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THE CHEMICAL PATHOLOGY

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RESPIRATION IN CHOLERA.

BY

WILLIAM SEDGWICK, M.R.C.S.

Read April 13th, 1886.

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It has been often asserted, and even still more often assumed, that cyanosis is not only distinctive of choleraic collapse, but that it is due to an excess of carbonic acid in the blood; and many useless, if not injurious, attempts have in consequence been made to increase the amount of oxygen in the blood of the pulmonary veins by the inhalation of hyperoxygenated air during the stage of collapse. The exceptional importance which has been ascribed to cyanosis in relation to cholera has not only led to much error both as regards diagnosis and treatment, but also to a widespread and an almost unquestioning belief that the disease is essentially associated with defective oxygenation of the blood. As regards diagnosis it will be sufficient for me to refer to one of my papers "On some Physiological Errors connected with Cholera,"[1] in which

[1] 'Lancet,' Nov. 11th, 1871, pp. 670, 671.

it has been shown that cyanosis is liable to occur during the collapse resulting from rapidly fatal poisoning by croton oil, by arsenic, by corrosive sublimate, and other preparations of mercury; by the mineral acids; from perforation of the stomach; and from obstruction, strangulation, rupture, and perforation of the small intestines. In such cases, which often closely simulate cholera, it has been observed that the skin is not unfrequently cyanosed, and is sometimes "even more blue than is usual in cases of true cholera." This occurrence of cyanosis in connection with gastro-intestinal affections had been fully recognised early in the present century by Broussais; and later and special writers on the subject have appropriately grouped some of these cases together under the heading of "gastro-intestinal cyanosis."[1]

In the above-quoted paper, "On some Physiological Errors connected with Cholera," attention was particularly directed to the fact that "there is a local disappearance of cyanosis during choleraic collapse, when galvanism is applied to a limb, which is independent of any effect produced on the pulmonary circulation." This influence of galvanism on the cyanosis of cholera is in no respect exceptional, for it will be found on referring to the joint report of Drs. Russell and Barry, dated "St. Petersburg, $\frac{27}{15}$ July, 1831," that, on the first introduction of the disease into Europe, it had been observed that "frictions remove the blue colour for a time from the part rubbed." The effect produced on these occasions by galvanism and by frictions evidently cannot be ascribed to any consequent increase of oxygen in the blood, for the only internal respiratory change which could result from thus urging on the blood through the tissues, would be a local increase of oxidation; as the oxygen already present in the blood would by such means be more quickly withdrawn from it

[1] Cited by F. G. Boisseau, "Mémoire sur la Cyanose Cholérique," 'Journal Univ. et Hebdom. de Méd. et de Chir. Prat.,' 1832, tome ix, pp. 277—298. See also F. J. V. Broussais, 'Le Choléra-Morbus Epidémique, observé et traité selon la Méthode Physiologique,' 1832, pp. 75, 76.

and used in that process of tissue change which is represented by an increased formation of carbonic acid. Before concluding these preliminary remarks it will be useful to direct attention to the fact, that even the normal change of colour from red to dark, which is chiefly effected in the capillary circulation, cannot be physiologically assigned to the larger quantity of carbonic acid which venous blood contains; since it has been shown by Pflüger, that "if equal quantities of oxygen be added to two portions of blood, and if carbonic acid be added to one of them, the colour is not changed."[1] Consequently, as the cyanosis of cholera fails to indicate the extent to which the aeration of the blood either has or has not been performed, it becomes necessary to analyse the air expired during life, and to examine the lungs after death in order to prove whether there is or is not any connection between this so-called asphyxia and choleraic collapse.

Those who are familiar with the literature of cholera know that it is very rich in evidence which proves that during the stage of collapse the respiration is usually much diminished, and that after death, in the case of those who die before reaction has begun, the lungs are always more or less collapsed. But when, in addition to such evidence, attention is directed to the numerous and exact analyses which have been made of the expired air, it will be found that the net result of the pulmonary interchange of gases in this disease has always been a relatively large gain in the amount of oxygen received by the blood in exchange for carbonic acid, as compared with that which is relatively gained by such interchange of gases during health. When referring to the works of those observers who have specially devoted their attention and skill to this subject, a decided preference should be given to M. Doyère's 'Mémoire sur la Respiration et la Chaleur Humaine dans le Choléra' (1863), as it is founded

[1] Cited by Landois, 'A Text-Book of Human Physiology,' translated from the fourth German edition. With additions by William Stirling, M.D., Sc.D., vol. i, 1885, p. 60.

on a very large number (nearly 300)[1] of careful observations made in 1849; as the results then obtained were confirmed by a second series of observations made in 1854, under the direction of a committee appointed for that purpose by the French Academy of Sciences, but of which the literary results were unfortunately lost; and, lastly, as the great value of the work was authoritatively recognised in 1858 by a subsequent committee, composed of MM. Serres, Velpeau, Cl. Bernard, Jules Cloquet, Jobert de Lamballe, and Andral, and whose report in its favour led to a prize of 5000 francs from the Bréant foundation being awarded to M. Doyère early in the following year (March 14th, 1859). Previous to the dates of these researches it had been analytically proved in 1819 by Dr. John Davy and Mr. Finlayson,[2] during an epidemic of cholera in Ceylon, that the air expired during choleraic collapse is "very deficient in carbonic acid;" the amount of carbonic acid, as compared at the time with that expired

[1] 'Comptes-rendus Hebd. des Séances de l'Acad. des Sciences,' October 22nd, 1849, p. 454.

[2] The importance of investigating the composition of the air expired by cholera patients was first recognised by Dr. John Davy at the latter end of April, 1819; and it was soon after this date that he had the opportunity of personally communicating his ideas on the subject to his "very intelligent and worthy friend, Mr. Finlayson," whose early death was due to phthisis, which was contracted during the following year in Siam. The first analysis of the air expired by a cholera patient was made jointly by these observers, and Dr. Davy states that "at my desire, Mr. Finlayson was so good as to continue the inquiry at a time I had no opportunity of continuing it myself." The results of these analyses were communicated to Dr. Davy in a letter dated "Kandy, 4th June (1819)." 'Report on Cholera, as it occurred in Ceylon in 1819' (published from a copy in the author's possession), by John Davy, M.D., F.R.S., &c.; 'Medical Times,' Aug. 31st, 1850, pp. 224—226; and also in his work 'On some of the more important Diseases of the Army, with contributions to Pathology,' 1862, pp. 113—122. Although this report remained unpublished for considerably more than thirty years after its transmission from Ceylon to the Medical Board of the Army, yet it was not immediately shelved; for Sir Gilbert Blane had the opportunity of reading it in manuscript soon after its arrival in this country, and he gave a summary of its contents at a meeting of the Medical and Chirurgical Society on June 6th, 1820 ('Med.-Chir. Trans.,' vol. xi, 1820, pp. 157—164).

by a healthy person of the same country and race, having been found in the first case to be only one fifth; in the second case one third; and in the several other cases examined, to be much below the normal standard. Whilst M. Rayer,[1] physician to "la Charité" Hospital, Paris, analytically recognised, in 1832, that there is a diminished quantity of oxygen absorbed. But it was reserved for M. Doyère to prove that in addition to these important but detached facts, which simply indicate a great reduction in the interchange of gases in the lungs, that there is a relatively large amount of oxygen absorbed, which, as regards the respiratory quotient of health, is constantly and sometimes very greatly in excess of that which can be accounted for by the carbonic acid eliminated.[2] Since the date of M. Doyère's researches there have been other, and some improved, methods for ascertaining the relative amounts of oxygen absorbed and of carbonic acid eliminated, both as regards health and disease; in consequence of which the respiratory quotient of health, according to the best authorities of the present day, $\frac{CO_2}{O}\left(=\frac{4{\cdot}38}{4{\cdot}782}\right)=0{\cdot}906$,[3] expresses a larger proportion of oxygen than that given, as the mean of twenty-one analyses, by M. Doyère in 1849, $\frac{CO_2}{O}\left(=\frac{4{\cdot}36}{4{\cdot}47}\right)=0{\cdot}977$.[4] But this does not affect the

[1] "Examen comparatif de l'air expiré par des Hommes Sains et des Cholériques, sous le rapport de l'oxygène absorbé," 'Gazette Médicale de Paris,' 26 Mai, 1832, pp. 277, 278.

[2] Notwithstanding this relatively large excess of oxygen aborbed, it was assumed by M. Doyère, in his introductory remarks, that asphyxia is "the constant phenomenon of cholera." The chief evidence, according to M. Doyère, in favour of asphyxia, is "the diminution of the proportion of carbonic acid produced and of oxygen absorbed;" and he proceeds to add, in accordance with the prevailing opinion of his day, that "the symptom most intimately associated with choleraic asphyxia is, I have hardly need to say, cyanosis."

[3] Dr. F. Landois, op. cit., p. 225.

[4] M. Doyère's observations in 1849, on the average amount of oxygen absorbed during healthy respiration, 4·47 per cent., agree very closely with those of M. Rayer in 1832, who found the mean of thirteen analyses to be 4·45 per cent.

general results of his researches as regards the relatively larger amount of oxygen absorbed in proportion to the carbonic acid eliminated during cholera, as compared with the relation between these two gases observed by him in the air expired during health. In the case (No. 6), for example, of a lad, æt. 16, who was admitted into the Hôtel Dieu, Paris, at 4 p.m., on April 28th, 1849, in a state of "extreme algidity," with strongly marked cyanosis and suppression of urine since the previous evening, the analysis of the air expired thirty minutes after admission showed that there was a reduction in the interchange of gases in the lungs to considerably less than half of the normal amount; and, at the same time, a relatively large excess of oxygen absorbed in proportion to the amount of carbonic acid eliminated. It was moreover observed during the progress of this case, in which, between April 28th and May 7th, fourteen observations were made on the composition of the expired air, that there was a relative excess of oxygen, associated with an absolute reduction in the pulmonary interchange of gases, both during reaction as well as during collapse.

This important fact in the chemistry of respiration in cholera shows that the blood which is conveyed to the lungs by the pulmonary arteries becomes relatively more oxygenated during its passage onwards to the pulmonary veins than is the case during health; and it has been fully established by numerous and trustworthy analyses of the air expired during cholera, that however low the absolute amount of oxygen absorbed may fall during the pulmonary interchange of gases, it is always relatively, and sometimes very largely, in excess of the amount of carbonic acid eliminated. For it has been clearly demonstrated that the blood which is brought to the lungs during choleraic collapse for the purpose of aeration, gives up a relatively diminished amount of carbonic acid in return for the oxygen taken in, owing to the formation of carbonic acid in the system having been greatly reduced, and that consequently when it leaves the lungs by the pulmonary

veins, it is relatively far richer in oxygen than is normally the case. This has been satisfactorily illustrated in the following case (No. 31), observed by M. Doyère, of a journalist, æt. 33, who was admitted into the Hôtel Dieu on May 24th, 1849 at 2.30 p.m., and who died, during choleraic collapse, at 9.15 p.m. on the same day. In this typical and rapidly fatal case of cholera there was, throughout the progress of the disease, a relatively large excess of oxygen absorbed in comparison with the amount of carbonic acid eliminated, as is well shown in the following series of analyses of the expired air. At 3 p.m., or thirty minutes after the patient's admission, the respiratory quotient was found to be $\frac{CO_2}{O}\left(=\frac{1{\cdot}61}{2{\cdot}23}\right)$ $=0{\cdot}72$; at 4 p.m., $\frac{CO_2}{O}\left(=\frac{1{\cdot}71}{2{\cdot}44}\right)=0{\cdot}70$; at 4·45 p.m., $\frac{CO_2}{O}$ $\left(=\frac{1{\cdot}62}{2{\cdot}32}\right)=0{\cdot}70$; and at 5.25 p.m., $\frac{CO_2}{O}\left(=\frac{1{\cdot}57}{2{\cdot}15}\right)=0{\cdot}73$. The average quantity of carbonic acid eliminated from the lungs in this case, according to these four analyses, was consequently reduced to 37 per cent., whilst the oxygen absorbed was only a fraction below 54 per cent. of the normal amount. When the concluding observation of the air expired in this case was made at 8.5 p.m., and when the temperature in the armpit was 37·8° C., there was found, as the mean of three analyses, to be a very much greater disproportion between the amount of oxygen absorbed and the amount of carbonic acid eliminated, for the respiratory quotient was then only $\frac{CO_2}{O}\left(=\frac{\cdot23}{1{\cdot}30}\right)=0{\cdot}18$. Consequently at the time of this last observation, which was made one hour and ten minutes before death, the carbonic acid eliminated from the lungs was not more than about $5\frac{1}{4}$ per cent., whilst the oxygen absorbed was 29 per cent. of the normal amount; or, in other words, the oxygen absorbed was equal to nearly six times the carbonic acid eliminated. A correspondingly large excess of oxygen absorbed shortly before death was also

very noticeable in other cases, and especially in that of a wood-sawyer æt. 37 (No. 12), who died during collapse sixteen hours after the commencement of the disease. Five minutes before death, and when the temperature of the armpit had risen to 38·3° C., the respiratory quotient, $\frac{CO_2}{O}\left(=\frac{\cdot 84}{2\cdot 10}\right)=0\cdot 40$, showed that whilst the carbonic acid eliminated was only 20 per cent., the oxygen absorbed was 47 per cent. of the normal amount.

There is no evidence, derived from the chemistry of respiration in cholera, in favour of the supposition that in well-marked and typical cases of the disease, carbonic acid is either accumulated in the system during collapse, or that there is an exceptional excess of it in the venous blood waiting, as it were, to escape through the lungs as soon as reaction should occur. On the contrary, it has been observed that in the same way that the first urine passed after its previously more or less prolonged suppression is deficient in urea, so the air expired during well-marked reaction is correspondingly deficient in carbonic acid ; and such deficiency is observable both in those cases in which reaction ends in death, as well as in those cases in which recovery occurs ofter a more or less prolonged and well-marked stage of convalescence. In the case (No. 2) of a young man, æt. 24, who was admitted into the Salpêtrière Hospital, Paris, on April 17th, 1849, with well-marked reaction consequent on a very severe algide stage of the disease, the pulse was 70 and fairly good, and there were only 20 to 22 very natural inspirations per minute, although the cyanosis was still very pronounced. The analysis of the air expired in this case, soon after admission, showed that the carbonic acid eliminated was only half of the normal quantity, whilst the oxygen absorbed was relatively in great excess, the respiratory quotient being $\frac{CO_2}{O}\left(=\frac{2\cdot 10}{2\cdot 78}\right)=0\cdot 75$. On April 20th, about thirty-four hours previous to death, and when the patient had been in a very grave typhoid state since the previous day, it was found,

on analysis, that the carbonic acid eliminated was reduced to one third of the normal quantity, whilst the oxygen absorbed was relatively in almost the same degree of excess as in the preceding analysis, the respiratory quotient being $\frac{CO_2}{O}\left(=\frac{1{\cdot}42}{1{\cdot}92}\right)=\cdot74$. In like manner, when the stage of reaction is followed by recovery, there is a corresponding reduction, as regards the interchange of gases, with a relatively more or less considerable amount of oxygen absorbed, as occurred in the preceding case, in which death occurred during reaction. This has been well illustrated in the case (No. 3) of a woman, æt. 30, who was admitted into the same hospital and on the same day as the last cited case; and who, at the time of her admission, was in the stage of commencing but very decided reaction, with 28 inspirations per minute, and with a slight return of the urinary secretion. The analysis of the air expired in this case, soon after admission, showed that the carbonic acid eliminated was only half of the normal quantity, whilst the oxygen absorbed was relatively in decided excess, the respiratory quotient being $\frac{CO_2}{O}\left(=\frac{2{\cdot}17}{2{\cdot}47}\right)=0{\cdot}88$. Three days later on, when reaction had been succeeded by convalescence, and the urinary secretion had been completely restored, the carbonic acid eliminated was still barely more than half of the normal quantity, whilst there was relatively a large excess of oxygen absorbed, the respiratory quotient being $\frac{CO_2}{O}\left(=\frac{2{\cdot}34}{2{\cdot}96}\right)=0{\cdot}79$.

These observations on the chemistry of respiration in cholera, and especially as regards the period of reaction, are strictly in accordance with the thermometric observations of MM. Briquet and Mignot, and of other recognised authorities on the subject. From the carefully tabulated observations of MM. Briquet and Mignot[1] on eighty-six patients suffering from the disease, it appears that although the period of reaction is usually accompanied by a compara-

[1] 'Traité Pratique et Analytique du Choléra-Morbus,' 1850, pp. 299, 300.

tively small elevation of temperature, which "at the most is not more than 2° to 3° Cent., more often 1°, and even only some tenths of a degree;" yet some of their observations have served to show that "there exists, not only during the algide period, but even during all the continuance of the choleraic phenomena, a tendency to coldness, in virtue of which the reduction of temperature is in some cases more pronounced at the period of reaction than in the cyanic period."

If any further evidence were needed to prove that cholera is unconnected with defective oxygenation of the blood, it would be unnecessary to do more than refer to that afforded by the pulmonary interchange of gases when the urinary secretion has been restored. For it has been clearly demonstrated that whilst the previously prolonged suppression of urine has always coincided with a great reduction in the amount of carbonic acid eliminated, and with a relative excess in the amount of oxygen absorbed, the restoration of the urinary secretion is not preceded, nor even for some days necessarily followed, by any corresponding difference in the interchange of gases in the lungs. In the case (No. 6) already cited, of a lad, æt. 16, in which the urine was completely suppressed from the evening of April 27th to the evening of April 29th, the lowest respiratory quotient during the intervening time was found to be $\frac{CO_2}{O}\left(=\frac{1{\cdot}58}{1{\cdot}92}\right) = 0{\cdot}82$; showing that whilst the carbonic acid eliminated was only $36\frac{1}{4}$ per cent., the oxygen absorbed was 43 per cent. of the normal amount. When the urinary secretion in this case had been restored about twelve hours (April 30th, 9 a.m.), the respiratory quotient $\frac{CO_2}{O}\left(=\frac{1{\cdot}95}{2{\cdot}50}\right) = 0{\cdot}78$, showed that the carbonic acid eliminated was 45 per cent., and the oxygen absorbed was 56 per cent. of the normal amount. Three days later on, May 3rd, 9 a.m., when the urine had become abundant, the respiratory quotient, $\frac{CO_2}{O}\left(=\frac{2{\cdot}09}{2{\cdot}46}\right) = 0{\cdot}85$, showed

that the carbonic acid eliminated was 48 per cent., and the oxygen absorbed was 55 per cent. of the normal amount. Finally, on May 7th, at 5.30 p.m., when the last analysis was made, the respiratory quotient, $\frac{CO_2}{O}\left(=\frac{2{\cdot}72}{2{\cdot}99}\right) = 0{\cdot}92$, showed that the carbonic acid eliminated was 62½ per cent., and the oxygen absorbed was 67 per cent. of the normal amount. It will be sufficient to add that in cases like this, which is typical of what occurs both during and subsequent to choleraic collapse, neither the previously prolonged suppression, nor the succeeding abundance, of the urinary secretion could have been influenced by any variations in the interchange of gases in the lungs; for during the ten days that the case was under special observation, the relative and continued excess of oxygen absorbed was limited to the comparatively narrow range of 4½ to 11 per cent. above the standard proportion of health.

The chemistry of respiration during the stage of choleraic convalescence has been as yet very imperfectly studied. But there is some evidence to show that the tendency to excess in functional activity, which, as regards the renal secretion, leads to temporary glycosuria, may also lead, as regards the pulmonary function, to an absorption of oxygen which may, for a comparatively short time, be absolutely greater than the standard of health. In one of M. Doyère's cases (No. 7) it was noted, fourteen days after the commencement of the disease, when the pulse was 64 per minute, and the health appeared to be "perfectly re-established," that the respiratory quotient was $\frac{CO_2}{O}\left(=\frac{3{\cdot}40}{4{\cdot}98}\right) = 0{\cdot}68$; showing that the carbonic acid eliminated was still only 78 per cent., whilst there was an absolute excess of oxygen absorbed to the extent of 11½ per cent. above the normal standard. In two other cases (Nos. 8 and 14) moderate reaction from slight collapse was observed to lead to an absolute excess in the absorption of oxygen, which, in each case, was also above, although only to a small extent, the normal standard

(analyses 43 and 66). Whilst in a fourth case (No. 38) it was observed during a convalescent period of five days, extending from the eighteenth to the twenty-third day after admission into the hospital, when the average temperature of the armpit was 37° C., and the average pulse was 57 per minute, that the amount of oxygen absorbed, although not quite up to the normal standard, was relatively very large; for the respiratory quotients, $\frac{CO_2}{O}\left(=\frac{3{\cdot}40}{4{\cdot}40}\right)=0{\cdot}75$, $\frac{CO_2}{O}\left(=\frac{3{\cdot}57}{4{\cdot}27}\right)=0{\cdot}83$, $\frac{CO_2}{O}\left(=\frac{3{\cdot}55}{4{\cdot}29}\right)=0{\cdot}83$, and $\frac{CO_2}{O}\left(=\frac{3{\cdot}39}{4{\cdot}14}\right)=0{\cdot}82$, showed that the average amount of carbonic acid eliminated was still below 80 per cent., when that of the oxygen absorbed was 96 per cent. of the normal standard. It is important also to note in this last case that during the succeeding eleven days which the patient continued to pass under special observation, when the average pulse was 63 per minute, and the average temperature was 37·4° C., there was a relative excess instead of a relative deficiency in the amount of carbonic acid eliminated; and at the same time loss of appetite instead of the previous desire for food. These observations on the chemistry of respiration during choleraic convalescence, like those on the occurrence of temporary glycosuria as a sequel to cholera,[1] show that "the tendency to excess during recovery from a central arrest of nutrition" does not readily cease.

There are some physiological facts connected with the chemistry of respiration in health which may with advantage be referred to in connection with the chemistry of respiration in this disease. It will be sufficient, however, for me on this occasion to state that the quantity of oxygen absorbed in the lungs is only to a very small, if any, extent influenced by an artificially produced excess of oxygen in the air for inhalation; and that if the deficiency of carbonic acid in the air expired by cholera patients during collapse, and to a less extent during convalescence, be

[1] 'Medico-Chirurgical Transactions,' vol. liv, 1871, pp. 63—93.

considered in connection with this as well as with other and allied physiological facts,[1] there will be less difficulty in understanding why such deficiency cannot be referred to any unsatisfied demand of the blood for oxygen. For whilst the analysis of the expired air demonstrates that the net result of the pulmonary interchange of gases is relatively very favorable as regards a clear gain of oxygen, all attempts to still further oxygenate the blood by the inhalation of additional supplies of oxygen have signally failed during each successive outbreak of the disease. Somewhat more than fifty-four years have passed since it was recorded by Dr. W. B. O'Shaughnessy,[2] whose name was at one time well known in connection with the chemical pathology of cholera, "that the inhalation of oxygen gas has failed remarkably in achieving the desired end is unhappily too notorious." This failure, it may be added, has not been due to any difficulty as regards inhalation, but simply to the absence of any demand on the part of the coloured blood-corpuscles for additional supplies of oxygen beyond what is contained in atmospheric air. For it has been very clearly shown that the great and remarkable affinity for atmospheric oxygen, which physiologically characterises the coloured blood-corpuscles, or rather the hæmoglobin which constitutes more than nine tenths of their bulk, instead of being lessened is increased in this disease.

[1] (*a*) That the amount of oxygen normally present in arterial blood is barely more than half the amount of carbonic acid; the proportion being 17 volumes of oxygen to 30 volumes of carbonic acid in 100 volumes of such blood.

(*b*) That the blood, in becoming venous, does not gain more per cent. than from 5 to 7 volumes of carbonic acid, whilst it loses from 8 to 12 volumes of oxygen; and that consequently the oxygen absorbed during the subsequent aeration of the blood in the lungs, is normally in excess of the carbonic acid eliminated.

(*c*) That during hybernation, when the pulmonary interchange of gases is extremely reduced, the oxygen absorbed ($\frac{1}{4}\frac{1}{1}$) is almost double the amount ($\frac{1}{7}\frac{1}{5}$) of the carbonic acid eliminated.

[2] "Proposal of a New Method of Treating the Blue Epidemic Cholera by the Injection of highly-oxygenated Salts into the Venous System," 'Lancet,' Dec. 10th, 1831, p. 367.

In thus attempting to recapitulate, as concisely as possible, some of the more important observations which have been made and recorded in connection with the chemistry of respiration in cholera, attention must be chiefly directed to the fact that whilst the absolute amount of interchange of gases in the lungs is always much reduced, in consequence of the formation of carbonic acid in the system having been partially arrested, that there is in this disease, and more especially during its stage of collapse, a relatively large amount of oxygen absorbed, which, as regards the amount of carbonic acid eliminated, is usually much above the standard proportion of health. This relative excess of oxygen absorbed necessarily leads to an almost exhaustive elimination of carbonic acid from the lungs, and to the blood, in its passage onwards to the pulmonary veins, becoming, as already stated, surcharged with oxygen. The great reduction in the supply of carbonic acid to the lungs, which is strictly in accordance with the continued ability of the patient, even during profound collapse, to make a moderately full inspiration, and also with the comparatively favorable character of the auscultatory signs of respiration, which indicate that there is no obstruction to the entrance of air, appears to be essentially connected with each stage of the disease. One of the earliest changes affecting the respiratory movements in cholera, and which is primarily due to this deficiency in the supply of carbonic acid to the lungs, is the ineffectual prolongation of the inspiratory murmur, and the exceptional shortening of the expiratory murmur, which lead to diminution, and ultimately to more or less complete failure of the voice. The duration of the inspiratory murmur has been observed, in a large number of cases of cholera, to be about twice as long as the expiratory murmur, during prolonged and well-marked collapse. In one of the cases specially noted by the late Dr. Parkes,[1] the relation between the two was as 12 to 5; in another

[1] 'Researches into the Pathology and Treatment of the Asiatic or Algide Cholera,' 1847, p. 67.

case, as 6 to 4; and in a third case it was twice as long; whilst the respiratory rhythm of health is as 6 to 7 or 8. This failure of the voice has been very commonly spoken of as the vox cholerica, but it is decidedly incorrect to refer to it as a diagnostic sign of choleraic collapse; for a corresponding failure of the voice, amounting in some cases to complete aphonia, has been noted by myself and by other observers in gastro-intestinal cases, in which there has been collapse simulating that of cholera. In such cases, as in cholera, there is a well-marked and characteristic change in the respiratory function during life, and, not unfrequently, a collapsed state of the lungs after death, which must be ascribed to a diminished supply of carbonic acid to the lungs, consequent on a previously diminished formation of carbonic acid in the system.

This failure from reduced production of carbonic acid, combined with the relative excess of oxygen absorbed, is moreover in accordance with the very decided influence of cholera on the dyspnœa of phthisis, which has for a long time attracted much attention; owing to the pathological effect of phthisis on the lung, as an organ for the elimination of carbonic acid, being necessarily to reduce its efficiency. For it has been carefully noted by MM. Briquet and Mignot[1] who, in common with other trustworthy observers, have had favorable opportunities for observing the not unfrequent occurrence of cholera in conjunction with this disease, that "in all our phthisical patients we have constantly seen the dyspnœa diminish, and the expectoration nearly or completely cease."

The physical signs of respiration and the analysis of the expired air show that the much reduced amount of blood supplied to the lungs continues to be well oxygenated during choleraic collapse. But it is chiefly by means of exact examinations after death of the extremely contracted lungs themselves, in those cases in which death has occurred before any reaction has commenced, that the extent to which carbonic acid has been eliminated during

[1] Op. cit., 1850, p. 360.

life can be fully estimated. With regard to the condition of the lungs after death, it should be noted that when attention was first directed to their contracted appearance in these cases, it was somewhat hastily, but not perhaps very unreasonably, assumed by some observers, that their condition must be due to the presence of air in the pleural cavities, which was thought to be alone capable of so completely overcoming the atmospheric pressure. At an early period in the first great epidemic of the disease in the Madras Presidency, an able observer, Dr. Pollock, of H.M's. 53rd Regiment, availed himself of an opportunity for opening, within two hours after death, the thorax of the dead body of a cholera patient under water; and as no gas was extricated, it became evident that the contracted condition of the lungs was not due to this, but to some intra-pulmonic cause.[1] Before however, any other suggestion on the subject could be reasonably offered, it obviously became important to demonstrate the exact nature as well as the extent of the pulmonary collapse; and this work has been satisfactorily done by the late Dr. Parkes,[2] whose researches have been fully confirmed by Dr. Sutton, by myself, and by very many other observers. Dr. Parkes has demonstrated that the lungs in these cases are less crepitant than usual, and that their specific gravity is diminished; showing that there is not only absence of air, but also of blood. The extent of the pulmonary collapse was found to be very considerable; for of thirty-nine cases in which the condition of the lungs was very carefully investigated by Dr. Parkes, it was ascertained that "in fourteen cases the lungs were completely collapsed, appearing in some cases almost like the lungs of a fœtus. In three cases they were considerably, and in eight cases they were slightly collapsed; and in the remaining fourteen cases, the collapse was in some cases altogether, and in other cases partially prevented by old

[1] Scot (W), 'Madras Report on Cholera,' 1824, p. 225, and Preface, p. xxxiii. See also Dr. Parkes, op. cit., 1847, p. 121.

[2] Op. cit., 1847, pp. 14—17.

adhesions." Dr. Parkes states, as the result of this collapsed condition, that "in twenty-four cases, the crepitation was totally abolished; in fifteen cases it was notably diminished in some part of the lung, and in one of these abolished completely in the upper lobes. The want of air was not owing to mechanical impediment, as on artificial respiration air passed readily in, distended the before collapsed lung, and partially or wholly restored the crepitation. This," Dr. Parkes proceeds to state, "I proved by many trials." Whilst the diminution of weight in the case of both lungs, consequent on reduced supply of blood, was found by Dr. Parkes to average 20 oz.; assuming the healthy standand weight for both lungs in males to be, according to Dr. Clendinning 46 oz.

The abolition of crepitation would thus appear to be both coextensive and coincident with the reduced supply of blood, and to be consequent on the smaller ramifications of the air-vessels having been gradually contracted so as to exclude the atmospheric air, at the same time that the previously reduced supply of carbonic acid has been more or less fully eliminated from the blood conveyed by the pulmonary arteries for aeration; and which passes onwards through the pulmonary veins, with a relative excess of oxygen to the left side of the heart. For whilst the relative excess of oxygen absorbed during health has the effect, so far as the pulmonary function is concerned, of assisting to promote the passage of blood through the lungs, the relatively larger excess of oxygen absorbed, during the collapse resulting from cholera and from allied conditions of the system, assists in still more effectually promoting the pulmonary circulation, which by this means is continued under great and increasing difficulties until the slowly diminishing supply of carbonated blood to the lungs almost or finally stops. The abolition of crepitation, like the diminished amount of blood, is in the same manner due simply to failure as regards both supply and demand; for although the well-known tendency to diffusion between the carbonic acid passing outwards from the air-

vesicles and the oxygen passing inwards from the bronchial tubes is relatively still unchecked, yet the chemical interchange of gases in the blood of the pulmonary capillaries steadily decreases with the advancing collapse, until, like the passage of the blood through the lungs, it slowly and completely fails. From the numerous observations which have been made on the progressively reduced frequency of breathing which immediately precedes death during choleraic collapse, it will be sufficient to select a fairly typical case reported by Dr. F. Paschall,[1] in which the respirations were specially timed "during the last five minutes of life, and were as follows: first minute 20; second 15; third 12; fourth 6; 5th 1 deep inspiration."

The resulting collapse of the lungs in such cases would therefore be due not to any morbidly excited contraction of the parietes of the smaller subdivisions of the pulmonary blood-vessels or of the air vessels, but to the natural elasticity of the lungs themselves, which specially favours the exclusion but not the entrance either of blood or of air, when the formation of carbonic acid in the system has been more or less extensively checked. From the thoroughly trustworthy observations of Dr. Parkes it is evident that as the lungs after death in some cases of cholera are so completely collapsed as to appear "almost like the lungs of a fœtus," the previous interchange of gases must have become less and less before it quite ceased; and that as the supply of blood sent to the lungs for aeration is to a great extent dependent on the amount of carbonic acid which it contains, this excretory product, which qualifies, as it were, the blood for aeration, must in like manner have been previously very much reduced before the pulmonary circulation could have so completely failed as to leave the lungs almost without blood as well as almost without air. The fact observed by Prof. Griesinger, that percussion during choleraic collapse gives a small area of cardiac dulness, shows that this failure in the supply of blood to the lungs is associated with a dimi-

[1] 'The Cholera Epidemic of 1873 in the United States,' 1875, pp. 18, 19.

nished amount of carbonated blood in the right cavities of the heart, and consequently in the pulmonary arteries, during life;[1] whilst the relative excess of oxygen, which is conveyed by the blood from the lungs to the left side of the heart, accounts not only for the remarkable integrity of the mental faculties during collapse, but also for the state of the left ventricle after death, which "is often found so firmly contracted that it must have closed forcibly on the last drops of blood that entered it."[2] The presence moreover of such relative excess of oxygen in arterial blood, thus stimulating into increased activity the vaso-motor centre, supplies a more satisfactory explanation of the emptiness of the brachial and other large arteries during advanced periods of collapse, which has been experimentally demonstrated by Magendie, Dieffenbach, and other observers, than the increased venosity of the blood, to which the general emptiness of the arteries after death has been very commonly referred. For this increased venosity of the blood, which occurs both shortly before as well as after death, is a capillary and not an arterial change; and it can therefore only have a secondary and an altogether indirect influence in contributing to any arterial expulsion of blood.

The not unfrequent association of collapse closely resembling that of cholera in cases such as those which have been referred to in my paper "On some Analogies of Cholera, in which Suppression of Urine is not accompanied by Symptoms of Uræmic Poisoning,"[3] with a similarly contracted condition of the lungs after death, shows that such pulmonary contraction is not only independent of any cause which is peculiar to cholera, but that it is necessary to seek elsewhere than in the lungs themselves for the primary change which has led to this result; and, in thus following analogy as a guide, we may not unreasonably expect that it will lead us to recog-

[1] Cited by Mr. Simon, 'Ninth Report,' 1866, p. 429, note.

[2] Dr. Parkes, op. cit., 1847, pp. 105, 106.

[3] 'Med.-Chir. Trans.,' vol. li, 1868.

nise that in the same way that the non-appearance of urine in the bladder is due to deficiency and arrest of urea formation in the system, and is independent, at least to a very great extent, of the kidneys; so, in like manner, the reduced interchange of gases and subsequent condition of pulmonary collapse are due to a corresponding deficiency and partial arrest of carbonic acid formation in the system, and are independent of any morbid condition of the lungs themselves. The greatly reduced but continued formation of carbonic acid during collapse, when that of urea has been thus almost if not completely stopped, is undoubtedly due to carbonic acid being a lower compound than urea, which, from a more or less strictly chemical point of view, might conveniently be referred to as a diamide of carbonic acid, or simply as a carbamide; and if, in accordance with recent progress in chemical science, we adopt one of these newer titles for urea, it would perhaps be more easy to recognise why, during choleraic collapse, the formation on a greatly reduced scale of carbonic acid in the tissues, or possibly in the blood itself, should continue, and the formation of a diamide of carbonic acid should cease.

It is perhaps almost unnecessary to add that the above cited facts connected with the chemistry of respiration in cholera do not admit of being otherwise explained. The great function of respiration is secured by being made to depend on simple and physical conditions, and it is therefore comparatively safe from such destructive influence of disease as is able in cholera to wreck the functions of those organs which are associated with nutrition, and which are affected, not by physical, but by peculiarly vital operations. This essential distinction between the function of the lungs on the one side, and the functions, for example, of the liver and the kidneys on the other, becomes still more noticeable when we pass from the consideration of the physically secured function of respiration, and from the vitally insecure and consequently wrecked functions connected with nutrition, to the rela-

tive influence of cholera on those structures and organs which are either directly or indirectly associated with reproduction. As this part of the subject has been already somewhat fully illustrated in my paper "On the Continuance of the Mammary Secretion during Collapse,"[1] it will be sufficient to state that the relative exemption there referred to is not limited to cases of this disease, but that it has been carefully noted in other cases in which there has been a central arrest of nutrition, and in which consequently the collapse has simulated that of cholera; as, for example, in acute poisoning by sulphuric acid.[2]

There remain to be noticed, and that very briefly, the great reduction of animal heat during collapse, and the remarkable increase of temperature shortly before death, which are both in accordance with the facts elicited by the chemical investigation of the respiratory function during life, and with the comparatively exsanguine and non-crepitant state of the lungs observed after death. As regards more especially the rise of temperature, which has been often recognised not only immediately before, but also after death, it is, as the result, at least to a very great extent, of temporarily increased oxidation, evidently dependent on a previous accumulation of oxygen. For it has been shown, by repeated analyses, that oxygen is continuously admitted into the system and to a great extent unconsumed during collapse; and therefore it would be ready to be thus used when life was becoming or had become extinct, and when consequently physical change was either ceasing or had ceased to be any longer checked by vital influence.

[1] 'British Medical Journal,' Sept. 19th, 1868.

[2] Casper, 'A Handbook of the Practice of Forensic Medicine, based upon Personal Experience,' translated from the third edition of the original by George William Balfour, M.D.St. Andrews, vol. ii, 1862, pp. 83, 84.

(For report of the discussion on this paper, see 'Proceedings of the Royal Medical and Chirurgical Society,' New Series, vol. ii, p. 102.)