ON SUDDEN HEART FAILURE IN TOXAEMIC CONDITIONS,

WITH A SPECIAL REFERENCE TO DIPHTHERIA AND BERI-BERI.

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HAVING had the unusual experience of being in charge consecutively of a comparatively large number of cases of diphtheria and beri-beri, I feel justified in treating of this important subject of sudden heart failure, as it is in these two diseases *par excellence* that degeneration of the heart muscle is so frequent and terrible a cause of death.

Shortly after making a clinical study of the heart condition in diphtheria while in charge of a diphtheria ward at the North-Western Fever Hospital, London, I came out to China, and was especially struck by finding an almost precisely similar heart condition in the beri-beri cases in the Shanghai Municipal Isolation Hospital. And this heart condition, compared with that caused by certain poisons, such as alcohol and arsenic, and associated with certain diseases, such as influenza, typhoid fever, and plague, appears to show a close relationship among many bacterial and chemical poisons in their action on the heart. Inasmuch as the heart is the most sensitive part of the human machine from the point of view of both prognosis and treatment, the subject is an important one and merits close attention.

In both diphtheria and beri-beri sudden heart failure is the most terrible complication, and one in which, as a rule, no treatment is available in preventing death. So marked a feature is this of beri-beri that the Japanese have given the name of "shio-shin" (signifying literally "heart stroke") to this mode of fatal termination; and this connexion with diphtheria—a disease which is also associated with peripheral neuritis—is a suggestive leading motive in etiology. In both these diseases the occurrence of vomiting is almost the invariable herald of a rapid fatal termination by heart failure.

Practically speaking, the main signs met with in heart failure occurring in any of these conditions are vomiting, restlessness, lilac-tinted pallor, dyspnoea, increasing weakness of the pulse, and coldness of the extremities. These symptoms occurring together in diphtheria or beri-beri denote, as a rule, a fatal termination. The syncopal attack is marked rather by duration than by intensity; loss of consciousness is rare. Heart failure may occur in diseases accompanied by neuritis before any skeletal muscular paralysis is obvious, and the usual time for death from this cause to take place appears to be about the end of the first week in diphtheria and towards the end of the first month in beri-beri.

Heart failure in diphtheria and beri-beri is always preceded and accompanied by physical signs of heart muscle degeneration. The heart signs are those induced by weakness of the heart muscle, namely, lowered pulse tension, feeble short pulse wave, feeble heart impulse, short first sound and relatively accentuated pulmonary second sound. The second sound is almost always reduplicated. Reduplication of the first sound is not unusual, and the cause of the cantering rhythm is so frequently met with just before death. Some dilatation of the heart is frequent, but not invariable. The cardiac impulse is usually feeble and, when there is dilatation, diffuse. Not rarely the heart's action is bounding and apparently forcible, but the actual circulatory output, as measured by the pulse, remarkably feeble by comparison, there being a marked difference between the violent over-action of the heart and the small feeble pulse.

Some change in the heart rhythm is invariable; changes in the length of the pauses of the heart cycle being frequent and of great importance in prognosis. Most common is a shortening of the long pause, giving rise to spacing of the heart sounds. The relative shortening of the long pause may be of all degrees up to "tic-tac" rhythm, where the short equals the long pause, so that the heart sounds are equidistant. The change in the relative length of the two pauses is almost always accompanied by a change in the character of the sounds, the first sound becoming like the second in quality, losing its deep so-called muscular sound, and making more audible the valvular sound, which resembles the ordinary valvular second sound. In this way the two sounds and the two intervals tend to become alike. This "tic-tac" rhythm, caused by the shortening of the long pause—the recuperative intervals, indicates diminished cardiac recuperative power, and prognosticates danger ahead—danger of heart-

failure. But of worse prognosis is that condition, where in addition to the long pause being shortened, the short pause is likewise shortened, so that the second sound follows very closely on the first. This condition is almost always a fatal sign, and occurs with or may be followed by heart failure.

A condition characterized by what may be termed delayed beats or "tumbling rhythm," is a common form of irregularity of the heart's action both in diphtheria and beri-beri. After a series of regular heart beats a pause occurs, followed by a sudden scramble of two or more heart beats, in order, as it were, to make up for lost time. This gives rise to an intermittent pulse, because all the beats do not reach the wrist.

Analysis of 500 Cases of Diphtheria with Regard to Fatal Heart Failure.

Fatal cases	...	...	...	80
Pulse tension lowered	...	...	...	446
Dilatation of the heart	...	...	...	11
Cases dying of heart failure	...	...	...	30
Of these, vomiting was associated in	...	...	...	27
Well-marked dilatation of heart in	...	...	...	3
Cases dying of heart failure before the onset of paralysis	...	...	...	22
Average day of the disease on which death took place in these cases	...	...	...	9.3
Cases dying of heart failure after the onset of paralysis	...	...	...	8
Average day of the disease on which death took place in these cases	...	...	...	28
Average day of the disease on which paralysis was first detected...	...	...	...	15.4

Analysis of 341 Cases of Beri-beri.

Fatal cases	...	...	...	72
Cases dying of rapid heart failure	...	...	...	31
Pulse tension lowered	...	...	...	254
Dilatation of the heart	...	...	...	98
Second sound reduplicated	...	...	...	245
First sound reduplicated	...	...	...	35
Long pause shortened	...	...	...	48
Short pause shortened	...	...	...	42
Cardiac murmur	...	...	...	84

DILATATION OF THE HEART.

Signs of dilatation of the heart were present in 11 out of 500 cases of diphtheria, and in 98 out of 341 cases of beri-beri. The comparative infrequency of dilatation in diphtheria may be due to the low arterial pressure which obtains; though the heart wall is degenerate and yielding, the blood pressure is insufficient to cause dilatation. In beri-beri, however, the process is a less acute one than in diphtheria, and though the toxin produces similar changes in the heart muscle, it acts through greater periods of time, causing more cardiac wear and tear.

The special effect of both beri-beri and diphtheria on the heart is to produce a marked diminution of force leading to defective arterial pressure, hence the low tension pulse and the frequency of syncopal attacks.

The degree of dilatation can be best measured by percussion of the deep cardiac dullness; the superficial cardiac dullness merely shows how much of the surface of the heart remains uncovered by lung and is no index of its actual size. Dilatation of the right auricle may be easily detected by percussion of the fourth right interspace and of the right ventricle by palpation of the epigastric region. It is, however, the dilatation of the left ventricle which causes the urgent danger of death from syncope, and neglect of this indication may cost the patient's life.

CHANGES IN THE HEART RHYTHM.

Changes in the heart-rhythm may be summarized as follows:—

1. Shortening of the long pause giving rise to spacing of the heart sounds or "tic-tac" rhythm.
2. Shortening of the short pause, the second sound following the first rapidly—a sign of grave import.
3. Lengthening of the long pause, causing infrequent heart beat and slow pulse.
4. Laboured over-action or excited action of the heart—a condition of irritable weakness where there is much show of force, but little circulatory result.
5. Delayed "heart-beat" occurring at rhythmic intervals, and giving rise to intermittent pulse: "Tumbling action" of the heart. "Hesitating heart" being a slight form of this.
6. Irregularities in force and frequency apart from above.
7. Reduplication of heart sounds, especially of the second sound. "Cantering rhythm," usually from reduplicated first sound—a fatal sign.
8. Murmurs.

The frequency of the heart's action in both beri-beri and

diphtheria is almost always above normal, and, as a rule, the lower the arterial tension the greater the frequency; but in beri-beri, as is found in some cases of diphtheria in adults, the pulse may occasionally be very slow.

In both diphtheria and beri-beri the second sound is almost always reduplicated. "Cantering rhythm" may occur, caused either by reduplication of the first or second sound; but more frequently by an apparent doubling of the first sound and nearly always accompanied by dilatation, and leads to a fatal termination.

The mechanism of the common heart changes is generally easily explained by weakness of the heart muscle. "Spaced rhythm" is caused by the shortening of the long pause or recuperative interval and leads to a vicious circle being established. The heart is weak, and is rendered still more so by diminished recuperative rest. The condition, therefore, leads to the still worse condition where the short pause is shortened, the second sound following the first sound more quickly than normal, due probably to the heart being brought up short by the resistance in front of it in the arterial system. The condition thus tends to go from bad to worse, and, as in the heart, it is "all or nothing." A stage is reached when the circulation can no longer be maintained, and the heart ceases function suddenly—sudden heart-failure, the "shio-shin" of the Japanese (literally "heart-stroke").

Murmurs are frequent, and are possibly due to some yielding of the mitral or tricuspid curtains, yet most usually come under the category of so-called "haemic murmurs."

CONCLUSIONS FROM CLINICAL OBSERVATIONS.

Heart failure may occur prior to any manifestation of disturbed innervation. As in diphtheria, so in beri-beri, heart failure often supervenes before any paralysis has appeared; about the end of the first week in diphtheria, towards the end of the first month in beri-beri. The cardiac muscle is the prime factor in the circulation. The heart, in contradistinction to the skeletal muscles, partakes of the nature of an automatic mechanism, though influenced through the vagus and sympathetic nerves. No extra-cardiac trophic nerve to the heart is as yet known. To attribute heart failure in beri-beri or diphtheria to a neuritis of the vagus is alike unnecessary, inadequate, and unproved.

To a certain extent heart failure and changes in the rhythm occur in other acute specific diseases which do not commonly produce peripheral neuritis, such as typhoid fever, influenza, plague, and acute rheumatism. In these and in arsenic and alcohol poisoning a somewhat similar condition of the heart is found *post mortem*, as in beri-beri and diphtheria, namely, one of parenchymatous degeneration of the heart muscle. To explain the unusual frequency of heart failure in beri-beri and diphtheria it is necessary, therefore, to establish that the degeneration of the heart muscle is more marked in these than in other toxin diseases where the heart degenerations are produced. Necropsy does establish this. That the toxin of diphtheria has a special predilection for heart muscle is also borne out by experiments on animals. Alcohol is another toxin, the product of a micro-organism, which produces peripheral neuritis, and has a specific degeneration action on the heart muscle. Some cases of alcoholic neuritis with dilated heart and oedema are almost indistinguishable from beri-beri, and death may take place from sudden heart failure. In arsenical neuritis also death not infrequently takes place from sudden syncope, and localized oedema has been described.

Muscle is less resistant and therefore more quickly acted upon than nerve, and hence the heart changes occur as a rule at an earlier date than nerve degenerations. The results of muscle degeneration through direct action of the toxin manifest themselves before those of muscle degeneration, the secondary result of trophic nerve change.

The suddenness of the heart failure does not, however, indicate a sudden lesion. In an involuntary muscular organ like the heart it is "all or nothing." Either it acts with sufficient force to maintain the circulation, or it ceases altogether, and often suddenly. The stoppage of the heart, though sudden, may therefore be really due to a gradual accumulating weakness, and this is borne out by clinical experience. That the heart failure, also, is not due to a general loss of vitality, but rather to a specific effect on the heart itself, is evident from the marked distinction between the condition of the heart and the comparatively good general, physical, and mental condition, even a short time before death from heart failure.

In conclusion, the circulatory physical signs point to a

weakness in circulatory power, due to primary degeneration of the heart muscle.

POST-MORTEM CONFIRMATION OF CONCLUSIONS FROM CLINICAL OBSERVATIONS.

Sidney Martin has shown² that the diphtherial albumoses produce an advanced degree of fatty degeneration in the heart muscle, and he was unable to find any degeneration in the vagus nerve. Mott³ found fatty degeneration of the heart muscle in each of four cases of diphtheria paralysis which he examined, but in only one of them was there degeneration of the peripheral nerves. Peyton⁴ has recently published a comparative study of the condition of the heart wall in diphtheria and rheumatism respectively, and has described very marked degeneration of many of the cardiac muscle fibres, and complete destruction of some parts of them. Mott and Halliburton,⁵ by making an alcoholic extract of the blood of a beri-beri case, filtering, evaporating to dryness at 40° C., dissolving the residue in normal saline, and injecting into the jugular veins of an anaesthetised cat, showed that the blood contained a substance which, like choline, produced a fall of arterial pressure, slowing of heart's action, and dilatation of heart. The beri-beri case was found *post mortem* to show extensive degeneration of the peripheral nerves and fatty degeneration of the muscles, including the heart. The substance in the blood therefore resembling choline may have been rather a product of this fatty degeneration.

Giacomelli⁶ has made a series of experiments on animals with the object of ascertaining the changes in the myocardium produced by various toxin diseases and poisons. More or less marked alterations were constantly seen, for the most part confined to the heart muscle itself, sometimes, but rarely, affecting the interstitial connective tissue or the vessels. The changes in the connective tissue were generally associated with the presence of micro-organisms and consisted of diffuse lymphoid infiltration. There was no causal relationship between the changes in the connective tissue and vessels and those in the heart muscle; the two existed independently. The changes in the heart muscle varied from simple atrophy to fatty degeneration and destruction. There were no definite anatomical lesions corresponding to definite specific poisons. The changes were due to the direct action of the bacterial toxin and poison on the muscle fibre itself, and were sufficient in themselves to cause cardiac failure.

The heart of a case of diphtheria dying by cardiac failure is to the naked eye usually flabby, soft, pale, wanting in lustre, and in sections it often has a greyish colour. Punctiform haemorrhages are common in the visceral layer of the pericardium and pleurae.

On teasing out the muscle under the microscope there may be seen small albuminous granules varying in size, which are insoluble in ether but swell up and become almost invisible on being treated with acetic acid, and they may be so abundant as to conceal the striation of the muscle.

The degeneration is usually general and uniformly distributed through the heart. This granular albuminous degeneration may be associated with the formation of fat globules, which are soluble in ether and brought out by osmic acid solution. Sometimes fatty degeneration only is seen and appears to be a later stage of the granular albuminous degeneration. Sometimes granular degeneration is seen which in certain parts has gone on to fatty change. While the granular degeneration is usually general, the fatty degeneration is more often patchy. Fragmentation of the contractile substance of the muscle is frequently seen.

The importance of the clinical evidence of heart degeneration lies in the fact of the warning it gives and the possibility of preventing the onset of heart failure by an unusual degree of care, with the object of saving the labour of the heart as much as possible.

Cardiac failure is undoubtedly the commonest cause of death in beri-beri and diphtheria, and this clinical association of beri-beri with diphtheria, influenza, alcoholism, and arsenic poisoning give an important etiological clue, which, in association with ergotism, pellagra, and lathyrism, it is proposed to closely follow.

CONCLUSIONS.

1. Beri-beri and diphtheria have a marked degenerative action on the heart muscle, which frequently causes fatal circulatory failure.
2. In this respect beri-beri and diphtheria resemble other toxæmias such as influenza and alcohol and arsenic poisoning.

which often cause peripheral neuritis, and also other toxæmic diseases, such as typhoid fever, plague and acute rheumatism, which do not or rarely give rise to peripheral neuritis.

3. Beri-beri and diphtheria are the diseases *par excellence* in which sudden fatal heart failure occurs.

4. The heart-muscle degeneration is not a secondary result of neuritis of the vagus.

5. The heart-muscle degeneration takes place as a rule before skeletal-muscle degeneration and is the result probably of direct action of the toxin and not a secondary result of nerve change.

6. Sudden heart failure does not indicate a sudden lesion, but rather is the result of a gradually-increasing heart weakness from cardiac-muscle degeneration, which may be precipitated by any sudden exertion, but more frequently is the result of the principle of "all or nothing," the transition from "all" to "nothing" being necessarily rapid.

7. The cardiac physical signs in beri-beri closely resemble those found in diphtheria and are of paramount importance in prognosis and treatment.

REFERENCES.

¹ Metropolitan Asylums Board Report, 1897, p. 180. ² *Goulstonian Lectures*, 1892. ³ *Croonian Lectures*, 1900. ⁴ *Lancet*, May 12th, 1900. ⁵ *BRITISH MEDICAL JOURNAL*, July 29th, 1899. ⁶ *Il Policlin.*, an. viii, f. 3, 4.

A CASE OF COMPLETE OPHTHALMOPLÉGIA OCCURRING DURING WHOOPING-COUGH.

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THE following are brief notes of the case:

J. B., a little boy, aged 4 years, was suffering from an attack of whooping-cough. Being of a particularly lively and mischievous disposition, his mother was surprised when he awoke one morning particularly subdued, unsteady in his walk, and only too willing to lie down. I saw him the day these symptoms appeared (March 9th), and noticed that there was ptosis of both eyes; the pupils were dilated, and failed to react to light or accommodation; there was a slight divergent strabismus; the child was perfectly conscious and extremely irritable. There was a bruise about the size of a florin on the forehead above the bridge of the nose, which the mother said was not due to a blow, and which she had only noticed that morning.

In two or three days' time he began to get about again, keeping the right eye closed or covered with his hand. In ten days' time the strabismus had disappeared, and with it the ptosis. The eyeballs appeared slightly protruded, and it became quite evident that the orbital muscles in both eyes were paralysed.

The fundi were normal, and the patient could evidently see fairly well except in a very bright light, although he occasionally made "bad shots" when reaching for anything he was playing with.

On April 5th he was taken to see Mr. Charles Higgins, who kindly wrote to me about the case. He expressed a doubt, after seeing my notes, as to the etiology, and gave a favourable prognosis.

The occurrence of acute nuclear paralysis, from whatever cause, is so remarkable and sufficiently uncommon to warrant recording. Occurring, as in this case, during an attack of whooping-cough, the interest is heightened.

Whether the case is to be rightly regarded as a complication of the disease, or a mere coincidence, or due to an attack of diphtheria occurring at the time or before the commencement of the whooping-cough it is difficult to determine. In the literature at my disposal I am unable to find any such complication of whooping-cough noted, which is the more strange in such a common disorder.

That such paralyzes of the orbital muscles sometimes follow an attack of diphtheria is well recognized. It is true this may have been the cause, but if so the disease was not clinically recognizable nor even suspected, and it is certain that no other member of the family, in a family of small children, suffered.

The mode of onset, too, was so sudden as to probably not warrant this supposition. I am inclined to regard the attack as one of acute inflammation in the nuclei, possibly accompanied by some hæmorrhagic lesion due to straining during a paroxysm of coughing, and akin to the process which produces acute anterior poliomyelitis, the child, as in this case, except for the cough, going to bed quite well and waking in the morning with the paralysis.

Two other children suffered at the same time from whooping-cough, but except that one had convulsions, there were no complications. I regret that no examination was made for the Klebs-Loeffler bacillus, but even this may not have been final, as it is said to occur sometimes in the throats of apparently healthy persons.

ACUTE RHEUMATISM: FIVE CASES OF APPARENTLY DIRECT INFECTION.

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IN THE *BRITISH MEDICAL JOURNAL* of August 8th last there is an interesting article by Dr. Turner, Nantwich, on three cases of acute rheumatism of apparently infective origin. I ask the courtesy of your pages for the insertion of particulars of five cases, and a probable sixth, of the above-mentioned disease occurring in or near one house, with intervals of from a few days to one week of each other, and in one family.

The first to suffer was the eldest son, aged thirty years, who came into town from his home, thirty-two miles distant, and was treated by Dr. N., who diagnosed acute rheumatism and treated him accordingly.

The second eldest a few days after complained in a similar manner and was at once brought to town by his mother and placed under the care of Dr. H., who diagnosed acute rheumatism and treated it in the usual way. His mother, contrary to the doctor's orders, to save expense returned home two days after with this son, although, as Dr. H. afterwards told me, he had a temperature 103° F.

About a week after his return I was wired for to go out at once to him as he was very ill. On arrival I found him suffering from acute rheumatism complicated with right pneumonia and pericarditis, temperature 103° F., and rising, delirious, and altogether in a bad way. I gave a grave prognosis, and prescribed suitable treatment.

The eldest daughter now presented herself for examination as she had been ailing for two days with pain and swelling in the joints, feverishness, loss of appetite, sleeplessness. As her temperature was 102° F. I ordered her to bed and prescribed salicylates with success, and she got all right in two weeks' time.

Three days after my visit I received a second hurried wire to visit the second boy, and on arrival found him dead, he having no doubt succumbed to pneumonia and heart trouble. Now the fourth and fifth cases presented themselves in the father and youngest son, both suffering similarly to the other members of the family. I ordered their removal to the hospital, where they are now being treated by Dr. N. for acute rheumatism.

A week later I received a wire to visit Mrs. C.'s eldest daughter who lived about half a mile from her parents, and on arrival found she had been confined a week, and was now suffering from pains in her joints, feverishness, rigors, almost complete cessation of lochia, cessation of milk. She had been a regular visitor up to her confinement at her parents' house. I could detect no evidence of puerperal fever, beyond a rise of temperature. I prescribed salicylates with success, and in a week's time she was able to go about her work. I have not included this last case, but merely mention it as being one probably of acute rheumatism.

The first case, who had now returned home as cured, consulted me for a return of his complaint, so diagnosing a relapse I ordered his removal to hospital, where he is now under the treatment of Dr. N.

That the diagnosis in the above cases could not be well wrong must be admitted, as all of them, with one exception, have been examined by two independent medical men, and some by three. Also, mere coincidence where so many cases have occurred could scarcely be thought of, and damp, cold weather could certainly not be assigned a cause as we are now suffering from a most disastrous drought in the colony. Therefore to my mind the only solution as to the cause is: direct conveyance from one patient to the other.

CHARITABLE BEQUESTS.—The late Mr. Charles Samuel, of Sutherland Avenue, Maida Vale, in addition to numerous other charitable bequests, has left £500 to the London Hospital, and £200 each to St. Mary's Hospital, the Metropolitan Hospital, the Royal Free Hospital, the City of London Hospital for Diseases of the Chest, Victoria Park; the National Hospital for Diseases of the Heart and Paralysis, Soho Square; the North London Consumption Hospital at Hampstead and the Earlswood Asylum for Idiots.—Under the will of the late Mr. Henry Brooke, of Huddersfield, £1,000 has been bequeathed to the Huddersfield and Upper Adbrigg General Infirmary.