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HONGKONG.

A RESEARCH

INTO THE

ETIOLOGY OF BERI-BERI

TOGETHER WITH A REPORT ON AN OUTBREAK IN THE PO-LEUNG-KUK,

BY

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1.—INTRODUCTORY LETTER.

HONGKONG, 29th December, 1905.

SIR.—We have the honour to forward, for the information of His Excellency The Governor, the following Report on our Researches into the Etiology of Beri-beri.

Beri-beri is a disease which is widespread in the Colony of Hongkong, and like many other disorders of widespread distribution is responsible for enormous national loss from an economic standpoint. A disease, occurring as it does in human beings during the most strenuous and wage-earning period of life, becomes of serious importance in a community like our own, where our commercial prosperity is largely dependent on the momentum for labour bestowed on it by the Chinese coolie who, unfortunately, is only too frequently its victim. Its importance from this point of view, as well as its power of rendering helpless many of the hard working natives of several of our prosperous Colonies, is at once apparent to any one sufficiently interested in the voluminous literature on Beri-beri and the numerous scientific memoirs published by eminent investigators belonging to the many unfortunate commissions which have been organised with the view of elucidating its etiology, and instituting measures likely to stay its march amongst the Oriental population.

3. In Hongkong where Beri-beri manifests its presence by the occurrence of the severest as well as the most chronic varieties of the disorder, opportunities for a careful study of the disease are obviously many. It was therefore considered that an investigation into the obscurities of Beri-beri as met with in Hongkong might well repay the labour of an earnest research. With a Bacteriologist in the Colony well equipped with scientific apparatus and a laboratory, and the assistance of another Medical Officer, the disease could be investigated fully from all points of view. Accordingly on arrangements having been made with the Government to start such an investigation, we drew out a plan of research, which appeared to us to afford the greatest hope of success in elucidating the etiological factor of the disease.

4. Our plan consisted of a thorough revision of the already known facts regarding the clinical and pathological features of the disease, accompanied by a searching investigation into the bacteriological side of the question and the carrying on of animal experiments on a hitherto unequalled scale.

5. For the opportunities afforded us in making these experimental researches a success our sincere thanks are due to the munificence of the Government and the ever-helping hand of the several Medical Officers of the Medical Department. Without such assistance the following Report could not have been made so complete and convincing as regards certain points of great importance in its etiology.

6. Further, considerable delay has been occasioned in the completion of the Report, our aim being to gather as much information together as possible, and to reconsider and verify many of the conclusions which had been collected by us during the earlier stages of our investigations.

7. Our actual research work commenced in the month of September, 1904. This date was chosen as one particularly favourable for a general consideration of the disease from all points of view, owing to the prevalence of a sharp but short outbreak of Beri-beri among the inmates of the Po Leung Kuk.

8. Previous to this date a considerable amount of work on Beri-beri was constantly being prosecuted at the Public Mortuary, where annually 400-500 cases of the disease are examined post-mortem and records of the most noteworthy features kept for reference. In addition to this, the bacteriology of the Beri-beri cadavers was studied from time to time. The results of these annual observations are embodied as far as possible in this Report.

9. With the advent of the outbreak of Beri-beri in the Po Leung Kuk our studies commenced, and the research was started from every point of view. The inmates of this Institution were removed and segregated, and their clinical condition noted daily. The treatment of these cases, as well as the prophylaxis against its further prevalence, is given in the preliminary part of our Report.

10. Subsequently the Institution was placed at our disposal, and with a little assistance the Po Leung Kuk was soon converted into an excellent experimental compound with the virus of the disease presumably working in the immediate vicinity.

11. Furthermore, the inmates of the Tung Wah Hospital suffering from Beri-beri were also at our disposal, and had it not been for the generous supply of cases the material used for our bacteriological and experimental researches would have suffered much depreciation.

12. We feel that we are deeply indebted to the Directors of the Tung Wah Hospital and the Po Leung Kuk respectively for the assistance they gave us in our work and the free access to, and utilisation of, the cases they afforded us.

13. The first part of this Report deals with the outbreak of Beri-beri in the Po Leung Kuk : the next part treats of certain points in the disease as regards its incidence with reference to (1) Age, (2) Sex, (3) Occupation—its diagnosis, prognosis, and treatment, etc.

14. The pathological section of the Report deals fully with the gross anatomy of Beri-beri cadavers. The œdematous and atrophic forms are dealt with under separate headings, and are presumably clear enough to afford one a picture of the morbid anatomy. The microscopic anatomy has not been investigated to any great extent. The literature on this question alone is voluminous, and so far investigation along these lines have led to no advance regarding the causation of the disease. The descriptions given recently by HAMILTON WRIGHT, MOTT and others are sufficiently extensive and minute to gratify even the most curious of pathologists.

15. The most interesting feature of this part of the Report is the question as to the presence of a primary lesion in Beri-beri. Medical papers at the present time are full of Beri-beri, and one of the most widely discussed questions in this connection is whether there exists in Beri-beri *a primary gastro—duodenitis, the premonitory syndrome of Hamilton Wright.* According to our results such a lesion does not exist. Gastric and duodenal changes, and indeed occasionally changes of variable pathological degree of the entire small gut are often found in Beri-beri cadavers. *These* however *do not appear to be primary and the seat of primary election of the so-called virus of Beri-beri.* Congestions, hœmorrhages, œdematous infiltrations and even patches of necrosis have often been found in the gastro-duodenal mucosa, but that these are due to the actual Beri-beri virus we have reason to doubt. Microscopically the changes found are difficult to class with active inflammation as found in diphtheria. They resemble more closely the changes consequent upon passive hyperæmia and congestion set up by precedent nerve degeneration. Arguing, a posteriori, little weight is to be given to the changes found in the alimentary canal, and our observations in this respect are more or less in accord with the recent investigations of DURHAM who lately studied Beri-beri in Christmas Island and the Federated Malay States.

16. The bacteriological investigations which have been made during the research were many, and of a varied character. Almost every tissue and fluid of the bodies of cases of Beri-beri have been submitted to a searching examination by almost all the methods available for the isolation of specific micro-organisms. On referring to this part of the Report in detail, it will be seen that we *found it impossible to find any micro-organism which could be brought into causal relationship with the disease.* Again and again cocci, bacteria, etc., could be obtained from Beri-beri patients or fresh cadavers. These were of the same nature as the micro-organisms isolated by other workers. Detailed bacteriological work and experiments proved, however, that such micro-organisms have nothing to do with the

production of the disease, and in the light of our present micro-biological knowledge must be regarded as extraneous organisms isolated and fully described by investigators using somewhat defective technique.

17. The bacteriological examination of WRIGHT's so-called primary lesion, *i.e.*, damaged gastro duodenal mucosa resulted in the isolation of many rod-shaped bacteria, the biology of which shewed them to be nothing more or less than ordinary intestinal micro-organisms. In summing up our bacteriological results, our investigations strongly point to the conclusion that *Beri-beri is not due to any micro-organism of the hitherto described types.* Indeed *we doubt if the disease is an acute specific infectious disorder.* So far our results are against its being so.

18. Coming to the experimental part of the Report, the results of our attempts to induce the disease in any of the common domestic animals are decidedly a failure. In no single instance, out of over 50 miscellaneous experiments upon monkeys, pigs, calves, sheep, fowls, rabbits, etc., were we able to call forth even the shadow of a symptom or sign of Beri-beri.

19. Comparing the results of these experiments with the series carried out by DURHAM who also had negative results, it would appear that it is impossible to convey Beri-beri directly from man to animals. So far as published records are concerned, monkeys are the only animals which appear to have contracted the disease, and then only under natural conditions. These—the experiments of HAMILTON WRIGHT and published in a recent number of "Brain"—however, are isolated observations, and judging from the recent remarks of DURHAM in the "Journal of Hygiene" some doubt would appear to exist as to the real condition of the monkeys described by WRIGHT as suffering from Beri-beri.

20. The question as to whether any animal can contract Beri-beri direct from man, or indirectly through some other channel must remain open. Our own opinion is decidedly against the conveyance from man to animals. With the exception of HAMILTON WRIGHT's experiments which must be received with due caution, *there are no reliable records of Beri-beri in animals.* Indeed it would be difficult to experiment along these lines with hope of success in the absence of the etiological factor and its point of invasion of the body.

21. Our experimental researches bring us further along the line of our conclusions as to the non-micro-organismal nature of Beri-beri. Up to the present time none of our researches have guided us to form a conclusion that it is a specific infectious disease. Indeed all the evidence contained in this Report is against such a conclusion.

22. The premises upon which we built up such a statement so antagonistic to the theories of HAMILTON WRIGHT are the following:—

(*a.*) There is no evidence of a primary lesion, *i.e.*, a point of invasion of the virus into the body. This however carries with it little weight as many specific infectious disease have a somewhat cryptogenous point of entry into the human tissues.

(*b.*) No specific micro-organisms can be found in any organ or tissue of any case of Beri-beri which can be brought into close causal relationship with the disease. The micro-organisms found in WRIGHT's so-called primary gastro duodenitis are to be regarded as ordinary bacteria belonging to the intestinal flora.

(*c.*) Experimental researches are negative. The blood contains no organisms and the transference of large quantities of Beri-beri blood to the tissues of healtly animals never induces disease.

Similar results are obtainable with the spleen, liver, brain, etc.

When we come to the gastro duodenal mucosa as found in acute and rapidly fatal cases of Beri-beri and use an emulsion of this for feeding monkeys—animals said by WRIGHT to contract Beri-beri naturally—and obtain uniformly negative results, our faith becomes somewhat shaken in the micro-organismal nature or the specific infectivity of Beri-beri.

23. In conclusion, the results of our researches are directly opposed to those of HAMILTON WRIGHT, and in more or less harmnoy with those of DURHAM.

24. Of late years a considerable diversity of opinion would appear to prevail as to the isolation of Beri-berics and the treatment of Beri-beri cadavers. From our researches we can see no valid reason to suppose that in Beri-beri we are dealing with a highly infectious disease. Indeed beyond the removal of such patients to surroundings light and airy, with the regulation of a liberal and wholesome diet nothing more would be required to add to the sum total of the necessary sanitation.

As regards the burial of Beri-berics, this, in our opinion, is of no vast importance apart from the question of the decomposition of the body. If provision during burial is made for rapid decomposition, as now laid down by all hygienists, no danger will accrue.

25. Having summed up the results of our investigations into this interesting disease it but remains to speculate on a theory as to its etiology. In these days everyone strives to have a theory in regard to the etiology of a disease like Beri-beri. Whether such a course is advisable, in the absence of any definite data, we leave open for speculation.—We have, etc.,

W. HUNTER,
W. V. M. KOCH.

The Hon. The Principal Civil Medical Officer.

2.—AN OUTBREAK OF BERI-BERI IN THE PO LEUNG KUK.

About the middle of the year 1904 a slight outbreak of Beri-beri occurred among the inmates of the Po Leung Kuk. This is an institution situated in the midst of the Chinese quarter of Victoria, Hongkong, and is intended for the reception of women and girls who are suspected to have been kidnapped or to have been brought into the Colony for immoral purposes, or who may for some other reason require protection. They are detained here until enquiries are completed regarding their case, and are then released. Owing sometimes to difficulty in these investigations it may happen that the detention of some of the inmates, and indeed it may be of most of them, is prolonged for months. Thus the number in residence may reach a high figure, on one or two occasions amounting to 92.

The Buildings.

The main building consists of a solidly built brick and stone building two stories high, opening on to a narrow courtyard about 10 feet wide, and guarded by a high wall. The upper two stories are used as dormitories, of which there are two on each floor; the ground floor is occupied by two rooms, one used as a dining-room, the other as a day-room, and a small kitchen and a lavatory. The dormitories are large, high rooms opening by doors on to a narrow verandah on the inner side over the courtyard, and on the outer side built solidly up to the roof. High up from the floor and beyond reach of the inmates, small windows are let in, well guarded. At right angles to this building and facing another street is an annexe containing two large dormitories, one above the other. Although these open on to the street they are dark and cheerless rooms.

During the months that this outbreak prevailed the population was dense. We find on examining the Register that the population varied during each month in the following manner:—

In January there were resident from:—	37—53
February,	37—52
March,	40—63
April,	46—59
May,	43—74
June,	47—65
July,	62—75
August,	51—92
September,	37—61
October,	49—64
November,	51—65
December,	48—63

Measurement of Rooms.

The following measurements have been courteously supplied us by the Medical Officer of Health:—

Room I. Ground floor—

Floor area, 401 sq. ft.
Cubic contents, 5,654 cub. ft.
Window area (courtyard), 72 sq. ft.
Do. (street), 28½ sq. ft.

Room II. Ground Floor—

Floor area, 327 sq. ft.
Cubic contents, 4,683 cub. ft.
Window area (courtyard), 48 sq. ft.
Do. (street), 19 sq. ft.

Room I. First Floor. Dormitory—

Floor area, 528 sq. ft.
Cubic contents, 6,441 cub. ft.
Window area (front), 90 sq. ft.
Do. (back), 45 sq. ft.

Room II. First Floor. Dormitory—

Floor area, 522 sq. ft.
Cubic contents, 6,375 cub. ft.
Window area (front), 90 sq. ft.
Do. (back), 45 sq. ft.

Room I. Second Floor. Dormitory—

Floor area, 526 sq. ft.
Cubic contents. 6,683 cub. ft.
Window area (front), 90 sq. ft.
Do. (back), 45 sq. ft.

Room II. Second Floor. Dormitory—

Floor area, 523 sq. ft.
Cubic contents, 6,649 cub. ft.
Window area (front), 90 sq. ft.
Do. (back), 45 sq. ft.

Room I. Annexe. Dormitory—

Floor area, 902 sq. ft.
Cubic contents, 8,305 cub. ft.
Window area, 223 sq. ft.

Room II. Annexe. Dormitory—

Floor area, 902 sq. ft.
Cubic contents, 8,020 cub. ft.
Window area, 223 sq. ft.

Ventilation.

All the rooms of the main building open out on to the verandahs which overhang the small narrow courtyard, the wall on the other side of which rises to a level with the floor of the second story. Small windows are let into the wall rising on the street The annexe has a verandah on each floor facing the street. These are closely barred and give on to a courtyard which serves as a waiting-room for the out-patients of the Tung Wah Hospital, which is also shut in by a high wall. The other side of these dormitories of the annexe consists of a solid wall, having a door at the southern end. As these buildings are placed among a crowd of others, many of which overshadow them in height, and narrow streets bound them on two sides only, scarcely ever does a good breeze blow through them, nor are the means of ventilation sufficient. To this may be added the fact that owing to the plan of construction and the surroundings the sun's rays never seem able to penetrate beyond the courtyard. They certainly do not flood the rooms, they scarcely ever reach them. When the sun shines highly in Hongkong it may be able to warm and to purify the air that reaches the Po Leung Kuk, but when the weather is wet, and the days dark, moist and gloomy, these rooms present a dismal and cheerless appearance which indicates a vitiated atmosphere, and suggests a nidus of disease. And such days in Hongkong are not remarkable for their rarity during some parts of the year.

The Beginning of the Outbreak.

On May 14th, two of the inmates, aged respectively 19 and 18 years, complained of numbness in the legs, weakness and difficulty in walking. They were examined and were found to be suffering from Beri-beri, and were transferred for treatment to the Tung Wah Hospital. The first had been in residence from April 22nd,—23 days: the second from March 14th,—62 days. Then a lull of a little more than a fortnight occurred, and two more were attacked—they had been in residence since the previous November. Then four more were attacked in June—on the 4th, 6th, 16th and 23rd. They had been in residence from three to two months.

Preventive Measures adopted.

These cases having occurred, though they only numbered eight up to now, led to measures being taken for the thorough and complete disinfection of the buildings. This was carefully done by the staff of the Sanitary Board, and the walls were completely lime-washed thereafter, and the floors scrubbed with a solution of strong carbolic acid.

Inefficacy of these Measures: Spread of the Disease.

These measures did not prove effective, for after 25 days cases began to break out again, and apparently followed each other with some rapidity. Four cases occurred in July—on the 17th, 19th, 25th and 31st. In August fourteen cases occurred—two on the 9th, seven on the 15th, and five on the 30th. In September three cases occurred on the 7th, two on the 19th, and one on the 27th. Then there was a lull.

Further Steps to stay the Outbreak.

Early in September this outbreak was represented to the Hon. The Principal Civil Medical Officer, and its gravity pointed out. Upon his recommendation His Excellency The Governor was pleased to appoint us a Commission to investigate this outbreak, and also to make such investigations into the disease as might tend towards elucidating certain points, notably its causation. On our recommendation the Committee of the Po Leung Kuk conferred with the Committee of the Tung Wah Hospital, and were able to arrange to transfer all the inmates from the former to the latter institution, where they were accommodated in two large airy well ventilated and sunlit wards. Upon this transfer taking place the premises of the Po Leung Kuk were handed over to us for purposes of investigation. On the completion of the greater part of the experimental portion of our work, the building was again disinfected on three several days, was lime and colour—washed, painted, and then handed over for occupation.

Symptoms of the Disease.

The disease as it affected these patients was of a very mild nature. The earliest symptom noticed was numbness of the legs, which generally extended from the dorsum of the foot upwards as high as the knee. The numbness was seldom evenly distributed, and did not always exactly follow the distribution of the cutaneous nerves of sensation. Soon after this, or almost coincident with its onset, there occurred pain and tenderness on pressure over the calf muscles, and then weakness of the legs set in. This was of varying degree, in some cases shewn only by slight difficulty in walking, in others reaching such an extreme degree as to render the patient completely bedridden. Between these extremes there occurred almost every degree of interference with locomotion. In the slighter degrees there was only slight paresis of the calf muscles—in the severer cases there was paralysis leading to ankledrop. Together with this there was loss of ankle clonus, and generally in all the cases loss of knee-jerk. The muscles of the thigh sometimes manifested tenderness on pressure. Generally there was some œdema perceptible over the tibia, but this seldom reached any great degree. In three cases there was some numbness over the hands and fingers. Apart from these cases the upper extremities did not shew any sign of being affected, nor was any part of the trunk affected. The weakness in the legs which the patients complained of was noticeable in the gait. Where the weakness was slight she would shuffle along planting the feet somewhat widely apart and taking deliberate steps, watching the floor carefully to avoid a fall. In more severe cases she would try to obtain assistance by guiding herself along the wall, or by holding on to the bed. In still more severe cases she would use one or two crutches, and the steps would be taken with an equine, high-stepping gait, the legs being helpless and out of control—resembling a pair of flails—and planted with care and deliberation though accompanied with some amount of inco-ordination. The action now was practically only confined to flexion of the thigh by the Psoas and Iliacus muscles. In the worst cases—and there were only four such—the patients were completely bedridden, and apparently to them only remained the power of flexion of the thigh on the abdomen. In such cases the accompanying anæsthesia was profound and extended as high as the groin.

Sometimes tingling and formication were present, and muscular tenderness was invariably present. Rapid wasting of the leg and thigh muscles occurred, together with loss of subcutaneous fat leading to a loss of rotundity and symmetry of the limb, and to a flabby "hanging" condition of the muscles. Appreciation of heat and cold was always present. In two cases the nerve symptoms were ushered in by a slight elevation of temperature which lasted a few days, and which was never of high degree. These were the only cases in which any elevation of temperature was present: in all the other cases the temperature remained steadily at the normal or perhaps may have varied about half a degree (Fahrenheit) above and below the normal. The digestive system in this series of cases was seldom deranged—the tongue was generally clean, the action of the bowels normal, the function of digestion performed normally, and there was no vomiting. As regards the circulatory system there was nearly always some cardiac debility, and in a few instances this was associated with a slight amount of dilatation of the cavities of the heart. There were no murmurs, however, except occasionally a pulmonary systolic blowing murmur propagated up the neck. The action of the heart was not "wobbly", and did not suggest that the vagus had given it a loose rein. There was sometimes slight palpitation—never to any uncomfortable or extreme extent. The pulse was regular, of normal tension, beating between 80 and 100 beats per minute. There was no suggestion in it of undue weakness. The respiratory system shewed no marked change—the lungs were not affected: but in some instances the respiratory act was somewhat accelerated and shallow. There was no irregularity. The urinary system was not affected—urine was passed freely, of normal quantity, and free from albumin: there was no excess of urates and the chlorides were not increased in quantity. The menstrual function was in about half the cases interfered with in the direction of suppression: in other cases it was normal and regular, and there was no dysmenorrhœa at any time. The nevous system, apart from what has been noted above, was not affected. The pupils shewed no irregularity. They were always equal and reacted normally to light and accommodation. As regards the cutaneous system, in some cases there was a condition of dryness of the skin to such a degree as to be almost patbological. The sweat glands seemed arrested in their action. Apart from the *nervous* symptoms in the lower extremity, the most prominent sign to be noticed was a condition of anæmia. This generally became more performed in proportion to the severity of the Beri-beri symptoms. Together with the diminution in the percentage of hæmoglobin, in some cases to 40, 30 or less, there was diminution in the number of red blood corpuscles to less than three millions, and an increase in the number of leucocytes to twelve or fourteen thousand. Of these there was a steady increase in the number of mononuclears and polymorphonuclears: the eosinophiles rose to about double the normal, and normoblasts were to be occasionally seen. This condition of anæmia was indicated plainly, not only by the pallor of the palpebral conjunctiva and the shallow, and in some instances, hurried respirations, but also by the pulmonary murmur which was undoubtedly hæmic in origin.

The Diagnosis.

The symptoms which have been detailed above are practically all that were present: and from a consideration of them it will be seen that all the cases were of a mild nature. The question arises then of the diagnosis of the disease. Into that it is not proposed to enter at length in this section. But it may be stated that the diagnosis was guided by the rapid and sudden onset of sensory derangements confined principally to the lower extremities, accompanied by hyperæsthesia of the musculature and followed by wasting: all this leading to difficulty in locomotion amounting in some extreme cases to complete paraplegia, necessitating guidance and assistance with the hands, or with sticks or crutches. Together with this, œdema of greater or less amount and extent principally confined to the area over the tibia was present. These symptoms occurring in a building ill-ventilated and remote from the sun's rays, generally damp, dark and sometimes overcrowded, and rapidly attacking one after another of a population stagnating in it for months without outdoor exercise and without an opportunity of breathing the fresh outer air—a population that is free of the vice of alcohol and of the taint of syphilis—such symptoms occurring in this Colony can only point to Beri-beri—very mild it is true, but still it is Beri-beri.

Probable Causation.

We do not here intend to discuss any of the theories regarding the causation of Beri-beri in general, but merely wish to call attention to a few points in connection with this particular outbreak. The predisposing causes we can point to fairly clearly. The disease broke out among an overcrowded, stagnant population resident in a building which we consider is ill-ventilated, and in addition is damp and ineffectually sunned. This much is easy of assertion and of proof. When however we come to consider what may be the exciting cause or causes we undertake a more difficult task. For we are unable to assign a cause to the outbreak. We can only point to the fact that when the conditions of residence were ameliorated the disease ceased spreading. As soon as the inmates were removed to the large, airy wards of the Tung Wah Hospital the incidence of the disease was arrested. Only two wards were occupied and the inmates crowded into them—but these were large, airy wards with wide doors on every side and the sun's rays penetrated into them all day. The food remaining the same in both establishments; it is perhaps a question whether it acts as a factor in causation, and if it does whether it requires certain conditions of crowding and surrounding to bring it into play. With this particular outbreak it was noticed that the patients improved on transfer, and that only one or two fresh cases occurred after transfer—these probably incubating at that particular period.

Prognosis.

With such mild, and mildly severe cases, the prognosis is invariably favourable. Of the 32 patients attacked all recovered except one. This patient had a rather more severe attack than the others. She quickly lost the power of movement and became confined to bed. The œdema of the legs became more pronounced and after a time the heart began to act badly—dilatation shewed itself, and after a time she contracted subacute pneumonia to which she sucumbed. Favourable points in prognosis are mildness of attack, as evidenced by power of locomotion if even slight, non involvement of the heart, and a moderate degree of anæmia. Then also the prognosis is most favourably influenced by prompt removal from the premises in which the disease developed or manifested itself—and removal if possible to well ventilated, sunny, airy premises.

Period of Incubation.

There is a diversity of opinion regarding the duration of the period of incubation of the disease, and in this series of cases also we meet with extremes. Assuming that the disease was contracted within the building, and that the infection was present or developed therein, we can calculate the length of time the patient was subjected to its influence before manifesting the earliest symptoms. And this period we might assume to be the period of incubation. From such an estimation we set a variation between a maximum period of 200 days in one case, and a minimum of 23 days in another. Between these periods we have varying periods—lengthy in some cases, such as 184, 147, 119, 117 and 131 days and comparatively short in others, such as 31, 53, 63 and 68 days. Calculating an average from these periods we set a period of 84 days, which we might call the period of incubation. [This of course only applies to this particular series of very mild cases : in very acute cases the incubation period has been known to be not much more than 40-50 hours].

During this period the symptoms are apparently very trifling and not such as to lead the patient to make any complaint nor such as to cause any inconvenience. Perhaps slight digestive disturbances or slight palpitation may be forerunners : certainly a condition of anæmia supervenes. Sometimes amenorrhœa may occur which in young females should lead to a suspicion of the cause, especially in a locality where the disease is endemic. So that it may be said that the incubation period is prolonged, the symptoms vague and indefinite, leading to the conclusion that the poison is slow working, and its result cumulative.

Age Incidence.

In considering this we must have in mind the fact that the inmates of the Institution are for the most part adults. It would appear to especially affect those between the ages of 15 and 25. In point of fact most cases occurred between the ages of 15 and 20—three occurred earlier, namely, one at 3 years of age, and two at 14, and no cases were seen in those over 25 years of age. No conclusions may be definitely drawn from these figures except perhaps that when the disease occurs among the female sex those between the ages of 15 and 25 are principally affected.

Duration of the Disease under Treatment.

The disease is as a rule very slow in resolving itself. This points to a degeneration of the nerve trunks and the muscles. Regeneration takes a prolonged time. The establishment of the path is first effected, and then after an appreciable period its conductivity becomes restored. This process takes a prolonged time to be accomplished, and considering the lengthy period during which treatment must be undergone it is doubtful whether any method of treatment is to be regarded as specific. In this series of cases the average length of time devoted to treatment before the patient was pronounced cured was 98 days :—17 of the cases remained under treatment from 117 to 156 days, 6 cases for the following periods, namely, 11, 20, 31, 21, 21, 16 days, and the remainder from 50-100 days. We might infer that except in the mildest cases treatment is not effective, that cases run their course, and arrive at a natural resolution—that is, that regeneration of the damaged nerves and muscles takes place in its own appointed time, and that gradually thereafter conductivity becomes established leading to a righting of the sensory and motor functions.

The one case that succumbed was of a rather more advanced nature than the others. She developed more œdema of the feet and legs ; the nervous apparatus of the circulatory and respiratory systems became more profoundly affected, leading to vaso motor paralysis and to consequent infiltration of the tissues, among which the lung became affected, and a sub-acute condition of pneumonia supervened. She was under treatment for 50 days.

Incidence with reference to Occupation.

The occupation of all these patients was returned as "destitute", a vague term which comprises many conditions in life. Some of them were occupied in household duties—not the majority of them ; some were looked after by parents or guardians and did no work ; a few enjoyed a considerable latitude in their mode of life. In this particular series of cases it could not be said that occupation in any way modified the incidence of the disease. The conditions that existed were eminently favourable for the development of Beri-beri, and it was a coincidence that the building was inhabited by these women at the time.

The Treatment.

There being no specific for Beri-beri, treatment was mainly directed towards keeping up the strength of the patient, and towards alleviating any special symptoms which arose.

As soon as the diagnosis was made the patient was put upon a mixture containing strychnine, arsenic and iron. If the pulse was weak, digitalis or strophanthus was added, and sometimes ether and ammonia given as well. Together with this routine treatment, massage was carried out in every case—either with the bare hand, or with a stimulating embrocation. This was found to be especially effective in removing the œdema and in maintaining the nourishment of the muscles. When symptoms of dyspepsia were present the usual hospital mixtures were administered, namely, soda and rhubarb, bismuth and pepsin, hydrochloric acid and nux vomica, and so on. For any pain over the heart or palpitation, a mustard poultice or a belladonna plaster was applied. Any diarrhœa on the rare occasions it appeared was checked with chalk and bael.

The paresis and paralysis of the muscles were improved by steady and assiduous massage.

No bed sores occurred, or such atrophy of the muscles as to lead to contracture.

The food remained the same throughout —rice, vegetables, salt-fish, salt-pork, condiments, etc.—the usual Chinese meals.

What undoubtedly proved the most effective means of treatment was the removal of the patient to the Tung Wah Hospital, and this measure was also effective in arresting the further spread of the disease, for, together with the patients all the other inmates were removed, and they mingled freely with each other, sharing the same rooms, meals, etc. No isolation was attempted, yet the outbreak was arrested.

3.—THE PREVALENCE OF BERI-BERI IN HONGKONG.

The Tung Wah Hospital in this Colony has been founded by the Chinese community and is carried on by them exclusively for their fellow-countrymen, who are freely admitted to its privileges without payment. Owing to this, and also to the fact that they may have their choice of Western or of Chinese methods of treatment, the sick fully avail themselves of the benefits afforded. Thus, considering the out-patient department, and the number of in-patients admitted annually, we are enabled to form some fairly accurate idea of the prevalence of various forms of disease among the Chinese community. For this reason we venture to think that an analysis of the statistics of this hospital with special reference to Beri-beri will prove instructive, not only as affording an index of its prevalence in the Colony, but also as regards certain other points, namely, its incidence amongst the different classes, its age incidence, its mortality and its diagnosis.

We have prepared an analysis of the cases admitted during the ten years, 1895-1904, being the years when a register was kept under Government inspection, and an accurate record made of the diagnosis.

The Admissions.

During this period the number of admissions has been high, and a regular and steady increase has been maintained each year as follows :—

	Males.	*Females.*
Admissions :—1895, ...	117	1
1896, ...	136	13
1897, ...	166	15
1898, ...	162	8
1899, ...	265	16
1900, ...	335	25
1901, ...	390	27
1902, ...	409	12
1903, ...	265	17
1904, ...	667	72
Total, ...	2,912	206

[*N.B.*—In the Table shewing the Aggregate Admissions month by month the total number of males admitted is set down as 2,890—the difference, representing 22, being males admitted in the first half of 1895, no note being entered in the Register of the month of admission.]

It will be noticed that there was a steady increase in the number of males admitted during the first four years of the period. There was then a sudden leap representing an increase of 103 in 1899. Thereupon a steady and progressive increase occurred until 1902, then as suddenly there was a drop of 144 in 1903, and the highwater mark was reached in 1904 with 667 admissions. Of those cases admitted in 1904, viz., 739, there were admitted from Singapore 50, from South Africa (repatriated coolies from the Transvaal) 40, from Peru 4, Siam 3, and from Manila and Canton 1 each—the remainder were residents of the Colony. Even deducting these 99, we have a total of 640 admitted who were resident in the Colony and presumably contracted the disease here.

The admission rate of the females was not high, and there was no noteworthy increase until the year 1904, when a total of 72 were admitted, being a third of the total admissions of females during the decennium. These were all, practically, residents.

Comparative Incidence on the Sexes.

Males are specially affected by the disease, 2,912 being admitted as against 206 females. This gives an incidence ratio of 14 to 1. We may consider this as representing fairly accurately the liability of the sexes, and may infer that the causes operative in the production of the disease are more prevalent among males rather than that females are less susceptible to it. In evidence of this statement we may point to the fact that when the disease breaks out under what we may assume to be favourable conditions, females seem to contract it very easily, as witness for example the outbreak among the inmates of the Po Leung Kuk.

The ratio of incidence for the period under analysis is as follows :—

	Males.	*Females.*
1896, ...	10	1
1897, ...	11	1
1898, ...	20	1
1899, ...	16	1
1900, ...	13	1
1901, ...	14·5	1
1902, ...	34	1
1903, ...	15·5	1
1904, ...	9·5	1

When we consider the prevalence of the disease among the total population with especial reference to sex, we find the ratio as follows :—

MALES.

Year.	Estimated Population.	No. of Cases.	Ratio.
1895, ...	173,500	117	1—1,483
1896, ...	165,499	136	1—1,217
1897, ...	171,558	166	1—1,033
1898, ...	174,624	162	1—1,078
1899, ...	177,748	265	1— 670
1900, ...	180,967	335	1— 540
1901, ...	204,811	390	1— 525
1902, ...	217,839	409	1— 532
1903, ...	224,147	265	1— 846
1904, ...	249,884	617	1— 405

[In the year 1904 there were 667 admissions of males—50 however being imported cases are omitted from this calculation].

The incidence among males is thus seen to be in the ratio of 1 to 823 of the population.

Among the female population we find the incidence as follows :—

FEMALES.

Year.	Estimated Population.	No. of Cases.	Ratio.	
1896, ...	61,211	13	1—4,701	The admission for 1895 being only 1, is not calculated.
1897, ...	63,452	15	1—4,230	
1898, ...	64,586	8	1—8,073	
1899, ...	65,742	16	1—4,108	
1900, ...	66,933	25	1—2,677	
1901, ...	75,753	27	1—2,805	
1902, ...	76,461	12	1—6,371	
1903, ...	82,903	17	1—4,876	
1904, ...	92,422	72	1—1,283	

This gives an average ratio of incidence of 1 case in 4,348 of the population.

This disparity of incidence on the sexes we are inclined to attribute to the facts as before mentioned, namely, that the female portion of the community are not subject to those conditions—surroundings, food, ventilation, fatigue, etc.—which might probably be considered as predisposing causes.

It is worth notice that the prevalence for all practical purposes increases year by year among both sexes, in spite of the steady increase of population. Among the males the increase is four times greater in ten years, and among the females the increase is about the same.

The figures we have obtained, through the courtesy of Dr. I. MITCHELL, of admissions to the Alice Memorial and the Nethersole Hospital are so small as not to affect the general result as stated above.

We have to express our thanks to the Medical Officer of Health, Dr. PEARSE, for kindly supplying us with the estimated population.

Age Incidence.

The accompanying Table (No. IV.) shews the age at which patients were admitted. We may postulate that patients seek admission as soon as possible after the onset of the illness, as soon in point of fact as they are unable to earn a livelihood, and indeed the majority as soon as they feel the early symptoms of the disease.

Analysing the total number of cases in quinquennial age groups, it will be noticed that the disease did not occur in the very early years of life, viz., between 1–5 years of age. In the next period 6–10 years 7 cases were admitted, and 35 cases between 11 and 15 years of age. Then the curve rises suddenly and quickly, from the quinquenniad 16–20 to its highest, 21–25, and maintain their height during the next period 26–30. After this the curve rapidly declines as far as the period 41–45, and then there is a gentle fall in the next and following periods.

Taking the male and female admissions separately, it will be seen that among the males the curve rises rapidly during the period 16–20, and reaches and maintains its maximum during the next two quinquenniads 21–25 and 26–30. There is then a notable fall to the next period 31–35, which continues during the next three periods. Thereafter the fall is gentle, steady and regular to the period 71–75.

The number of females admitted though small may be taken as fairly representative of the incidence among them. We notice that the earlier age periods are those especially affected, there being a steady rise up to the period 16–20, after which there is a slow fall of the curve during the next two periods 21–25, and 26–30, then a rapid fall and the curve remains steady except one rise during the period 36–40.

Thus we see that the disease has its greatest incidence during the two quinquennial periods 21–25 and 26–30, namely those years when the person is most vigorous and most fit for wage-earning. The extremes of life are affected to a very slight degree, but after the age of 30 although the curve drops fairly quickly we get large numbers, especially among the men, affected at the succeeding periods.

Seasonal Prevalence.

We have drawn up a chart to shew the admissions month by month during the ten years. Premising that the incubation period is from 20-30 days, and that the patients seek admission on the onset of the more severe symptoms which render them unfit for work, the chart is instructive.

We notice that the disease maintains a fairly uniform level during the first four months of the year. There is then a rapid rise in May and the level is maintained during June. Then a further rise occurs rapidly in July and the curve maintains a high level in August and September. After that a sharp drop takes place in October, followed by a temporary rise in November, and a further sharp drop in December.

The height of the prevalence and incidence of the disease is thus seen to be during July, August and September. These months, together with the two preceding months when the curve commences to rise are the wet, damp and humid months of the year in this Colony, and it is a question whether these atmospheric conditions are contributory factors in the production and development of the disease.

It will be noted that though the curve for females is uniformly flat there is a marked rise in May and in August.

The Varieties of the Disease.

As we meet it here the disease presents itself in two varieties, known as the dropsical, moist or wet form, and the atrophic or dry form. The disease however is a single entity—in its inception certain common symptoms manifest themselves, in its development it assumes the characters of the one or the other variety. In the rapid onset and development of the first variety modified slightly in some respects but with an accentuation of the cardiac symptoms we get the acute pernicious variety. This form is very rarely met with here and is usually very fatal. The two varieties—the dropsical and the atrophic—occur in about equal proportions in their developed form, but it must be remembered that one form may pass into and shew the characters of the other, that is, that œdema, etc., may be implanted on the dry form and so convert it into the dropsical, or that the œdematous variety may pass through changes resulting in its assuming the atrophic form. Beri-beric residual paralysis is a term which has been used in an analogous manner and with a similar meaning to diphtheritic paralysis. The pathology of the diseases being different, clear in one case, unknown in the other, the comparison does not hold, and any attempt to introduce new varieties, names, etc., is to be deprecated.

A Picture of the Disease and its Diagnosis.

In a country where the disease is sometimes epidemic and always endemic the diagnosis on the one hand should present no difficulty, and on the other hand because so easily made not infrequently leads to errors. Indeed, so well are the symptoms known that patients frequently present themselves for treatment, having already diagnosed their condition.

What then are the symptoms upon which we rely for a diagnosis? In the first place, and we are here discussing the early stages, we find there is a feeling of malaise and lassitude, and then there is weakness of the legs and numbness, which is characteristic. Then comes on pains in the muscles of the calf of the leg, elicited by compressing the calf muscles, which amounts to exquisite pain sometimes. The patient is unable to walk easily and freely, and he has a feeling as if he were treading on cotton wool or walking on a carpet. These signs by themselves are sufficient for the patient and his friends. They indicate that he has Beri-beri. Further examination by an expert shews that there is loss of the knee reflexes, that there is anæsthesia of the legs to a varying degree—that slight œdema exists over the shin bones, and that there may be shortness of breath and palpitation. The patient has progressive weakening of the muscles of the hand and forearm. His grip is weak, and there is wasting of the muscles of the thumb. The more advanced stages of the disease present no difficulty in recognition. There is wasting or there may be œdema of the leg—the calf muscles in the former case being flabby and the skin dry, and there is loss of subcutaneous fat; or the whole leg is swollen and tense with a subjective feeling of fulness. In either case the sensibility of the skin of the leg is altered, either in the direction of total loss over the whole area or over irregular patches not necessarily corresponding to any particular nerve distribution, or there may be paræsthesia, viz., sensations of heat and cold, of pins and needles, of lancing pains, etc. In the early stages there is a loss of knee reflexes, an exaggerated reflex being seen perhaps in the first few days after onset. Then in the later stages corresponding with the loss of power in the leg muscles we have ankledrop marked. At this stage the patient is generally bedridden.

In the *dropsical variety* the picture in the later stages is characteristic. The tissues are all water-logged, and there is general œdema. The face is swollen and bloated, the eyes closed owing to œdema of the lids, and the skin over the abdomen is puffy. There is a purplish cyanotic look. All the parts pit on pressure and there is anæsthesia to a varying extent. The patient is unable to move with any freedom and in point of fact takes to bed. He suffers from dyspepsia, from palpitation. The heart acts irregularly, and there is a weak, soft and perhaps intermittent pulse. His faculties are unclouded. He may have a slight cough from œdema of the lungs. The tongue is clean, the digestive functions unimpaired though there may be present a watery diarrhœa. The temperature does not become elevated. The functions of the kidneys shew no signs of being interfered with, the urine being normal in amount and in constitution. He lies a dropsical water-logged mass incapable of locomotion and very helpless.

On the other hand in the *atrophic variety* the picture is equally characteristic in the later stages. The pronounced emaciation, the steady, gradual and progressive wasting of the muscles especially of the lower extremities, the wasting of the connective tissue over the body, the loss of the reflexes, particularly the knee-jerks, the gradually increasing and spreading anæthesia rendering him finally bedridden, present a picture which is diagnostic. The organic reflexes are not interfered with, and the body temperature keeps at the normal or perhaps may run a degree or more under the normal. The cardiac muscle apparently undergoes a progressive wasting and atrophy pari passu, leading to weakened action, and a feeble, soft and compressible pulse. When the disease reaches its worst point, death may occur either from the extreme general atrophy or from some intercurrent pulmonary affection to which such cases are specially liable, or recovery takes place very gradually. In the latter cases the muscles recover themselves soonest but the anæsthesia continues and is prolonged. Gradually strength comes back and the muscles slowly, very slowly, regain their functions, and as the leg muscles were the earliest to manifest weakness, so are they the earliest to recover themselves. The patient tries to use his legs with the aid of crutches at first, and he balances himself on them being unable to secure the assistance of his legs. Then gradually he is able to move the legs, to flex the thighs and to raise the feet off the floor instead of scraping his toes on the floor as he walks. Then he slowly acquires control of his feet, and from letting it fall purposelessly on the floor he is able to draw up his foot and to plant it flat—but he still drags it along after him and feels as if he were walking on cotton wool or paper. In the next stage he discards crutches and takes to the assistance of a stick, and so with returning power and returning feeling he gradually comes to use his feet in a normal manner. Convalescence is slow but is steady, normal sensation returning last of all. When recovery occurs in the dropsical variety its progress is slow—gradually the œdema of the extremities and of the body becomes resolved, the turbulent action of the heart is regulated, sensation becomes normal, and power of locomotion is regained. The last returns most slowly of all.

In the *atrophic form* the first sign that shews itself is a sensation of weakness in the legs accompanied by shooting pains in the front of the legs and calves, and there is tenderness in the calf muscles. This pain is striking, because on examination of the skin over the affected muscles and the other part of the leg large areas of partial or total anæsthesia are met with. This weakness is accompanied with inco-ordination of the gait which may become so pronounced as to lead to the necessity of keeping in bed. Weakness of the muscles of the hand also sets in so that the grasp is lost: and there may be tremulousness. Later the finer movements of the hand are impaired and anæsthesia to greater or less extent sets in. Then actual wasting of the muscles of the legs and arms occurs, and a typical picture is presented. An extremely emaciated man is seen lying helplessly—able to perform some of the coarser muscular movements, but unable to stand or walk: he has wrist drop and also ankle drop—the knee reflexes are lost, but the organic reflexes remain intact. The tongue is clean, the appetite good, the breathing is quiet and regular, and the pulse is normal. Sometimes a degree of anæmia may be co-existent when hæmic murmurs may be heard at the base of the heart. The mental faculties are not impaired. Gradual recovery may now take place with slow convalescence, or death may take place from progressive atrophy or from some intercurrent complication.

Mild laryngeal and tracheal catarrh are often said to usher in the disease, or to be present in an aggravated form in the later stages. Such, however, we have never found in our cases.

The Diagnosis.

This presents no difficulty at all to any one who has the least acquaintance with the disease. The points upon which we rely are :—

(1.) Anæsthesia over legs.
(2.) Œdema over the shin.
(3.) Pain on pressure of calf muscles.
(4.) Loss of knee reflexes.
(5.) Heart touble—palpitation, &c.

Cases in the later stages present no difficulty whatever—their appearance is diagnostic.

It may happen, however, that in some cases difficulties may present themselves and, therefore, we should be careful to eliminate such diseases as may shew some likenes to Beri-beri.

A.—Alcoholic Neuritis.—In this there is a history of alcoholism to guide us—there is progressive weakening of the legs, and anæsthesia, general tremulousness and perhaps albumin in the urine.

B.—Arsenical Neuritis.—Symptoms of arsenical poisoning are present, viz., diarrhœa, abdominal pains, numbness, tingling, bloody urine. There is no œdema. Sensation may be lost. No ankle clonus or knee-jerk.

C.—Lead Poisoning.—Characterised by pains in joints, blue line on gums, colic, wrist drop—no pain in affected muscles.

D.—Malarial Cachexia.—No loss of reflexes. History of repeated attacks of fever. Anæmia—perhaps enlarged spleen. Microscope may help—shewing parasites ; no anæsthesia. No rapid wasting of muscles.

E.—Locomotor Ataxia.—Characterised by girdle pains, Argyll Robertson pupil, anæsthesia of soles of feet—loss of reflexes—chronic course—history of syphilis.

F.—Epidemic Dropsy.—Sets in with sudden dropsy, fever, vomiting, diarrhœa —no pain in muscles, no loss of reflexes, no anæsthesia.

G.—Heart Disease.—Signs of affection, such as murmurs, enlargements : œdema of lower extremities, albumin in urine—no paralysis, no anæsthesia.

H.—Bright's Disease.—Indicated by swelling under eyes and in legs : albumin in urine : no loss of sensation, of reflexes, of power of movement.

I.—Ankylostomiasis.—This is very insidious—progressive anæmia and perverted appetite characterise it. No paralysis or loss of reflexes, or anæsthesia. Miscroscope shews ova in fœces.

J.—Pellagra.—History of eating maize—knee-jerks exaggerated—very chronic course--tremors and tetany—inco-ordination of gait. No tenderness of muscles.

K.—Ergotism.—History of eating rye. Gangree of extremities sets in. Tingling in skin. Knee reflex lost.

L.—Lathyrism.—History of eating pulse. Knee-jerks increased. No tenderness of muscles, no inco-ordination, no paralysis, no anæsthesia.

M.—Myelitis.—Rapid onset and fatal result—loss of reflexes—paræsthesia—incontinence of urine. No pain or tenderness over paralysed muscles.

All these diseases and conditions enumerated above run their own course and shew their individual particular symptoms : a careful consideration of the case and a recollection of the fundamental symptoms and signs should lead to no difficulty in the diagnosis.

Duration of the Illness.

This varies much and is proportionate to the intensity and the development of the disease on admission. The slighter degrees of the illness get well within a short time, but the more severe the illness the more prolonged is the period that it has to be subjected to treatment, and the more prolonged the convalescence. Some cases were in hospital under treatment for upwards of one hundred and two hundred days; one indeed for as long as 360 days. In an analysis of nearly 3,000 cases we find that the average duration of treatment was 40 days for males, and 42 days for females. Nothing definite, however, can be laid down. Variations occur as in all diseases that run an acute, sub-acute or chronic course.

Its Mortality.

In the majority of countries where the disease is endemic or epidemic the percentage rate of mortality is low. Thus in Japan SCHEUBE noted a percentage of 3·7%, but BALZ only 2·5%. In one hospital in Tokyo it was barely 1% for men, and 3%, for women. In the Dutch Indies the troops suffered to the extent of 2% to 6%. Among the Chinese in Sumatra and native Javanese and Filipinos it was stated at one time to be from 60% to 70%. Latterly, however, the mortality is low. The last figures are exceptional.

In Hongkong the death-rate has been persistently high. The Table No. XI shews this.

Of 3,118 cases analysed, 1,510 died—males contributing a percentage of 49%, and females 35·4%. Each year there was a slight variation, but a uniformly high level was maintained; among the males the variation was from 58·5% to 34·8% with an average mortality of 49·5%—among the females the variation was greater, from 62·5% to 15·4% with an average of 35·4%.

We are unable to offer any explanation of this very high mortality, save that we might take into consideration the fact that a fairly large number of cases was admitted moribund, dying within a few hours, or so ill that they died within one, two, or three days of admission.

Year.	Moribund.		Died within One Day.		Died within Two Days		Died within Three Days.	
	Males.	Females.	Males.	Females.	Males.	Females.	Males.	Females.
1896,	...	...	17	...	2	...	5	...
1897,	42	2	2	1	7	1	2	1
1898,	24	3	8	0	3	0	4	0
1899,	39	2	9	3	8	1	6	0
1900,	83	3	23	0	13	3	8	0
1901,	54	2	31	1	17	0	8	0
1902,	90	2	...	...	10	0	11	0
1903,	61	1	22	0	7	0	2	0
1904,	115	4	10	0	25	3	21	1
	508	19	122	5	92	8	67	2

Duration of Treatment (in cases which succumbed).

The duration of treatment in hospital varied greatly. A few cases were under treatment for long periods—for instance, one died 210 days after admission, a few

others after long periods varying between 101 and 182 days: the majority however succumbed after much shorter periods which varied each year.

Average Residence in Days.

Year.	Males.	Females.
1896,	20	16
1897,	32	42
1898,	18	28
1899,	32	4
1900,	23	38
1901,	23	12
1902,	25	36
1903,	45	35
1904,	14	15

We may conclude from this Table that the severity of the disease varies from year to year: that in some years it runs a rapid course and carries off the patient quickly, that in other years when the type is not so grave it runs a slower course. We may also infer, from the prolonged duration of treatment that the type and severity may undergo variation in the same year.

The Mortality with reference to Age.

On reference to Table No. VII, and a study of the curve it will be seen that the aggregate mortality during the ten years under review reaches its height in the quinquennial age-period 26-30. From the age of 6 to 15 years the curve is flat; thereafter there is a rapid rise in each of the next periods 16-20 and 21-25: and the curve reaches its height during the years 26-30. After that there is a consistent rapid fall till the age-period 41-45: and there a slow fall till it approaches the base line and runs fairly flat during the last three quinquenniads 61-65, 66-70, 71-75. Here we note a similarity to the admission curve (*q.v.*). The largest number of admissions occurs between the ages of 21-30: the largest number of deaths between the same ages. It would seem that the fatality of the disease is great in early adult life, and bears a proportionate relation to the numbers attacked.

The mortality curve for females runs a fairly level course though there is a heightening of it during the quinquenniads 16-20, 21-25, 26-30.

Rate of Mortality according to Sex and Age Periods.

Period.	Total Percentage.	Percentage of	
		Males.	Females.
6-10	43	50	40
11-15	40.6	37.5	43
16-20	38.4	43	17.5
21-25	45	46.3	23
26-30	51	51.4	39
31-35	50	50	57
36-40	55	55	58
41-45	51	50.3	75
46-50	45	45	33
51-55	59	59	50
56-60	70	66.6	100
61-65	41.5	30	100
66-70	90	75	100
71-75	33	0	50

A study of the foregoing Table shews that the percentage mortality is high at all the age-periods but especially high in males between 51 and 60 years, and between 66 and 70 years. In females it is high from 6 to 15 years, then there is a drop in the next 5-year period, a gradual rise from 21-25 which continues into the next quinquenniad. After this the percentage is very high from 31-45 years of age, and then there is a noticeable drop during the period 46-50 followed by a rise from 51 to 55. In the next three quinquenniads the percentage reaches 100, after which it drops to 50 during the period 71-75.

It would thus be seen that the mortality percentage rules high in adult life, and that the disease especially among females is very fatal in the more advanced periods of life, the capacity of resistance among them decreasing with advancing years.

Incidence with reference to Occupation.

We append a Table No. VI in which we have analysed the occupation of the patients in the case of males 2,710, and females 197.

A very large majority of cases occurred among the coolie class, of whom 878 were relieved and 857 died. Under the heading "Workman" 178 were treated, 88 being relieved and 90 died. This term refers simply to those employed in manual unskilled labour. Masons come next in the list, numbering 165, of these 86 were relieved and 79 died. Seamen constitute a fair number—59, with 29 deaths and 30 recoveries. Hawkers constitute a large proportion—79, of whom 30 were relieved and 49 died. Carpenters, Boatmen, Barbers all contribute a fair share, and so do Tailors, Rattan-chair makers, Servants and Cooks. Other trades and occupations furnish a very small proportion of cases. The list serves to shew that practically no trade is exempt from the disease. From a consideration of the Table we may draw the following inferences:—

(1.)—That the disease is universally prevalent among the community.

(2.)—That it especially affects the working classes.

(3.)—That the professional classes, leisured classes and merchants are practically exempt, though a case here and there testifies to inference (1) above.

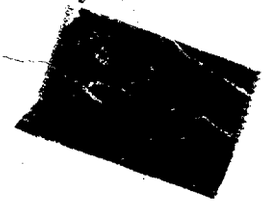
The total number of coolies admitted amounted to 1,730 constituting a percentage of nearly 60. It is well known that their surroundings, domestic and otherwise, and their food and habits, are not altogether unexceptionable. Generally they are crowded together at work and in the house, natural sanitary laws are set at defiance, their personal habits are unclean, their food is of the poorest quality and the cheapest. In all Beri-beri countries these are the conditions which obtain among those that contract the disease. We are compelled, therefore, to regard them as having a causative relation to the disease in the direction of predisposition; a similar statement may be made with reference to other classes, especially of workmen.

The Question of Contagion and Infection.

From our observations we are of opinion that the disease is neither contagious nor infectious—(*vide* Part III). When a case is removed from any locality, say for instance some institution where the disease has appeared, and is freely allowed to go among other people, we have not seen any cases develop. Cases are constantly taken into the wards of a General Hospital but no fresh cases arise. From facts like these and from the result of our experimental work we are of opinion that the evidence against contagion and infection is very strong. Cases are sometimes produced which are stated to refute this statement, but the underlying fallacy in these is one practical ignorance of the length of the period of incubation.

Length of Exposure before Manifestation of the Disease.

This varies within wide limits. We were able to calculate this very exactly in the outbreak which occurred in the Po Leung Kuk. The first two cases occurred on May 14th. The inmates who were admitted into the Institution, (and who were all found to be healthy on examination), after this date—May 14th—were obviously



subjected to the influence of the noxa of the disease. These being under daily medical inspection and supervision the first signs of Beri-beri were carefully sought for and noted if found. An exact record was made and shews a very wide variation from 31 days' exposure to 103 days. As we do not know exactly the period of incubation, nor with any certainty what are the symptoms which manifest themselves during this incubation period, we must include the incubation period in this period of exposure.

We found the first signs shew itself as follows :—

2	cases	in	31	days.	1	case	in	72	days.
2	,,	,,	33	,,	1	,,	,,	78	,,
1	,,	,,	37	,,	1	,,	,,	84	,,
1	,,	,,	53	,,	1	,,	,,	90	,,
2	,,	,,	58	,,	1	,,	,,	93	,,
2	,,	,,	62	,,	1	,,	,,	103	,,
1	,,	,,	68	,,	1	,,	,,	77	,,

We may justifiably conclude that a lengthened period of exposure is necessary in order to contract the disease.

Recurrence or Re-infection and Relapse.

Beri-beri is a disease which does not confer immunity upon those who have suffered from it. Indeed one attack of it may be a predisposing cause for another attack and perhaps to repeated attacks. We were informed by a medical man that he knows a patient, a domestic servant, who contracts it regularly every year for the past 18 or 20 years. The proportion of cases of re-infection is about 1 in 10 or 12 cases.

With reference to the question of a relapse, we are of opinion that relapses do not occur and that cases classed as such are really cases of re-infection.

The Cause of Death.

Death may occur from heart failure principally, or from some sub-acute or acute pulmonary complication. It may sometimes ensue with appalling suddenness. A patient who may apparently be progressing favourably and may shew signs of a favourable issue may without warning succumb to cardiac failure. On the other hand the disease may drag a slow length towards an unfavourable termination. The dry form of Beri-beri becomes steadily worse, the general atrophy progressively becomes more intense, until death ensues.

Acute infectious diseases may sometimes supervene on Beri-beri and be fatal-small-pox, plague and enteric are known to occur. Malaria also co-exists and may prove fatal. In point of fact the majority of cases of Beri-beri which are of a chronic or sub-acute nature are liable to be infected with any other disease.

Prophylaxis.

In order to prevent the outbreak of Beri-beri amongst people who are liable to be confined in buildings for any period of time the following measures should be adopted :—

(1.) The buildings should be well ventilated.

(2.) There should be no overcrowding.

(3.) The food supply should be ample in quantity and of good quality.

(4.) The drainage should be perfect.

(5.) The buildings should be so constructed as to get all the sunshine possible.

(6.) Damp in the buildings should be avoided.

(7.) The inmates should have regular exercise in the open air.

(8.) The greatest personal cleanliness should be ensured.

On the outbreak of the disease in an institution the inmates should be promptly removed from it, and the following measures taken :—

(1.) Building should be disinfected and then all the doors and windows should be kept open and fresh air and sunlight allowed to enter.

(2.) The clothing should be disinfected.

(3.) The furniture should be disinfected.

The Treatment.

As long as the cause remains undiscovered treatment must be empirical and symptomatic, and cannot be specific. For this reason it is unnecessary to go into any detailed account of the remedies administered. Benefit seems to be derived from the administration of a variety of drugs. In our hands iron, arsenic and strychnine in a mixture have proved of great benefit. Strychnine injected into the substance of the muscles has also given good results in some of our cases. Mercury varies in its effect. Massage daily for half an hour at a time does much good—indeed we have great belief in its use. Electricity also does good and should be applied along the course of the nerve and also to the affected muscles. The most effective therapeutic measure is removal of the patient from the locality where the disease manifested itself. Some observers assert that too much stress is laid on this and that the good results are not more apparent than if the patients are permitted to remain. Our observations, however, distinctly recognise the beneficial results of such removal. How this acts is unknown—it may be that the removal is generally to a more hygienic part or it may be that the noxa of the disease is escaped from. Whatever the explanation, the fact remains that removal is one of the most effective measures at our disposal.

The following Tables, etc., are attached :—

I.—Admissions, 1895-1904.

II.—Aggregate monthly admissions, 1895-1904.

III.—Comparative monthly admissions.

IV.—Admissions in quinquennial age-periods.

V.—Monthly admissions, 1895-1904.

VI.—Occupations.

VII.—Deaths, 1895-1904.

VIII.—Comparative monthly deaths.

IX.—Chart of death curve.

X.—Deaths in quinquennial age-periods.

XI.—Percentages of deaths.

TABLE I.

ADMISSIONS, 1895–1904.

Age.	January.		February.		March.		April.		May.		June.		July.		August.		September.		October.		November.		December.		Total.	
6–10.....	1	0	...	...	...	...	...	1	...	1	...	1	1	...	...	...	...	...	...	1	...	...	...	1	2	5
11–15.....	2	4	...	...	2	2	...	1	...	...	...	1	3	1	1	2	1	4	1	2	3	2	2	1	15	20
16–20.....	19	2	7	1	6	2	10	2	23	6	26	6	34	6	39	15	47	6	25	7	27	3	20	4	283	60
21–25.....	26	3	28	1	29	4	34	2	49	7	58	3	90	2	78	4	79	4	65	5	62	6	58	2	656	43
26–30.....	33	2	24	1	38	3	37	0	73	5	46	3	62	1	69	2	79	2	70	2	76	3	56	2	663	26
31–35.....	17	1	21	1	22	0	26	0	41	1	52	1	53	1	44	0	42	0	41	0	51	0	39	2	449	7
36–40.....	8	3	15	2	21	0	24	0	24	1	32	3	38	...	37	0	27	3	34	0	35	2	28	1	323	15
41–45.....	9	0	10	0	11	0	7	0	11	0	10	0	23	...	31	2	35	1	13	0	17	1	10	...	187	4
46–50.....	5	0	4	0	8	0	5	0	13	1	8	0	16	1	18	1	18	1	21	0	19	1	13	1	148	6
51–55.....	2	0	3	0	4	0	5	1	11	1	14	0	4	...	14	0	6	1	9	1	10	1	5	1	87	6
56–60.....	2	1	2	0	2	0	1	...	2	1	4	0	5	3	4	0	10	...	6	1	5	0	5	...	48	6
61–65.....	2	0	...	...	1	0	...	...	4	0	3	0	5	1	1	2	1	...	1	1	1	...	1	...	20	4
66–70.....	2	0	...	1	1	1	...	...	1	0	...	...	...	...	1	...	1	...	2	0	...	...	...	...	8	2
71–75.....	0	1	...	...	...	...	...	...	1	0	...	...	...	...	...	1	...	...	...	...	...	...	...	...	1	2
75–80.....	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	128	17	117	7	145	12	149	7	253	24	253	18	334	16	337	29	346	22	288	20	306	19	237	15	2,890	206

TABLE VI.

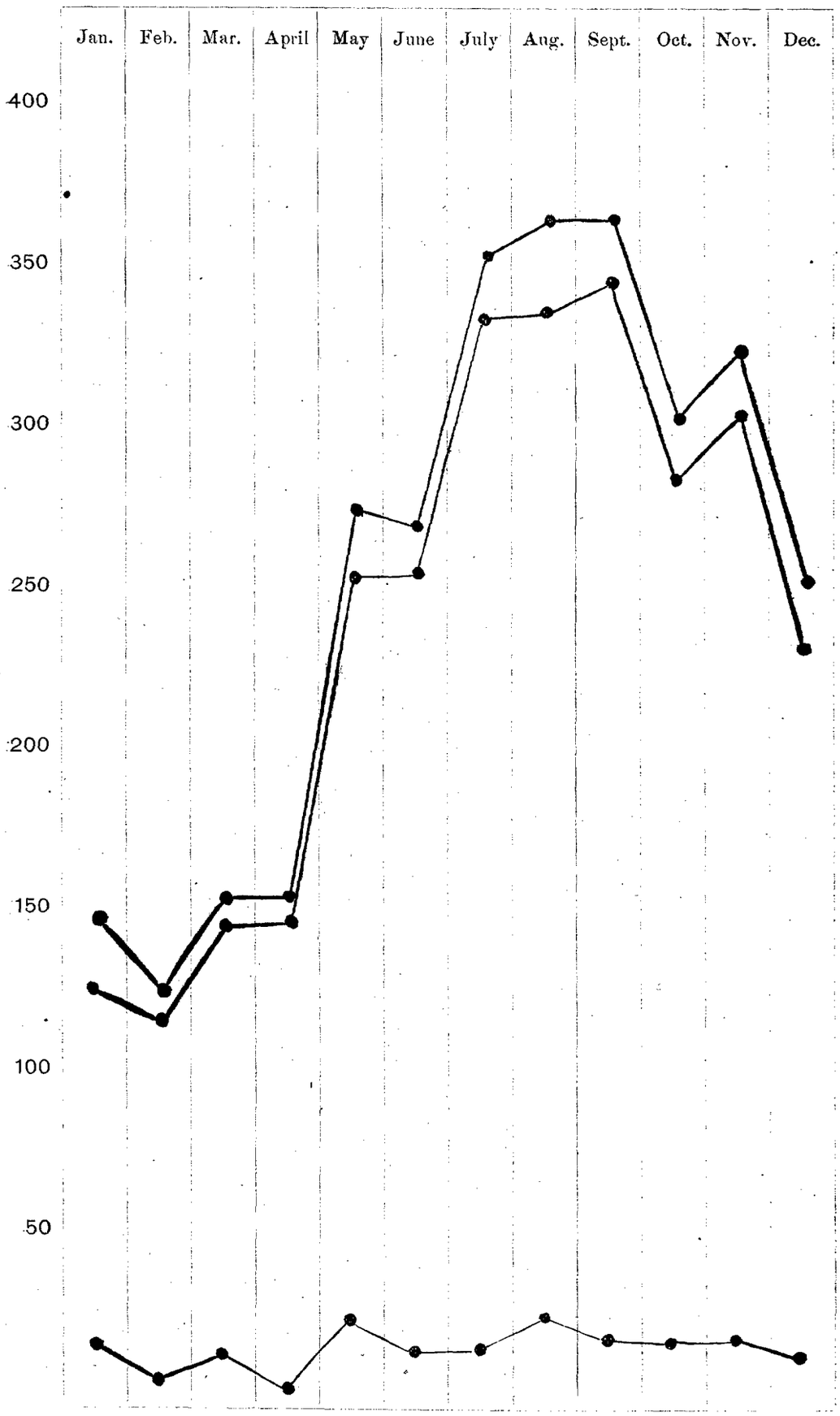
OCCUPATIONS.

Males,—2,710. Females,—197.

Occupation.	Relieved.		Died.		Total.	Occupation.	Relieved.		Died.		Total.
	Male.	Female.	Male.	Female.			Male.	Female.	Male.	Female.	
						Brought forward,	1,092	34	4,117	39	2,282
Accountant,	3	...	...	...	3	Machinist,	...	...	1	...	1
Apprentice,	1	..	3	...	4	Mechanic,	5	...	3	...	8
Actor,	1	...	...	...	1	Miller,	1	...	...	...	1
Beggar,	2	...	3	...	5	Miner,	4	...	...	...	4
Boatman,	16	...	17	...	33	Merchant,	1	...	1	...	2
Barber,	13	...	15	...	28	Money-changer,	...	...	1	...	1
Brass-smith,	4	...	3	...	7	Not stated,	39	17	17	5	78
Blacksmith,	4	...	6	...	10	No occupation,	22	62	78	30	132
Butcher,	...	...	1	...	1	Paper-maker,	...	...	1	...	1
Baker,	...	...	1	...	1	Painter,	6	...	3	...	9
Coolie,	877	1	853	4	1,735	Photographer,	...	...	1	...	1
Chair-maker,	2	...	1	...	3	Printer,	1	...	...	...	1
Carpenter,	20	...	30	...	50	Prostitute,	...	...	...	2	2
Copper-smith,	3	...	1	...	4	Preacher,	1	...	...	...	1
Cook,	9	...	9	...	18	Rattan Chair-maker,	20	...	6	...	26
Cracker-maker,	...	...	1	...	1	Rattan Shaver,	...	...	1	...	1
Chair Coolie,	1	...	...	...	1	Rope-maker,	1	...	1	...	2
Compositor,	...	...	1	...	1	Rice Pounder,	2	...	2	...	4
Cotton Spinner,	2	...	...	...	2	Sack-maker,	...	...	1	...	1
Druggist,	...	...	2	...	2	Scavenger,	1	...	...	...	1
Doctor,	...	...	1	...	1	School Boy,	1	...	...	...	1
Destitute,	7	2	17	1	27	Seaman,	30	...	29	...	59
Engineer,	2	...	2	...	4	Servant,	9	1	5	...	15
Electrician,	1	...	...	..	1	Shoe-maker,	2	...	1	...	3
Excise Officer,	...	...	1	...	1	Shipwright,	1	...	1	...	2
Fireman,	1	...	...	...	1	Silver-smith,	3	...	4	...	7
Fisherman,	2	...	3	...	5	Singer,	...	...	1	...	1
Fishmonger,	...	...	1	...	1	Stone Cutter,	3	...	5	...	8
Farmer,	2	...	3	...	5	Sugar Tester,	...	...	1	...	1
Flower Seller,	...	...	1	...	1	Tailor,	22	...	19	...	41
Foreman,	...	...	3	...	3	Tallyman,	1	...	...	...	1
Fortune Teller,	...	...	2	...	2	Telephone Boy,	1	...	...	...	1
Glass-blower,	...	...	1	...	1	Tin-smith,	2	...	3	...	5
Godown Keeper,	...	...	1	...	1	Washerman,	4	...	3	...	7
Gardener,	3	...	6	...	9	Watchman,	3	...	2	...	5
Hawker,	30	...	49	...	79	Workman,	88	...	90	...	178
Mason,	86	...	79	...	165	Widow,	...	1	4	...	5
Married,		31		30	61	Wrapper,	1	...	1	...	2
Carried forward,	1,092	34	1,117	39	2,282	*Total,*	1,367	115	1,343	82	2,907

Table II.

Chart shewing Aggregate Monthly Admissions during Ten Years 1895-1904.



Highest line—Aggregate. Middle line—Males. Lowest line—Females.

Table III.

Comparative Monthly Admissions 1895—1904.

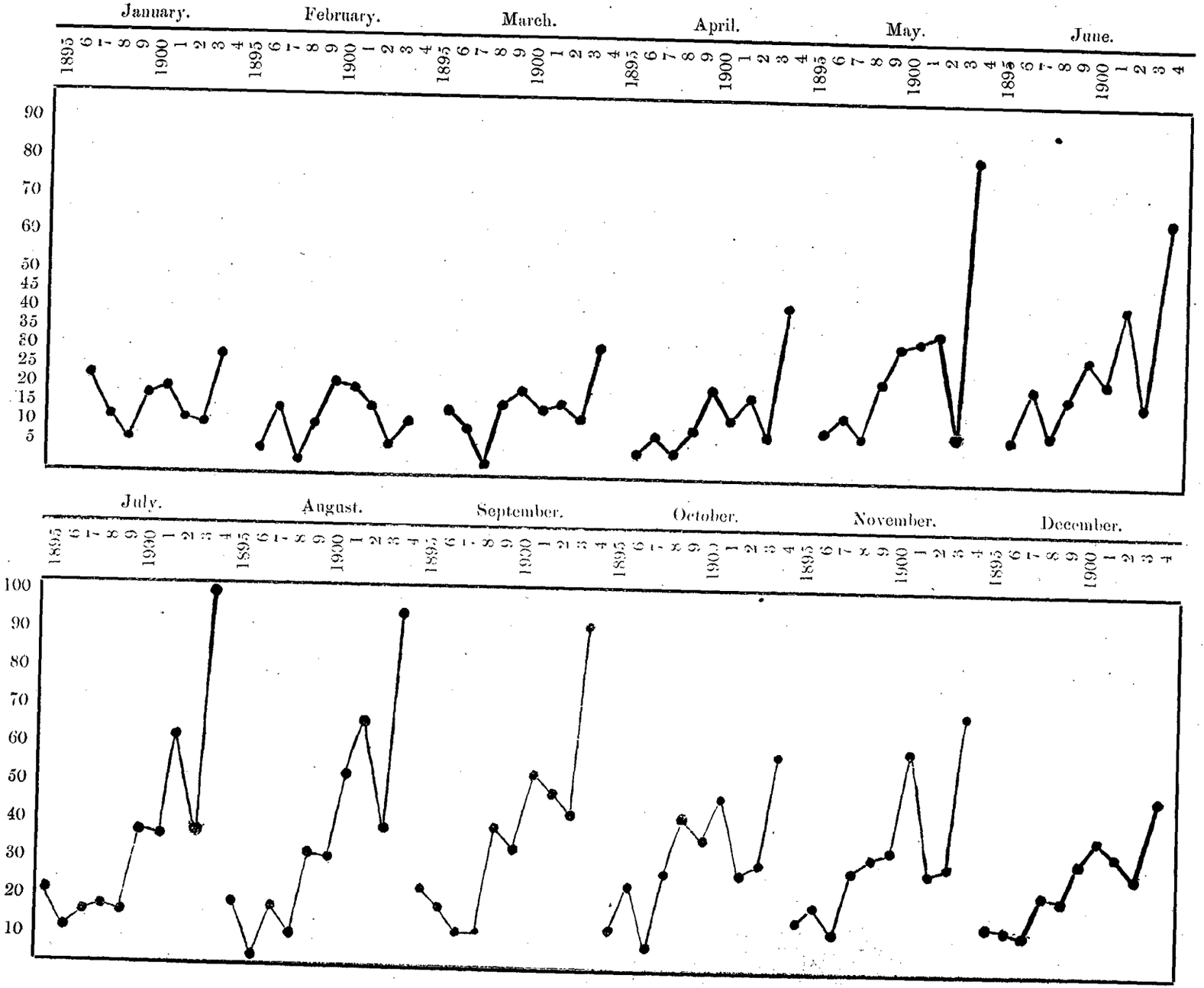
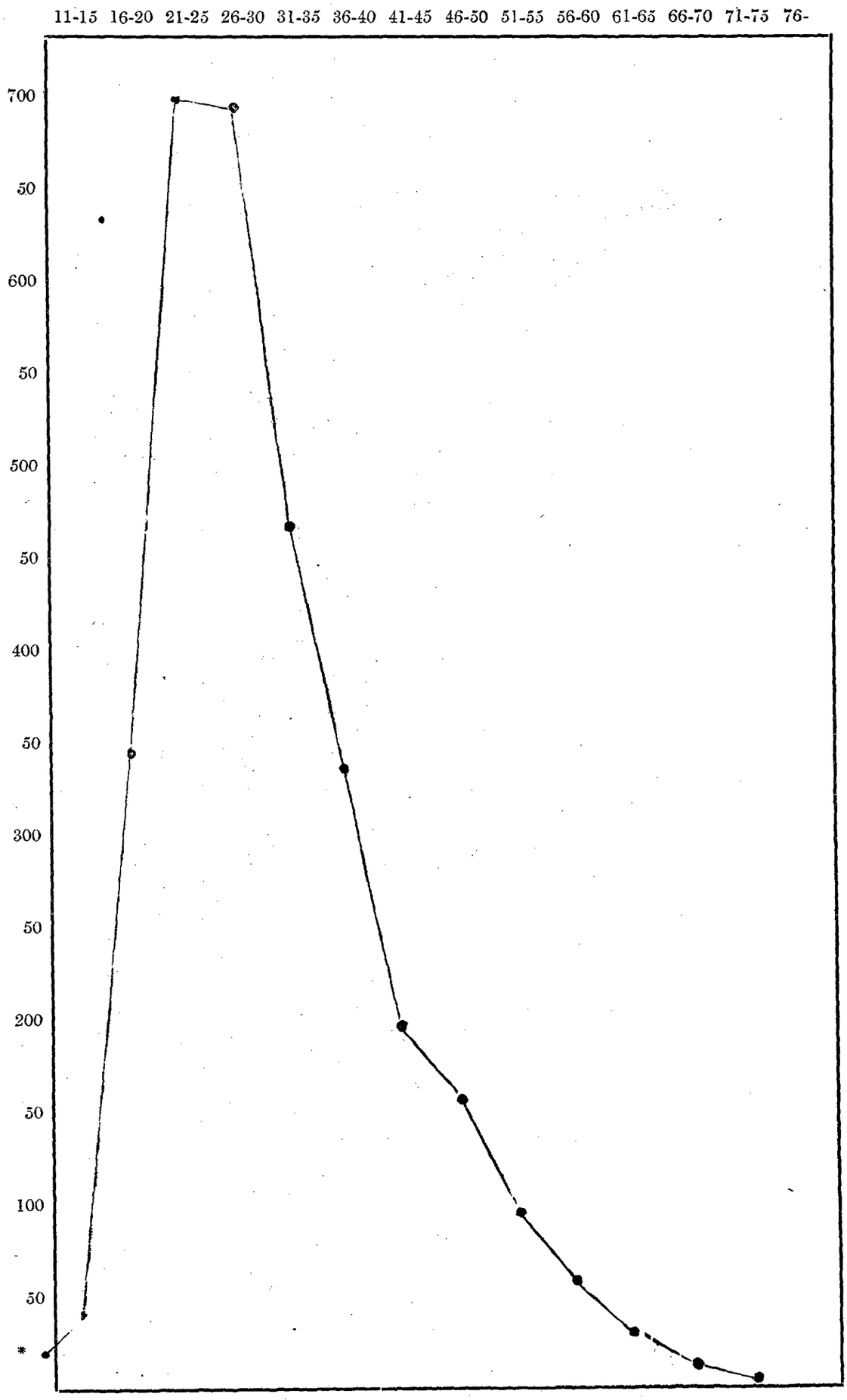


Table IV.

Admissions in Quinquennial Age Periods for 10 Years. 1895-1904.



* N.B.—7 cases were admitted between 6 to 10 years of age.

Table V.

Chart shewing Admissions month by month for ten years 1895-1904.

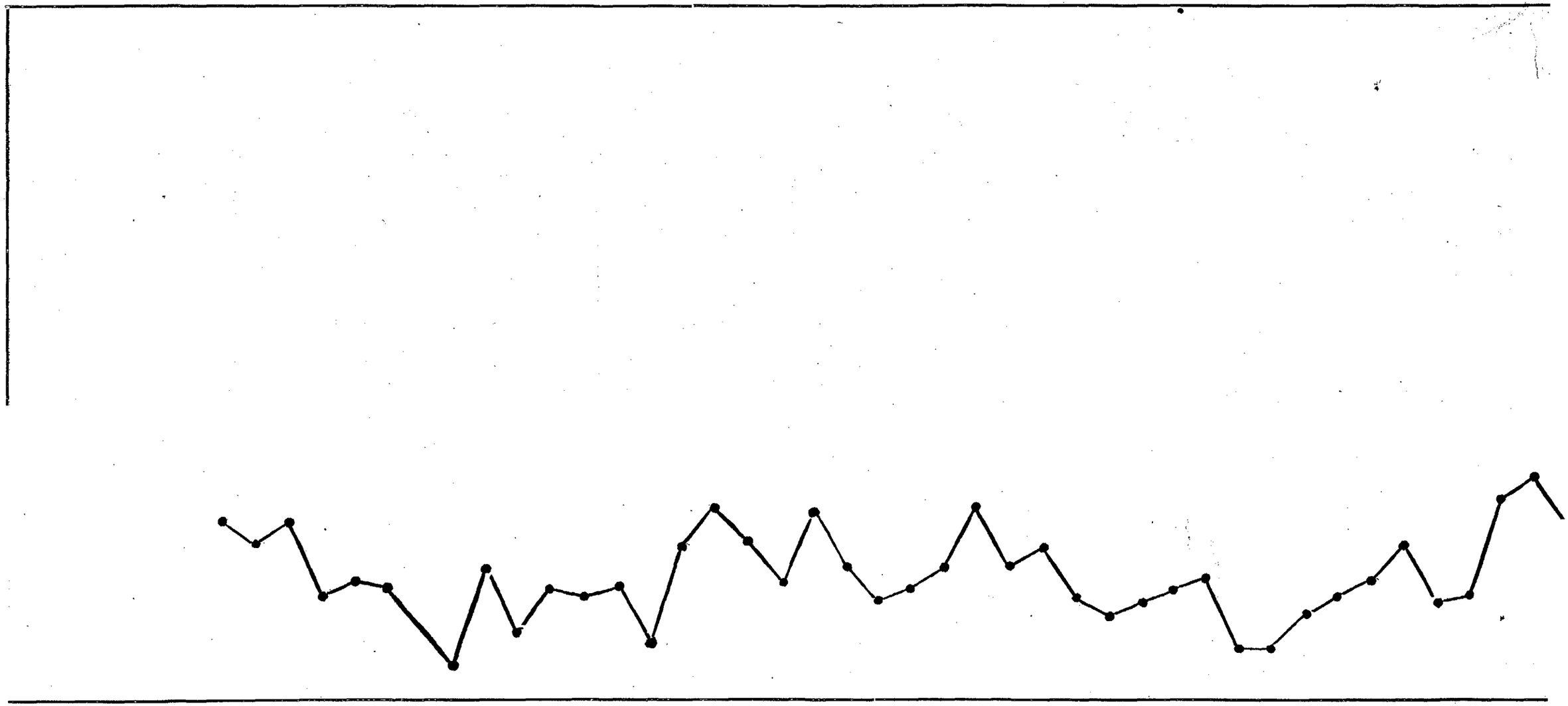


Table V.

Chart shewing Admissions month by month for ten years 1895-1904.

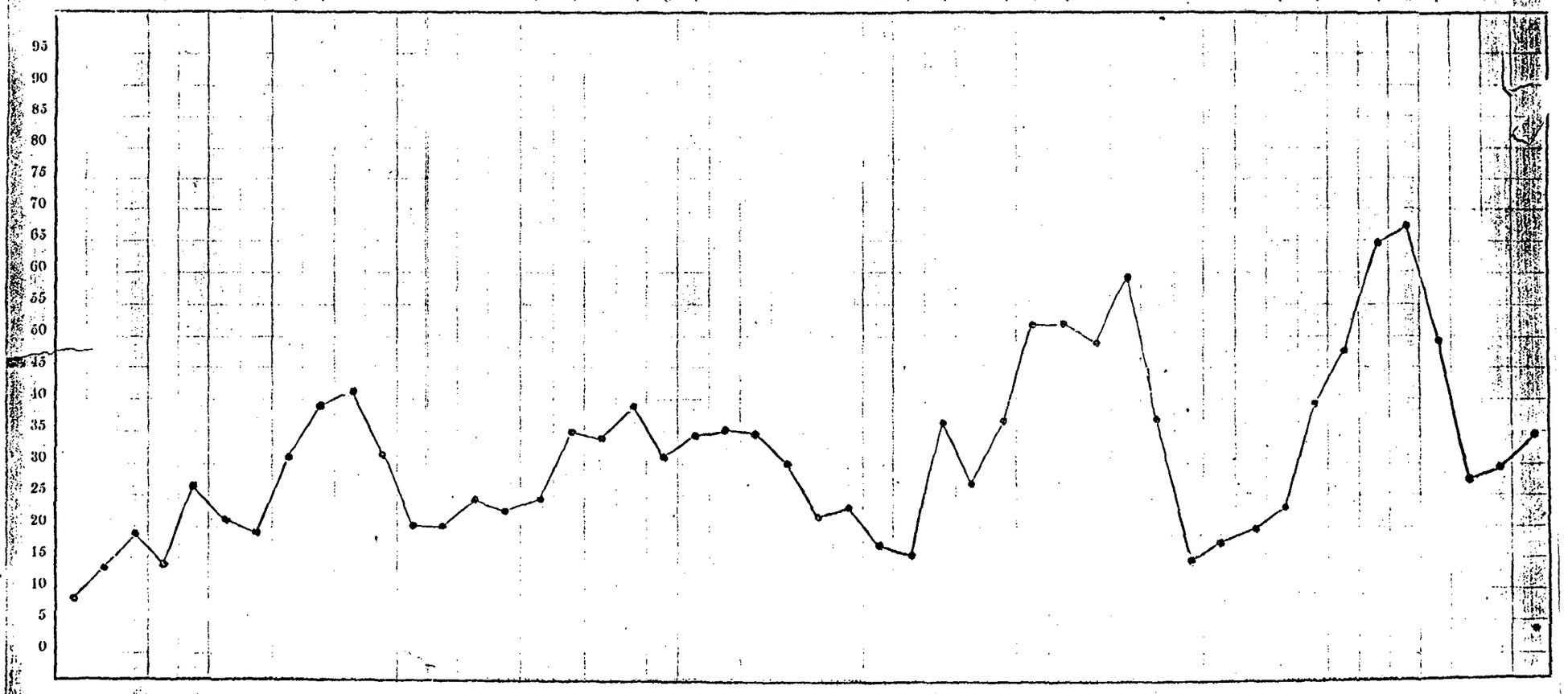


Table V.

Chart shewing Admissions month by month for ten years 1895-1904.

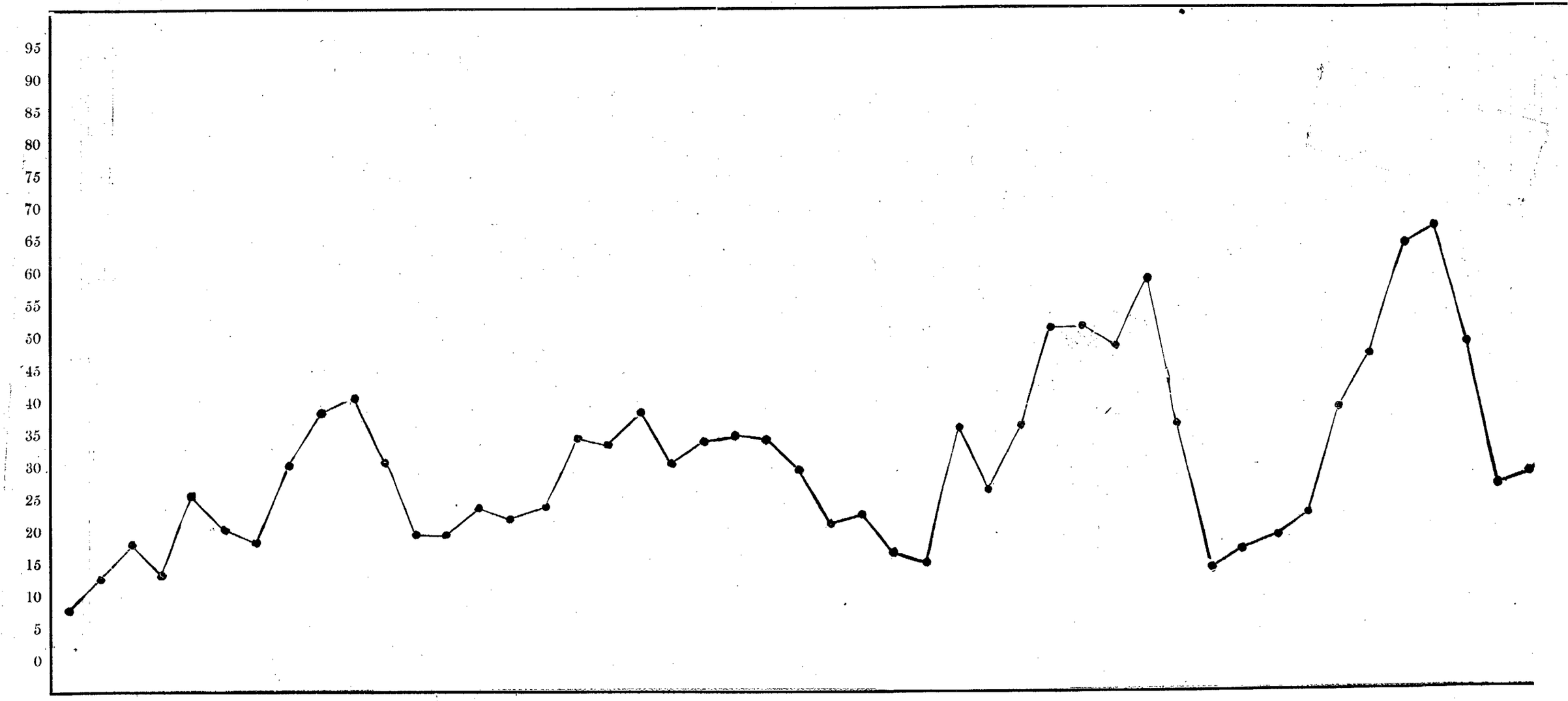


Table V,—*Continued.*

Chart shewing Admissions month by month for ten years 1895-1904,—Continued.

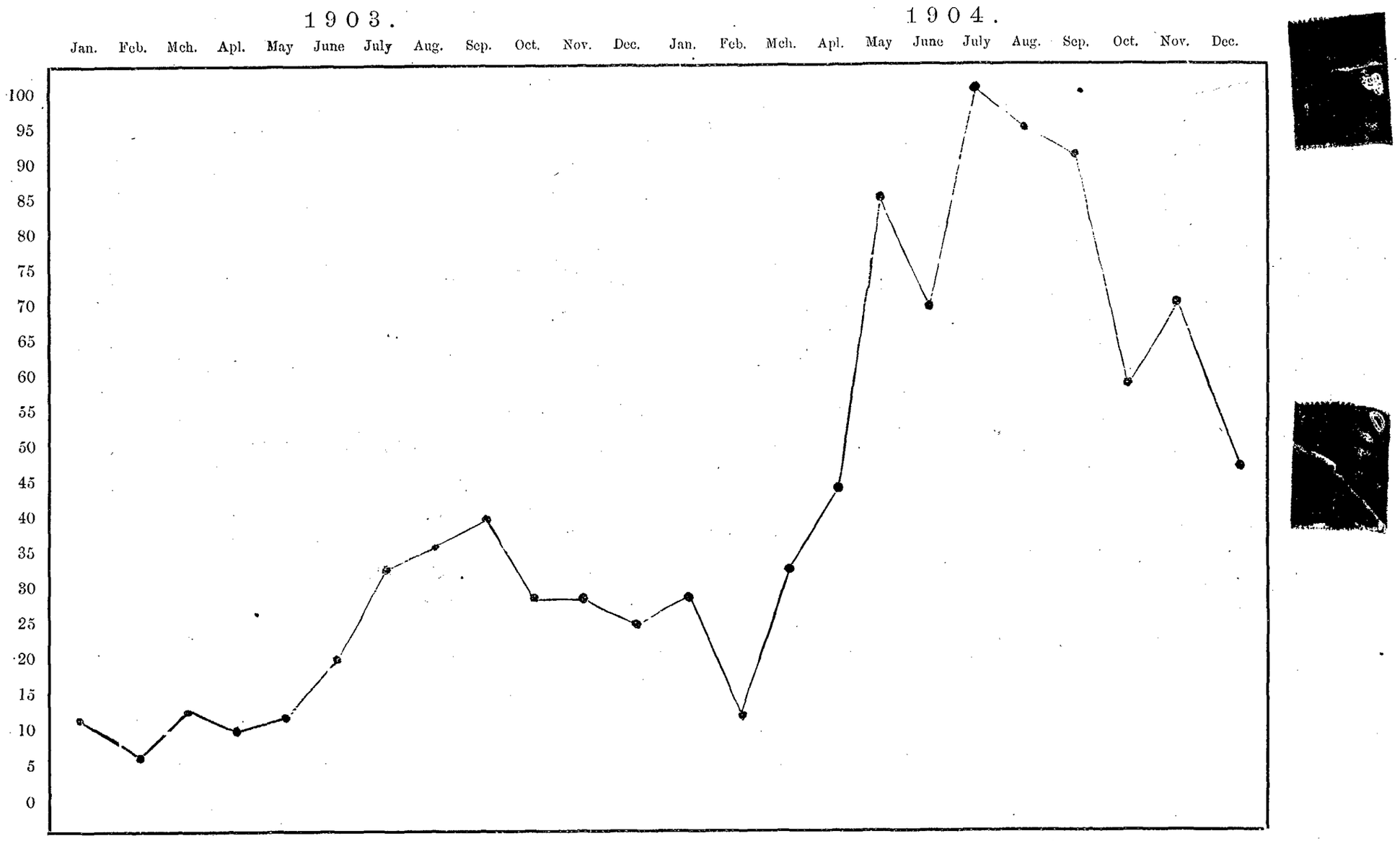


TABLE VII.

AGGREGATE DEATHS PER MONTH, 1895-1904.

Age.	January.		February.		March.		April.		May.		June.		July.		August.		September.		October.		November.		December.		Total.	
6–10.....	...	...	...	...	...	...	...	1	...	...	...	...	1	...	...	...	...	...	...	...	...	...	...	1	1	2
11–15.....	3	2	...	1	1	...	...	...	...	...	...	1	...	1	...	...	...	2	...	1	1	...	1	1	6	9
16–20.....	10	2	5	1	4	...	4	1	10	1	8	1	16	...	11	...	24	1	9	2	9	2	12	...	122	11
21–25.....	10	...	19	...	9	...	18	2	27	...	23	1	39	1	36	3	33	1	36	...	31	...	23	2	304	10
26–30.....	14	1	18	1	19	2	23	...	38	1	30	1	30	1	41	...	30	...	36	2	37	1	25	1	341	11
31–35.....	9	...	11	...	11	2	17	...	19	...	17	...	25	2	23	...	26	...	27	...	26	...	16	...	227	4
36–40.....	5	2	13	2	9	...	15	...	12	...	15	2	25	...	20	...	15	...	16	...	18	1	15	...	178	7
41–45.....	6	...	6	...	5	...	5	...	3	...	5	...	6	...	16	1	19	1	10	...	7	...	6	1	94	3
46–50.....	2	...	4	...	3	...	2	...	6	1	1	...	5	...	7	...	10	...	8	...	10	...	9	1	67	2
51–55.....	1	...	3	...	2	...	3	...	5	...	10	1	5	...	4	...	4	...	7	1	6	1	2	...	52	3
56–60.....	2	...	1	1	1	...	1	...	2	1	1	...	3	3	3	...	6	...	5	1	4	...	3	...	32	6
61–65.....	...	...	...	...	1	...	...	...	1	...	1	...	2	1	...	2	1	..	...	1	...	...	...	...	6	4
66–70.....	1	...	1	1	...	1	...	1	1	...	...	...	...	...	...	...	...	...	2	...	1	...	...	...	6	3
71–75.....	...	1	...	...	...	...	...	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	1
75–	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	63	8	81	7	65	5	88	5	125	4	111	7	157	9	161	6	168	5	156	8	150	5	112	7	1,437	76

TABLE XI.

PERCENTAGES OF DEATHS.

Year.	Admissions.			Deaths.			Total Per-centage.	Percentane of	
	Males.	Females.	Total.	Males.	Females.	Total.		Males.	Females.
1895, ...	117	1	118	63	0	63	53.4	53.8	0
1896, ...	136	13	149	46	2	48	31.5	34.8	15.4
1897, ...	166	15	181	90	8	98	53.0	53.6	53.3
1898, ...	162	8	170	80	5	85	50.0	49.4	62.5
1899, ...	265	16	281	115	7	122	43.4	43.4	43.7
1900, ...	335	25	360	191	11	202	56.1	57.0	44.0
1901, ...	390	27	417	195	11	206	49.4	50.0	40.7
1902, ...	409	12	421	212	3	215	51.0	51.8	25.0
1903, ...	265	17	282	155	6	161	57.1	58.5	35.3
1904, ...	667	72	739	287	23	310	42.0	43.0	32.0
	2,912	206	3,118	1,434	76	1,510	48.6	49.5	35.4

Table VIII.

Table to shew Comparative Monthly Deaths.

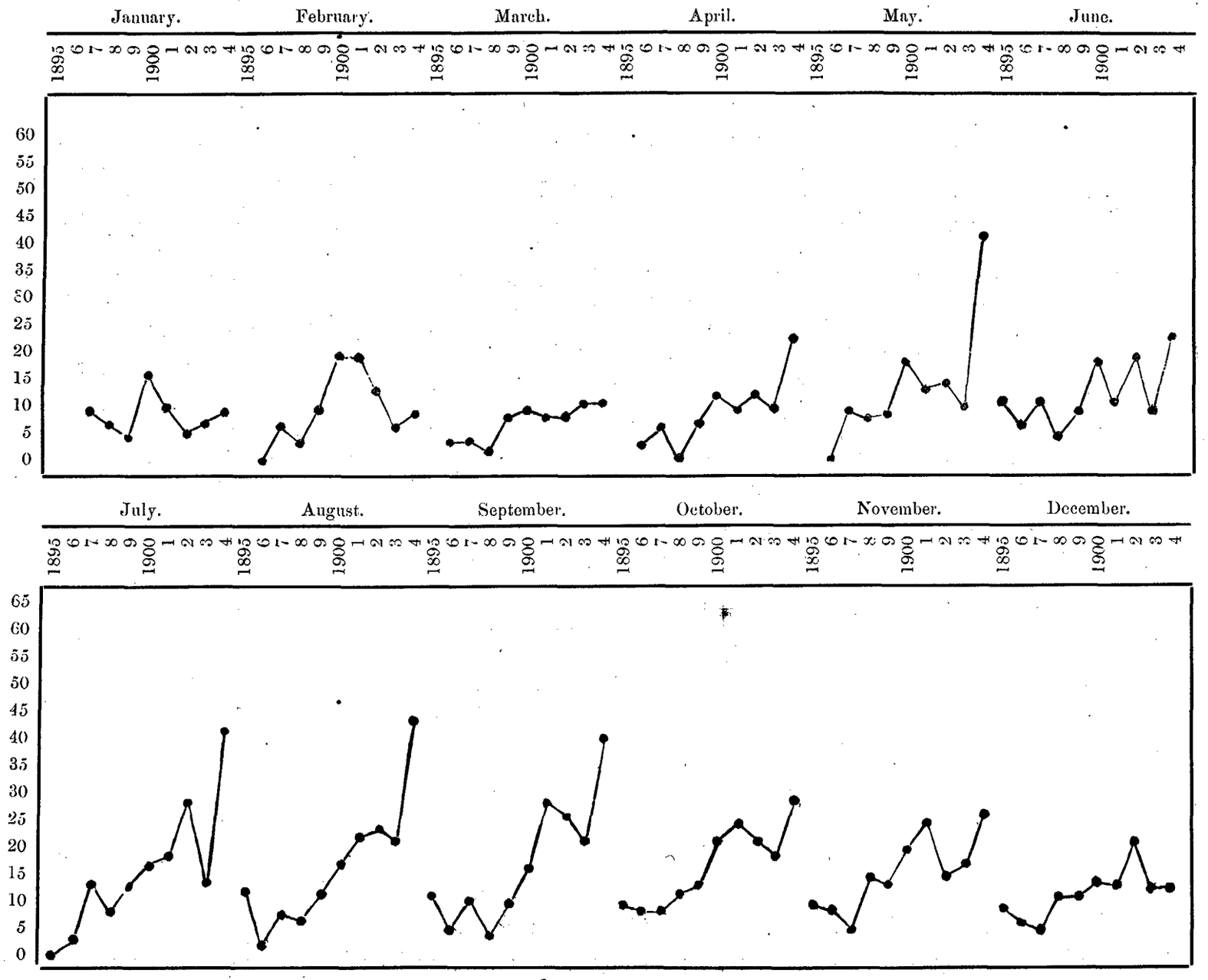


Table IX.

Chart shewing Death rate for 1895-1904.

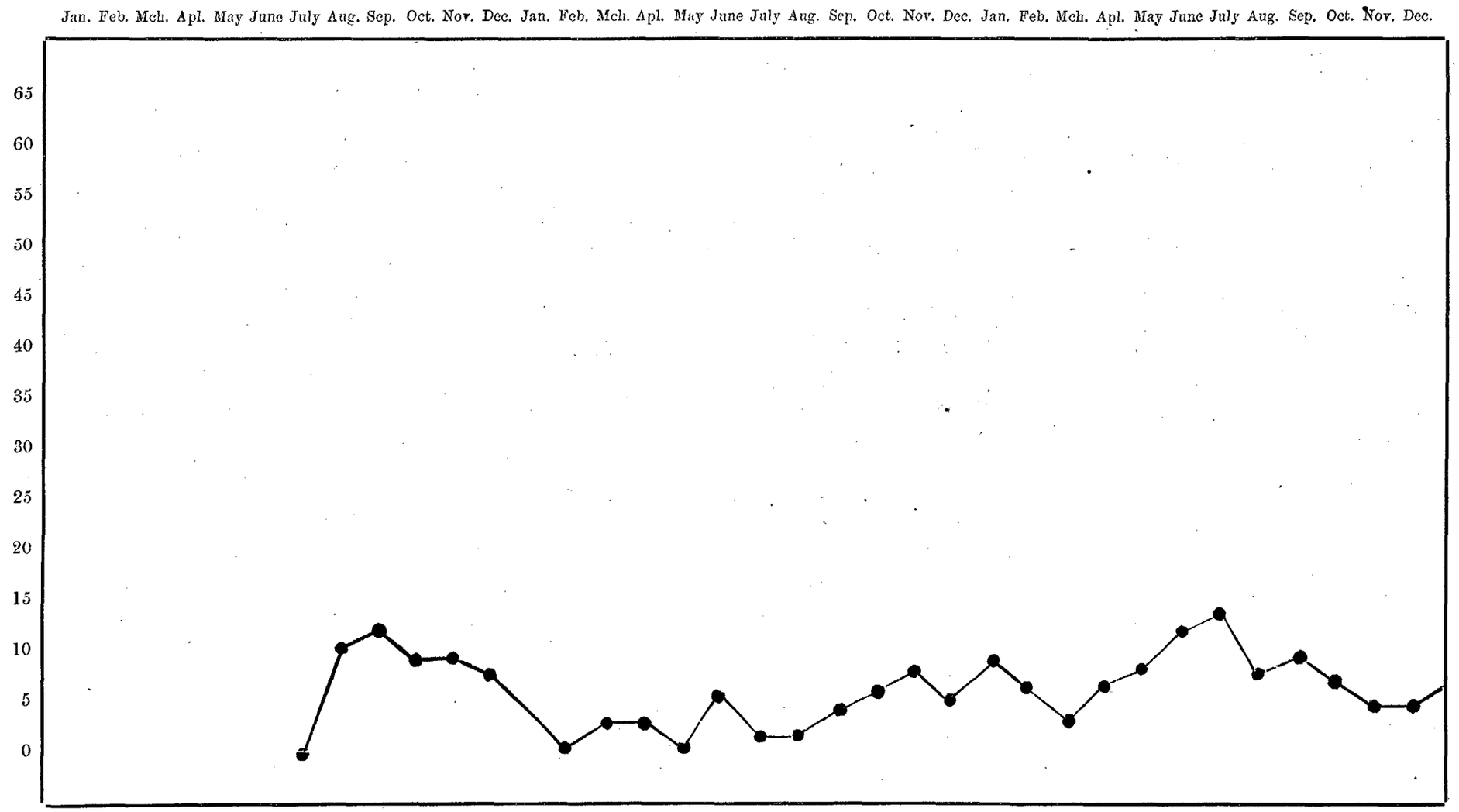


Table IX.

Chart shewing Death rate for 1895-1904.

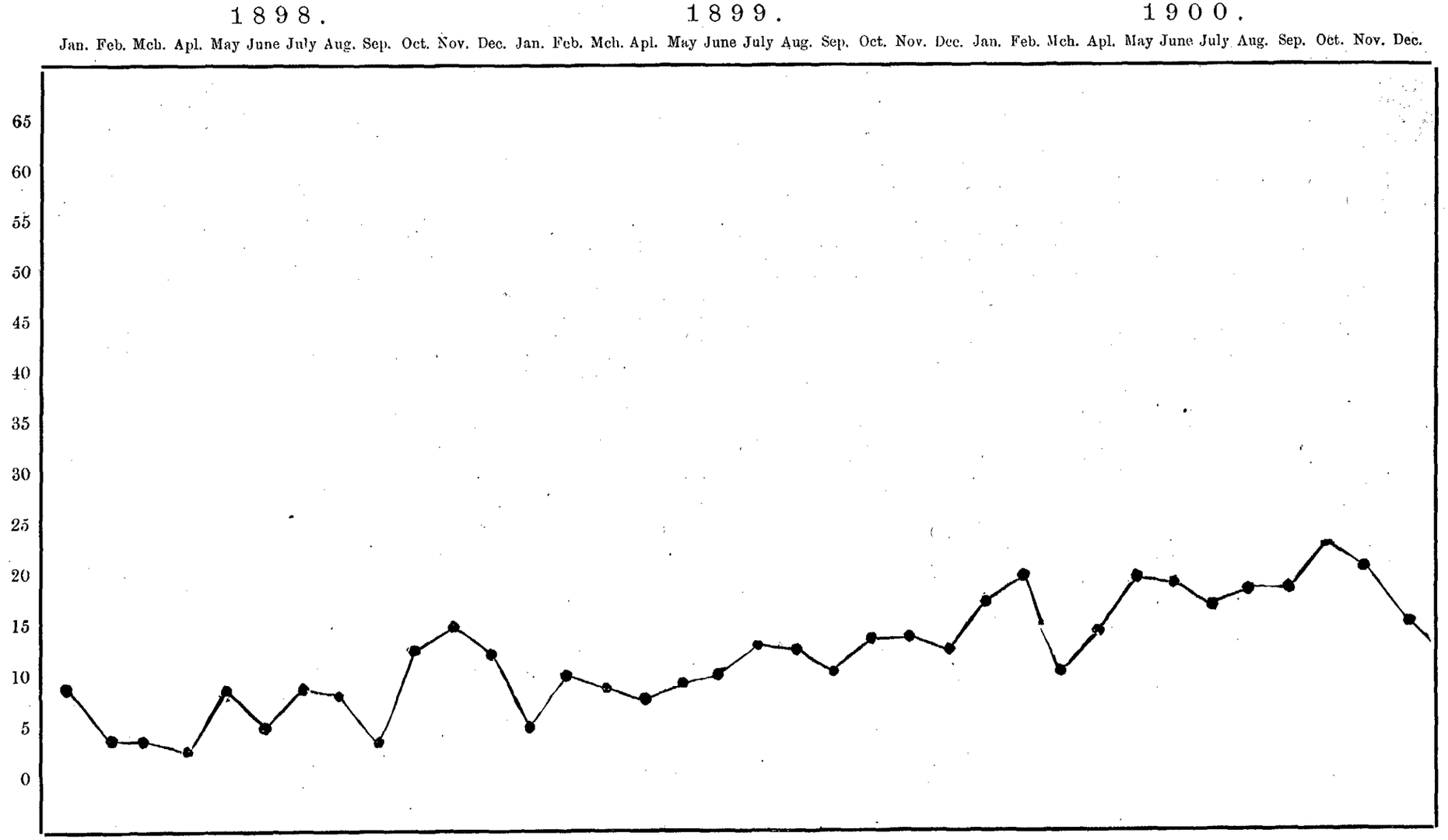


Table IX.

Chart shewing Death rate for 1895-1904.

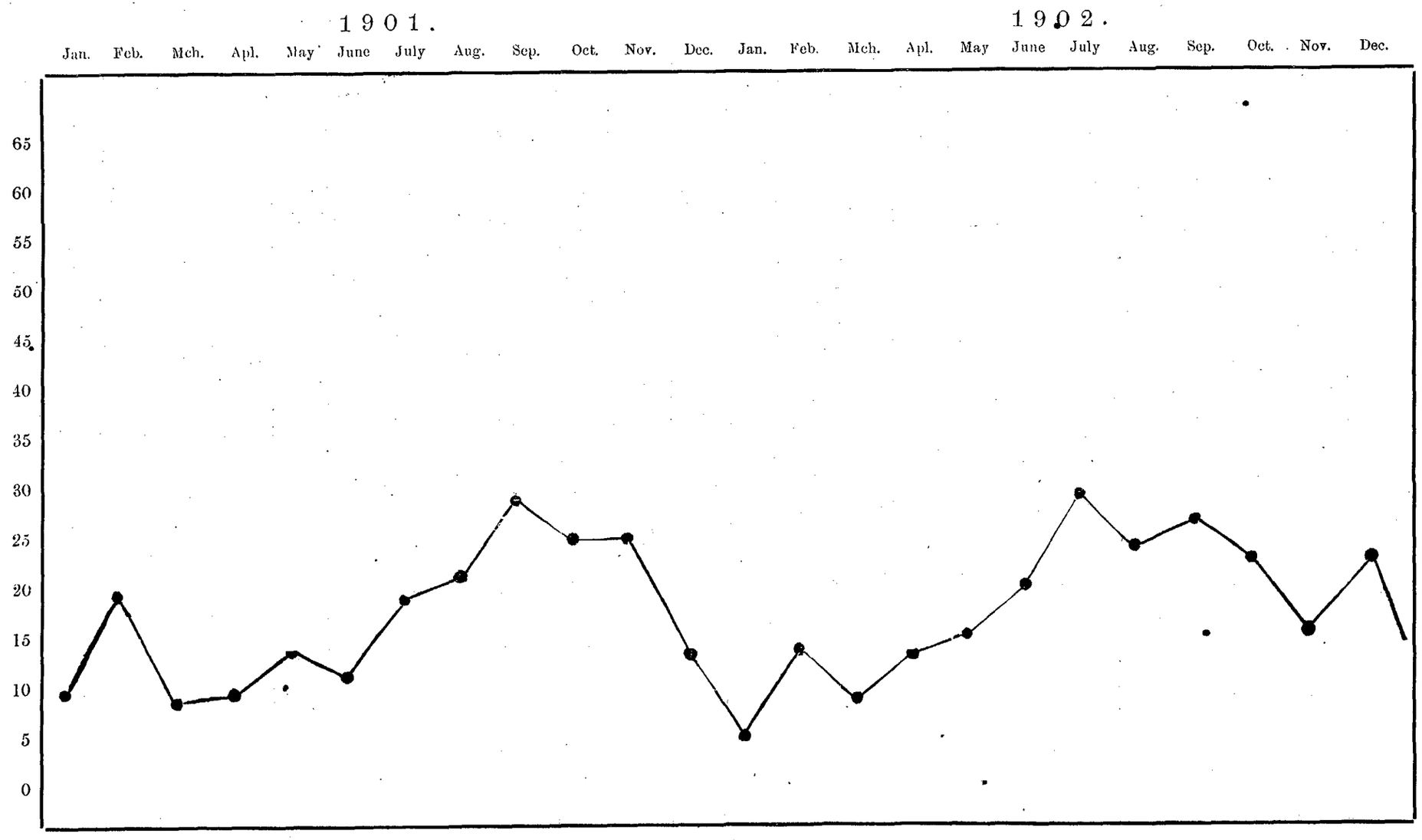


Table IX.

Chart shewing Death rate for 1895-1904.

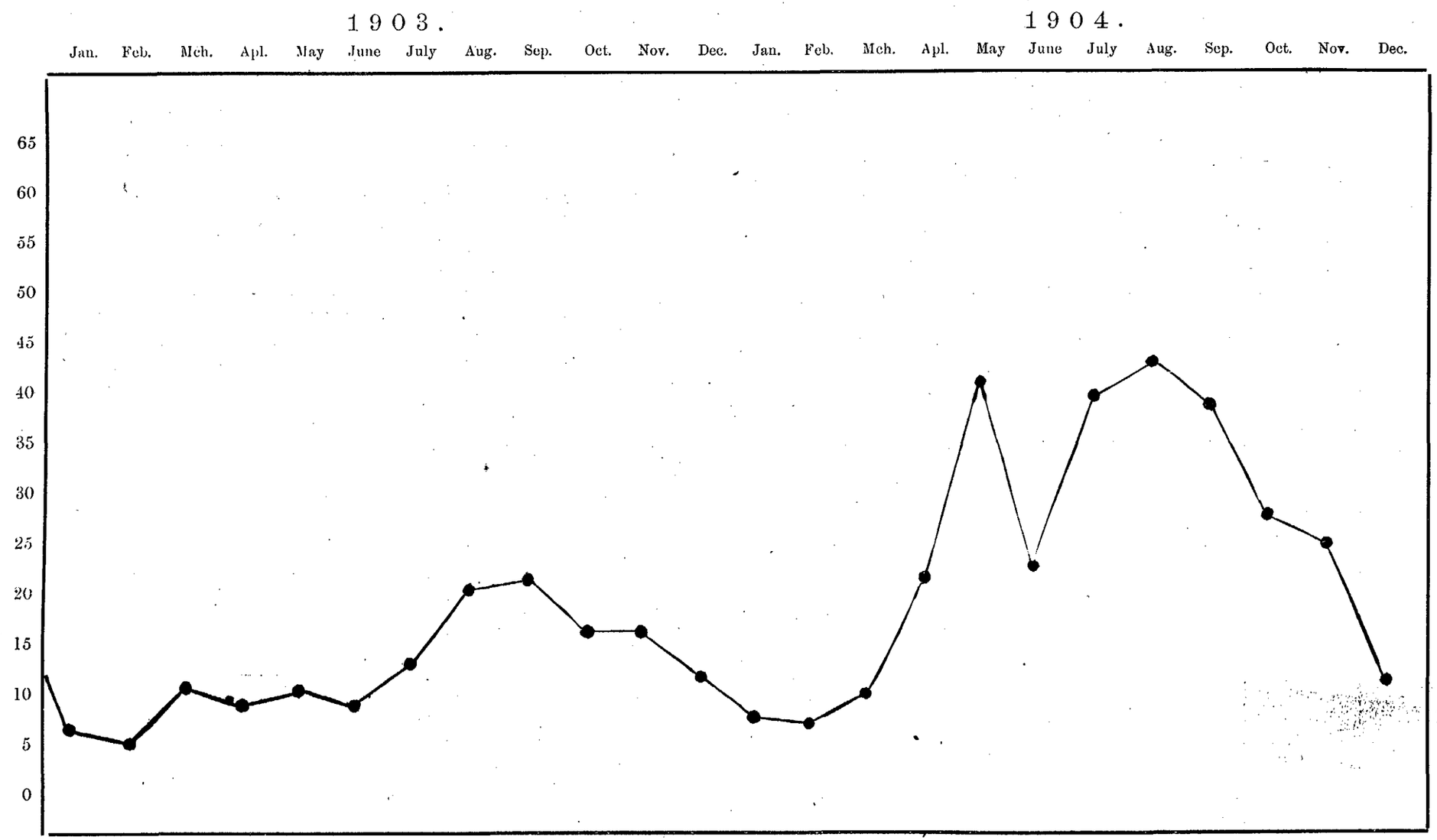
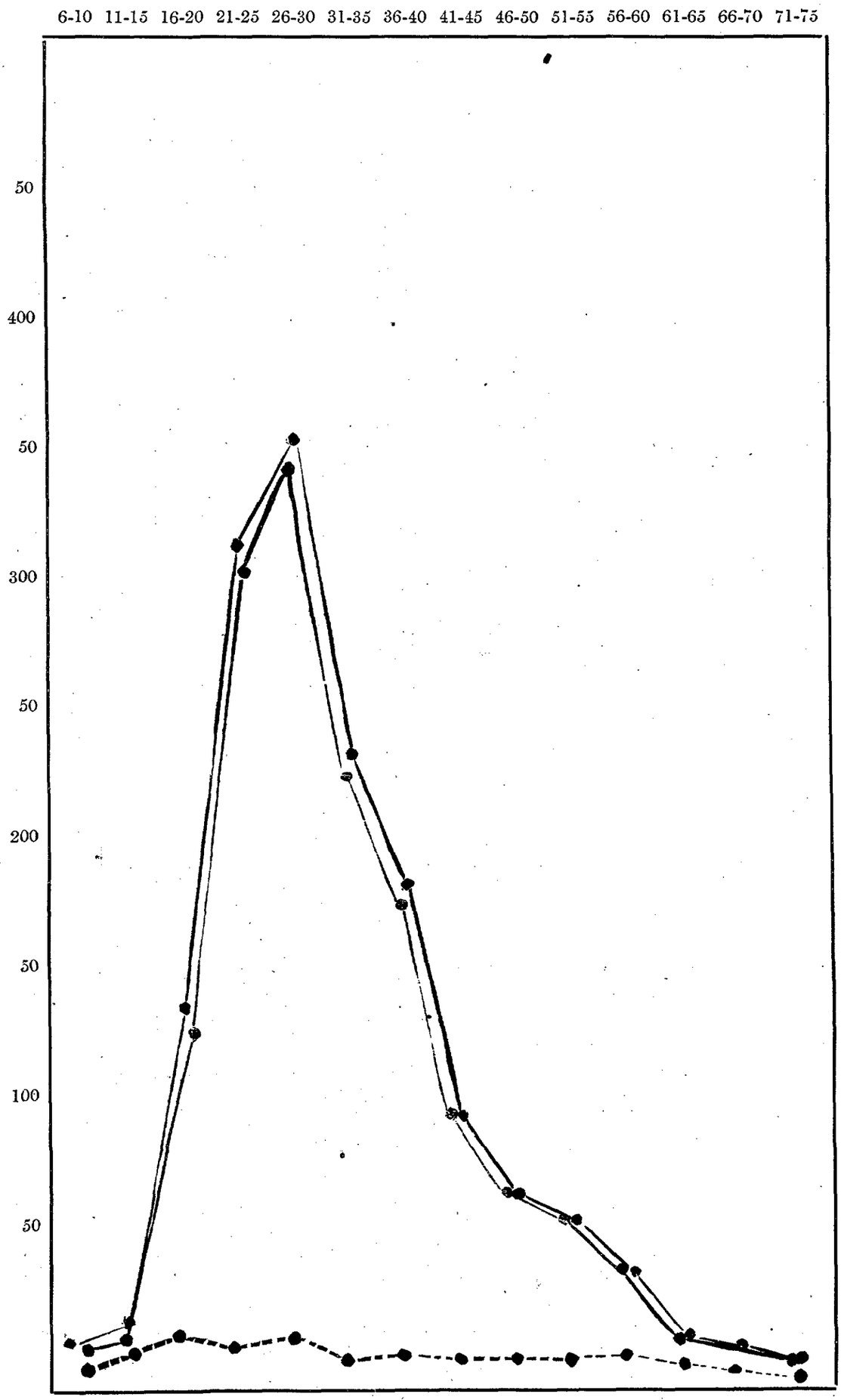


Table X.

Chart shewing Deaths in Quiquennial Age Periods. 1895-1904.



4.—PATHOLOGICAL ANATOMY.

Excellent opportunities are afforded at the Government Public Mortuary for a careful study of the Pathology of Beri-beri. During the past three and a half years over 500 cases of Beri-beri have been examined post-mortem, and the chief lesions and changes noted. All varieties of the disease have been found, but for general purposes, it has been found preferable to divide the cases into Dropsical forms and Atrophic forms.

From our experience in Hongkong, the dropsical form of the disease has formed the larger number of the cadavers sent for pathological examination. This type of the disease would appear to be the most frequent in Hongkong, and this frequency of one particular form of Beri-beri in different parts of the world has been noted repeatedly by other observers. Variations in different places in the same country are also found, and the malignancy of the disease often varies in different years.

The post-mortem examinations which have been held in Hongkong have been upon cadavers of all ages and both sexes. A few cases have occurred in young adults and children but whether the occurrence of Beri-beri symptoms and pathological appearances in the latter, are to be regarded as true Beri-beri is still a matter for dispute. The discussion of this question will be dealt with under a separate heading.

By far the largest number of autopsies have been made upon male cadavers. The female sex would appear to enjoy a comparative immunity from the disease. During the period mentioned only 5% of the total number of post-mortem examinations on cases of Beri-beri have been made upon female cadavers. An explanation of this freedom is difficult to offer. In all probability it is dependent upon the differences in the manner of living, between the sexes.

It is to be regretted that in the majority of cases examined a history of illness was not ascertainable. This was due to the fact that most of the bodies sent for section were found in the streets, in deserted houses, or on the hill-sides.

Beri-beri cadavers shew pathological changes which are of great interest. These structural alterations are generalised throughout the body and are usually so profound as to be easily recognised. Taken individually none of the pathological changes can be regarded as distinctive of the disease. It is only by careful collection of the lesions present, and by a process of exclusion, that a diagnosis of true Beri-beri may be arrived at.

As no recent references regarding the pathology of the disease as met with in Hongkong have been made within recent years, an account of the results obtained during the past 3½ years is of interest.

As already mentioned two types of the disease have been distinguished, namely, the Dropsical form and the Atrophic form. The following is a description of the post-mortem appearances of each.

The Dropsical Form.

To an expert the external appearance of the dropsical Beri-beri cadaver is fairly typical. The cyanotic swollen face with starting eyes, the engorgement of the veins of the head and neck, appearing as blue cords below the skin, the bloody froth about the nose and mouth, and the general corpulent appearance of the body and extremities, coupled with occasional subcutaneous hœmorrhagic extravasations, lead us to suspect the cause of death. In countries in which Beri-beri is endemic, these external appearances presented by a cadaver are held by many tropical sanitary experts to be sufficient to establish a correct diagnosis and thus obviate the necessity of post-mortem examination. In our opinion such methods of corpse inspection are unscientific and much to be deprecated, and with the gradual disappearance of native prejudice, corpse inspection ought to be completely supplanted by routine post-mortem examination. If this be not done such statistics as may be compiled are of little value, and the relative incidence of the disease throughout our Colonies determined by a method directly opposed to the principles and practice of medicine.

In Dropsical Beri-beri the bodies externally appear to be well nourished. This appearance, however, is but a false impression, and is largly dependent upon the development of general anasarca before death. The rate of decomposition of the bodies is when compared with those of the acute infectious fevers, relatively slow. Further, the condition known as foaming organs is not so frequently found in Beri-beri corpses as amongst those of the acute specific fevers.

Post-mortem lividity is usually pronounced especially on the face, neck and back. This discolouration is not so pronounced as one finds in the case of a constitutional infectious disease, *e.g.*, Pest. Rigor mortis may be present. In some cases it is practically absent.

The skin is usually normal in appearance. Old scars which have nothing to do with the disease are frequently found scattered over the body surface. Eruptions may be present but it is questionable if they have anything to do with the disease. Subcutaneous hœmorrhages may be found but are not frequent in the type of cases met with here.

No special pigmentation of the skin or mucous membranes has ever been noted.

On section of a Beri-beri corpse the first thing which strikes the eye is the amount of watery fluid in the subcutaneous tissues and body spaces. In well-marked cases of the dropsical variety, a mere cut in the skin occasions a regular outflow of clear serous fluid. The subcutaneous tissue has a jelly-like or mucoid appearance and from this the fluid pours continuously. Subcutaneously a considerable quantity of fatty tissue may be found, but its consistence and colour, etc., shew this layer to be in a state of degeneration. Indeed the appearance of the subcutaneous tissue, apart from the large amount of fluid present, in a well-marked cadaver resembles that found in newly-born children. This great infiltration of the subcutaneous tissue with serous and mucoid-like fluid is characteristic of dropsical Beri-beri.

The pericardial sac in marked œdematous cases is usually distended with fluid. The parietal layer is usually slightly congested and may shew a few petechial hæmorrhages. On opening the sac a clear straw-coloured fluid, free from flaky material, wells out often in enormous quantity. Milky patches are frequently found present scattered over the surface of the epicardium. These, as well as the tissue along the course of the main coronary vessels are usually infiltrated with fluid and have a swollen, mucoid and translucent appearance. Occasionally the coronary vessels look as if they were embedded in a clear yellowish jelly-like substance. Usually there is no evidence of pericarditis.

In all cases of dropsical Beri-beri the **heart** as a whole is enlarged. The extent of this enlargement varies within wide limits. Occasionally hearts of enormous size are found like the so-called "bullock's heart." Coupled with this enlargement one usually finds a considerable increase in the weight of the organ. The amount of fatty infiltration on the heart also varies. In the majority of cases the fatty deposit is in excess. The coronary arteries are usually normal. The auricles, especially the right, are usually dilated. The right ventricle in the majority of cases is markedly dilated and contains a large solid and firm blood clot. Occasionally a certain amount of hypertrophy of the wall of the right ventricle is found, especially in cases of a more chronic nature. As HAMILTON WRIGHT puts it—dilatation and more or less hypertrophy of the right ventricle is the rule in cases of beri-beric residual paralysis. The left ventricle is usually only slightly dilated, and its walls are often found in a state of marked hypertrophy, especially when the cases have run a chronic course. In acute cases, on the other hand, dilatation may exist without hypertrophy. The walls of the ventricle are usually pale in colour and greasy and friable to touch. The cardiac muscle is almost always in a state of fatty degeneration, although the degree of this degeneration varies extremely in each individual case. On opening the heart enormous quantities of extremely dark-red blood escapes which is perfectly fluid. On allowing it to stand for a few minutes freely exposed to the air, it becomes of a brighter red colour and begins to clot. As is generally now accepted, this peculi-

arity on the part of Beri-beri blood is accounted for by the fact of the presence of an excess of CO_2. The valves of the heart are usually competent. Tricuspid incompetence may however be met with. Scattered over the inner surface of the cavities of the heart numerous small petechiæ are frequently found.

The **aorta, arteries** and **veins** are frequently the seat of extensive atheromatous degeneration. This however has little to do with the disease, and is a common pathological change among the Chinese over 30 years of age.

The **upper respiratory passages** are in almost all cases normal. Hyperæmia and œdema of the epiglottis is found rarely. Occasionally the mucous membrane of the entire **larynx** is in a similar condition. The **trachea** may also be found congested, and on its mucous membrane a thick yellowish secretion is frequently found. The **bronchi** usually contain an appreciable quantity of secretion which may be simply bubbly mucus, or of a purulent or semi-purulent nature.

The **lungs** on opening the chest only partially collapse. They are usually crepitant throughout. As a rule these organs are full of œdematous fluid which wells out profusely from the cut surface. On squeezing the latter a bloody frothy fluid and watery mucus oozes in large quantity. In addition to the presence of œdema, emphysema to a varying degree is usually present and this is occasionally so pronounced as to cause the anterior edges of the lungs to meet over the percardial sac. Hypostatic congestion of varying degree is usually present in the posterior and lower portions of the lung tissue. A considerable proportion of cases of Beri-beri end fatally owing to the supervention of pneumonia.

The **pleural cavities** are usually normal. Adhesions are frequently present but these are common amongst the Chinese who often suffer from sub-acute and localised pleurisies. Bilateral Hydrothorax is the rule in all well-marked cases of dropsical Beri-beri —both cavities being more or less full of clear yellow-coloured fluid. The bronchial glands are usually normal. In extreme cases of general anasarca they may be slightly enlarged owing to the presence of œdematous infiltration and cortical congestion. Amongst the Chinese old tubercular deposits are frequently found in these glands.

The **thymus gland** in young adults may be slightly enlarged owing to œdema and congestion.

The **peritoneum** is almost always normal. It may be thickened owing to the presence of œdema. Hydroperitoneum is usually present and may be extreme. The fluid, as in the other cavities, is clear yellowish and viscid in character.

The condition of affairs found in the **alimentary canal** in Beri-beri, has within recent times been the subject of considerable dispute. Most authorities state definitely that the digestive tract in this disease present nothing of any great pathological importance. Other investigators as HAMILTON WRIGHT and his colleagues in Malaya, however, attach considerable weight to the presence of certain alimentary lesions. They regard the changes present as more or less constant, as typical for Beri-beri, and the point of entrance of the materies morbi of the affection. HAMILTON WRIGHT in his most recent publication on the pathology of Beri-beri describes what he calls the primary lesions, namely, a gastro-duodenitis, and in his conclusions follows up this statement by a considerable amount of weighty evidence in favour of his view. Whether this theory, which up to the present is an isolated one, will be confirmed by subsequent workers, will be awaited with considerable interest. If this conclusion be established that "the premonitory gastro-duodenal syndrome of Beri-beri has as its pathological basis a definite gastro duodenitis", and that this is the primary lesion of the disease, all that remains to be done is to establish the presence of a definite exciting cause of such a lesion. So far no micro-organism has been brought into definite causal relationship with the disease and all attempts by HAMILTON WRIGHT and others to isolate a biological cause of Beri-beri have failed up to the present time.

The following is a brief resumé of the results of our post-mortem observations:—

The **mouth**, including the teeth and tongue, is usually normal. The **pharynx** may be congested and its mucous membrane swollen owing to œdematous infiltration. The **œsophagus** is in almost every case normal—congestion is uncommon. The condition of the **stomach** varies according to the severity and duration of the disease. In well-marked cases of moderate duration, this viscus will be found dilated and in a condition of muscular atony. The peritoneal coat is normal. The other coats and especially its mucous membrane are usually thickened, soft and œdematous. On opening and cleansing the organ the appearance of the mucous membrane is very variable. It may be normal, and all grades from this to the presence of passive congestion, necrosis, and hæmorrhagic extravasation, are to be found on examination of a large number of cases. In a few, as already stated, the mucosa is normal to the naked eye. In others the cardiac end is normal, whereas the pyloric end is congested, angry-looking, and presents a few blood extravasations. At other times small points of necrosis of varying size may be found in addition. In still another series of cases the whole mucous coating of the stomach is congested, reddish-black in colour, and contains numerous scattered extravasations of blood of variable size. The necrosed areas may or may not be present. If they are, they are of varying size and shape, and the dead tissue may be removed easily, leaving a raw but dead-looking floor. These irregularities in the mucous membrane caused by sloughing are not marked by the presence of surrounding cellular infiltration, and their edges and floors shew but little attempt at re-organization. Lying between the folds of the mucosa one usually finds a considerable amount of thick, greyish-yellow, tenacious mucus.

The condition of the **duodenum** also varies within wide limits. The gut may be normal or it may shew the changes already described under the stomach. The hæmorrhages, punctiform or diffuse, into the mucous membrane of the duodenum, are chiefly found on the coats of the valvulæ conniventes. Necrosis of the mucous membrane has not been observed.

The **jejunum** is frequently congested, but in many cases nothing abnormal is to be noted.

The **ileum** may be normal. At other times congestion to a varying degree is present and may be accompanied by the presence of a few punctiform blood extravasations.

The **lymphatic tissues** of the small intestine do not appear to be affected

The condition of the **cæcum** resembles that of the other portions of the small intestine.

The **large intestine** presents no characteristic change of a pathological nature. The mucosa may be thickened and soft owing to the presence of œdematous infiltration. Otherwise it is usually normal.

The **rectum** is usually normal.

In dealing with the large gut one has to be careful to exclude any lesions of a dysenteric nature which may be present. A thickened colon with old scars and increased pigmentation is frequently found amongst the Chinese, and is to be referred to recent or remote inflammations of a dysenteric nature.

The **mesenteric lymphatic glands** may be normal. Frequently, however, they are found moderately enlarged owing to œdematous infiltration and congestion. The latter is only slight and cortical.

The **mesentery** is thickened and sodden, being drenched with œdematous fluid.

The foregoing description of the pathological changes found in the alimentary canal have been formulated from the results of a large number of typical cases of dropsical Beri-beri. It will be noted that such changes as are found are subject to considerable variation. Congestions, mostly of a passive character, are common, and, as a result of this and other factors, which will be discussed later, necrosis of limited extent, and hæmorrhages make their appearance. Tissue changes of a

true inflammatory nature do not appear much in evidence. Indeed, on the other hand, the conditions met with in the stomach and other parts of the gut suggest an absence of trophic nerve influence, nerve degeneration, and consequent vascular engorgement, stasis, hæmorrhage, etc.

The descriptions and interpretations of the condition of the alimentary gut given by us, are totally different from that recently furnished by HAMILTON WRIGHT; who somewhat forcibly drives home his theory of gastro-duodenitis as the primary lesion of Beri-beri, indicating thereby the existence in this part of the gut of a definite acute inflammation, excited by some particular germ, and resulting in the advent of the well-known symptoms and signs of Beri-beri.

The **liver** is usually increased in size, weight and specific gravity. Its consistence is firm and capsule is stretched and usually has a congested parenchyma shining through it. Hæmorrhages into the capsule are rare. In cases of Beri-beri of short duration, the capsule of the liver is normal, but in the more chronic cases thickenings are frequently found in it. These are localised and scattered over the surface of the organ. They are greyish-white in colour, and ramify and branch in a tree-like fashion. This peculiar form of capsular thickening is also found in connection with the spleen and some other organs. It is not specially characteristic of Beri-beri and is found in other diseases, such as chronic malaria, but in the disease under consideration it is usually peculiarly well defined. On section the liver frequently drips with blood and watery fluid. The colour of the parenchyma is usually normal, or darker than normal. Fatty changes are often found well marked. Cirrhosis of the intra-lobular variety is frequently found in chronic dropsical cases. The gall bladder is usually distended with bile. The walls are thickened, soft and œdematous. Blood extravasations are rare. The bile is thick, tenacious and dark-green in colour.

The **spleen** varies extremely in size and weight. It may be normal but in other cases spleens 3-4 lbs. in weight and of enormous dimensions have been found. This variation, however, would not appear to depend wholly upon Beri-beri and is due probably to other causes, *e.g.*, malaria. Capsular thickenings of the spleen are very common, and may reach 3-6 m.m. in thickness. The organ is usually moderately congested and on section bleeding surfaces are left. A general fibrosis of the organ is frequently present.

The condition of the **kidneys** varies. They may be normal, at other times cloudy swelling and congestion is present. Usually the capsule peels readily from the surface. Slight cirrhosis is not infrequently present. Hæmorrhages are rare.

The other **genito-urinary** organs are normal. Œdematous thickenings are found in marked dropsical cases, being part of the generalised anasarca.

The **supra-renals** and **pancreas** are normal.

The membranes of the **brain** and **spinal cord** are thickened. This is either patchy or generalised. Their contained vessels are full of dark-red fluid blood. The **cerebro-spinal** fluid is usually in excess. The brain and spinal cord are usually normal to the naked eye, but are firmer owing to œdematous infiltration below the pia mater, and the existence of slight increase of fibrous tissue.

To recapitulate—the naked eye pathological changes found in dropsical cases of Beri-beri may be summed up as follows :—

1. General anasarca and dropsical accumulations.
2. Venous hyperæmias and their results.
3. Fibrotic accumulations of varying degree.

The Atrophic Form.

The external appearances of atrophic Beri-beri cadavers are vastly different from that of the foregoing variety. There is a typical picture of anæmia and advanced emaciation. In old standing examples of the disease the cadaver is practically skin and bone, and as the body is viewed on the post-mortem table the posture assumed is varied owing to the presence of muscular contractures and other deformities.

The general nourishment is extremely poor, the eyes are sunken, rigor mortis is variable in its degree, and post-mortem lividity is usually present in traces about the most dependent parts. The skin may shew atrophic changes, and sores of various kinds are frequently present especially over the bony prominences of the posterior parts of the cadaver, and there is increased pigmentation. In general, the impression produced by the corpse inspection of a typical and advanced case is that some constitutional disease of an extremely chronic nature was the cause of death and that the latter supervened only after the individual had been reduced to a condition almost approaching mummification.

On opening the body one notes the extreme wasting of the muscles. They are soft and flabby and tinged of a yellow colour. The subcutaneous fat is at a minimum. The tissues often appear as if dried and shrivelled. In some cases a slight quantity of thin, serous fluid oozes out from the tissue spaces.

The **pericardial sac** usually contains a slight excess of fluid. This is of a clear yellow colour and watery character. The pericardial layers are thickened, and often present an opaque white appearance due to an increase in the amount of dense white connective tissue. Frequently the mucoid and swollen appearance is found, similar to the condition met with in the dropsical forms of the disease. Pericarditis is scarcely ever found.

The condition of the **heart** varies. It may be enlarged and flabby. Usually however the organ is normal in size, in a condition of systole and its walls thickened. A certain degree of hypertrophy of the right ventricle is found associated with more or less dilatation. The left ventricular wall is also thickened. The walls of the heart are usually somewhat hard and friable. The amount of granular and fatty degeneration of the cardiac muscle varies in each individual case. Sometimes the already mentioned jelly-like substance is found in considerable amount in the walls. It lies embedded between the layers of the cardiac muscle, under the epicardium, and also along the course of the coronary vessels. The **valves** are usually competent. The presence of petechiæ is uncommon.

The **blood** is similar to that found in the dropsical variety. It is fluid, very dark in colour, and clots after its removal from the body. Firm clots are frequently found in the ventricular cavities. Frequently these are of ante-mortem origin.

The **lungs**, on opening the chest, do not collapse. They are usually hypercrepitant throughout and emphysematous changes are predominant. Œdema to a varying degree may be present, particularly about the posterior and basal regions of the organs. The visceral layers of the pleura are usually thickened owing to fibrosis and in this membrane and lying beneath it one frequently finds accumulations of varying amount of the clear jelly-like substance of a yellow colour.

The **pleural cavities** usually contain a small but varying amount of clear yellow fluid.

Pleurisy is rarely met with.

The **peritoneum** is usually normal. Thickenings of the membrane are occasionally found, and are due in most cases to localised modules of mucoid tissue. A varying increase in the amount of peritoneal fluid is usually present and its character is identical with that found in the other serous cavities of the body.

The **alimentary canal** presents nothing of any great significance. The variable changes found in the dropsical variety are rarely met with in this type. Generally speaking the whole of the gastro-intestinal tract is in a state of atony, its walls are thinner and pigmented, and jelly-like material is present in varying amounts, especially along its mesenteric attachment. There is nothing in the alimentary tract to stamp it as the primary focus of the disease.

The **liver** presents little alteration in size and shape. Its consistence is firm usually owing to the presence of an increased amount of connective tissue. The peculiar thickenings of the capsule described in the other variety are often present to a marked degree.

The **spleen** varies much in size, is usually fibrotic and shews the thickenings of its capsule as already described. It presents nothing further worthy of note.

The **kidneys** apart from slight interstitial changes present nothing abnormal.

The **brain** and **spinal cord** are usually normal to the naked eye. Under the pia mater the mucoid substance may be found in varying quantity.

Conclusions :—

1.—Emaciation, variable in degree, due to chronic wasting and degeneration of tissues.

2.—Fibrosis of the organs and tissues.

3.—The infiltration of jelly-like material into the various organs and tissues, consequent upon the degeneration of the latter.

5.—BACTERIOLOGY.

Like most diseases of wide geographical distribution and even recurring incidence amongst the natives of many of our most important colonies, the Etiology of Beri-beri has been the subject of much careful investigation. Prior to the days of the microbic theory of disease, Beri-beri was attributed to causes such as cold, heat, rains, fatigue, etc., upon which the investigator placed great significance, and which are now recognised as mere general predisposing causes of the majority of diseases affecting man.

It would be out of place in such a Report as the present to attempt to unravel the chaos of theories which has accumulated within the past few years, and especially since the advent of Bacteriology and Pathological Chemistry. It will be sufficient to note here that since this date, the theories regarding Beri-beri have, in the main, run along two lines, namely, the Diet Theory and the Germ Theory.

Regarding the Diet Theory, Nitrogen Starvation, Deficiency of Fat, and Infected Poisonous Foods all these have been adduced, with many plausible arguments, as excitants of the disease. On the other hand, the Bacteriological Theory includes the discovery in Beri-beri of the most varied species in biology from worms down to amœbæ and bacteria. In the presence of such a chaotic mass of theories and literature regarding the etiology of Beri-beri, it is obvious that the subject still requires much investigation along absolutely unbiassed lines of research. It has seemed to us that so far as the bacteriological theories are concerned and the results of bacteriological investigation, too much attention has been paid to the fashionable cause of disease at the present day, namely, bacteria. In such investigations of the unknown causes of certain diseases, one must always bear in mind, that although the tendency at the present day is to cause everything to be bacteriological, there must be many diseases affecting man the etiology of which has nothing to do with biology. The significance of this is at once apparent regarding the disease at present under consideration, as many recent investigations shew. Although some experts on Beri-beri who have dealt voluminously with the subject declare that the factors regarding the diet theories can be reduced *ad absurdum*, and that the only theories which may hold sway are bacteriological, we believe that still much remains to be done from the point of view of pathological chemistry. Indeed we doubt if the disease has ever been dealt with thoroughly by an expert pathological chemist.

During the present research our investigations have been necessarily limited to the bacteriological side of the question and the negative results which have been obtained as regards the etiology of the disease have much to recommend further research, not along bacteriological principles, but along the lines pursued by the expert pathological chemist.

If it be granted that the disease is bacteriological in its etiology there is little to recommend the theory of gas-intoxication of MANSON. We cannot conceive a disease such as Beri-beri with its many manifestations being stirred up in such a manner. Noxious or non-noxious gaseous effluvia could scarcely cause Beri-beri. The results of PEKELHARING and WINKLER may be verified by anyone posses-ing bacteriological knowledge. Cocci, pigment producing or otherwise, bacteria, etc., may be isolated from almost every case of Beri-beri and from almost every organ in such cadavers. Such micro-organisms, however, have no great pathogenic effect on animals and so far as one can judge they bear no causal relationship to the disease. The isolation of such micro-organisms as cocci, bacilli or bacteria, is not limited to Beri-beri cadavers, they may be isolated from almost any cadaver of a few hours old. With a knowledge of the rapid post-mortem wanderings of micro-organisms and the influence of the tropical climate on the degree of rapidity of decomposition, one cannot be surprised at the advent of such organisms in our culture tubes, particularly if the technique employed is in the slightest degree defective. Again, therefore, we wish to emphasize that, in our opinion, the micro-organisms isolated by PEKELHARING and WINKLER have no connection with Beri-beri, and their isolation by these workers was due to the circumstances mentioned in the foregoing.

Coming to the most recent of germ theories of Beri-beri, namely, that formulated lately by HAMILTON WRIGHT, it has been our chief aim to follow out this as carefully as possible during the present enquiry. Put before the medical profession as it has been by WRIGHT, such a theory of Primary Gastro-duodenitis due to a micro-organism (probably not unlike the B. Diptheriæ in its action) lying latent in some unknown form and multiplying in the stomach and duodenum, requires earnest consideration before it can be accepted or refuted. At the outset HAMILTON WRIGHT accepts the dogma that Beri-beri is to be classed as an acute specific infectious disease. The arguments for and against such a statement are many, and it is our intention to deal with this branch of the subject under a separate heading. Given the infectivity of the disease, WRIGHT shews us the primary lesion of the disease in the gastro-duodenal mucous membrane and notes the incidence of bacteria in such tissue, as are pathological in this locality. He likens the growth of such bacteria in the mucous membrane to that of diphtheria and is inclined to attribute all the well-marked evidence of the presence of Beri-beri to secondary degenerations called forth by the action of an assimilable toxin elaborated by the bacilli locally in the gastro-duodenal mucosa and absorbed directly into the general blood stream. According to WRIGHT hoards of a particular form of bacillus are found between the epithelial cells of the pathological mucous membrane, and the number of these gradually diminish as the healthy mucosa is reached.

Further than these bland statements as to the incidence of bacteria in the mucosa of the alimentary tract in Beri-beri, we find little in WRIGHT's paper on the subject regarding the isolation of his special bacteria and the results which he obtained on testing his cultures experimentally. Without such data one feels bound to attribute little importance to that part of WRIGHT's researches which deal with the bacteriology of the disease. Indeed we may go further and point out that as the alimentary tract throughout its entire course is a regular hotbed of all sorts of biological life, the mere finding microscopically, in sections of the damaged gut, of hoards of bacteria can excite no surprise or suspicion that these micro-organisms are actually the causal agents of the disease. In the pathological section of our report we mention that in our opinion the pathological condition as found in the gastro-intestinal mucous membrane was not an active process, but one due in the main to passive congestion. Hæmorrhages and broken down areas of mucosa were described, and necrosis was mentioned as being present in a certain number of the cases. Given therefore such a mucosa lining a gut full of milliards of biological life, it is to be expected that should such a membrane become pathological, the morbid areas must afford an excellent nidus for the growth of such organisms, and their presence in section in enormous numbers would certainly be noted. In the experimental part of our research, it will be seen that the bacteria of the gut and its membranes of cases of Beri-beri are non-pathogenic when introduced into the alimentary tract of other animals.

Apart from our experimental studies our researches along bacteriological lines have been directed as follows :—

I.—BLOOD.

(*a.*) Blood films from several hundred cases of Beri-beri of all types have been examined according to the latest tinctorial methods including LEISHMAN's modification of ROMANOWSKY's method. In every case a negative result as regards organisms was obtained.

(*b.*) Large quantities 10-20 *c.c.* of blood have been taken ante-mortem from acute cases of Beri-beri, in nearly 50 cases, and transferred to a variety of nutrient media either in flasks or in test tubes. Subsequently some of these were incubated, and others were grown at the room temperature. The flasks and tubes were kept under observation for at least 14 days. In every case in which the technique was faultless, the flasks and tubes remained sterile.

(*c.*) Blood was directly transferred from Beri-beri cases to a number of animals. The result was constantly negative (*vide* Experimental section).

II.—SPLEEN PUNCTURES during life were made in nearly a hundred cases. The blood obtained was treated in exactly the same way as that described under "Blood" (*a.*), (*b.*) and (*c.*). In every case a negative result followed.

III.—The Dropsical Accumulations.

Fluid from the pleural and abdominal cavities and subcutaneous tissues has been examined bacteriologically (culturally and experimentally). In a certain proportion of the tests the presence of the inhibiting alexins in such fluids was destroyed by heat. Subsequently all the flasks containing the fluid and nutrient media were incubated. All tests made in this way were negative.

IV.—The Cerebro-spinal Fluid (lumbar puncture and post-mortem).—This fluid was also examined microscopically and bacteriologically, the examinations being made after thorough centrifugalisation in order to obtain a suitable deposit. Bacteriologically the tests were similar to those given under the foregoing headings. The results were negative as regards organisms in every instance.

Post-mortem Results.—Microscopic examinations of smears of almost every organ and tissue of fresh Beri-beri cadavers have been made in a large number of cases. Indeed in every case of Beri-beri examined post-mortem smears of the blood spleen and liver are always prepared stained by Leishman's method and examined microscopically. All our microscopic examinations in these cases have given a negative result.

Bacteriologically.—The tests applied were those usually adopted in order to isolate micro-organisms, namely, plate cultivations, tube inoculations and the employment of a variety of nutrient media. The experimental tests were also applied (*vide* Experimental part of the research).

In fresh cadavers inoculations were made into nutrient media from every organ. In many of the cases cocci and bacteria of various species were obtained in pure culture, thus agreeing with the results of Pekelharing and Winkler. On applying further tests, inclusive of experimentation, with these micro-organisms, the results obtained shewed that these cocci and bacteria, bore no causal relationship to Beri-beri.

Repeatedly cultures were made from the gastro-duodenal mucous membrane especially from the areas of necrosis and hæmorrhagic extravasations. Bacteria were isolated according to the aerobic and anaerobic methods, but these on further examination proved to be organisms having nothing in common with the disease and whose natural hatitat is the intestine.

From these examinations which have extended over several years, and from the general negative results as regards a specific biological excitant of the disease, we feel assured that the organisms hitherto isolated by many observers are of extraneous origin, and have no causal relationship to Beri-beri. Again, the bacteria noted by Hamilton Wright in his recent memoirs on this subject can be demonstrated again and again in the pathological areas of the gastro intestinal mucosa, but their presence must be regarded as the result of secondary bacterial invasion of the pathological mucosa.

Supplementary evidence of these all-round negative results is supplied in the experimental part of our research. There, it will be observed, experiments of the most varied character were undertaken, and notwithstanding the application of all the methods known to induce the incidence of the disease amongst animals, the results were uniformly negative throughout.

In conclusion, therefore, it may be said that the bacteriological methods so far applied to cases of Beri-beri have failed to isolate for us a specific pathogener of the disease. Naturally we cannot definitely say that the disease is of a non-bacteriological nature, yet we are strongly of opinion that in the absence of positive results after many searching biological investigations by ourselves and others, a specific infectivity as regards Beri-beri must lose much of its significance, and the disease, in the future, relegated to the confines of the pathological chemist.

ON THE PRESENCE OF MICRO-ORGANISMS IN THE BLOOD STREAM OF BERI-BERICS.

Previous workers on this subject have described micro-organisms which were formed in cultures made direct from the blood. The organisms described by these investigators were usually of the nature of cocci and rod-shaped bacteria. The cocci were often of the chromogenic variety, and so far as one can gather from the descriptions given of such organisms, they would appear to differ but slightly, indeed if at all, from the micro-organisms found ubiquitous in nature, and in the deeper folds and sebaceous ducts of the normal human skin.

The bacteria described up to the present would also appear to come under the same category, and so far as one can gather have but little to do with the disease under consideration, and much less with its etiology.

During this research experiments were undertaken on an extensive scale, and under very favourable conditions for the final determination of the presence or absence of any forms of micro-organisms in the blood stream of Beri-beri patients. In our examinations acute cases of Beri-beri were chosen to begin with, and later on the experiments were supplemented by the examination of the blood streams of the dropsical and atrophic varieties of the disease.

The technique employed was the following:—Peptone bouillon was prepared according to EYRE's method, and transferred to tubes. Each tube contained approximately 20 *c.c.* of bouillon. These bouillon tubes were kept under incubation for at least a week previous to being used for purpose of cultivation. Great care was always exercised in maintaining absolute sterility of the medium used. The tubes of bouillon were prepared in the Bacteriological Laboratory and transferred to the Tung Wah Hospital for inoculation. The patient was prepared for a venesection of the arm. The arm having been rendered aseptic by the use of thorough washing, alcohol, sublimate, etc., one of the superficial veins was completely severed at the bend of the elbow. The blood was allowed to flow into a porcelain dish and escape slowly for at least 30 seconds. Thereupon the bouillon tubes were brought to the bedside, the cotton wool plugs carefully removed and from 10-20 *c.c.* of blood were allowed to pass into each tube. Several tubes were inoculated with the blood of each patient. After the operation, pressure was applied over the wound and in no instance did adverse conditions shew themselves subsequently. The tubes were removed to the Laboratory as soon as possible and incubated for definite periods. In other cases tubes of agar-agar and other media were used and filled with blood extracted from the patient in the same way. All these were subsequently incubated for long but indefinite periods. Further flasks of a capacity of 1,000 *c.c.* were filled with bouillon to the extent of 250 *c.c.* These were tested before use as to their sterility by incubation at 37° C. for over a week. They were inoculated with blood from typical cases of the disease—one flask being used for each patient, and each receiving at least 50 *c. c.* of blood.

By these methods it is obvious that if micro-organisms were present in the blood in cases of Beri-beri these means would undoubtedly settle the question. A large number of experiments were made because of the difficulty of rendering the skin absolutely aseptic and the prevention of extraneous organisms entering the flask when exposed in the airy wards of a tropical and Chinese Hospital.

The following is a description of the results obtained :—

Experiment No. I.

Nature of case.	Media.	No. of Tube.	Quantity of Blood.	Period of Incubation.	Result.
Acute Beri-beri, 7 days ill.	Bouillon.	1	10 c.c.	7 days.	Mould.
		2	15 c.c.	„	Sterile.
		3	10 c.c.	14 days.	„
		4	10 c.c.	„	„
		5	10 c.c.	„	„

Experiment No. II.

Nature of Case.	Media.	No. of Tube.	Quantity of Blood.	Period of Incubation.	Result.
Acute œdematous Beri-beri, 10 days ill,	Bouillon.	1	10 c.c.	14 days.	Sterile.
		2	10 „	14 „	„
		3	10 „	14 „	„
		4	10 „	21 days.	„
		5	10 „	21 „	„

Experiment No. III.

Nature of Case	Media.	No. of Tube.	Quantity of Blood.	Period of Incubation.	Result.
Acute Beri-Beri, 1 week ill,	Bouillon.	1	5 c.c.	21 days.	Sterile.
		2	5 „	21 „	„
		3	10 c.c.	21 „	„
		4	10 „	21 „	„
		5	10 „	21 „	„

Experiment No. IV.

Nature of Case.	Media.	No. of Tube.	Quantity of Blood.	Period of Incubation.	Result.
Atrophic Beri-beri, 4 months ill,	Bouillon.	1	5 c.c.	21 days.	Sterile.
		2	10 c.c.	14 „	„
		3	5 c.c.	21 „	Mould.
		4	10 c.c.	30 „	Sterile.
		5	10 c.c.	30 „	„

Experiment No. V.

Nature of Case.	Media.	No. of Tube.	Quantity of Blood.	Period of Incubation.	Result.
Acute Beri-beri, 10 days ill.	Agar-agar.	1	5 c.c.	14 days.	Sterile.
		2	5 „	14 „	„
		3	5 „	14 „	„
		4	5 „	14 „	„
		5	5 „	14 „	„

Experiment No. VI.

Nature of Case.	Media.	No. of Tube.	Quantity of Blood.	Period of Incubation.	Result.
Acute, Pernicious, Beri-beri, 1 month ill.	Agar-agar.	1	10 cc..	1 month.	Sterile.
		2	10 „	1 „	Mould.
		3	5 c.c.	1 „	Sterile.
		4	5 „	1 „	Mould.
		5	5 „	1 „	Sterile.

Experiment No. VII.

Nature of Case.	Media.	No. of Tube.	Quantity of Blood.	Period of Incubation.	Result.
Acute, Pernicious Beri-beri, 1 week ill.	Blood-Serum Agar.	1	5 c.c.	14 days.	Sterile.
		2	10 c.c.	14 „	„
		3	5 c.c.	14 „	„
		4	5 c.c.	21 days.	„
		5	5 c.c.	21 „	„

Experiment No. VIII.

Nature of case.—A Chinese male adult, aged 50, suffering from acute œdematous Beri-beri. The duration of the illness was approximately 14 days.

Method of Experimentation.—One litre flask containing sterile peptone bouillon was inoculated with 50-60 *c.c.* of this patient's blood. The technique as regards prevention of extraneous contamination was found to be rather more difficult than in the case of the test tube experiments. The flask was subsequently incubated at 37° C.

In 24 hrs.—a diffuse turbidity of the broth was found with the formation of a delicate membrane on its surface.

In 72 hrs.—the turbidity was more pronounced with the accumulation of a considerable amount of greyish-white granular deposit. The surface membrane was now found to be thick and wrinkled of a greyish-white colour, and covering the entire surface of the bouillon. It was tough and with difficulty could be broken up on severe agitation of the bouillon.

Microscopically—the growth was found to consist of rod-shaped organisms. These were found to be single or in pairs, and occasionally in threads, they were mobile, and could be easily stained with any ordinary dye. Spore formation was present. Subsequent plate and sub-cultivation on different media shewed this micro-organism to be the only micro-organism present, and it was later identified as the *Bac. mesentericus vulgatus* or potato bacillus, which is so commonly found in nature, and has no relationship to the disease under consideration.

Experiment No. IX.

Nature of case.—A Chinese male adult suffering from acute Beri-beri of 10 days' duration, was bled in the usual way, and according to the technique already described. A flask of peptone bouillon was inoculated with about 30-40 *c.c.* of blood (venous) which was introduced into the flask and well mixed with the broth.

Subsequently the flask was incubated at 37-C.

After 24 hrs.—the bouillon was turbid and the flask shewed the presence of a granular deposit.

Microscopically—a drop of the bouillon shewed the presence of cocci and rod-stained preparations of this medium shewed the cocci lying singly, in pairs, and in small groups. They stained well by GRAM'S method and generally resembled staphylococci. The rod-shaped organisms were found to be identical with those found in Experiment No. VIII.

The cocci were isolated in pure culture and proved to be a mixture of staphylococcus pyogenes albus and aureus, organisms which are found ubiquitous in nature and on the body surfaces of all human beings.

The micro-organisms present in this flask were utilised for the purpose of experiment.

Experiment No. IX A.

One rabbit was inoculated subcutaneously on November 3rd, 1904, with the bouillon containing both varieties of organisms.

On the following day a small localised swelling was found over the seat of inoculation. The temperature was normal.

The animal continued in a good state of health until November 8th, 1904, when it received 2 *c.c.* of a 24-hr. old bouillon culture of the staphylococci present in this flask.

During the next few days the rabbit remained well.

November 12th, 1904.—Another 2 *c.c.* of the bouillon culture of the micro-cocci were inoculated subcutaneously.

November 18th, 1904.—2 *c.c.* injected as on November 12th.

November 20th, 1904.—The animal is well, feeds, and has no diarrhœa. A small abscess has developed over the site of the injection of November 12th. The knee-jerks are present, there is no apparent terderness on pressure over the abdomen, and the rabbit moves and functionates as other animals do.

November 25th, 1904.—2 *c.c.* of the flask used for Experiment No. XI were injected subcutaneously.

From this time onwards until the middle of January, 1905, the rabbit remained in a fair state of health. There was never any sign of Beri-beri. About the latter end of January subcutaneous abscess formation took place and the animal died from general septic poisoning.

Although the animal was frequently examined during the experiment, which lasted about three months, no sign of Beri-beri was elicited. There was never any distension of the abdomen or epigastric tenderness on gentle pressure. The knee-jerks could always be elicited and pressure on the leg muscles did not appear to evoke any discomfort.

Experiment No. IX B.

The experiment is similar in almost all respects to the previous one.

November 3rd, 1904.—One rabbit was inoculated subcutaneously with 3 *c.c.* of the bouillon.

November 8th, 1904.—5 *c.c.* of the contents of the flask used for Experiment No. XI, inoculated subcutaneously.

The result of these injections was negative. Apart from localised swellings over the site of inoculation, the animal shewed no discomfort. The temperature remained normal. It will be obvious from these inoculations tnat the micro-organisms present in the flask possess practically no pathogenicity.

November 19th, 1904.—The animal contracted pneumonia and died the following day.

There never was any sign of paralyses, epigastric tenderness, œdema, or tenderness of the muscles. The knee-jerks could always be elicited.

Post-mortom Examinatien.—Double fibrinous pneumoina; no evidence of lesions indicative of Beri-beri found.

Experiment No. IX C.

For details of this Experiment reference should be made to Observations on Sheep—Experiment No. 2.

Experiment No. X.

The nature of this experiment and the technique employed were identical with that found in Experiments Nos. VIII and IX.

After incubation of the flask at 37° C. for 48 hours, a mixed growth of cocci were found. These proved to be staphylococci, chromogenic and non-chromogenic varieties being both present. There was nothing distinctive about these micro-organisms. They answered to all the characteristics and cultural tests of the ordinary ubiquitous staphylococci.

The contents of this flask were utilised for the carrying out of the following experiments :—

Experiment No. X A.

One Monkey.

The animal was previously tested as to its good health and during the experiment the temperature was tested twice daily.

November 7th, 1904.—The animal received subcutaneously 10 *c.c.* of the culture in the flask.

November 8th, 1904.—The inoculation made yesterday appeared to have no effect upon the animal. There was a slight local swelling over the site of the inoculation. There was however no fever.

Thereupon, 10 *c.c.* of the flask used for Experiment No. XI was injected subcutaneously.

November 11th, 1904.—Diarrhœa set in to-day. The animal appears weak and very apathetic. It can only with difficulty be made to stir from the crouching position.

November 12th, 1904.—The diarrhœa has become more pronounced. The animal appears to be in a condition of septic poisoning. The knee-jerks are present and the monkey shrieks when touched. It is evidently in great pain. There are no evidences present of acute Beri-beri.

November 14th, 1904.—The animal died to-day.

Post-mortem Examination.—The body was greatly emaciated. Rigor mortis was present (4 hours after death). The subcutaneous tissues shewed no œdema or mucoid appearance. The lungs were normal. There was no excess of fluid in the pleural cavities. The heart was dilated and contained dark fluid blood. Several small ante-mortem clots were found present. The cardiac muscle was found to be soft and flabby and degenerated. There was no endocarditis. The mucous membrane of the stomach was injected and eroded, with numerous patches of hæmorrhagic extravasation. The intestine throughout was in a condition of acute follicular enteritis. The mesenteric glands were enlarged and soft and shewed points of hæmorrhagic extravasations. The spleen, apart from congestion, was normal. The kidneys were congested. Smear preparations were made from the spleen and the heart blood, and shewed the presence of staphylococci. This was confirmed bacteriologically. The cause of death was put down as staphylococcic ptomaine poisoning.

Experiment No. X B.

One Monkey.

The conditions were the same as those of Experiment No. I. The usual preliminary precautions were taken.

November 7th, 1904.—The monkey was inoculated subcutaneously with 6 *c.c.* of the culture in the fluid.

November 8th, 1904.—A small localised swelling was found over the site of the inoculation. There was no rise in temperature.

November 9th, 1904.—5 *c.c.* from the same flask was again incorporated subcutaneously.

November 10th, 1904.—No reaction found except a small localised swelling. The temperature became subnormal.

November 11th, 1904.—10 *c.c.* of the contents of the flask used for Experiment No. X was injected subcutaneously.

November 12th, 1904.—Local reaction found but no elevation of temperature.

November 13th, 1904.—Diarrhœa set in.

November 14th, 1904.—The animal died to-day.

Throughout the experiments, no signs of symptoms of Beri-beri shewed themselves. The doses of the culture given were large but it must be remembered that previous experiments had shewn the culture to be possessed of but small virulence.

Post-mortem Examination.—The condition of the internal organs was similar to that found in Experiment No. I, and need not be detailed.

The cause of death was chronic poisoning due to the incorporation of large amounts of staphylococci and their ptomaines.

Experiment No. X C.

One Rabbit.

After determining that the animal was in perfect health, the following experiment was made.

November 7th, 1904.—2 *c.c.* of the bouillon growth was injected subcutaneously.

November 8th, 1904.—The temperature is 104° F. The animal is dull and apathetic, and refuses food.

November 9th, 1904.—The temperature was normal. The animal was livelier to-day. The swelling at the site of inoculation is fully developed but shews no signs of softening. The animal was tested for the presence of signs of Beri-beri. The knee-jerks were present. There was no epigastric tenderness and no tenderness on pressure over the muscles.

November 10th, 1904.—2 *c.c.* of the same bouillon again injected beneath the skin of the abdomen.

November 13th, 1904.—Still no signs of Beri-beri.

November 15th, 1904.—2 *c.c.* again injected.

November 18th, 1904.—No evidence of Beri-beri.

November 21st, 1904.—2 *c.c.* again injected.

November 25th, 1904.—There is no evidence of a sign of Beri-beri. The animal moved and functionated like other normal rabbits.

November 29th, 1904.—Diarrhœa set in.

December 2nd, 1904.—The animal died to-day.

Post-mortem Examination.—Cause of death was diarrhœa. Absolutely no sign of Beri-beri.

Experiment No. XI.

The conditions and technique of the experiment were the same as in the previous experiments. A well marked case of œdematous Beri-beri was chosen for the venesection.

The flask was subsequently incubated at 37° C.

Micro-cocci in pure culture were found and agreed in all points with the ordinary staphylococcus epidermidis albus.

The following experiments with this culture were made. All of these have been noted under the following different headings :—

Experiment No. XI A.—*Vide* Observations on Sheep. Experiment No. 1.

Experiment No. XI B.—*Vide* Observations on Sheep. Experiment No. 2.

Experiment No. XI C.—*Vide* Observations on Fowls. Experiment No. 1.

Experiment No. XI D.—*Vide* Observations on Fowls. Experiment No. 3.

Experiment No. XI E.—*Vide* Experiment on Rabbit, under Experiment No. IX A. (Blood in Beri-beri).

Experiment No. XI F.—*Vide* Experiment on a Monkey. Experiment X A. (Blood in Beri-beri).

Experiment No. XII.

Nature of experiment was the same as No. XI.

Mixed cocci were found—chromogenic and non-chromogenic—and agreeing with the characteristics of staphylococcus albus and aureus.

The contents of this flask were not used for experimental purposes.

Experiment No. XIII.

The nature, technique employed, and the result of the bacteriological examinations were identical with Experiment No XI. One variety of micro-coccus was present, namely, staphylococcus albus.

No experiments were made.

Experiment No. XIV.

This experiment was carried out in the same way as the previous one. A well marked atrophic case of Beri-beri was used for venesection. The result of the bacteriological examination was the isolation of cocci and rod-shaped bacteria. The cocci were of the ordinary staphylococcic variety and the rods shewed themselves closely related to the colony group.

Owing to the mixed growth of micro-organisms no experiments were made with this bouillon.

Conclusions.

The results of these experiments shew more or less clearly, that micro-organisms of the common type are absent from the blood during an attack of Beri-beri. The repeated sterile result after inoculating bouillon and agar tubes with appreciable quantities of freshly flowing blood, demonstrates more or less clearly the non-bacteriæmic nature of the disease.

The findings of other workers who have pinned their faith in the micro-organismal nature of the disease must, as a result of our investigations, be looked upon in a different light. The prevention of contamination is a difficult matter even in the hands of an expert, and the description of the presence of micro-cocci and bacteria of several kinds must be regarded as the result of defective technique in the methods applied for the determination of this important question.

6.—EXPERIMENTAL RESEARCHES.

These researches occupied the greater part of our time and seemed to offer us the best opportunity of locating the exact etiological factor in Beri-beri. After the account given by HAMILTON WRIGHT of natural Beri-beri infection of monkeys, coupled with the negative results obtained by other methods of investigation, it appeared to us experimental methods would in all probability bring to light this much sought for factor in Beri-beri. Naturally these experiments were undertaken from as wide a standpoint as possible. Monkeys were used on a large scale and subjected to experimentation by almost every method known. In addition, pigs, sheep, calves and a horse, rabbits and fowls were made extensive use of. The following is a resumé of the methods adopted, with a detailed account of the experiments themselves:—

1.—Observations on Monkeys.

A.—Natural Infection.

B.—Feeding experiments—

(1) With Beri-beri blood.
(2) With spleen substance.
(3) With gastro duodenal mucosa.

C.—Subcuntaneous Inoculation—

(1) With Beri-beri blood.
(2) With spleen blood.
(3) With cerebro-spinal fluid.

D.—Intraperitoneal inoculation with Beri-beri blood.

2.—Observations on Pigs.

A.—Feeding experiments—

(1) With Beri-beri blood.
(2) With spleen substance.
(3) With brain substance.
(4) With cerebro-spinal fluid.
(5) With gastro duodenal mucosa and other abdominal organs.

3.—Observations on Sheep.

A.—Vaccination experiments with spleen pulp.
B.—Feeding experiments with Beri-beri blood.

4.—Observations on Calves.

Subcutaneous inoculation with Beri-beri blood.

5.—Observations on Rabbits.

A.—Natural infection.
B.—Subcutaneous inoculation with Beri-beri blood.
C.—Feeding experiments—

(1) With Beri-beri blood.
(2) With spleen substance.

6.—Observations on Fowls.

A.—Feeding experiments with spleen substance and blood.

7.—Observations on a Horse.

A.—Subcutaneous inoculation with Beri-beri blood.

Observations on Monkeys.

A.—Natural Infection.

This series of experiments was undertaken in order to confirm, if possible, the recent observations of Hamilton Wright on Beri-beri in Monkeys. [*Vide* "Brain," Winter 1903].

Description of Experiment.—The rooms of the Po Leung Kuk in which the majority of the cases of Beri-beri had occurred (in the outbreak in that Institution) were reserved for this test. The rooms were left in exactly the same condition as when they were used by the inmates of the Po Leung Kuk.

Two monkeys were placed in each room, and in order to facilitate the onset of the disease, the windows of the rooms were kept shut, and the light excluded as far as possible.

Previous to the commencement of the experiments, the monkeys were kept under observation for several days, and their blood microscopically examined.

The following is a resumé of the experiments:—

Experiment No. I.

Animals—Two monkeys.

Nature of Experiment :—

The monkeys were incarcerated in a presumably infected room in the Po Leung Kuk. The shutters were closed and the room darkened. The animals were allowed their full freedom in the room. Their diet consisted of bananas, sugar cane, peanuts and boiled rice bought in one of the local markets, and was strictly the same as that of the other monkeys under observation.

They were placed in the room on September 26th, 1904, and kept prisoners in the room without a break until the end of January, 1905, *i.e.*, for over four months. The condition of the animals was noted daily. They lost weight slightly but were able to climb and scramble over the furniture and walls like normal monkeys. They eagerly devoured their food; there was no diarrhœa, and their temperature never varied beyond normal limits.

At the end of their incarceration, the monkeys, except for a slight loss in weight, were healthy and their movements and reflexes were normal.

Subsequently the monkeys were kept in cages under continued observation for a further period of four months, at the end of which the animals shewed no sign of disease, and could eat, walk and climb as well as many other monkeys. At the present time—the middle of October, 1905, *i.e.*, over twelve months since they were first placed in the infected room—these two animals are in sound health.

During the period of their incarceration the blood of the animals was examined microscopically on several occasions. Its contents was without exception normal.

Experiment No. II.

Animals—Two monkeys.

Nature of Experiment: —Identical with No. I.

The animals were incarcerated over five months. They were subsequently under close observation up to the date of writing, namely, the 19th October, 1905, that is, over one year. Both animals are alive and healthy at the present time.

Experiment No. III.

Animals.—Two monkeys.

Nature of Experiment:—The same as that described under Experiment No. I.

Period of incarceration—5 months.

Total period of observation—One year.

Result.—Both animals are alive and well at the present time.

Conclusions:—

The conclusion to be drawn from these experiments is that the incarceration for months of monkeys in rooms presumably infected with the so-called Beri-beri virus, failed to induce the occurrence of the disease in them. We were unable to confirm the results of HAMILTON WRIGHT.

B.—FEEDING EXPERIMENTS.

After the publication by HAMILTON WRIGHT of his observations on the nature of Beri-beri and his theory of a definite primary lesion in the disease, feeding experiments were resorted to as a possible means of inducing infection. Again, as certain observers, as PEKELHARING and WINKLER, GERRARD and others, claim to have found micro-cocci, etc., in the blood stream of Beri-beri patients, feeding animals with the blood of such cases seemed to afford the best opportunity for a successful mode of conveyance of Beri-beri from man to animal. By this method the organisms said to be present in the blood would reach that part of the gut, namely, the gastro duodenal mucosa, alleged to be the site of primary Beri-beri infection, and in susceptible animals set up the disease. It seemed to us that by resorting to such experiments, the question as to the presence of a definite primary lesion in Beri-beri, and our hopes of obtaining positive evidence of the transmission of the disease to monkeys by this method were strengthened by the publication of WRIGHT dealing with natural infection in monkeys incarcerated in presumably infected prison cells.

As already noted under a separate paragraph our results as regards natural infection of monkeys are directly opposed to those of HAMILTON WRIGHT. In every instance a negative observation was made. At the same time our experiments regarding natural infection might have been unsuccessful for other unknown adverse circumstances, so that the prosecution of other methods of experimentation in monkeys would decide definitely whether these animals (or indeed any animal) can suffer from Beri-beri naturally, or can be infected artificially by simple or drastic methods of incorporation of Beri-beri infected tissues.

The following feeding experiments on monkeys were undertaken :—

Experiment No. I.

Animal—One monkey.

Nature of experiment :—

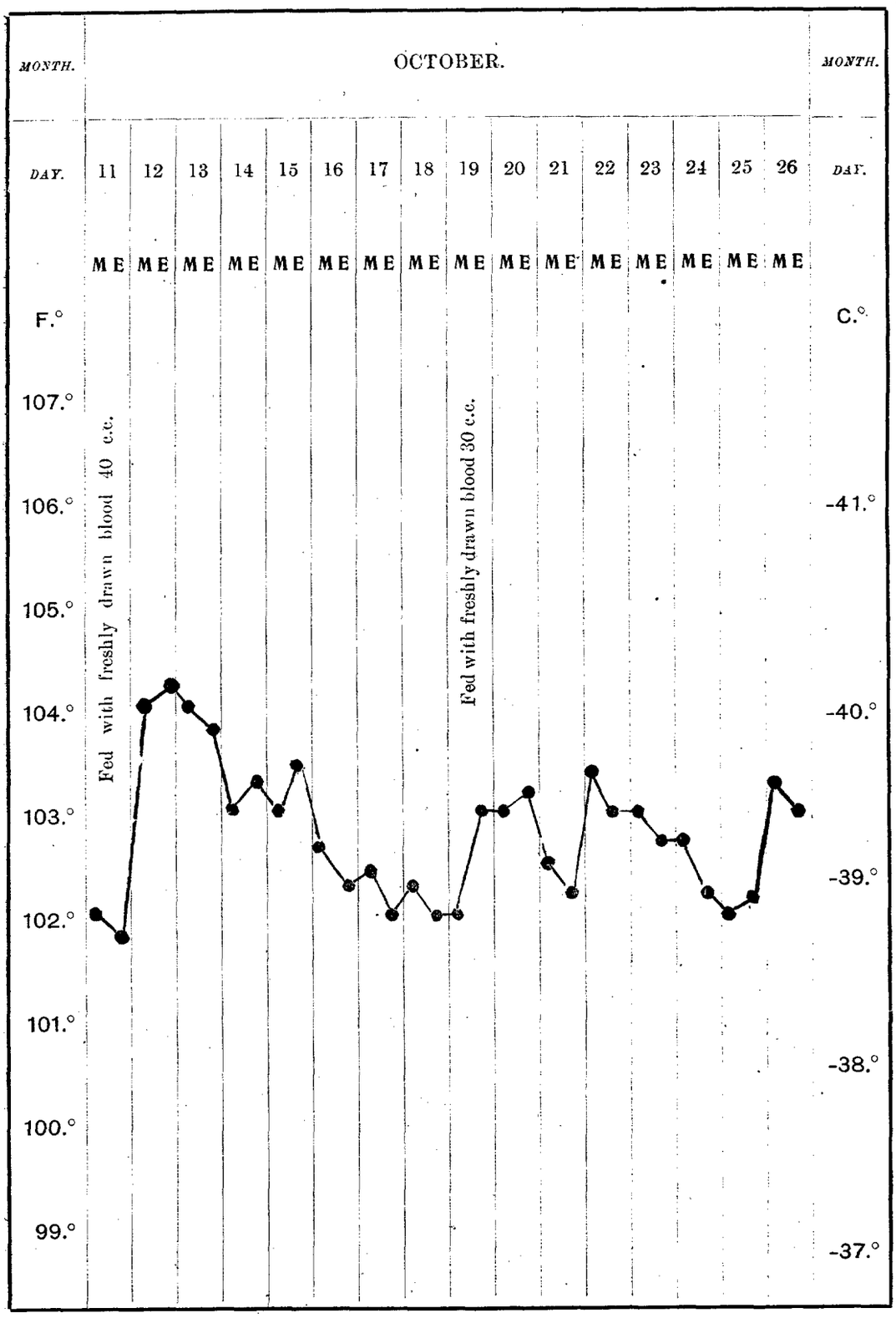
Feeding with freshly drawn defibrinated venous blood of acute Dropsical Beri-beri patients.

The blood was obtained under sterile conditions from one of the veins in front of the elbow joint, defibrinated, and immediately poured down the animal's throat.

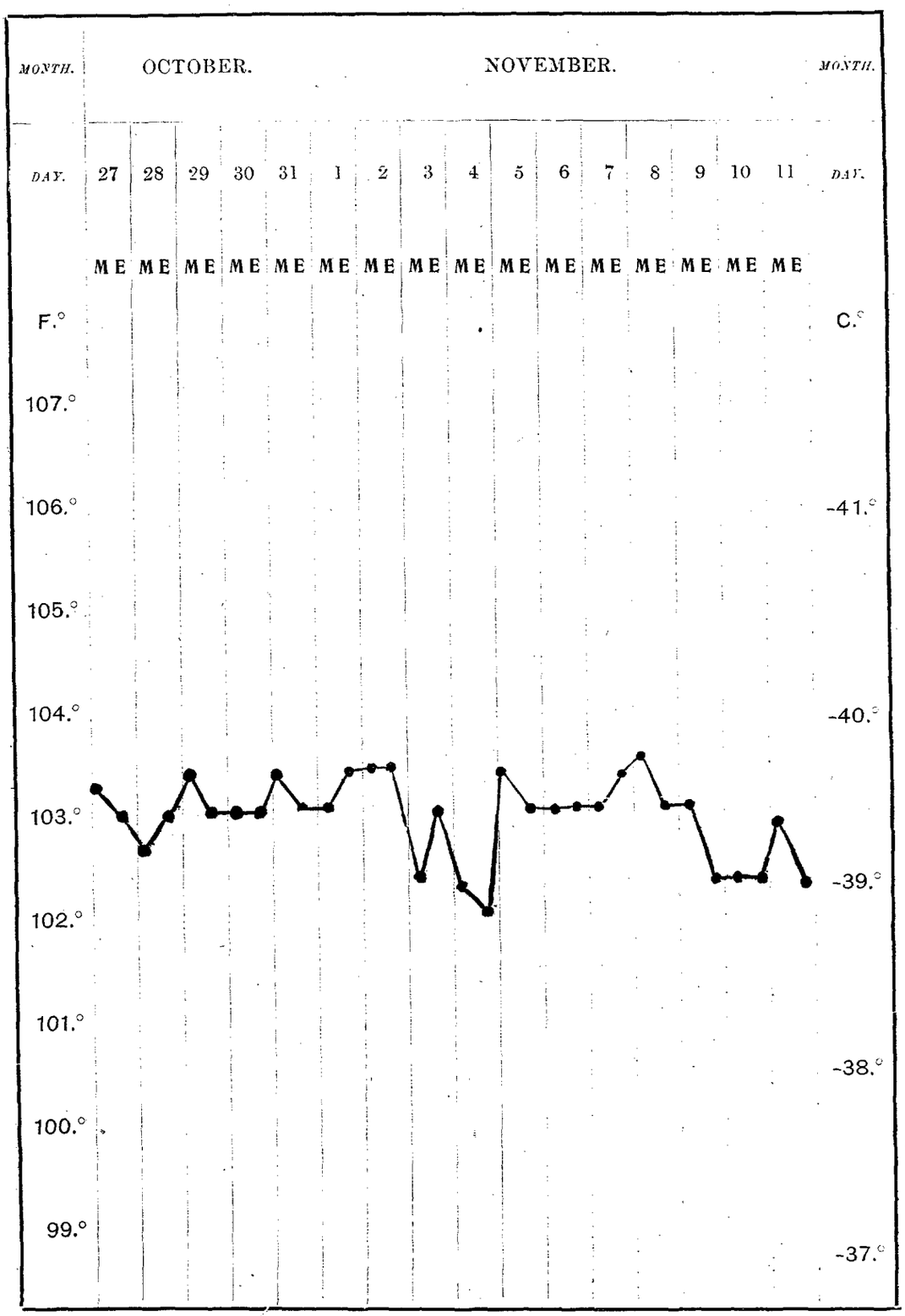
Quantities of blood varying from 40-50 *c.c.* were administered for a dose. Several doses of the same quantity were given. The animal was fed with blood from different cases of Beri-beri.

The experiment was commenced on the 11th October, 1904. For some days previous, the animal was kept under observation and during this period shewed no signs of disease. The temperature was normal. During the whole period of observation, the temperature of the animal was taken twice daily per rectum. Its food consisted of bananas, nuts and rice. The condition of the animal was also tested daily, particularly in regard to emaciation, motor and sensory disturbances, knee-jerks and the presence of epigastric tenderness and diarrhœa.

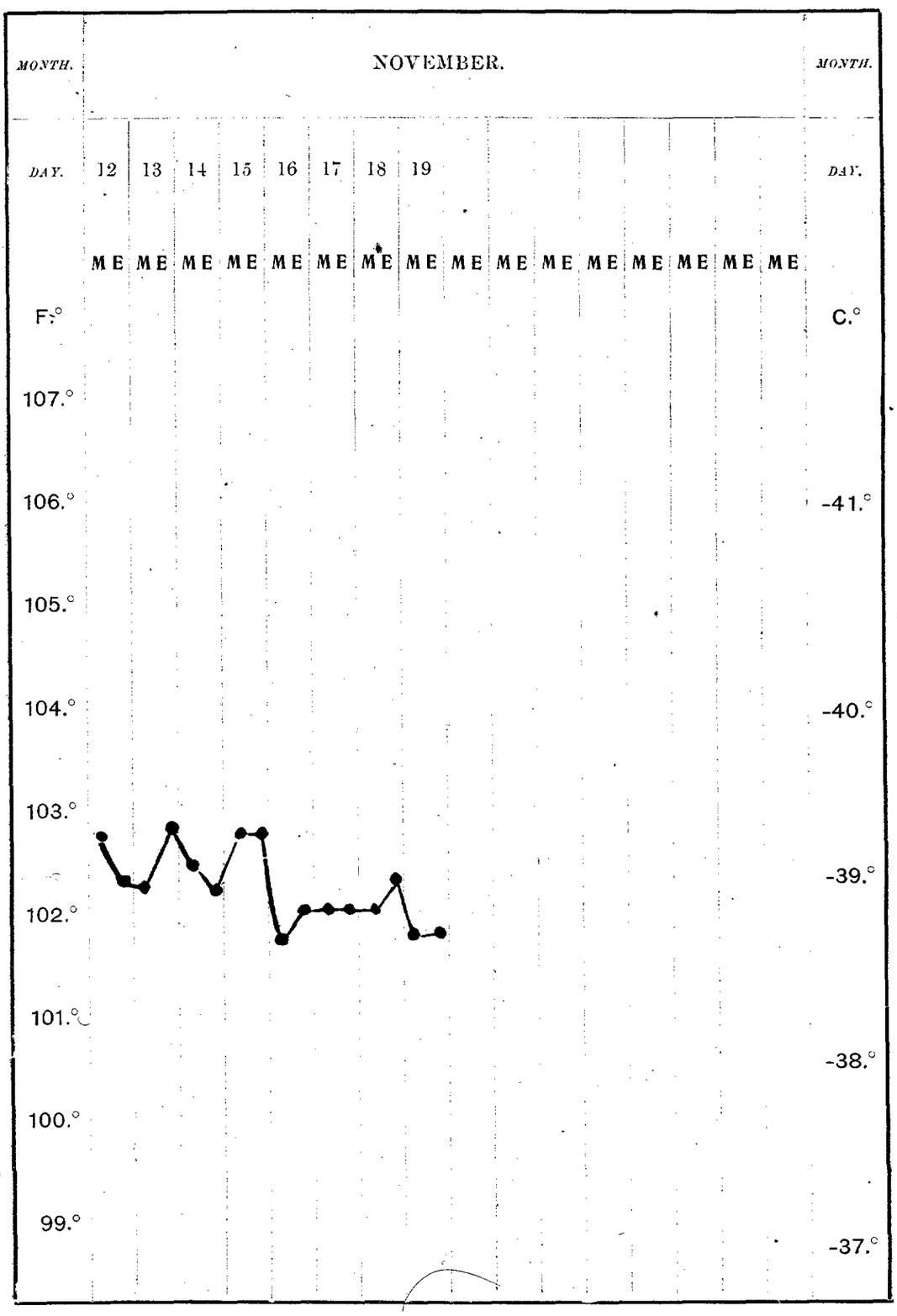
Feeding Experiment.



Feeding Experiment.



Feeding Experiment.



On the 11th October, at 3 p.m., the animal was fed with freshly drawn blood. 40 *c.c.* was swallowed. The temperature was 102° F., *i.e.*, practically normal for this animal. From the attached temperature chart it will be seen that during the following 5 to 6 days a distinct elevation of temperature was noted. During this time, however, the monkey shewed no signs of discomfort, being bright and lively and displaying a good appetite; the bowels being normal. An examination of the blood was negative as regards micro-organisms. The other elements of the blood were normal as regards number and nature.

On the 16th October, the animal was examined thoroughly. It could run and jump and was lively, taking its food well with apparent relish. The knee-jerks were normal. Sensation appeared to be normal. No œdema was found and the animal did not object to pressure over the epigastric region.

On the morning of the 19th October, the animal was again fed with blood from an acute case of Beri-beri. The amount swallowed was about 30 *c.c.* The technique was the same as that already described.

This feeding was followed by a slight rise in temperature which continued until the 10th November, when the temperature became steadily 102° or under. The oscillations of temperature were slight during this period, the fever rarely exceeding 103° F.

During this period, *i.e.*, from the 16th October to the 16th November, the animal remained in perfect health. It never shewed the slightest disinclination for food. There was no diarrhœa or loss in weight and the motor and sensory apparatus appeared normal after repeated examination.

After the 16th November the temperature and the condition of the animal were noted until the beginning of February, 1905. The temperature remained steady between 101·5 and 102° F. The condition of the animal remained good. No evidence of disease was at any time found present. At the present time (October, 1905,) the animal is alive and well, *i.e.*, one year after the commencement of the experiment.

Experiment No. II.

Animal—One monkey.

Nature of experiment:—

The animal was fed with an emulsion of the Medulla, and Pons Varolii obtained from a recently dead case of Beri-beri.

The usual preliminary precautions were observed as regards the animal, and the temperature was noted daily.

For one month the animal remained in perfect health. There was no rise in temperature, no epigastric tenderness, no loss of knee-jerks, and no paralysis.

About five weeks after the commencement of the experiment the animal contracted dysentery from which it died after about 7 days' illness.

Post-mortem examination:—

Cause of death—Acute bacillary dysentery.

No evidence of Beri-beri.

Experiment No. III.

Animal—One monkey.

Nature of experiment:—

Feeding with freshly drawn defibrinated blood of an acute case of Beri-beri.

The technique was the same as that described in Experiment No. I (above).

After a month's observation of the monkey it was fed with an emulsion of fresh spleen in normal sterile saline, obtained post-mortem from a Beri-beri cadaver of a few hours old. The temperature was taken twice daily as before, and the physical condition of the animal noted weekly. The temperature chart is not recorded for this experiment. It practically runs the same course as that recorded for Experiment No. 1.

The experiment was commenced on 11th October, 1904, the temperature and the physical conditions of the animal were recorded until the 27th January, 1905, *i.e.*, for 3½ months.

At the present time (October, 1905), *i.e.*, one year since the commencement of the experiment the animal is alive and healthy.

C.—Subcutaneous Inoculation.

(1) With Beri-beri blood.

Experiment No. I.

Animal—One monkey.

Nature of experiment :—

The animal was inoculated subcutaneously with 5 *c.c.* blood obtained, under sterile conditions, from the median basilic vein of a patient suffering from acute Beri-beri. The monkey was kept under observation for a few days previous to the commencement of the experiment, its temperature and physical condition being noted. When the experiment was made, the monkey was brought to the bedside of the patient and the blood transferred directly from the arm of the patient to the monkey by means of a sterilised syringe.

The inoculation was made on the 27th September, 1904. 5 *c.c.* of blood was injected into the subcutaneous tissue over the abdomen. The attached temperature chart shews the course of the body heat during the period of observation. The blood of the animal was examined previous to the commencement of the experiment. It shewed nothing abnormal.

The injection of the blood caused a slight rise in temperature which continued for about 8 or 9 days. During this period the animal remained in perfect health, eating well, with no diarrhœa, and all sensory and motor phenomena were carried out and responded to in a normal fashion. The blood was negative as regards organisms.

After observing the animal for a fortnight a feeding experiment was performed. On the 11th October the animal was fed with 30 *c.c.* of freshly drawn blood from an acute case of Beri-beri. The technique employed was the same as that described under Feeding Experiments.

This caused a transient rise in temperature, but notwithstanding, the animal fed well, and moved and responded to all stimuli in a normal manner. The blood was again examined but with a negative result.

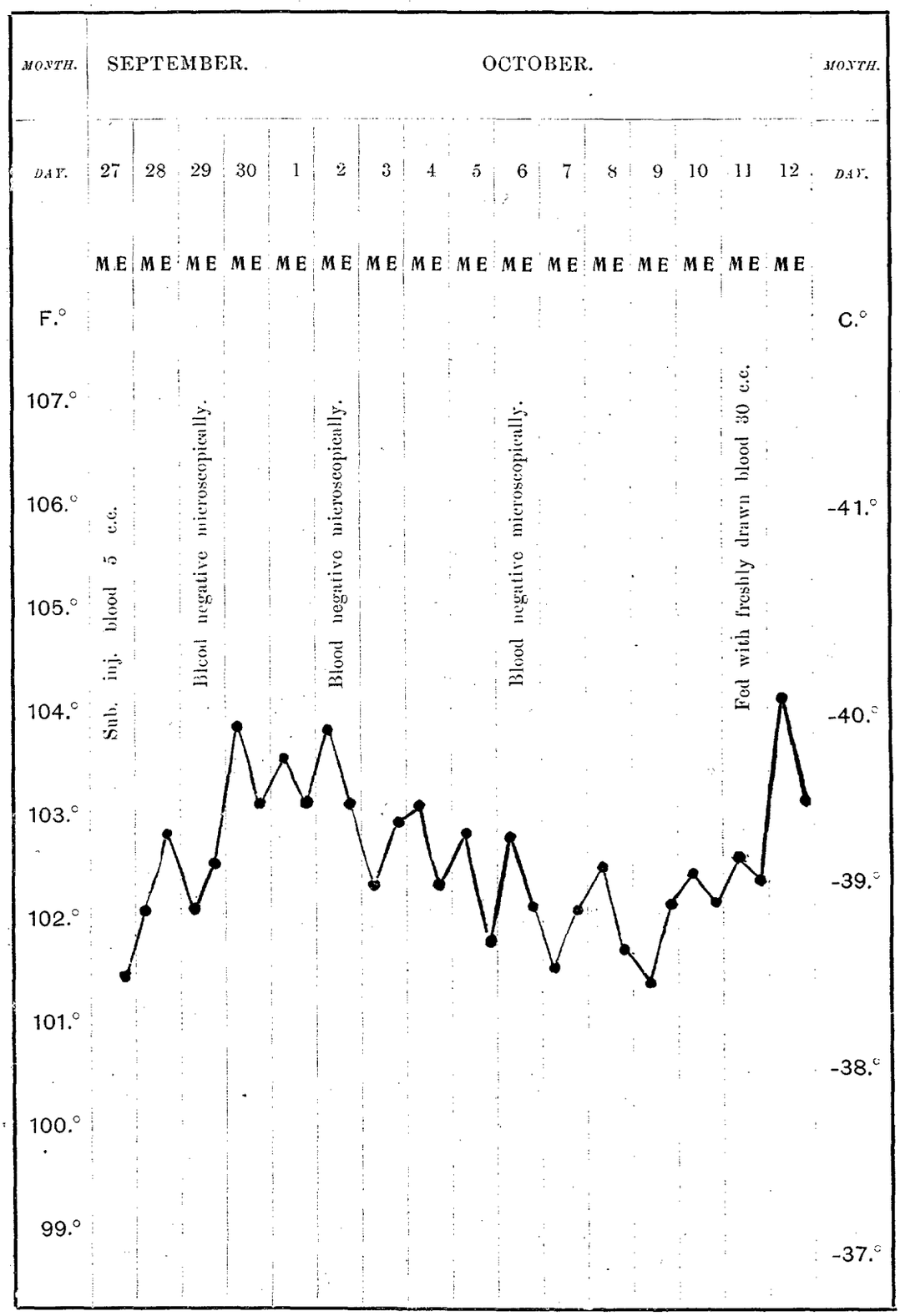
After another forthnight had passed, the monkey received another subcutaneous injection of blood, nearly 5 *c.c.* taken as before from an acute œdematous case of Beri-beri.

This was followed by a rise in temperature lasting 3-4 days. During this period—a month after the first injection—the monkey remained in perfect health.

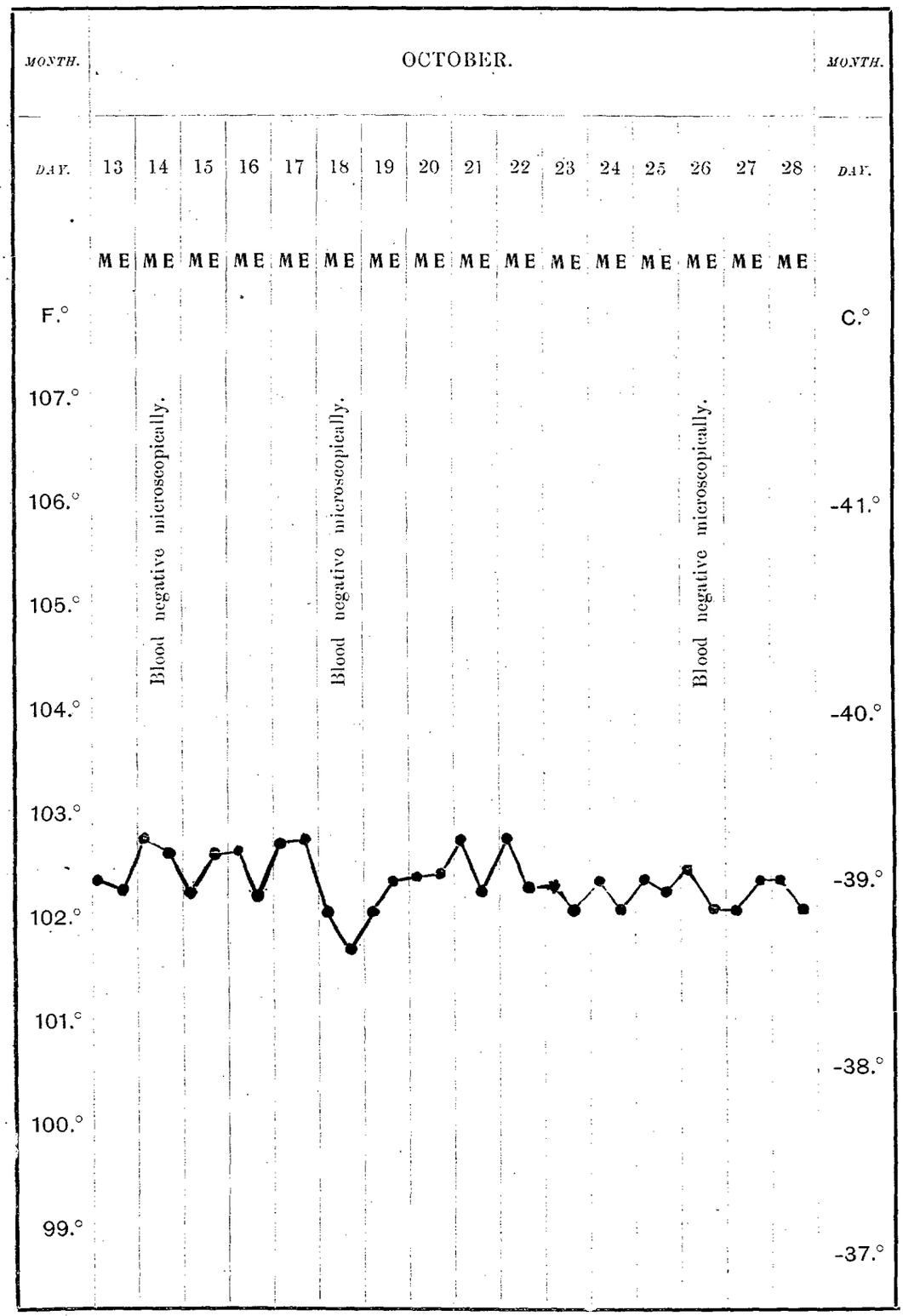
From this time onwards the temperature remained normal and for this reason the curve has not been continued on the chart.

During the middle of December, 1904, the animal contracted dysentery and died on the 26th December.

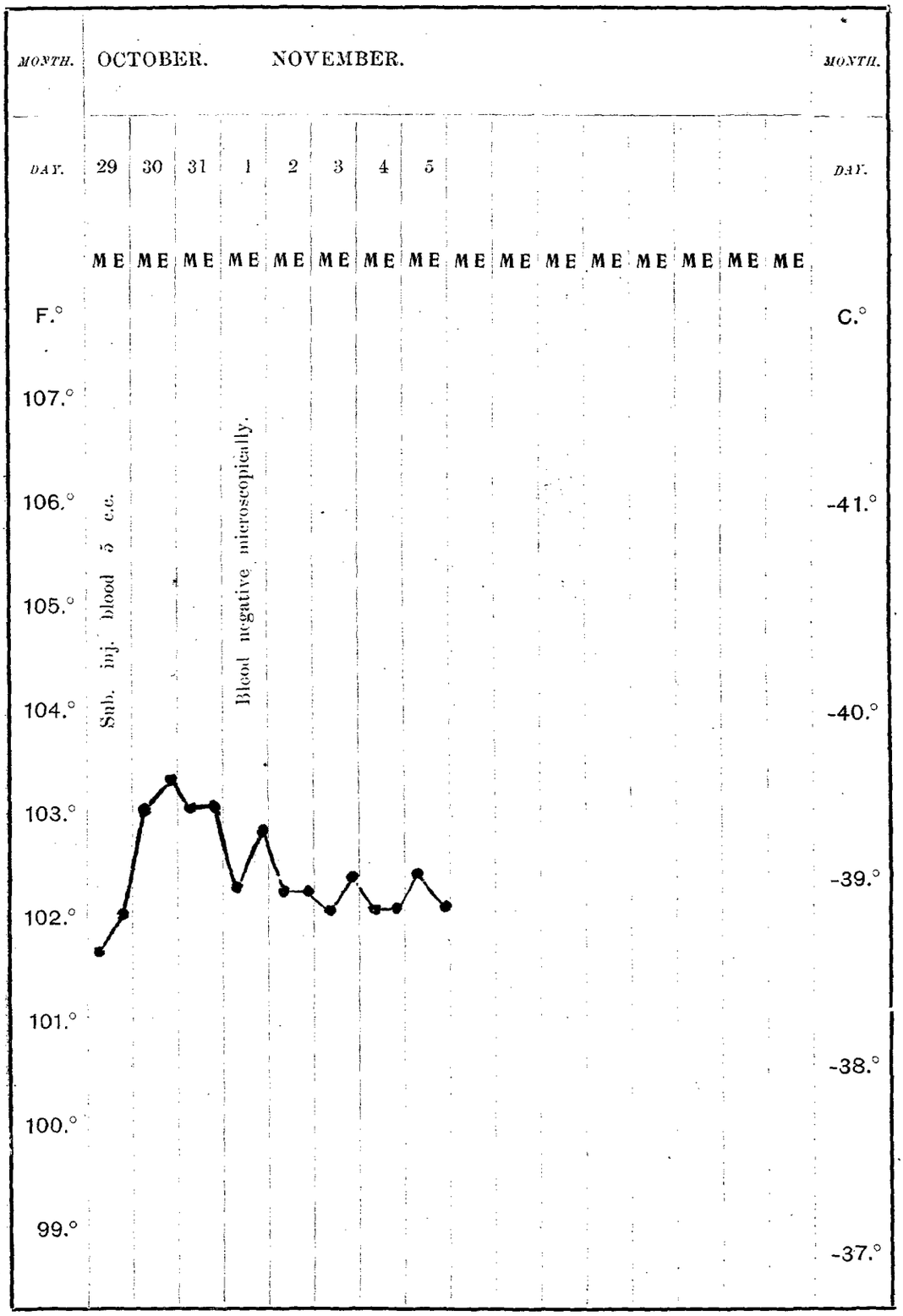
Subcutaneous Inoculation with B.B. Blood.
One Monkey.



Subcutaneous Inoculation with B.B. Blood.
One Monkey.



Subcutaneous Inoculation with B.B. Blood.
One Monkey.



Up to the date of death the animal never shewed the slightest symptom of Beri-beri. Its movements and sensations were normal at all times. There was never any epigastric tenderness or œdema of the extremities. The knee-jerks were normal.

Post-mortem Examination.—The large intestine shewed marked dysenteric ulceration and necrosis. The stomach and duodenum were normal. The organs of the thorax were normal. There were no dropsical accumulations and a miscroscopical examination of the blood and spleen were negative as regards organisms.

[A large number of experiments have been undertaken by this method. The subcutaneous inoculation of considerable quantities of Beri-beri blood, obtained from patients suffering from the disease in the acute form, seemed to us to offer good chances of transference of the disorder to animals, especially monkeys, and for the following reasons. Given that the experiments of HAMILTON WRIGHT on natural Beri-beri infection in monkeys are valid, and that there exist, according to certain observers, micro-cocci or other germs on the blood stream, such an experimental method of conveyance of the infection would be almost bound to result in a successful issue.]

Experiment No. II.

Animal—One monkey.

Nature of experiment :—

The technique employed was the same as that employed in Experiment No. I. The blood was obtained from a vein in the arm of an acute and œdematous case of Beri-beri.

After a few days' observation the monkey was inoculated with 5 *c.c.* of blood on the 4th of October, 1904.

As will be observed from the attached temperature chart the injection of the blood occasioned no fever. The blood was also negative bacteriologically.

Up to the 20th October, 1904, *i.e.*, over a fortnight since the commencement of the experiment the animal remained in perfect health. Its motor and sensory apparatus were normal and there was no epigastric tenderness.

On the 20th October, 1904, 5 *c.c.* of venous blood from another similar case of Beri-beri was injected subcutaneously. This inoculation was followed by a rise in temperature.

On the following day, namely, the 21st October, 10 *c.c.* of blood was subcutaneously inoculated from an acute case. On this date the temperature was maintained at 150° F. From this time onwards there was a gradual defervescence.

Still another injection of 5 *c.c.* of venous blood was given on the 27th October, 1904. This however occasioned no perceptible alteration in the temperature chart.

The temperature curve reached its normal about the beginning of November, that is, about 10 days after its initial rise.

During the febrile period the animal shewed but little signs of being ill. The appetite was poor, but there was no epigastric tenderness and all motor and sensory functions were carried out in a normal fashion. The blood was examined microscopically and bacteriologically on several occasions with a negative result.

From the beginning of November, 1904, the temperature remained normal, so that a continuation of the curve was unnecessary.

The monkey has remained in perfect health and is alive at the present time (October, 1905) functionating normally and to all appearance as well as other monkeys.

[REMARKS: There is always the possibility that monkeys, or even any animal, are not susceptible to Beri-beri. WRIGHT'S experiments were positive, ours negative. Given WRIGHT'S experiments as positive, then in all probability there are no micro-organisms in the blood of Beri-beri cases.]

Experiment No. III.

Animal—One monkey.

Nature of experiment:—

This was carried out in the same way as the previous two experiments. The usual preliminary observations were made and precautionary measures were taken.

October 8th, 1904.—The monkey received 10 *c.c.* blood from a moribund case of acute Beri-beri.

October 20th, 1904.—10 *c.c.* of blood injected from another case of œdematous Beri-beri, in the morning.

October 20th, 1904.—In the afternoon 8 *c.c.* blood injected.

October 25th, 1904.—4 *c.c* blood injected.

October 28th, 1904.—8 *c.c.* blood injected.

Total amount injected, 40 *c.c.* blood.

(*Vide* temperature chart).

Nothing found in the blood microscopically or bacteriologically.

No ill health of animal, no paralyses, sensory or motor, no epigastric tenderness.

From November, 1904, to October, 1905, the animal has remained in perfect health.

Experiment No. IV.

Animal—One monkey.

Nature of experiment:—

This was carried out in a similar fashion to the three preceding experiments.

(*Vide* temperature charts).

Five different inoculations of blood from different cases of Beri-beri were made.

Total quantity of blood injected—30 *c.c.*

The blood of animal was negative microscopically and bacteriologically. The animal was never ill: there was no paralysis: no epigastric tenderness: no œdema. It was alive and well 9 months after the beginning of the experiment and presented no signs of Beri-beri.

Experiment No. V.

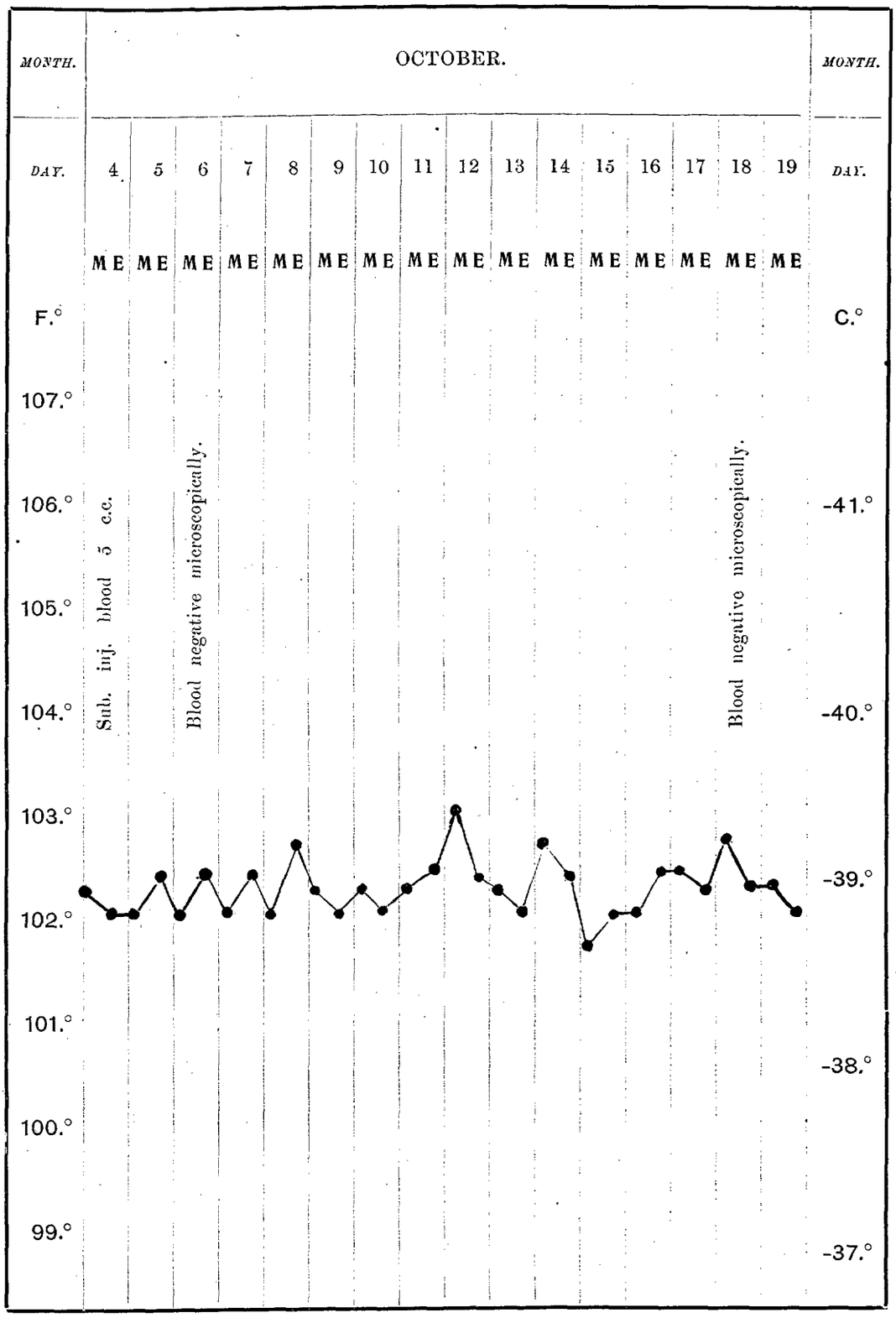
Animal—One monkey.

Nature of experiment:—

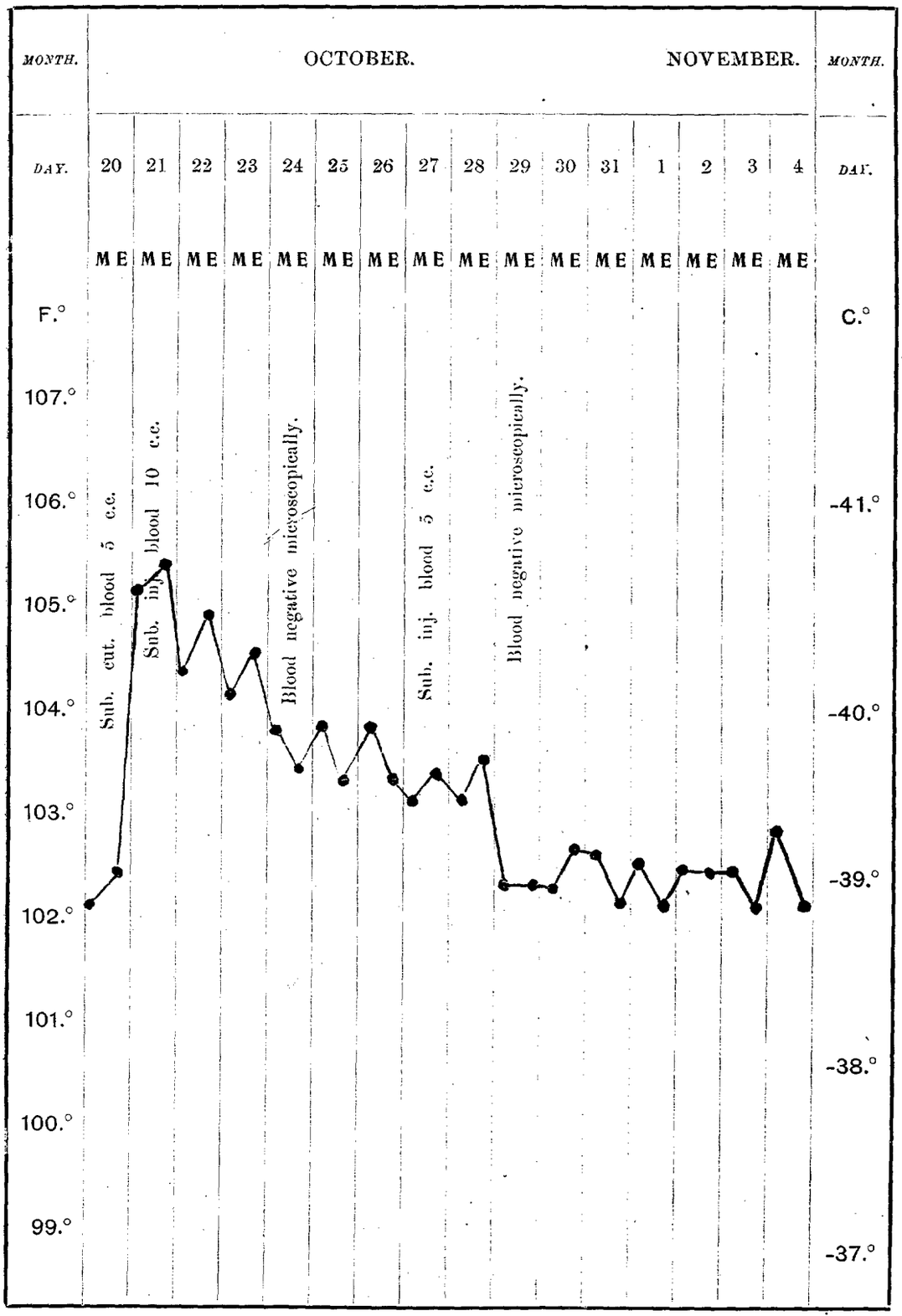
This was performed as in the preceding experiments. The usual precautionary measures were taken. The cases of Beri-beri from which the blood was taken were acute and œdematous and atrophic.

Four different inoculations at different periods were performed. In all the animal received subcutaneously 45 *c.c.* of human Beri-beri blood.

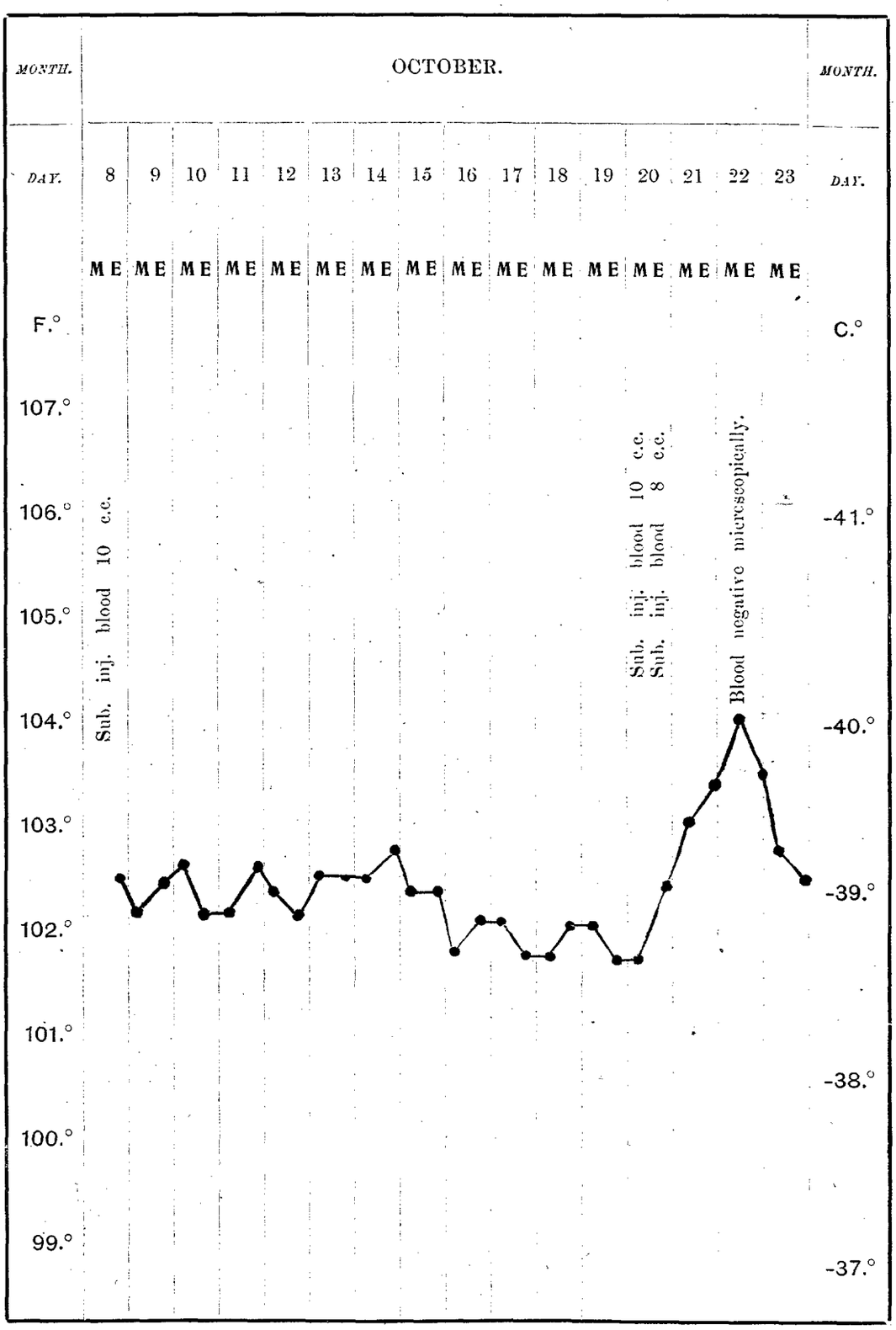
Experiment No. 2.—Inoculation.



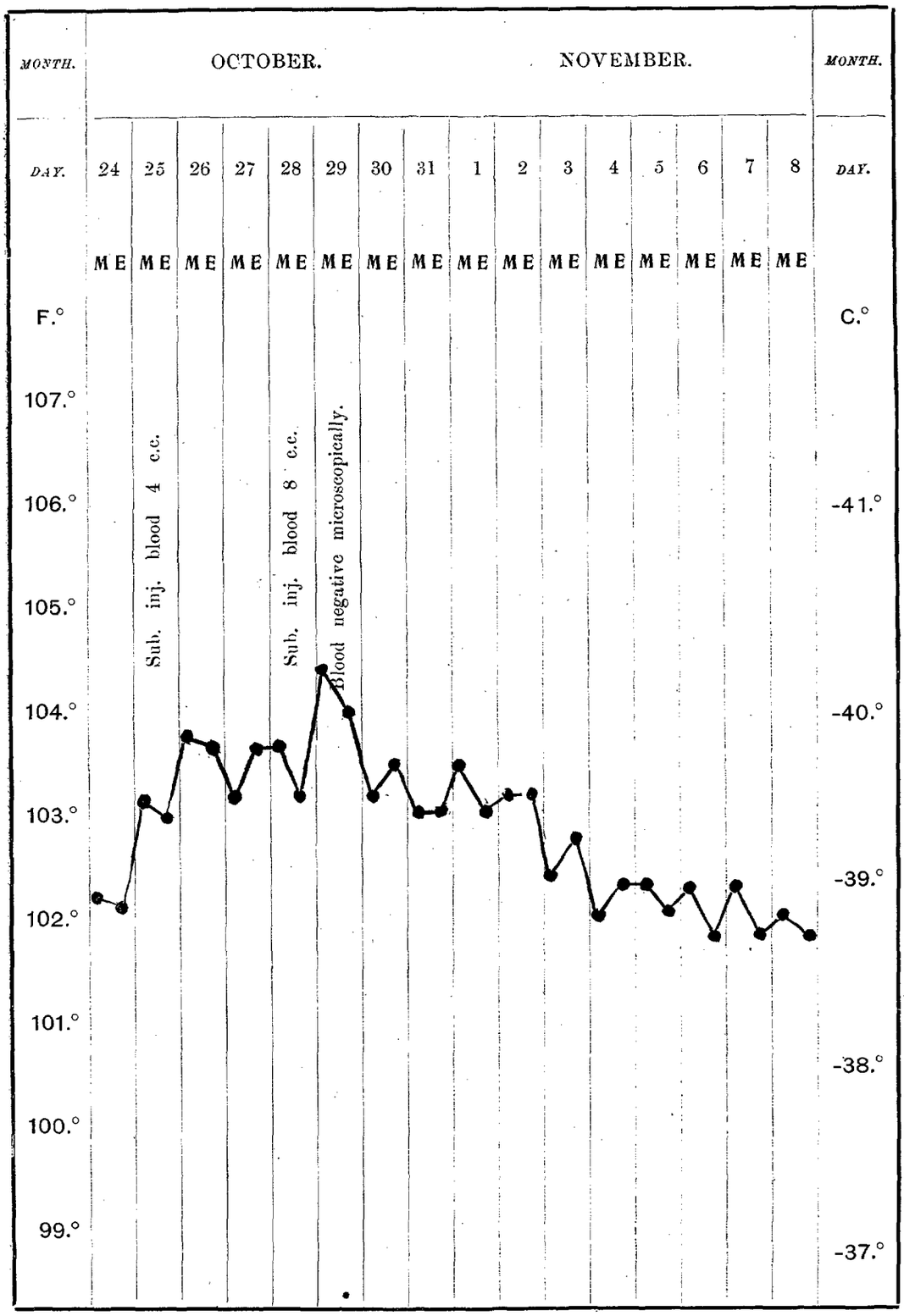
Experiment No. 2.—Inoculation.



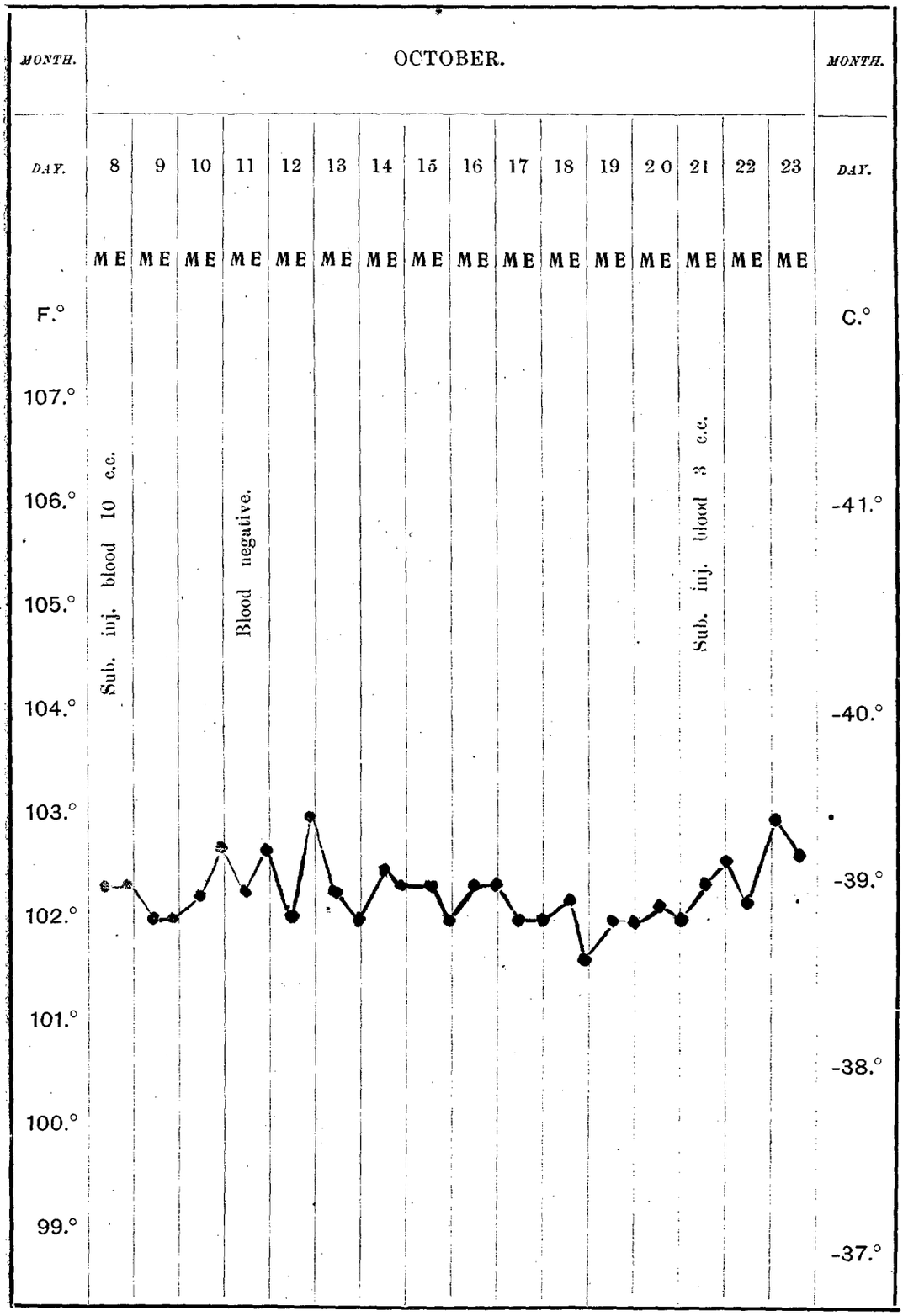
Experiment No. 3.—Inoculation Monkey.



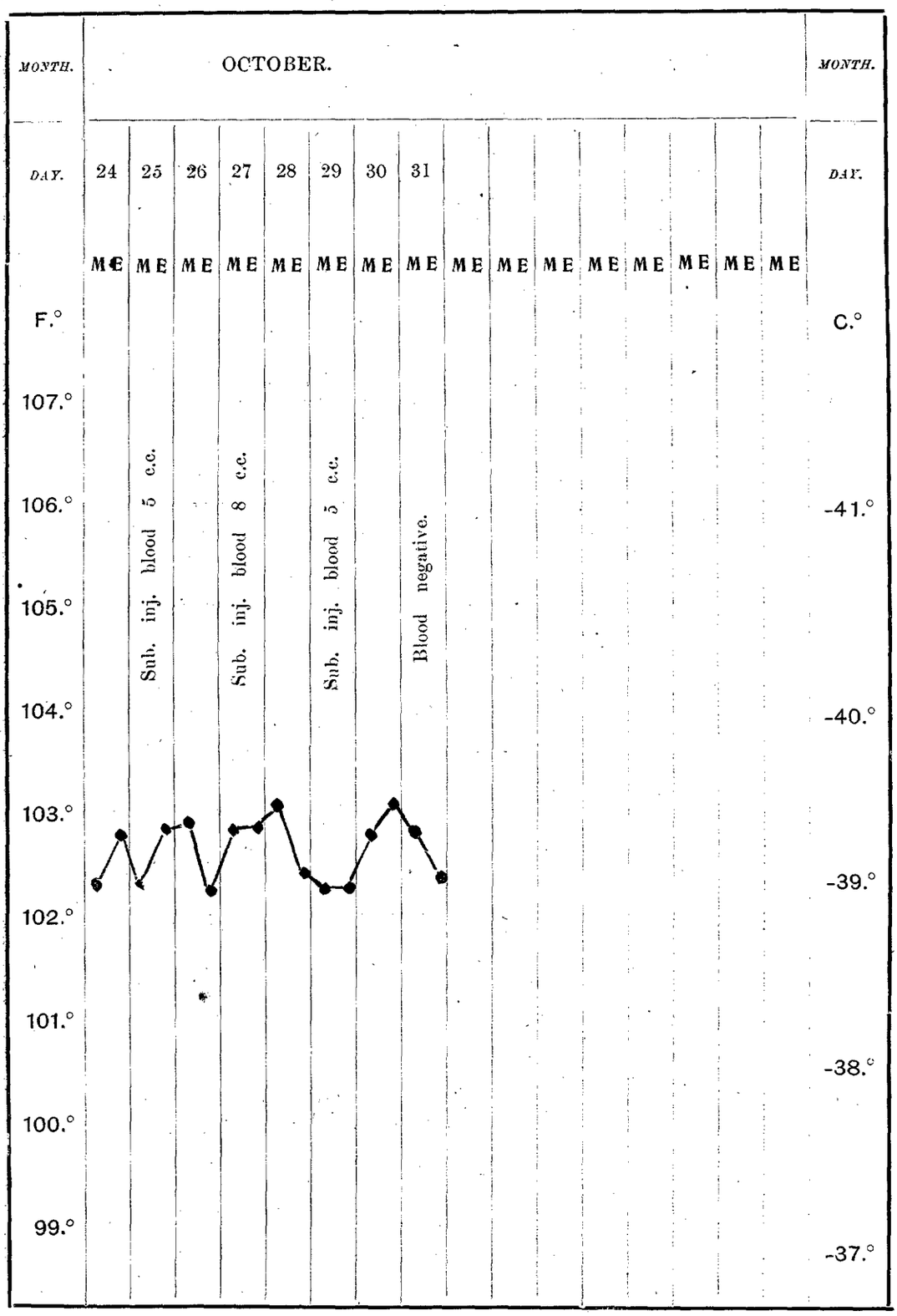
Experiment No. 3.—Inoculation.—Monkey.



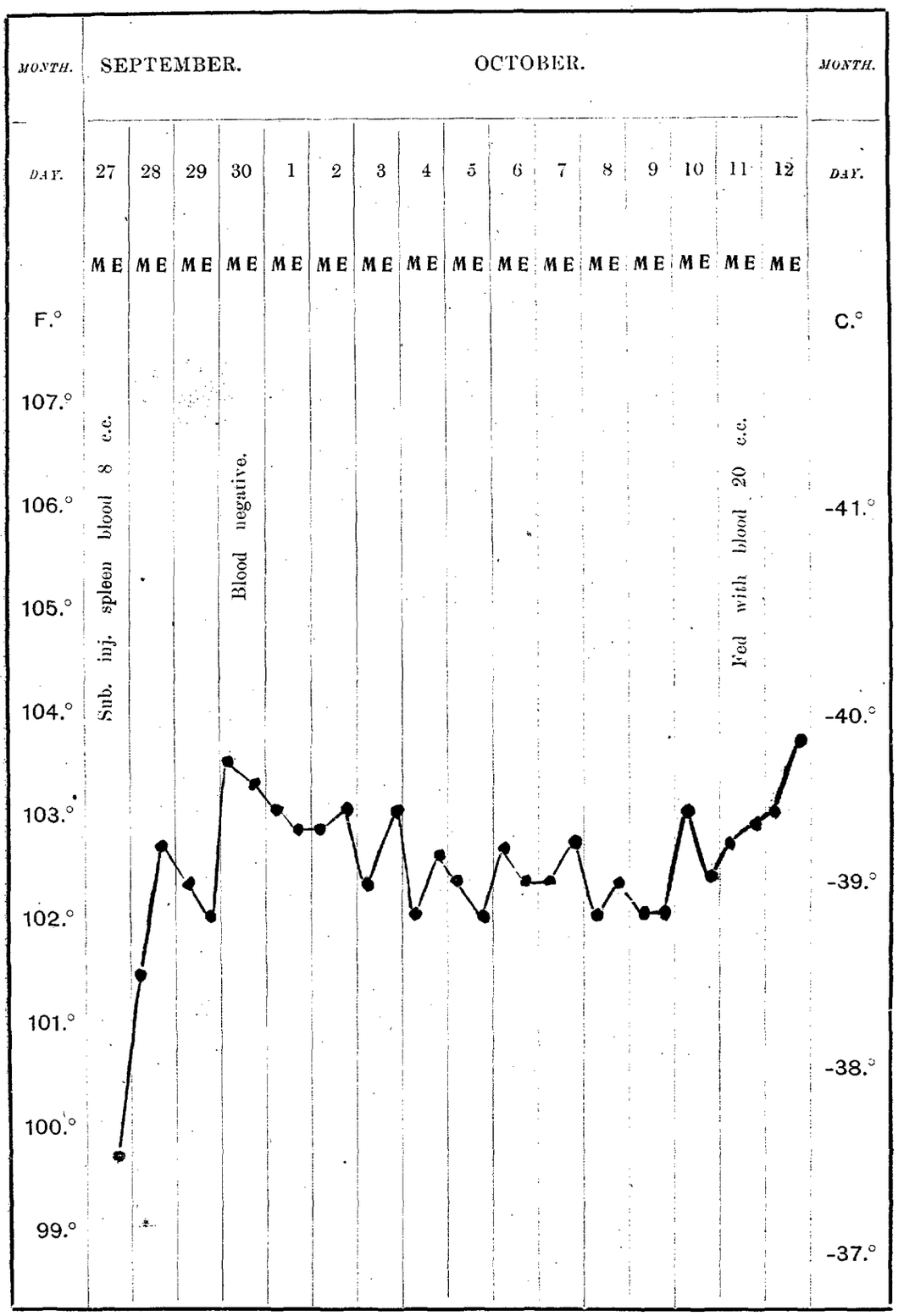
Experiment No. 4.—Inoculation with Blood.



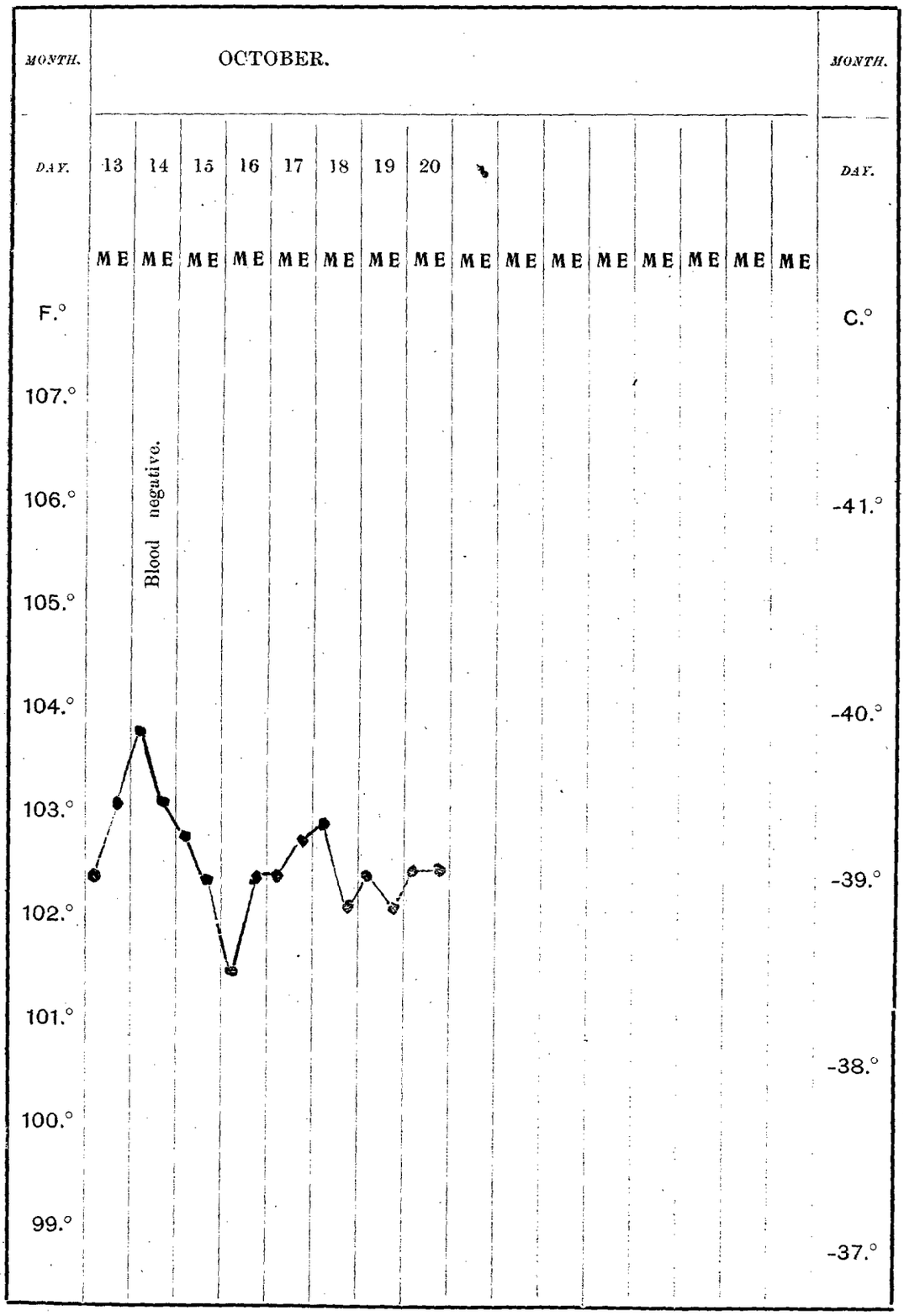
Experiment No. 4.—Inoculation with Blood.



Spleen Blood.—Monkey.



Spleen Blood Experiment.



A temperature chart is not appended as the course of the fever when present was really the same as in the other experiments. At no time while the animal was under these observations did it shew any change from its normal condition. After being kept in its cage for 6 months it escaped and was lost.

Experiment No. VI.

Animal—One monkey.

Nature of experiment :—

The same as the previous ones and under the same conditions.

Forty *c.c.* of blood from four different recurrent cases of Beri-beri were injected.

The animal lived for 3 months and was healthy. It contracted dysentery and died. Post-mortem, there was no evidence of Beri-beri, no œdema, no changes in stomach and duodenum.

Experiment No. VII.

Animal—One monkey.

Nature of experiment :—

As before.

Three injections of blood 33 *c.c.* were given and the animal is alive and well after one year.

(2) With Beri-beri Spleen Blood.

Experiment No. 1.

Animal—One monkey.

Nature of experiment :—

The animal was kept under observation for several days prior to commencing the experiment. A case of acute Beri-beri with enlarged spleen was selected and blood films prepared for examination. No malarial parasites or other organisms were found. The case containing the monkey was brought along the bedside, and splenic puncture performed under aseptic conditions. The bloody fluid obtained was at once injected subcutaneously into the animal in all about 8 *c c.* was used. This inoculation was made on September, 27th, 1904. A drop of this fluid was spread on a microscope slide, stained and examined. Nothing was found microscopically. Bacteriologically this fluid gave a negative result.

The attached temperature chart shews that the injection was followed by a slight degree of fever with gradual defervescence, and lasting 5 to 6 days. This transitory temperature can be reasonably ascribed to the result of the injection. There was no evidence that it had anything to do with the onset of Beri-beri. A day or two after the inoculation the blood of the animal was examined but was negative as regards germs. No change in the physical appearance of the monkey was observed after the injection.

On the 11th October, namely, fourteen days after the inoculation of splenic blood, the animal was fed according to the methods already described, with 20 *c.c.* of freshly drawn blood of a dropsical case of Beri-beri. This again occasioned an evanescent rise in temperature lasting 3-4 days. Subsequent to this the temperature became normal, so that a prolongation of the curve on the attached chart was unnecessary.

From this time onwards the animal kept in perfect health. It functionated normally and all its motor and sensory apparatus responded normally to the usual stimuli. There was never any epigastric tenderness, and the knee-jerks could be daily elicited with ease.

At the present time—one year after the commencement of the experiment—the animal is alive and quite lively.

(3) With Cerebro-Spinal Fluid.

Animal—One monkey.

After observing the monkey for several days 5 *c.c.* of freshly drawn cerebro-spinal fluid from a marked case of œdematous Beri-beri was injected subcutaneously, on October 4th, 1904, and the animal was subsequently examined daily.

October 19th, 1904.—Still healthy and functionates normally. The injection of the fluid has practically caused the animal no inconvenience.

October 20th, 1904.—Was injected subcutaneously with 10 *c.c.* venous blood of a recent and acute case of Beri-beri. This injection caused no elevation of temperature, and the animal functionated like other monkeys.

October 26th, 1904.—There is a suspicion of weakness in the hind limbs, but a positive opinion on this matter is difficult to give as the animal appeared dull and apathetic. The knee-jerks were exaggerated however, and the animal resented pressure on its epigastrium. There was no evidence of disturbance of sensation. There was no œdema and no muscular tenderness.

October 7th, 1904.—The animal received another injection of 8 *c.c.* of blood from an acute case of Beri-beri.

November 1st, 1904.—The last injection caused no inconvenience to the animal. There was no temperature and the animal took its food and functionated normally. On careful examination the weakness of the hind legs is apparently lost. The animal could climb, grasp firmly, and behave on its legs like other monkeys. There was no change in the knee-jerks, and no epigastric discomfort on gentle pressure. The monkey in fact appears to be in perfect health.

November 8th, 1904.—Diarrhœa set in to-day. This is mucoid and bloody in character. No fever.

November 10th, 1904.—The animal died to-day, the result of persistent diarrhœa. It exhibited no signs of Beri-beri infection up to the date of its death.

Post-mortem Examination.—Mucous colitis. Other organs normal. No signs of Beri-beri, and no evidence of a gastro duodenitis (localised) as described by Hamilton Wright. Microscopical examination of smears of the various organs gave a negative result, and the bacteriological examination of the blood and the spleen resulted in nothing of a definite nature being found.

D.—Intra-peritoneal Injection of Freshly drawn Blood.

Experiment No. I.

Animal—One monkey.

Preliminary precautions taken as before.

October 27th, 1904.—4 *c.c.* of blood from an acute œdematous case of Beri-beri injected intraperitoneally.

October 31st, 1904.—6 *c.c.* blood again injected into the peritoneum from another acute case of Beri-beri.

The animal was kept under close observation. The temperature was noted twice daily, but never deviated from normal.

The animal moved and functionated normally, took its food well, had no diarrhœa or epigastric tenderness and no œdema was ever present.

Five months after the date of the last injection the animal was well. There was not the slightest sign of Beri-beri. The knee-jerks were normal.

The animal then contracted dysentery and died a few days after.

Experiment No. II.

Animals—One monkey.

The animal was normal previous to the commencement of the experiment, and the usual precautions were taken.

October 27th, 1904.—10 *c.c.* of freshly drawn venous blood from an acute case of Beri-beri was inoculated.

October 31st, 1904.—8 *c.c.* of blood freshly drawn from an œdematous case was injected. No change was noted in the general behaviour of the animal. The temperature was always normal. The knee-jerks were frequently tested but were always present and not exaggerated.

The period of observation of this animal extended over one year. At the end of this time the condition of the animal was that of a normal monkey. Beri-beri-like symptoms or signs never manifested themselves.

E.—Feeding Experiments with gastric mucous membrane taken from fresh and fatal cases of acute Beri-beri.

Experiment No. I.

Animal—One monkey.

Healthy, fed well and moved like other monkeys.

November 12th, 1904.—The animal was fed with a mixture of boiled rice and broken down gastric mucosa obtained an hour after death from an acute case of Beri-beri. The pieces of mucosa used for the experiment contained small erosions and hæmorrhages, presumably the pathological changes described by Wright, and insisted on by him as the primary lesion in Beri-beri.

The bolus was coaxed down the animal's throat. No sickness followed and the animal was carefully observed until the following day, lest it might vomit the mixture. Nothing followed however, and on the next morning the monkey appeared to be in good health. The temperature was normal.

From November 13th, 1904, until March, 1905, the monkey was kept under close watch. It never shewed any sign of Beri-beri. It moved, climbed, ate, and behaved generally like any other monkey. The result therefore was negative, although the bolus administered contained presumably Wright's primary lesion and his diphtheriod bacillus and toxin, and was brought into actual contact with the gastro duodenal mucosa of the monkey.

Experiment No. II.

Animal—One monkey.

This was fed in exactly the same way and with the same material, including pieces of the duodenum.

Result—Negative as regards Beri-beri after four months' observation.

Experiment No. III.

Animal—One monkey.

This animal was fed in the same way with pieces of gastro duodenal mucosa from a very acutely fatal case of Beri-beri lasting four days.

Result—Negative after three month's observation.

Observations on Pigs.

Feeding Experiments.

Feeding experiments were made with pigs under conditions similar to those used in connection with other animals.

In dealing with these animals, no difficulty was found in getting considerable quantities of the presumably infected material swallowed. As will be seen from the following experiments in certain cases very considerable amounts of Beri-beri tissue were consumed.

Experiment No. I.

(Temperature Chart attached.)

This pig, an adult, in good health and fat. was kept under observation for a few days previous to the commencement of the experiment. It was found to be normal.

September 28th, 1904.—The animal was given as food the stomach, intestines, kidneys, liver, pancreas and spleen of a fresh Beri-beri cadaver. The post-mortem examination was made an hour or two after death, and these organs were sliced into small pieces, mixed with boiled rice and warm water, and placed in a wooden trough before the pig. In order to ensure consumption, the animal had been kept without food of any description for the previous 24 hours. The pig attacked the bolus with considerable vigour, and in a short time had consumed practically the whole of the contents of the trough.

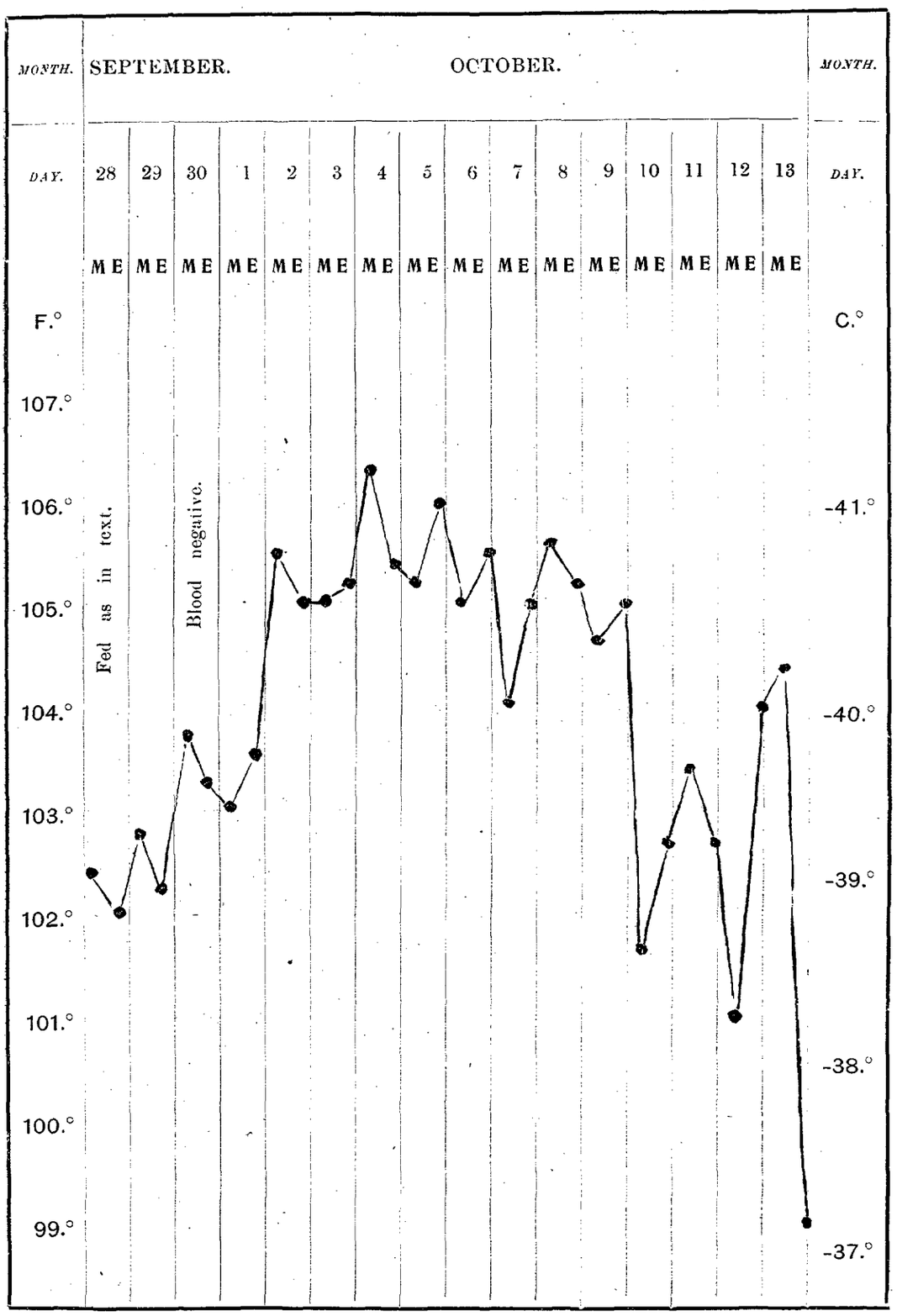
September 29th, 1904.—To-day the animal is bright and lively and anxious to obtain more food. It suffered no immediate bad effects from its gorge on the previous day. Its temperature is normal.

October 1st, 1904.—The animal is dull, and does not eat its food with much relish. It now lies in its pen throughout the day, and on urging it to move it bellows with great force. Fever is present. An examination of the blood gave a negative bacteriological result.

October 3rd, 1904.—The animal has lost a considerable amount of flesh. Its temperature is now maintained over 105° F. It practically refuses all food, and if left alone, lies apparently sleeping in a corner of its pen, emitting short groans frequently. It has great thirst. There is no vomiting or diarrhœa. On urging the pig to move over the compound slight weakness of the hind legs is seen. The gait is groggy, and the animal appears to have difficulty in placing its hind legs firmly upon the ground. There is no œdema of the legs. Pressure on the muscles of the thighs is greatly resented by the animal. The knee-jerks could be elicited with difficulty. No definite disturbances of sensation could be made out. Pressure on the epigastrium was not resented.

October 5th, 1904.—The pig refuses all food but drinks voraciously. Its temperature is the same. There is no diarrhœa. Emaciation is proceeding rapidly. It is now difficult to get the animal to progress. After considerable stimulation, the gait is found to be very feeble, the animal swaying from side to side in a drunken manner on forward progression. The hind legs are with difficulty placed straight on the floor and infringe the one against the other on progression. Pressure on the muscles of these limbs call forth loud grunting from the animal. The anterior extremities were normal. In the affected legs the knee-jerks could not be obtained. There was no œdema. No epigastric tenderness could be found. The blood was examined but gave a negative result as regards organisms.

Feeding Experiment with Pig.—Experiment I.



October 10th, 1904.—The animal has been reduced to skin and bone. The gait irregular, muscular movements, etc., are still present, but not more pronounced. If anything the pig is somewhat brighter to-day. Its temperature has fallen and a certain amount of food (boiled rice) has been consumed. There is no diarrhœa.

October 13th, 1904.—The animal died to-day.

Post-mortem Examination.—There was great emaciation. All the organs and tissues were found to be markedly anæmic. Slight œdema of the subcutaneous tissues was present. The blood was watery and did not coagulate for some time after it had been withdrawn from the body. Both lungs distinctly crepitant throughout. There was no excess of fluid in either pleural cavity. The cardiac muscle was pale, yellowish, and anæmic. The right ventricle was dilated, the left ventricle dilated and slightly hypertrophied. There was a slight amount of mucoid-like tissue lying beneath the epicardium, especially along the course of the main coronary vessels and at the auriculo-ventricular junction. The valves were normal. The ventricles contained several small ante-mortem blood clots. The pericardium was normal and contained about 50 *c.c.* of clear yellowish serous fluid.

The spleen was enlarged, soft and friable.

The liver was soft and yellowish. On section the bile channels were dilated and contained a thin yellowish fluid. Slight cirrhosis was also present.

The stomach was normal, there was no congestion or reddening of the mucosa.

The intestines were normal.

The mesentery was thickened owing to the presence of œdema and gelatinous infiltration. The mesenteric glands were slightly enlarged and showed cortical congestion.

The kidneys were normal.

The brain and spinal cord were congested.

Smear preparations were made from the heart, blood, spleen, liver and kidney, and cerebro-spinal fluid, and shewed the presence in the tissues of a small worm which resembled the embryos of Filaria. Several of these were found in each slide. So far we have been unable to identify them, and have found them in this pig alone. Nothing further, worthy of note, was found in these smear preparations.

Cultures were also made from the heart blood and the spleen but gave a negative result as regards specific organisms.

The sciatic nerves were excised and examined for degenerative changes but the result was negative.

Cause of Death.—*Vide* Conclusion of Experiment No. IV.

Experiment No. II.

Animal.—One pig.

Preliminary conditions as in Experiment No. I.

The pig was fed with an emulsion of the spleen, heart blood and cerebro-spinal fluid of a recently dead acute case of Beri-beri.

The pig ate the mixture with great relish.

On the following day it appeared to be normal. There was no temperature.

On the 3rd day of the experiment the animal died suddenly.

Post-mortem Examination.—There was no pathological lesion to indicate the cause of death, and nothing was found microscopically or bacteriologically.

Experiment No. III.

Animal—One pig.

Preliminary observations, the same as before.

October 7th, 1904.—To-day the pig was fed with a spleen and blood obtained from a recently dead case of Beri-beri (acute). The post-mortem examination was performed within two hours after death, and the heart blood and spleen mashed and mixed with boiled rice.

October 8th, 1904.—Pig lively, no diarrhœa, slight loss of appetite, and apathy. It scarcely ever moves in its pen preferring to lie sleeping in a corner of the enclosure.

October 15th, 1904.—The animal has kept well, the appetite has returned, and it moves in a normal fashion. There has been no rise in temperature since the commencement of the experimental.—*Vide* Chart.

October 16th, 1904.—Fed again to-day with a large amount of mashed Beri-beri organs. The liver, spleen, stomach and duodenum, heart and kidneys with blood of an extremely acute and œdematous case of Beri-beri were obtained one hour after death. These were sliced into small pieces, mixed with the blood and boiled rice, and placed before the animal. The pig made a hearty meal finishing every particle placed before him.

October 17th, 1904.—To-day the animal is dull and apathetic and refuses to move from a corner of its pen. During the day it has had severe vomiting and diarrhœa. The former consisted of undigested pieces of the tissues eaten. The latter was composed of loose bile-stained fœces which apart from their fluidity were normal. The animal is able to locomote normally and has no recognisable epigastric tenderness.

October 18th, 1904.—The pig was again fed with post-mortem tissues, namely, the internal organs of the pig used for Experiment No. IV. (*q.v.*). These the animal devoured heartily.

October 20th, 1904.—The temperature has commenced to rise (*v.* Chart) and from this day onwards the fever followed a course similar to that observed under Experiment No. I. The total duration of this fever was 7 days. During this time the pig became much reduced in weight and ate but little food. There was never any diarrhœa, and the animal locomoted and functioned exactly as other pigs. There was no œdema or recognisable epigastric tenderness.

October 27th, 1904.—From this date onwards the temperature became normal and never again went above 102° F. It is unnecessary therefore to continue the fever chart at greater length. The animal was much thinner but in the course of a few days commenced to recover its normal condition.

Continued observation of the animal was kept up for the following five months, during which time nothing abnormal was noted. The temperature continued normal, the appetite was good. There was no diarrhœa, no epigastric tenderness, and no trace of general or local œdema. The motor and sensory apparatus of the animal appeared at all times to be perfectly normal.

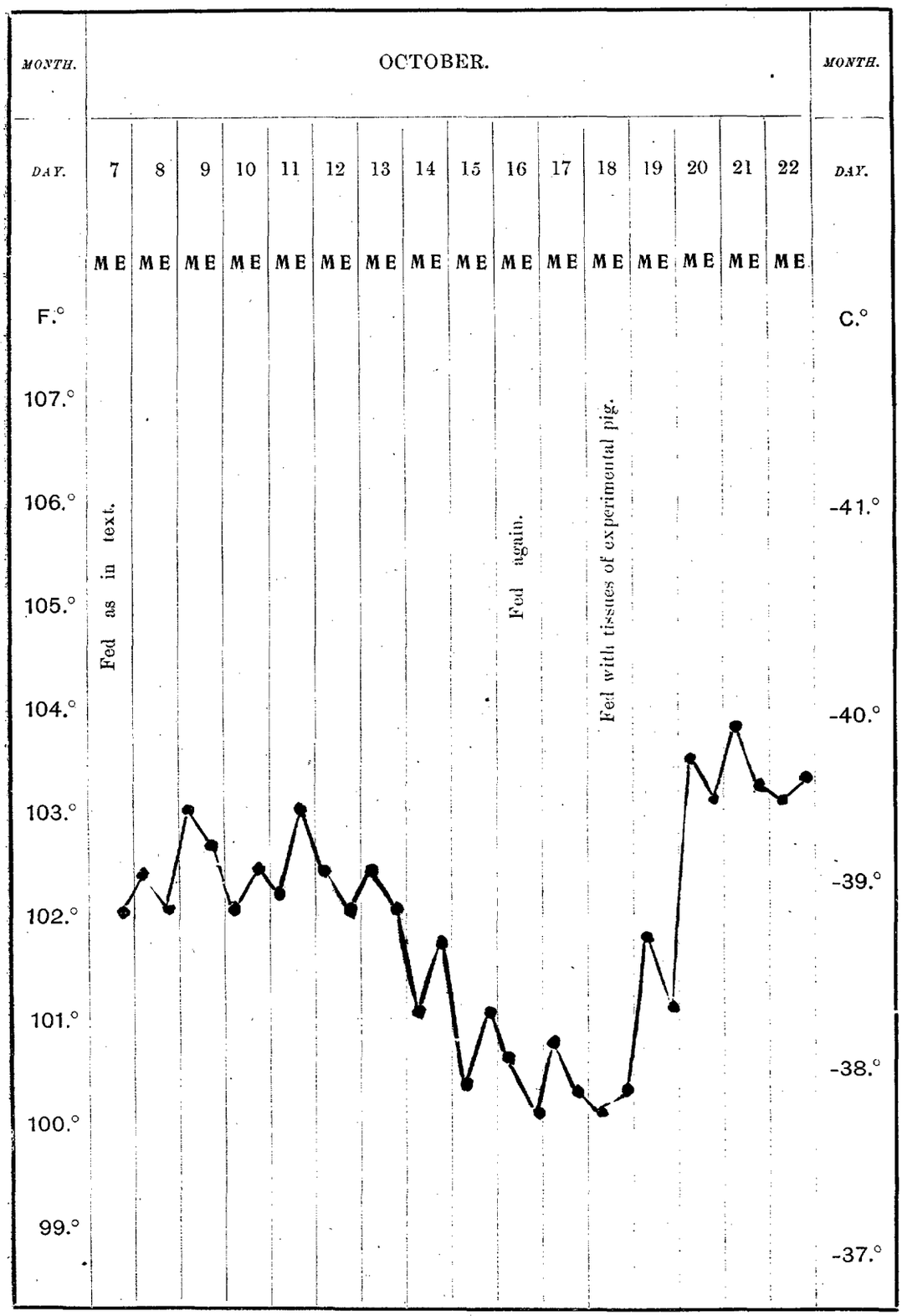
At the present time, a year after the commencement of the experiment, the pig is as healthy and fat as any pig could be.

Experiment No. IV.

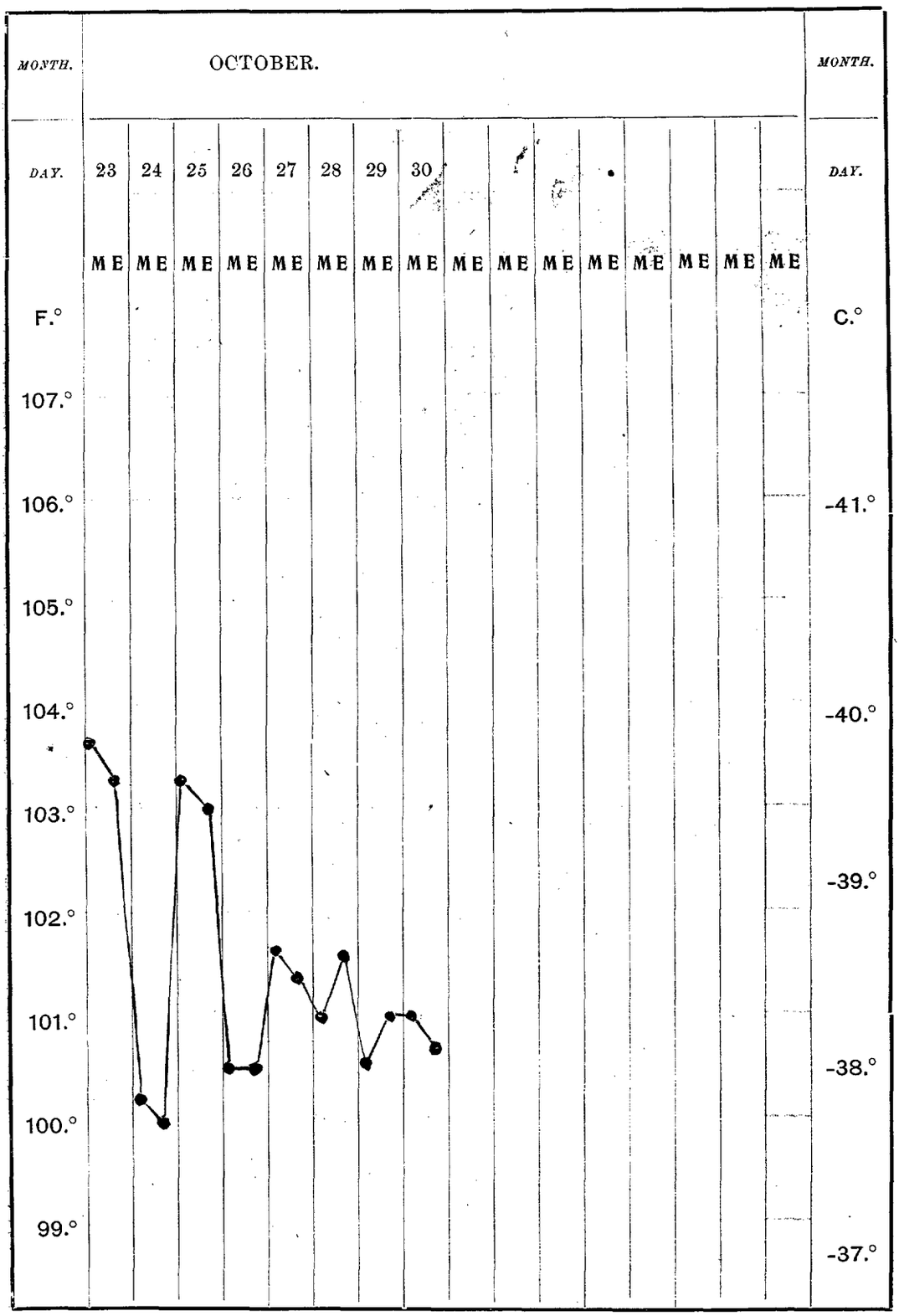
Animal—One pig.

Preliminary observations, as before.

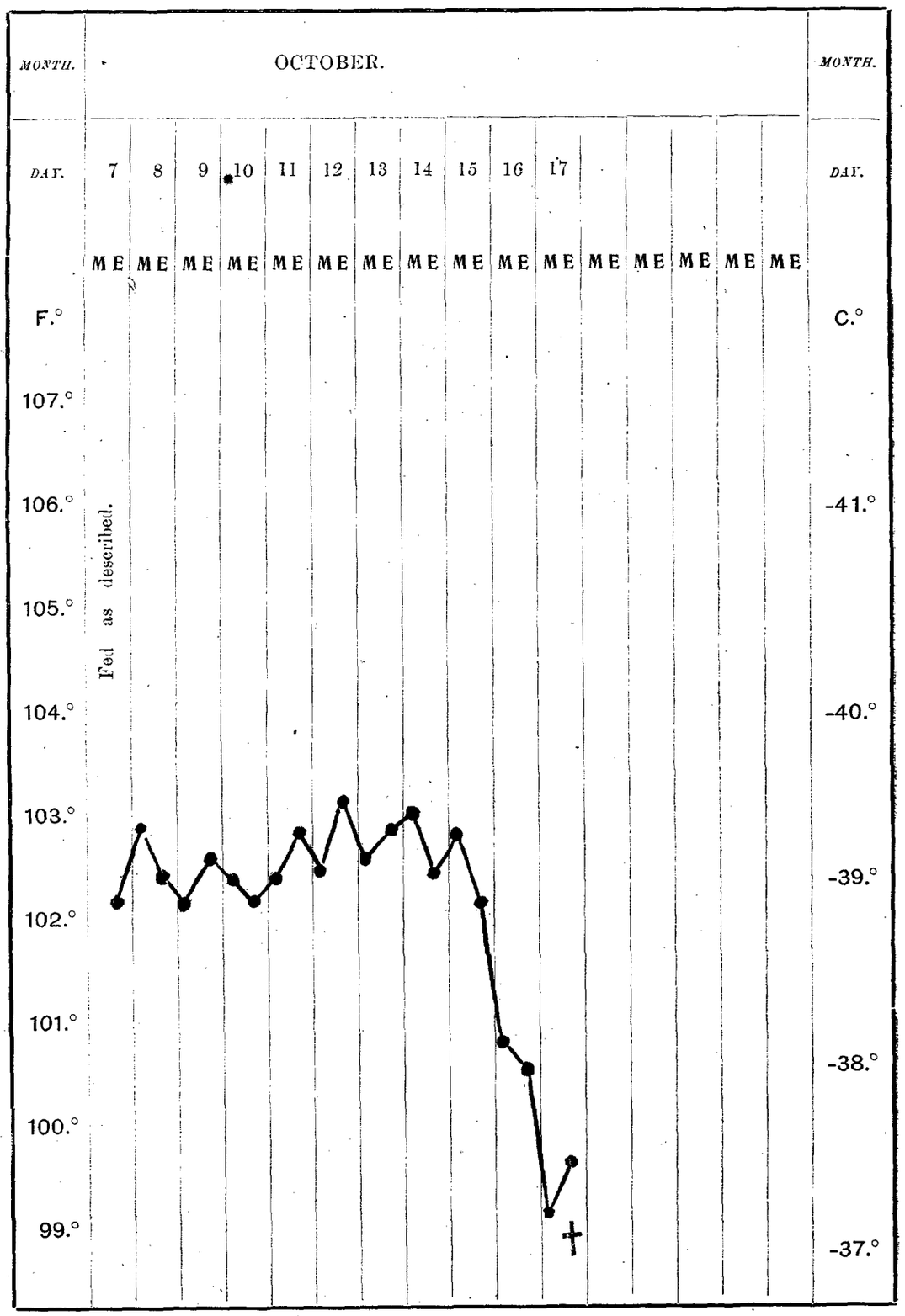
Feeding Experiment. Pig.—Experiment III.



Feeding Experiment. Pig.—Experiment III.



Feeding Experiment. Pig.—Experiment IV.



October 7th, 1904.—The pig was fed with an emulsion composed of the whole brain of a Beri-beri cadaver mixed with boiled rice. The brain was obtained from a freshly dead case and emulsified within one hour after death.

The animal ate voraciously, having been kept without food for 24 hours previously.

The attached temperature chart shews that during the experiment there was no fever.

October 17th, 1904.—The animal died to-day rather unexpectedly. Up to the date of its death, it never shewed any signs of Beri-beri infection. There was no epigastric tenderness, no œdema, and no disturbance of locomotion and sensation. During the greater part of the time the pig was dull and refused food. It became progressively weaker.

Post-mortem Examination—No sign of Beri-Beri. No gastro duodenitis. No œdema. Heart normal.

Cause of Death.—Chronic cachexia, the result of ptomaine poisoning.

[On October 15th, 1904, was again fed with internal organs of pig of Experiment No. I.]

Experiment No. V.

Animal—One pig.

Preliminary precautions, and the animal's condition carefully noted previous to the commencement of the experiment.

October 25th, 1904.—To-day the animal was fed with the emulsified brain of an acutely fatal case of Beri-beri. The brain was obtained within two hours of the death of the patient. It was broken down and mixed with boiled rice and water and then given to the animal, which consumed it entirely.

November 1st, 1904.—Another brain was obtained from a similar case, treated exactly as before and eaten by the pig.

On the following day an examination of the animal shewed nothing of note. It ate well, had no diarrhœa, moved about in a normal fashion, and had no tenderness over any part of the body surface. There was never any rise in temperature.

November 5th, 1904.—The pig died to-day, and post-mortem examination shewed the cause of death to be a form of hæmorrhagic septicæmia. There was no evidence of Beri-Beri.

Experiment No. VI.

Animal—One pig.

Preliminary precautions were taken as in previous experiments.

October 25th, 1904.—The animal was fed with an emulsion composed of boiled rice, water, and broken down liver substance, and one pint of the blood of a well marked Beri-beri cadaver. The organs were obtained almost immediately after death and the pig fed at once.

October 27th, 1904.—The animal appears to have lost its appetite, but has no vomiting or diarrhœa. There is no apparent surface tenderness over the body. The legs, especially the posterior pair, appear to be weak. They lock somewhat on forward progression, and the feet are not firmly planted on the ground. The legs are not tender however, and there is no sign of œdema. The knee-jerks were present.

A temperature chart is not attached. The temperature was noted daily and shewed no variation from the normal.

November 1st, 1904.—The animal has lost flesh. It eats little but has no diarrhœa. There is no epigastric tenderness. The knee-jerks are present, but the weakness and stiffness of the hind legs has become progressively worse. On rapid forward progression the animal staggers considerably. There is no œdema.

November 7th 1904.—The condition of the animal remains the same. It has occasional rigors. Food is all but refused. There is no diarrhœa.

December 1st, 1904.—The animal cannot walk. The hind legs are in a condition of spasticity. The knee-jerks are present and exaggerated. There is no diarrhœa. The temperature has remained normal since the commencement of the experiment.

January 12th, 1905.—The animal died to-day. From the date of the last examination, the pig had become progressively weaker, was quite unable to walk, but ate its food and had no diarrhœa. There was never any œdema, and the knee-jerks were always present.

Post-mortem Examination.—This was made within four hours after death. The body was very emaciated, and on cutting open the cadaver the subcutaneous tissues were found bathed with a yellowish watery fluid, and they themselves presented a mucoid appearance. There was about 20 *c.c.* of clear watery fluid in the pericardial sac. There was no pericarditis. The heart shewed a mucoid like infiltration near its surface under the epicardium. This was especially well marked at the auriculo-ventricular groove and along the course of the main coronary vessels. The cardiac muscle was soft, yellowish in colour, and very flabby. Both ventricles were dilated, with a small amount of compensating hypertrophy of the wall of the left ventricle.

The lungs were normal apart from a small amount of œdema. The pleural cavities each contained about 30 *c.c.* of clear watery fluid There was no pleurisy.

The spleen was not enlarged. Its capsule shewed irregular thickenings due to localised growths of connective tissue. The spleen pulp was firm, dark in colour, and beset with firm bands of fibrous tissue. It was not congested.

The liver was in a condition of cirrhosis of the interlobular type, and its naked-eye appearance was not unlike a miniature of the hob-nailed liver met with in the human subject.

The kidneys were anæmic but otherwise normal.

The stomach shewed small areas of hæmorrhagic extravasation scattered over the mucosa. Towards the cardiac end a patch of hæmorrhagic mucous membrane was found. It was about the size of a dollar-piece, and raised above the general surface of the remaining mucosa. It had thickened edges, and its surface was covered with yellowish necrosed material in the form of a membrane. This was difficult to remove from the underlying area. The latter was found to be red and congested. In general this patch appeared to be of the nature of a slowly spreading chronic ulceration.

The duodenum and remaining mucosa of the intestines were normal.

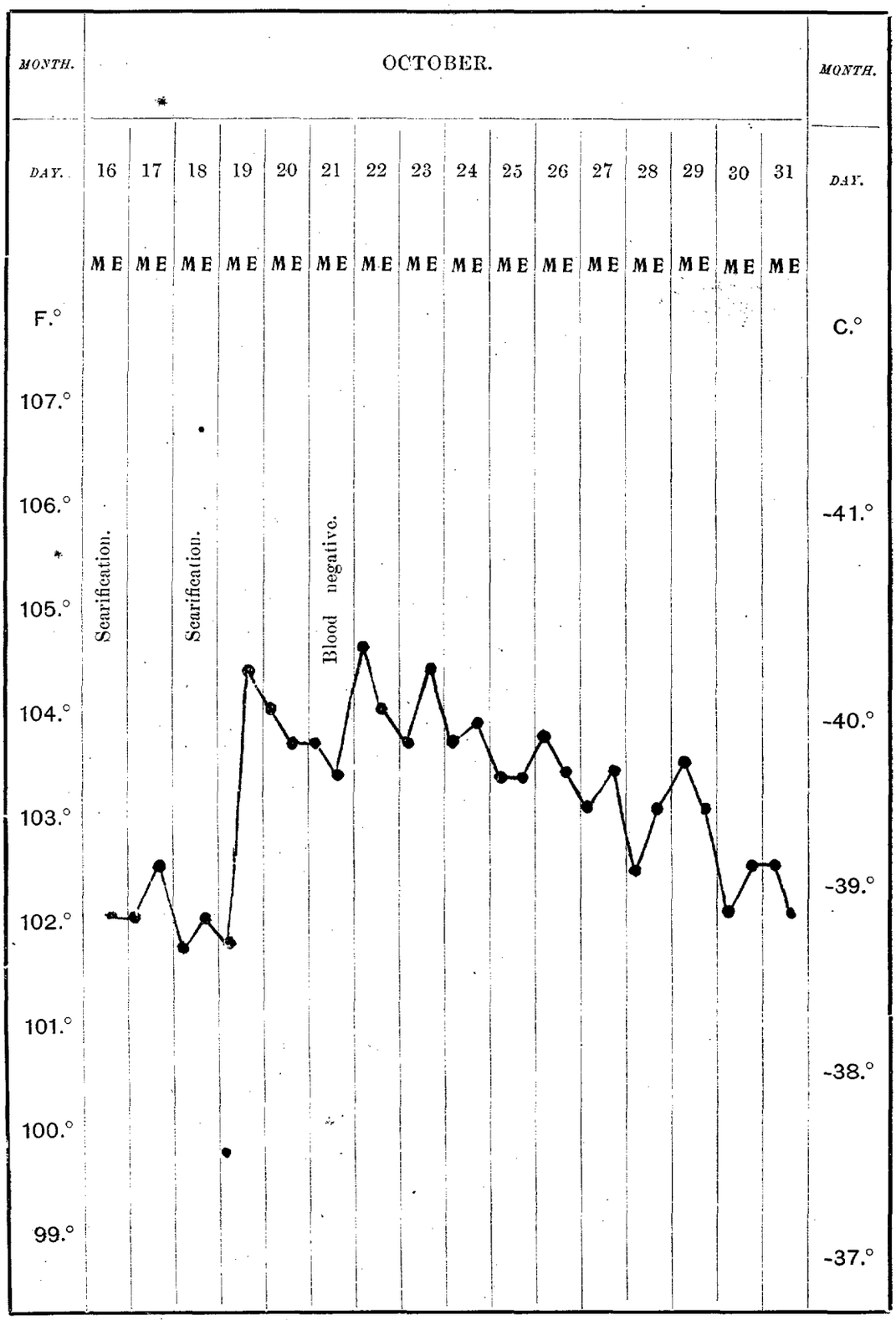
The peritoneum was normal to the naked eye and the mesenteric glands were not enlarged. There was no visible change in the pancreas, and the pelvic viscera were normal. A small quantity of clear yellow fluid, namely, about 40 *c.c.* was present in the peritoneal cavity.

The heart blood and the spleen substance were examined microscopically after staining by LEISHMAN'S method, but nothing was found.

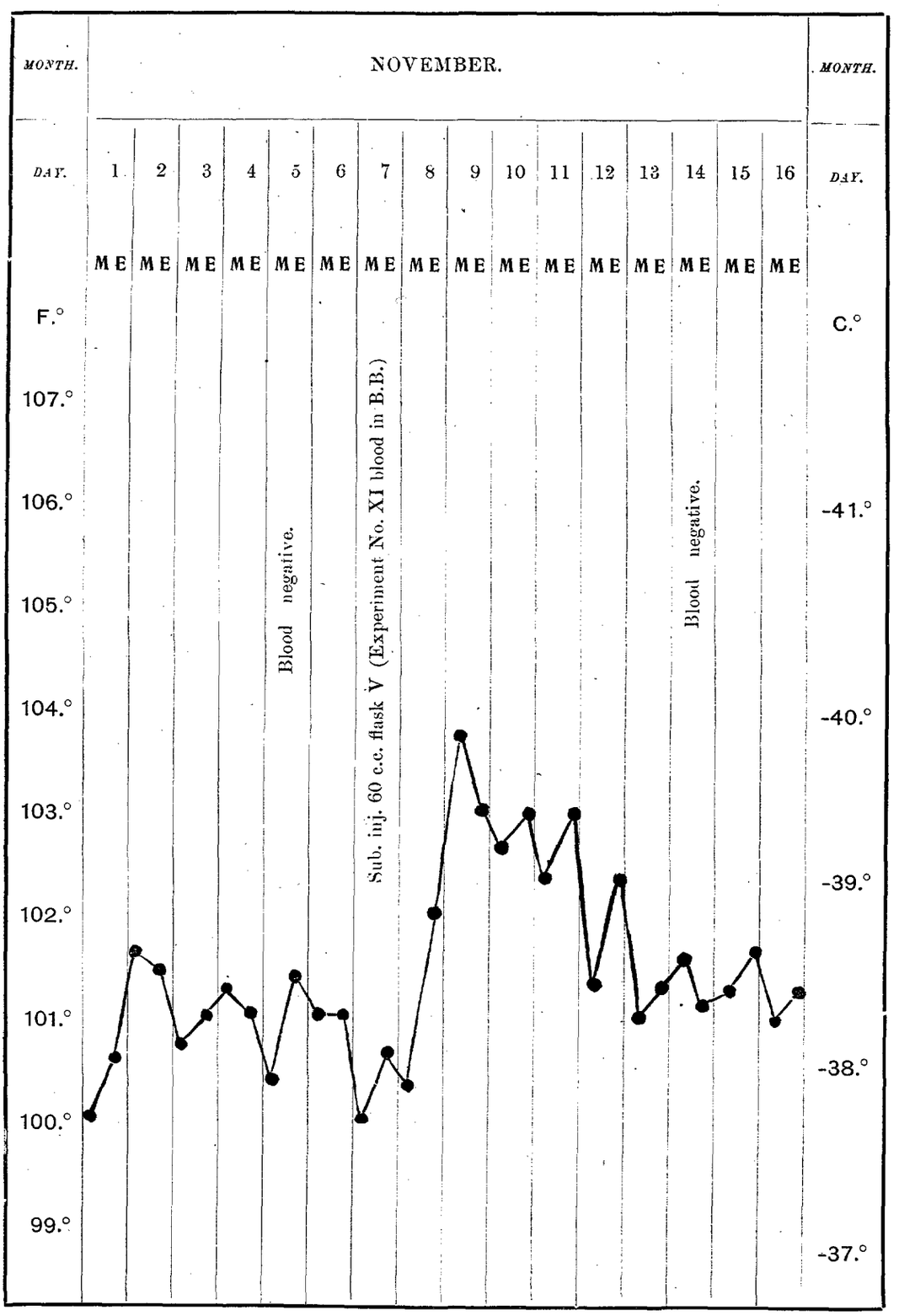
Bacteriologically the blood and the spleen were negative apart from the presence of a few colon-like bacteria which were obviously of post-mortem origin.

A microscopical examination of the sciatic nerves of the animal by the osmic acid method shewed no evidence of Wallerian degeneration.

Experiment on Sheep.—No. I.



Experiment on Sheep.—No. I.



Observations on Sheep.

Experiment No. I.

Animal—One sheep.

October 16th, 1904.—The animal had been kept under observation for several days. It was normal in every respect. To-day, on the death of an acute œdematous case of Beri-beri, the spleen was removed as soon as possible, and used for this experiment. The sheep was thoroughly scarified over the abdominal wall which had previously been shaved and rendered as aseptic as possible. After the scarification the cut surface of the spleen was well rubbed into the scars over the scarified area.

October 17th, 1904.—To-day the animal is quite well and feeds and functionates as other normal sheep.

October 18th, 1904.—Another scarification was done to-day, the cut surface of the spleen of a pig (Expt. No. IV) was well rubbed into the abdominal wall.

October 19th, 1904.—The temperature rose to-day (*v.* chart.)

October 20th 1904. Pustulation over the area of vaccination has occurred, which accounted for presence of the fever: this lasted, with a gradual defervescence, for nearly 14 days.

During this time the animal became much emaciated. It took but little food, but there was no diarrhœa. The urine was normal and an examination (bacteriological) of the blood gave a negative result as regards organisms. There was some apparent weakness of the hind limbs: the animal walked with seeming difficulty, and there was a tendency to lock on the part of the posterior limbs, during forward progression. There also seemed to be some wasting of the muscles of the hind limbs. There was no œdema or evidence of discomfort on pressure over the epigastric area.

This weakness and difficulty in walking we do not ascribe to actual nerve degeneration, and consequently Beri-beri in nature. The animal lost such a considerable amount of weight, and the emaciation was so extreme that in our opinion this difficulty in walking was the result of weakness only. The inability to progress normally disappeared entirely after the animal regained its weight and strength and the temperature became normal.

November 7th, 1904.—The animal's temperature has now been normal for at least a week. The weakness of the hind limbs has now all disappeared, and the sheep moves as other normal sheep. It eats well and has no trace of diarrhœa.

To-day a subcutaneous inoculation was made. 60 *c.c.* of the contents of the flask used for Expt. XI (Blood in Beri-beri) was injected subcutaneously under the skin of the neck.

November 13th, 1904.—The result of the inoculation was a rise in temperature, lasting with gradual lysis, about 6 days. The animal again refused food, became somewhat thinner. There was no diarrhœa however, and no œdema or epigastric tenderness. The inoculation was not followed by any return of the apparent partial paralysis of the posterior extremities. A bacteriological examination of the blood gave a negative result as regards organisms. From this time onwards the temperature remained normal and the animal behaved in every way like any other normal sheep.

At the present time, November, 1905, the animal is alive and well, never having shewn any sign of Beri-beri.

Experiment No. II.

Animal—One sheep.

The conditions of this experiment were similar in every respect to those of Experiment No. I.

October 16th, 1904.—Scarification.

October 17th, 1904.—No result from vaccination. No rise in temperature.

October 18th, 1904.—Scarified again with the substance of the fresh spleen of an experimental pig. (*Vide* Experiment No. IV.—Pigs).

October 19th, 1904.—Scarification a failure so far. Animal apparently healthy. No rise in temperature. Blood examined microscopically with a negative result. From this date onwards until November 1st, 1904, the animal remained in perfect health.

November 1st, 1904.—The animal was fed with 8 ounces of blood from a moribund case of acute Beri-beri.

November 3rd, 1904.—Fed again with 8 ounces of contents of flask used for Experiment No. IX. (Blood in Beri-beri).—*Vide* Bacteriological Experiments.

November 4th, 1904.—Again fed with 10 ounces of 96-hour growth of bouillon from flask used for Experiment No. IX. (Blood in Beri-beri).

November 8th, 1904.—Injected subcutaneously with 60 *c.c.* of the flask used for Experiment No. XI. (Blood in Beri-beri).

During this time when the animal was being subjected to so much experimentation the temperature remained normal, and the sheep fed well. There was no diarrhœa, no epigastric tenderness, and no difficulty in walking. The feeding experiments certainly brought any Beri-beri micro-organisms present in the blood into close relationship with the gastro-duodenal mucosa. Similarly the micro-organisms growing in the bouillon of the different flasks were incorporated in large quantity per the alimentary canal and the subcutaneous tissues.

From the 8th November onwards the sheep was kept under close observation, and frequent tests were made to detect Beri-beri symptoms or signs. Briefly it may be said that such signs were never found, and the animal maintained itself in good health for at least a year after the date of the last subcutaneous inoculation.

Observations on Calves.

Two calves were experimented with. Each was inoculated subcutaneously with the freshly drawn blood of an acute case of Beri-beri. Approximately 30 *c.c.* of blood was injected into each animal. Both animals lived for a week only, contracting hæmorrhagic septicæmia.

Owing to the great risks attached to the introduction of hæmorrhagic septicæmia by cattle among our animals, it was considered advisable to stop further experiments with calves and confine our attention to other animals.

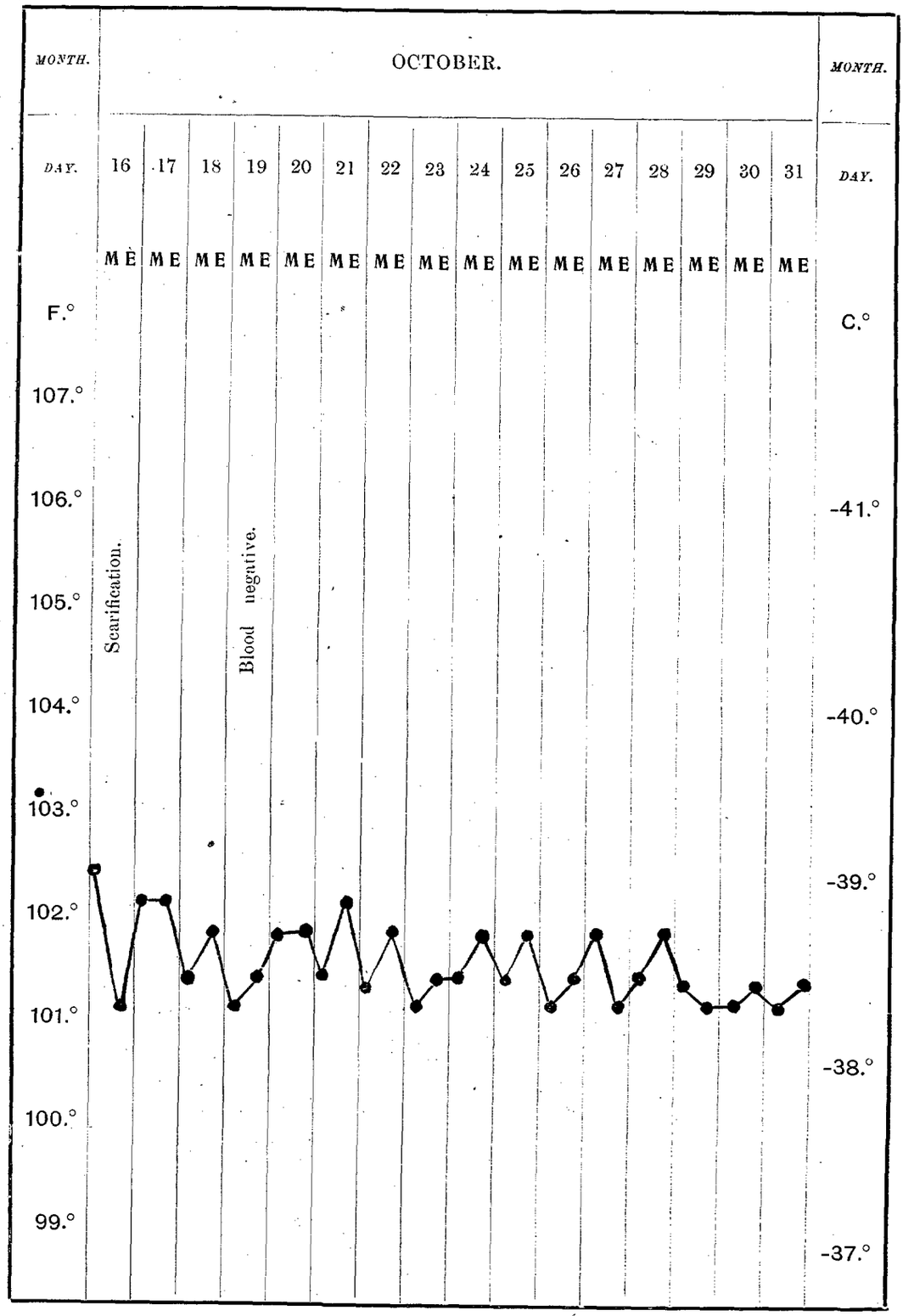
Observations on Rabbits.

A.—Natural Infection.

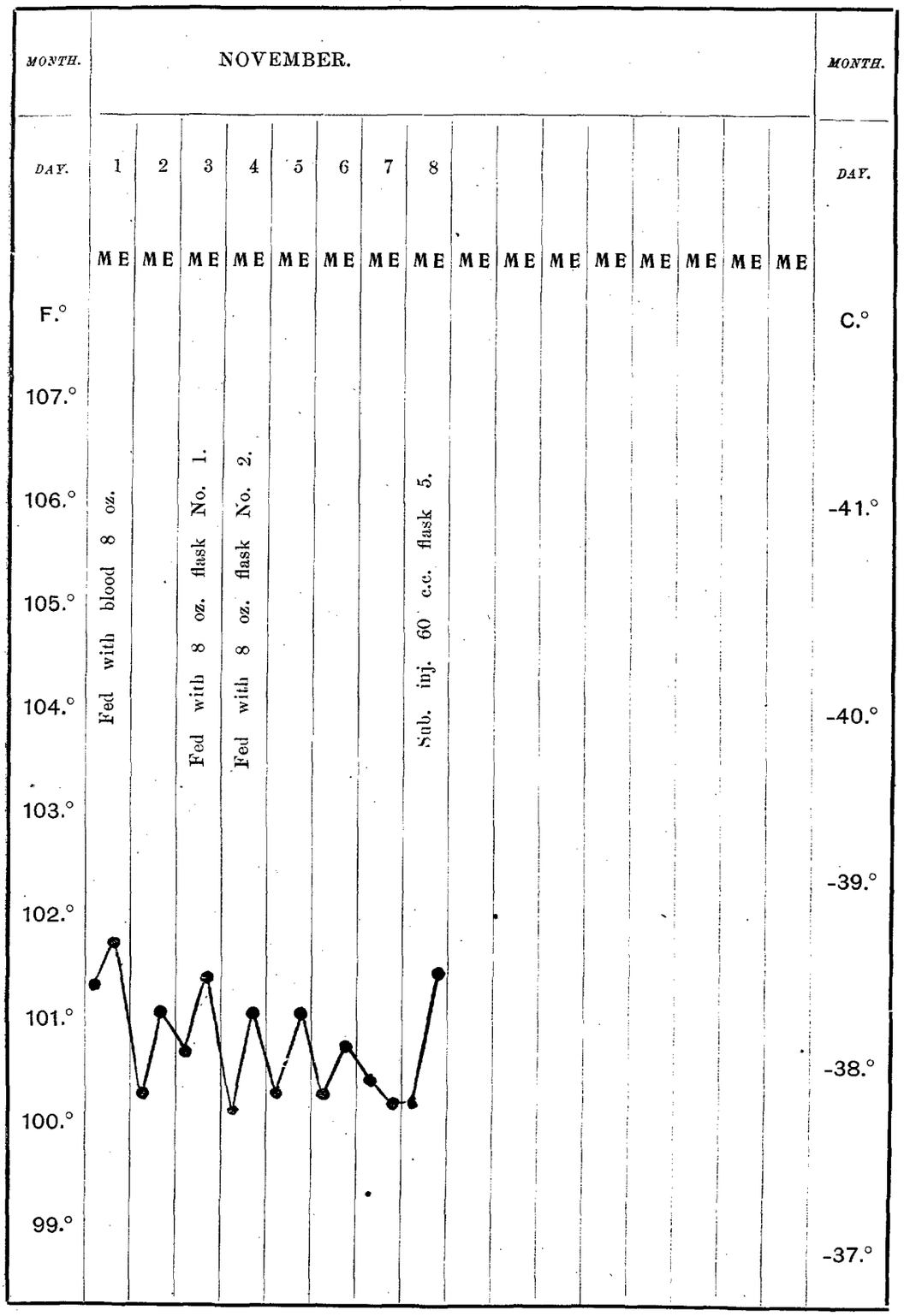
One experiment of this nature was undertaken under similar conditions to those already detailed under "Natural Infection of Monkeys." Four rabbits were placed in one of the rooms of the Po Leung Kuk, in which the inmates resided who contracted Beri-beri. The windows were shut and the light excluded as rigidly as possible. Previous to the commencement of the experiment, the animals were kept under observation, and their blood tested microscopically.

The experiment lasted 6 months. The diet consisted of rice, vegetables, etc. At no time did they exhibit any sign of disease, and were as healthy when removed as when they were first incarcerated.

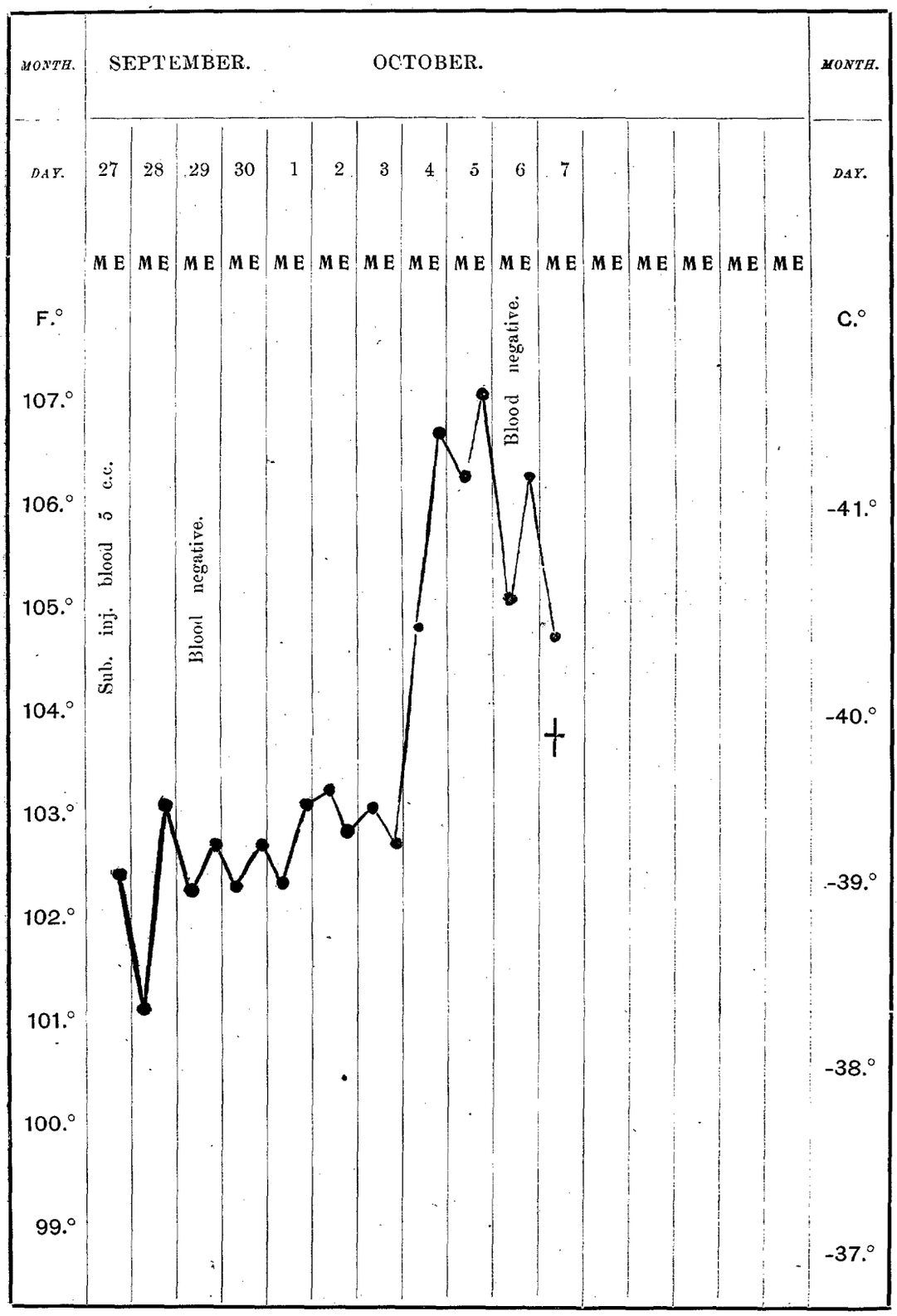
Experiment on Sheep.—No. II.



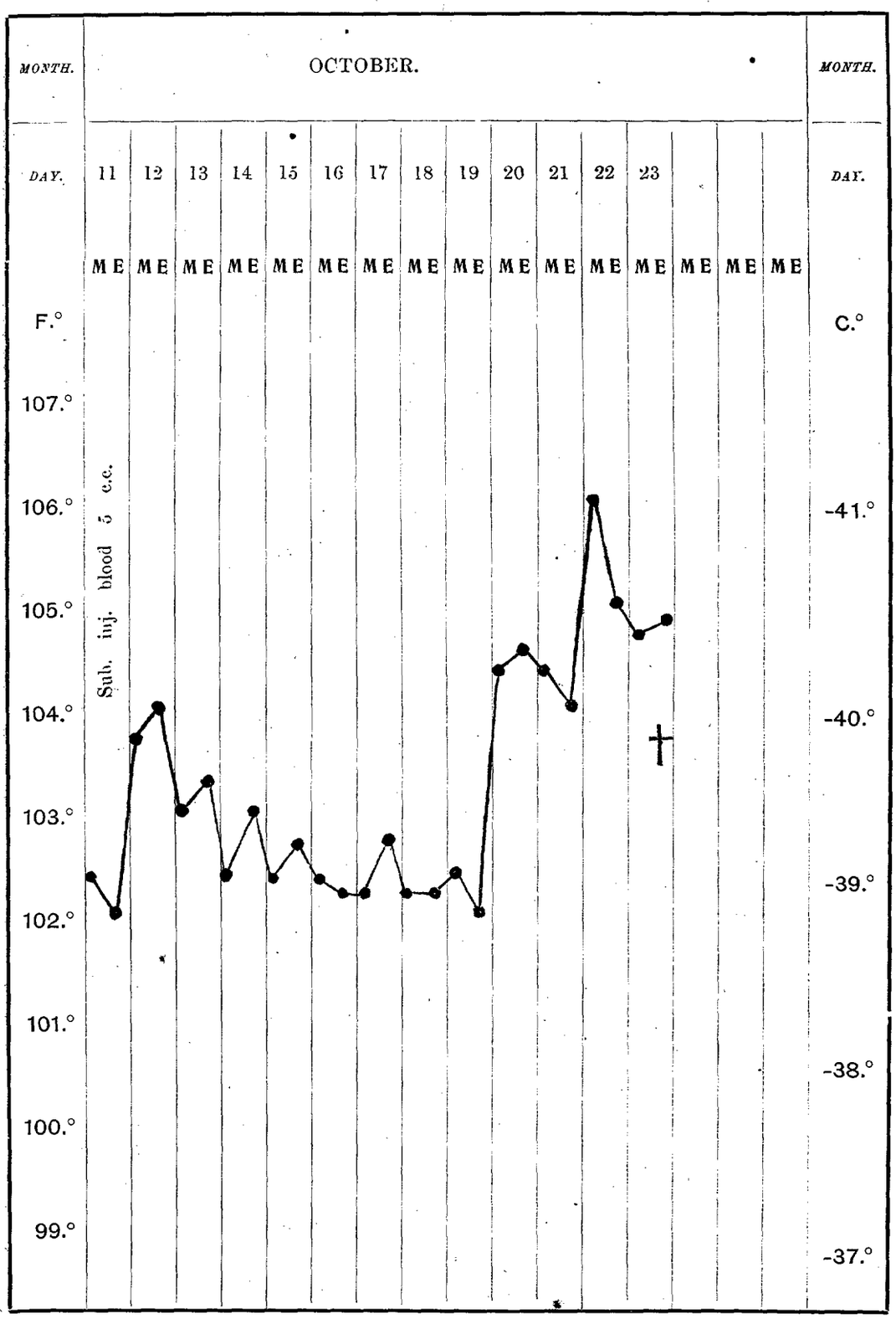
Experiment on Sheep.—Experiment. II.



Experiment with Beri-beri Blood.—Rabbit.
Subcutaneous Inoculation.—Experiment I.



Sub. Inoculation.—Rabbit.—Experiment II.



B.—Subcutaneous Inoculation with Beri-beri Blood.

Experiment No. I.

Animal—One rabbit.

Similar to the experiments on monkeys.

The animal was kept under observation for a few days, its general health and temperature being noted. An examination of the blood revealed nothing abnormal.

On September 29th, 1904.—The rabbit was injected subcutaneously under aseptic conditions with 10 *c.c.* of venous blood of an acute cace of Beri-beri. As a result of this no change was observed in the condition of the animal. Its blood was examined and proved negative to organisms as before. The animal continued well until October 3, 1904, *i.e.*, for six days after the inoculation, when it contracted severe diarrhœa and its temperature rose rapidly (*v.* Temperature Chart). It died on October 10th, 1904, ten days after the commencement of the experiment.

Post-mortem examination.—Acute follicular enteritis. No changes characteristic of Beri-beri. Stomach and duodenum normal. Spleen smears and cultures negative.

Experiment No. II.

Animal—One rabbit.

Previous to the commencement of the experiment the animal was kept under observation and was found to be normal in every respect.

October 11th, 1904.—To-day the animal was inoculated subcutaneously with 5 *c.c.* of freshly drawn venous blood taken from an acute case of œdematous Beri-beri.

October 12th, 1904.—There is slight fever to-day, the result of the inoculation of the blood. The animal is otherwise well, has no diarrhœa, and moves about freely. (*v.* Chart).

October 14th, 1904.—The fever has disappeared.

October 19th, 1904.—The animal is well and shews no signs of any indisposition. There is no evidence of the onset of Beri-beri.

October 20th, 1904.—To-day the animal developed pneumonia with all the accompanying symptoms.

October 23rd, 1904.—It died this evening.

October 24th, 1904.—Post-mortem.—Typical double pneumonia. No evidance of Beri-beri. Pneumo-cocci and strepto-cocci found in lungs. No organisms is spleen.

Feeding Experiment.

Animal—One rabbit.

After the preliminary measures in regard to experimentation had been taken, the animal was fed (November 1st, 1904) with an emulsion of boiled rice and the broken down spleen pulp obtained from a fatal case of Beri-beri. The spleen was extracted from the cadaver within two hours after death and the animal was at once fed.

Subsequently the rabbit was kept isolated and observed daily.

The experiment was negative after three months. No sign of Beri-beri was ever noted.

Observations on Fowls.

Experiment No. I.

One fowl.

The animal was kept under observation for a week previous to the commencement of the experiment. Its temperature was normal varying from 105°-106° F.

November 1st, 1904.—Fed with broken down spleen substance obtained from a cadaver with typical acute Beri-beri lesions.

November 8th, 1904.—Fed with 30-40 *c.c.* of the contents of the flask used for Experiment No. XI (*vide* "Organisms in Blood of Beri-berics").

From this date onwards, the animal shewed no departure from its normal state of health. A temperature chart is not appended as no fever was ever present. The bird was kept under observation for at least six months from the last date of feeding and at no time shewed any symptom or sign of Beri-beri.

Experiment No. II.

Five fowls.

Kept in a hen coop isolated.

Normal previous to commencement of experiment.

October 25th, 1904.— Fed with broken down spleen of a recently dead acute case of Beri-beri. The spleen was enlarged and weighed 1½ lbs. The fowls devoured the whole organ.

November 1st, 1904.— Fed with a second spleen under similar conditions. This was also actively devoured.

The birds were kept under close observation and tested almost daily as regards their powers of locomotion. Their temperature never appeared to vary, and at no time during the following six months was there the slightest evidence of Beri-beri infection.

Experiment No. III.

One hen.

November 1st, 1904.—Fed with the broken down spleen pulp of a recently dead case of acute Beri-beri.

November 8th, 1904.—Fed with an emulsion of boiled rice and 100 *c.c.* of contents of flask used for Experiment No. XI (*vide* "Blood in Beri-beri.")

The animal was kept under observation for at least three months. The temperature was noted daily. It continued to move and functionate like any other normal fowl. Up to the date of the last observation, it never shewed the slightest trace of Beri-beri.

Observations on a Horse.

A horse, China pony, was placed under observation and its temperature and general health noted for some days.

October 25th, 1904.—Inoculated subcutaneously (over left side of neck) with 60 *c.c.* of defibrinated fresh venous blood taken from a case of acute Beri-beri. As the result of the injection a hard brawny swelling occurred around the site of inoculation. This gradually subsided and was entirely gone in about 3 weeks. It occasioned no rise in the temperature of the animal and apparently gave him no discomfort. The animal fed well, had no diarrhœa, and moved and functionated like a normal horse.

October 27th, 1904.—The animal was again inoculated subcutaneously with with 80 *c.c.* of freshly drawn venous blood from a patient suffering from acute œdematous Beri-beri. This occasioned another hard swelling about the size of a child's head which gradually subsided.

This injection caused no rise in temperature, and the general health of the horse was well maintained.

November 7th, 1904.—The swellings have entirely gone and the animal is well in every respect.

November 11th, 1904.—Rheumatism with swelling of the knees set in, rendering the animal unable to walk. This condition set in suddenly, and, in our opinion, had nothing to do with the disease under consideration. The knee-jerks were present and not diminished or exaggerated, and there was no evidence otherwise of the presence of Beri-beri.

November 15th, 1904.—The horse is able to move slowly, although crippled. The swelling of the knee joints has practically disappeared. There is no pain or tenderness on pressure over the hip muscles, and the knee-jerks are present.

November 16th, 1904.—The temperature has remained normal since the commencement of the experiment. The animal is unable to stand to-day. The hind legs are stiff and spastic. The knee-jerks are greatly increased. The breathing is rapid and laboured, and there is some distension of the abdomen.

November 23rd, 1904.—The former symptoms have all but disappeared. The animal is now able to rise and walk on all-fours. The temperature is normal, and the horse enjoys its feed and has no diarrhœa.

From this time onwards the horse maintained good health. There were no paralyses. The knee-jerks were normal and the animal fed well.

January 27th, 1905.—The animal died to-day from inanition. Previous to its death it shewed no evidence of Beri-beri.

Post-mortem examination.—Nothing of note found.

Comments.—The stiffness and lameness of the animal during part of the experiment is, in our opinion, to be attributed to rheumatism. This was probably contracted by exposure and cold, the animal having but meagre house accommodation. Again, it must be noted that the animal was old and decrepit when bought for experimental purposes. Taking everything into consideration the cause of death cannot be attributed to Beri-beri.

GENERAL CONCLUSIONS ON EXPERIMENTAL RESEARCHES.

1. It has been found impossible to convey Beri-beri to any of the animals used for the experiments.

2. Monkeys have been used extensively and experimented upon in a great variety of ways, including that recommended by HAMILTON WRIGHT. In no instance has any one of them exhibited the slightest trace of Beri-beri infection.

3. The Pigs used for the experiments shewed signs of lameness, etc., and a condition simulating Beri-beri was once or twice reproduced. The animals, however, were frequently subjected to somewhat rough handling by the attendants, and this, coupled with the continued observation of their progress, and the result of post-mortem examination, leads us to the conclusion that a condition of true Beri-beri never existed.

4. In regard to the other animals, viz., Sheep, Calves, Rabbits, Fowls, etc., notwithstanding vigorous experimental efforts, we have been unable to call from them the slightest evidence of Beri-beri infection.

5. As a result of our extensive experiments *it would appear that the transference of Beri-beri infection from man to animals is impossible.* It may be possible that animals contract the disease through other channels. This, however, we doubt.

6. These experimental researches, negative though they may be, possess in our opinion great value as they practically prove in opposition to H. WRIGHT and others, *that in Beri-beri we are not dealing with an infectious disease, but with one of an entirely different etiology.*