, however, been allowed to remain in undisputed possession of the field, for at various times other and opposing explanations have been advanced. For example, Leyden considered that the asthmatic dyspnœa is caused by irritation of the vagus terminations in the bronchi produced by minute sharp-pointed crystals; but this explanation, after all, involves the production of a spasmodic constriction of the bronchi by reflex irritation. Wintrich denied that spasmodic contraction of the bronchi is possible, and maintained that the only explanation consistent with the phenomena is to be found in tonic spasm of the diaphragm, or of the diaphragm aided by the other ordinary muscles of respiration. Traube, Weber, and Sir

Andrew Clark have ascribed the paroxysm to sudden congestive swellings of the bronchial mucous membrane, through the agency of vaso-motor nerves, the changes produced being likened by Clark to the swellings of the skin in nettle rash.

These views represent the more important of the contending explanations that have been advanced. It cannot be pretended that any single explanation has yet been established by the evidence that has been produced in its favour, although I think that the explanation which accounts for the essential phenomena of an asthmatic paroxysm by spasmodic contraction of the bronchial muscles is still the most generally accepted one. But while a spasmodic influence has thus been fully recognised in the production of the dyspnœa and of other of the essential phenomena of asthma, the existence of a spasm element in bronchitis has been but partially acknowledged. Indeed, so far as my acquaintance with the literature of this disease is concerned, spasm of the bronchial muscles is by the greater number of writers ignored as a condition that is ever, much less that is frequently, present. Bronchitis, however, resembles asthma in so far, at least, that in a considerable number of cases dyspnœa is frequently an important symptom, and that rhonchi and sibilations are among the most significant of its phenomena. The production of these râles has generally been attributed to stenosis of the bronchial tubes caused by engorgement, or swellings, or puckerings of the lining membrane, or to deposits of adhesive mucus upon this membrane.

It cannot, gentlemen, be too frequently impressed upon your consideration that the ultimate objects of all our observations, studies, and investigations in pathology and medicine are the relief of suffering and the cure of disease. These objects will be the more certainly accomplished, the

more accurate our knowledge is of the conditions that produce the symptoms of the diseases. I am not without hope that an illustration of this almost self-evident proposition may be found in some facts bearing upon the causation of the dyspnœa in asthma and in bronchitis, which I shall now proceed to describe. Let me first remind you that there are several well-recognised homologies in the structure and nerve connexions of the bronchi and of the smaller blood-vessels. They both contain non-striped muscle, and both are innervated by partly independent centres distributed in their walls, and by nerves proceeding to and from centres remote from themselves.

Although the effects of pharmacological agents upon the functions of the muscles and nerves of blood-vessels have been elaborately studied, their effects upon the functions of these structures in the bronchi have been but little investigated. Among the most striking of the results that have been obtained by pharmacology in the study of the influence of agents upon the blood-vessels is the demonstration that various nitrites cause a dilatation of the blood-vessels by an action restricted to the blood-vessels themselves. It was suggested to me by this fact that light might be thrown upon the production of dyspnœa in asthma and bronchitis by examining how far the dyspnœa and some of its associated phenomena could be modified by the action of nitrites. It seemed to be of importance to include in this observation not only the influence upon the dyspnœa (for any influence on it alone might be explained by an action upon nerve structures remote from the bronchi themselves), but also the influence upon the associated phenomena which have their seat of origin, without doubt or ambiguity, in the bronchi themselves. The associated phenomena, to which I attach the greatest importance, are the dry râles, audible in these diseases when the

chest is auscultated, and conspicuously present along with the dyspnœa.

The first observation I made with these objects in view was in 1880, on a patient twenty-two years of age, of markedly nervous diathesis, who had suffered from asthma for several weeks. The chest was auscultated during an asthmatic paroxysm of moderate severity, and it was found that cooing, whistling and creaking râles were abundantly present. She inhaled during fifty seconds a few minims of nitrite of amyl. Two minutes after the inhalation had been commenced, the râles had entirely disappeared, and her breathing had become quite easy. In another minute the râles had returned and the breathing had become more difficult. After an interval of six minutes, when both the râles and dyspnœa were present in their original abundance and severity, she again inhaled nitrite of amyl, this time for thirty seconds, and in forty-five seconds after commencing the inhalation the râles had entirely disappeared and the breathing had become perfectly unembarrassed. In five minutes afterwards, the original state of breathlessness, with its accompanying auscultatory phenomena, had returned. After an interval of ten minutes, nitrite of amyl was a third time inhaled, with essentially the same results as on the previous two occasions.

This observation showed in a very striking manner that nitrite of amyl very rapidly caused every sensation of dyspnœa to disappear. The coincident effects of the highest interest were that so long as the dyspnœa was removed, and only so long, were the cooing, whistling, and creaking sounds silenced, and so long also were there present those well-known modifications in the pulse characteristics which indicate dilatation of blood-vessels. Since this observation was made I have accumulated much evidence of a similar kind. In a few other cases nitrite of

ethyl, as well as nitrite of amyl, were given by inhalation, but in the greatest number of the observations the administration was effected by the introduction of the nitrite into the stomach, and thus a much more prolonged action was obtained. In this manner, not only has the influence of nitrite of amyl and of ethyl been examined, but also that of nitrite of sodium and of the nitrite-acting substance, nitro-glycerine. Further, in several cases of severe asthmatic orthopnœa occurring during the night, remarkable alleviation, with coincident silencing of the râles previously abundant in the chest, were obtained in several observations made for me by Dr. Vaughan and Mr. Toft on patients in the wards.

In bronchitis, accompanied with dyspnœa, similar effects were also obtained. The dyspnœa was removed, and at the same time the previously existing dry râles disappeared. Let me illustrate this action of nitrites in two patients suffering from bronchitis, now placed before you. One of the patients has been in the wards for several weeks, and from previous experience I can confidently predict the changes that will occur. He has suffered at intervals during the last fifteen years from bronchitis, the lungs are emphysematous, and his chief complaints at present are breathlessness and cough with a rather adhesive and slightly frothy sputum of small quantity. The other patient was admitted into the hospital only yesterday, but I shall be much disappointed if the observation I shall immediately invite you to make on her should fail as an illustration. Her cough originated four months ago from a severe wetting. You observe that she has very obvious dyspnœa, and the sputum which I show you is large in amount, watery, and contains much froth. Both patients are suffering at the present moment from dyspnœa, and as you have heard from the four members of the class who

are examining the patients, two of whom are continuously auscultating the chest of each patient, there are now associated with the dyspnœa an abundance of snoring, whistling, and cooing râles. I now ask Dr. Jeffcoat, the resident physician, to give to one patient four minims of nitrite of amyl in a little water, and to the other two minims of a 1 per cent. solution of nitro-glycerine also mixed with a little water; and the gentlemen who are auscultating will at once inform us of any change in the sounds which they hear, while I have asked the patients to announce the first change which they experience in their sensations. It is only a very few minutes since the medicines have been given, and already you have heard, almost simultaneously, that silence prevails in the chests where before there was a continuous succession of sounds, and that both patients find that they no longer experience any dyspnœa.

The significance of the facts I have now brought you in connexion with the influence of nitrites upon the dyspnœa of asthma and bronchitis, some of which you have yourselves assisted in observing, is almost self-apparent. They appear to throw light upon the production of the dyspnœa of asthma, and in doing so to confirm the conclusion otherwise arrived at by Biermer that the dyspnœa cannot find its chief explanation in spasm of the diaphragm. They appear also to show that this dyspnœa does not depend on suddenly produced and vanishing constrictions of the bronchial tubes, caused by swellings of a hyperæmic, herpetic, or urticaria-like character; for the means that have been successfully employed to control and terminate the dyspnœa are the very means which should, according to the theory which involves constrictions of this kind, be the most efficient for increasing and prolonging it. Relief of the dyspnœa and removal of the accompanying râles were simultaneously or nearly simultaneously produced by

nitrites, whose action is to increase hyperæmia by dilating blood-vessels. As nitrites, however, lessen the contraction of non-striped muscle, it appears to follow that the râles which accompany the dyspnœa of asthma are produced by spasmodic contractions of the bronchial muscles, that the dyspnœa is mainly the result of spasmodic constrictions of the bronchial tubes, and that therefore the old doctrine which attributes the asthmatic paroxysm to spasm of the bronchi is in all probability the correct doctrine. In reference to their bearing upon the dyspnœa of bronchitis we have these facts to assist us: that whenever rhonchi and sibilations accompanying dyspnœa were removed by nitrites, the dyspnœa was also removed or lessened; but when the rhonchi or sibilations were unaffected the dyspnœa was not appreciably lessened. It could not be expected that in all cases of bronchitis the administration of nitrites would be followed by complete relief of the dyspnœa and complete removal of the auscultatory phenomena. In this disease dyspnœa is sometimes produced by mucus or other inflammatory products accumulated in the bronchial tubes, and rhonchi are sometimes heard which are caused by a viscous condition of the accumulated products, and even by accumulations of a similar kind in the throat. In such cases nitrites fail to give complete relief, and they fail to silence the abnormal sounds. That they should fail is a confirmation rather than a refutation of the opinion which I wish emphatically to state—that stenosis of the bronchi due to spasmodic contraction of the bronchial muscles is a frequent cause of the dyspnœa of ordinary bronchitis.

I have not obtained any facts that would justify the preference of any one of the nitrites because it possesses therapeutic advantages over the others in the treatment of asthma or bronchitis. There are, however, conveniences of

administration which lead me to give a preference to nitrite of sodium and to nitro-glycerine. They are both extremely stable, and they can readily be given in solution, either by the stomach or by subcutaneous injection. These advantages are not possessed by nitrite of amyl and nitrite of ethyl, and even the latter substance in the alcoholic solution of the *spiritus ætheris nitrosi* of the Pharmacopœia is notoriously a very uncertain preparation. It is probable that the favour with which this preparation is, notwithstanding, regarded, may be due not only to the action on the circulation which it shares with the other nitrites, but also to its previously unrecognised influence on dyspnœa, which is no doubt exerted when it is administered, as it so frequently is, in the treatment of bronchial catarrh. When the volatile nitrites are given by inhalation the effects are only of brief duration, but when they are given by the stomach the effects are similar in their relatively prolonged duration to those of the non-volatile nitrites. Nitrite of amyl, nitrite of ethyl, nitrite of sodium, and nitro-glycerine have each proved successful in my observations in relieving the dyspnœa of asthma and bronchitis. I believe they do so, gentlemen, by removing bronchial spasm, and the remarkable power which they possess in doing this will probably lead to their being more largely used than they hitherto have been in the treatment of disease. Where their administration is successful in removing the auscultatory evidences of such spasm, it is difficult to imagine anything more convincing of the beneficial influence that can be exerted upon the conditions of disease by pharmacological agents. The observer has presented to him a patient in whose thorax a continuous succession of varying sounds is heard. Within a few minutes after a nitrite has been administered, the endless succession of noisy breath accompaniments gives place to an

almost complete silence in which only the subdued quiet of normal respiration is heard, and at the same time, what to us is of even greater interest and importance, the distress of dyspnœa, or, it may be, the intense suffering and anxiety of orthopnœa, is entirely removed.