quite unconscious though the swallowing reflex was still present. The pupils were unequal, the left being dilated and the right medium. Ophthalmoscopic examination revealed a double optic atrophy but no tubercles were to be seen anywhere in the fundus. The head was retracted and the abdomen was slightly retracted but was quite soft and doughy to the touch. Tache cérébrale was well marked. The temperature was 98° F., the pulse was 133, and the respirations were 25. During the first few hours after admission twitching movements were at intervals noted in the right arm and leg, also more extensive movements in both arms and legs. The respirations all this time were sighing in character, but after midnight the breathing assumed the Cheyne-Stokes character, the respiratory cycle lasting 50 seconds and consisting of 80 separate respiratory movements. The pupils likewise showed rhythmical movements. During the pause they became contracted, while with the respiratory movements they began to dilate, till at the acme of respiration they were widely dilated. While thus dilated the pupils reacted slightly to light. Rhythmical movements corresponding in time to the above were also observed in the arms, especially in the right arm. The arms it is to be noted were at this time more or less rigid and they presented slight tremor. They were extended, with the thumbs adducted and the fingers flexed at the inter-phalangeal joints. During the advent of the Cheyne-Stokes respiration, then, this tremor exhibited a rhythmical activity of such a nature that during the pause the tremor was scarcely perceptible, increasing, however, with the breathing till at the height of the respiratory cycle the tremor presented movements of considerable amplitude. As the respiratory movements lessened so did the extent of the tremor movement. These various rhythmical phenomena were observed at frequent intervals until the time of death, about 30 hours after admission into hospital.

On post-mortem examination the convolutions of the brain were found to be much flattened and the soft membranes and ventricles contained a large quantity of clear serous fluid. Numerous tubercles were to be found scattered throughout the soft membranes. The brain substance generally was very soft, but otherwise it presented no abnormal appearances. Both lungs were studded with miliary tubercles of comparatively large size and there was extensive tuberculous consolidation and excavation of the upper lobe of the right lung. The right bronchial glands were enlarged and caseous, but the left seemed healthy. Miliary tubercles were to be seen in the liver, spleen, and kidneys, and some small and evidently recent tuberculous ulcers were found in the colon and ileum. The mesenteric glands seemed healthy. The medulla and pons were fixed in formol and stained with theonin according to Nissl's method. Numerous sections were examined at different levels, special attention being paid to the sections passing through the *alæ cinereæ*. In none of the sections, however, could any distinctive change be found in the ganglion cells of either the tenth, the twelfth, or of any of the other nerve nuclei. Many of the ganglion cells I found to be quite normal. Some showed what has been termed a "polar" or "apical" chromatolysis and some were very faintly stained like to the so-called "ghost-cells." But these changes were seen throughout the whole medulla and pons, not confined to any special level or nucleus, and I take it that they were due to the meningitis or the high temperature (the temperature reached 107.6° before death) and not to be specially associated with the Cheyne-Stokes respiration.

That, then, very briefly is the record of this case and it would seem to be of some interest in that (1) careful microscopic examination of sections of the medulla through the *alæ cinereæ*—the supposed rhythmical respiratory centre—showed no distinctive change, at least not more than in the rest of the medulla and pons; and (2) in that rhythmical movements were also present in the arms, showing the extent of the affection. Some time ago Dr. Terrien¹ reported a case of Cheyne-Stokes respiration where not only was there a rhythmical movement of the pupils, but also a rhythmical anæsthesia of the parts of the face supplied by the fifth nerve. During the pause this anæsthesia was present, passing off again as soon as the respiration began. In explanation of this Dr. Terrien points out that the cilio-spinal centre and the sensory nucleus of the fifth nerve lie close to the respiratory centre and that whatever was causing

the Cheyne-Stokes breathing had evidently extended its influence to these adjacent centres. In my case tactile sense over the area of the fifth nerve could not be tested as the child was unconscious all the time the Cheyne-Stokes breathing was present. But to it Dr. Terrien's explanation would not seem to be applicable, for the arm-centres are certainly in no way adjacent to those of the pupil and respiration. My case seems rather to favour the view advanced by Dr. G. A. Gibson² that Cheyne-Stokes breathing and its accompanying rhythmical phenomena "are instances, among many others, of the common tendency towards 'pulsatile or rhythmic activity' manifested by all living matter."

Glasgow

THE DIASTOLIC MURMUR OF MITRAL STENOSIS.

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It is generally recognised that, as stated by Bristowe,¹ the murmur of mitral stenosis may be early, middle, or late diastolic; but the clinical significance of the variation in time of these murmurs is practically unknown; and it was the attempt to discover wherein cases with the early and middle diastolic murmur differed from those with the more ordinary presystolic murmur which led me to examine a series of cases of mitral stenosis. From clinical examination of a considerable number of cases I have arrived at the following conclusions, in support of which I am unable to give figures, but they will probably be found to agree with the experience of most.

1. The murmur in an early compensated case of mitral stenosis, such as is seen in the out-patient room and often discovered only on routine examination, is always presystolic. Early diastolic murmurs are practically never heard while compensation remains good.

2. On the other hand, when cardiac failure supervenes and the patient is troubled with dropsy, cyanosis, and other symptoms of mitral stenosis, the murmur is frequently heard in the first half of diastole, although even now it is not so common as the presystolic murmur. (A long diastolic murmur running right up to the thrust and increasing in loudness and roughness as it approaches the systole is included as a variety of the presystolic murmur.)

3. A presystolic murmur may or may not be accompanied by a systolic bruit, but an early diastolic murmur is almost always preceded by a systolic murmur. A single, early diastolic murmur at the apex is very rare in mitral stenosis and strongly suggests aortic regurgitation even if no murmur is heard at the base.

4. A presystolic murmur frequently changes into a diastolic murmur or *vice versa* in a short time and the period of diastole occupied by the murmur may even vary in the erect and recumbent postures. The difference in the cause of these murmurs is therefore not likely to be found in any structural condition of the affected valves, but rather in the way in which the heart is working at different times.

I have examined the records of University College Hospital for the past few years in order to see if in the fatal cases of mitral stenosis any post-mortem differences could be substantiated between the hearts of those in which during life the murmur was presystolic and those in which it was in the first part of the diastole. Such cases are not easy to collect, as it is frequently found in mitral stenosis that before death there may be no murmur or it may be confined to the systole, so that unless the case is under observation for some time it may be useless for this purpose. I have, however, collected 21 suitable cases of well-marked mitral stenosis with necropsies.

In 15 cases there was either during life a presystolic murmur or a very long murmur running up to the thrust. In 12 of these the left ventricle was either small, normal in size, or slightly hypertrophied without dilatation; in two the left ventricle was slightly dilated; and in one patient who died, not from the cardiac condition, but from septicæmia, it

¹ Le Progrès Médical, Jan. 8th, 1898.

² Cheyne-Stokes Respiration (Edinburgh, 1892).

¹ Proceedings of the Medical Society of London, 1888, p. 41.

was considerably dilated. In six cases the murmur was in the first part of the diastole and in every one of these the left ventricle was found to be markedly dilated and usually also hypertrophied. So it seems that the early diastolic murmur is heard in those cases of mitral stenosis in which the left ventricle is dilated. Now, in mitral stenosis alone the left ventricle does not dilate; it may either become smaller, as it receives less blood, or it may become slightly hypertrophied, possibly to increase its suction power, as suggested by Giuffré.² If with mitral stenosis we find distinct left ventricular dilatation we may be sure, excluding other valvular or visceral disease, that during life there was considerable mitral regurgitation, in which condition dilatation is of course frequent. This great frequency of dilatation of the left ventricle in cases of mitral stenosis with early diastolic murmur, together with the clinical association of such murmurs with systolic bruits, and the fact that this murmur is only heard when compensation is failing, leads to the conclusion that the murmur in the first part of the diastole is only heard in cases of mitral stenosis in which there is free mitral regurgitation. The objection might be raised that with the rigid and useless valves of mitral stenosis there must be very frequently regurgitation and that the early diastolic murmur should be therefore more common. But there are frequently no signs during life or after death that regurgitation has taken place and, as suggested by Samways,³ this may be due to hypertrophy of the left auricle which, until it gives way, prevents by its more forcible contraction any great mitral regurgitation. The rapid changes in the time of the murmur of stenosis may be due to alterations in tone of the muscle of the left auricle and auriculo-ventricular ring, allowing greater or less regurgitation.

Although there have been no suggestions as to the significance of the early diastolic as compared with the presystolic murmur, yet there are several explanations as to the mode in which it is produced. There is the view supported by Fagge⁴ that it is caused by an increased duration of the auricular systole, so that it drives the blood through the narrowed orifice as soon as the ventricle dilates. Apart from the difficulty of conceiving such a cardiac rhythm on physiological grounds there is the obvious objection that such murmurs are very frequently heard with, but separated from, presystolic murmurs which would be most unlikely if they were both due to the auricular contraction. Balfour⁵ ascribes this murmur to the high tension in the pulmonary system forcing blood through the narrow mitral orifice to fill the left ventricle as soon as it is emptied. If this were sufficient by itself to produce a bruit we should expect an early diastolic murmur in all advanced cases of mitral stenosis until the right side gives way, relieving the high pulmonary pressure, whereas such murmurs are only heard in a minority of cases. There is also the attractive theory put forward by Rolleston⁶ and adopted by Gibson⁷ and others that the early diastolic murmur is due to the negative pressure in the expanding left ventricle sucking blood through the constricted orifice. If the early diastolic murmur is associated with a dilated left ventricle, as appears from my analysis of post-mortem examinations, which unfortunately includes only a small number of cases, it can hardly be explained by this *vis a fronte*. For even if we suppose the wall of the left ventricle to remain of the same thickness and elasticity when the cavity is dilated there would be as a question of physics less negative pressure within it; and as the wall of a dilated ventricle is always softer and less elastic, this loss of negative pressure would be increased. Also, as shown by Roy and Adami,⁸ a dilated heart does not thoroughly empty itself and this, again, would diminish its suction-power. So that if, as I have endeavoured to show, cases with early diastolic murmur have a dilated left ventricle the murmur cannot be explained by the negative intra-ventricular pressure, as this would be considerably less in such hearts than in those with a left ventricle of normal size. Another great objection to all these views is that they make no attempt to explain why the murmur should only occasionally be

in the early part of the diastole, as such causes would be equally potent in all cases of stenosis. There is, lastly, the explanation put forward by Petit⁹ that the diastolic murmur is only heard when the heart is beating slowly, as then the ventricular systole being more complete the left ventricle is better emptied, and there is therefore a more energetic flow of blood into the ventricle at the beginning of diastole, producing a murmur immediately after the second sound. This connexion between the early diastolic murmur and a slow strongly-beating heart is, however, quite disproved, as mentioned before, by clinical examination, the murmur being rather heard with a failing heart.

For these reasons it seems to me that the suggested causes of this murmur in the early half of the diastole are insufficient. If, as I suggest, this early diastolic murmur is always associated with free mitral regurgitation the explanation is simple. The ventricular systole drives a certain quantity of blood back through the constricted orifice into the already over-distended left auricle and pulmonary veins, and at the beginning of diastole these cavities by their elastic recoil drive some of the blood back through the narrowed mitral valve, thus producing the murmur.

This view of the dependence of the early diastolic murmur of mitral stenosis on co-existing regurgitation thus seems to be supported by some clinical and post-mortem evidence: it affords a simple solution of the mechanism of this rather obscure murmur and also explains why it is only heard in a certain number of cases of mitral stenosis.

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THE ACTION OF THE WATER OF LLANGAMMARCH WELLS ON URIC ACID.

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THE well-known efficacy of waters containing salts of the alkaline earths in the treatment of lithæmia has induced us to record the following observations on the water of Llangammarch Wells which contains the chlorides of barium and calcium in solution.

A man, aged 66 years, who had suffered for many years from symptoms of renal calculus, consulted one of us (Dr. W. Black Jones) in September, 1896. For the past 10 years he had been taking Contrexéville and Wildungen waters, but without relief. In 1895 he began taking the water of Llangammarch Wells, but in the following year was still suffering from the same symptoms. His urine was acid and the specific gravity was 1020. There was no albumin or sugar present, but he passed a large quantity of uric acid crystals. He suffered from obscure pains in the abdomen and had also well-marked signs of osteo-arthritis in the right knee and in the phalanges of the fingers. In May, 1897, he consulted Dr. Lauder Brunton who reported that all the symptoms of calculus had disappeared. Since then his urine has been free from deposit of uric acid, his rheumatism is much better, and his health is generally improved. He has continued to take a glass of Llangammarch Wells water daily.

The success of the above case induced one of us (Mr. Edward Russell) to make the following series of experiments upon himself. As a preliminary the alkalinity of the following waters was tested with a decinormal solution of hydrochloric acid, 20 cubic centimetres of the water being used in each case. It was found that distilled water was neutralised by 0.1 cubic centimetre of acid, tap water (New River) by 0.8 cubic centimetre, and the Llangammarch Wells water by 0.36 cubic centimetre. The direct action of the above waters on uric acid was then tested in the following manner. 250 cubic centimetres of the water with about one gramme of powdered uric acid were kept at 100° F. in a bath for some hours; 20 cubic centimetres of the solution were then taken, filtered, and treated with standard solution of permanganate of potassium. The results, which are denoted by the amount

² Giuffré: Cinquième Congrès de la Société Italienne de Médecine, Octobre, 1892.

³ Brit. Med. Jour., vol. i., 1897, p. 200.

⁴ Text-book of Medicine, vol. ii., p. 74.

⁵ Diseases of the Heart, third edition, p. 132.

⁶ St. Bartholomew's Hospital Reports, 1888, p. 200.

⁷ Diseases of the Heart, p. 532.

⁸ Philosophical Transactions, 1892.

⁹ Charcot's Traité de Médecine, vol. v., p. 250.