Cheyne-Stokes Respiration.

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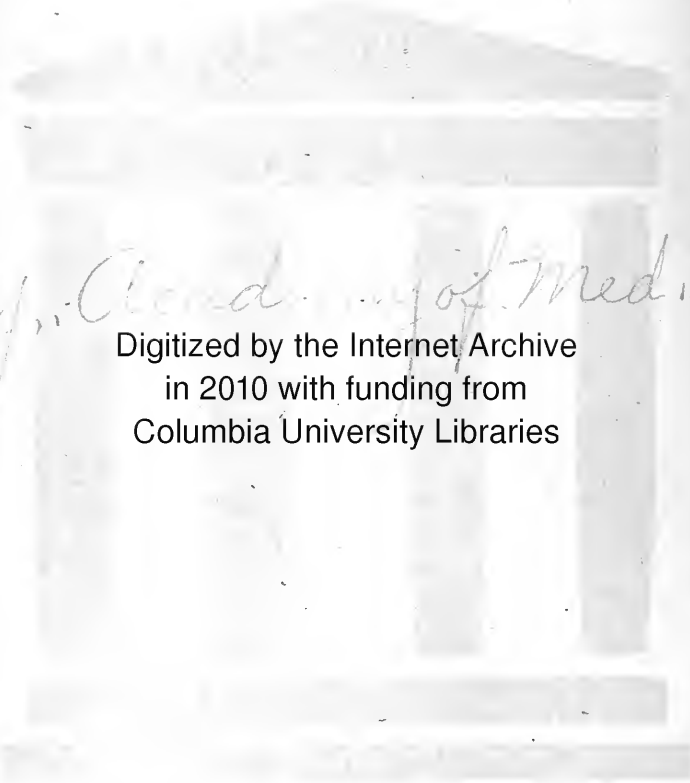

TO

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THIS LITTLE WORK IS DEDICATED

IN TOKEN OF

ADMIRATION AND AFFECTION.

PREFACE.

THE contents of the following pages have appeared from time to time during the last three years in the pages of the *Edinburgh Medical Journal* under the title of "An Examination of the Phenomena in Cheyne-Stokes Respiration." The somewhat lengthy period over which the publication of these papers has extended has not, perhaps, been altogether a disadvantage, as it has allowed full opportunities for considering the many questions involved in the explanation of a symptom so complex as that with which this work is concerned.

It is a duty as agreeable to, as it is incumbent upon, me to express my warm thanks to those who have rendered me assistance in ascertaining the views which have previously been advanced by others on the subject. I desire gratefully to acknowledge my obligations in this respect to Drs Berry, Edinburgh; Billings, Washington; Bull, Christiania; Cowan, Dordrecht; Edes, Washington; Grawitz, Greifswald; Langendorff, Königsberg; Pepper, Philadelphia; and Schepelern, Copenhagen.

I wish further to express my thanks for copies of the Transactions of their respective societies, which could not be obtained except through their kindness, to the Secretaries of the *k. k. Gesellschaft der Aerzte zu Wien, Société de Médecine et de Pharmacie de l'Isère, Société médicale de la Suisse romande, Upsala Läkareförenings Selskab, and Wisconsin State Medical Society.*

17 ALVA STREET, EDINBURGH,
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CHEYNE-STOKES RESPIRATION.

FEW symptoms have within an equally brief space of time excited so much discussion as that peculiar modification of the respiratory rhythm which in every language bears the names of Cheyne and Stokes, and, as so much has already been written on the subject, there cannot fail to be some hesitation before adding another to the many contributions towards its elucidation. In our own country, however, the symptoms which frequently accompany the type of breathing in question are but imperfectly known, while of the many explanations that have been advanced to account for its appearance, very few have been seriously considered, and it therefore seems unnecessary to give any reasons for bringing the matter forward once more. During the last four years several excellent examples of this type of breathing have been under my observation, and these have led me to study the phenomena which are linked with it, as well as to criticise the theories that have been formed to explain its mode of origin. In the following pages the results of these investigations are fully embodied, and as they naturally fall into three classes, it will be of advantage to group them in three divisions: historical, clinical, and critical.

Historical.

The type of breathing which forms the subject of the present remarks has aroused a great amount of interest and produced a corresponding number of contributions to medical science. Occurring as it does in the course of many varied conditions, the symptom is, as might be expected, referred to in works on many different diseases. The literature of the subject has therefore assumed large proportions. Many of the writings which have been devoted to it are of but little value, and yet they have served a useful purpose by throwing light upon some of its phases,

or by recording its presence in conditions where it had not been observed before. Others again are remarkable at once for their clinical acumen and critical insight. Many even of the most important are utterly unknown to the literature of this country, and it seems to be my duty, even at the risk of being here and there somewhat tedious, to mention, to an extent proportionate to their value, the different writings on the subject.

Hippocrates, like many other writers of antiquity, has suffered at the hands of his admirers, and his works have so often been wrested to suit the individual views of subsequent authors, that his name is only mentioned here with a certain degree of reluctance. It seems almost beyond doubt, however, that in the First Book of the Epidemics he makes reference either to the type of breathing about to be considered or to some nearly allied form of respiration. In describing the case of Philiscus, who died of an acute disease of a somewhat indefinite kind, accompanied by an enlargement of the spleen, he remarks:[1]—"Τουτέῳ πνεῦμα διὰ τέλεος, ὥσπες ἀνακαλουμένῳ αραιὸν, μέγα. In this case, the respiration until the end, like that of some one recollecting himself, was infrequent and deep;" or, as it has been rendered by Adams,[2] "The respiration throughout, like that of a person recollecting himself, was rare and large." The last-named author remarks in a footnote,—"The modern reader will be struck with the description of the respiration, namely, that the patient seemed like a person who forgot for a time the *besoin de respirer*, and then, as it were, suddenly recollected himself. Such is the meaning of the expression as explained by Galen in his Commentary, and in his work, On Difficulty of Breathing."

In his learned address on Medicine, delivered before the Edinburgh meeting of the British Medical Association, Warburton Begbie[3] called attention to this observation of Hippocrates, and the matter is put so clearly that it will be well to quote his words:—"It is, however, in respect to the peculiar character of the breathing that the case of Philiscus acquires its chief interest, and it is in this particular that a resemblance is to be found between the ancient and the modern examples now quoted. The attention of Hippocrates had been arrested by the peculiar char-

[1] *Œuvres complètes d'Hippocrate*, par É. Littré, tome ii. p. 684. Paris, 1840.
[2] *The Genuine Works of Hippocrates*, vol. i. p. 371. London, 1849.
[3] *British Medical Journal*, vol. ii. for 1875, p. 164.

acter of the breathing which existed throughout the fatal illness of Philiscus. Surely it is matter of interest and for reflection that the respiration described by Hippocrates as *αραιὸν μέγα*, 'rare and large,' and to which Galen has attached the meaning, 'like a person who forgot for a time the need of breathing, and then suddenly remembered,' or 'the respiration throughout, like that of a person recollecting himself, was rare and large,' has attracted great attention in quite recent times. The expression used by French writers, 'besoin de respirer,' corresponds in some measure to the meaning which is sought to be conveyed by the Greek words. In Latin the rendering is, 'Spiratio huic perpetuo rara et magna fuit.' Daremberg, the learned French editor of Hippocrates, thus translates the passage: 'La respiration fût constamment grande, rare comme chez quelqu'un qui ne respire que par souvenir.'"

Attention has recently been called by Gallois[1] to the fact that the type of respiratory rhythm about to be considered was observed towards the close of last century. In a work by Nicolas, a physician of distinction at Grenoble, entitled, *Histoire des maladies épidémiques qui ont régné dans la province de Dauphiny depuis l'année* 1780, and published at Grenoble in 1786, there is a description of a respiratory phenomenon which appears to be identical with Cheyne-Stokes breathing. Narrating the case of a general officer, aged 81, suffering from a complication of senile affections, he describes the respiratory phenomenon, after referring to the state of the pulse which was extremely irregular, in the following manner:—"Mais ce qui était bien plus extraordinaire que cette irrégularité, c'était une suspension absolue, une fériation des mouvements du poumon pendant vingt-cinq ou trente secondes, à chaque trente-cinquième ou trente-sixième respiration; alors le jeu de l'organe se rétablissait peu à peu, et par une gradation très sensible, il reprenait son énergie ordinaire, pour cesser de nouveau à peu près à l'instant marqué."

It will be observed that the ascending phase of Cheyne-Stokes respiration is accurately described in the quotation just given, although there is no mention of a period of descending respiration, and it is impossible to avoid coming to the conclusion that

[1] *Journal de la Société de Médecine et de Pharmacie de l'Isère*, 8me année, p. 267, 1884.

Nicolas had before him a typical example of the breathing now under consideration.

With the exception of the observations made by the Father of Medicine and by the learned physician at Grenoble, the peculiar form of breathing which we are about to consider remained unnoticed until Cheyne, who carried the torch of medical science from our own shores to those of the sister island, observed it anew. In reporting[1] a case of fatty degeneration of the heart, he thus describes the type of the respiration:—"The only peculiarity in the last period of his illness, which lasted only eight or nine days, was in the state of the respiration. For several days his breathing was irregular; it would entirely cease for a quarter of a minute, then it would become perceptible, though very low, then by degrees it became heaving and quick, and then it would gradually cease again: this revolution in the state of his breathing occupied about a minute, during which there were about thirty acts of respiration." In the description of the dissection, it is noted that there were between three and four ounces of fluid in the ventricles of the brain. A very interesting observation, which has most frequently escaped the notice of subsequent writers, is contained in a footnote, where Cheyne remarks:[2]—"The same description of breathing was observed by me in a relative of the subject of this case, who also died of a disease of the heart, the exact nature of which, however, I am ignorant of, not having been permitted to examine the body after death."

Berton[3] mentions changes in respiratory rhythm as being a common symptom in cerebral inflammations, and quotes some remarks by Dance, in which breathing, not very unlike that under consideration, is described. Subsequent French writers on children's diseases follow in the same path.

It has been stated that Flourens, in the course of his celebrated experiments, observed the occurrence of periodic breathing as the result of injury to the nerve centres. But in the first edition of his work[4] there is no reference to such a phenomenon, while in

[1] *Dublin Hospital Reports*, vol. ii. p. 216, 1818.

[2] *Ibid.*, p. 222, 1818.

[3] *Traité des Maladies des Enfants*, p. 67. Paris, 1837.

[4] *Recherches Expérimentales sur les Propriétés et les Fonctions du Système Nerveux, dans les Animaux Vertèbrés*, p. 168. Paris, 1824.

the second edition the exact condition which is mentioned admits of considerable doubt. In the second edition, when criticising the observations of Marshall Hall, and describing the results of some experiments on the medulla oblongata,[1] he says:—"Je répétai cette expérience, sur un lapin. L'animal survécut à l'opération pendant à peu près vingt-deux minutes: sa respiration n'était plus, à la vérité, continue; mais elle se reproduisait de temps en temps, et surtout quand on irritait l'animal." Such arrests of the respiration, as will be seen later, are regarded by some authors as belonging to the same series as Cheyne-Stokes respiration; they are looked upon as essentially different by others.

West[2] briefly refers to irregularity of breathing as frequently occurring in inflammations of the brain and meninges, and later authors in this country also do so.

Stokes, whose name, as well as Cheyne's, is now indissolubly bound up with the peculiarity of breathing in question, made it pathognomonic of fatty degeneration of the heart. Speaking of the symptoms of this condition he says:[3]—"But there is a symptom which appears to belong to a weakened state of the heart, and which, therefore, may be looked for in many cases of the fatty degeneration. I have never seen it except in examples of that disease. The symptom in question was observed by Dr Cheyne, although he did not connect it with the special lesion of the heart. It consists in the occurrence of a series of inspirations, increasing to a maximum, and then declining in force and length, until a state of apparent apnœa is established. In this condition the patient may remain for such a length of time as to make his attendants believe that he is dead, when a low inspiration, followed by one more decided, marks the commencement of a new ascending and then descending series of inspirations. This symptom, as occurring in its highest degree, I have only seen during a few weeks previous to the death of the patient. I do not know any more characteristic phenomena than those presented in this condition, whether we view the long continued cessation of breathing, yet without any suffering on the part of the patient, or the maximum point of the

[1] *Recherches Expérimentales sur les Propriétés et les Fonctions du Système Nerveux, dans les Animaux Vertébrés*, Deuxième edition, p. 206, 1842.

[2] *Lectures on the Diseases of Infancy and Childhood*, p. 16. London, 1848.

[3] *The Diseases of the Heart and of the Aorta*, p. 324. Dublin, 1854.

series of inspirations, when the head is thrown back, the shoulders raised, and every muscle of inspiration thrown into the most violent action; yet all this without râle or any sign of mechanical obstruction. The vesicular murmur becomes gradually louder, and at the height of the paroxysm is intensely puerile.

"The decline in the length and force of the respirations is as regular and remarkable as their progressive increase. The inspirations become each one less deep than the preceding, until they are all but imperceptible, and then the state of apparent apnœa occurs. This is at last broken by the faintest possible inspiration; the next effort is a little stronger, until, so to speak, the paroxysm of breathing is at its height, again to subside by a descending scale."

Hasse,[1] writing a year later than Stokes, observes, in describing the symptoms of tubercular meningitis, that "long pauses occur now and then, as if the patients had for the time forgotten inspiration." This may, however, have been an allied type of intermittent respiration.

Schweig,[2] writing in ignorance of previous observations, brings forward periodic breathing as a new symptom, and it is clear from his remarks that he had the true phenomenon of Cheyne and Stokes before him. He records several cases. In all there was a comatose tendency preceding or accompanying the onset of the symptom in question. After death, one was found to have thickening of the skull, several ounces of fluid in the left ventricle, a flabby, but otherwise healthy, heart, old tubercular masses in the pulmonary apices, and abdominal adhesions. No notice is taken of the state of the kidneys. The second, in which the author states there was no change in the pulse during the phases of the breathing, had thickening of the skull, dropsy of the ventricles, old tubercular lesions in the lungs, and atheroma with cardiac hypertrophy. The state of the kidneys is not mentioned. The third was a case of renal disease with hypertrophy of the heart, dropsy of the pleuræ, and œdema of the legs. Here again it is noted that neither phase of the respiration had any influence on the pulse. The head was not examined after death. In the fourth case there was atheroma of the vessels with fatty degeneration of the heart,

[1] *Handbuch der speciellen Pathologie und Therapie*, redigirt von Rudolf Virchow, iv. Band, i. Abtheilung, S. 473. Erlangen, 1855.

[2] *Aerztliche Mittheilungen aus Baden*, xi. Jahrgang, S. 49, 1857.

thickening of the skull, and a considerable quantity of fluid in the left ventricle of the brain. The kidneys receive no notice. He lays stress in all these cases on the comatose tendency, and in the three whose heads were examined on the sclerosis of the skull, and the chronic hydrocephalus, but especially emphasizes the fact that on the left side in these three cases the foramen jugulare was greatly narrowed, and thus caused pressure on the vagus and accessorius nerves. After these remarks he describes another case in which, after various affections especially connected with the brain, pneumonia ensued, and was followed, after severe mental troubles, by periodic respiration with gradual development of coma. The author diagnosed thickening of the skull, narrowing of the left cranial cavity, left-sided hydrocephalus, and stenosis of the left foramen lacerum. The necropsy revealed thickening of the skull with osseous deposits, œdema of the pia mater, bleeding points throughout the brain substance, distention of the left ventricle by fluid and some also of the right, atheroma of the basilar-artery, and great stenosis of the left jugular foramen, which was only one-third of the size of the opposite one. The heart was adherent to the pericardium and enormously hypertrophied, with atheroma of the mitral and aortic valves, great dilatation of the right side of the heart, a considerable amount of fluid in the pleuræ, which were adherent in great part, and tubercular lesions in the lungs. The kidneys escape observation. A sixth case is mentioned, still alive when the paper was published, in which cardiac disease was followed by mental affections accompanied by periodic breathing.

Soon afterwards similar phenomena were produced experimentally, for we find that Schiff[1] observed the characteristic breathing as the result of hæmorrhages involving the medulla oblongata, but not directly affecting the vital spot. He says:— "Injury of other parts of the medulla oblongata than that described above permit indeed life and breathing to go on, but probably through the accompanying hæmorrhage, which influences the respiratory centre, it may modify the respiration in two ways.

"*a*. Every slight hæmorrhage upon the medulla oblongata, and

[1] *Cyclus organisch verbundener Lehrbücher sämmtlicher medicinischen Wissenschaften*, herausgegeben von Dr C. H. Schauenburg, ix. Theil, i. Band, S. 324. Lohr, 1858-59.

every pressure upon it, makes the breathing less frequent and more laboured.

"*b.* If the hæmorrhage be larger or the pressure greater, a peculiar symptom is observed in different mammals, the like of which I have as yet sought in vain for in human pathology, and to which I may direct the attention of physicians. The respirations entirely cease for a quarter of a minute or half a minute, then begin gradually, increase their rate, and afterwards wane, until a new pause occurs. This appears to be caused by variations in the amount of the pressure, which is of necessity dependent on the power of the heart beat." From this it is evident that Schiff's attention had never been called to the observations of Cheyne, Stokes, or Schweig.

Reid,[1] in reporting two cases of aneurism with this symptom, one of a man aged 60, the other that of a woman aged 59, notes that the pulse was periodically irregular, becoming less frequent during the respiratory distress, and more so when the distress was lessened.

In another paper[2] the same author describes a case of aortic and mitral disease, without any change in the texture of the muscular walls on dissection, and from a study of it he concludes "that the symptoms of respiratory distress must henceforth cease to be looked upon by me as pathognomonic of fatty degeneration of that organ." He observes that in this patient "*the pulse became invariably slow when the distress was greatest, and as invariably quick when it was subsiding, or whilst the patient had ceased to breathe.*" He is inclined to think that this change in the pulse is not a mere coincidence, "but that it and the distress stand towards each other in the relation of cause and effect;" he does not, however, venture upon any theory.

Trousseau[3] mentions, as characteristic of cerebral inflammations, a symptom, which, if not exactly the same as Cheyne-Stokes respiration, has a great resemblance to some forms of that type of breathing, as it has not only the cessation of respiration, but also the ascending and descending phases.

Referring to this subject in the third edition of his treatise,

[1] *The Dublin Hospital Gazette*, vol. vi. p. 308, 1859.

[2] *Ibid.*, vol. vii. p. 133, 1860.

[3] *Clinique Médicale de l'Hôtel-Dieu de Paris*, tome ii. p. 318. Paris, 1862.

Walshe[1] remarks:—"I cannot avoid inferring that the proximate cause lies in a failure of the special nervous excitant of the respiratory act—in anæsthesia either of the vagus or of the medulla oblongata itself." This opinion is simply adhered to in the last edition of the work.[2]

In a lecture by Laycock, reported by Ropes,[3] there is a description of the peculiar breathing, and it is stated that the most probable explanation of the phenomena "is that a sentient palsy of the respiratory centre occurs, or a paresis of reflex sensibility of the mucous membrane of the lung."

In a research undertaken with a view to solve some physiological and pathological questions connected with the brain, Leyden[4] notes that when the pressure is abnormally raised in animals there are changes in the respiration. The breathing became irregular, long pauses separating periods, during which respirations rapidly succeeded each other, so that, as the author states, there was a similarity to Cheyne-Stokes respiration; there was never such a regular periodicity of the events or transition from the breathing to the pause. It is of interest to observe that in this contribution, in addition to changes of sensibility, mobility, and intelligence, the author noted alterations in the pupils.

Head[5] recorded a case which presented this symptom, and in which fatty degeneration of the diaphragm was found after death, with atheromatous degeneration and dilatation of the aorta, and aortic incompetence. In this paper is a full notice of the condition of the pulse during the two stages of apnœa and dyspnœa; from tracings taken by Grimshaw it was observed that the pulse was as strong during the former as the latter phase, while tracings obtained from another case under the care of Little showed stronger pulsations during the cessation of respiration.

This type of respiration is said by von Dusch[6] to occur in

[1] *A Practical Treatise on the Diseases of the Heart and Great Vessels.* Third edition, p. 345. London, 1862.

[2] *Ibid.* Fourth edition, p. 407. London, 1873.

[3] *The Medical Journal* for 1864, p. 116.

[4] *Archiv für pathologische Anatomie und Physiologie und für Klinische Medicin*, xxxvii. Band, S. 519, 1866.

[5] *Dublin Quarterly Journal of Medical Science*, vol. xliv. p. 405, 1867.

[6] *Lehrbuch der Herzkrankheiten*, S. 153. Leipzig, 1868.

affections of the brain, and in uræmic coma, and he also states that he has observed it in one severe case of pericarditis.

Little[1] published a few cases in which the symptom was prominent, one being an example of fatty degeneration of the heart, another of aortic stenosis and hypertrophy of the left ventricle, and a third of renal disease with atheromatous degeneration and dilatation of the aorta, and thickening of the aortic valves. The author of this contribution ingeniously argues that the cause of the peculiar respiration is a loss of balance between the two sides of the heart, either through diminished force of the left ventricle, as in fatty degeneration, or when some abnormal burden has been imposed on the left ventricle, under which it is unable to get rid of blood as quickly as it is supplied to it, and the blood accumulates in the left auricle and the pulmonary veins and capillaries. Being fully oxygenated, this blood fails to excite the terminal filaments of the vagus, as venous blood does, and the respiration ceases. A few pulsations then displace this blood, and the venous blood streaming in excites the respiration anew. He also states his belief that the altered rhythm of the respiration is only found when the lesion which has destroyed the balance between the two ventricles has been rapidly produced; that when this is not the case the ventricles adapt themselves to the changed conditions.

Benson[2] describes a case of mitral disease in which cerebral hæmorrhage occurred followed by the type of respiration which we are considering, and he gives expression to his opinion that the theory propounded by Little is a "true account of the essential mechanism of the phenomenon," but adds that he thinks "a certain nervous complication is necessary to determine the accession of this peculiar form of respiration, and without which it would not occur." He also notes, in the description of his case, that it was only while the patient was allowed to remain in the semi-comatose state that the peculiar respiratory rhythm showed itself; when roused up, the respiration became almost normal, and assumed the ascending and descending character when the condition of stupor was permitted to return. He distinctly states his belief that the

[1] *Dublin Quarterly Journal of Medical Science*, vol. xlvi. p. 46, 1868.
[2] *Ibid.*, vol. xlviii. p. 127, 1869.

nervous centres were incapacitated for work by the cerebral lesion; that this produced arrest of the respiration, that the centres after a certain time regained their excitability sufficiently to reflect a motor impulse, thus re-establishing respiration, but that being weak, the centres could not sustain the effort and apnœa again occurred, and so on. He therefore concludes that there must in every case be a diseased condition of the circulatory and of the nervous mechanism, a double pathological condition, which he states as follows:—

"1. A certain diseased state of the heart, by reason of which, indirectly, the excito-motor impulse upon the nervous centres, conveyed through the pulmonary branches of the pneumogastric, is diminished.

"2. A certain weakened state of those nervous centres, by reason of which the reflecto-motor impulse is diminished."

This brings us to the period of the classical clinique, in which Traube expounded his theory, published by Fräntzel,[1] and reprinted in his collected works.[2] Describing a case of aortic and mitral disease, with hypertrophy of the left and dilatation of the right ventricle, in which the phenomenon appeared after a subcutaneous dose of morphine, he takes the opportunity to mention the first case in which he had met with this symptom—one of cerebral hæmorrhage—and refers to other instances of cerebral hæmorrhage, as well as cerebral tumours, tubercular meningitis, and uræmic coma, which presented it. He concludes, therefore, that the peculiar type of respiration may occur in two classes of patients: 1. Those with healthy hearts, but diseased contents of the cranial cavity; 2. Those with healthy contents of the cranial cavity, but diseased hearts. He further observes that the duration of the periods may be so short, and the pauses so inappreciable, that the phenomenon may escape notice; that, towards the end of long pauses, muscular twitchings may occur closely resembling those seen when the artificial respiration is suspended in slightly curarised animals; and that sometimes during long pauses the tension of the arteries rises, while the pulse-rate diminishes. He proceeds to point out that all the cases in which the pheno-

[1] *Berliner klinische Wochenschrift*, vi. Jahrgang, S. 277, 1869.

[2] *Gesammelte Beiträge zur Pathologie und Physiologie*, ii. Band, S. 882. Berlin, 1871.

menon is present have one characteristic—they have all a diminution of the supply of arterialized blood to the medulla, where the respiratory centre is situated. There is thus a smaller supply of oxygen, of which we know that it, in a higher degree, influences the irritability of the cellular nervous elements. Through this lessened amount of oxygen the irritability of the nerve cells becomes so much lowered that a larger quantity of carbonic acid is required to cause an inspiration, and therefore the time within which the carbonic acid will accumulate in sufficient quantity is lengthened. This is similar to the effects of section of the vagi, in which long pauses occur in the respiration, attended by dyspnœa. The respiration may be excited in two ways: 1. By the pulmonary fibres of the vagus, whose peripheral terminations are probably washed by the blood, and whose central ends are connected with the respiratory centre; and 2. By the afferent nerves coming from all parts of the body, which are able to send a sufficient stimulus to the medulla, as in the case of dashing cold water on the skin, and the well-known effect of the gastric portion of the vagus on the respiration. The difference between these two is this, that the pulmonary endings of the vagi are bathed in blood containing much carbonic acid, while the others have a supply of blood which contains but little. If both be equally irritable, then in health only the pulmonic vagi will be called into action. If the vagi be cut the respiratory centre can only be excited by the other nerves, and this can only happen when the blood circulating throughout the body is as rich in carbonic acid as that normally passing into the lungs. It must be borne in mind that the number of the vagus fibres is incomparably smaller than that of the other nerves; when these latter act, therefore, the effect is correspondingly greater, and simple respiration becomes dyspnœa. Applying this reasoning to the phenomenon in question, we find that the lessened irritability of the respiratory centre, caused by the cerebral pressure, or uræmic blood, or deficient arterial supply, requires a larger amount of carbonic acid as a stimulus, and thus there is a long pause. When this gas has accumulated in sufficient quantity it first stimulates the pulmonary terminations of the vagi, but, as was shown long before by Traube, the strongest stimuli applied to the vagi never cause dyspnœa, and this only causes the shallow breathing which appears first after the pause. The amount of carbonic acid

meantime increases sufficiently to cause stimulation of the nerves coming from the skin and other parts of the body, and hence the dyspnœa sets in. The quantity of the gas is greatly diminished by the forcible breathing, and the excitement of the other nerves ceases, so with the action of the vagi alone shallow breathing again occurs, until there is not enough carbonic acid gas to excite the pulmonary endings of the vagi, and a pause sets in anew. Traube ends by calling attention to the fact that the morphine directly induced the peculiar respiratory rhythm by reducing the irritability of the respiratory centre in a case where it was already at a low ebb.

Mader[1] describes five cases in which Cheyne-Stokes respiration was present; an extravasation into the floor of the fourth ventricle; a tumour between the medulla, pons, and cerebellum; an extravasation reaching from the right optic thalamus to the medulla; an enlargement of the vertebral artery compressing the medulla; and, lastly, renal disease with a tumour of the pons. He maintains that the cause of the phenomenon must be sought in anatomical changes in the medulla oblongata, and opposes the view of Traube that the respiratory change can take place, without any palpable changes in its structure, through alterations in the circulation.

Hesky,[2] observed the occurrence of Cheyne-Stokes breathing during the course of a fatal case of enteric fever. The chief point of interest in his description is the fact that the pulse almost ceased during the long pauses; the pulsation, indeed, appeared to become less before the respiration began to diminish. The section gave evidence, in addition to the characteristic abdominal lesions, of congestion of the brain and medulla, particularly of the floor of the fourth ventricle, and more especially of the points of origin of the vagus and hypoglossus. The author is of opinion that the cause of the symptom is a smaller access of oxygenated blood to the centres, produced by the lessened activity of the circulation.

Esenbeck[3] describes the case of a man, aged 62, belonging to an apoplectic family, and subject to no affection beyond nervous palpita-

[1] *Wiener medicinische Wochenschrift*, xix. Band, S. 1447 und 1464, 1869.

[2] *Wiener medicinische Presse*, x. Jahrgang, S. 1107 und 1133, 1869.

[3] *Aerztliches Intelligenzblatt*, S. 253, 1870.

tion, who had about a year and a half before been attacked by apoplexy, which passed away without leaving any distinct sequelæ in its train. He was again suddenly seized with unconsciousness accompanied by convulsive twitchings of the face and right arm, which became absolutely paralysed. Seven days after the attack the patient died in a comatose state. Thirty-six hours before death the rhythm of Cheyne-Stokes breathing appeared, and continued until death occurred. On section, fatty degeneration of the heart was found. The skull was very thick, the meninges and ventricles of the brain contained a considerable amount of exudation, the vessels were turgid, and the brain substance showed "capillary apoplexy," but no patch of cerebral hæmorrhage. The medulla was quite normal in appearance. The author points out that the result of the post-mortem examination agrees with what has been described by Stokes and Traube, and gives his adhesion to the theory advanced by the latter.

Leube [1] mentions three cases which he observed in von Ziemssen's clinique presenting this symptom, one being an instance of fatty degeneration of the heart, another of cerebral hæmorrhage, and a third, which he narrates at length, of mitral stenosis with dilatation of the right ventricle, venous pulsation, hydrothorax, ascites, and albuminuria, in which the characteristic rhythm of the respiration came on after a subcutaneous injection of morphine. He remarks that at the beginning of the pause the pupils were contracted and underwent no change in size with alteration of light, and continued in this state throughout the pause. With the first returning breath, or, rarely, immediately before it, they dilated again. With the movement of the pupils there was a peculiar lateral deviation of the globes of the eyes, which was repeated with each change of the size of the pupils. With the commencement of respiration the globes became still, and during the respiratory period they performed the usual movements in every direction. He also observes that consciousness was entirely lost during the pauses, and further notes that during this phase the pulse was always smaller and more irregular than during the periods, but that the rate was unaltered or slightly increased. He attributes the pupillary changes to the action of the excess of carbonic acid in the blood on the oculo-

[1] *Berliner klinische Wochenschrift*, vii. Jahrgang, S. 177, 1870.

pupillary centre, and refers to the observations of Vigouroux on the action of the iris in inspiration and expiration, and to the researches of Küssmaul on the influence of the circulation on it, as well as to the investigations of Adamük on stimulation of the corpora quadrigemina. Lastly, he mentions that in spite of deep inspirations produced by electric stimulation of the phrenic nerves, the onset and course of the period of breathing were unaffected. He notes that each deep inspiration thus produced by artificial stimuli was accompanied by dilatation of the pupils; this, however, he says may be due to stimulation of the sympathetic in the neck by the current.

Haehndel[1] enters very fully into the whole matter in his inaugural dissertation. After some historical and critical observations he mentions that he had frequently noticed the appearance of groups of shallow or superficial respirations without any pause. Such a phenomenon he considers to be a transition towards the more fully developed form, and he explains it in a manner similar to Traube's theory. He thereafter narrates seven cases of Cheyne-Stokes breathing which he had personally observed:—Mitral incompetence, with embolism of the right Sylvian artery; chronic endocarditis, with mitral and aortic lesions and thrombosis of the left internal carotid artery; aortic incompetence, with fatty degeneration of the muscular structure and hypertrophy and dilatation of the heart; sclerosis of the coronary arteries, with cardiac hypertrophy, and stenosis of the inferior vena cava from hepatic fibro-sarcoma; mitral stenosis, with atheroma of the arteries of the base of the brain, and softening of the left optic thalamus; chronic renal disease with uræmia; and, lastly, chronic renal disease with mitral incompetence. In his remarks on these cases he calls attention in one instance to the persistence of consciousness throughout all the phases of the breathing, and in another to the pupillary changes which were present, but which did not in all respects coincide with the appearances described by Leube.

In this thesis the author refers to a case which he attributes to Erb, in which cerebro-spinal meningitis was accompanied by Cheyne-Stokes respiration, the cause of which had been supposed

[1] *Ueber das Cheyne-Stokes'sche Respirations-Phänomen.* Breslau, 1870.

to be the presence of purulent exudation surrounding the medulla oblongata. No trace of this observation is to be found in literature elsewhere, and Professor Erb informs me that he has never written or spoken on the subject.

Lutz[1] describes a case of scarlatina followed by suppuration of the ear and cerebral symptoms, during the presence of which the respiration assumed this peculiar rhythm.

Björnström[2] says that the phenomenon is probably not so rare as might be imagined from the paucity of literature concerning it, and describes three cases which he had seen. The first, a child three months old, was ill with capillary bronchitis, and during the last four days of life manifested this phenomenon. The second patient, aged seventeen years, suffered from tubercular meningitis, but here the symptom was not typical, and was accompanied by divergent strabismus. The last case was that of a patient of the age of seventy years affected by fatty degeneration of the heart. The author regards Cheyne-Stokes respiration as lethal. He does not approve of Traube's theory, but declines to formulate another. He further objects to the name by which the symptom is known.

In the discussion which followed the reading of this paper, Glas mentioned that he had seen stoppages of breathing in a case under his care, and a description of the case is given further on[3] in the same publication. The patient in this case, who was a man aged 70, suffering from traumatic gangrene, had pauses in the respiration, without any change in the state of the circulation.

Heidenhain,[4] in a most interesting paper on Cyon's theory of the central innervation of the vaso-motor nerves, points out that he has observed the Cheyne-Stokes phenomenon in chloralized animals, and he gives a tracing showing the rhythm of the respiration, which perfectly corresponds with that which we obtain in cases of disease in man. He draws attention to the fact that during the respiratory period the blood-pressure rose slightly.

[1] *Deutsches Archiv für klinische Medicin*, viii. Band, S. 123, 1870.

[2] *Upsala Läkareförenings Förhandlingar*, vi. Band, S. 307, 1870–1871.

[3] *Ibid.*, vi. Band, S. 315.

[4] *Archiv für die gesammte Physiologie des Menschen und der Thiere*, iv. Jahrgang, S. 554, 1871.

Brückner[1] makes a brief reference in 1871 to the fact that his deceased father had, twenty-two years before the date of his communication, called his attention to the phenomenon of Cheyne-Stokes respiration, and given it the name of "pendulum-like breathing," because the alternation of the breathing and the pauses is as regular as the swinging of a pendulum. The author mentions that he has frequently watched the symptom, particularly in cases of tubercular meningitis.

Rehn[2] describes two cases of pulmonary disease in children, which presented this symptom. One was a child of one year of age, suffering from pneumonia; the other an infant six weeks old labouring under bronchitis. For the explanation of the phenomenon he accepts the theory that there is a lessened access of arterialized blood.

Merkel[3] records a case in which the patient, who suffered from renal disease with cardiac dilatation and pulmonary emphysema, was attacked by apoplexy a year before his death. During the cerebral symptoms, Cheyne-Stokes respiration made its appearance, and during the pause, narrowing of the pupils and absence of reaction to light were observed, along with dulness of the mind. The author mentions that when a question was asked at the end of a period of breathing, it was answered at the beginning of the next period after the termination of the intervening respiratory pause. The patient recovered from this seizure, and on his death, about a year later, it was found that in addition to granular kidneys, emphysematous lungs, and a dilated and hypertrophied heart, with cyanotic atrophy of the liver and spleen, there was destructive disease in the corpus striatum, optic thalamus, and pons. In another case narrated subsequently,[4] the same author found this type of respiration in association with endocarditis and embolism of one of the posterior branches of the right artery of the Sylvian fossa. He found that even with total absence of reaction to light the pupils became distinctly smaller at the beginning of the pause.

[1] *Archiv für pathologische Anatomie und Physiologie und für klinische Medicin*, lii. Band, S. 155, 1871.

[2] *Jahrbuch für Kinderheilkunde und physische Erziehung*, neue Folge, iv. Jahrgang, S. 432, 1871.

[3] *Deutsches Archiv für klinische Medicin*, viii. Band, S. 424, 1871.

[4] *Ibid.*, x. Band, S. 201, 1872.

Schepelern[1] describes several cases in which he met with this type of breathing, and adds to the rapidly advancing store of knowledge in regard to the symptoms associated with it. The first patient was a man, aged 54. In this case the phenomenon appeared after a period of breathlessness and palpitation. The patient felt most comfortable at the beginning of the apnœa, and became unconscious towards the end of it, but could be awakened out of this state, and was able to talk during the pause. No convulsive or involuntary movements were present in the muscles or eyes. Ophthalmoscopic examination of the eyes showed nothing beyond a slight patch of hæmorrhage near one papilla, and fulness of the veins. There was no variation in the size of the vessels of the fundus during the changing phases of respiration. The patient could be caused to breathe during the pause of respiration by constantly ordering him to do so, and this lessened the subsequent period of dyspnœa. Electric stimulation of the phrenic nerves during the pause produced no result. The relative duration of the apnœa and dyspnœa was not affected by sleep. The pulse remained small throughout the different phases of respiration, without apparent change in strength or tension, but the number of pulsations was less during the period of breathing, probably from intermission which was present. On section the heart was fatty, the aorta and arteries, especially the vertebral and basilar, atheromatous, the liver was fatty, and the kidneys cyanotic.

The second case was that of a man, 75 years old, suffering from bronchitis with ascites and albuminuria. The Cheyne-Stokes respiration was well marked, but was not attended by muscular twitchings or pupillary variations. The patient could be made to speak during the pause, but could not be caused to breathe during that phase, and electric stimulation of the phrenic nerves produced no result. There was no alteration in the rate or strength of the pulse during the changing respiratory phases. There was no examination after death.

The third case was that of a man, aged 69, of gouty habit, suffering from aortic disease and cardiac hypertrophy with albuminuria. There was no autopsy in this case.

The fourth patient, a woman about 60 years old, was affected

[1] *Hospitals-Tidende*, xv. Aargang, S. 77, 81, og 85, 1872.

by mitral disease. On section there was stenosis and incompetence of the mitral orifice and valve, with hypertrophy of the left and dilatation of the right ventricle, and a fatty heart. There was degeneration of the cerebral arteries and old tubercular disease of the apex of the right lung.

Schepelern supports the theory of Traube, and believes the dulness of the mental faculties to be caused by the presence of an excess of carbonic acid in the blood. He does not approve of the view advanced by Traube, that the mental obscurity is the result of cerebral anæmia. The dyspnœa he attributes to the action of the carbonic acid on the sensory nerves, and he compares this to the forced breathing seen after section of the vagi, when the sensory nerves alone act as the respiratory stimulants. He states that he has never seen any deepening of the symptoms after the use of morphine or chloral.

In conclusion, he describes another case, that of a man, aged 39, who, after paralysis of the left side with loss of speech, suddenly became uræmic, with delirium and sopor, and paralyzed on the other side. During the unconsciousness, which deepened into coma, the characteristic Cheyne-Stokes respiration appeared, and with it changes in the pupils were observed. They became larger during the period of respiration, even after the application of atropine, and the author regards the dilatation, therefore, as purely due to the influence of the sympathetic nerve. Nothing noteworthy could be seen on ophthalmoscopic examination of the eyes. On section, the kidneys were found to be granular, the heart degenerated, the arteries atheromatous; there was also thrombosis of the cerebral vessels and patches of softening of the brain, but the pons and medulla were healthy.

Roth places two cases on record,[1]—one, that of a child, aged 7 months, suffering from meningitis, the other, that of a girl, with uræmia and eclampsia, in which the typical respiration was present.

Körber[2] describes the symptom as it occurred in a boy of 9 months, suffering from tubercular meningitis, and notes that during the pause a certain stiffness of the paralyzed limbs came on, while during the period of breathing they were quite flexible.

[1] *Deutsches Archiv für klinische Medicin*, x. Band, S. 310, 1872.

[2] *Ibid.*, x. Band, S. 600, 1872.

A paper by Filehne[1] deserves mention here, as in it he points out that after section of the vagi it is possible to cause apnœa, and carefully discriminates between true apnœa, or arrest of respiration from excessive oxidation of the blood, and arrest of respiration caused by other conditions.

Laycock[2] enters very fully into the phenomenon of "Brief Recurrent Apnœa," as he terms the Cheyne-Stokes respiration, in a very interesting lecture, but he cannot be regarded as adding anything of importance to the pathology of the condition. It is a singular, nay, even startling fact, that he makes no mention of Traube in his remarks, although in them he does full justice to most of those who had written on the subject in the vernacular. He refers to the case which has been already mentioned in connexion with his name.

The same writer immediately afterwards contributed another paper on this subject to medical literature[3] which is substantially the same as that to which reference has just been made.

Two or three months after the publication of Laycock's remarks, Bernheim,[4] who had the good fortune to be present at the historic clinique when Traube expounded his theory, gave an excellent review of much of the work that had been done on the Continent, along with an account of four cases which he had himself observed. These four cases were respectively—heart disease with emphysema; chronic alcoholism with nephritis; pulmonary tuberculosis and dilated heart; and the result of a fall from a great height. He points out that Cheyne-Stokes respiration is only the highest expression of a series of similar phenomena, in the less marked of which there is no pause, but alternations of deep and shallow breathing, and he gives the result of a careful study of the eye and pulse during the phases of the respiration. The pulse he describes as being sometimes altered, and at other times unchanged during the alternations of dyspnœa and apnœa. Like Leube he found that electricity would stop the pauses for a time.

[1] *Archiv für Anatomie, Physiologie, und wissenschaftlichen Medicin*, Jahrgang 1873, S. 361.

[2] *The Medical Times and Gazette*, vol. i. for 1873, p. 433.

[3] *The Dublin Journal of Medical Science*, vol. lvi. p. 1, 1873.

[4] *Gazette Hebdomadaire de Médecine et de Chirurgie*, Deuxième Série, tome x. p. 444 et p. 492, 1873.

Monti, in an exhaustive research into the physical examination of the thoracic viscera of children,[1] gives it as his opinion that Cheyne-Stokes respiration in children only occurs during the last stages of life, and that it is always to be attributed to disturbances of the centres of the nervous system.

Rohrer[2] describes a case of tubercular meningitis in which Cheyne-Stokes breathing was present, and explains it by means of Traube's theory.

Chvostek[3] records a case of mitral incompetence in which the phenomena of Cheyne-Stokes respiration were fully developed, and goes on to discuss and criticise the various symptoms present, as well as those mentioned by other writers, after which he states the theory of Traube. This paper is of extreme interest, as it gives one of the best critical studies of the various appearances which attend the type of respiration.

So far no one had ventured to oppose the theory of Traube, but in the following year it entered upon a period of storm and stress which has continued ever since. In that year Filehne[4] subjected the theory to a searching criticism, and insisted on such modifications of it that we are quite justified in saying that he propounded a rival theory. He states in his contribution that he has produced Cheyne-Stokes respiration by the administration of ether and chloroform to animals poisoned by means of large doses of morphine, and grants that, for the production of this symptom, there must be lowered irritability of the respiratory centre; he asserts that this, however, is not enough, and that the irritability of the respiratory centre must be less than that of the vaso-motor centre, which is the converse, according to him, of the normal relationship existing between these centres and the condition of the blood. He states, further, that the phenomenon may occur, although in a modified form, after both vagi have been cut; and he, therefore, is of opinion that it is not dependent on the integrity of these nerves, whence he concludes that a new theory is absolutely necessary. He points out that the centres remain at rest so long as they are supplied with a sufficient amount of blood

[1] *Oesterreichisches Jahrbuch für Pädiatrie*, neue Folge, ii. Band, S. 173, 1873.

[2] *Correspondenz-Blatt für schweizer Aerzte*, iii. Jahrgang, S. 225, 1873.

[3] *Wiener medizinische Wochenschrift*, xxiii. Jahrgang, S. 899 und 922, 1873.

[4] *Berliner klinische Wochenschrift*, xi. Jahrgang, S. 152 und 165, 1874.

containing an adequate quantity of oxygen; that they are excited whenever the blood-supply is insufficiently arterialized, or when, although sufficiently arterialized, the supply is deficient in quantity; and that the excitement is greatest when the blood-supply is too small and at the same time inadequately arterialized. He asserts that in health venous blood excites,—1st, the respiratory, 2nd, the vaso-motor, and 3rd, the convulsive centres. Picturing a case in which the phenomenon is present, he says that during the pause the blood gradually becomes more venous and develops the stimulus for the centres, but that, from the lessened irritability of the respiratory centre, no respiration is caused, and the pause therefore continues until the point is reached when the vaso-motor centre is brought into action. This produces a diminution of the blood-supply, which causes the respiratory centre to act and originate the superficial breathing which is first observed. It is some time, however, before the blood arterialized by these respirations can reach the vaso-motor centre, and the time is lengthened by the contraction of the arterioles caused by its activity; it takes time, moreover, before the vaso-motor apparatus can induce contraction of the arterioles, and time also before the contraction can pass away; there is therefore a lengthening of the pause and deepening of the dyspnœa. He states that when Cheyne-Stokes respiration is produced in animals by the administration of large doses of morphine, followed by the inhalation of ether or chloroform, there is always a gradual diminution of the pulse-rate during the pause, which sometimes goes the length of complete cessation of the pulsation; while during the period of respiration there is a gradual acceleration until the normal rate is regained towards the end of this phase. He states further, that in the animals thus experimented on, the blood-pressure rises during the pause and falls during the period of breathing. He mentions the case of a man dying from a lethal dose of morphine and chloroform, who showed during the narcosis Cheyne-Stokes respiration exactly in the same form as seen in his experimental investigations. The pulse underwent the same changes as he observed in the animals on which he performed his experiments. Finally, in his criticism of Traube's theory he asserts that the periodicity of the Cheyne-Stokes respiration could only depend upon a periodicity of action of the respiratory centre which has not been proved.

In the discussion which followed Filehne's paper, Ewald[1] stated that he had examined during breathing as well as pause the retina of a patient in whom the pulse underwent alterations, but had been unable to detect any distinct changes.

Traube[2] promptly came forward in defence of his theory. In his reply he points out that Filehne had arbitrarily postulated that the respiratory centre must have less irritability than the vaso-motor centre, and that this postulate had been based on the gratuitous assumptions,—1, that the vaso-motor system is always implicated; 2, that the vaso-motor is normally less irritable than the respiratory centre; and 3, that two centres are not proportionately affected by a proportional diminution of oxygenated blood. He states, with regard to the first of these points, that there is very often no change in the arterial tension during the different phases of the phenomenon; with reference to the second, that the vaso-motor is more irritable than the regulator, while this is more sensitive than the respiratory centre; and he curtly dismisses the third as absurd. He holds that a rhythmic periodicity of the respiratory centre has been proved as distinctly as in the case of the vaso-motor and inhibitory centres—all being dependent on the changing quantity of carbonic acid and consequent stimulation and exhaustion of the centres. Traube concludes his reply with a restatement of his theory, pointing out that all cases in which the phenomenon appears have lessened irritability of the respiratory centre, and therefore require more carbonic acid to excite respiration, which of necessity requires a longer interval of time. At first the necessary carbonic acid will be in the lungs, and the peripheral endings of the vagi are the earliest to be stimulated. This, however, causes no dyspnœa, only the superficial breathing, but when the carbonic acid has accumulated in sufficient quantity to excite the sensory nerves dyspnœa is produced. In consequence, however, of the diminution of the carbonic acid, as well as on account of the exhaustion of the respiratory centre by the powerful irritation, the breathing loses its dyspnœic character, and as the exhaustion of the centre gains ground more rapidly than the accumulation anew of carbonic acid, the breathing becomes more

[1] *Berliner klinische Wochenschrift*, xi. Jahrgang, S. 169, 1874.

[2] *Ibid.*, S. 185 und 209, 1874.

and more superficial, ending in another pause. It is to be observed that in this second enunciation of his theory Traube introduces the factor of exhaustion.

Filehne[1] again returned to the charge. In his answer to Traube he reasserts the action of the vaso-motor system as the basis of the Cheyne-Stokes phenomenon. He refers to his own experiments and to the observations of Heidenhain on chloralized dogs in support of his position, as well as the rise of arterial tension in patients before the commencement of respiration, and the dilatation of the pupil at the same stage, which, if not due to a dilator pupillæ muscle, must be caused by contraction of the vessels. In this connexion he asserts that the finger cannot be accepted as any criterion of the tension of the radial artery. He brings forward the state of the fontanelles in little children presenting this phenomenon as a proof of his theory, and states that he observed in one case a depression of the fontanelles before the commencement and during the early part of the period of breathing. The normal condition was regained towards the end of the respiratory period. This he holds to prove contraction of the vessels. In the case of a child when the Cheyne-Stokes respiration disappeared it could be brought back by the application of pressure upon the fontanelles. He mentions the case of a woman suffering from degeneration of the cord and medulla, in whom Cheyne-Stokes respiration was present; when nitrite of amyl was administered the phenomenon disappeared and remained absent as long as the inhalation was continued. He gives details of experiments in which the peculiar type of respiration was produced by interference with the supply of blood to the brain by alternate compression and relaxation of the carotids and vertebral arteries in the rabbit. He further mentions a rise of tension found in some persons before the act of inspiration which is not normal, and which he holds to prove that in them the vaso-motor is affected before the respiratory centre. The paper ends with a criticism of Traube's reply to his previous communication.

Heitler[2] begins an interesting study of this symptom, by pointing out that although far more common in unconsciousness it is not

[1] *Berliner klinische Wochenschrift*, xi. Jahrgang, S. 404 und 435, 1874.

[2] *Wiener medizinische Presse*, xv. Jahrgang, S. 649 und 672, 1874.

invariably associated with that condition. He states that he has seen Cheyne-Stokes respiration in chronic hydrocephalus; in typhoid fever; in pneumonia; in tubercular meningitis; and in tubercular laryngeal perichondritis where tracheotomy had to be resorted to. He calls attention to the fact, that although the fully developed symptom cannot be regarded as common, less pronounced forms of the same phenomenon are yet of frequent occurrence, and constitute a gradation between slight irregularity of the breathing and the Cheyne-Stokes respiration. A critical description of the breathing follows, in which the author mentions that he has not observed any very characteristic changes in the condition of the circulation except in the most pronounced cases where the pulse underwent slight modifications. He then states the later theory of Traube, and goes on to describe two of his cases, one being chronic hydrocephalus and the other tuberculosis.

In the course of a case of insolation from which perfect recovery took place, Zimmerhans[1] observed the phenomenon of Cheyne-Stokes breathing, for the explanation of which he accepts some medullary change as the cause.

Hœpffner[2] describes a case of cerebral disease in which Cheyne-Stokes respiration was one of the prominent symptoms. In this case electricity was applied along the course of the pneumogastric nerve without effecting any change in the respiratory symptoms.

An excellent summary of the discussion between Traube and Filehne appeared at this time from the pen of Ricklin,[3] in which, however, no new facts or views were brought forward.

In some observations on intermittent respiration in the insane, Zenker[4] narrates six cases in which he states that Cheyne-Stokes breathing was developed. Some of these cases do not give in their intermitting respiration the true features of Cheyne-Stokes breathing, but in three of them it appears to have been undoubtedly present. In none of the cases described was there any periodic

[1] *Wiener medizinische Presse*, xv. Jahrgang, S. 771, 1874.

[2] *Gazette médicale de Strasbourg*, xxxiii^e^ année, p. 101, 1874.

[3] *Gazette médicale de Paris*, xlv^e^ année, 4^e^ Serie, tome iii. pp. 519, 530, et 565, 1874.

[4] *Allgemeine Zeitschrift für Psychiatrie und psychischgerichtliche Medicin*, xxx. Band, S. 419, 1874.

variation in the state of the pupil or pulse. It is interesting to notice that in two of these cases the periodic breathing was associated with epilepsy, and Zenker points out in this connexion that it is due to the proximity of the respiratory and convulsive centres. In regard to the causation of the phenomenon, Zenker says that there can be no doubt it is due to a disturbance of the respiratory centre, for the explanation of which it is necessary to clear up several physiological and pathological questions.

Baas[1] describes the phenomenon under the name of "intermittent respiration," which he prefers to the designation by which it is commonly known. In his contribution he records the case of a female child, not quite eight weeks old, who suffered from diarrhœa and hydrocephalus; the patient, amongst other symptoms, such as coma with left-sided ptosis, and later, right-sided mydriasis, developed Cheyne-Stokes respiration, which continued for the last five hours of life until death took place. The author calls attention in this case to the early period of life at which the symptom occurred; shows that it was caused by acute hydrocephalus; that it was associated with unconsciousness; that in this, as in some other observations, the increase and decrease of the respiratory energy was less characteristic than the regular intervals of both phases of the breathing; and points to the probability that the condition was caused by one-sided pressure on the respiratory centre, as shown by the ptosis and dilatation of the left pupil in the early stage.

Benson, whose previous observations on this subject have been already referred to, brought the matter before the Medical Society of the Irish College of Physicians,[2] and in briefly detailing the facts of a recent case, took occasion to mention some of the theories which had been propounded, and to compare Traube's explanation with his own. He points out that in the case which he recorded, in which there was hemiplegia followed by cardiac failure, the peculiar type of respiration did not appear until the *cardiac* symptoms had added themselves to the *cerebral*, adding that in the previous case which he narrated the phenomenon only appeared after the *cerebral* symptoms had added themselves to the *cardiac*.

[1] *Deutsches Archiv für klinische Medicin*, xiv. Band., S. 609, 1874, and *Zur Percussion, Auscultation und Phonometrie*, S. 264, Stuttgart, 1877.

[2] *The Dublin Journal of Medical Science*, vol. lviii. p. 519, 1874.

Following Benson's remarks, Henry Kennedy mentioned[1] that he had been led to the conclusion that the symptom was more or less connected with the nervous system generally rather than with any particular organ connected with the chest, which view was confirmed by some common phenomena, such as the alteration of breathing in sleep, showing that the breathing may vary in health; the cerebral breathing of Graves in fever; or the changes of respiration in hydrocephalus. He thought there was evidence enough to prove that a temporarily modified state of the nervous system might be capable of altering and modifying the breathing. He mentioned an interesting fact that, in patients showing this type of respiration, the ascending and descending character disappeared when they were placed on their sides.

A case of diphtheria in a boy 2½ years old afforded v. Hüttenbrenner[2] the opportunity of studying Cheyne-Stokes breathing, which he attributes in this instance primarily to weakness of the heart from the diphtheritic poison. He refers to the Traube-Filehne controversy, but refrains from criticism.

Bull[3] has placed three cases on record in which the peculiar breathing in question was noticed. The patients in whom it appeared suffered from chronic renal disease, with sclerosed arteries, hypertrophied heart, and cerebral haemorrhage; granular kidney, arterial atheroma, cardiac hypertrophy, and pericarditis; and duodenal cancer, in which, after the use of morphine for the agony caused by the disease, Cheyne-Stokes breathing appeared. In a letter which the author has kindly addressed to me, he states that he is not satisfied with any of the present theories.

Hayden fully discusses the phenomenon in his work,[4] and gives the following explanation of it:—"I have already stated," he says, "that the only lesion of structure with which rhythmical irregularity of breathing has been always found associated is atheromatous or calcareous change, with dilatation of the arch of the aorta, involving loss of elasticity in its walls. I think these changes supply the conditions of a rational theory of the pheno-

[1] *The Dublin Journal of Medical Science*, vol. lviii. p. 521.

[2] *Jahrbuch für Kinderheilkunde und physische Erziehung*, neue Folge, viii. Jahrgang, S. 420, 1875.

[3] *Norsk Magazin for Lægevidenskaben*, iii. Raekke, v. Bind, S. 255, 1875.

[4] *The Diseases of the Heart and of the Aorta*, p. 632, Dublin, 1875.

menon. During the period of greatest tranquillity of the heart's action, viz., in sleep or repose, the systemic capillary circulation fails, from want of the contributory aid rendered in health by the elastic reaction of the aorta. Hence arises a suspension of tissue-respiration, *besoin de respirer*, and accelerated or suspirious breathing, as shown by the experiments of Flint already referred to. Accelerated respiration must strengthen capillary circulation; first, through the lungs, and then through the tissues of the body generally, by quickening the action of the heart and increasing its force. In proportion as the systemic capillary circulation becomes established, the *besoin de respirer* is less urgent, and respiration gradually subsides, till a period of apnœa arrives. The descent of respiration below the normal standard would seem to arise from its previous excessive activity and the exhaustion of the patient. Now, again, comes a period of feeble action of the heart, and failure of capillary circulation, with its consequence of paroxysmal breathing. That imperfect circulation of arterial blood in the respiratory centre contributes in a special manner, and in a great degree, to the production of the respiratory derangement I have no doubt; but the effect of this is not easily distinguished from that of a want of oxygen in the tissues of the body generally." Hayden also states that he has not observed marked alterations in the rate of the cardiac pulsations with the different phases of the phenomenon; only, "as in one or two cases, a slight acceleration during the period of dyspnœa, and a gradual decline in that of descent, till a minimum rate was reached on the accession of apnœa."

Hazard[1] records the case of a gouty lawyer, aged 54, who met with injuries in a railway accident at the age of 32; these caused paraplegia, from which there was only partial recovery. A blow on the head when 48 years of age impaired all his powers, and, in addition to some mental symptoms, there was after this date such evidence of a weak circulation as a frequent and irregular pulse, cyanosis, and dyspnœa. When seen he had weakness of both cardiac sounds without any symptom of valvular disease, and soon afterwards symmetrical gangrene of both feet set in, with absence of pulsation in any of the vessels of the lower extremities below

[1] *St Louis Clinical Record*, vol. ii. p. 54, 1875.

Scarpa's triangle. The patient had a great tendency to fall asleep, and when he dozed Cheyne-Stokes respiration appeared. He died from gradual extension of the gangrene upwards, and unfortunately no post-mortem examination was obtained. The author's diagnosis was fatty heart and thrombosis of the arteries of the lower extremities. He enters into a long physiological argument without reaching very definite conclusions with regard to the causation of the respiratory rhythm.

Claus[1] entered upon a criticism of Filehne's theory, based upon the observation of two cases under his care. The first part of his paper is historical, entering fully into the controversy between Traube and Filehne, and laying special stress on the statements made by the latter in regard to the oscillation of the blood-pressure seen when the vagi are intact, and absent when these have been divided. He then describes a case in which nitrite of amyl had no effect on the periodicity of the respiration, which he tries to explain away by supposing that in Filehne's case the abnormal irritability of the vaso-motor centre was less pronounced than in his own. He will not allow that there is any evidence in favour of the view that the cause of the phenomenon lies in any change of the quantity of blood supplied to the respiratory centre. From sphygmographic tracings, Claus concludes that there is an increase of blood-pressure at the end of the pause and beginning of the period of respiration, with a return to the normal pressure during the period of breathing and beginning of the pause, and that there is an increase of vascular contraction during the pause. He therefore supports Filehne's theory as to the cause of the phenomenon. In a postscript to the paper the author narrates a second case, in which one inhalation entirely removed the periodic character of the breathing, while a second administration only partially modified its type. These results, however, he considers as being in favour of the theory to which he appears to have been predisposed.

In an elderly patient, who died apparently from cardiac failure, de Wette[2] watched the phenomena of Cheyne-Stokes breathing for thirteen days, and after a brief description of the case, he refers to Traube's theory.

[1] *Allgemeine Zeitschrift für Psychiatrie und psychischgerichtliche Medicin*, xxxii. Band, S. 437, 1875.

[2] *Correspondenz-Blatt für schweizer Aerzte*, vi. Jahrgang, S. 140, 1876.

In a case of thoracic aneurism in an old man, described by de Cérenville,[1] Cheyne-Stokes respiration was present for some days. No mention is made of the state of the pulse in the varying phases of the breathing, but the pupils are said to have remained in a condition of excessive contraction. The author takes the opportunity of bringing forward an occurrence which seems to be unique —a case of intermittent respiration in a baby, one month old, caused by morphine taken by his mother. The mother had been suffering from neuralgia, for which she took a large dose of morphine, and next day the baby lost his appetite, became cyanotic, and fell into convulsions, attended by periodic breathing, during which the pupils varied in size, becoming larger with inspiration. The infant recovered under appropriate treatment. In a case of cardiac disease presenting Cheyne-Stokes respiration, de Cérenville found that morphine caused a diminution in the extent of the respiratory phenomenon, while neither digitalis nor bromide of potassium had any effect of the kind.

Ross[2] describes the occurrence of Cheyne-Stokes breathing after the hypodermic administration of half a grain of morphine to an intemperate person of 40, who was found in convulsions almost entirely confined to the left side, with pupils of natural size. After the use of the morphine the convulsions ceased and the pupils became contracted, while typical Cheyne-Stokes breathing made its appearance. The author notes that during the pause in the respiration the limbs became rigid, and relaxed again when the breathing began. This type of breathing made its appearance within four and a half hours of the time of the administration of the morphine, it remained for about six hours, and ceased five hours before death. The thoracic organs presented no abnormal symptom, and the urine was healthy. At the post-mortem examination the various organs of the body were found to be perfectly healthy.

Biot[3] carefully describes this type of breathing as it occurred in the case of a patient suffering from aortic and mitral disease, and for the first time publishes tracings of the pulse and respira-

[1] *Bulletin de la Société médicale de la Suisse romande*, dixième année, p. 152, 1876.

[2] *Canada Medical and Surgical Journal*, vol. v. p. 544, 1876.

[3] *Contribution à l'étude du phénomène respiratoire de Cheyne-Stokes.* Lyon, 1876.

tion. The pulse was relatively more frequent during the pause than during the breathing, and the tension fell during the former phase. He mentions several of the writings which preceded his work, and criticises the rival theories of Traube and Filehne. He especially refers to the lessened arterial pressure during the apnœa, shown by his tracings, as being antagonistic to the theory of Filehne, which requires stimulation of the vaso-motor centre, and consequent contraction of the arteries during that phase. He mentions that the pupil was contracted during the pause, and states that chloral produced considerable benefit to the patient. In summing up he points out that the theory of Filehne is not applicable to all cases, but he declines, for the present, to formulate another. As a postscript he mentions the pauses of the respiration in meningitis, which he describes as being entirely irregular and sighing in character. He will not admit that such cerebral breathing belongs to the type of Cheyne-Stokes respiration, although it is related to it.

Pepper[1] calls attention to the significance of Cheyne-Stokes respiration in cases of tubercular meningitis, and records two such instances in an interesting paper on the subject. In both the cases which he describes there were variations in the condition of the circulation coincident with the changes in the state of the respiration, the pulse becoming less frequent during the cessation of the respiratory movements. The author regards the phenomenon as being caused by "a paresis or state of impaired sensibility and activity of the nervous centres of respiration," in which they cease to respond to the small quantity of carbonic acid in the blood when it has been oxygenated by active respiratory movements. It is worthy of note that Pepper refers to Begbie's mention of the case of Philiscus, described by Hippocrates, alluded to in the early part of this monograph, and it is permissible to quote his words. "On reading the description of the case," he says, "which may probably have been one of acute nephritis, with uræmia, in the original and in Daremberg's translation, however, I cannot see that anything more is intended than the infrequent, deep breathing with long intervals, which is so often met with in states of partial or complete coma."

[1] *Philadelphia Medical Times*, vol. vi. p. 416, 1876.

Hein[1] begins an elaborate contribution to the subject by stating that all arrests of respiration are not to be regarded as instances of Cheyne-Stokes respiration. He says that such irregular interferences with the usual rhythm are common in infants and children. He mentions that he has observed six cases of true Cheyne-Stokes breathing—two in patients suffering from Bright's disease, one of whom had a fatty heart, and the other œdema glottidis and pneumonia; one in a patient who had induced fatty degeneration of the heart through alcoholism; and three in patients dying of tubercular meningitis. He gives full details of a seventh case. The patient on this last occasion was an old lady, who had suffered for a long time from bedsores with profuse suppuration, in consequence of being confined to bed after a severe bruise to her left hip, and in whose case Hein diagnosed fatty degeneration of the heart. During the course of the illness Cheyne-Stokes breathing made its appearance, and, as it remained for five weeks, the author of this paper was able to make careful observations in regard to its phenomena. He calls attention particularly to the condition of the consciousness. He noticed, when she was sitting up, that during the respiratory pause, which took place with the thorax in the position of expiration, the head sunk forward as if in sleep, while with the commencing respirations she raised it again like one awaking from slumber. During the pause the eyes were shut as in sleep; she could be roused from this condition by loud speaking, showed her tongue when asked to do so, swallowed a mouthful of water, and could even speak a word or two, but the senses were dull; with the first superficial respirations, however, the consciousness returned, she opened her eyes and spoke spontaneously, complaining particularly of her breathlessness. During the pause she could not be induced to breathe. At the end of the pause slight twitchings about the mouth were to be seen, but otherwise there were no involuntary muscular movements. No pupillary changes corresponding to the varying phases of the breathing could be determined, but this point was rendered difficult by the fact that there was a cataract in the left eye, while the lens and a piece of the iris had been removed from the right eye in a previous cataract operation.

[1] *Wiener medizinische Wochenschrift*, xxvii. Jahrgang, S. 317 und 341, 1877.

Hein points out that the fluctuations in the condition of the consciousness must be accounted for by the same causes as those which give rise to the respiratory phenomena, and asserts that this gives a new position from which to consider the condition of the medulla oblongata. He allows that changes in the state of the consciousness have previously been noted in this condition, but shows that no one has called attention to the simultaneous return of the consciousness and the respiration, and holds that this fact is of such importance that he can only reject every theory that does not account for the return of the cerebral and medullary functions at the same time. He points out that the relation between the irritability of the respiratory centre and the degree of respiratory stimulation must undergo a periodic change.

Criticising the rival theories of Traube and Filehne, he remarks, in regard to the latter, that he has observed in a child, aged seven months, a fall of the blood-pressure in the great fontanelle at the time of the return of the breathing, and states, on the authority of Mayer and Friedrich, that amyl nitrite directly stimulates the respiratory centre and may thus cause regular breathing. He shows that the theory of Traube cannot account for the simultaneous return of consciousness and respiration, while his own observation is in direct opposition to the hypothesis of Filehne, for it does not agree with his experience that in a patient suffering from cardiac weakness and its consequences, the dulness of the sensorium would be removed by means of a sudden contraction of the arteries and anæmia of the brain. Such an effect would sooner be produced by an arterial hyperæmia through paralysis of the vessels, but such an explanation is negatived by the fact that the fulness of the vessels of the face and neck remained equal during both phases. He points out further that the variations of the consciousness and respiration must have the same cause, and shows that in all his cases cyanosis was present, which, although arising from different conditions, has the same result. Just as is the case with the vitality in general, so in the medulla oblongata the irritability is lessened, and hence interruptions in the breathing are caused; it is open to question whether these breaks may not cause an influence on the circulation, so that what was a consequence may in other conditions be a cause. With a normal circulation such an effect he holds to be impossible, as Cheyne-Stokes respiration may be

imitated by the hour without any noticeable modification of the circulation. It is otherwise, however, when the blood-stream is retarded and oxygenation reduced, for if interruptions to the respiration take place, the functions are alternately increased and diminished, and such effects are shown in the medulla oblongata through variations in its irritability.

The blood which has been arterialized during the respiratory period reaches the capillaries in greatest part at the beginning of the pause, at which time the circulation which had been quickened by the breathing becomes slower, while the tissue change is most active. The result is that the irritability of the medulla is again increased and the breathing begins. By means of the passage, during the breathing period, of the blood which has become venous during the pause, the tissue-change for the vitality necessary to the functional activity of the organ cannot be supported, the oxygen in the tissues is consumed without adequate compensation, and the irritability of the respiratory centre is lessened and suspended. It is again restored after arterialized blood has coursed through the vessels of the medulla and promoted internal respiration, as occurs at the end of the pause. That the irritability shows a stage of increase and a stage of decrease is due to the fact that the alternation in the conditions of the circulation and diffusion is gradual, not sudden. From the analogous conditions of the brain and medulla it is to be concluded that the respiratory nerve centre does not simply undergo a change in the degree of stimulation, but a periodic alteration of its own condition.

Hein is of opinion that, although this theory of a periodic activity of the brain and medulla caused by variations in the amount of the tissue change is only hypothetical, it yet explains what he thinks cannot be otherwise accounted for. He holds that the frequent occurrence of the phenomenon in unconscious persons does not oppose his theory, for in such cases the periodic demand of tissue change may be so insignificant that, although it is in a position to affect the activity of the respiratory centre, it may not be able to influence the functions of the brain.

Carrer[1] describes the case of a man, aged 60, who died of renal disease and cardiac failure. Cheyne-Stokes respiration appeared

[1] *Gazeta medica Italiana*, Provincie Venete, tomo xx. p. 403, 1877.

after the patient had presented various head symptoms for some days, and remained long enough to allow the author to make a number of interesting observations. He mentions that during the period of breathing the pupils were dilated, while they were contracted in the pause. The pulse was less frequent during the former than during the latter phase; and sphygmographic tracings taken during these phases showed a difference in character, the pulsations being larger, but less regular, during the dyspnœa than during the apnœa. It is of interest to note that the author found the apnœa could be interrupted by powerful stimuli: the aspersion of cold water, for example, caused a deep breath followed by dyspnœa. The peculiar rhythm of the respiration remained until the death of the patient—twenty-five days after its first appearance. At the post-mortem examination it was found that the ventricles of the brain and subarachnoid spaces were distended with fluid; the pleural cavities contained each a litre of fluid; the heart was hypertrophied; the aorta dilated and atheromatous; and the kidneys contracted. There was, in addition, a perforating ulcer of the duodenum. Carrer, in conclusion, passes the opinions of other authors in review.

Broadbent[1] describes the occurrence of Cheyne-Stokes breathing in a case of apoplexy with right-sided hemiplegia. There was no alteration in the state of the pulse or heart during the varying phases of the symptom, but movements of the left leg were observed towards the end of the pause. He states that he has often watched it in uræmic coma, and on some occasions in sinking from exhaustion, as well as something very like it once in the case of an elderly gentleman in his usual health. He thinks that the effect of the phenomenon on the pulse varies, and remarks, "All the theories on the subject are unsatisfactory, and I have none of my own to offer."

Wharry[2] places on record four cases in which the symptom occurred. These were mitral disease with aortic dilatation, aortic and mitral disease, nephritis, and typhoid fever with pneumonia.

Andrew[3] describes the phenomenon as occurring in a case of typhoid fever, which ended in recovery.

[1] *The Lancet*, vol. i. for 1877, p. 307.
[2] *Ibid.*, p. 368.
[3] *Ibid.*, p. 385.

Treves[1] mentions the development of Cheyne-Stokes respiration after hæmorrhage followed by operation, and notes that drawing the tongue forward diminished the pauses. On section the heart was found to be healthy.

Frost gives some notes of a case of apoplexy[2] in which the symptom appeared, and where no variation could be perceived in the pulse during the different phases of the breathing.

One of the most valuable contributions to the subject is a study of respiratory pauses by François-Franck.[3] Having observed that the respiration which followed tracheotomy had a great resemblance to that with which we are concerned, and being inclined to explain this as the result of a free supply of oxygen, he investigated the conditions which influenced the phenomenon. He states that with a larger supply of oxygen the pause arrives sooner and lasts longer, while with a smaller supply the pause is later and shorter, and that the pause (or apnœa, in the sense of Filehne) can be stopped by compression of the carotids, which hinders the carriage of oxygen to the brain, just as in calm breathing compression of these vessels induces forced respiration. He attributes the pause following the suspension of artificial respiration in animals to excessive oxygenation. Mentioning the pause in respiration which is observed after the cessation of cardiac inhibition caused by stimulation of the peripheral portion of the vagus, he explains it as being due to excessive oxygenation of the blood lying in the lungs during the cardiac inactivity, which is thereafter supplied, on the recommencement of cardiac action, to the centres, as observed by Mayer. He describes experiments in which, after stimulation of the central portion of the vagus, there is complete arrest of respiration without any change in cardiac action. This pause, on the cessation of the stimulation, is succeeded by large and frequent respirations, which in turn are followed by a complete pause due to excessive oxygenation of the blood. He further calls attention to the pause which follows forced voluntary respirations in man—a pause accompanied by total absence of the *besoin de respirer*—as being caused in precisely the same manner. Turning now to the phe-

[1] *The Lancet*, vol. i. for 1877, p. 481.

[2] *Ibid.*, vol. ii. for 1877, p. 238.

[3] *Journal de l'anatomie et de la physiologie normales et pathologiques de l'homme et des animaux*, 1877, p. 545.

nomena of Cheyne-Stokes respiration, he mentions a case of uræmia in which this type of breathing occurred. He points out that the form of arrest in it differs completely from that of apnœa in the strict sense of that term, inasmuch as in Cheyne-Stokes respiration the pauses are gradual in their development and cessation, while in true apnœa they are abrupt. In connexion with this case he mentions some experiments performed by Cuffer, along with himself and Jolyet. They injected ammonium carbonate into the veins of dogs, in accordance with one of the theories of uræmia, and found that these injections were followed by arrests of respiration. These, however, were very similar to the stoppages in apnœa, and had little resemblance to the pauses of Cheyne-Stokes respiration. He also describes another example of Cheyne-Stokes respiration observed in a case of mitral disease with cerebral embolism, in which also the pauses had no resemblance to the arrests of respiration in apnœa. He mentions that in both the cases referred to there was an adynamic condition, and thinks that perhaps the suspension of the respiration may simply be due to the absence of voluntary participation in the acts performed.

Sacchi[1] describes a case of aneurism of the ascending and transverse aorta in which Cheyne-Stokes respiration made its appearance. The pause of apnœa could be broken by opening the closed eyelids or by speaking to the patient. Cold affusion and inhalation of amyl nitrite produced no effect, but the inhalation of oxygen prevented the return of the pauses for an hour and a half. The pupils contracted during the pause and dilated during the breathing, and when the apnœa was broken by means of speaking to or in any way rousing the patient, they also dilated. The pulse was very irregular, and sphygmographic curves showed no constant relation between the circulation and respiration. The sensorium was clouded during the existence of the symptom. The post-mortem examination showed that there was an aneurismal dilatation of the ascending portion and arch of the aorta with hypertrophy of the heart. Both vagi were found to be compressed by means of inflamed lymphatic glands below the origin of the recurrent laryngeal nerves, a point of interest, inasmuch as Traube states that for the occurrence of this phenomenon both vagi must be intact. The brain was anæmic, and there was some effusion.

[1] *Rivista clinica di Bologna*, Secondo Serie, tomo vii. p. 33, 1877.

The author will not give his adhesion either to the theory of Traube or to that of Filehne, and he holds that the result of the oxygen inhalations is enough to disprove the view that the apnœa is caused by too little carbonic acid in the blood.

Mosso[1] describes periodic breathing of the Cheyne-Stokes type as being a natural feature of the hibernation of the myoxus during winter, when the temperature did not exceed a certain limit. If the thermometer registers a heat of more than from 10°–16° C., however, the animal awakes from the hibernating condition Mosso further states that Cheyne-Stokes breathing is to be seen in the sleep of healthy men, and this paper contains several tracings of the respiratory movements taken in such conditions.

Ottilie[2] takes the opportunity, in describing a case of senile degeneration of the brain, in which this symptom occurred, of discussing the phenomena and causation of Cheyne-Stokes respiration. He holds that however varying the cases may be in which it appears, one condition is constant, an insufficient supply of arterial blood to the medulla.

He further calls attention to the fact, that if the pulmonary portions of the vagus are rendered incapable of performing their functions, the sensory nerves from the rest of the body can induce inspiration when the blood contains the amount of carbonic acid gas which, under normal circumstances, is only found in the blood of the pulmonary artery, and that this gives rise to long pauses.

Filatow[3] describes two cases of Cheyne-Stokes respiration from which recovery took place. One of these was a child, aged three months, who suffered from dyspepsia and inanition; the other was also a child, ten months old, labouring under whooping-cough accompanied by wasting.

The observations of Cuffer[4] throw some light on certain aspects of the subject. These have already been referred to in mentioning the work of François-Franck. After stating that

[1] *Archiv für Physiologie*, Jahrgang 1878, S. 441, 1878.

[2] *Transactions of the Wisconsin State Medical Society*, vol. xii. p. 66, 1878.

[3] *Centralzeitung für Kinderkrankheiten*, Band ii. S. 35, 1878.

[4] *Recherches cliniques et expérimentales sur les alterations du sang dans l'urémie et sur la pathogénie des accidents urémiques—De la respiration de Cheyne-Stokes dans l'urémie.* Paris, 1878.

the authors who have written on the subject of uræmia make no mention of the state of the blood corpuscles, or of the affinity for oxygen shown by the blood in cases of Bright's disease, he describes a series of experiments performed to discover what changes are undergone by the blood in that disease, and what rôle is played by such changes. He shows that injections of urea have no effect on the number of the blood corpuscles nor on the capacity of the blood for the absorption of oxygen, while injections of ammonium carbonate and of kreatin reduce the former and diminish the latter. Along with these effects the injection of these two substances causes the appearance of a respiratory rhythm similar to that of Cheyne-Stokes breathing. When the actions of these substances upon the blood are tested *in vitro* it is found that urea has no effect, but that carbonate of ammonium and kreatin destroy the blood corpuscles. In Bright's disease the same effects are produced—lessened number of corpuscles and diminished quantity of oxygen. Cuffer thinks it logical to conclude that in diseases accompanied by a diminution of urea there is generally a lessened number of blood corpuscles; that the retention of urea, its possible transformation into ammonium carbonate, along with the retention of other waste substances such as kreatin and kreatinin, form the point of departure in that alteration of the blood; and he regards these substances as causing the effects known under the term uræmia by their action on the blood. In Bright's disease the corpuscles are fewer as well as more resistent; they do not undergo changes under the influence of reagents—they are, in short, paralyzed, and their capacity for absorbing oxygen is extremely diminished. Turning to dyspnœa, the author shows that the reason of the frequent occurrence of this symptom in Bright's disease is the reduced number of corpuscles, and that the acceleration of the respiratory movements is in direct ratio to the diminution of the number of the corpuscles, in connexion with which he mentions that in leukæmia, chlorosis, and anæmia the same symptom depends on a similar cause. Carbonate of ammonium is much more active in the destruction of the blood corpuscles than kreatin, and it is worthy of note that the effects upon the respiration are much more profound after injections of the former than is the case with injections of the latter substance. In cases of Bright's disease the author notes a spasm

of the arterial system, which he holds to be a powerful factor in determining the accession of the exacerbations of the respiratory disturbance. Entering next upon the consideration of Cheyne-Stokes respiration as seen in uræmia, he deals, firstly, with this as a clinical symptom, and, secondly, with the experimental production of similar phenomena by means of injections of ammonium carbonate and kreatin. He states that cases of Cheyne-Stokes breathing fall into two classes, in one of which there is marked dyspnœa, and in the other little more than a cessation of respiration. These two classes he holds to correspond to the effects produced respectively by carbonate of ammonium and by kreatin.

He briefly narrates seven cases of renal disease in which Cheyne-Stokes breathing was present, and which may be shortly summarized as follows:—Mitral disease with consecutive disease of the kidneys, in which no cerebral symptoms were to be seen; mitral disease followed by renal affection; lead poisoning resulting in interstitial nephritis with cardiac hypertrophy, where dilatation of the pupils and muscular agitation accompanied the dyspnœa; chronic renal disease and cardiac hypertrophy; interstitial nephritis, in which the respiratory pauses were not complete, but were represented by periods of shallow breathing; chronic disease of the kidneys; mitral and renal disease; gout and chronic renal disease, in which Cheyne-Stokes breathing seemed to have persisted for years; and chronic inflammation of the kidneys, in which case the vascular spasm previously referred to was well marked.

Turning to the experimental aspect of the subject, he describes his work in Marey's laboratory, where he had the assistance of François-Franck. The first series of experiments was performed by injecting ammonium carbonate and kreatin into a vein, and the results may be briefly summed up. After injections of the former drug, the respirations assumed the character of Cheyne-Stokes breathing, with violent dyspnœa and muscular agitation, as well as dilatation of the pupils during apnœa. Injections of kreatin, on the other hand, simply produced Cheyne-Stokes respiration of a tranquil description. The employment of urea in similar experiments caused no respiratory symptoms.

The second series of experiments was intended to elucidate the cause of apnœa. After performing tracheotomy on animals, which manifested symptoms of agitation during the experiment, apnœa

appeared; and the author refers in this connexion to the same symptom as it occurs after opening the trachea in children. Apnœa was induced by keeping up artificial respiration in animals after tracheotomy; and Cuffer, by means of several ingenious experiments which cannot be described here, proved that this condition was due to superoxygenation of the blood.

He, therefore, regards the stage of apnœa in the type of respiration which we are considering as arising from excessive oxygenation of the blood, caused by dyspnœa; the recommencement of the breathing and subsequent dyspnœa as caused by the want of oxygenation due to the arrest of respiration; the superoxygenation of the blood and accompanying muscular fatigue determining in turn a new period of apnœa. He regards the phases as caused by the action of the blood on the medulla as well as by the influence of a reflex action having its point of departure in the lung, the lung being the special regulator of the quantity of oxygen needed, and having its essential stimulus in the condition of the blood which it contains. The author, in concluding this most admirable investigation, finally directs attention once more to the arterial spasm at the beginning of the respiratory period, already mentioned as characteristic of uræmia, and points out how it influences the condition of the breathing.

Further observations having been made by Biot, subsequent to the publication of his paper already reviewed, he embodied them in a work[1] of much value. After quoting the clinical descriptions, given by Cheyne and Stokes, he lays stress on the differences existing between such breathing as may be frequently seen in meningitis and that known as Cheyne-Stokes respiration, to emphasize which he quotes from, or refers to, the writings of many authors who have described the former. He analyzes the cases narrated by Bernheim, and asserts that the type of respiration in some of these was not that of Cheyne-Stokes breathing, which he would like to keep quite apart from all other varieties of respiratory rhythm. Passing from this subject he describes several cases, which may be briefly referred to.

1. Man, aged 74, with atheroma, aortic dilatation, cardiac hypertrophy and degeneration, and pleurisy. 2. Man, aged 57, with

[1] *Étude clinique et expérimentale sur la respiration de Cheyne-Stokes.* Paris, 1878.

atheroma, and aortic and mitral disease. Pulse less frequent in dyspnœa; pupil dilated during that phase. 3. (Reported by Lépine.) Man, aged 47, with saturnine renal disease, cardiac hypertrophy, and hemiplegia. Pupils contracted during apnœa. 4. (Reported by Clement.) Man, aged 70, with mitral disease and cardiac hypertrophy. Pupils contracted in pause. 5. Man, aged 74, with cardiac hypertrophy and fatty degeneration. Pupils contracted during apnœa, and muscular spasms in that phase. 6. (Reported by Frost, and already mentioned.[1]) Man, aged 63, suffering from apoplexy. 7. (Reported by Rocher.) Man, aged 46, with aortic stenosis and incompetence as well as hemiplegia. Pupils small during apnœa, but pulse less frequent instead of more so, as in most cases. 8. (Reported by Clement.) Man, aged 60, with cardiac failure, pulmonary apoplexy, anasarca, and hydrothorax. Pupils contracted during apnœa. 9. Man, aged 77, with mitral disease and cardiac hypertrophy. No pupillary changes.

The author proceeds afterwards to analyze the symptoms presented by these cases. Taking up the apnœa, he speaks of its duration and frequency, and, as regards its causes, shows that it may be produced physiologically by superoxygenation, and pathologically by want of reaction of nerve centres. Turning to the dyspnœa, he speaks of its duration and frequency; and attempting to account for its causation, he describes how he repeated Filehne's experiments on the blood supply of the brain without attaining similar results, which causes him to conclude that the theory of that observer cannot be supported, and that the views of Traube are correct. Taking up the state of the pulse, he finds the tension less and the rate greater during apnœa. With regard to the condition of the eyes, he usually observes contraction of the pupils and conjugate deviation of the globes during apnœa. As to the intellect, it is usually clouded during apnœa. Muscular spasms are often seen at the end of apnœa, due to vagus irritation. As a means of diagnosis, he holds the symptom to be a sign of a double affection —cerebral and cardiac. As regards prognosis, he considers it to be of very grave if not fatal significance. With reference to medicines, he points out the uselessness of all remedies tried, and lays stress on the hurtful influence of many drugs, such as

[1] *Vide antea*, p. 36.

hypnotics, narcotics, and substances reducing reflex action. In this connexion he narrates another case. 10. Woman, aged 53, with bronchitis and emphysema, along with tricuspid dilatation. Cheyne-Stokes breathing appeared, and after being present for some time disappeared. To relieve dyspnœa she had 7 mg. of hydrochlorate of morphine, which caused the reappearance of the Cheyne-Stokes breathing, followed by death. He shows, finally, by experiment that drugs which induce or increase this type of respiration do so by lessening the amplitude and frequency of the respiratory movements, and by developing a pause at the end of each expiration.

Filehne promptly replied[1] to the strictures of Biot, and pointed out that the latter had *not* repeated his experiments, which were performed by stopping the current through the vertebrals as well as the carotids, while Biot had only compressed the carotids, and therefore left the blood supply to the medulla almost untouched. He further observes that the clinical arguments advanced by Biot are not more convincing, for the fact that the frequency of the pulse is greater during the pause than during the period is not against the theory of the author. The nuclei of the pneumogastric nerves may be excited at the end of the pause at the same time as the vaso-motor centre; or, later than this, at the same time as the respiratory centre, so that the lessened frequency of the pulse may be found during the end of the pause or beginning of the ascending respirations. Filehne refers Biot to his own tracings, which he holds to be proof of this. He further expresses his opinion that the phenomena of the pupils may be explained in a similar way. He ends his paper by remarking that he is not called upon again to refute the theory of Traube which Biot wishes to resuscitate, and adds that in 1875 Traube addressed an oral communication to him, in which, recognising how well founded were his objections to that theory, he accepted his views.

Biot at once answered[2] the criticisms of Filehne by the publication of an additional note on the subject. He regrets that, from an error in the medium from which he obtained his knowledge of Filehne's observations, he had been led to make a mistake in his control experiments, and accepts Filehne's assertion that the pheno-

[1] *Revue mensuelle de médecine et de chirurgie*, deuxième année, p. 668, 1878.
[2] *Ibid.*, p. 935, 1878.

mena of Cheyne-Stokes may be produced by alternately allowing and preventing the afflux of blood to the brain. He again states the distinction between Cheyne-Stokes respiration and other, more or less irregular, modifications of respiration. He further reiterates his statement that the arterial tension is higher during the period of apnœa than during that of hyperpnœa, basing this upon tracings and the application of Marey's law. He brings forward an interesting fact, that when breathing is suspended the effect on the pulse-rate depends on the phase of respiration during which the stoppage takes place. When the breathing is stopped during the phase of inspiration, there is usually slowing of the heart's action; when, on the contrary, it ceases during expiration, there is always acceleration. He refers to his previous work, in which he states that the apnœa in Cheyne-Stokes respiration begins in the phase of expiration; and again mentions that during the pause the arterial tension falls, while the rate of pulsation rises. On the other hand, with the period of breathing the reverse occurs.

He further criticises the work of Cuffer, in which he regrets the absence of tracings, and expresses his opinion that Cuffer attributes the dyspnœa of uræmia to a cerebral anæmia caused by a vascular spasm—a theory which he regards as cousin to that of Filehne.

He concludes by maintaining his conclusions, that Cheyne-Stokes respiration has a double origin—cerebral and cardiac.

Mickle[1] has recorded three cases of insanity in which Cheyne-Stokes respiration made its appearance. The diseases with which the symptom was associated were in these three cases respectively, general atheromatous change with cardiac hypertrophy and chronic renal disease, pulmonary phthisis with dilated heart, and apoplexy with epilepsy. The author fully discusses the pathological conditions accompanied by the type of respiration in question, the state of the pulse during its phases, the duration of these phases, the disappearance of the symptom in some cases before death, and the arrest of the peculiar breathing by means of various stimuli.

Zimmerman[2] describes the case of a drunken tailor, aged 55, who was seen in an epileptic attack caused by excess. He had been healthy up to within a few years of this attack, but latterly he had suffered from breathlessness, and he had also been affected by

[1] *British Medical Journal*, vol. ii. for 1878, p. 308.

[2] *Canadian Journal of Medical Science*, vol. iv. p. 112, 1879.

phlegmonous inflammation of the leg. After the epileptic seizure he became œdematous, with a return of the inflammation of the leg and severe dyspnœa. The urine contained neither albumen nor tube-casts. About a month after being first seen the breathing assumed the Cheyne-Stokes character, and traces of albumen appeared in the urine, but without casts. The patient died in a comatose state, and it was found on post mortem examination that there was chronic renal disease with cardiac hypertrophy, arterial atheroma, and cerebral congestion. The author quotes Cuffer's cases and explanation, and refers to the work of Biot. He further states that since the paper was read he had met with Cheyne-Stokes respiration in an old man of 80, dying of chronic bronchitis and emphysema, and in a child 18 months old suffering from pneumonia of the right lung. In this last case the patient had many symptoms pointing to tubercular meningitis, but recovered, and the Cheyne-Stokes breathing in this instance was not continuously present, but appeared and disappeared irregularly.

Luciani[1] prefaces one of the most valuable contributions ever made to this subject by stating that he had, in the year 1873, commenced a series of experiments under the superintendence of Ludwig at Leipzig, but that on account of various circumstances he had not been able at the time to complete his investigations. This paper begins with a brief retrospect of the work done by previous observers, after which the author describes some of the results which he obtained by experiment. Finding, by means of operations on the heart of the frog, that its rhythmic contractions became periodic, the analogy between this phenomenon and the character of the rhythm of Cheyne-Stokes respiration led him to seek for their causes in a common condition. His experiments were conducted by fixing a rabbit in Czermak's apparatus; ligaturing the carotid arteries to control hæmorrhage during subsequent operations on the medulla; connecting the respiratory passage, by means of a canula, with a manometer, whose index recorded the respiratory movements on a revolving cylinder; exposing the medulla oblongata; and dividing it above the origin of the vagi. The respiratory movements after section of the medulla in this way fell into groups, but each group began with a deep

[1] *Lo Sperimentale.* Anno xxxiii. Tomo xliii. p. 341 e p. 449, 1879.

inspiration and expiration, followed by a series of diminishing respirations. Luciani states that if he had published these observations when they were conducted he would have deprived Filehne of some of the novelty of his work, but he would at the same time have been led to different conclusions. He was induced, however, by the hope of obtaining more precise information, to postpone the publication of these results.

He afterwards turned himself to the study of apnœa caused by excess of artificial respiration. The method employed was to fix the dog or rabbit; to inject laudanum into the veins of the dog, when such an animal was subjected to experiment, this proceeding not being resorted to in the case of the rabbit; to perform tracheotomy and insert a canula into the trachea for the purpose of supporting artificial respiration and recording respiration; to expose the vagi; to keep up artificial respiration until apnœa was present; to divide the vagi; and in some cases to join the canula to a reservoir of air leading by a tube to a Marey's tambour, by which means the result of gradual asphyxia could be recorded. He found that, after the production of apnœa by excessive artificial respiration, and without section of the vagi, the respiration did not at once begin as ordinary respiration, but in an ascending series; at the same stage, with previous section of the vagi, an ascending series of respirations was seen, but in this case the ascent was much more rapid; after profound narcosis had been caused and apnœa induced, it was succeeded by groups of ascending and descending respirations, separated by long pauses; after section of one vagus, the breathing became deeper but less frequent, and after section of the other also it became laboured and very infrequent; when the animal was allowed to breathe the air of the reservoir until death from asphyxia took place, it was found that section of the vagi caused but little effect, and the respiration became periodic when the animal was almost asphyxiated.

Turning to the clinical aspect of the subject, Luciani remarks that Cheyne-Stokes respiration may occur in diseases of the brain, and of the heart and great vessels, in the coma produced by different intoxications, during the agony of certain affections, and also in the sleep of healthy persons and the lethargy of hibernating animals. He refers to its appearance after the use of morphine in disease; after the administration of morphine followed

by ether or chloroform; after the injection of chloral, kreatin, and ammonium carbonate; after injury to the parts near the nœud vital; after the employment of artificial respiration, subsequent to the injection of opium into the veins, so as to cause apnœa; and during the last stage of asphyxia.

The respiratory phenomenon may appear in different forms. The movements may increase or decrease in amplitude without change in frequency, or there may be more of the descending than ascending phase—in fact, the latter may be absent. The number of respirations during a period may vary from two to thirty, but the larger numbers are only found in the Cheyne-Stokes breathing of disease. The length of the pauses is very variable, and there may be a similarity in the duration of the successive pauses or a total want of equality.

The author then enters upon a long and careful criticism of the theories of Traube, Filehne, and Hein,—into which it is, for obvious reasons, impossible to follow him,—after which he submits his own views on the subject.

He is of opinion that it is impossible to solve the problem of Cheyne-Stokes respiration while resting upon the principle now generally admitted or sustained, that the capacity and functional activity of a nervous organ has always a direct and immediate dependence on the stimulant and nutritive conditions extrinsic to itself. That the life of an organ is intimately bound up with the surrounding conditions and influences cannot be denied without stifling science in the old vitalism; but it does not follow from this that the organ does nothing in every case but to transform as much as it receives in a given time, both in the same measure and in the same rhythm with which it receives it. Drawing a clear line of distinction between reflex and automatic movements, Luciani points out that the determining cause of the former is extrinsic, while in the case of the latter it is intrinsic, and consists in oscillations of the internal nutritive movements, to which correspond as many oscillations of the excitability of the organ itself. He was led to this new conception of automatism by the discovery of the periodic grouping of the movements of the frog's heart, before referred to, for no one could doubt that when extrinsic conditions remained unchanged the cause of the alternate groups of pulsations and pauses in repose was intrinsic.

Luciani therefore regards the diverse forms of respiratory rhythm as extrinsic expressions corresponding to the oscillations of the nutritive changes taking place in the structure of the respiratory centre. If it be granted that the respiratory centre is automatic, it follows that the different forms of rhythm which constitute Cheyne-Stokes phenomenon may be regarded as effects of diverse kinds of automatic oscillations in the excitability of the centre itself.

In a study of the action of morphine on the respiration, Filehne[1] again discusses the respiratory and circulatory phenomena of Cheyne-Stokes breathing, and somewhat modifies his original statements. He says:—"To my former theory of periodic breathing would I now make the addition that for its appearance it is quite sufficient that the arteries of the medulla oblongata be stimulated simultaneously with the stimulation of the respiratory centre; a previous contraction will strengthen the phenomenon, and may occur in the most pronounced cases; it is, however, not indispensable, and perhaps not always present." He further says that the difference of opinion existing between his own and Biot's explanations of identical observations is a purely verbal misunderstanding; and he also replies to Hein by saying that the latter has concerned himself more with the *how* than the *why*.

To Rosenbach[2] we owe a new explanation of the symptom in question. After pointing out that the different phenomena accompanying Cheyne-Stokes respiration really constitute a complex of symptoms, he disputes Biot's statement that true Cheyne-Stokes respiration only occurs in cardiac diseases, and not in cerebral affections. He points out that the descending part of the phase of respiration is not so regular as the ascending, and agrees with most observers that the circulation is sometimes involved and at other times not. In some cases he mentions that there is a rise of the pressure and fall of the rate during the ascending respiration, while with the descending respiration the contrary takes place, and in other cases there is no increase of rate, only lessened frequency at the end of the pause. He shows that Filehne's observation on the sinking of the fontanelles of the child's head

[1] *Archiv für experimentelle Pathologie und Pharmakologie*, x. Band, S. 442, und xi. Band, S. 45, 1879.

[2] *Zeitschrift für klinische Medicin*, i. Band, S. 583, 1879.

before the beginning of the respiratory phase is not correct for all cases; the recession may occur after the phase has begun or during the height of the breathing, from which he concludes that the sinking may be caused by an acceleration of the blood-flow from the brain by means of the respiration. He recalls Leube's statement regarding stimulation of the phrenic nerves, and says that stimulation of the vagi, causing a change in the pulse rate, effects no change in the phenomena of Cheyne-Stokes respiration, showing that they are independent of the supply of arterialized blood to the brain. He lays stress on the contraction of the pupils during the pause and their dilatation during the period of breathing, as well as on the rolling of the eyeballs or conjugate deviation, and the general twitchings of the body occurring during the period of respiration. He further dwells on the changes in the sensorium, and on the influence of such drugs as morphine, chloral, and bromide of potassium, and recapitulates that there are changes in Cheyne-Stokes respiration connected with the cortical as well as with the basal centres, such as those of intellection, the muscular system, the vision, the circulation, and the respiration.

Passing by Traube's first explanation, he states his second, which, though not entirely tenable, has yet some good points. He points out that it does not explain the *ascending* character of the respiration. He then enunciates Filehne's earlier theory, based on periodic changes of blood-supply, caused by a higher degree of excitability of the vaso-motor centre, and without hesitation rejects it, inasmuch as in some cases the blood-pressure rises before the recommencement of breathing, and when this rise is present it attains its maximum at a point between the ascending and descending respirations. Filehne's later theory, that the stimulation of the respiratory centre and medullary vessels may occur simultaneously is also rejected. Rosenbach is of opinion that both phenomena are co-effects, and he is strengthened in his views by the fact that other phenomena, such as the mental, visual, and muscular, are bound up with the respiratory, not with the circulatory, symptoms. He emphasizes the differences between the circulatory and respiratory phenomena in this type of breathing, the great variability of the former and the monotonous similarity of the latter being noteworthy. He brings forward the fact, noted by Leube and confirmed by himself, that artificial respiration during

the pause (which prevents accumulation of carbonic acid in the blood) does not alter the next phase, as well as his own observation that stimulation of the vagi and slowing of the pulse during the descending period do not alter that phase, and holds that these facts prove that within wide limits the condition of the blood does not modify the type of respiration. He points out that the eye phenomena are not dependent on the state of the blood, as the widening of the pupils takes place along with the first inspiration, and therefore before any change can be effected in the state of the blood. In this connexion he refers to the work of Küssmaul, Rählmann and Witkowski, Sander, Plotke, and himself, on the relations of the eye and the central nervous system. He is therefore led to conclude that the beginning and ending of breathing in Cheyne-Stokes respiration are independent of the blood-pressure and the amount of gas in the blood, and that the changes of the pupils have no relation to the circulation or the blood, but to the excitability of centres not directly dependent on the condition of the blood. He points out that in health the vagus and vaso-motor centres are more excitable than the respiratory, but that in this phenomenon (with the highest pressure accompanying the deepest respirations) they are sunk to the level of the respiratory. He asserts that Filehne's theory postulates, in rhythmic contraction and dilatation of the arterial system, conditions without analogy in nature. He points out that at the end of the period of breathing there is no apnœa, for the pupils, eyeballs, and mental state speak of fatigue, not better arterialization, that amyl nitrite has often no influence or very little, and that the drug is believed by some to act on the respiratory centre itself. He refers to Hein's explanation of the observation that unconsciousness is present during the pause and consciousness during the period as incompatible with Filehne's theory.

Rosenbach seeks for an explanation of the phenomenon in the alternation of activity and repose characteristic of nature. In the respiration there is inspiration, expiration, and pause; in the circulation, systole, diastole, and pause; in the nervous system, waking and sleep; while in curarized animals there are periodic changes in the rate and tension of the circulation which are quite independent of the respiration. The origin of activity is in the *cell*, not the *blood*, and it is illogical to seek a cause of respiratory and other

phenomena in the blood. Periodicity of activity of all nervous apparatus, therefore, depends on immanent peculiarities of elementary structures, and the blood is not the direct stimulus for the cells, but has its power in giving the cells the possibility of regulating tissue change. When the blood is altered there is necessarily a modification in the absorption of oxygen and removal of tissue change products, and the mechanism will therefore be indirectly affected; the blood is thus only one link in the chain of apparatus needful for life.

The regular alternation of activity and repose characteristic of life is seen in the complex of pathological phenomena, of which periodic breathing is only one symptom, and Cheyne-Stokes respiration is therefore a condition in which the exhaustibility of the central apparatus, normally following its activity, is greatly increased. The respiratory centre has its irritability lowered, as the breathing is at first shallow, but the irritability progressively increases, for in spite of better aëration dyspnœa gradually develops. The irritability then diminishes and the descending phase begins. The supposition may be hazarded that the first descending respirations following the deepest have their origin in better arterialization of the blood, or in removal of waste products from the centre, and that the fall in irritability begins with the first normal breathing.

Rosenbach shortly summarizes his views in this way:—Through certain disturbances of nutrition, the brain suffers from lessened flow of blood or altered quality of blood, and the processes of tissue change are modified in the entire central organs, or in particular parts of it, especially in the medulla oblongata, and here again more particularly in the respiratory centre, so that the normal irritability of the parts is lowered more or less, and the normal periodic exhaustibility is increased even to complete paralysis.

Rosenbach mentions, as an appendix to his paper, a case in which a patient ill with tubercular meningitis suddenly ceased to breathe except once or twice per minute, the pulse continuing to beat. After artificial respiration had been employed the phenomena of Cheyne-Stokes breathing appeared.

Purjesz[1] describes a case which he met with in the University

[1] *Pester medicinisch-chirurgische Presse*, xv. Band, SS. 771, 787, u. 846, 1879.

clinique of Wagner in Buda-Pesth. The patient, a man aged 57, was suffering from emphysema, renal cirrhosis, cardiac hypertrophy, and general dropsy. During the last three days of his life typical Cheyne-Stokes breathing was present. No changes in the state of the pupils or alterations in the conditions of the brain cortex were to be seen. The author mentions another patient, in the same clinique, suffering from chronic renal cirrhosis, who had Cheyne-Stokes breathing. In this case an improvement in the patient's condition took place, and he left the hospital. Purjesz reviews at considerable length several of the theories which have been advanced to account for the phenomenon, but gives no opinion of his own.

Edes[1] has described five cases in which Cheyne-Stokes breathing made its appearance; and it is a most interesting point to find that four of these instances belonged to the same family—a father, aged 80; his wife, whose age is not stated; and two sons, aged respectively 50 and 45. The father was subject to attacks of unconsciousness, during which the pulse was completely lost and the periodic respiration appeared. The mother and the two sons were affected by chronic renal disease. The fifth case was that of an old woman with chronic renal disease, atheromatous arteries, and hypertrophy of the heart, in whom left hemiplegia occurred from plugging of the middle cerebral artery.

Kronecker and Marckwald,[2] by a series of experiments on the rabbit, have shown some results of interest in this connexion. The medulla was severed between the respiratory centre and the brain, in such a way that the respiration was not much altered, and the lower part was stimulated by single opening induction shocks. At the right time such shocks strengthened the inspiration and expiration, and when given during the interval between the acts they induced others quite normal in character. When the animal was brought into the condition of apnœa by means of artificial respiration, the most powerful induction shocks failed to cause any inspirations. When long pauses in the respiration with intervening periods of dyspnœa were produced by partial removal of the respiratory centre, every induction shock given during the

[1] *Boston Medical and Surgical Journal*, vol. ci. p. 734, 1879.

[2] *Archiv für Physiologie*, Jahrgang 1879, S. 592.

pauses was followed by an apparently normal respiration. When during a respiratory pause successive rhythmic induction shocks were given, phenomena were seen analogous to the changes in the ventricle of the frog's heart observed by Kronecker and Bowditch (Bowditch's stair).

From the pen of Rosenbach[1] came an excellent article on the subject, based upon the views to which full reference has been made. In this article he again advances his opinions that the phenomena are not chiefly dependent on changes in the circulation, that they are independent of any periodicity in the blood-supply to the brain, and that they are co-ordinated by and joint effects of one and the same cause occurring periodically in the central organs, this cause being a periodic exhaustion of the centres. The whole brain may be affected, when the entire complex of symptoms, to be termed Cheyne-Stokes phenomenon, is produced; or only limited tracts may be implicated, giving simply Cheyne-Stokes breathing. He points out that, just as the respiratory centre alone may be deranged, so the vaso-motor or vagus centre may be disturbed, as in tubercular meningitis, and cause changes in the tension or rate of the pulse. Rosenbach compares the periodic exhaustion with the normal pauses for rest shown by all rhythmically acting systems. The different phases resemble natural phenomena, but with longer intervals; the period of breathing, for example, is to be compared with a respiration, and the period of apnœa with the short pause following expiration. The vagus and vaso-motor centres show similar variations. The exhaustion of the brain induces sleep, during which the pupils behave as in ordinary slumber.

The centres are not only more easily exhausted, requiring longer rest, but their irritability is reduced, and dyspnœa comes on in spite of better arterialization of the blood (which involves reduction of stimulus). The meaning of this is that the centre is becoming more irritable although the stimulus is lessening. After a time the normal irritability is regained, which is accompanied by gentler breathing until the pause occurs.

The author holds that this theory differs from all previous explanations in being based, not on periodic variations in the

[1] *Real-Encyclopädie der gesammten Heilkunde*, Herausgegeben von Dr Albert Eulenberg, iii. Band, S. 150. Wien und Leipzig, 1880.

amount of stimuli, but on periodic changes in the irritability of the centre.

Caizergues[1] describes the case of a man, aged 64, suffering from mitral disease, in the course of which he laboured for some days under severe dyspnœa, which was replaced afterwards by Cheyne-Stokes respiration. During the pause the intelligence became very cloudy, but the patient could be awakened by a loud noise; the eyelids drooped and the pupils contracted in this phase. When awakened by a loud noise the regular periodicity of the breathing was for a time arrested. During the period of breathing the eyes were opened, and the face bore a look of anxiety. The pulse, of which tracings are given, was more frequent during the pause than during the breathing, and during this latter phase it was extremely irregular.

After death it was found that there was mitral incompetence with extensive arterial atheroma, more especially of the cerebral vessels, with congestion of the kidneys and other internal organs.

Bull[2] describes an interesting case in which the patient, belonging to a neurotic family, and herself the victim of many nervous symptoms, was seized, when 20 years old, with a hysterical affection of the breathing. This consisted in spasms of the thoracic muscles in the position of deep inspiration and deep expiration alternately, the former lasting as long as forty seconds, and the latter to thirty-five seconds. This condition cannot be compared with Cheyne-Stokes breathing, as the only point of resemblance lies in the pauses.

Blaise and Brousse,[3] in a joint communication on this subject, give a brief historical review of previous opinions as to the cause of the phenomenon, and then pass on to the description of a case in which it occurred. The patient in this case was a man, aged 88, suffering from bronchial and pulmonary inflammation associated with pleurisy, and accompanied by renal disease, as shown by albuminuria and uræmia. The authors watched the type of breathing under consideration for ten days; it invariably ceased during sleep, and it disappeared finally two days before death.

[1] *Gazette hebdomadaire des Sciences médicales de Montpellier*, tome ii. p. 337, 1880.

[2] *Norsk Magazin for Lægevidenskaben*, 3 Raekke, v. Bind, S. 165, 1880.

[3] *Montpellier médical*, tome xliv. p. 287, 1880.

During the pauses the eyes closed, and the pupils became small and reactionless; two or three seconds before the return of the breathing the pupils dilated, and sometimes executed a series of oscillations during the dyspnœa; during the period of breathing they were sensible to light. There was considerable agitation at the height of the dyspnœa, at which time consciousness was unimpaired, and there were no convulsions. By speaking to the patient during the period of breathing this phase could be prolonged considerably. Sphygmographic tracings showed during the pause a fall of tension and an increase in rate; during the respiratory period the reverse occurred along with irregularity of the pulse. There was never a rise of tension at the end of the pause, but, on the contrary, sometimes a fall.

After an excellent description of this case, accompanied by admirable tracings, the authors give a brief notice of another case, under the care of Caizergues, which appears to be that previously referred to.

They then proceed to analyze the symptoms attending this phenomenon with great care, and subsequently criticise the views of previous observers, to which they, in the early part of their paper, had called attention. This brings them to consider the view of their teacher Grasset, which they fully expound. According to him, the dyspnœa is the primordial fact, the apnœa being merely a consequence of it; and the type of breathing is a symptom of excitement. The anæmia of the medulla, far from lowering, increases the irritability of that organ. In anæmia of the nerve-centres such phenomena of excitement as convulsions are common. The diminution of the blood-current and consequent lessening of the nutrition reduce the vitality of the nerve-cells. This increases the irritability, but at the same time tends to produce weakness and liability to exhaustion of the nerve centres. In short, it leads to what the authors call, "that peculiar condition which the English have so happily termed irritable weakness." This gives the key to the causation of Cheyne-Stokes breathing: bulbar anæmia produces greater irritability of the centres which it contains; their usual excitant, carbonic acid, acts upon them with unaccustomed intensity; the breathing assumes the character of dyspnœa, which will be more marked if excitement of the vaso-motor centre causes constriction of the arterioles, thus increasing

the bulbar anæmia. As the centres are easily fatigued, however, their excitement progressively diminishes, until it passes away entirely, whence the pause. After a time, the nervous elements repair their forces, and the cycle recommences.

Franz,[1] in the course of a paper on artificial respiration, takes occasion to refer to the observation of Leube, pressed by Rosenbach in opposition to Filehne's theory, that during the pause stimulation of the phrenic nerves has no influence on the respiration. He expresses his opinion that periodic breathing is not induced by a periodicity in the respiratory centre apart from the degree of arterialization of the blood, but that the origin of the periodic event is a certain degree of venosity of the blood. He states that in animals under the influence of morphine showing periodic breathing, faradization of the phrenic nerves, when the trachea is open, causes respiration, which he holds to show how little ground Rosenbach has for citing Leube's and his own observations in opposition to the theory of Filehne.

Marckwald and Kronecker,[2] as the result of further observations on the respiratory movements, state that they have fully confirmed Traube's observations, that the occurrence of Cheyne-Stokes respiration is connected with the integrity of the vagi, for after cutting these nerves in the neck the phenomenon never appeared, and if present before section, it disappeared; in fact, with division of the vagi, all regulation of the respiration was lost.

Hein[3] asserts that neither the theory of Traube nor that of Filehne can account for what he had previously described, *i.e.*, variations in the state of consciousness, and he believes that there must be the same cause for the cerebral and bulbar phenomena. He therefore again states his theory. He quite agrees with Biot that cerebral breathing is not the same thing as Cheyne-Stokes respiration. In the former there is periodic breathing of atypical form, often with long pauses, sometimes ascending and descending in character, and having no constant relation between the eye and breath symptoms; but if the eye signs are present, the pupils are wide during the breathing and narrow in the pause. It occurs in many diseases, and the prognosis is not always unfavourable.

[1] *Archiv für Physiologie*, Jahrgang 1880, S. 398.

[2] *Ibid.*, S. 441.

[3] *Deutsches Archiv für klinische Medicin.*, xxvii. Band, S. 569, 1880.

Periodic breathing of the Cheyne-Stokes type he holds to be, as a rule, associated with a state of unconsciousness. Sometimes consciousness returns during the period of breathing, but is absent in the pause, and if this is the case, the consciousness and the breathing reappear simultaneously. If pupillary variations are to be seen, the pupils are of middle size during respiration, become narrower during the descending phase, and are small and insensitive during the pause, gradually widening with the ascending respirations. If the vaso-motor nerves are affected, there is higher arterial tension during the respiratory period. This may pass from regular Cheyne-Stokes respiration into the atypical form at times. The type of the respiration may be due to periodic variations in activity of the respiratory centre alone or associated with similar variations of other centres.

Löwit,[1] from a careful study of tracings obtained by means of the polygraph in a case of Cheyne-Stokes respiration, forms the opinion that this symptom is not to be regarded as identical with the periodic breathing produced experimentally by Filehne. He holds that Cheyne-Stokes breathing does not depend upon variations in the condition of the circulation, but upon fluctuations in the activity of the nervous mechanism of the breathing, such as changes in the irritability of the respiratory centre from exhaustion and recovery. The irritability of the respiratory centre alters under conditions not yet perfectly known, but no doubt belonging to the processes of tissue change. He regards this as the cause of the symptom.

Winternitz,[2] writing of Cheyne-Stokes respiration in children, describes a case in which the patient, who was a highly hysterical girl, was thrown into a state of great nervous irritability after a painful operation on the teeth, and in this condition developed the type of breathing in question. It was present during a period of thirty-six hours, and then disappeared. Another case described is that of a little boy suffering from catarrh of the nose and throat, with vomiting and diarrhœa, in whom the Cheyne-Stokes breathing was present for twelve hours, until the patient improved. During the pauses the pupils were contracted. He is of opinion that in such a case the determination of blood to the intestines,

[1] *Prager medicinische Wochenschrift*, v. Band, SS. 461, 473, 481, u. 499, 1880.
[2] *Archiv für Kinderheilkunde*, i. Band, S. 142, 1880.

acting on a delicate and nervous organism, caused anæmia of the medulla, and thus induced the Cheyne-Stokes breathing. He suggests mechanical compression of the abdomen in similar cases, but says he omitted it in his own.

Solokow and Luchsinger, in giving the results of a careful series of experiments, contribute some interesting observations[1] to this subject. They state that when frogs, which have been immersed for some hours in water, begin to recover from their stupor, they show the Cheyne-Stokes phenomenon; that when frogs in winter are exposed to the action of heat, and the aorta is clamped, the same phenomenon occurs on the removal of the clamp and on its being again replaced; that the periodic respiration is also seen on clamping the aorta, after cutting the cord in the neck and destroying the spinal cord below that point, showing that it is quite independent of conditions of blood-pressure; that its occurrence is not affected by any changes of pressure, or by the substitution of saline solutions in place of blood; and that the vagi are not necessary for its appearance. They state that the conditions of periodicity are no other than such as are developed in every tissue, with growing asphyxia. Describing the administration of picrotoxin hypodermically during ether narcosis, they mention that the Cheyne-Stokes respiration and convulsions occurred synchronously, and that on the administration of more ether the convulsions ceased while the periodic breathing went on. They compare the phenomenon with the periodicity of lymph hearts as seen by themselves; with the periodicity of blood hearts described by Luciani; with the periodicity of the heart observed by Rosenbach when a supply of defibrinated blood has been allowed to circulate too long and has lost its colour; and with the occurrence of the contractions of exhausted Medusæ in groups. They conclude that the observations of comparative physiology as well as the results of experimental analysis agree in showing the conditions of this grouping of movements. Increase of stimulus and decrease of elasticity show themselves to be the important factors. It may without hesitation be supposed that the cause of the periodicity is to be sought in the lessened elasticity and greater exhaustibility of the organ, and this view is supported by direct observation.

[1] *Archiv für die gesammte Physiologie des Menschen und der Thiere*, xxiii. Band, S. 283, 1880.

In answer to Filehne's question,[1] why the exhaustion does not follow each respiration, instead of showing itself after a series of respirations, they reply that the irritability of a nervous organ will rise when after repose it is awakened to activity by stimuli, but it will sink if the activity has lasted too long. They refer to the observations of Kronecker and Marckwald, already mentioned, as being entirely analogous to the phenomena of Cheyne-Stokes respiration.

O'Neill[2] lays stress on the fact that the respiratory pause may be present without any ascending and descending phenomena, but is not prepared to say that arrests of this kind should be classed as Cheyne-Stokes respiration. He mentions the case of a lady suffering from chronic bronchitis and emphysema, with dilatation and hypertrophy of the heart, in whom arrests of respiration appeared, after an exacerbation of her pulmonary troubles, accompanied by general anasarca. The arrests of breathing disappeared when the chest improved and the dropsy passed away. He describes a case in which there was difficulty of articulation and deglutition along with Cheyne-Stokes breathing, and he supposes there was an affection of the medulla as well as of other nervous centres. In this case the pauses appeared after the use of chloral. O'Neill states that in two cases nitrite of amyl produced no effect, but that another patient suffering from renal disease, accompanied by Cheyne-Stokes respiration, felt much relief from this drug, which on several occasions "restored and reinvigorated the breathing when it was about to cease."

Lereboullet gives an excellent summary of the various views held by several writers on the phenomena of Cheyne-Stokes respiration.[3] He is evidently of opinion that Filehne's investigations have tended to show that the primary cause of the symptom is an affection of the vaso-motor centre, while the respiratory centre is only concerned in its production in a secondary manner. Lereboullet adds no original observations of his own to the subject with which he deals.

Rosenbach[4] gives another critical study of the phenomena of

[1] *Ueber des Cheyne-Stokes'sche Athmungsphänomen*, S. 17. Erlangen, 1874.

[2] *Lancet*, vol. ii. for 1880, p. 691.

[3] *Dictionnaire encyclopédique des sciences médicales*, Première série, tome xxv., p. 322. Paris, 1880.

[4] *Deutsche medicinische Wochenschrift*, vii. Jahrgang, SS. 27, u. 39, 1881.

Cheyne-Stokes respiration, in which he asserts that to this type of breathing are to be referred all forms of respiration in which the respiration is intermittent, or there is any periodic change in the depth of the inspirations. He therefore includes the effects of morphine in the group of periodic changes of respiration, and points out that as this drug lowers all the vital centres there are usually changes in the functions linked with the respiration. He then refers to the various symptoms associated with Cheyne-Stokes respiration, and holds that any valid theory must account for all of them. He goes on to state that the common characteristic of these phenomena is an alternation of activity and repose, which belongs to all nervous processes, and which is present in this case with longer periods of repose. In addition, he points out how far reaching is the analogy between the phenomena of Cheyne-Stokes respiration and the normal physiological processes. He ends his contribution by stating the differences between the theory of Traube and that which he proposed as follows:—1. His own theory is wider, and is concerned with symptoms unknown or insufficiently appreciated before; 2. It takes little account of fatigue, and looks to the excitability and non-excitability of centres; and 3. It holds the different phenomena to be independent of the changes of the circulation.

A somewhat warm discussion took place between Filehne[1] and Rosenbach[2] in regard to their respective theories, in which no new facts or views were advanced on either side. The only points of interest in Filehne's two articles are contained in his allegation that Rosenbach's theory is not a new one, but merely a modification of Traube's exhaustion hypothesis, and in his statement that its author has only supported it by purely speculative reasoning—a statement full of unconscious irony against its maker. Rosenbach's reply to these strictures is a strong refutation of the charges brought against his views, in which he has unfortunately followed the polemical style of his critic.

Saloz[3] devotes his inaugural dissertation to the subject of Cheyne-Stokes respiration, and embodies in its pages a large

[1] *Zeitschrift für klinische Medicin*, ii. Band, SS. 255 u. 472, 1881.

[2] *Ibid.*, S. 713.

[3] *Contribution à l'Étude clinique et expérimentale du Phénomène Respiratoire de Cheyne-Stokes.* Genève, 1881.

number of interesting facts, clinical and experimental. After defining this type of respiratory rhythm, and distinguishing it from such respiratory phenomena as are common in meningitis, he proceeds to analyze its symptoms, taking up, in the first place, the phenomena shown by the respiration, and, in the next place, those connected with the circulatory, psychical, visual, and motor apparatus. He lays stress on the variability of the circulatory phenomena; on the necessity that any theory explaining the origin of Cheyne-Stokes respiration must give a reason for the changes in the mental state frequently accompanying it; on the support which the oculo-pupillary symptoms give to Rosenbach's theory; and on the inconstancy of the muscular phenomena.

He states that the appearance of Cheyne-Stokes breathing is frequently preceded, and its disappearance followed, by a form of respiratory rhythm which may be termed "intermediate," as it forms a transition from the normal rhythm to that of Cheyne-Stokes breathing, and calls attention to the fact that sleep is very favourable to the development of the symptom. Casting a glance at the views of Cuffer and his division of the type into two classes, he proceeds to review several of the theories advanced to account for it, particularly those of Traube, Filehne, Luchsinger and Solokow, and Cuffer. In the course of this criticism he enunciates the following proposition:—That the pathological physiology of Cheyne-Stokes respiration must be based on the three conditions,—(1), Diminution of the excitability of the respiratory centre; (2), Rapid exhaustion of this excitability by excessive action; and, (3), Gradually increasing recovery of this excitability, even amounting to transitory exaggeration. In reviewing Cuffer's work he observes that in the renal cases which he has seen presenting this symptom there have been,—(1), Alterations of the arterial system, embracing the vessels at the base of the brain, leading to defective irrigation of the medulla; (2), Consecutive cardiac lesions augmenting the circulatory troubles; and, (3), An abnormal state of the blood, which presented a great tendency to coagulate and cause thrombosis.

After some brief remarks on diagnosis, prognosis, and treatment, the author goes on to describe his experiments. These, briefly stated, were as follows:—

1. Pressure on the medulla, which caused phenomena somewhat resembling those of Cheyne-Stokes respiration.

2. Compression of the arteries supplying the brain, which produced effects distantly resembling Cheyne-Stokes breathing, but not presenting a regular ascending and descending type, or corresponding in time to the intermittent compression.

3. Injection of morphine, with or without subsequent administration of chloroform, giving results closely resembling Cheyne-Stokes breathing.

4. Injection of carbonate of ammonium and kreatin, with or without previous nephrotomy, producing respiratory pauses and spasms in no way comparable to Cheyne-Stokes breathing.

5. Various operations on frogs, leading to many phenomena like those of Cheyne-Stokes breathing.

This leads to the description of ten cases personally observed by the author, and of another communicated to him by Dr Mermod. Summarized as shortly as possible, these cases were as follows:—(1), Chronic renal disease in a man, aged 60; (2), Hæmophylia in a boy, aged 3½; (3), Chronic renal disease in a man, aged 48; (4), Chronic renal disease in a woman, aged 84; (5), Chronic renal disease in a man, aged 77; (6), Chronic renal disease in a woman, aged 41; (7), Atheroma and chronic renal disease in a man, aged 70; (8), Chronic renal disease in a man, aged 74; (9), Atheroma with thrombosis of the carotid artery and cerebral embolism in a man, aged 65; (10), Chronic renal disease in a man, aged 50; and (11), Mitral and aortic disease, with consecutive renal affection, in a man, aged 70. Some of these cases presented the fully developed phenomena of Cheyne-Stokes breathing with its associated symptoms; others were simply accompanied by the respiratory changes alone.

The author concludes this excellent dissertation by drawing up the following conclusions:—

1. The fundamental condition causing the phenomenon is diminished excitability of the respiratory centre.

2. This diminished excitability is most commonly the consequence of some obstacle to the supply of blood to the medulla, such as some change in the vascular walls, some cardiac affection, or some compression of the medulla.

3. This diminished excitability may also be caused by hæmorrhages and poisons.

4. The apnœa is not produced by excess of oxygen, but by exhaustion of the respiratory centre.

5. The peculiar characters of the hyperpnœa are caused by the gradually increasing recovery of the centre and by progressive diminution of its excitability.

6. The role attributed to spasm of the vessels in the causation of the symptom does not appear to rest on sufficiently certain facts.

7. The frequency with which the symptom is associated with chronic renal disease depends less on the kidney affection than on the vascular degeneration with which it is associated. The urinary troubles only play a secondary part, by producing cardiac or pulmonary affections, and by altering the state of the blood. The development of the phenomenon in these cases does not seem to have a direct relation to an intoxication by extractive matters or ammonium carbonate.

8. Occurring in very diverse conditions Cheyne-Stokes breathing has no precise diagnostic value.

9. The intermittent appearance of the phenomenon and its complete disappearance prove that it does not depend on a profound alteration in the structure of the respiratory centre.

10. Although most commonly the precursor of a speedy fatal issue, the symptom may be compatible with survival for a long period.

11. Without extolling narcotics it may be stated that in cases of Cheyne-Stokes respiration they may render good service, and that their dangers have been considerably exaggerated.

Langer[1] describes a case of tumour of the pons in a young woman, where Cheyne-Stokes respiration was present in its typical development.

In an investigation into the periodic breathing of frogs, Langendorff and Siebert[2] note that after the blood-supply to the medulla has been cut off, frogs show a periodic rhythm of respiration, and that the result is the same, whether the blood-supply is cut off by tying the aorta or bleeding the animal, while substitution of a physiological solution of common salt for the blood sometimes allows the ordinary type of respiration to continue, but often modifies it in various ways. Stimulation of the skin during the pauses between the periods of breathing causes the appearance of

[1] *Medizinische Jahrbücher der k. k. Gesellschaft der Aerzte in Wien*, S. 515, 1881.

[2] *Archiv für Physiologie*, Jahrgang 1881, S. 241.

a group of respirations. They regard periodic respiration as conditioned by disturbance of irritability induced by modifications of nutrition. The ascending character they attribute to the gradual disappearance of exhaustion—the descending phase is not so often seen.

Langendorff[1] has further observed periodic respiration in frogs after the administration of muscarine, which he regards as acting directly on the respiratory centre, causing a true disturbance of its nutrition. In the same paper he describes periodic respiration caused by digitalin, which he attributes to the influence of the drug on the heart, as the respiratory phenomena only appear when the heart is brought nearly into the condition of arrest.

Sansom[2] is of opinion "that the respiratory nerve centre is *directly* influenced—that it suffers a paralytic lesion, and so its irritability is impaired," but adds that "it may be doubted whether, in some cases, the symptom may not be initiated by disease of the heart-muscle itself."

Davy[3] describes the case of a man, aged 70, subject to attacks of cardiac asthma, who at times presented characteristic breathing of this type.

Langer[4] commences an excellent contribution to the study of this subject by defining the symptom and describing the phenomena with which it is so often associated, after which he refers to modifications in its type, and states that his observations lead him to agree with Rosenbach that true Cheyne-Stokes respiration may occur in cerebral cases. He afterwards analyses the various phenomena, especially dwelling on those connected with the state of the consciousness, the muscular condition, the changes in the eyes, and the circulatory modifications. All of these he holds to be explicable by one of two possibilities—either that the excitability of the centres increases and diminishes, or that the stimuli vary while the excitability remains constant. This leads him to mention the rival theories of Filehne and Rosenbach.

He then narrates the case of a mason, aged 29, suffering from

[1] *Archiv für Physiologie*, Jahrgang 1881, S. 331.

[2] *Manual of the Physical Diagnosis of Diseases of the Heart.* Third edition, p. 38. London, 1881.

[3] *Cincinnati Lancet and Clinic.* New series. Vol. viii. p. 492, 1882.

[4] *Wiener medizinische Presse*, xxiii. Jahrgang, S. 1253 u. 1289, 1882.

chronic Bright's disease. In this case Cheyne-Stokes breathing was developed with changes in the condition of the consciousness and in the movements of the eyeballs, but without any alteration in the pupils corresponding to the two phases of the breathing. After this had continued for twenty-four hours, periodic changes in the condition of the circulation showed themselves, the tension of the pulse rising, and its rate sinking with the ascending phase of the respiration, and the converse taking place during the descending phase and the subsequent pause. After these conditions had existed for two days a change ensued, and on account of an alteration in the relation of the pulse and respiration, it often happened that the highest tension and lowest rate of the former coincided with a pause of the latter.

The author regards this observation as giving support to the theory of Rosenbach, to which, as well as to the work of Solokow and Luchsinger, and Hein, he refers in concluding his paper.

De Witt[1] records a case in which the patient, an elderly man, fell down and probably struck the back of his head. He became unconscious, and developed long pauses in the breathing. It is open to question whether this case may be regarded as having any close connexion with the subject under discussion.

Paterson[2] narrates the case of a middle-aged gentleman, suffering from Bright's disease, who presented the symptoms of Cheyne-Stokes respiration, which he is inclined to attribute to cardiac hypertrophy and pulmonary œdema, acting injuriously on the medulla oblongata.

Knoll,[3] in a contribution to the study of irregular and periodic breathing, distinguishes between spontaneous alterations in the state of the respiratory centre and changes which are produced reflexly. He holds the latter class to be very much more extensive than the former, traces out the mode of origin in both, and gives examples of each. Amongst periodic breathing the author dwells on that of the "meningitic type" of Biot, which he holds to be dependent on a sinking of the irritability of the respiratory centre rather than on a stimulus caused by the blood, leaving it in doubt, however, whether other factors may not also be concerned in its production.

[1] *Cincinnati Lancet and Clinic*. New series. Vol. ix. p. 200, 1882.

[2] *Lancet*, vol. i. for 1883, p. 121.

[3] *Lotos*, neue Folge, iii. u. iv. Band, S. 109, 1883.

He also devotes some remarks to Cheyne-Stokes phenomenon, mentioning the various methods by means of which appearances more or less like it may be produced, and concluding that he would not be justified in regarding the symptom as a reflex phenomenon of deeply depressed irritability of the respiratory centre, in opposition to any theory of blood stimulus.

Fano,[1] in the course of some investigations on the red blood corpuscles, observed that after removing the heart from a tortoise the breathing persisted, not indeed with its previous regularity, but in a periodic manner, the respirations being grouped together and the different groups separated by long pauses. This observation, which he repeated more than once with different forms of tortoise, and which he compares with the results of Solokow and Luchsinger, led him to consider the origin of Cheyne-Stokes respiration. Such experiments he holds to have entirely overthrown the theory of Filehne, already refuted by Luciani. Fano proceeds to detail the methods which he adopted in his investigations, and afterwards criticises the theories of Filehne, Traube, Solokow and Luchsinger, Langendorff and Siebert, and Luciani.

This is followed by a description of his experiments with carbonic oxide and carbonic acid gases. He found that tortoises were able to live and breathe for many hours when in an atmosphere solely composed of either of these gases; and he concludes this fact to be enough to show that there may be some doubt as to the production of respiratory movements by the state of the blood. Other experiments, performed with oxygen, hydrogen, and carbonic acid, confirmed his conclusions; but at the same time, as he remarks, made some of the nervous functions involved even more mysterious and difficult of explanation.

The occurrence of Cheyne-Stokes breathing in a case of apoplexy of the cerebellum, due to degeneration of the cerebellar arteries, has been placed on record by Hurd.[2] In this case marked congestion of the whole medulla oblongata was found at the examination after death.

In an exhaustive article on variola, Zuelzer[3] says of that disease that the respiration in the early stages is usually hard and laboured,

[1] *Lo Sperimentale*, tomo li. p. 561, 1883.

[2] *Boston Medical and Surgical Journal*, vol. cix. p. 195, 1883.

[3] *Real-Encyclopädie der gesammten Heilkunde*, xiv. Band, S. 393. Wien und Leipzig, 1883.

and not infrequently shows at a later stage the irregularity of the Cheyne-Stokes respiration phenomenon, which continues more or less regularly and distinctly, until towards the end in fatal cases pneumonia or pleurisy appears.

Puddicombe[1] records a case of apoplexy occurring in a man, aged 64, who towards the end of the disease, in the last days of his life, developed Cheyne-Stokes respiration. This characteristic form of breathing only appeared during sleep. The pauses could be interrupted by strong stimuli, but as soon as these ceased the patient again fell into the condition of apnœa. Drugs which increased the tendency to sleep made the patient worse instead of better. The effect of nitrite of amyl is worthy of note. "Nitrite of amyl," says the author, "on being held to his nostrils, stopped the symptoms temporarily, but only by causing him to wake up, which he invariably did after it had been held to his nose for seven or eight seconds."

Dunin[2] describes three cases in which Cheyne-Stokes respiration was present, two being in cerebral hæmorrhage, and the third in enteric fever. He is of opinion that in the last-mentioned case, at any rate, the cause of the symptom was exhaustion of the nerve centres in the medulla.

Murri,[3] after some historical remarks, considers the nature of the phenomenon and the type of breathing to be designated by the term Cheyne-Stokes respiration, which leads him to mention the investigations which he had previously carried out. He holds that there is in this condition a regular increase and decrease of the activity of the respiratory centre caused by a mechanism as yet unknown. This definition is followed by a reference to some of the views advanced by previous observers, particularly Traube, Filehne, Luciani, Luchsinger and Solokow, Rosenbach, Löwitt, Langer, Saloz, and Fano, and this is in turn succeeded by a description of some of the more important work done by them, and a thorough criticism of their theories.

Murri then turns to the influence of stimulants, and finds that variations in the amount of carbonic acid in the blood, as well as

[1] *The Lancet*, vol. i. for 1883, p. 816.

[2] *Gazeta lekarska*, Rzad 2, tom iii. S. 945, 1883.

[3] *Rivista clinica di Bologna*, serie terza, tomo iii. p. 737, 1883; and *Archives italiennes de Biologie*, tome v. p. 143, 1884.

sensory stimuli, the effects of coughing, or of changes in the brain circulation from pressure on the neck, together with the result of moral impressions and the exercise of the will, can modify the periodic breathing. He thinks that the respiratory centre has several zones of different degrees of excitability corresponding to different groups of muscles. In health the most sensitive zone responds promptly to stimuli, and is therefore sufficient for the function of respiration. If impaired, however, it needs stronger stimuli, and these rouse the other zones, causing dyspnœa, by means of which more oxygen is supplied to the blood, and there is a more rapid current in the medulla, leading to a slowing of respiration which ends in the pause, during which there is again an accumulation of carbonic acid and a repetition of the cycle. The decreasing or descending respirations are due to the continuance of activity after the interruption of the stimuli; the dyspnœa is caused by the delay in the aeration of the medulla. It must be admitted, as postulated by Traube, that the irritability of the respiratory centre is impaired in order to have the necessary conditions for the development of Cheyne-Stokes respiration, but it is unnecessary that the pneumogastric nerves should be intact.

Tizzoni[1] describes the lesions which he observed in two cases under the care of Murri in which Cheyne-Stokes breathing was a prominent symptom. In one of these, where the primary disease was a cardiac lesion, there was chronic neuritis of the trunk of the vagus, with sclerosis and atrophy of the gray matter of the medulla. In the other case, where death was caused by renal disease and uremia, the vagi were healthy, but there were inflammatory changes in the internal or median nucleus of the vagus as well as in the posterior nucleus common to the vagus and spinal accessory nerves.

Bramwell,[2] in his admirable and exhaustive work on cardiac diseases, devotes considerable attention to Cheyne-Stokes respiration as one of the symptoms of circulatory affections. After describing its appearances and significance, he refers to the conditions which may lead to its development, and gives a brief sketch of the views of Traube, Sansom, and Filehne. This brings

[1] *Memorie dell' Accademia delle Scienze di Bologna*, serie quarta, tomo v. p. 331, 1883; and *Archives italiennes de Biologie*, tome v. p. 226, 1884.

[2] *Diseases of the Heart and Thoracic Aorta*, p. 68. Edinburgh, 1884.

him to state the opinion which he has been led to form, and as his explanation of the phenomenon is given with equal lucidity and brevity, it will be satisfactory to quote his own words.

"The respiratory centre in the medulla oblongata probably consists of two parts—one connected with inspiration (the inspiratory centre), the other with expiration (the expiratory centre). Now, according to Rosenthal (quoted by Dr M. Foster), the inspiratory centre is the seat of two conflicting forces,—one tending to generate inspiratory impulses (the discharging portion of the inspiratory centre, as we may call it), and the other offering resistance to the generation of these impulses (the restraining or inhibiting portion of the inspiratory centre), the one and the other alternately gaining the victory, and thus leading to a rhythmical discharge.

"Further, we may probably with truth suppose that the two parts of the inspiratory centre are differently acted upon by the same stimulus; venous blood, for instance, which excites the action of the discharging portion, depresses the action of the restraining portion, *vice versâ* arterial blood depresses the action of the discharging portion, but strengthens the action of the restraining part.

"Now, if we suppose that the discharging portion is in a condition of irritable weakness, in which it is more easily excited to discharge, but in which it tends to become more speedily and more completely exhausted than in health—(or, better still perhaps, that both portions of the centre are in this abnormal condition, *i.e.*, a state of irritable weakness), we have, I conceive, a condition of things which will satisfactorily explain the phenomena.

"Let us suppose, as it is simpler, a case in which the discharging portion is in a condition of irritable weakness, the restraining portion remaining normal. Starting, as we did in considering Filehne's theory, with the end of the period of apnœa, *i.e.*, with the blood in a highly venous condition, we may suppose:—

"(1.) That the venous blood gradually excites a paroxysm of dyspnœa:—*Firstly* and chiefly by acting directly upon the inspiratory centre itself, depressing the action of the restraining portion, and arousing the action of the discharging portion, which has, during the stage of rest or apnœa, been gradually recovering from the condition of exhaustion occasioned by the excessive discharge, which produced the preceding paroxysm of dyspnœa. *Secondly*, by stimulating the action of the vaso-motor centre, in consequence

of which the arterioles are contracted, and the supply of oxygen to the respiratory centre is still further diminished.

"(2.) That in consequence of the *excessive irritability* of the discharging portion of the inspiratory centre, the discharges become excessive, and a condition of dyspnœa is produced.

"(3.) That in consequence of the *weakness* of the discharging portion of the inspiratory centre it speedily becomes exhausted—over-exhausted; and the dyspnœa tends to subside.

"(4.) That in consequence of the excessive respiratory efforts during the paroxysm of dyspnœa, the blood (which was previously venous) becomes arterialized; stimulation of the discharging portion of the inspiratory centre ceases; stimulation of the restraining portion is produced; and in consequence of the deficient stimulation and over-exhaustion of the discharging portion, the restraining portion has full swing, and the condition of apnœa is produced.

"The arterialized blood acts *firstly* and chiefly upon the inspiratory centre itself, strengthening the action of the restraining portion and depressing the action (removing the stimulation) of the discharging portion; *secondly*, by removing the stimulation of the vaso-motor centre, in consequence of which the arterioles dilate, and the supply of oxygen (arterial blood) to the respiratory centre is still further increased.

"During the stage of apnœa the discharging portion, which was exhausted by excessive action during the period of dyspnœa, gradually regains its irritability, and the condition required for its stimulation, and for the removal of the control of the restraining portion, viz., a venous condition of the blood, is, in consequence of the absence of the respiratory movements, gradually developed.

"By this theory we can, I think, satisfactorily explain:—

"(*a.*) The occurrence not only of diminished respiratory movements after the period of dyspnœa, but the complete arrest of respiration which occurs during the stage of apnœa—a point which it is difficult to explain by the other theories.

"(*b.*) The remarkable fact that the respiratory centre is at one moment violently discharging, and at the next in a state of absolute quiescence.

"(*c.*) That the dyspnœa and apnœa follow one another with rhythmical regularity; and that the one condition gradually passes into the other, and *vice versâ*."

Fano,[1] in reply to the criticism of Murri, defends the views which he previously advanced, and in turn criticises the theory proposed by the latter.

O'Connell[2] mentions the occurrence of Cheyne-Stokes respiration in the case of a male infant who died in one of the respiratory pauses twelve hours after birth. No post-mortem examination was allowed, and the cause of the symptom therefore remained unknown.

Fano[3] describes the respiration of the alligator as not being naturally periodic, but as assuming this character when the surrounding atmosphere is cold. By spraying the animal with ether, for example, it was easy to render the respiration, which was regularly rhythmic previous to the use of cold, periodic in character.

Fabian[4] gives an excellent critical survey of Cheyne-Stokes respiration in regard to the various theories advanced to explain its origin; he gives the theory of Murri credit as being the most satisfactory hitherto proposed, and gives a very good summary of the views of that writer.

Piaggio[5] devotes his graduation thesis to this subject. Beginning with some introductory observations, followed by a brief historical retrospect, he gives a clinical study of the phenomenon and its associated symptoms, passes in review the normal physiology of the respiration, and concludes that it is not the degree of arterialization nor the arterial tension, nor the rapidity of the blood current, nor the action of the heart and lungs, but the cell itself that regulates the amount of oxygen consumed by the organism. He supposes that there are two respiratory centres, one of which presides over the respiration of the tissues, and controls the respiratory centre as usually understood. Passing on to consider the pathological physiology, Piaggio grants for the appearance of Cheyne-Stokes breathing a diminished excitability of these centres, and ex-

[1] *Lo Sperimentale*, anno xxxviii., tomo liii. p. 132, 1884.

[2] *British Medical Journal*, vol. i. for 1884, p. 220.

[3] *Lo Sperimentale*, anno xxxviii., tomo liii. p. 233, 1884.

[4] *O zjawisku oddechowém Heyne-Stokesa. Matlakovski Ksiega pamietkowa Hoyerowi*, S. 277, 1884.

[5] *Sur une nouvelle Théorie du Phénomène Respiratoire de Cheyne-Stokes.* Paris, 1884.

presses his opinion that the various circulatory changes which accompany the symptom are of a compensatory nature. He does not allow that the forced breathing is true dyspnœa, and compares it with analogous symptoms seen in hysteria and other nervous affections. After criticising some of the most recent work done immediately before the appearance of his thesis, he sums up his views, stating that there is in Cheyne-Stokes respiration a constant force whose intensity is invariable and subnormal, and whose source is in the condition of the tissue, not in the state of the blood; that the tissue centre of respiration controls its subordinate, the automatic centre of respiration, and that this latter may be affected indirectly through disturbance of its superior centre or by means of influences acting directly upon itself.

In an investigation into the action of sulphuretted hydrogen on the respiration, Smirnow[1] found that when the air breathed contained from one-eighth to one-seventh per cent. of this substance, "a classical Cheyne-Stokes breathing," as he calls it, appeared, accompanied by variations in the diameter of the pupils, the sensibility of the conjunctiva, and the rate of the pulse. The condition was present as long as the animal breathed the mixture, and disappeared when ordinary air was allowed to replace it. The author mentions that on the periodicity and ascending and descending character of the respiratory movements section of the vagi and of both laryngeal nerves had no effect. He states that the blood-pressure fell during the cessation of respiration and rose when it recommenced, while the pulse became less frequent during the pause. On dividing the vagi the change in frequency did not appear, but the falling of blood-pressure remained. Smirnow was able, therefore, to produce almost all the features of the Cheyne-Stokes respiration phenomenon, and from his study of it he is of opinion that the periodicity of the breathing is only conditioned by weakness of the respiratory centre. He thinks that the appearances presented by the circulation, pupils, and other organs depend upon a synchronous affection of the other corresponding nerve centres, which is not connected with the type of the respiration.

[1] *Centralblatt für die medicinischen Wissenschaften*, xxii. Jahrgang, S. 641, 1884.

Kaufmann[1] contributes a paper on some artificially produced phenomena in Cheyne-Stokes breathing, which he observed in the case of a man, aged 54, suffering from general tuberculosis, where it was developed after the use of chloral and morphine. The periodic breathing was accompanied by changes in the size of the pupils, in the movements of the eyeballs, and in the state of the intellect, but not, so far as could be made out by means of the finger, by any changes in the state of the circulation. Kaufmann found that during the pause of the breathing, respiration could be excited by the application of cold, by striking the surface of the body, by tickling the sole of the foot, and by speaking loudly to the patient, and he gives tracings of the respiration showing these effects. These results were usually accompanied by opening of the eyelids and widening of the pupils. He is of opinion that such effects could not be produced if there were a total absence of irritability of the respiratory centre or a condition of true apnœa, and he also thinks theories based upon a conception of exhaustion of the centre require the additional hypothesis that the increase of irritability induced by external stimuli is so great as to prevent the exhaustion from giving expression to itself. He comes to the conclusion that much observation and experiment is required before we can arrive at a satisfactory solution of the phenomenon.

Cantieri[2] records a case of cardiac disease in a man aged 59, who presented the symptom of Cheyne-Stokes respiration during the course of the affection. After death it was found that there was great hypertrophy of the heart with pericarditis, myocarditis, and endocarditis—the latter especially affecting the left side and particularly the mitral valve—associated with atheroma of the aorta.

Bordoni[3] describes two cases presenting Cheyne-Stokes respiration, one being that recorded by Cantieri, which has just been referred to, and the other patient being a man aged 76, who died under the care of a colleague in consequence of pneumonia and cardiac degeneration. In the former case the pulse increased in

[1] *Prager medicinische Wochenschrift*, ix. Jahrgang, S. 344 u. 354, 1884.

[2] *Bolletino della Società tra i Cultori delle Scienze mediche in Siena*, anno ii. p. 250, 1884.

[3] *Ibid.*, anno ii. p. 253, 1884.

rate and tension during the pause; the pupil contracted during that phase, and dilated during the period of breathing. In the latter case the rate and tension were greater during the period of breathing than during the pause, and there were no periodic changes in the size of the pupils. Bordoni mentions several of the writers who have concerned themselves with Cheyne-Stokes breathing, but restricts himself to facts, and abstains from making any theoretical remarks.

Oser[1] describes the occurrence of this form of respiration in a woman aged 74, suffering from aortic and mitral disease. The symptom occurred during an attack of intestinal catarrh, and again a few days before death; and it is noteworthy that it could at any time be produced when it was not present by compression of the two common carotid arteries. At the post-mortem examination, besides the cardiac lesions, nothing but the usual senile changes could be found, along with some discoloration of the medulla oblongata and upper part of the spinal cord.

Howard,[2] in a paper on some of the varieties of dyspnœa met with in kidney disease, after referring to the appearance of Cheyne-Stokes respiration in one of his puerperal cases, suffering from uræmic eclampsia, briefly describes its occurrence in a man, 52 years old, who was the subject of chronic renal disease. The chief interest of the case lies in the fact that the periodic breathing had persisted for two months before the author saw him in consultation with another medical man, and that there was no appearance of imminent danger when he was seen. Howard mentions another opportunity which he had of observing Cheyne-Stokes breathing in an aged man sinking apparently from senile decay. He is now inclined to think that failure of the renal functions may have been the immediate occasion of the symptom, and suggests that this is probably the underlying cause of the symptom in many cases. The author makes passing reference to the work of Cuffer, but shrinks from entering into any discussion of the numerous explanations that have been advanced.

Mosso, in an exhaustive monograph,[3] has materially contributed

[1] *Wiener medizinische Blätter*, vii. Band, S. 1480, 1884.

[2] *Canada Medical and Surgical Journal*, vol. xiii. p. 193, 1884.

[3] *Atti della Reale Accademia dei Lincei*, anno cclxxxii., 1884-86, serie quarta, p. 457, 1885; and *Archives italiennes de Biologie*, tome vii. p. 48, 1886.

to the knowledge we possess of this symptom. He begins by pointing out that the movements of respiration are not always uniform and regular. In the profound repose and more especially the deep sleep of man and animals, the respirations are grouped in periods, and this periodic breathing is quite physiological. When this periodic respiration becomes more intense, pauses appear from the remission or cessation of inspiration, and the author terms such breathing remittent when there is a slight respiratory movement during a pause, and intermittent when there is complete cessation for a time. He mentions breaks in breathing, as if a respiration had aborted or failed, but points out that there is no connexion between such a break and the succeeding respirations. Intermittent respiration may be caused by injections of chloral, and this cannot be modified by making the animal breathe pure oxygen through the tracheal canula, or by artificial respiration from electric stimuli to the respiratory nerves, from which the author concludes that the intermittences cannot be altered by the influence of oxygen. He states that there are periods of tonicity of the respiratory muscles independently of the rhythmic movements of breathing, and that the circulatory vessels take no part in the phenomena of periodic breathing, which disposes of the complicated and imaginary theories of Traube, Filehne, and others. Oscillations in the tonicity of the respiratory muscles are closely united with the phenomena of periodic breathing. In general, when this tonicity is lessened there is a tendency on the part of the respiratory centre to lessen the force of the movements of respiration, and a pause often ensues. It has been thought that the greater or less activity of the respiratory centre represents a greater or less need of provision by pulmonary ventilation for the chemical wants of the organism; but the author is of opinion that he is not far from the truth in thinking that the respiratory movements modify themselves according to the states of sleeping or waking, of greater or less activity of the nervous system. He holds that the mechanical and chemical parts of respiration are distinct, that the mechanical is more representative of the vitality of the nerve centres than of the chemical wants of the organism; that if the nervous excitability increases more air is inspired than is needed for chemical wants, while on the contrary during sleep the mechanical may lessen or become periodic without disturbance of

the chemical function of tissue respiration; and further, that when the excitability of the centres is much lowered, it can be determined that the accumulation of carbonic acid by asphyxia causes almost no effect on the respiratory movements.

Mosso agrees with Fano in hesitating to accept the hypothesis of Luciani, but does not see how Fano's hypothesis can explain remittent respiration, for, if it were true, periodic breathing would always appear in animals whose nervous excitability gently died away, which it does not. He points out that the ascending part of the breathing is not due to arterialization of the blood, for it appears just as before after the diaphragm has been cut, so as to render the respiration useless. The periods of breathing appear during sleep without any consciousness. The pauses have no effect on the vaso-motor centre if they are not very long. If any influence is shown, it is opposite in effect to that of psychic phenomena; during the intermittences there is a diminution in the tonicity of the bloodvessels, while under the influence of psychic activity there is an increase. Referring, again, to the hypothesis of Filehne, he says it is a mere supposition, and adds that his results are contrary to his hypothesis. He has observed the fact described by Murri, that during the pause there is an increase in the bulk of the arm as tested by the plethysphygmograph, and is of opinion that it is caused by dilatation of vessels during profound slumber.

Although periodic respiration is not in direct or immediate relation with vascular phenomena, alterations in the circulation of the nervous centres may cause periodic respiration; in chloralized animals it appears on raising the head, and disappears when the head is again lowered.

Mosso points out the intimate relations of periodic breathing with sleep, as shown by the variations of the iris and the intelligence. In discussing the phenomena of consciousness he points out that there is no distinction in kind, simply a variation in degree. He refers to a case under the care of his colleague, Bozzolo, where all the reflexes, even those of swallowing, were abolished during the pause. He does not believe that all cases are due to conditions resembling sleep; he has seen it, for instance, under the influence of curara, where the arrest of the respiratory movements caused by the motor paralysis produced sufficient

excitement of the nervous activity to overcome the influence of the curara on the nerves.

Davies[1] gives an explanation by Foster of a case in which it was noted "that the heart and respiration alternated in rhythm, the heart being in full swing at the pause of the respiration, and being inhibited during the height of the respiratory period." This circumstance is explained by Foster as follows:—"Apparently coincident with changes in the medulla oblongata leading to Cheyne-Stokes respiration was a stimulation of the cardio-inhibitory centre in the medulla, occurring alternately with the former."

Fazio[2] has described Cheyne-Stokes respiration as a symptom occurring in the course of two cases of cholera.

Langendorff[3] points out that a change from regular to periodic rhythm is not peculiar to the respiration, and as examples of similar change of rhythm mentions the frog's heart nourished by means of serum instead of blood; the ventricle of the frog's heart separated from the auricle; and the heart of the embryo of the fowl. He then starts from the point of view that the commonest cause of the periodicity of rhythmic movement is asphyxia, and seeks to determine whether it can be produced experimentally in this way. In mammals asphyxia is too rapid to induce periodic breathing, but in frogs, as he showed before, he is able to do so. He calls attention to the increased motor activity during the period of breathing, which may even reach the stage of convulsions. Frogs poisoned by strychnine and then asphyxiated show convulsions during the breathing. The movements appear even after the removal of the brain, and cannot therefore be voluntary. It has been observed, further, that before the respiratory period the heart and lymph-hearts cease for a time to beat. Langendorff interprets the various manifestations of activity associated together in an attack as being the co-ordinated effects of a periodic excitement of the gray substance of the brain and cord. But in order to explain this periodicity in the Cheyne-Stokes phenomenon it is necessary to admit some opposition to the normal

[1] *Lancet*, vol. i. for 1885, p. 1183.

[2] *Rivista Clinica e Terapeutica*, anno vii. p. 494, 1885.

[3] *Breslauer ärztliche Zeitschrift*, vii. Band, S. 161, 1885, and *Biologisches Centralblatt*, vi. Band, S. 370, 1887.

stimulation, and the author regards the lowered irritability of the respiratory centre in this light.

Bernabei[1] records a case in which Cheyne-Stokes breathing made its appearance as a symptom of meningitis following fracture of the temporal bone. The patient was a man, aged 60, subject to vertigo for two months, who, after having, contrary to his usual custom, taken some spirits while fasting, became suddenly giddy, and fell on coming down-stairs. The left temporal bone was fractured, and, in consequence, there was left-sided facial paralysis and deafness. This was followed by double broncho-pneumonia, more on left, and meningitis, specially of right frontal region, during which Cheyne-Stokes respiration appeared, and could not be altered by any stimuli.

Wellenbergh[2] begins a valuable and interesting contribution to the study of Cheyne-Stokes respiration by a consideration of the anatomical relations of the respiratory centre and nerves, and of the bloodvessels which supply the nerve centres. He shows that the quantity of blood within the skull may increase or decrease under certain circumstances, and that such changes, when compensated by movements of the cerebro-spinal fluid, may not interfere with the physiological balance of function; but that beyond a certain point such alterations in the blood-supply must produce disturbances. This leads him to draw an analogy between certain mechanical contrivances and the probable causes of Cheyne-Stokes respiration. He imagines a brook whose stream moves a wheel, the motion of which is transmitted by means of an endless rope to the sails of a mill. He compares the brook to a bloodvessel, the water to the blood, the wheel to the respiratory centre, and the revolutions of the sails to the respiratory movements. He then imagines such an obstacle to the flow of the brook as a lock with a trap-door, whose resistance is greater than the pressure of the water, in consequence of which the door cannot open until the accumulating water has sufficient pressure to overcome the resistance. Before the trap opens the water beyond the lock will have flowed away and the wheel will have gradually stopped. As soon as the pressure of the water has overcome the resistance of the trap the

[1] *Bolletino della Società tra i Cultori delle Scienze mediche in Siena*, anno iii. p. 61, 1885.

[2] *Psychiatrische Bladen*, iii. Jaargang, S. 30, 1885.

water will flow down the brook in greater quantity and with greater force than under ordinary circumstances. The brook will be filled, the wheel will revolve, at first slowly, but afterwards with greater velocity than under ordinary circumstances, and as the brook falls to its usual size the rate will lessen until, from the closure of the trap, the stream again fails and the wheel stops. This is represented by a graphic schema, in which the wheel revolves normally three times a minute, as follows:—

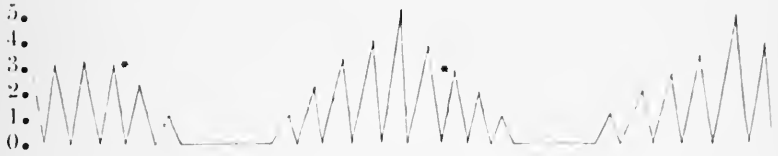


Fig. 1.—The figures 1 to 5 represent the number of revolutions per minute, and the asterisk denotes the moment when the trap-door is closed.

The amount of resistance of the trap-door and the amount of pressure of the flowing water are the two factors upon which the endless varieties which the tracing may undergo depend, the size of the wheel remaining constant.

The schematic tracing reproduced above is then compared by the author with tracings from the chests of patients showing Cheyne-Stokes respiration.

The author finds that although there is no apparatus within the vessels analogous to the lock and trap-door, there is an external force, viz., intracranial œdema, and he regards intracranial œdema as the principal, if not the only cause of Cheyne-Stokes respiration. He regards the phenomenon as the result of a struggle between the pressure of the blood within the vessels and the pressure of the œdema outside of them, a struggle in which these forces are alternately supreme.

He thereupon compares the appearances accompanying Cheyne-Stokes breathing with the symptoms which would naturally be expected to follow an alternate increase and decrease of pressure, and is strengthened in his views by the comparison. The author afterwards reviews a number of the theories which have been advanced, and concludes that the series of symptoms can hardly be caused but by such a cause as he has supposed.

Murri[1] combats the opinion of Mosso that Cheyne-Stokes respiration presents a condition analogous to sleep. During sleep the respiratory movements may cease without any injury to the interchange of gases in the tissues and blood, because there is less need for oxygenation. Remittent and intermittent respiration accordingly appear where a condition analogous to sleep is developed in the central nervous system. There is lowering of the irritability of the medulla oblongata, and Mosso differs from other observers in his opinion that in this lessened irritability there is a state analogous to sleep, whence intermittent breathing is a physiological appearance instead of a rare phenomenon. He therefore seeks to draw the conclusion that Cheyne-Stokes may have a twofold origin—physiological and pathological. Under ordinary circumstances the phenomenon is certainly associated with sleep, but just as certainly in pathological conditions this is not always the case. The origin of the symptom is often in such lesions as interfere with the harmonious successive and gradual working of the different parts of the respiratory centre. By means of such disturbances of particular phases of its activity, its functions are no longer continuous but periodic.

Storch[2] records intermittent respiration, perhaps not a typical instance of Cheyne-Stokes breathing, in a horse, 18 years old, which died from what is known in Germany and Austria as "Pferdetyphus," an affection characterized by general extravasation and exudation. In this case there was much extravasation into the mucous and serous membranes.

The author discusses several of the well-known explanations of Cheyne-Stokes respiration, and states that he considers Rosenbach's theory as the most probable.

Fano[3] criticises Mosso's work, and points out that the views therein expressed on the automatism of the respiratory centre are essentially the same as those advanced by Luciani and himself. He has some hesitation, however, in regard to Mosso's sleep hypothesis.

Fenoglio,[4] to test the accuracy of Mosso's observation that in sleep the respiration may become periodic, watched the sleep of a

[1] *Revista clinica di Bologna*, serie terza, tomo v. p. 161, 1885.
[2] *Revue für Thierheilkunde und Thierzucht*, viii. Band, S. 145 u. 165, 1885.
[3] *Lo Sperimentale*, tomo lvii. p. 1, 1886.
[4] *Ibid.*, tomo lvii. p. 113, 1886.

hundred old men, whose ages averaged 75 years, and an equal number of old women averaging 70 years of age. He found periodic breathing in six men, but not in any of the women. In two cases, where long pauses had been seen, post-mortem examinations were obtained. In one case there were no changes in the brain; in the other there were chronic meningeal lesions, but the medulla was healthy. Fenoglio is inclined to attribute the phenomenon to excessive fatigue and great need for rest, which speak of exhaustion of the system through severe disease.

Poole[1] has enunciated some views on the subject which are singular in themselves, and are probably based upon an imperfect appreciation of physiological facts. Stating that all the theories previously brought forward are based upon the assumption that impure venous blood acts as a stimulus to the nerve centres, he asserts that venous blood is a depressant of nerve function. He grants that for the appearance of Cheyne-Stokes respiration there must be a condition of partial paralysis of the respiratory centre, and that the blood is imperfectly arterialized. The heart, however, continuing to beat sends some blood through the lungs during the pause, which becomes oxygenated by means of the residual air; this reaching the nerve centres revives them and causes a dilatation of the arterioles, which occurs simultaneously with the laboured breathing. The inrush of blood into the lungs is too great to allow of proper oxygenation, and the imperfectly arterialized blood depresses the medullary centres, whence a pause again takes place.

Bordoni[2] begins his inaugural dissertation on this subject by a historical retrospect, and mentions that he has seen the symptom on six occasions—twice in fatty heart with pneumonia; once in inflammation of the endo-myo-pericardium (referred to at p. 73): twice in cerebral apoplexy; and once in fracture of the temporal bone (referred to at p. 78). This is followed by a consideration of the conditions present in the medulla oblongata, and of the circumstances, physiological and pathological, under which Cheyne-Stokes breathing may appear. The author then considers the phenomena presented by the symptom and the various changes

[1] *The Canada Lancet*, vol. xviii. p. 197, 1886.

[2] *Sul Tipo Respiratorio di Cheyne e Stokes, osservazione e ricerche sperimentali.* Siena, 1886.

which are associated with it, entering into a masterly examination of these appearances and of the conditions giving rise to them.

He then proceeds to discuss the occurrence of the symptom in lower animals and its production by various agencies, and describes some experiments performed by himself, whereby he found that in frogs periodic breathing could be caused by digitalin, scillain, and gelsemine.

The second part of his thesis is devoted by the author to an able criticism of the various theories which have been advanced by previous writers, and this leads him to support the views of Luciani:—Firstly, that the normal type of respiration is the result of continuous irritability of the respiratory centre and of the influence of varying stimuli; and, secondly, that Cheyne-Stokes respiration and all forms of periodic breathing depend upon variations of this irritability, having their origin in transitory or permanent changes in the respiratory centre.

Piaggio,[1] whose inaugural dissertation on this subject has already been noticed, again deals with the subject in an interesting paper. This communication begins with a review of Langendorff's observations and a criticism of his views. The author then calls attention to the phenomena which accompany the respiratory symptom. He is of opinion, as previously stated in his thesis, that an asphyxia or insufficient access of oxygen to the tissues is the determining cause of the phenomena, and he regards the forced respiration of the period of breathing as a false dyspnœa. He does not think that Langendorff has penetrated into the secrets of the internal mechanism which account for the symptoms. He holds that his interpretation implies an idea of resistance to the passage of nerve force, thus determining periodic discharges, and cannot admit it.

Unaware of the observations of earlier writers on the connexion between the respiratory and pupillary phenomena, Robertson[2] brought forward the rhythmic contraction of the pupils in Cheyne-Stokes respiration, as seen in two patients who had been under his care. He gives a full and clear description of the eye symptoms as well as of the alternate contractions and relaxations of the muscles

[1] *Le Progrès médical*, xiv. année, ii. série, tome iv., deuxième semestre, p. 690, 1886.

[2] *The Lancet*, vol. ii. for 1886, p. 1016.

of the limbs, which were especially well marked in one of his cases.

Being unacquainted at the time with the observations of Rosenbach and others who have disproved the statement that amyl nitrite invariably produces a disappearance of the symptom, the opportunity afforded by a case of chronic renal disease in a woman aged 60, accompanied by Cheyne-Stokes respiration, was employed by me[1] as a means of testing the efficiency of that remedy. In this case the drug, although effecting its usual changes as regards the circulation, failed to produce any modifications in the respiratory rhythm. The injection of nitrate of pilocarpine was in this case resorted to for the relief of the respiratory and other symptoms. It was followed by a disappearance of the pauses, which only continued for about a minute. It seemed to me, as stated in the paper referred to, that this brief disappearance of the periodic cessation of breathing was caused by the shock of the injection, and it also appeared extremely probable that in cases where nitrite of amyl had been found efficacious, its action was to be regarded as due to a stimulant effect upon the respiratory centre. It has since come to my knowledge that this view, as mentioned in an earlier part of this contribution, has also been previously advanced.

Finlayson[2] prefaces some interesting remarks, made at the Medico-Chirurgical Society of Glasgow, on the state of the pupil in Cheyne-Stokes respiration, by expressing his opinion that the distinction drawn by several writers between Cheyne-Stokes breathing and the less regularly intermittent respiration of cerebral disorders is one of degree only, and that there is a perfect gradation between the two varieties. The author enters upon the well-known phenomena of the pupils which usually accompany Cheyne-Stokes breathing, and states that although the reversed relationship has been described, *i.e.*, a dilatation of the pupil during the pause and a contraction in the period of breathing, he has never himself seen it.

The interest of Finlayson's communication, however, lies chiefly in this, that he for the first time describes a rhythmical enlargement of the pupil with each individual inspiration, and a subse-

[1] *The Practitioner*, vol. xxxviii. p. 85, 1887.

[2] *Glasgow Medical Journal*, fourth series, vol. xxviii. p. 221, 1887.

quent narrowing with the succeeding expiration. He is inclined to regard this phenomenon as being possibly but an exaggeration of a physiological variation which has been alleged to occur in the pupil with each respiration.

In the discussion which followed the reading of Finlayson's paper, M'Vail[1] lays stress upon the reversal of the pupillary phenomena to be seen in some cases of Cheyne-Stokes breathing.

Gowers,[2] after briefly describing the phenomenon and shortly mentioning some of the explanations advanced to account for it, makes the following remarks:—"On the whole it may be said that, unless the simple rhythmical tendency of the depressed centre is adequate to produce the phenomena, they can be best explained by the assumption that this rhythmical tendency is modified by some other periodical influence, of which vaso-motor spasm is the only one which, according to our present knowledge, can be conceived as acting and adequate. The gradual onset of the respirations may be due to the fact that the vaso-motor dilatation exceeds the normal (as it often does after contraction), and thus the quantity of blood reaching the respiratory centre lessens the stimulating influence of its quality."

Vierordt[3] allows that the phenomenon undoubtedly depends upon a disturbance of the functions of the respiratory centre in the medulla oblongata, but is of opinion that all more explicit theories are unavailing to explain it. He thinks that a simple diminution of the excitability of the cells of the centre from the presence of venous blood could only give rise to infrequent and possibly irregular respiration, which might either be deep or shallow, and that to ascribe a different degree of excitability to particular cells or groups of cells is at least a refinement—in short, that we are in want of a distinct explanation of the phenomenon.

Marckwald[4] devotes a section of his admirable work on the

[1] *Glasgow Medical Journal*, fourth series, vol. xxviii. p. 224, 1887.

[2] *A Manual of Diseases of the Nervous System*, vol. ii. p. 118. London, 1888.

[3] *Diagnostik der inneren Krankheiten auf Grund der heutigen Untersuchungs-Methoden*, S. 64. Leipzig, 1888.

[4] *The Movements of Respiration and their Innervation in the Rabbit.* Translated by Thomas Arthur Haig, student of medicine, University of Glasgow, and revised by the Author; with an Introductory Note by John G. M'Kendrick, M.D., LL.D., F.R.S., Professor of Physiology, University of Glasgow, p. 45. London, 1888.

respiration to the subject of periodic breathing. He shows that the medulla may be divided in the region of the acoustic tubercles without inducing any alteration in respiratory rhythm, but that if the section is made lower down at the level of the alæ cinereæ the breathing at once becomes periodic. Periodic respiration may follow the higher section if a blood-clot has caused pressure upon the respiratory centre, or if the respiratory centre has been exposed to the air. During periodic respiration he finds that the excitability of the centre has not in any way suffered, for stimuli to the skin during the pauses are immediately followed by movements of respiration. Marckwald was never able to produce periodic breathing by means of pressure upon the medulla in the region of the alæ cinereæ, the result of which was a cessation of respiration. Section below the upper level of the alæ cinereæ was always followed by destruction of the respiration, which could not be restored by any means. The author has never seen an ascending and descending series of respirations produced artificially, only a descending group, but he recalls the fact that in Cheyne-Stokes breathing the groups are sometimes also of this latter kind alone. He is of opinion that periodic breathing only takes place when at least a part of the higher brain tracts has ceased to act and has lost its influence upon the respiratory centre, which he believes to accord well with the mode of occurrence of Cheyne-Stokes breathing, as, for example, in sleep and hibernation; after the use of certain drugs, which paralyze the upper nervous centres, or lessen the circulatory supply to the brain; and from various experiments upon the nervous and circulatory systems. In this connexion Marckwald mentions a case of hemiplegia which he observed under the care of Lichtheim, where only the descending series of Cheyne-Stokes breathing was present. The patient in this case was able to modify the breathing, but when left to herself it was always periodic. In this case one-sided deficiency of the upper brain tracts was sufficient to produce Cheyne-Stokes breathing.

Marckwald points out that after the production of periodic breathing experimentally, section of the vagi causes it at once to disappear, and he is therefore of opinion that for the appearance of periodic breathing it is necessary to have the peripheral branches of the vagi in connexion with the respiratory centre. As stimuli during the pause produce respirations, he cannot admit that a diminished

excitability of the respiratory centre is the cause of the phenomenon.

Descourtis[1] describes a case of Cheyne-Stokes breathing in a man, aged 68, suffering from general paralysis. In this instance the pulse, as ascertained by the sphygmograph, remained constant in its characters throughout the varying phases of the respiration.

In a short abstract by Smart[2] of a paper read by him at the Medico-Chirurgical Society of Edinburgh, cerebral respiration and Cheyne-Stokes respiration are grouped together as "Multiple Complex Respiratory Neuroses," but the author insists on their independence of each other.

Stillman[3] has placed three cases on record in which Cheyne-Stokes breathing was present. These cases were:—A man, aged 47, who had received injuries in a fall, from which he recovered perfectly; a woman, aged 76, dying of cerebral hæmorrhage; and a man, aged 27, who had received an injury to the skull, from which he died. The author is of opinion that "the starting point in the chain of causation is found in the equilibrium between the respiration and circulation being always disturbed by a relatively weak heart."

A communication was recently made by me[4] with the view of showing that, whatever may be the nature of the condition underlying the associated symptoms of Cheyne-Stokes respiration, it may produce the effects which depend on it by affecting the lower centres in the first place, and spreading upwards to the higher, or by acting upon the higher first, and afterwards invading the lower centres. This was illustrated by reference to the presence of Cheyne-Stokes breathing in a case of pneumonia, in which small doses of bromide of potassium had been administered, without any changes in the pulse, pupil, mind, or muscles; to its appearance in a case of cardiac failure, in which it was accompanied by circulatory, pupillary, and mental symptoms; and to its occurrence in cases of uræmia in association with periodic alterations in the circulatory, visual, psychical, and muscular condition. These different classes of cases were regarded as presenting a

[1] *L'Encéphale*, vol. viii. p. 431, 1888.
[2] *The Edinburgh Medical Journal*, vol. xxxiv. p. 529, 1888.
[3] *The Medical News*, vol. liii. p. 555, 1888.
[4] *The Birmingham Medical Review*, vol. xxv. p. 30, 1889.

regular series of symptoms, commencing with those showing consequences depending upon some affection of the respiratory centre alone, and passing through others having a progressive tendency to involve different centres. The paper next attempted to show that the periodic changes produced by alterations of the centres may commence in, and be limited to, those which are not concerned in vital phenomena. The case of a child suffering from what clearly seemed to be tubercular meningitis, but which, owing to the recovery of the patient, may appear to have been possibly an error in diagnosis, was taken to illustrate my meaning. The patient was a little girl, aged three years, presenting all the symptoms of subacute tubercular meningitis. During the course of the disease, when watching her carefully one day, a periodic closure of the eyelids attracted my attention, and on further observation it was easy to determine that along with this closure of the lids there was a simultaneous contraction of the pupils, and a state of complete unconsciousness. This condition remained for several seconds, the eyelids were then raised, the pupils dilated, consciousness returned, and the child raised her head to look about. The conscious state was present for some time, how long it is not possible for me to say, as it did not occur to me to notice the interval, and was in its turn followed by the unconscious condition. In this case there was never, so far as my observation went, any tendency to a periodic change in the rhythm of the breathing. It seemed to me that such a phenomenon can only be regarded as analogous in every way to intermittent respiration, and, if this be granted, it follows that my contention is to be regarded as highly probable.

This brings us to the end of the examination of the facts and views embodied in the different works on the subject. In addition to the authors who have been mentioned, reference might have been made to many others who incidentally touch upon the subject, but, in so far as my acquaintance with the literature is concerned, these authors neither add anything to the store of facts nor throw any light upon their explanation. It is, in consequence, unnecessary to devote time and space to them.

Before leaving this division of the subject, a few remarks must be made upon three unpublished observations which have been communicated to me.

Dr Muirhead, of Edinburgh, informs me of an elderly gentleman, who for many years during his daily sleep after dinner breathed in the characteristic Cheyne-Stokes type.

Dr Edes, of Washington, writes to me with regard to a lady whose breathing has for many years been periodic or cyclical, as he prefers to term it, during sleep. A most interesting fact is that this lady tells him the phenomenon had been observed by her mother in herself and her sister from childhood.

Finally, Dr Tuke has placed the following interesting communication in my hands:—

"Balgreen,
"Edinburgh, 28*th February* 1889.

"Dear Gibson,—Knowing you are specially interested in 'Cheyne-Stokes breathing,' I send you a short report of a case which came under my observation last Saturday. On that afternoon my two favourite Dandie Dinmonts were poisoned by strychnine, which had been laid down for rats in the stable; the one fatally—dying in opisthotonus—the other recovering after fifteen hours of suffering. During all that time he was under my most careful observation. After five violent spasms (opisthotonus) I bolstered the dog in such a way that he could not move, as the slightest stimulus induced the attacks. By this means the general spasms were averted, and only occasional jerks were observed. But fifteen minutes after he was thus restrained well-marked Cheyne-Stokes breathing set in—the number of respirations was about 25, and the interval was somewhat longer than I have generally noticed in the human subject. The pupils were fully dilated during the breathing, the iris contracting slightly during the interval. So far as I could judge, the dog was conscious all the time, often trying to wag his tail. The rate of the heart was 120, and its action was regular, which is curious, as, under ordinary circumstances, this dog's heart, like that of most dogs, is very irregular, and sometimes intermitting. Its usual rate is 104. The femoral pulse was full and steady. When violent spasms showed themselves, the Cheyne-Stokes breathing ceased. I kept my hand slightly pressed on the ribs; when doing so the breathing never reached dyspnœa, but when the pressure was removed the symptom tended to show itself. After thirteen hours all the symptoms disappeared—the Cheyne-Stokes breathing gradually growing less pronounced—except stiffness of the hind legs.—I am, yours sincerely,

John Batty Tuke."

So far as my knowledge goes, Cheyne-Stokes respiration has not been observed as a consequence of the action of strychnine on mammals by any of the authors who have devoted attention to the subject.

Clinical.

In approaching the consideration of Cheyne-Stokes respiration from the clinical point of view, it will be necessary to group the conditions, already mentioned in the historical sketch, in which it has been observed. Before doing so, however, it must be stated that by the term employed to designate the phenomenon is meant a periodic form of respiratory rhythm. It would be out of place to attempt, at this stage of the inquiry, any definition of the symptom, but it will certainly tend to simplify the subject if it be distinctly understood that the term employed is limited in its application. It will not, in this paper, be held to include any irregular arrests of breathing, such as are frequently observed in diseases of the brain, and which are generally classed together under the term cerebral breathing. But in making this distinction there is no intention of drawing a hard and fast line between the regular periodicity of events seen in classical Cheyne-Stokes breathing and the altogether irregular stoppages of respiration characteristic of cerebral breathing. So many intermediate links are to be found between the two extremes, that the existence of an uninterrupted series of similar symptoms may safely be assumed.

From the observations of some authors there can be no doubt that there is a hereditary tendency in certain families towards the conditions under which Cheyne-Stokes respiration arises, and in some cases an inherited liability to the symptom itself has been found.

Amongst general diseases, Cheyne-Stokes respiration has been observed in the course of enteric fever, small-pox, diphtheria, cholera, and whooping-cough.

The nervous diseases in which it has been described are:— meningitis, encephalitis, cerebral hæmorrhage, cerebral embolism, cerebral thrombosis, insolation, insanity, hysteria, cerebellar hæmorrhage, extravasation on the medulla oblongata, pressure of an aneurism on the medulla, and tumour of the medulla and pons.

The symptom has been very frequently recorded as a consequence of general arterial degeneration, attended in some cases by gangrene or degeneration. It has been observed in hæmophilia,

as well as hæmorrhage following severe operation, and it has been seen in such more restricted diseases of the circulation as pericarditis, myocarditis, fatty degeneration, valvular diseases, and aneurism.

The respiratory affections in which Cheyne-Stokes respiration has been found are:—bronchitis, pneumonia, and phthisis, and it has been described as a sequel to tracheotomy.

Amongst digestive disorders, the symptom has been placed on record as occurring in the course of severe catarrhal diarrhœa.

Chronic renal disease is, without doubt, the most common cause of Cheyne-Stokes breathing, a large percentage of uræmic cases presenting the symptom in some part of their course.

Before leaving this summary of the diseases in which Cheyne-Stokes respiration has been observed, reference must be made to two singular conditions in which it was present. Fatty degeneration of the diaphragm was in one case associated with this symptom, but disease of the aortic valves was also present. Narrowing of the foramen jugulare was found in several cases presenting this symptom, but in all of these there was also cardiac or renal disease.

Cheyne-Stokes respiration has frequently been observed in the ordinary sleep of apparently healthy persons, and it has often made its appearance after the administration of bromide of potassium, chloral hydrate, and morphine. In one most interesting observation the symptom was developed in an infant whose mother, while nursing, had taken some doses of the latter drug.

In the lower animals, phenomena identical with Cheyne-Stokes respiration have been of frequent occurrence. Such appearances have been present during the deep sleep which has followed prolonged exertion, and also during the condition of hibernation. Intermittent respiration has been produced by the administration of chloral, morphine followed by ether or chloroform, ether along with picrotoxin, muscarine, picrotoxin, digitalin, strychnine, sulphuretted hydrogen, urea, kreatin, and ammonium carbonate.

Periodic breathing has further been produced by considerable changes of external temperature, by prolonged immersion (in amphibians), by bleeding, by removal of the heart, by alternate compression and relaxation of the carotid and vertebral arteries, by section of the medulla oblongata, with or without section of the

vagi, by pressure on the medulla, and by various injuries to the brain and medulla, even after the aorta had been tied. It is particularly worthy of notice, that section of the medulla at the level of the *alæ cinereæ*, seems invariably to produce a periodicity of the respiration. When the medulla is divided above that level, no change in the rhythm of the breathing occurs, while section below that level produces an entire cessation of respiration.

Turning now from the consideration of the different conditions in which Cheyne-Stokes breathing has been observed, the nature of the symptom in itself must be dwelt upon at somewhat greater length.

The descriptions given of this phenomenon by Cheyne and Stokes, which have so often been quoted, have never been surpassed, and no attempt will be made here to describe a symptom which is now so well known. The purpose of this part of the paper is rather to analyze the different phenomena which make up the symptom.

In Cheyne-Stokes breathing the normal rhythm is interrupted by distinct arrests of respiration; there is an alternation of periods of respiratory activity, and periods of respiratory repose. Under ordinary conditions, the inspiration, the expiration, and the short pause which succeeds the latter phase, have a definite relation in duration, and they are perfectly rhythmic in their recurrence. The arrests of respiration occur usually at definite intervals of time; they are therefore periodic, and it may be said that there is a secondary, superimposed upon the primary, rhythm. This, however, is not all; for an essential feature is that the period of activity consists of two distinct phases, termed by Cheyne ascending and descending. During the former phase there is a gradual increase, not only in the amplitude of the respiratory movements, but also in their rate; while during the latter phase there is a gradual decrease, both in extent and rate, of these movements. The contrast between the period of repose and the period of activity is very striking. During the former phase there is an entire absence of all movement, and during the latter the patient often appears as if labouring under severe dyspnœa, which is frequently accompanied by a fit of coughing at the height of the breathing. Such are the appearances in a simple instance of Cheyne-Stokes breathing. But Cheyne-Stokes breathing is frequently associated with other symptoms,

and attention must be directed to changes in other systems besides the respiratory.

There are in many cases alterations in the state of the circulation. These appear to have been first observed by Reid, whose descriptions of the state of the pulse must be stated in passing to be extremely careless in the use of terms. Such circulatory alterations are at once inconstant and variable, presenting a marked contrast to the regularity of the respiratory phenomena. In many cases no change in the state of the circulation can be observed on the closest investigation, as in cases described by different writers.

Sometimes the rate of the pulse is diminished during the pause in respiration, as in cases narrated by several observers. As has been mentioned in the previous part of this paper, Hesky observed an entire arrest of the radial pulse during the period of repose. On the other hand, the rate of pulsation has been observed to be greater during the period of repose than during the period of breathing.

Variations also in the volume and tension of the pulse have been met with. The pulse has been described as of larger volume and lower tension during the arrest of breathing than during the period of respiratory activity. In other instances no such changes could be detected, or the converse has been observed.

Filehne observed a recession of the fontanelles of children before the arrest of respiration; and, on the other hand, Rosenbach describes the recession as occurring late in the pause, or even during the period of respiratory activity.

In this connexion reference must be made to the experiments of Heidenhain, who observed an increase in the blood-pressure during the period of activity.

There are also certain appearances connected with the eyes which occur in association with Cheyne-Stokes breathing. In many cases the periodic rhythm of the respiration only takes place during sleep, when, as may readily be understood, no changes are observed in the eye. But in a large number of instances the symptom is present during the waking, as well as the sleeping hours. In a certain number of such cases Cheyne-Stokes breathing is unaccompanied by any eye-changes. In a certain number, however, definite appearances make themselves manifest in con-

nexion with the visual apparatus, and these must have attention devoted to them. As was first noticed by Leube, the eye is open during the period of breathing, and closed during the cessation of respiration. The eyes, further, glance about while the patient is breathing, while, during the pause, on lifting up the eyelids, a conjugate deviation of the eyeballs may be observed. A still more interesting fact is to be seen in some of the cases which present eye-symptoms. During the breathing the pupil is widely dilated, and tightly contracted during the pause. As Leube pointed out, the dilatation begins along with the early superficial respirations, or the dilatation may even precede the active phase of the breathing cycle. Appearances exactly similar in character were observed by Leyden as the result of experiments on the medulla. This is, however, not all, for Finlayson, on close scrutiny of the pupil, found that it dilates a little with each inspiration, and contracts slightly with each expiration, until the height of the respiratory phase is attained, and the pupil is widely dilated, after which the converse occurs, and the contraction with each expiration somewhat exceeds the dilatation accompanying each inspiration, until at the end of the active phase the pupil becomes fixed in the contracted condition. The contracted condition of the pupil during the cessation of respiration is evidently analogous to the appearances observed during sleep, and in this connexion it may be remarked that the pupil in some persons enjoying perfect health undergoes a considerable dilatation on deep inspiration and contracts to an equal degree on forced expiration. As Merkel first pointed out, the pupil reflex is absolutely abolished during the cessation of respiration, and no reaction to light can be elicited.

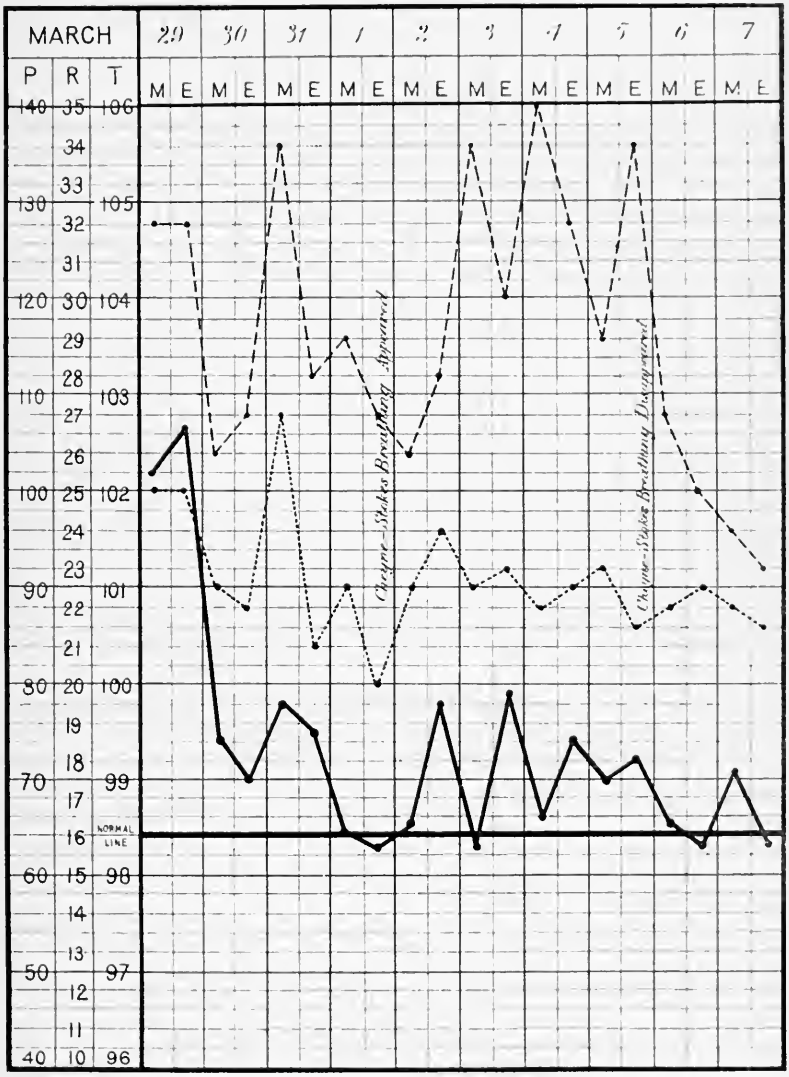
It is a most important fact that no changes have been seen in the condition of the vessels of the retina during the varying phases of respiration. Both Schepelern and Ewald, who have devoted themselves to the investigation of this point, are perfectly confident in regard to the absence of any alterations in the calibre of the vessels.

In many cases showing Cheyne-Stokes respiration, the condition of the mental powers undergoes fluctuations. The most usual state of matters is, as Leube first showed, that the patient is conscious during the period of breathing, while during the interval of repose he is bereft of perception and volition. This alternation of

consciousness and unconsciousness is frequently, but not invariably, associated with the variations in the appearances of the eyes just referred to. The interesting observation of Merkel has occasionally been repeated since. He put a question to one of his patients towards the end of the descending phase of the period of breathing. The patient sunk into the state of absolute repose, but on the return of respiration he made a suitable reply to the question which had been put to him. This observation, to compare small with great matters, is somewhat similar to the classical account of the officer who was wounded in the head at the Battle of the Nile, when in the act of uttering a command to his men, and who, after fifteen months of unconsciousness, finished his order after the operation of trephining. Such cases as these, in which patients are only in possession of their mental faculties during the phase of breathing, form a marked contrast to others in which the patients are conscious throughout, and often employ the pause in the breathing for the purpose of conversing with other people.

Out of the many cases showing this symptom which have come under my observation, a few will now be narrated in illustration of the various appearances, and these will be arranged as far as possible in a definite series, in order to emphasize the difference which they present in the association of phenomena.

Case I.—Lady, aged 73; seen for the first time 29th March 1888, about the ninth or tenth day of an attack of croupous pneumonia affecting the lower lobe of the right lung. The rate of the pulse and respiration and the height of the temperature may be seen on the accompanying chart, Plate I., which is based upon the very excellent graphic clinical chart of my friend Dr Handford. There was free expectoration of rusty sputum, increased vocal fremitus over the base of the right lung, dulness on percussion over that region, and bronchial breathing, with increased vocal resonance in the same situation. The pulse was of moderate volume, low tension, and regular rhythm. The state of the heart was healthy. The urine contained no abnormal constituent. There was no delirium during either day or night. On the evening of 1st April, three days after the crisis took place, during the administration of ten grains of bromide of potassium with ten minims of tincture of digitalis three times a day, Cheyne-Stokes


MARCH
29
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NORMAL LINE
Oxygen—Stokes Breathing Appeared
Oxygen—Stokes Breathing Disappeared
Pulse ..... Respiration _ _ _ _ _ _ _ _ _ Temperature

breathing made its appearance in typical fashion. This symptom persisted throughout the following four days, during waking as well as sleeping moments, and disappeared during the afternoon of 5th April, on the withdrawal of the bromide of potassium. The periodic changes in the respiration were accompanied by no corresponding alterations in the circulatory, visual, or mental processes. The patient's pulse beat with a steady uniformity during the waxing and waning phases of the breathing; no modification in the rate or rhythm was present, and not the least alteration in volume or tension could be determined in relation to the ascending and descending respiration. In the same way not the slightest tendency to closure of the eyelids during the arrest of respiration was at any period present, and it was therefore an easy matter to determine that the pupils underwent no modification in size, except when vision was accommodated to near or distant objects, or a change in the amount of light caused the usual reflex alteration in size. Similarly, the state of the consciousness was absolutely independent of the phases of the respiration. The patient had a tendency towards somnolence, but when waked had as much mental activity during the cessation of respiration as during the period of breathing; in fact, as is often the case, she employed the pause by preference for the purpose of talking with those around her.

This case forms an excellent example of the occurrence of Cheyne-Stokes breathing in a patient who, in spite of advanced years, showed no vascular degeneration, no cardiac affection, and no renal disease, and who, it may be added, made an entirely satisfactory recovery from the attack of acute pneumonia. It is to be regarded as a specimen of the simplest type of periodic respiration, in a patient entirely conscious of all her surroundings, unattended by any of the other symptoms often associated with it.

Case II.—Lady, aged 63, who showed the usual signs of chronic vascular degeneration without very obvious renal complications. On 7th February 1888 she was suddenly attacked by an apoplectiform seizure. When seen during the afternoon she was lying with a dusky flush on her cheeks, and beads of perspiration on her forehead, in a state of profound unconsciousness. The periodicity of breathing was very marked, nothing like the irregular

arrests of respiration, commonly called cerebral breathing, being present, but the regular ascending and descending respiration, with pronounced stertor and flapping out and in of the lips and cheeks at the culmination of the ascending phase. The sensory and motor functions were entirely abolished. The eyes were closed, and on separating the eyelids the pupils were observed to be contracted to the size of a pin-point, and to undergo no variations in diameter with the changing phases of respiration. The pulse was extremely frequent and of very high tension, but perfectly regular, and manifesting no alteration in tension, fulness, or rate corresponding to the respiratory phases.

The Cheyne-Stokes type of breathing persisted until a few hours before the death of the patient, which occurred during the morning of the following day.

On post-mortem examination the cause of death was found to be thrombosis of some of the branches of the middle cerebral arteries. The arterial system was somewhat degenerated throughout, the heart slightly hypertrophied, but otherwise healthy, and the kidneys showing to a certain extent, although not very markedly, granular changes.

This case is to be regarded as furnishing an example of Cheyne-Stokes respiration in a patient absolutely unconscious, which was not associated with any of the other symptoms often linked with it.

Case III.—Farmer, aged 74, suffering from chronic arterial and renal degeneration. On 6th March 1888, in spite of every precaution, he showed symptoms of uræmia, and, notwithstanding the most energetic treatment, he sunk gradually into a comatose condition. During the last two days of his life he had, as one of his symptoms, Cheyne-Stokes respiration almost without intermission. Before the fully comatose stage of uræmia was reached, the patient was, during the arrest of respiration, in a state of unconsciousness, from which he could not be roused by any form of stimulation. But with the superficial respirations which ushered in the period of respiratory activity, the patient opened his eyes and looked around him, speaking, during this phase, to those who were with him. It was singular that the most rigid scrutiny of the eyes entirely failed to reveal the slightest difference in the size of the pupils during the opposite conditions of the respiration, and there never was the

least tendency to conjugate deviation of the eyeballs. The pulse was infrequent, of high tension and absolute regularity, undergoing no changes in rate, volume, or tension throughout the varying phases of the respiration.

This case gives a good example of Cheyne-Stokes respiration attended by varying degrees of consciousness, but without any visual or circulatory phenomena accompanying the respiratory phases.

Case IV.—Housekeeper, aged 60, suffering from chronic renal disease.

Present condition, 6th November 1885.—The patient is of medium height and slender build, with a pallid complexion, tending towards an icteric tint, which is distinctly present in the conjunctivæ. The expression is anxious and restless, with staring eyes and dilated pupils. The tongue is covered with a thick yellow fur. The temperature is 98°·2 F.

The pulse is 96 per minute, regular, tardy, and of extremely high tension. The radial artery, like the arteries throughout the body, is atheromatous.

The impulse of the heart is somewhat diffuse, and the diastole is accompanied by a sinking inwards of the fourth, fifth, and sixth left intercostal spaces. The apex-beat has its point of maximum intensity in the fifth intercostal space, 3½ inches to the left of the mid-sternal line. The impulse is forcible, and is followed by a well-marked shock accompanying the second sound. No thrill is present.

The first sound is dull and thumping in its character, and in the aortic area the second sound is much accentuated. No murmur is present, but a to-and-fro friction sound is to be heard very distinctly over the base of the heart.

There are no morbid symptoms connected with the lungs.

The urine amounts to 25 ounces in twenty-four hours. It is of a pale yellow colour, with a specific gravity of 1013, and a highly acid reaction. It contains about one-fourth of albumin, and 7·5 grains of urea per ounce, or 187·5 grains per day. Microscopically, the urine contains broken granular tube-casts, and amorphous urates.

Diagnosis.—Chronic granular kidney, with some roughening of the pericardium as the result of an intercurrent pericarditis.

The patient continued to grow worse in spite of free purgation

and other remedies employed. On the 12th November, after two nights of wandering delirium, Cheyne-Stokes respiration was first observed towards evening, and on the 13th it was fully developed. It was accompanied by most of the appearances usually associated with the symptom, but, as will be seen from the sequel, there were few variations in the state of the circulation. During the pauses in the breathing the patient lay perfectly motionless with the eyes closed; immediately before the first shallow inspiration of the ascending series of respirations she opened her eyes, and the pupils dilated; as the respiration deepened into dyspnœa her eyes began to roll about, her head was thrown from side to side, and her hands jerked violently in various directions; at the height of the breathing she attempted to rise up in bed and muttered to herself; with the descending series of respirations these phenomena passed away, and when the phase of arrest was reached she had resumed her motionless attitude. The pupils during the pause were found to be contracted. The pulse varied very slightly, if at all, in its rate throughout the cycle of events, never being less than 24 or more than 26 beats in a quarter of a minute. The tension, so far as could be estimated by the finger, varied still less.

The following day, with the kind assistance of my friend Dr James, some tracings were obtained with the cardiograph and the stethograph, one of which is given in Fig. 1, Plate II. This tracing, which, like the others, is to be read from left to right, shows the respiratory curve above and the cardiac curve below, with signals from a time-marker registering every fifth second. It shows that the number of respirations during the period of breathing was about 36; that the period occupied about 25 seconds, and the pause about 5 seconds; and that the pulsations of the heart did not vary much in rate, although the tracing is naturally modified by the heaving of the chest during the period of dyspnœa. Unfortunately all attempts to obtain a tracing with the sphygmograph failed on account of the jerking which took place during the breathing.

On the 15th the patient was in the same condition, and it was deemed advisable to have recourse to the use of nitrite of amyl. A few drops were administered by inhalation during a period of respiration. The drug at once caused flushing of the face and

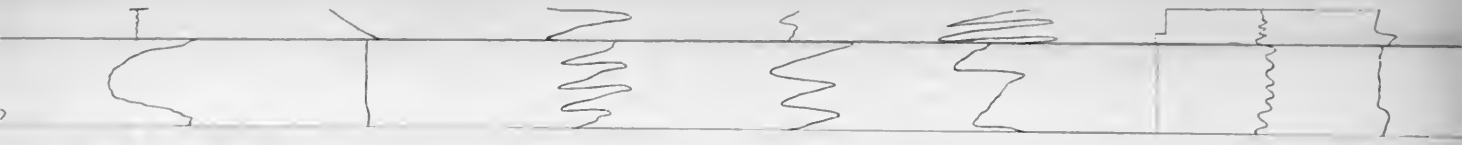


Fig 1

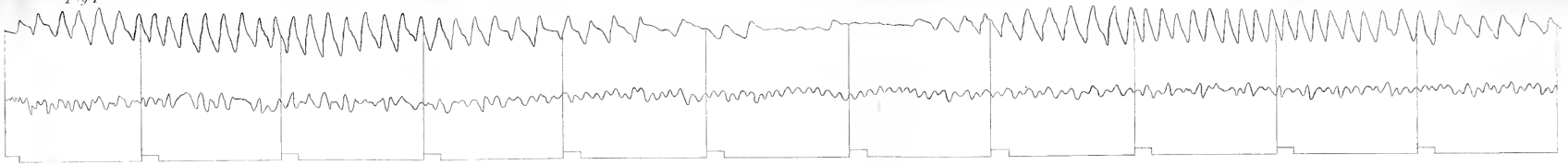


Fig 2

Fig 3

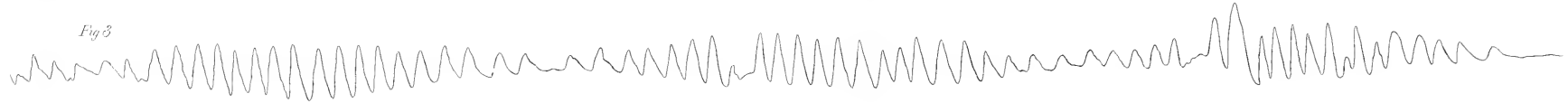


Fig 4

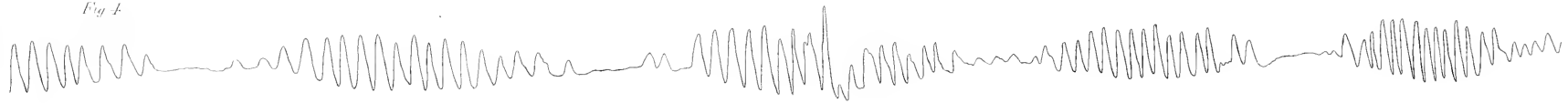


Fig 5

Fig 6

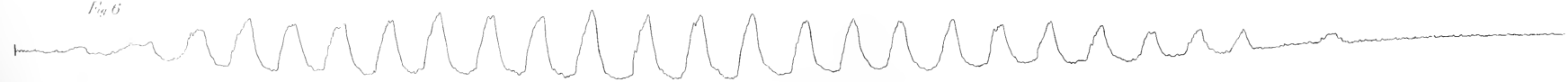
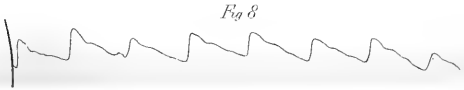


Fig 7

Fig 8



neck, but did not interfere with the periodic pause in the respiration. Its action was tested by several inhalations, during some of which tracings were obtained from the chest. Fig. 2, Plate II. shows the curve obtained while the drug was administered, and it proves how slight was the effect of nitrite of amyl on the respiration. The first pause after the use of the drug appeared with its wonted regularity, and before the second pause a period of shallow breathing was found to intervene.

By the 16th the urine had almost become suppressed, and as a last resource it was resolved to employ pilocarpine. One-quarter of a grain of the nitrate was administered subcutaneously, and in order to ascertain whether this substance had any effect on the conditions leading to Cheyne-Stokes respiration, tracings were taken with the stethograph. Fig. 3, Plate II., was taken immediately after the injection, and therefore before the drug could have caused any direct effects upon the central nervous system. It shows that three pauses were only present in the form of shallow breathing, but that the fourth pause was clearly marked. Fig. 4, Plate II., taken five minutes after the injection, has three complete pauses and one incomplete. Fig. 5, Plate II., taken ten minutes after administration, shows very irregular breathing, with pauses intervening between the periods.

On the 16th the power of swallowing was lost, and the patient could not be roused; on the 17th she sank steadily, and on the 18th she died. To the last the Cheyne-Stokes respiration was present.

A post-mortem examination of the body was made, the day after death, by my friend Dr Russell, to whose kindness I am indebted for the following description:—

The body was fairly well nourished. There was a decided icteric tinge in the skin and conjunctivæ. Rigidity and lividity were present. There was no anasarca.

Thorax.—There were 6 oz. of brownish-coloured fluid in the right pleural cavity, and 13 oz. of a similar fluid in the left. There were some old pleural adhesions on the right side. Both lungs were congested and œdematous, especially posteriorly. Otherwise they were normal.

The pericardium contained no fluid. The heart was firmly contracted. It was considerably enlarged. There was a large

deposit of fat on its surface, more especially on the anterior aspect of the right ventricle. The coronary arteries were markedly atheromatous, segments of them being converted into rigid calcareous tubes. The anterior one contained a thrombus not far from its origin, which may have been formed during the process of dying. The muscle of the left ventricle was firm and of a good colour, it varied in thickness from $\frac{3}{8}$ inch to $\frac{1}{2}$ inch; at the apex, however, it only measured $\frac{1}{4}$ inch, and part of the muscle was replaced by fat. At this point a firm decolorized clot about the size of an almond, and not of very recent formation, had been moulded into a depression in the ventricular wall. The mitral cusps were somewhat thickened, and their free edges slightly retracted. At the junction of the posterior cusp with the cardiac wall there was a thick nodular crescent of calcareous matter over which the endocardium was intact. The *chordæ tendineæ* were also thickened. The aortic valve was competent, but its cusps presented a few small and hard calcareous nodules at their junction with the ventricular wall. The aorta immediately above the valves showed a considerable tract of atheroma. The muscle of the right ventricle was deeply covered with fat, the muscle itself measuring $\frac{1}{8}$ inch in thickness. There was much tough blood-clot entangled in the meshes of the *columnæ carneæ* and *musculi papillares*. The tricuspid and pulmonary valves were normal.

Abdomen.—The abdomen contained 20 ozs. of brownish-stained serum. The surface of the organs was bile-stained. The intestines in places presented traces of recent peritonitis, their coils being agglutinated to one another by soft lymph.

Both kidneys were very small, hard, and tough. On section the normal arrangement could be traced with difficulty and only at a few points. There were numerous cysts both on the surface and in the substance of the organs. The cortex was practically obliterated in places. The interlobular vessels were much thickened. The capsules were firmly adherent, and when torn off left a coarsely granular surface. The organs, in fact, presented the ordinary appearances of advanced atrophic cirrhosis.

The liver had some old and firm adhesions at its posterior edge, and at this point there was a depressed cicatrix in the centre, on section of which there was found a calcareous mass

twice the size of an almond. Its left edge extended far into the left hypochondrium, and was united to the upper border of the spleen by old adhesions. The organ itself was congested and fatty, with a slight increase of its connective tissue arranged in a polylobular fashion.

The spleen was of normal size and somewhat firm consistence.

An examination of the *head* was not permitted.

The point which calls more especially for remark in a clinical respect, in addition to the persistence of the chief symptom, is the fact that the pericardial serous membrane was quite healthy —there were no adhesions, and there was no roughening of the surface. The pericardial friction, therefore, was apparently caused by the irregular and projecting anterior coronary artery rubbing against the parietal layer of the pericardium.

In this case nitrite of amyl caused no change in the type of the breathing, although, as shown by the flushing of the face and neck, it produced its usual effects on the circulation. The injection of pilocarpine caused a temporary disappearance of the periodic pauses in the respiration.

In this case the periodic variations in the respiration were attended by associated changes in the mental, visual, and muscular functions, but in so far as could be ascertained by the most rigid scrutiny, there was not any synchronous modification of the condition of the circulation.

Case V.—Gentleman, aged 63, with a history of chronic alcoholism, who had for four years suffered from paralysis of the right leg. For some weeks he had been confined to bed on account of general weakness, and when seen on the 7th June 1889 he had general anasarca. The urine was increased in quantity, but markedly deficient in urea; it contained albumin, but no tube-casts were present. The pulse was of high tension, showing, however, a tendency to failure of arterial pressure. The heart was dilated and hypertrophied; the second sound in the aortic area was somewhat accentuated; in the mitral and tricuspid areas there were soft systolic murmurs. The lungs, in the presence of crepitations at their bases posteriorly, gave evidence of pulmonary œdema. The case was obviously an instance of chronic granular kidney, with cardiac failure.

The last phase of his malady was characterized by the occurrence of uræmia, during the presence of which Cheyne-Stokes breathing was a prominent and persistent symptom. Fig. 6, Plate II., is a tracing of the respiratory movements of the thorax, obtained on the 13th June by means of Marey's stethograph with the kind assistance of my friend Dr Aitken, with whom the case was seen. During the pauses in the respiration the patient lay quietly in a state of unconsciousness, with the eyes shut, and it was difficult to rouse him even by powerful stimuli. On forcibly opening the eyes during this pause, the pupils were seen to be contracted to their smallest diameter. At this period the pulse was small, regular, and of high tension. After the lapse of from twenty to thirty seconds, the patient moved his head a little and partially opened his eyes. The pupils dilated to a slight extent, the pulse lost some of its tension, and these changes were followed by a superficial respiration. This respiration was succeeded by a slight and momentary contraction of the pupils, followed immediately by dilatation to a greater extent than at first, and succeeded by another respiration of greater depth than the first. This alternate dilatation and somewhat slighter contraction of the pupil respectively preceded and followed each of the ascending respirations, until at the culminating point the pupil was widely dilated. The pulse during the phase of waxing respiration gradually became fuller in volume and less in tension.

Fig. 7, Plate II., is the tracing obtained by means of Marey's sphygmograph during the period of repose ; Fig. 8, Plate II., during the phase of activity. They show that the pulse was smaller and more frequent during the arrest of respiration than during the period of breathing. The patient became more and more restless as the breathing deepened, until at the point of the most profound dyspnœa he showed considerable tendency to spasmodic jerkings of the arms and legs, and made efforts to converse with those near him. From this point the reverse series of phenomena began to be manifest. The respiratory movements became less in amplitude, the pupils after each breath contracted to an extent greater than the dilatation preceding it, the pulse-rate increased and its volume lessened, the eyes gradually closed, and the patient sank into the state of profound unconsciousness.

In this case the entire complex of symptoms constituting the

Cheyne-Stokes phenomenon of the modern German School formed a striking and complete clinical picture.

This group of five cases presents an almost perfect series of phenomena, from the simplest form of Cheyne-Stokes breathing, unattended by any other periodic changes, to the complex of symptoms—respiratory, circulatory, and nervous—known as the Cheyne-Stokes phenomenon. In the sequel an attempt will be made to analyze the conditions underlying the different appearances.

Another case, somewhat anomalous in certain respects, and of much interest as throwing a strong side-light on the occurrence of the periodic respirations, must, in conclusion, be described.

Case VI.—Gentleman, aged 65, seen 24th April 1886, suffering from arterial degeneration and cardiac failure. Face somewhat cyanotic; ankles slightly œdematous. Pulse extremely irregular in rhythm and variable in rate, of low tension in spite of some atheroma of the radial artery, as well as of the general arterial system. Heart considerably dilated, with diffuse pulsation. No murmur could be detected, but the first sound was feeble, and the second sound in the pulmonary area considerably accentuated. The rhythm was extremely irregular. The lungs presented no abnormal phenomena. The urine contained no albumin.

During calm waking moments and during sleep the breathing of the patient was perfectly regular, but whenever he was engaged in any mental effort the breathing fell into groups of ascending and descending respirations, and in conversation he found it necessary to employ the pauses for speaking. In this case the pulse showed no corresponding periodicity in any respect, and there was not the slightest approach to any changes in the opening of the eyelids or in the size of the pupil. It goes without saying, from what has just been described, that no alternations in the mental state attended the respiratory changes.

This observation appears to me to be quite unique in the fact that excitement produced the cyclical breathing, the converse of what has so often been previously observed.

Critical.

The most satisfactory method of entering on the consideration of the conditions underlying the complex of symptoms, already discussed from the clinical point of view, is obviously to be found in a survey of the ground traversed by previous observers. In the earlier pages of the present work the gradual development of clinical knowledge in regard to the phenomena, and the continuous evolution of ætiological doctrines with reference to their causation, have been dealt with in simple chronological order. But to have a thorough grasp of the entire subject it will be necessary, in weighing the different views which have been advanced, to arrange them in groups. The discussion of these opinions will lead in due course to certain definite and substantive conclusions.

The earlier observers advanced no theories in explanation of the periodicity of the respiration, for although Stokes regarded this as a consequence of fatty degeneration of the heart, and Schweig associated it with stenosis of the jugular foramen, causing pressure on the vagus, neither observer offered any opinion in regard to the possible means by which such lesions might produce the symptom.

Somewhat analogous in its vagueness is the opinion of Broadbent. In a work which made its appearance after the earlier portions of this work had passed through the press, and which will be more fully referred to in the sequel, he refers Cheyne-Stokes breathing to high arterial tension, and cites some cases of this kind in which its presence was determined by the supervention of some complication. From the consideration of these observations he is led to conclusions adverse to any hypothesis with regard to the respiratory centre, whether of exalted or diminished sensibility, and he is of opinion that they point to a loss of the normal adjustment between the systemic and pulmonary circulations. He gives no explanation of the mode of operation of the loss of balance.

It seems a sufficient answer to these views to recall the fact that periodic breathing occurs under very varied conditions. It is undoubtedly true that Cheyne-Stokes breathing is more commonly found in cases presenting high arterial tension than in patients who have a low arterial pressure; but it is necessary to take into

account cases belonging to the latter class, and no hypothesis can be accepted as even plausible if it fails to do this.

Broadbent's views, moreover, make no attempt to explain why the high arterial tension, whether with or without a disturbance of the normal adjustment between the systemic and pulmonary circulations, should induce such a striking change in the rhythm of the respiration, and they do not take into consideration the various associated symptoms occurring with the periodic breathing. For these reasons, as well as on account of the fact that Cheyne-Stokes respiration often occurs without high arterial tension, his views cannot be entertained.

The earnest attempts to explain the occurrence of the periodic phases of the breathing will now be considered according to the classes into which they naturally fall.

There are, firstly, certain vague and indefinite views based upon the hypothesis of a persistent diminution of the functional activity of the respiratory nervous mechanism.

Walshe mentions "anæsthesia of the vagus or of the medulla oblongata itself," a hypothesis which appears to be simply repeated in a transposed form by Laycock with his "sentient palsy of the respiratory centre," or "paresis of reflex sensibility of the mucous membrane of the lung." The conceptions of many other writers, such as Sansom, are equally hazy.

No hypothesis of this kind is adequate. Simple reduction of the excitability of the respiratory centre might cause infrequent and irregular respiration, but it most assuredly could not by any possibility lead to the regular periodicity of phenomena seen in Cheyne-Stokes respiration.

In the second place, many attempts have been made to explain the regular periodicity of the breathing by varying conditions of the stimuli which act upon the nervous mechanism controlling the muscular functions of the respiratory apparatus.

Undoubtedly the earliest attempt of this kind is that of Little. He thinks that the cause is a loss of balance between the two sides of the heart, either when there is diminished force of the left ventricle, as in fatty degeneration, or when some abnormal burden has been imposed on the left ventricle, under which it is unable to get rid of blood as quickly as it is supplied to it, and the blood accumulates in the left auricle and the pulmonary veins and

capillaries. Being fully arterialized, this blood fails to excite the terminal filaments of the vagus, as venous blood does, and the respiration ceases. A few pulsations then displace this blood, and the venous blood streaming in excites the respiration anew.

This explanation forms in some respects a transition towards the renowned hypothesis of Traube. It postulates an intermittent stimulation of the vagus-endings by alternating conditions of the blood contained in the lungs. It cannot be regarded as meeting the case, for many diseases produce Cheyne-Stokes breathing in which no disturbance of the circulation occurs. It fails, moreover, in not giving any adequate reason for the ascending and descending phases of the breathing; and the assumed loss of equilibrium between the two sides of the heart is absolutely unproved.

Traube begins his explanation, as we have already seen, by pointing out that all cases presenting Cheyne-Stokes breathing have one common feature—a lessened supply of arterial blood to the medulla, in which the respiratory centre is situated. There is in consequence less oxygen, which influences the irritability of the nervous elements. Through this lessened amount of oxygen the irritability of the nerve cells becomes lowered, and a larger quantity of carbonic acid is required to cause an inspiration; the time, therefore, within which the carbonic acid will accumulate in sufficient quantity is lengthened. This is similar to the effects of section of the vagi, in which long pauses, attended by dyspnœa, occur in the respiration. The respiration may be excited in two ways: 1. By the pulmonary fibres of the vagus; and 2. By the afferent nerves coming from all parts of the body. The difference between these two is this, that the pulmonary endings of the vagi are bathed in blood containing much carbonic acid, while the others have a supply of blood which contains but little. If both be equally irritable, then in health only the pulmonic vagi will be called into action. If the vagi be cut, the respiratory centre can only be excited by the other nerves, and this can only happen when the blood circulating throughout the body is as rich in carbonic acid as that normally passing into the lungs. The number of the vagus fibres is incomparably smaller than that of the other nerves; when these latter act, therefore, the effect is correspondingly greater.

Applying this reasoning to the phenomenon in question, the lessened irritability of the respiratory centre, caused by cerebral pressure, or uræmic blood, or deficient arterial supply, requires a larger amount of carbonic acid as a stimulus, and thus there is a long pause. When this gas has accumulated in sufficient quantity it first stimulates the pulmonary terminations of the vagi, but, as was shown long before by Traube, the strongest stimuli applied to the vagi never cause dyspnœa, and this only causes the shallow breathing which appears first after the pause. The amount of carbonic acid meantime increases sufficiently to cause stimulation of the nerves coming from the skin and other parts of the body, and hence the dyspnœa sets in. The quantity of the gas is greatly diminished by the forcible breathing, and the excitement of the other nerves ceases, so with the action of the vagi alone shallow breathing again occurs, until there is not enough carbonic acid gas to excite the pulmonary endings of the vagi, and a pause sets in anew.

This beautiful and ingenious explanation appears at first sight to fulfil all the requirements of a good working hypothesis. It is only on close inspection that it is found wanting. The initial difficulty is that a simple and constant reduction of the functional activity of the respiratory centre could not by any possibility induce a change from regular rhythm to periodic rhythm of the respiratory movements, and that no real cause for the fluctuations in the blood-supply is advanced. Under the trenchant criticism of Filehne, indeed, the author found himself obliged to shift his ground, and in restating his theory, as we have previously seen, he fell back upon a tendency to rhythmic periodicity in the respiratory centre, as well as upon exhaustion of that centre produced during the phase of breathing, and causing the subsequent pause. Even this addition, however, leaves the ascending or crescendo phase quite unaccounted for, and gives no valid cause for the beginning of the periodicity.

It is hardly necessary to refer to the fact that Traube only deals with the respiratory phenomenon, and leaves untouched the different associated symptoms brought before the scientific world by the clinical acumen of Leube. And it is equally needless to add that no theory can be complete that does not account for the occurrence of the entire complex of symptoms which may be present.

Hayden, reasoning from the fact that the only lesion with which rhythmical irregularity of the breathing has been, in his experience, found, is degeneration and dilatation of the aortic arch, involving a loss of elasticity in its walls, considers that during the period of greatest quiet of the heart's action, such as occurs in repose or sleep, the systemic capillary circulation fails, from want of the aid rendered in health by the elastic reaction of the aorta; and there are a suspension of tissue-respiration, *besoin de respirer*, and accelerated or suspirious breathing. Increased respiration will aid capillary circulation, first, through the lungs, and then through the tissues of the body generally, by quickening the action of the heart and increasing its force. As the systemic capillary circulation is stimulated, the *besoin de respirer* is less urgent, and respiration gradually subsides, till a period of apnœa arrives. The descent of respiration below the normal standard arises, he thinks, from its previous excessive activity and the exhaustion of the patient. A period of feeble action of the heart succeeds, with failure of capillary circulation, and paroxysmal breathing. That imperfect circulation of arterial blood in the respiratory centre contributes in a special manner, and in a great degree, to the production of the respiratory derangement he has no doubt; but he thinks that the effect of this is not easily distinguished from that of a want of oxygen in the tissues of the body generally.

In this explanation the train of reasoning bears considerable resemblance to the arguments advanced by Traube in his second hypothesis. All the objections which have been, or may be, urged against the views of Traube may be, with equal cogency, brought forward in opposition to the views of Hayden; and it is hardly necessary to add that in a considerable number of cases, exhibiting the Cheyne-Stokes phenomenon, there is no structural alteration of the aortic walls, or of any part of the circulatory apparatus.

Hein, starting from the consideration that the fluctuating conditions of the cerebral and respiratory functions must have the same cause, considers that the irritability of the tissues in general, as well as of the medulla in particular, must be lessened by some underlying condition, which in his own experience was cyanosis. From the diminished excitability of the medulla pauses are produced which may, he thinks, have an effect on the circulation, so that what was a consequence may in other circumstances be a

cause. With a normal circulation such an effect is impossible, as Cheyne-Stokes respiration may be imitated by the hour without any noticeable modification of the circulation. It is otherwise, however, when the blood-stream is slowed and oxygenation lessened, for if interruptions to the respiration take place, the functions are alternately increased and diminished, and such effects are shown in the medulla oblongata through variations in its irritability. The blood which has been arterialized during the respiratory period reaches the capillaries in greatest part at the beginning of the pause, at which time the circulation which had been quickened by the breathing becomes slower, while the tissue change is most active. The result is that the irritability of the medulla is again increased and the breathing begins. By means of the passage, during the breathing period, of the blood which has become venous during the pause, the tissue change necessary to the functional activity of the organ cannot be kept up, the oxygen in the tissues is consumed without adequate compensation, and the irritability of the respiratory centre is suspended. It is again restored after arterialized blood has coursed through the vessels of the medulla and promoted internal respiration, as occurs at the end of the pause. That the irritability shows a stage of increase and a stage of decrease is due to the fact that the alternation in the conditions of the circulation and diffusion is gradual, not sudden. From the analogous conditions of the brain and medulla it is to be concluded that the respiratory nerve centre does not simply undergo a change in the degree of stimulation, but a periodic alteration of its own condition.

The explanation advanced by this author, so far as it is possible to understand his meaning, seems to rest upon the conception that alterations in the metabolic processes lead to an alternate increase and decrease of the functional activity of the centre for respiration. But in this theory there is absolutely no attempt to find a real cause for the initial phenomena of periodic alternations—in short, as was remarked by Filehne, it is solely concerned with the *how*, and leaves the *why* untouched.

At the conclusion of his argument, however, it must be noted, he makes mention of a periodic variation of the condition of the respiratory centre; and, in his later contribution to the subject, he lays still more stress upon the periodic variations in the activity

of the respiratory centre, with or without analogous fluctuations in the activity of other nerve-centres. He leaves us, notwithstanding, under the belief that this periodic variation of functional activity is produced by variations in the condition of the blood-supply, and offers no explanation of the original cause of this.

Filehne allows that for the production of Cheyne-Stokes respiration there must be a lowering of the irritability of the respiratory centre, but he asserts that the irritability of this centre must be diminished to a greater degree than that of the vaso-motor centre. He holds that these centres remain at rest as long as they have a sufficient amount of oxygenated blood, and that they are excited whenever the blood-supply is sufficiently arterialized, or when, although sufficiently arterialized, the supply is deficient in quantity. He asserts that in health venous blood excites in regular order,—1st, the respiratory; 2nd, the vaso-motor; and 3rd, the convulsive centres. When the phenomenon is present, the blood during the pause gradually becomes more venous and develops the stimulus for the centres, but, from the lessened irritability of the respiratory centre, no respiration is caused, and the pause therefore continues until the point is reached when the vaso-motor centre is brought into action. This produces a diminution of the blood-supply, which causes the respiratory centre to act and originate the superficial breathing which is first observed. Some time, however, elapses before the blood arterialized by these respirations can reach the vaso-motor centre, and this is delayed by the contraction of the arterioles caused by its activity; it also takes time before the vaso-motor apparatus can induce contraction of the arterioles, and time also before the contraction can pass away; there is therefore a lengthening of the pause and deepening of the dyspnœa.

Filehne states that when Cheyne-Stokes respiration is produced in animals by the administration of large doses of morphine, followed by the inhalation of ether or chloroform, there is a diminution of the pulse-rate during the pause, which sometimes goes the length of complete cessation of the pulsation; while during the period of respiration there is a gradual acceleration until the normal rate is regained towards the end of this phase. In animals thus experimented on the blood-pressure rises during the pause and falls during the period of breathing. In a man dying from a lethal dose of morphine and chloroform, who showed during the narcosis Cheyne-

Stokes respiration, the pulse underwent the same changes as in the animals on which he performed his experiments.

During his controversy with Traube, Filehne refers, as previously mentioned, to the fact, observed by him, that the arterial tension rises before the beginning of the phase of respiratory activity; to the depression of the fontanelles in children, who present the symptom, before the active phase of breathing; to the disappearance of Cheyne-Stokes breathing on the administration of amyl nitrite; to a rise of tension in some persons before inspiration; and to the production of periodic breathing by alternate compression and relaxation of the carotid and vertebral arteries in the rabbit. In later contributions Filehne found himself driven to admit that the arterial changes may be synchronous with the periodic changes in the respiratory activity.

This exceedingly complicated hypothesis rests, in the first place, on certain assumptions which have not been proved; and, in the second place, on several observations which have, without exception, been proved to be, to say the least of them, inconstant.

The statements in regard to the relative excitability of the centres in the medulla rest upon no basis of fact, and with reference to an arterial spasm, upon a misconception.

Filehne's observations on the alterations of pulse-rate and tension have been found by numerous writers to be altogether incorrect, inasmuch as the changes, when present at all, have been seen to be the converse of what he described, and to occur at a period entirely different from that stated by him. An arterial spasm, moreover, in a patient with a condition of lessened cerebral activity would probably lead to consequences quite the opposite of those seen at the beginning of the phase of breathing. His description of the cerebral movements seen in the fontanelles of an infant is absolutely controverted by the observations made on similar cases by Rosenbach and Hein. Even the result of amyl nitrite has been found by later observers to be in many cases negative, and if any change has been produced by this drug it has been through its effects as a stimulant, as has been pointed out by Mayer and myself. The results of his experiments will be discussed at a later stage. Meantime it is only necessary to state that no basis for his elaborate hypothesis is left.

The views of Bramwell are essentially those of Filehne, inas-

much as he postulates an arterial spasm, produced by the venous blood, as the proximate cause of the excessive respiratory action, and this excessive action as the cause of the subsequent pause, through free oxygenation of the blood. The main points in which he differs from Filehne are in his considering the possibility of a different state of excitability in the discharging and restraining portions of the inspiratory centre, and in his holding that there is a state of irritable weakness in the centre, rendering it more easily fatigued, and yet also producing more powerful effects when sufficiently stimulated.

It is obvious that all the objections which have been advanced against the theory of Filehne may be brought forward in opposition to this hypothesis, and neither of them does account for the starting-point of the periodic breathing.

Cuffer, as we previously saw, seems to have proved by his researches with François-Franck that excessive oxygenation of the blood produces arrest of respiration. He has been led to consider the stage of apnœa as arising from excessive oxygenation of the blood, caused by dyspnœa; the recommencement of the breathing and subsequent dyspnœa as caused by the want of oxygenation due to the arrest of respiration; the superoxygenation of the blood and accompanying muscular fatigue determining in turn a new period of apnœa. He thinks the phases are caused by the action of the blood on the medulla as well as by the influence of a reflex action having its point of departure in the lung; the lung being the special regulator of the quantity of oxygen needed, and having its essential stimulus in the condition of the blood which it contains. He directs attention to the arterial spasm at the beginning of the respiratory period, which is characteristic of uræmia, and holds that it influences the condition of the breathing.

There seems but little difference between this view and that of Filehne, and the same arguments may be brought against both.

The theory of Grasset, as stated by Blaise and Brousse, holds that from deficient nutrition there is loss of vitality of the nerve-cells producing a condition of irritable weakness, upon which the venous blood acts strongly, producing dyspnœa. This oxygenates the blood to a high degree, which removes the stimulus to respiration, and a pause ensues, allowing the blood again to become venous. So far the theory is similar to that of Traube, *except* that

its author thinks the deficient nutrition of the nervous elements produces an excessive irritability, whereas that of Traube refers the condition to a lessened irritability. But Grasset goes on to state that excitement of the vaso-motor centre may produce an arterial spasm. Here we have the theory of Filehne almost in its entirety.

On similar lines, but considerably less definite than most of the hypotheses summed up in the preceding pages, are several opinions stated by different observers.

The view of Piaggio, for instance, fully stated in the earlier part of this work, is that a tissue-centre of respiration controls an automatic centre, and that the condition of the tissues, not the state of the blood, is the determining cause of the periodicity.

Kaufmann is even less precise, and thinks that theories based upon a conception of exhaustion of the centre require the further hypothesis that the increase of irritability induced by external stimuli is so great as to prevent the exhaustion from giving expression to itself.

Wellenbergh points out that, under ordinary conditions, there is a provision for an increase or a decrease in the quantity of blood in the cranium up to a certain point, but that, when the limit is passed, changes in the blood-supply must cause disturbances. Reasoning from the analogy of the mechanical contrivance described previously in the extract from his paper, he seeks for some mechanical cause of interference with the blood-supply, and is of opinion that this is to be found in œdema of the brain, and he advances the hypothesis that the periodic breathing is the result of a struggle between the pressure of the œdema outside the blood-vessels and the blood-pressure within them, in which struggle each is alternately supreme.

It is a sufficient reply to this hypothesis to point out that many cases have no œdematous condition, and that the explanation is therefore not valid.

Many observers simply give in their adhesion to one or other of the foregoing hypotheses based upon assumed alterations of the external stimulation, and it is therefore unnecessary to refer to them in this place.

We have to consider, thirdly, the theories which seek to explain the regular periodicity of the respiration by variations in the intrinsic condition of the respiratory centre.

Observing, as we have previously seen, that in certain circumstances the contractions of the frog's heart fell into groups, or became periodic, Luciani was led by the resemblance of this phenomenon to the character of Cheyne-Stokes breathing to seek for some condition common to both as the cause of the two phenomena. The experiments and observations which he has made have already been fully referred to.

He does not think that Cheyne-Stokes breathing can be explained by means of the principle, that the capacity and activity of a nervous organ depend on extrinsic stimulant and nutritive conditions. No doubt the vitality of any organ is intimately connected with surrounding conditions and influences, but it does not follow that the organ in every case transforms only as much as it receives in the same measure as well as in the same rhythm with which it receives it. Drawing a clear line of distinction between reflex and automatic movements, Luciani points out that the determining cause of the former is extrinsic, while in the case of the latter it is intrinsic, and consists in oscillations of the internal nutritive movements, to which correspond as many oscillations of the excitability of the organ itself. He was led to this conception of automatism by the discovery of the periodic grouping of the movements of the frog's heart, for it could not be doubted that when extrinsic conditions remained unchanged, the cause of the alternate groups of pulsations and pauses was intrinsic. Luciani therefore regards the diverse forms of respiratory rhythm as extrinsic expressions of the nutritive changes in the structure of the respiratory centre. If it be granted that the respiratory centre is automatic, it follows that the different forms of rhythm which constitute Cheyne-Stokes phenomenon may be regarded as effects of diverse kinds of automatic oscillations in the excitability of the centre itself.

This theory presents us with views entirely different from any which we have hitherto criticised. It is quite true that Traube, in his later hypothesis, makes mention of a tendency to rhythmic periodicity in the respiratory centre, and that Hein somewhat briefly refers to a periodic variation in the activity of that centre; these authors, however, clearly indicate that such changes are conditioned by extrinsic agencies. Luciani therefore makes quite a new departure in advancing the view, that the change

from regular to periodic rhythm is due to intrinsic conditions.

The chief difficulty, as regards this theory, appears to be placed in the question whether the respiratory centre can be regarded as really automatic. As will be shown in the sequel, there can now be no manner of doubt that the respiratory centre is truly automatic in its action. And this being granted, it must of necessity follow that, although it is perhaps more influenced by external agencies than any similar organ, the nerve centre mainly concerned in the maintenance of respiration can modify its functions independently of such extrinsic conditions. There can, therefore, be no great obstacle in the way of accepting Luciani's conclusions.

Rosenbach finds an explanation of Cheyne-Stokes breathing, with its attendant symptoms, in the alternation of activity and repose characteristic of Nature. In the respiration we see inspiration, expiration, and pause; in the circulation, systole, diastole, and pause; in the nervous system, waking and sleep; while in curarized animals there are periodic changes in the rate and tension of the circulation which are quite independent of the respiration. The origin of activity is in the *cell*, not the *blood*, and it is illogical to seek a cause of respiratory and other phenomena in the latter. Periodic activity of all nervous apparatus, therefore, depends on immanent peculiarities of elementary structures, and the blood is not the direct stimulus for the cells, but has its power in giving the cells the possibility of regulating tissue change. When the blood is altered there is necessarily a modification in the absorption of oxygen and the removal of the products of tissue change, and the mechanism will therefore be indirectly affected; the blood is thus only one link in the chain of apparatus needful for life.

The regular alternation of activity and repose characteristic of life is seen in the complex of pathological phenomena, of which periodic breathing is only one symptom, and Cheyne-Stokes respiration is therefore the result of a condition in which the exhaustibility of the central apparatus, normally following its activity, is greatly increased. The respiratory centre has its irritability lowered, as the breathing is at first shallow, but the irritability progressively increases, for in spite of better aëration,

dyspnœa gradually develops. The irritability then diminishes, and the descending phase begins.

The phenomena, therefore, according to Rosenbach, occur in conditions of disturbed nutrition, but they are independent of any periodicity in the blood-supply to the brain, and are co-ordinated by, and joint effects of one and the same cause occurring periodically in the central organs, this cause being exhaustion of the centres. The whole brain may be affected, when the entire complex of symptoms termed Cheyne-Stokes phenomenon is produced, or limited tracts only may be implicated, giving Cheyne-Stokes breathing. He points out that just as the respiratory centre alone may be deranged, so the vaso-motor or vagus centre may be disturbed, as in tubercular meningitis, and cause changes in the tension or rate of the pulse. Rosenbach compares the periodic exhaustion with the normal pauses for rest shown by all rhythmically acting systems. The different phases resemble natural phenomena, but with longer intervals ; the period of breathing, for example, is to be compared with a respiration, and the period of repose with the short pause following expiration. The vagus and vaso-motor centres show similar variations. The exhaustion of the brain induces sleep, during which the pupils behave as in ordinary slumber.

The centres are not only more easily exhausted, requiring longer rest, but their irritability is reduced, and forced breathing comes on in spite of better arterialization of the blood (which involves reduction of stimulus). The meaning of this is, that the centre is becoming more irritable, although the stimulus is lessening. After a time the normal irritability is regained, which is accompanied by gentler breathing until the pause resulting from exhaustion occurs.

This theory runs on the lines laid down by Luciani, and assumes variations in the intrinsic condition of the centres as the cause of the periodicity of the phenomena. This, as has been stated, is an opinion which is difficult to refute. But the chief import of Rosenbach's work is the masterly grouping of the different phenomena, whether inherent or accidental, as one complex of symptoms, conditioned by one and the same cause. The great value of his contributions lies in the fact that he has marshalled all these appearances, and given a satisfactory explanation of their origin.

Mosso, from the consideration of a long series of interesting observations and experiments, concludes that the respiratory movements are modified according to the amount of activity present in the nervous system, and points to the intimate relations existing between periodic breathing and sleep. It has been thought that the greater or less activity of the respiratory centre represents a greater or less need of provision by pulmonary ventilation for the chemical wants of the organism; but the author is of opinion that he is not far from the truth in thinking that the respiratory movements modify themselves according to the states of sleeping or waking—of greater or less activity of the nervous system. He holds that the mechanical and chemical parts of respiration are distinct, that the mechanical is more representative of the vitality of the nerve centres than of the chemical wants of the organism; that if the nervous excitability increases more air is inspired than is needed for chemical wants; while, on the contrary, during sleep the mechanical may lessen or become periodic without disturbance of the chemical function of tissue respiration; and further, that when the excitability of the centres is much lowered, it can be determined that the accumulation of carbonic acid by asphyxia causes almost no effect on the respiratory movements.

These views are in the main in accord with the opinions of Luciani and Rosenbach, but they embrace one or two extensions in different directions. In regard to the relations existing between periodic breathing and sleep, it has been urged that sleep is impossible when ordinary stimuli are maintained; it must nevertheless be borne in mind that, when the nervous centres are exhausted, sleep occurs even during the presence of ordinary stimuli.

Greater exception may probably with justice be taken to the hypothesis that the mechanical and chemical functions concerned in respiration may undergo quantitative changes irrespective of each other. There can, however, be no doubt, as will be fully proved in the sequel, that the centres engaged in the processes of respiration are endowed with a large measure of automatism, and it may fairly be concluded that there is no absolute quantitative relation between the mechanical and chemical functions.

With regard to the main theory, that the respiratory movements

in periodic breathing are modified according to the amount of activity present in the nervous system, it is only necessary to remark that, like the two just discussed, it rests upon a sure basis.

Murri has more especially attacked Mosso for holding the view that Cheyne-Stokes breathing presents a condition analogous to sleep, and he urges that if this were really the case, periodic breathing would be a common appearance instead of a rare symptom. But Murri is entirely incorrect in considering periodic respiration as a rare phenomenon. In very many different but physiological conditions various degrees of this type of respiratory rhythm may be seen, as will be shown in the sequel.

The interesting observations of Langendorff and Siebert have led them to the somewhat indefinite conclusion, that periodic breathing is caused by disturbance of irritability produced by changes of nutrition. Their views, notwithstanding a considerable degree of vagueness, appear to accord for the most part with the conclusions of most of the observers who are embraced in this section, and they merit a similar place in regard to their scientific value.

From the results of their observations, which have already been fully referred to, Solokow and Luchsinger have come to the conclusion, that the phenomena are absolutely independent of changes in blood-pressure, and that the conditions underlying the periodicity of the respiration are such as are developed in every tissue with increasing asphyxia; that the cause is, therefore, to be found in the lessened elasticity and greater exhaustibility of the centre.

These views are founded on a series of observations so complete as to leave no room for any doubt in regard to the validity of conclusions reasonably deduced from them, and the opinions of these observers naturally fall in with and complete the teaching of Luciani and Rosenbach.

The experiments and conclusions of Fano may briefly be classified as strictly analogous to those of the two authors just referred to.

Löwit, from his clinical studies, and Saloz, from his experimental investigations and clinical observations, have apparently arrived at conclusions which closely resemble those already discussed as belonging to the third group.

Murri thinks that in periodic breathing there is a regular increase and decrease of the activity of the respiratory centre, caused by some mechanism at present unknown. He holds, however, that the irritability of the respiratory centre is depressed; and he is of opinion that the respiratory centre must have several zones, corresponding to different groups of muscles, and endowed with various degrees of irritability.

So far his views are in accord with those placed in this group. But he proceeds to argue that in health the most sensitive zone responds promptly to stimuli, and is therefore sufficient for the function of respiration. If impaired, however, it needs stronger stimuli, and these rouse the other zones, causing dyspnœa, by means of which more oxygen is supplied to the blood, and there is a larger supply to the medulla; this gives rise to a slowing of respiration which ends in the pause, with accumulation of carbonic acid and a repetition of the cycle. The decreasing or descending respirations are due to the continuance of activity after the interruption of the stimuli; the dyspnœa is caused by the delay in the aëration of the medulla. It must be admitted that the irritability of the respiratory centre is impaired in order to have the necessary conditions for the development of Cheyne-Stokes respiration.

In this there is a complete adoption of the theory of Traube, and Murri's explanation, therefore, embraces, firstly, fluctuations of activity in the centre, caused by some mechanism as yet unknown, but probably intrinsic; and, secondly, alterations occurring reflexly in response to extrinsic stimuli. The first part of his hypothesis is probably founded on correct views; the second, as has been seen, is in itself at once inadequate and unnecessary. It is, however, not improbable that as an additional and accidental part of the phenomenon, such processes are sometimes linked with the more important automatic action of the centre.

In order to arrive at a real understanding in regard to the conditions underlying Cheyne-Stokes breathing, it is necessary to grasp the results of physiological investigation into the nervous mechanism controlling the respiratory movements.

In these complex movements there is one of the most wonderful examples of co-ordinated muscular acts. The precision with which the different movements—facial, faucial, laryngeal, and thoracic—

are brought into harmony with each other, speaks for a highly specialized nervous apparatus. These various movements are not merely complementary to each other under ordinary conditions, but they may in altered circumstances become also compensatory. If the phrenic nerves, for example, are severed, so that the diaphragm is paralyzed, the intercostal muscles act much more powerfully in an attempt to compensate for its inactivity. Such observations prove that the centres controlling the respiratory movements have the power of increasing the activity of certain muscles in order to supply what is lacking on account of deficient efforts elsewhere.

It is, perhaps, unnecessary in this place to refer to the question whether more centres than one are concerned in the maintenance of the respiration, but a brief allusion to it will conduce to the thorough comprehension of the subject. From the results of experiments performed by severing the connexions of the medullary centres, it is quite clear that in young animals at least there are spinal, as well as bulbar, centres engaged in the movements of respiration. This is analogous to the now thoroughly established and more widely-known fact, that there are vaso-motor centres in the spinal cord as well as in the bulb. In both cases there are probably lower spinal, under the control of higher bulbar, centres. In the respiratory mechanism of the adult mammal, the functions of the lower spinal centres, however, appear to be allowed to fall into desuetude.

It will serve no purpose to enter upon any attempt to draw distinctions between inspiratory and expiratory centres: no such differentiation is of the least use in the present inquiry.

The nervous mechanism concerned in respiration is remarkably subject to the influence of external agencies. The movements of respiration may not only be modified by processes taking place in the higher nervous tracts, such as volitional impulses or emotional impressions, but they are subject also to alterations in consequence of any considerable stimulus of any part of the lower nervous system.

The functions of the respiratory centre are also modified by changes in the blood circulating through the nervous textures. The presence of venous blood augments the respiratory movements; even after section of the vagi and spinal cord below the bulb, a venous state of the blood increases the facial respiratory move-

ments. A lessened supply of blood, as after ligation of the carotid and vertebral arteries, produces dyspnœa, and the same result is produced if the blood flowing upwards in the carotid arteries is heated. Against these facts must, however, be placed the interesting observation, that if by transfusion the normal blood circulating in the bulb is replaced by a fluid containing little or no hæmoglobin, and therefore but little oxygen, dyspnœa is not produced.

The condition of apnœa may be caused by forced respiration, but it has been found that this cannot be brought about so easily after section of the vagi; this is what might be expected, seeing that the inhibition of inspiratory movements is largely the function of the vagi, and, more especially, of the superior laryngeal branches. The production of apnœa may be effected by forced breathing of such an indifferent gas as hydrogen, and the positive ventilation, as it is termed by Foster,[1] appears to act more as a mechanical stimulus to the vagus terminations, than as a chemical stimulus acting through the blood.

The regulative influences normally ascending the vagus nerves are apparently twofold, and probably run along different sets of fibres. No other conclusions can be drawn from the fact, that when, after section of the vagi (producing deep and infrequent respiration), the upper ends are stimulated, the respirations are sometimes rendered more, and at other times less, frequent.

Very many of the phenomena produced by external agencies are purely reflex in their nature, but when this has been granted there remain other facts which point to something more than simple reflex action in the respiratory centre.

After section of the vagi, for example, the respiration is maintained, although considerably modified by the lack of the ascending regulative influence of these nerves. This observation proves that the movements of respiration are in their causation independent of, although modified by, stimuli from the lungs.

If the spinal cord be severed from the bulb, and all the accessible sensory cranial nerves be divided, so that the respiratory centre is set free from almost all sensory stimuli, the respiratory movements of the face and larynx continue, although the thoracic movements necessarily come to an end. In this observation there is clear

[1] *A Text Book of Physiology*, fifth edition, Part ii. p. 595, 1889.

proof that the respiratory movements are independent of all sensory stimuli.

Such facts demonstrate, beyond the shadow of a doubt, that the respiratory centre is in its nature truly automatic.

The most scientific conception of the respiratory centre, therefore, seems to be that it is one endowed with an independent automatism, but that it is subject to modifications of its activity by impressions from without.

The next step in the inquiry is to find out whether periodic changes in the rhythmic action of the respiratory centre may occur under physiological conditions. Mosso, as has already been seen, pointed out that in men and domestic animals, perfectly healthy, but fatigued by exertion, the breathing tended to become periodic and intermittent during sleep. This is an observation which has been verified by subsequent investigations, and which may be confirmed by anyone who has any doubt on the subject. During the after-dinner nap of elderly persons there is also a great tendency to periodic respiration, which may exhibit the phenomena of Cheyne-Stokes breathing in its most pronounced form. This may, as in the case communicated to me by Dr Muirhead and previously referred to,[1] occur day after day for years. But it is not necessary to look for such periodic variations in the rhythm of respiration in conditions of fatigue or of advanced life, where it may possibly be said that the conditions are not absolutely physiological. Edes has, as was previously mentioned,[2] observed that in certain individuals the breathing during sleep is constantly periodic, and it seems probable that the members of some families have a peculiar tendency to the development of the symptom.

The periodic breathing may therefore be regarded as in many instances a perfectly physiological appearance. This conclusion divests the symptom in itself of any prognostic significance, and any importance which it may have in this respect is to be estimated by the conditions in which it is seen. In hibernating animals, as Mosso showed,[3] the breathing is very similar to Cheyne-Stokes respiration. The case described on a previous page,[4] in which during mental efforts the breathing fell into groups of ascending and descending respirations, must be referred to in this connexion.

In all the diverse forms of disease, classified on a previous page,

[1] *V.* p. 88. [2] *V.* p. 88. [3] *V.* p. 38. [4] Case VI., p. 103.

presenting Cheyne-Stokes breathing, one condition may be held to be constant—a reduction of the activity of the higher nervous structures. Whether the cause be in the nerve centres primarily, or in other structures, such as those of the digestive, circulatory, respiratory, or renal systems, or in general affections, such as the specific fevers, there is, when Cheyne-Stokes breathing is present, the one constant condition of lowered nerve activity, such as normally occurs in deep sleep, or after a full narcotic dose. It must not be imagined, from the reference just made to circulatory changes as a cause of Cheyne-Stokes respiration, that there is any such direct nexus between the state of the circulation and the condition of the breathing as has been postulated by Filehne and his followers. The fact that there is no cyanosis during the pause is in itself enough to negative such views, against which valid objections have been fully urged previously. There is, however, a more general connexion between the state of the circulation and the condition of the nerve centres. If at any time the quantity or quality of the blood should depart from the normal, the activity of the nervous structures suffers in a direct ratio. In this way, but in no other, is there in Nature a connexion between the function of the circulatory and nervous mechanisms.

The explanation of all these phenomena is supplied by the interesting series of investigations of Marckwald,[1] from which he has been led to the conclusion that periodic breathing can only occur when some of the higher brain tracts have ceased to exert their influence upon the respiratory centre. During sleep the action of these higher tracts is in abeyance to a greater or lesser extent; in certain individuals a greater degree may habitually be present, in others it only takes place after great fatigue. It is more likely to occur during the process of digestion, as in the after-dinner nap, because the nervous energy is then carried off in another direction. In Case VI. the accession of the periodic breathing was obviously determined by the deviation of nervous influences into other channels by mental effort.

The effect of many drugs which produce periodic breathing amply confirms this view, as all of them which have been found to produce such changes have the power of lessening cerebral activity.

[1] V. p. 84.

It is, however, extremely probable that in addition to the removal of the higher influences the activity of the respiratory centre itself must be lessened.

Such periodic phenomena are not confined to the respiration. Luciani [1] has observed analogous phenomena in the amphibian heart when removed from its normal nervous control, and Waller and Reid, in a recent investigation,[2] have observed analogous phenomena in the excised mammalian heart. Fano [3] and Langendorff and Siebert [4] have seen similar appearances in the excised heart of the embryo, and Solokow and Luchsinger [5] in the lymph hearts of dying frogs.

It was previously seen that the periodic movements of the respiratory muscles in hibernation had been observed by Mosso [6] to become regularly rhythmic on elevation of the external temperature. A periodicity of respiratory rhythm was caused by Fano [7] in the alligator by subjecting it to the influence of cold. In these instances it is only a fair inference that the depressing influence of the low temperature lowers the vitality of the animal and diminishes the control of the higher nervous centres, while it no doubt at the same time lessens the activity of the respiratory centre.

It seems to be in accordance with some great natural law, that rhythmic phenomena tend to become modified when the organs have their vitality lowered or are still imperfectly developed. This conception appears to be confirmed by Steiner's observations on Medusæ. He points out [8] that the rhythmic contractions of the calyx fall into periodic groups separated by pauses from each other when Medusæ are kept in water which has not been sufficiently often renewed.

Phenomena analogous to those seen in Cheyne-Stokes respiration are observed in various conditions. Changes in the rhythm of the pulse lead in many cases to more or less periodicity of

[1] *V.* p. 45.

[2] *Philosophical Transactions of the Royal Society of London*, vol. clxxviii. page 218, 1887.

[3] *Lo Sperimentale*, tomo lv., p. 143 e 252, 1885. [4] *V.* p. 63.

[5] *V.* p. 58. [6] *V.* p. 38. [7] *V.* p. 71.

[8] *Archiv für Anatomie, Physiologie, und Wissenschaftlichen Medicin, Jahrgang* 1875, s. 174.

groups of pulsations, and in certain circumstances, more especially perhaps when the heart has undergone degenerative changes, the pulse-tension manifests a marked tendency to show periods of elevation and depression. The Traube-Hering curves seen on physiological investigation are probably in every way analogous to this symptom.

Reasons have been adduced by me on a previous page for believing that in certain states of the nervous system there are periodic fluctuations of consciousness which may be regarded as similar to the periodic changes of respiration.

In most of the instances brought forward, the obvious character of the change is the induction of a larger secondary upon the smaller primary periodicity of the phenomena.

It has already been proved that the respiratory centre is to a great extent endowed with automatism. It is like the other organic centres possessed of much more vitality than the higher centres, and can resist influences fatal to their integrity. When from any cause the higher centres are rendered incapable of performing their proper functions, the influence normally exerted is in abeyance, and the organic centres are allowed free play for their automatism.

From the investigations of Marckwald it must be concluded that the automatic centre for respiration is under the control of a higher regulating centre. Whether the periodic respiration produced by section of the bulb in its upper part may not be in part caused by disturbance of the automatic centre, by which its activity is lessened, is a point that might be discussed. It seems clear that when the activity of the automatic centre is reduced, its functions have a tendency, common as has been seen to all vital structures, to become periodic.

The relation of Cheyne-Stokes respiration to what is termed cerebral breathing has from time to time been referred to in the preceding pages. The essential difference between the two types, when fully developed, consists in the perfectly regular periodicity, as well as in the waxing and waning character of the former, in contrast to the very irregular occurrence and the absence of any uniform onset or end of each period of activity. But it cannot be held that there is any absolute line of distinction between the two phenomena; there are not only many intermediate gradations by

which they are linked together, but the same cerebral affections may produce at times the periodic, and at other times the irregular form of interrupted breathing. No reason has ever been given to account for the different characters of the extreme varieties. It appears to me not at all unlikely that the difference may lie in the total removal of the higher brain influences in the case of perfectly periodic Cheyne-Stokes breathing, and in the irregular discharge of unequal impulses from the higher tracts in the case of that type which is commonly called cerebral.

A careful study of the entire phenomena must lead to the adoption of the view that Cheyne-Stokes breathing is but one of a complex group of associated symptoms, as has been so clearly pointed out in the suggestive contributions of Rosenbach. Why there should be such diversity of phenomena connected with the pulse, eye, and mind, it is at present impossible to answer. In one case there may be no periodic phenomena except the respiratory, and in another the entire complex of symptoms—mental, visual, circulatory, and respiratory—may be present. It is only possible at this time to hazard the suggestion, that the centres involved in each group of symptoms may be affected singly or collectively. Reasons have been given for believing that there may be well-marked periodicity of mental functions or of circulatory functions without any similar change of rhythm in the other systems. In what respect these various symptoms are linked it is not with our present knowledge possible to state, and it is equally difficult to assign any reason for the fact, that it may appear as an isolated phenomenon or as part of a complex of symptoms.

The essential cause of the symptom is without doubt a periodic variation in the functional activity of the automatic centre for respiration, and the philosophical work of Luciani must be credited with having for the first time established this fact. Whether the periodic variation depends simply upon the loss of the influence of higher regulating centres, or whether it is also at the same time the result of diminished vitality, in accordance with some great natural law, it is not at present in our power to decide.

APPENDIX.

Since the earlier portions of this work appeared several contributions have been made to the subject, but it cannot be said that much new light has been thrown upon the symptom.

Tizzoni[1] has continued and extended his researches on changes in the medulla oblongata in a very interesting article, while Mancini[2] and Hauer[3] devote their attention to careful studies of the clinical features of the symptom.

In the recent edition of Foster's work on Physiology, the author briefly considers Cheyne-Stokes breathing. After a short description of its phenomena he says:[4]—"A secondary rhythm of respiration is thus developed, periods of normal or slightly dyspnœic respiration alternating, by gradual transitions, with periods of apnœa. Whether the waning and the waxing of the respiratory movements be due to corresponding rhythmic changes in the nutrition of the respiratory centre itself, or to a rhythmic increase and decrease of inhibitory impulses playing upon that centre from other parts of the body—for instance, from higher regions of brain—has not yet been settled. . . . Closely similar phenomena have been observed during sleep under perfectly normal conditions; and this fact is rather in favour of the latter of the two explanations just given. The phenomena present a striking analogy with the 'groups' of heart-beats so frequently seen in the frog's ventricle placed under abnormal circumstances."

In the above statement there appears to be a misconception of the results obtained by Marckwald, as the experimental production of periodic breathing depends not upon "rhythmic increase and decrease of inhibitory impulses," but follows upon the removal of such inhibitory influences altogether.

Macdonnell[5] gives a description of some of the principal characters of periodic breathing, and Dixon Mann[6] describes

[1] *Memorie dell'Accademia delle Scienze di Bologna*, tomo viii., p. 3, 1886-88.

[2] *Bolletino dell' Ospedale di Santa Casa di Loreto*, tomo i., 533, 1887-89.

[3] *Prager medicinische Wochenschrift*, Band xiv., s. 373, 1889.

[4] *A Text Book of Physiology*, fifth edition, Part ii. p. 605, 1889.

[5] *Montreal Medical Journal*, vol. xviii., p. 294, 1889-90.

[6] *The British Medical Journal*, vol. i. for 1890, p. 427.

changes in the bulb in connexion with Cheyne-Stokes respiration.

West,[1] describing at the Pathological Society of London the long continuance of Cheyne-Stokes breathing in a case of granular kidney, mentions that the pauses at times disappeared, leaving respiration of an ascending and descending type.

Mackenzie,[2] in the discussion which followed West's remarks, asked if patients ever recovered after they had developed Cheyne-Stokes respiration; and in answer to his question several cases are recorded. Hingston Fox[3] narrates one of influenza with broncho-pneumonia, O'Neill[4] one of a febrile affection, Mallins[5] one of cerebral hæmorrhage, Flux[6] one of puerperal septicæmia, Adams[7] one of epilepsy and one of hydrocephalus, Aylward one of phthisis[8] in which morphine produced the symptom, Lawford Knaggs[9] one of renal disease, and Square[10] one of cerebral softening—all of which recovered. It is very interesting to note that Knaggs found a brother and a sister both suffering from renal disease and both showing periodic respiration.

Pilkington[11] describes a case of cardiac disease with softening of the left cuneate lobe, third right temporal convolution, and right anterior pyramid of the bulb.

Downs[12] has described a case of uræmia in which Cheyne-Stokes breathing occurred, and criticises some of the recent work on the subject, while Brush[13] records the case of an insane patient with chronic degenerative changes in the heart and bloodvessels who showed the same symptom.

An important contribution to the subject is contained in Broadbent's recent work on the Pulse.[14] He is of opinion that the symptom is mainly conditioned by a state of high arterial tension. No doubt the periodicity of the respiration is very frequently found in association with affections in which high arterial tension is a prominent symptom, as, for instance, granular

[1] *The Lancet*, vol. i. for 1890, p. 545.
[2] *Ibid.*, *loc. cit.* [3] *Ibid.*, p. 571. [4] *Ibid.*, p. 260.
[5] *Ibid.*, *loc. cit.* [6] *Ibid.*, *loc. cit.* [7] *Ibid.*, p. 674.
[8] *Ibid.*, *loc. cit.* [9] *Ibid.*, p. 744. [10] *Ibid.*, p. 776.
[11] *The British Medical Journal*, vol. i. for 1890, p. 819.
[12] *Medical News*, vol. lvi. p. 589, 1890.
[13] *Ibid.*, vol. lvi. p. 592, 1890. [14] *The Pulse*, p. 169, 1890.

degeneration of the kidney. But it has to be remembered, on the one hand, that both the high blood-pressure and the periodic breathing are consequences of the same change, while, on the other hand, that Cheyne-Stokes breathing is often seen with low arterial pressure. Hence, as was shown before, this view is untenable.

Wertheimer[1] holds that Cheyne-Stokes breathing is produced by inhibitory influences resulting from irritation, and not pushed so far as to cause total arrest of respiration, as it would do if the inhibition were absolute.

Boyd[2] describes the earlier part of the forced respiration as mainly inspiratory, and the latter as principally expiratory, and refers to tracings of the pulse to prove this. It may be mentioned, however, in passing, that the respiratory curve shows nothing that can be held to support this view, and that the numerous cases unaccompanied by any pulse changes disprove it.

Huber[3] describes a very interesting case of aortic aneurism, in which, as shown by pulse-changes, the first inspiration after the pause caused an increase in the activity of the vagus and vaso-motor apparatus.

Waller[4] takes a broad and philosophic view of periodic breathing. "*Cheyne-Stokes breathing*," he says, "is characterised by a waxing and waning of the amplitude of the respiratory movements. In a typical and well-marked case, the movements alternately decline to complete cessation and return to an amplitude much above the normal. No definite or conclusive cause can be assigned to this peculiarity of rhythm; it is not—as was once believed to be the case—characteristic of fatty degeneration of the heart, but makes its appearance in a variety of diseases, or in the absence of any disease at all; during normal sleep, particularly in children, a waxing and waning respiratory rhythm is of common occurrence. All we can say in explanation is to point to the fact that the Cheyne-Stokes rhythm is to the respiratory system what the Traube-Hering rhythm is to the vaso-motor system; both rhythms are originated by medullary centres, and are of about the same

[1] *Archives de Physiologie normale et pathologique*, v. série, tome ii. p. 31, 1890.
[2] *The British Medical Journal*, vol. i. for 1891, p. 1337.
[3] *Deutsches Archiv für klinische Medicin*, Band xlvii. s. 13, 1891.
[4] *An Introduction to Human Physiology*, p. 127, 1891.

frequency, viz., one to three per minute; indeed, the association is sometimes most definite and exact. On the rabbit, for instance, after hæmorrhage, phases of increasing and diminishing amplitude of respiration coincide with rise and fall of arterial blood-pressure. They are instances, among many others, of the common tendency towards 'pulsatile or rhythmic activity' manifested by all living matter."

Since this expression of opinion, so far as it goes, closely agrees with the views urged in the concluding pages of this work, it is as unnecessary as it is impossible to criticise it.

INDEX OF AUTHORITIES REFERRED TO.

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Cheyne-Stokes Respiration

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