Dictionnaire des maladies éponymiques et des observations princeps : Felty (syndrome de)

FELTY, Augustus Roi. - Chronic arthritis in the adult, associated with splenomegaly and leucopenia. A report of 5 cases of an unusual clinical syndrome

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patient was very toxic, and the presence of an extraperitoneal abscess in the left flank was very definite. Immediate operation seemed necessary, but we decided to inject mercurochrome intravenously. Time of injection, 11 A. M., July 16; dose 27 c.c. of a 1% aqueous solution—5.4 mg. per kilo of body weight.

The above chart, with its careful colorimetric tests, which were made at my request by Dr. E. C. Shaw, shows the remarkable rapidity with which mercurochrome appears in fairly high percentage in the urine, stools and stomach contents (vomitus). Within four hours mercurochrome was present in both urine and stools in a strength of 1 to 10,000. As shown by Miss J. H. Hill, a solution of 1 to 5,000 kills B. coli in urine and salt solution in one hour, and a solution of 1 to 10,000 kills staphylococci in one hour. It remained in this strength apparently for at least three hours, after which it gradually diminished; but twenty-four hours later was still at a strength of 1 to 100,000.

The improvement of the patient, after recovering from the primary reaction in which the temperature rose to 106°F. was most gratifying—the subsidence of pain, tenderness, muscle spasm and mass in the left flank and back being indeed remarkable. The patient was discharged on the sixth day after the intravenous injection, in excellent condition. Nov. 1, 1923 (4 months later), Letter: patient well.

One cannot, of course, draw positive or general conclusions from a single instance, but coming as it does after definite laboratory proof that mercurochrome, intravenously administered, will sterilize the blood and urine (Hill and Colston) in animals infected with the bacillus coli or other bacteria, and after our case of a patient, almost moribund with colon bacillus septicaemia who was promptly cured by 34 c.c. of a 1% solution, and cases of pyelitis which Colston and I have sterilized in this way, it makes me feel confident that the effect of the drug in this case was very definitely curative and that the procedure is worthy of further clinical experimentation. I wish to express my thanks to Dr. E. C. Shaw and to Miss J. H. Hill for valuable assistance.

Conclusions

In the case, here recorded, it is shown that a colorimetric method can be used to determine the strength in which mercurochrome, after intravenous injection, may appear in urine, stools and vomitus. A strength of 1 to 10,000 was maintained in the voided urine for three hours, and also in stools. The immediate sharp febrile reaction (to 106°F.) followed by a rapid fall to normal, and a disappearance of definite symptoms and signs of a retroperitoneal abscess, seem to verify previous animal experiments which show a pronounced general and local germicidal effect from intravenous injections of mercurochrome.

CHRONIC ARTHRITIS IN THE ADULT, ASSOCIATED WITH SPLENOMEGALY AND LEUCOPENIA

A REPORT OF FIVE CASES OF AN UNUSUAL CLINICAL SYNDROME

By A. R. Felty, M. D.

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The occurrence of slight splenic enlargement associated with the arthritides has occasionally been noted by various writers. McCrae found it to be present in a small group of his studied cases (among which were included cases of deforming arthritis of children); but he states that splenomegaly is much more common in acute arthritis than in the chronic type. So, too, leucopenia may occasionally be present in arthritis, though it is not commonly believed that the white cell count of the blood is characteristic or of particular significance, since variations above and below the normal are of about equal occurrence. However, the association of all three conditions is a rather more unusual circumstance, and a recent observation of such a case has led us to search the hospital records for similar pictures. Five cases, of striking similarity in many respects, have been collected, presenting a syndrome which is not only of interest by itself, but offers certain diagnostic difficulties which will subsequently be mentioned.

Report of Cases

Case 1.—(Medical No. 49918.) A white man of 46, an American, was admitted to the hospital August 12, 1923, with the complaint of generalized aching in the muscles and joints, of three years' duration. There was no history of arthritis in his family. He gave a personal history of several mild short attacks of malaria, the last attack ten years before admission. Three years before coming to us he began to have attacks of arthralgia, the aching being more or less generalized, but worse in his ankles and wrists, which sometimes were swollen. There were intervals, however, during which there was almost complete freedom from symptoms. Since the onset he had lost about 40 pounds; and in recent months his appetite had been poor, with occasional nausea after meals.

Physical Examination.—A sparely nourished man, who has evidently lost considerable weight. Slight pallor. Exposed surfaces deeply pigmented. Axillary, epitrochlear, and inguinal glands slightly enlarged and firm. Pupils and eye-grounds normal. Throat clear. Pyorrhea about the few remaining teeth. Heart and lungs clear. Pulse regular, no radial thickening. B. P. 115/75. Abdomen soft, symmetrical, not tender. Spleen felt as a firm, rounded mass extending to the level of

the umbilicus, 6 cm. below the costal margin in the mammillary line. A thin, soft liver edge comes just to the costal margin. A little swelling and tenderness of the 2nd and 3rd metacarpo-phalangeal joints of both hands, and slight fusiform enlargement of the interphalangeal joints. Some soreness on passive motion of the fingers, elbows, shoulders, ankles, and toes, but no objective changes except in the fingers. Slight grating in both knees. Left elbow somewhat limited in mobility, apparently from voluntary spasm. There is general soreness of the muscles of the extremities. No local heat nor muscular atrophy. Spine negative. Slight hyperreflexia.

Blood Examinations.

8/14/23. R. B. C. 3,750,000; Hb. 70%; W. B. C. 2680.
Differential formula.
P. M. N. 26%; P. M. E. 2%; S. M. 54%; L. M. and Trans. 18%.
Slight diffuse and punctate basophilia.

8/27/23. W. B. C. 3000.

9/ 2/23. W. B. C. 2800; Hb. 80%.
P. M. N. 34%; P. M. E. 2%; S. M. 54%; L. M. and Trans. 9%.

9/ 7/23. W. B. C. 3000.
P. M. N. 47%; P. M. E. 4%; S. M. 30%; L. M. and Trans. 9%.
R. B. C. show diffuse and punctate basophilia.
Platelets, 330,000.
Bleeding time, 2½ minutes.
Coagulation time (Howell method), 10 minutes.
Reticulated R. B. C., 0.8%.
Fragility of R. B. C.
Hemolysis begins at..... 0.46% NaCl
Hemolysis of control begins at.. 0.44% NaCl
Hemolysis complete at..... 0.32% NaCl
Hemolysis of control complete at 0.34% NaCl

Urine.—Negative except for slightly positive urobilin test obtained on three occasions.

Test Meal.—No free acid present.

Stool.—Negative.

Wassermann reaction.—Negative.

8/17/23. Blood culture negative.

9/ 7/23. Blood chemistry—
Non-protein Nitrogen ...28 mgm. per 100 c.c.
Sugar .....85 mgm. per 100 c.c.
Uric acid ..... 3.2 mgm. per 100 c.c.

X-ray of chest.—Lungs clear. Heart and aorta normal.

X-ray of joints.—Knee and elbow show practically no bone or joint changes.

Pathological report on section of excised epitrochlear gland—"Chronic lymphadenitis."

Examinations by the laryngologist and dentist were negative.

Temp. 99°—100.5° (rectal) for two weeks; normal thereafter until discharge.

Summary of Case.—White man, 46 years old, with a history of joint pains for three years. Undernutrition. Pigmentation of exposed parts. Splenomegaly. Objective changes in joints which, however, are not proportionate to the symptoms. Slight glandular enlargement. Slight anemia and frank persistent leucopenia. Slight urobilinuria. Gastric anacidity.

Impressions of case (by different observers) (1) Syndrome in adult comparable to that of Still's disease; (2) Possible Banti's disease associated with chronic arthritis.

CASE 2.—(Med. No. 19,574.) A Lithuanian woman, 45 years of age, sought admission to the clinic on April 16, 1906, on account of generalized aching in her joints. Family history irrelevant. Her husband had died of phthisis in 1899. Her own health had always been fairly good, though she had had typhoid fever, and occasional sore throats. Of late her appetite had been poor. Menopause six months before admission. Occasional cough in winter. She had lost about six pounds in the past four or five months. Her present illness began six years before admission with pains in her joints, which had been present more or less constantly since then—varying, however, in severity and distribution. About four months before admission she was confined to bed for three weeks with fever, and swollen, painful feet.

Physical Examination.—The patient has a cachectic sallow appearance, is undernourished, and somewhat anemic. Light brown pigmentation over abdomen, on flexor surfaces of arms and in axillae. Conjunctival inflammation characteristic of trachoma. Teeth in bad condition. The cervical, axillary, and epitrochlear nodes are slightly enlarged and firm. Heart normal. Lungs negative except for slight emphysema. Visible peristalsis present. Spleen extends 13.5 cm. diagonally below the costal margin, and 5 cm. below the level of the umbilicus, measuring 8 cm. in width at the rib edge. A notch is felt. Liver not enlarged. Slight crepitus felt in the shoulders and right knee, although mobility is not restricted. Both wrists show limitation of motion, but no pain nor swelling. Left knee is held flexed and the joint is tender. Fingers and toes abducted and somewhat flexed.

Blood.—R. B. C. 4,624,000. Hb. 72%. W. B. C. 1000.

Urine.—Negative (urobilin not tested for).

No fever during stay on ward. Patient discharged after five days on account of trachoma.

Summary of Case.—Woman of 45, who has had symptoms of arthritis for six years. Undernutrition and mild anemia. Brownish pigmentation of skin. Great enlargement of spleen. Slight arthritic changes in joints. Very marked leucopenia.

Diagnosis.—Arthritis deformans; splenomegaly; trachoma.

CASE 3.—(Med. No. 35,980.) The patient was a white man, aged 65, an American, who was admitted to the hospital April 24, 1916, complaining of articular aching of the extremities. The affection had had a rather sudden onset eight months before with swelling, redness, and pain in one ankle, with subsequent rapid involvement of all the other joints of the extremities—especially the ankles, knees, wrists, and elbows. The arthralgia persisted with exacerbations and remissions. There was an indefinite history of a somewhat similar attack fifteen years before, which had left no residuum after its disappearance. The patient had lost forty pounds since the onset of the present illness. The past and family history were non-contributory.

Physical Examination.—Poorly nourished man, who has evidently lost considerable weight. Exposed surfaces of skin show brownish pigmentation. Fundi normal. No general glandular enlargement. Teeth in poor condition. Throat clear. Lungs normal except for slight emphysema. Heart normal. Blood pressure 140/80. Liver not palpable. A firm spleen reaches to the level of the umbilicus. Slight limitation of mobility of the shoulders. Periarticular swelling of both elbows, which are held in partial flexion, with slight limitation of motion. Slight thickening of both wrists and metacarpo-phalangeal joints, with normal mobility. No Heberden's nodes. There is a small collection of fluid in both knee-joints, which are limited in mobility. Ankles somewhat swollen, but freely movable. Spine normal. Rectal examination negative.

Blood Examination.—R. B. C. 4,800,000. Hb. 80%. W. B. C. 2720. Differential, P. M. N. 74%. S. M. 19%. L. M. and Tr. 5%.

Urine.—Negative.
Stool.—Normal.
Wassermann reaction.—Negative.
X-ray Examination.—"Infectious arthritis with some slight bone change."
Special Examination of the nose and throat revealed nothing abnormal.
The patient was afebrile throughout his six weeks' stay in the hospital.
Summary of Case.—White man, 65 years of age, with symptoms of arthritis in arms and legs for a period of eight months. Undernutrition. Pigmentation of exposed surfaces. Splenomegaly. Leucopenia. Slight periarticular swelling, pain on motion, and slight limitation of mobility of some of the joints of the extremities.
Impression of case: Chronic infectious arthritis; splenomegaly. Possibility of Banti's disease suggested by the enlarged spleen and leucopenia.

Case 4.—A white woman, 50 years of age, was admitted to the hospital October 31, 1914, complaining of pains in her joints, of about ten years' duration. Her general health prior to this had been good, and her past history, except for an attack of pleurisy 25 years before admission, was singularly negative. She had never had malaria. Her two children were living and well. The menopause occurred in July, 1914. Since 1908, when she weighed 190 pounds, she had gradually lost 65 pounds to her present weight of 125 pounds. In 1904 her present symptoms began with an attack of pain and swelling in both ankles which confined her to bed for a few days. After the subsidence of the acute attack she continued for five years to have slight aching with swelling of her ankles, and during this period she had three or four attacks similar to, but less severe than, the first. The ankle joints had become somewhat stiff and continued to give pain. In the past five years other joints had become involved in succession—the metacarpo-phalangeals, the wrists, knees, toes, and elbows. The swelling and pain in the joints had been variable, at times acute with reddened skin and slight local heat, and at no time had there been complete subsidence of the symptoms. For the past six months the articular pains had been more generalized and more severe, especially in the ankles.
Physical Examination.—The patient is distinctly undernourished and has obviously lost weight. Sallow pigmentation of exposed parts, especially about the eyes. Fundi normal. Marked pyorrhea. Tonsils adherent to pillars. No lymph-node enlargement. Heart and lungs clear. Radial vessels soft. The spleen comes to the costal margin. Liver edge not felt. Symmetrical, soft, painless swelling of the metacarpo-phalangeal joints of both hands, with no redness or local heat. Slight ulnar deflection of the fingers with slight limitation of motion. No Heberden's nodes. Small muscles of hands a little atrophied. Right elbow and both knees slightly limited in mobility, but are neither red nor tender. No crepitus in any of the joints. Pelvic examination, negative.

Blood Examination.

10/31/14. R. B. C. 4,528,000. Hb. 70%. W. B. C. 2080. P. M. N. 46%. P. M. E. 11%. P. M. B. 0.5%. S. M. 24%. L. M. and Tr. 18%.
11/23/14. R. B. C. 4,000,000. Hb. 74%. W. B. C. 2440. P. M. N. 41%. P. M. E. 11%. P. M. B. 1%. S. M. 20%. L. M. and Tr. 27%.
11/23/14. R. B. C. 5,228,000. Hb. 80%. W. B. C. 2040.
12/ 1/14. R. B. C. 5,000,000. Hb. 80%. W. B. C. 2000.
12/ 6/14. W. B. C. 2,240. P. M. N. 25%. P. M. E. 13%. P. M. B. 1%. S. M. 38%. L. M. and Tr. 23%.
12/ 9/14. R. B. C. 4,700,000. Hb. 79%. W. B. C. 2040. P. M. N. 37%. P. M. E. 12%. P. M. B. 1%. S. M. 28%. L. M. and Tr. 22%.
1/11/14. R. B. C. 4,500,000. Hb. 76%. W. B. C. 1760.

Urine.—Negative.
Stool.—Negative.
Wassermann.—Negative. Gonococcus complement fixation test negative.
Vaginal Smears.—Negative.
X-ray of wrist and ankle joints showed chronic infectious arthritis.
X-ray of sinuses was negative.
Special nose and throat examination was essentially negative.
The patient ran a low irregular fever which subsided after six days.
Summary of Case.—A white woman, 50 years of age, with symptoms of arthritis of the extremities for ten years, with exacerbations and remissions but never complete subsidence of articular pain. Marked undernutrition. Pigmentation of the exposed surfaces of the skin. Splenomegaly. Slight objective changes in many joints of both arms and legs. Slight secondary anemia and frank leucopenia.
Impression of case: Chronic infectious arthritis; splenomegaly.

Case 5.—(Med. No. 30,042.) A white man, aged 51 years, an American, came to the hospital December 3, 1912, complaining of rheumatic pains of two and one-half years' duration. Prior to this he had always been in good health, with no serious illnesses. Acute urethritis once 25 years before admission. He had lost 40 pounds in the last two years. The gradual onset of his arthritic symptoms dated back to April, 1910, when he began to have aching pains and swelling of the left foot. A few weeks later both wrists and shoulders became affected. In September, 1910, the left and then the right knee became hot, swollen and painful, but after a short time there was complete subsidence of symptoms in both knee-joints for eighteen months. A year before admission the left hip became painful. For the past two months there had been a flare-up of symptoms in all the joints (knees, hips, wrists, fingers, and shoulders).
Physical Examination.—The patient shows poor nutrition, with evident loss of weight, and poor muscular development. Pigmentation similar to tanning on backs of hands and exposed parts of head. Labial herpes. Lips rather pale. Throat clear. Axillary, inguinal, and epitrochlears a little enlarged. Persistent fine moist râles at right apex. Heart negative. Blood pressure 120/80. Abdomen scaphoid; the spleen extends below the costal margin. Polyarthritis involving especially the knees, hips, fingers, wrists, and elbows with slight swelling, periarticular infiltration of the soft parts, and limitation of motion, partly voluntary, partly organic. Practically all the joints of the extremities are sore. Crepitus in knees, and wrists, with slight muscular atrophy.
Blood Examination.—R. B. C. 4,304,000. Hb. 85%. W. B. C. 4200.
Sputum Examination.—Negative for tubercle bacilli (numerous examinations).
Urine.—Negative.
Wassermann reaction.—Negative.
X-ray of left knee and foot. Slight infectious arthritis of knee; foot negative.
X-ray of chest.—Infiltration of both apices.
Temperature remained normal throughout the patient's stay in the hospital.

Summary of Case.—White man, 51 years of age, with a history of generalized articular pains for two and a half years, and loss of forty pounds during this time. Undernutrition. Slight enlargement of lymph-nodes. Tan-like pigmentation over exposed parts. Râles at right apex. Enlarged spleen. Arthritis of numerous joints of the extremities. Leucopenia.

Impression of case: Chronic infectious arthritis; pulmonary tuberculosis (inactive); splenomegaly.

ANALYSIS AND DISCUSSION

Certain features of these five cases are outstanding and worthy of comment. The syndrome occurred in individuals of middle age (45-65), the average being 50 years. All the patients gave a history of marked loss of weight since the onset of symptoms (from 40 to 65 pounds in four out of five cases), and all were undernourished. The arthritic process is distinctly chronic, and all but one of the patients had symptoms of over two years' standing, the average duration being four and one-half years. With either an acute or gradual onset, there develops more or less generalized articular aching in the extremities, mild but persistent, and accentuated by occasional acute exacerbations. In striking contrast to the prolonged course of the disease, and the ubiquitous distribution of the pain which is the presenting symptom of all the patients, the objective findings both by physical examination and roentgenographic study are neither wide-spread nor indicative of a very damaging or destructive process. Indeed, one is rather impressed by the relatively benign nature of the involvement when compared with the typical chronic deforming arthritis of equal duration and extent.

In every case the spleen was palpably enlarged—just below the costal margin in two cases; in two others, extending to the level of the umbilicus; and in the fifth case reaching a point 5 cm. below this level. The spleens were firm and not tender. None of the patients had symptoms referable to the splenic tumor. No abnormalities in the size or consistence of the liver were noted. The lymph glands were not enlarged in two cases; but in the other three, the axillary, inguinal, and epitrochlear nodes showed definite enlargement. In every instance there was noted a yellowish-brown pigmentation of the skin, which in four cases was confined to the exposed surfaces, but in the fifth had a wider distribution over the abdomen, axillae, and flexor surfaces of the arms. None of the patients had hypertension. The heart, lungs, and eyegrounds were essentially normal.

In all cases save one there was a slight secondary anemia—the red cells varying from 3,750,000 to 4,800,000; the hemoglobin from 70-80%. The average red count was 4,400,000, and the hemoglobin 75%, giving a color index of 0.85. More striking was the leucopenia, which was a distinctive feature in every case. The leucocyte counts varied from 1000 to 4200, in four cases being below 3000. The differential formula was not characteristic. The urine was normal except for the one case in which urobilin was found to be present. Stool examinations were negative. None of the patients showed any evidence of lues either serologically or on general examination. Three patients were afebrile during their hospital stay; two ran a low fever which subsided after one to two weeks.

The question immediately arises as to a proper classification, or at least an explanation of this unusual clinical syndrome. There are but two likely possibilities:

1. The several features are manifestations of one pathological process, caused by a noxa which simultaneously affects the joints, the spleen, and the blood leucocytes (and in three of the five cases the lymph glands). On such a basis, the picture might be comparable to that occasionally seen in young children, and first described by Still—a syndrome of chronic arthritis, splenomegaly, and general gland enlargement which has since been designated as Still's disease. But whereas Still's disease occurs only in the young, usually before the second dentition, this disease is distinctly one of middle life (45-65 years). So, too, the leucocyte count in Still's disease is not characteristic, and, if altered at all, is more commonly increased, whereas in the present series of cases there is a constant and very striking leucopenia.

2. The syndrome is merely the confusion of two separate clinical entities, occurring coincidently in the same individual. Taken separately, without regard for the arthritis, the enlarged spleen, with leucopenia and slight secondary anemia, the slight pigmentation of the skin, and the presence in the urine of urobilin, in the one case in which this was sought for—these findings are typical features of early Banti's disease. This possibility was indeed broached in two of the cases. Joint changes, however, are not a part of the Banti syndrome, and Eppinger, in his exhaustive discussion of this disease, fails to mention any observations of its occurrence. One would need to assume, then, that the arthritis is quite independent of the rest of the complex. However, on the law of probability alone, such a coincidence seems highly unlikely, and this view would violate a fundamental rule of diagnostics—that a symptom-complex should, if possible, be explained on the basis of one pathological process rather than on the assumption of the existence of two or more. In one case, to be sure, the history of several short malarial attacks many years ago might possibly explain the existing splenomegaly (though not the urobilinuria nor the leucopenia). In the other cases there was no preexisting disease recognized to explain the findings. In short, one is more or less forced to the conclusion that this syndrome is a distinct clinical entity, of which the outstanding symptoms are those related to the joints, and

the outstanding signs are the enlarged spleen and the blood picture.

SUMMARY

Five cases, strikingly similar in their essential features, are described, presenting an unusual but unmistakable clinical picture, characterized by arthritis, splenomegaly, and leucopenia. The etiology is entirely obscure, though the various findings seem best accounted for as manifestations of a single disease process.

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RESULTS OF THE INJECTION OF ENCEPHALITIC SPINAL FLUID INTO RABBITS

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Experimental encephalitis and experimental herpes, now so closely associated and believed by some to be identical, were in the beginning widely separated in the minds of experimental pathologists.

Loewe and Straus,[1] in 1920, reported the transfer of epidemic encephalitis to rabbits by the intracerebral injection of filtered nasopharyngeal washings and of spinal fluid from human cases. Levaditi and Harvier,[2] Kling,[3] and Thalhimer [4] soon confirmed this report.

In a totally separate line of investigation Loewenstein [5] produced keratitis in rabbits by applying to the scarified cornea the contents of herpetic vesicles. Some of the rabbits died of convulsions suggesting that the virus had invaded the central nervous system.

Doerr with Vöchting [6] and with Schnabel,[7] injected the vesicular contents intracerebrally into rabbits and found that a diffuse encephalitis was provoked by the virus. Doerr noted the close similarity between herpetic virus and the virus of epidemic encephalitis, and Levaditi from a thorough experimental study believed that the two viruses are identical and adduced immunological evidence to substantiate his views. Kling, on the other hand, from immunological studies does not agree. In spite of the great amount of work on the subject of the identity of herpes and encephalitis there still remains some doubt in the minds of many. One of the questions to be decided relates to the authenticity of the so-called encephalitic strain.

There is no doubt that some sort of virus supposed to have come from human encephalitis has been propagated among rabbits, but it cannot be said definitely that this strain represents the true encephalitic virus. There are at least two possibilities, (a) that some virus peculiar to rabbits and producing the lesions indistinguishable from encephalitis, as described by Oliver [8] and Wright,[9] has been propagated, and (b) that the so-called encephalitic virus is really a human herpetic strain which entered the spinal fluid on account of an increased permeability of the meningeal choroidal complex.[10] Netter and McNalty report a very low incidence of herpes simplex in epidemic encephalitis.

Efforts to transmit spontaneous rabbit encephalitis during the past year have been in vain. Likewise, attempts to isolate a strain of herpes from the spinal fluid of a few patients with marked labial herpes but without signs of encephalitis have yielded negative results.

EXPERIMENTAL

Fifteen young rabbits were given intracerebral injections of 0.4 c.c. spinal fluid withdrawn from two patients on the second and third days after the development of labial herpes. Laboratory examination of these fluids was entirely negative. None of the rabbits injected showed any signs of herpes encephalitis.

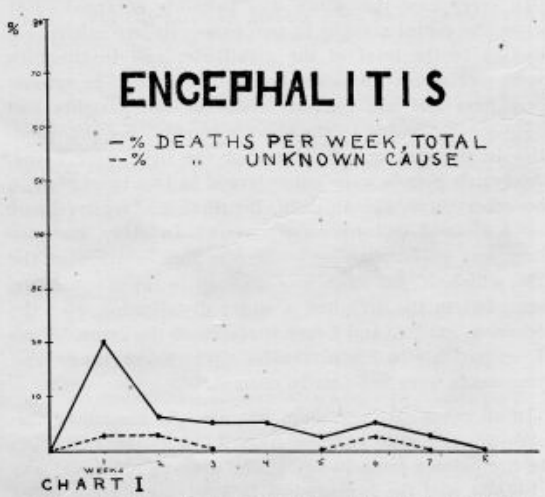

CHART I

40 inoculated in all; 20 died in 2 months, 50%; 7 died from coccidiosis; 5 died from pneumonia; 2 died from inoculation; 1 died from fractured spine; 1 died from diarrhea; 1 died from brain abscess; 3 died from unknown cause.