Rat Bite Fever Due to *Streptobacillus Moniliformis*

A CASE TREATED BY PENICILLIN

By F. F. KANE, M.D., M.R.C.P.I., D.P.H.

Medical Superintendent, Purdysburn Fever Hospital, Belfast

It is unlikely that rat-bite fever will ever become a public health problem in this country, so the justification for publishing the following case lies rather in its rarity, its interesting course and investigation, and in the response to Penicillin.

PRESENT CASE.

The patient, D. G., born on 1st January, 1929, is the second child in a family of three sons and one daughter of well-to-do parents. There is nothing of importance in the family history or the previous history of the boy. Before his present illness he was in good health, was about 5 feet 9½ inches in height, and weighed, in his clothes, about 10½ stone. The family are city dwellers.

On the afternoon of 18th March, 1944, whilst hiking in a party along a country lane about fifteen miles from Belfast city centre, he was bitten over the terminal phalanx of his right index finger by a rat, which held on until pulled off and killed. The rat was described as looking old and sickly. The wound bled slightly at the time, but with ordinary domestic dressings it healed within a few days. Without missing a day from school and feeling normally well in the interval, the boy became sharply ill at lunch-time on 31st March, i.e., thirteen days after the bite. He had acute loss of appetite, with rigor, vomiting, and headache, and his temperature, when taken shortly afterwards, was 105°. He took to bed that day, but after about three days the malaise disappeared and his temperature returned to normal. He tried to get up, but was unable to stay, and returned to bed. Two similar attacks followed periods of apparent normality before he was admitted to a general hospital on 12th April, for investigation. This revealed a white cell count of 1,200 per cm., a negative Paul Bunnell, X-ray of chest and abdomen apparently normal, urine normal. The Widal was positive to a titre of 1/50 to *B. typhosus* (H) and negative to *B. para. A*, *para. B*, and *abortus*. On this finding he was transferred to Purdysburn Fever Hospital as a possible enteric infection.

On admission, although he was actually in an acute pyrexial phase, there was nothing outstanding to note in his clinical condition. He was dull, but not to the degree consistent with even a mild enteric infection. He could detail his story without confusion, and denied any disturbance of sleep, made light of his headache, and admitted rigors, so that altogether he was not clinically suggestive of enteric fever. His tongue was moist and lightly furred. He had a healthy throat and no palpable glands. His abdomen was distended without any tenderness. The spleen was not palpable. For some days he had difficulty with micturition, apparently entirely postural. He had been constipated since taking to bed, and for some weeks afterwards required enemata at intervals. There was a small well-healed scar on his right index finger where the rat had bitten, but there was no tenderness

Fig. 1
 Morning and Evening Pulse and Temperature Chart
 M—Myocrisin. B—Blood transfusion. P—Penicillin.

or induration and no lymphatic involvement whatever. There were no abnormal findings in heart, lungs, or C.N.S., and there was no sign of any rash.

The temperature and pulse chart during the entire sixty-two days of his stay in this hospital indicates the course of his illness (fig. 1). The outstanding feature is the relapsing nature of the condition. At first relapse occurred at regular five-day intervals, but later became irregular, tending towards shorter and milder attacks with longer free periods.

In the afebrile periods the boy was bright and cheerful, completely without symptoms, with a rather fickle appetite, and a pale white skin. The approach of

Fig. 2
Four-hourly Temperature and Pulse Chart of One Week
(6th—12th May)

a relapse became evident by his quietness, loss of interest in his radio and papers, a puffiness of his features, especially of the eyelids and nose, and a sharp loss of appetite. The dulness and loss of appetite were the only features common to all relapses. His temperature and pulse were recorded four-hourly throughout, and the second chart (fig. 2) shows a week's record with two typical relapses. It shows the temperature rising gradually over two days to a peak, with a sharp fall to subnormal terminating the relapse. (This contrasts with the impression of Douglas, Colebrook and Fleming,¹³ who record the fall of temperature as being more gradual than the onset.) There was no disproportion between the temperature and pulse-

rate. Once epistaxis of mild degree occurred during a relapse. There were no chest symptoms or signs.

The boy's tongue remained moist and lightly furred throughout. On several occasions his lips inclined to crack and bleed. On only two occasions was his spleen palpable: thirty-second and fifty-sixth days, both immediately following the termination of a relapse. The viscus was only slightly enlarged and not tender. At no time while in hospital was there any reaction about the scar of the bite or in the lymphatics. Headaches were never severe and were easily relieved. Sweating was not a prominent feature, and rigors at the onset of the first few attacks were of a mild degree. Blood-pressure readings varied from 86/60 to 104/64. Sleep and rest were little disturbed at any time throughout the course. The fluid exchange, charted throughout his illness, was always liberal, from five and a half to eight pints intake and a urinary output varying from three and a half to seven pints daily. Only on three days throughout the course was a trace of albumen found in the urine, twice after his first injection of Myocrisin and once in convalescence. Loss of weight was not pronounced: his ward record shows that when first weighed on his twenty-sixth day of illness he was 9st. 5lb., his lowest was 8st. 6lb. at his forty-fourth day, and at his seventy-first day he had returned to 9st. 5lb. There was never any sign of arthritis as a complication, although he had a very slight degree of myalgia upon full extension of elbows and knees, but not more than could be attributed to his long spell in bed. There was never delirium, confusion was minimal, and giddiness was present only in the early relapses, when the boy was allowed to sit erect in bed.

It was not until the twenty-sixth day of illness that a rash was seen. Then the patient drew attention to what he thought were "hives" on his left arm, although at no time did the spots itch. During this particular exacerbation—the third in hospital—he was entirely without symptoms, apart from loss of appetite and dulness, and did not even feel feverish. The rash on this occasion comprised six dusky red, ill-defined spots of about $\frac{1}{4}$ in. diameter, not raised and without induration, and limited to the left arm. There were no lesions on mucous surfaces. Next day there were another six spots of similar nature distributed over chin, neck, and chest, which had faded the following day with the remission of temperature. In every subsequent relapse these spots reappeared, especially about the face, neck, and shoulders. They were always ill-defined and blotchy and accompanied by the puffy features, described as "measly," but bearing little resemblance to morbilli. There was no photophobia or conjunctivitis, although in these exacerbations the boy usually lay with closed eyes (plate I).

INVESTIGATIONS.

At first it was considered necessary to exclude the possibility of typhoid fever, and although the agglutination titre of 1/50 for *B. typhosus* (H) was confirmed, blood culture in trypsin broth was reported sterile and the stools showed no enteric organisms. Thereafter, with appreciation of the relapsing nature of the condition, steps were taken to exclude malaria and establish connection with the rat-bite.

The following investigations were subsequently carried out.

Blood film—daily from twenty-first to twenty-fifth days—showed no malarial parasites.

	Day of Disease	
Red blood cells	32	4,120,000 per cmm.
	40	4,225,000 Hæmoglobin approximately 100%.
	46	3,850,000
	57	4,000,000 immediately before transfusion.
	62	4,890,000 immediately before Penicillin.
	63	5,100,000
White blood cells	21	3,200 per cmm.
	23	3,200
	24	2,300
	25	2,200 polymorphs 66%, mononuclears 11%, lymphocytes 23%.
	26	2,100 polymorphs 72%, mononuclears 18%, lymphocytes 10%.
	28	2,104
	29	3,120
	30	2,808
	32	2,496
	35	3,800
	37	1,300
	40	2,900
	46	3,800
	55	4,056
	57	4,000 immediately before transfusion.
	58	4,900
	60	4,300
	62	4,300 immediately before Penicillin.
	63	3,500 polymorphs 39%, mononuclears 37%, lymphocytes 24%.
	64	4,600
	68	7,100 polymorphs 65%, mononuclears 15%, lymphocytes 20%.
	70	8,300
	75	8,500 polymorphs 45%, mononuclears 25%, lymphocytes 30%.
Blood sedimentation rate	26	5.5
	30	5.0
Widal	18	B.T. 1/50 (H), negative para A, para B, and abortus.
	21	B.T. 1/50 (H), negative para A, para B, and abortus.
	25	B.T. 1/50 (H), negative B.T. (0), para A, para B, abortus.
	75	Completely negative.

	Day of Disease	
Weil-Felix	25	Negative OX.K, OX.L, and OX2.
Paul Bunnell	26	Negative (also negative at 14th day before admission)
	75	Positive 1/2,560.
Serum test for syphilis	25	Harrison negative, Fleming negative.
	46	Harrison + +, Fleming negative.
	55	Harrison + +, Fleming negative, Dreyer 0.
	75	Harrison + +, Fleming negative, Kahn + + +.
Throat and naso- pharyngeal swabs	39	No growth of streptobacillus.
Fæces	18	No enteric organisms.
	25	No enteric organisms.
	39	No growth of streptobacillus.
Urine	...	Daily examination throughout course revealed a trace of albumen on only three occasions.
	25	No enteric organisms.
	33	Two guinea-pigs inoculated intraperitoneally with- out effect.
	39	No growth of streptobacillus.
Blood culture	21	No growth in Trypsin broth.
	25	Streptobacillus moniliformis grown on Loeffler slopes and serum broth.
	31	Streptobacillus moniliformis grown on Loeffler slopes and serum broth.
	36	Streptobacillus moniliformis grown on Loeffler slopes and serum broth.
	37	Streptobacillus moniliformis grown on Loeffler slopes and serum broth.
	40	No growth on Loeffler slopes or serum broth.
	46	No growth on Loeffler slopes or serum broth.
	47	No growth on Loeffler slopes or serum broth.
	50	No growth on Loeffler slopes or serum broth.
	62	No growth on Loeffler slopes or serum broth.
	75	No growth on Loeffler slopes or serum broth.
Blood by animal inoculation	22	Two guinea-pigs inoculated intraperitoneally.
	25	Two guinea-pigs inoculated intraperitoneally.
	31	{ Two guinea-pigs inoculated intraperitoneally. Six white mice inoculated intraperitoneally.
Agglutination tests	...	Deferred to obtain agglutinable cultures of the streptobacillus; meanwhile samples of the patient's serum are frozen.

DIAGNOSIS.

Following the lines suggested by Brown and Nunemaker,⁴ investigations included attempts to recover the causal organisms by culture and animal inoculation. The first blood culture at the twenty-first day in ordinary trypsin broth was to exclude enteric infection, and was reported negative. It is unlikely that the streptobacillus would grow primarily on an unenriched medium such as this. Next day, at the end of a relapse, two guinea-pigs were inoculated intraperitoneally with patient's blood.

The subsequent attempts at culture were made on Loeffler slopes and 50 per cent. serum broth. On the twenty-fifth day blood was withdrawn when the temperature was 103 and in the early phase of a relapse. The streptobacillus moniliformis grew abundantly on both media. Of the two guinea-pigs inoculated intraperitoneally, one died immediately and the other twelve hours later, and in neither was there any abnormal post-mortem finding.

The next cultures were taken in relation to the phases of the relapses, and those of the thirty-first, thirty-sixth, and thirty-seventh days, at peak, rise, and peak respectively of two successive relapses, all gave pure growths of streptobacillus. Further intraperitoneal inoculation of two guinea-pigs and six mice was done on the thirty-first day. One guinea-pig died seven days later, and the streptobacillus was cultured from its heart-blood and peritoneal fluid.

Blood culture at the fortieth day, i.e., in a trough or remission, immediately before commencing gold therapy was sterile. Further attempts to culture the organism on the forty-sixth, forty-seventh, and fiftieth days, i.e., twice in a remission and once on a falling temperature, were in vain. Another culture on the sixty-second day, immediately before starting Penicillin, at first appeared to give a growth, but was eventually reported negative. This was regarded as an important culture in relation to therapy, as was also that of the fortieth day. The ultimate culture on the seventy-fifth day, during convalescence, was also sterile.

Upon the evidence of four successive cultures of the organism from the patient's blood, together with its transmission by inoculation to a guinea-pig, and recovery therefrom, the diagnosis of septicæmia due to streptobacillus moniliformis is established. No evidence of simultaneous spirillary infection was found from the animals inoculated. Difficulty as yet in obtaining an agglutinable culture of the streptobacillus has prevented agglutination tests being carried out, but samples of the patient's serum are in storage, and the results of these tests will be recorded later. Details of the animal inoculations will also be reported later.

TREATMENT.

No specific therapy of any kind was considered until the diagnosis was established beyond doubt, meanwhile little treatment, apart from nursing care, was required. The boy was allowed full scope of his appetite, and his other treatment included vitamins A, B, C, and D, and ultra-violet radiation.

As spirillary infection had not been established, arsenical therapy was deferred, and following the experiences of Brown and Nunemaker,⁵ and Heilman,¹⁹ that

hospital—fourteen days—was never above normal. Fig. 3 illustrates the amazing rapidity of his response to Penicillin in temperature, and his clinical improvement was similar. His appetite improved greatly, and he had a very pleasant sense of well-being. He was allowed up for increasing periods from his seventieth day, and left hospital seven days later (15th June), apparently completely well in every way.

HISTORICAL.

It is likely that human illness following rat-bite is as old as the association of the species, and from the literature it appears that in Japan, where the disease is common, the condition has been recognised for many years (Miyake³⁰). Cases are also common in India (Das Gupta,¹⁰ Dalal,⁹ Surveyor⁴⁷). Many reports of cases in America are available, and the review of the disease by Brown and Nunemaker⁴ provided the basis of investigation of this present case. The review by McDermott²⁷ is concerned mainly with the spirillary form of the disease.

In Europe, Millot-Carpentier²⁹ first reported the condition in 1884, and in 1900 Miyake³⁰, and eight years later Ogata³⁶ described in detail the features of the disease under the title of "Rattenbisskrankheit." The Japanese term for the condition is "Sodoku": 'So'—rat, and 'doku'—poisoning.

Horder,²² in 1910, was the first to record the disease in Britain with a report of three cases presented to the Association of Physicians. In 1909 von Ofenheim⁵¹ described autogenous vaccine treatment of a septicaemia following a rat-bite, from which he recovered micrococcus tetragenus by blood culture. Since then cases have been recorded in Britain by Middleton,²⁸ Cruickshank,⁸ Nixon,³⁴ Douglas, Colebrook, and Fleming,¹³ Burton-Fanning,⁶ Low,²⁵ Thorp,⁴⁸ and Hickling.²¹ In 1912 O'Carroll reported a case in the west of Ireland.³⁵

As the title implies, the disease usually follows the bite of a wild rat, but the literature records cases arising after bites by a laboratory rat (Caldwell and Templeton⁷), field mouse (Reitzel et al.,⁴¹ Moore and Davis³²), weasel (Dick and Tunnicliff¹²), ferret (Nixon³⁴), cat (Mock and Morrow³¹), and squirrel (Schottmüller⁴⁴), and from a dog (Ripley and van Sant⁴²). It appears to have followed the bite of a monkey and also that of a parrot, and Walker⁵² suggested the possibility of transmission by infected soil. There is, however, no record of rat-bite fever assuming epidemic proportions.

The relapsing nature of the fever probably led to the therapeutic transmission of Sodoku to patients suffering from general paresis, as recorded by Solomon et al.⁴⁵ in 1926. At that time Solomon wrote of this treatment that it was comparatively simple and harmless, less severe on the patient than malaria, and could be used in patients immune to malaria. Hershfield²⁰ found the disease was not transmissible from man to man, but through the medium of infected guinea-pig heart blood. He reported a further example of artificial Sodoku in seventy-two cases of paresis so treated. In his cases, after an incubation period of eight to fifteen days, he recorded paroxysms of fever up to 106°, becoming progressively lower and shorter, with an average total duration of thirty-two days. Nine of his cases recovered spontaneously from the fever, the others were controlled by .3G.

nearsphenamine. The last report of this form of Sodoku by Neyman and Koenig³³ probably put an end to Sodoku-inoculata, as they found it difficult to control the disease, and much preferred diathermy for the treatment of their cases of paresis.

The bacteriology of rat-bite fever has been, and still appears to be, a subject of controversy. Text-books of medicine still identify the spirillum minus as the causal organism, and either ignore entirely the role of the streptobacillus or dismiss it as a common secondary invader. Ogata, in 1908, appears to have been on the trail of the causal organism, but to Schottmüller goes the credit for the first description of an organism he designated streptothrix muris ratti. In 1916, Blake³ confirmed Schottmüller's finding, but later in the same year Futaki et al.¹⁶ described as the cause of the disease an organism which they later named spirochæta morsus muris, and which was subsequently designated spirillum minus. Since then the controversy has been waged, and in their summary, Brown and Nunemaker⁴ admit the evidence that spirillum minus causes an illness which may be indistinguishable from that produced by the streptobacillus. There is as yet no reported case of simultaneous infection by both organisms, although some cases are suspicious, but do not appear to have been followed to the degree necessary. Of recent years the majority of cases appear to be due to the streptobacillus, but this may be due to investigations being directed more towards that end. The streptobacillus can be cultured from infected body fluids, whereas, in spite of the claim of Joekes²³ and that of Futaki et al.¹⁶ (subsequently withdrawn), the spirillum has not yet been cultured outside the body.

In 1926, Place et al. and Parker and Hudson³⁸ described the condition of erythema arthriticum epidemicum, or Haverhill fever, occurring in epidemic form, and in 1934 Place and Sutton³⁹ summarised the findings in the outbreak. Eighty-six persons were involved in the epidemic, which was established as a septicæmia, due to the Haverhillia multiformis, identical with the streptobacillus moniliformis. The source of the outbreak was traced to the consumption of unpasteurised milk, in one case taken as ice-cream, and the probable contamination of the milk arose in the udder of one cow of many concerned in the farms supplying the particular dairy. This cow alone showed specific antibodies in her blood and had lesions of two quarters, but further investigation was impossible, due to "the hostility of the farmer." Evans¹⁴ records symptomless streptothrix infection of cows' udders with recovery of the organism from the milk. The main features of the outbreak of Haverhill fever were an incubation period of two to four days, abrupt onset with rigor, headache, vomiting, relapsing fever to 105°, rash probably in every case, with arthritis of the large joints the most persistent symptom. In the cases investigated the white cell count was from 5,680 to 19,000 per cmm., and as well as being present in the blood, the organism was cultured from the joint fluid. Agglutinins were present in the blood of cases to a titre of 1/100. All patients recovered spontaneously, and there was no response to any therapy. A similar epidemic of 1925 involving some six hundred persons is commented upon.

It appears that either spirillum or streptobacillus is harboured as a saprophyte by many rats and some other similar animals. Strangeways⁴⁶ suggests the naso-

pharynx as the site of the infection, while other authors suggest a blood infection transmitted by abrasion of the gums at the moment of biting. As well as the present case, where the rat is described as looking old and sickly, the rats in the cases of Cruickshank⁸ and Low²⁵ were described as being "mangy." Individual susceptibility must play some part in the development of the disease, for in the cases of Miyake,³⁰ Dick and Tunnicliff,¹² and Thorp,⁴⁸ one alone of the persons bitten by the infecting animal developed rat-bite fever. In the case of von Ofenheim,⁵¹ the dog bitten by the same rat as his patient suffered for six weeks afterwards with an uninvestigated illness, as did the cat, which ate part of the rat in Thorp's case. The disease has been transmitted experimentally by rat-bite to rabbits, as recorded by Savoor and Lewthwaite,⁴³ and likewise rat-bite is the likely path of infection of cows' udders. Topley and Wilson⁴⁹ mention as a fact the excretion of the streptobacillus in the urine of infected mice and possibly rats, and suggest this means of contaminating milk. A dog has been infected experimentally by the spirillum, and recovered after treatment with an arsenical preparation (Ripley and van Sant⁴²).

The age-limits of susceptibility appear to be extreme between the infant of four days at the time of the bite, recorded by Tunnicliff and Mayer,⁵⁰ and the man of 79 years, reported by Leadingham.²⁴ Colour appears no bar nor is sex any deterrent to the biter. The two cases published by Ripley and van Sant⁴² were both of medical students.

The incubation period in cases following a bite appears to be from seven to twenty-one days. In this case a thirteen days' period is established. In almost every case note has been made of bleeding at the time of the bite, followed by rapid healing of the wound, although in the case of Cruickshank⁸ the bitten finger was eventually amputated on account of its gangrenous condition. The healed wound appears well during the incubation period, only to show local induration and lymphatic involvement during paroxysms of fever. In the present case no local exacerbation occurred after primary healing.

The onset of general symptoms seems to have been sharp in every case. It was frequently diagnosed as influenza, and in the case of von Ofenheim,⁵¹ as well as the present case, the patient eventually came to hospital as suspected enteric fever. The case reported by Douglas, Colebrook, and Fleming was originally admitted to a sanatorium as possible phthisis.¹³ Rigors with vomiting and a moderate degree of headache are the most constant symptoms. Sweating is not recorded as profuse, and there is no mention of disturbance of sleep. Allbritten et al.¹ seek to distinguish clinically between the disease due to the streptobacillus and that caused by the spirillum, and suggest in favour of streptobacillary infection a short incubation period, joint pains, fine petechial rash, and leucocytosis. In this case the attempted clinical distinction on these points would have been completely wrong.

The prominent constant feature of the fever is the paroxysmal nature of the temperature, very suggestive of a malarial infection. In the early stages the chart shows a regular five-day cycle. Later it loses its symmetry, with longer remissions and lower and shorter paroxysms. The bacteriology of the streptobacillus suggests

a life-cycle comparable to that of the malarial parasite, and it was hoped to be able to correlate the bacterial cycle with the clinical phases of the disease. The desire to get the patient well precluded this investigation. In this case the highest temperature recorded was 106.2 at the peak of the relapse immediately following the first Myocrisin. As mentioned earlier, the rise of temperature was always more gradual than the fall, which was invariably dramatically sudden, but without gross sweating. No disproportion between temperature and pulse-rate was noted and there was no alteration in respiratory rhythm. There was nothing of note in the blood-pressure readings. Daily blood films excluded malaria, and revealed the red cells to be apparently normal and hæmoglobin was likewise unaltered. The transient fall in R.B.C. count was reasonable with the clinical course of the illness. On the two occasions upon which the spleen was palpable it was not suggestive of a malarial infection. This palpable enlargement of the spleen following a crisis suggests the possibility of this viscus being the reservoir of infection.

The outstanding blood finding in the case is the extreme degree of leucopenia, for which no parallel can be found in the literature of rat-bite fever. The lowest count recorded before is 4,400 by Reitzel.⁴¹ Rather is leucocytosis stressed in the majority of cases with counts up to 32,000 and increased polymorphonuclears characteristic. In this case the attempt to increase the white cells by transfusion was disappointing, and it is remarkable that only with apparent recovery after Penicillin did the W.B.C. count return to normal. The differential count varied throughout and presents no diagnostic feature.

The blood sedimentation rate in this case on two occasions was within normal limits. In a case by Beeson² a similar finding is recorded.

The Widal reaction, giving a titre of 1/50 to *B. typhosus* (flagellar), was obviously false and persisted for some time, but was eventually completely negative at seventy-fifth day. No agglutination of O strain typhosus or of the paratyphoid and abortus strains occurred. No former record of this false positive Widal in this condition is to be found. Many authors report negative findings.

Savoor and Lewthwaite⁴³ record positive Weil-Felix reactions in the blood of rabbits experimentally infected with spirillum minus, and suggest a polysaccharide common to the spirillum and proteus OX.K, with which the test was done. In this present case the Weil-Felix reaction was negative with OX.K, OX.L, and OX.2, and it might be suggested that on this single finding this was not a spirillary infection. Allbritten¹ records a negative Weil-Felix in his streptobacillary case, as does Beeson in one of his cases. Ripley and van Sant⁴² report positive Weil-Felix reactions in their two medical students with spirillary infection.

The Paul Bunnell reaction, negative on admission to hospital, was still negative at twenty-sixth day, but on repeating at seventy-fifth day was positive to a titre of 1/2,560. The development of heterophile antibodies, not claimed as peculiar to glandular fever, has not been previously noted in rat-bite fever.

There are many references in the literature to the results of serum tests for syphilis (S.T.S.) in this condition. In most cases the complement fixation tests, such as Wassermann, Harrison, Fleming, and Kolmer, are negative or faintly

positive, whereas the flocculation tests of Kahn, Kline, and Hinton are frequently positive and often strongly so. Positive S.T.S. are familiar in yaws, leprosy, malaria, sleeping sickness, and tuberculosis in rapidly descending order of frequency, and rarely in other febrile conditions.⁴⁹ Apparently the reaction can develop with either infection, streptobacillus or spirillum. In Dawson's¹¹ cases, both due to streptobacillus, both complement fixation and flocculation tests became positive. Beeson² reports of his two spirillary cases that one was Kahn negative, the other, at first negative, eventually became ++. Two of Marshall's²⁶ cases are recorded as ++++ Kahn, one of them with a ++++ Wassermann. (He notes a negative Mantoux in this case.) In the case of the infant of eleven days, published by Greengard and Hess,¹⁷ the Kahn, at first negative, became ++ before death. Woolley⁵³ deals largely with S.T.S. findings, and reports twelve out of fourteen Kahn tests in this disease, taken after at least four weeks from infection, showing some degree of modification, and suggests that the positive reaction fades with the conclusion of adequate therapy. He suggests the greater sensitivity, and as a corollary, lesser specificity of the flocculation test as the explanation of the findings of positive Kahn with negative Wassermann. In the case under discussion, the S.T.S. is traced from negative Harrison to ++, Fleming negative throughout, Kahn + + +, and Dreyer 0.

The examination of throat and nasopharyngeal regions for the streptobacillus was suggested from Strangeway's⁴⁶ finding of the organism in these regions in rats. Likewise, the investigation of stools and urine for the organism arose from consideration of the food-borne nature of the same organism in the Haverhill outbreak.^{38 39} Attempts to identify the causal organism from these sources were in vain. Allbritten,¹ in addition to negative throat and stool findings, records a negative sputum in the search for the streptobacillus.

There were no complications to record in this case. Blake³ mentions as important complications nephritis, severe anæmia, and emaciation, whilst O'Carroll³⁵ described hydrothorax as a sequel. In the case of Reid and Ritchie,⁴⁰ rat-bite fever developed in a child already in hospital suffering from nasal diphtheria without aggravation of either condition. The patient was bitten before admission to hospital!

The course of the illness to recovery usually occupies months. Surveyor's⁴⁷ patient suffered for eight years, and in one other case recovery took place after seventeen years. Mortality from the disease amounts to 10 per cent. in Japan, and is probably limited to the extremes of life.

Four cases recorded respectively by Blake,³ Greengard and Hess,¹⁷ Pappenheimer,³⁷ and Tunnicliff and Mayer,⁵⁰ died and came to autopsy. Tunnicliff's case, an infant of four days old, when bitten, survived a further twenty-six days, and at post-mortem gave a growth of streptobacillus from the heart blood without any significant pathological finding. Greengard's patient of eleven days old when bitten, displayed a hæmorrhagic broncho-pneumonia at death without bacteriological findings. Pappenheimer's patient, a man of 44 years, died after four months in hospital with streptobacillus septicæmia, and post-mortem examination revealed

a vegetative aortic endocarditis with demonstration of the organisms on section of the vegetations. Blake's patient, a woman of 67 years, died after fifteen days in hospital, and post-mortem revealed an acute ulcerative endocarditis of the mitral region only, with infarcts in the spleen and kidney. Culture of heart blood gave the identical organism previously cultured during life, and a morphologically similar organism was pictured, on section of the mitral vegetations.

Treatment in the past has been largely empirical, and Farrell¹⁵ actually writes : "In cases where there was continued fever, no therapy seems to have been effectual." Spontaneous cure must occur ultimately in some cases and, in others, hitherto no remedy applied was of avail. Most cases to date have had arsenical preparations exhibited, and as early as 1913 Hata¹⁸ recorded eight cases treated with Salvarsan. Heilman and Herrell⁵⁴ report the results of their experiments with Penicillin upon experimentally produced infections by spirillum minus and streptobacillus moniliformis. Their results are most impressive, and suggest that Penicillin will prove effective in the treatment of human infections with either spirillum minus or streptobacillus moniliformis. It is of interest that no success is recorded with sulphonamides, and the present case affords the unique occasion to report cure of streptobacillus septicæmia by Penicillin.

SUMMARY.

A case of septicæmia due to streptobacillus moniliformis, following a rat-bite, is recorded.

Detailed clinical investigations are discussed.

Treatment of this condition with Penicillin is reported, it is believed, for the first time. Complete recovery resulted.

I am happy to acknowledge the keen interest displayed, and the enthusiastic assistance given throughout the course of the case by the staff of this hospital and of The Institute of Pathology, Belfast. In addition, the help of Major J. Oliver, R.A.M.C., with Penicillin is warmly appreciated.

The pure bacteriology of the case will provide the material for further publication by Dr. N. C. Graham and colleagues of The Institute of Pathology.

BIBLIOGRAPHY.

1. ALLBRITTEN, F. F.; SHEELY, R. F.; and JEFFERS, W. Z. : *J.A.M.A.*, 1940, 114, 2360.
2. BEESON, P. B. : *J.A.M.A.*, 1943, 123, 332.
3. BLAKE, F. G. : *Jour. Exp. Med.*, 1916, 23, 39.
4. BROWN, T. McP., and NUNEMAKER, J. C. : *Bull. Johns Hopkins Hosp.*, 1942, 70, 201.
5. BROWN, T. McP., and NUNEMAKER, J. C. : *Jour. Clin. Investigation*, 1940, 19, 768.
6. BURTON-FANNING, F. W. : *B.M.J.*, 1921, 1, 886.
- *7. CALDWELL, R., and TEMPLETON, F. : *Wisconsin M.J.*, 1932, 31, 705.
8. CRUICKSHANK, R. W. : *B.M.J.*, 1912, 2, 1437.

9. DALAL, A. K. : *Practitioner*, 1914, 92, 449.
10. DAS GUPTA, B. M. : *Brit. Encycl. Med. Pract.*, 1938, 10, 477.
11. DAWSON, M. H., and HOBBY, G. L. : *Tr. A. Am. Physicians*, 1939, 54, 329.
12. DICK, G. F., and TUNNICLIFF, R. : *Jour. Infect. Dis.*, 1918, 23, 373.
13. DOUGLAS, S. R.; COLEBROOK, L.; and FLEMING, A. : *Lancet*, 1918, 1, 253.
14. EVANS, A. C. : *Jour. Infect. Dis.*, 1918, 23, 373.
15. FARRELL, E.; LORDI, G. H.; and VOGEL, J. : *Arch. Int. Med.*, 1939, 64, 1.
16. FUTAKI, K.; TAKAKI, I.; TANIGUCHI, I.; and OSUMI, S. : *Jour. Exp. Med.*, 1916, 23, 249.
17. GREENGARD, J., and HESS, E. R. : *J.A.M.A.*, 1941, 116, 2393.
- *18. HATA, S. : *Munch. Med. Woch.*, 1912, 854.
- *19. HEILMAN, F. R. : *Science*, 1940, 21, 366.
20. HERSHFELD, A. S.; KIBLER, O. A.; COLBY, S., et al. : *J.A.M.A.*, 1929, 92, 772.
21. HICKLING, T. : *B.M.J.*, 1932, 2.
22. HORDER, T. J. : *Quart. J. Med. Oxford*, 1910, 3, 121.
23. JOEKES, TH. : *Lancet*, 1925, 2, 1225.
24. LEADINGHAM, R. S. : *Am. Jour. Clin. Path.*, 1938, 8, 333.
25. LOW, G. C. : *B.M.J.*, 1924, 1, 236.
26. MARSHALL, T. J. : *Arch. Pediat.*, 1936, 53, 664.
27. McDERMOTT, E. N. : *Quart. Jour. Med.*, 1928, 21, 433.
28. MIDDLETON, G. S. : *Lancet*, 1910, 1, 1618.
- *29. MILLOT-CARPENTIER, G. : *L'Union Medicale*, 1884, 38, 1069.
- *30. MIYAKE, H. : *Mitt. a.d. Grenzgeb. D. Med. u. Chir.*, 1900, 5, 231.
- *31. MOCK, H. E., and MORROW, A. R. : *Illinois M.J.*, 1932, 61, 67.
32. MOORE, J. J., and DAVIS, D. J. : *Jour. Infect. Dis.*, 1918, 23, 252.
33. NEYMANN, C. A., and KOENIG, M. T. : *J.A.M.A.*, 1931, 96, 1858.
34. NIXON, J. H. : *B.M.J.*, 1914, 2, 629.
35. O'CARROLL, J. : *Dublin M.J.*, 1912, 1, 6.
- *36. OGATA, M. : *Deutsch. Med. Wchn. Schr.*, 1908, 34, 1099.
37. PAPPENHEIMER, A. M., and SATCHELWELL, H. H. : *Jour. Infect. Dis.*, 1907, 4, 617.
38. PARKER, F., JUN., and HUDSON, N. P. : *Am. Jour. Path.*, 1926, 2, 357.
39. PLACE, E. H., and SUTTON, L. E. : *Arch. Int. Med.*, 1934, 54, 659.
40. REID, T., and RITCHIE, J. : *Edin. M.J.*, 1915, 15, 186.
41. REITZEL, R. J.; HAIN, A.; and PRINDLE, K. : *J.A.M.A.*, 1936, 106, 1090.
42. RIPLEY, H. S., and VAN SANT, H. M. : *J.A.M.A.*, 1934, 102, 1917.
43. SAVOOR, S. R., and LEWTHWAITE, R. : *B.J. Exp. Path.*, 1941, 22.
- *44. SCHOTTMULLER, H. : *Dermat. Wchn. Schr.*, 1914, 58, 77-103.
45. SOLOMON, H. C.; BERK, A.; et. al. : *Arch. Int. Med.*, 1926, 38, 391.
46. STRANGEWAYS, W. I. : *Jour. Path. and Bact.*, 1933, 37, 45.
47. SURVEYOR : *Lancet*, 1913, 2, 1746.
48. THORP, E. : *B.M.J.*, 1925, 2, 255.
49. TOPLEY, W. W. C., and WILSON, G. S. : *The Principles of Bact. and Immun.*, 1937, 2.
50. TUNNICLIFF, R., and MAYER, K. M. : *Jour. Infect. Dis.*, 1918, 23, 555.
51. VON OFENHEIM, F. : *Proc. Roy. Soc. Med.*, 1909, 2 (Clin.), 159.
- *52. WALKER, H. : *Virginia Med. Monthly*, 1937, 64, 272.
53. WOOLEY, P. V., JUN. : *Jour. Pediat.*, 1936, 2, 693.
54. HEILMAN, F. R., and HERRELL, W. E. : *Proc. Staff Mayo Clinic*, 1944, 19, 257.

*Quoted, by permission, from Drs. T. McP. Brown and J. C. Nunemaker (4).

RAT BITE FEVER

Plate I