

stances which, as Jacques Loeb has shown, enhance the proliferating power of the cell. While it is self-evident that no chemical will be absolutely innocuous to the cells of the organism, a chemical substance may arrest the proliferating power of a cell and not kill it. The influence of the racial differences on immunity is neutralized in our work by the great number of animals used. I stated that the question of organ immunity as well as general immunity in human cancer cannot be discussed at present for lack of properly analyzed material, but that my own investigations on eugenics in human cancer seem to indicate that there may exist a condition of resistance or immunity in human cancer. Metastases occur after an inoculation into a parenchymatous organ of tumors which do not metastasize on a subcutaneous inoculation. It is my personal belief that ferment activity underlies the condition of susceptibility as well as immunity in cancer. But at present the knowledge of the chemical nature of the ferments is so limited that it is impossible to ascertain their true functional significance.

#### FOUR CASES OF TYPHUS FEVER (BRILL'S DISEASE) IN ONE FAMILY

WITH SUCCESSFUL INOCULATION INTO GUINEA-PIGS  
AND MONKEY \*

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The recent work of Anderson and Goldberger of the Hygienic Laboratory at Washington establishing, experimentally, the identity of typhus fever and so-called Brill's disease, together with the mode of transmission of typhus fever by body-lice as shown by these writers, and Nicolle and his co-workers abroad, and by head-lice as lately shown by Anderson and Goldberger, greatly increase the interest in cases of what we must now regard as endemic typhus fever, so well studied by Drs. Brill, Louria and others as it occurs in this country and especially in New York City.

\* From Research Laboratory, Department of Health, New York.

For many months before the occurrence of those reported, no cases of typhus fever had occurred in New York to the best of our knowledge. Those that we present are unique in the history of the endemic form of the disease as it has been studied in New York, in that they affected four members of one family, and that two of them were young children. These cases, furthermore, represent types of the disease varying from the comparatively mild, to an example of typhus fever such as is commonly seen in epidemics, thus giving, as it were, a clinical demonstration of the identity of the endemic (Brill's) and epidemic form. But one member of this family escaped the disease, a child of 1½ years of age.

A careful investigation of the premises (a large tenement house) in which these cases occurred failed to reveal the occurrence of any other cases previously, and an extensive inquiry among physicians and hospitals has brought to light but three additional cases of the disease up to the present time.

The patients were typical east-side residents, Russian Hebrews of the poorer class. They had been in the country for about eight months.

#### REPORTS OF CASES

CASE 1.—Ida K., aged 28, (Chart 1), the mother, was admitted to the Har Moriah Hospital, April 9, 1912, with a temperature of 105 F. She had previously been healthy and there was nothing in her past history to throw any light on her present condition. About six days before admission she had a severe chill followed by fever, sweating and intense headache. She was obliged to take to her bed. Four days before admission she vomited some bilious material. These symptoms continued, together with a profuse watery diarrhea, up to the time of her entrance to the hospital. On admission the patient's condition was fairly favorable; a few hemorrhagic spots were noted on the abdomen. The general physical examination, together with two Widal tests, proved negative. On April 10, the leukocytes were 12,600 per c.mm. of which 66 per cent. were polynuclears. A second count on April 13, showed 11,200 leukocytes and 64 per cent. polynuclears. The case was regarded as one of intestinal toxemia, the true cause not being suspected until after the entrance to the same hospital of other members of the family.

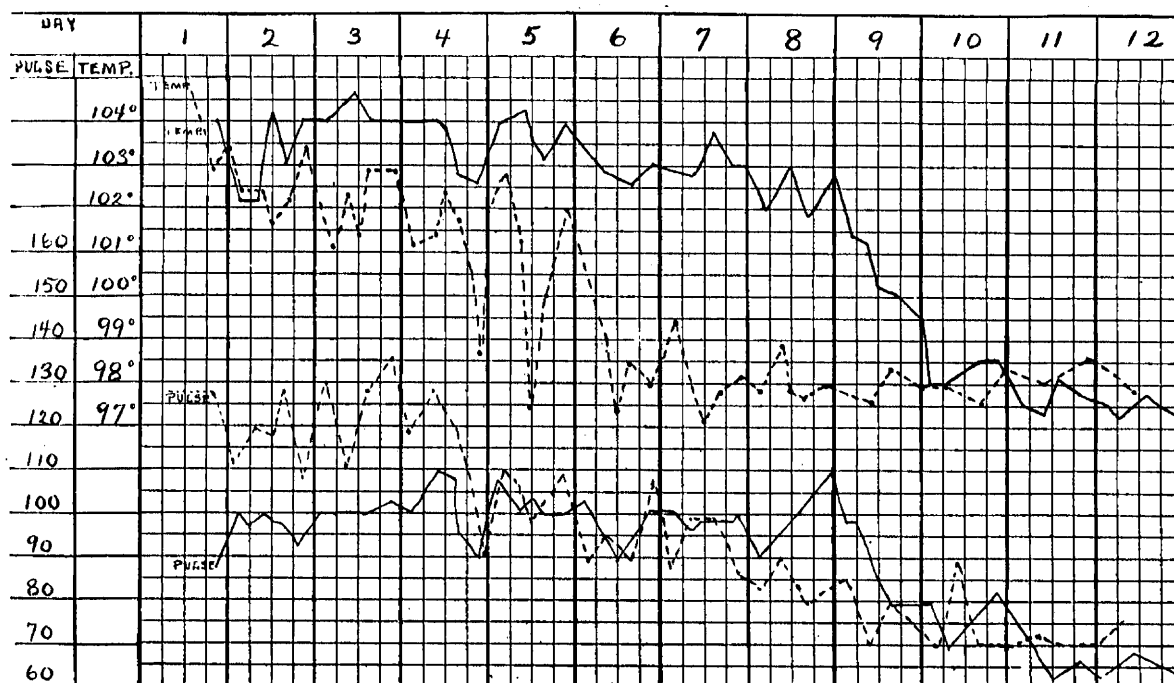


Chart 1.—Pulse and temperature in cases of Israel K. (solid line) and Ida K. (line composed of dashes).

CASE 2.—Israel K. (Chart 1), the husband of Ida K., was admitted to the hospital, May 4. There was nothing in his personal history of importance except that the patient had suffered for some ten years with a functional gastric condition, but had otherwise been in good health. He used alcohol moderately and was a heavy smoker. Six days before admission to the hospital he went to bed feeling very ill with severe frontal headache and fever. He had a slight cough. He was treated symptomatically by a private physician until his admission to the hospital where he was seen by two of us three days later and showed the following picture: The entire body from the neck down was covered with a discrete, somewhat morbilliform type of eruption, which included also the palms of the hands. The lesions were fairly widely separated, much more so than in measles, were of bluish-red color, and disappeared on deep pressure. The throat was intensely red, the head somewhat retracted, the neck stiff, and Kernig's and Babinski's signs were marked. The patient's picture was that of typical coma-vigil, the eyes wide open and staring. There was no resistance or evidence of pain caused by taking blood from the arm for purposes of inoculation. The heavy beard,

nuclears. Seen on the second day after admission, the patient did not seem particularly ill; there was a maculopapular rash over the body and extremities, the number of lesions being few and widely scattered. They were of the same general type as those seen on the father but much less marked. A physical examination on the day of his transfer to the Willard Parker Hospital, May 11, showed a fairly well-developed child with hair full of vermin, flushed face and somewhat apathetic. The rash was still present but fading. The lungs, heart and liver were negative, the spleen was enlarged and somewhat tender. An examination of the spinal fluid gave the following results: 23 c.c. clear fluid, pressure considerably increased. Cytology: no cellular elements—coarse shreds of fibrin. There were no bacteria in either smear or culture. Albumin ++. Globulin +. The progress of this case was uneventful to recovery. The pulse after the fall in temperature was frequently quite weak and irregular. The patient had a slight cough for a few days.

CASE 4.—Lena K. (Chart 2), aged 10, was admitted to the hospital on the same day as her brother, having been taken ill four days previously with headache, fever and loss of appe-

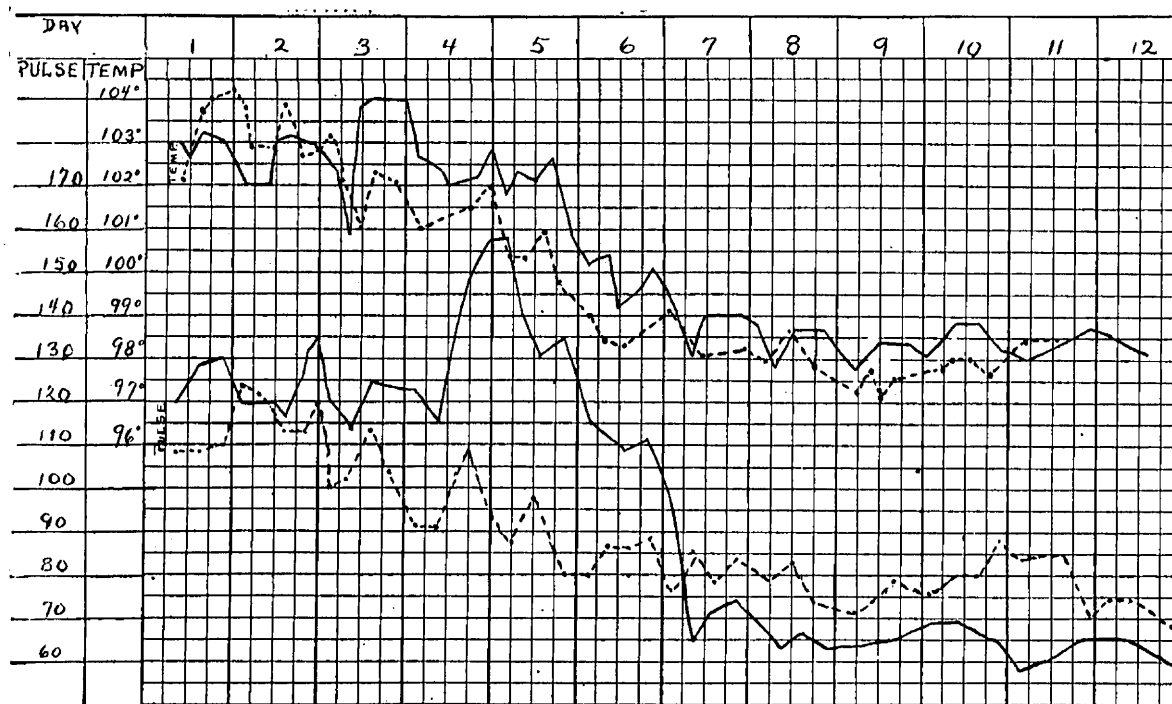


Chart 2.—Pulse and temperature in cases of Harry K. (solid line) and Lena K. (line composed of dashes).

axillæ, scalp and chest were full of lice. Blood-count, May 5, showed 17,000 leukocytes of which 84 per cent. were polynucleated; May 7, 16,000 leukocytes, 80 per cent. polynuclears. The patient was transferred to Willard Parker Hospital, May 11. A physical examination at this time showed the eruption still present with the addition of some petechiæ. The throat was moderately congested, the tongue dry and covered with sordes, as were also the teeth; the conjunctivæ were injected. The patient was emaciated. The lungs showed the presence of bronchitis of moderate extent; the liver was normal, the spleen enlarged and tender, the urine negative. May 12, the patient still coughed and the pulse was very weak. May 15, the patient had greatly improved with the fall of temperature; the rash was still visible and the pulse occasionally weak. Apart from a rather long-continued subnormal temperature his recovery was uneventful. Three Widal's proved negative and the stools showed no typhoid bacilli.

CASE 3.—Harry K. (Chart 2), aged 8 years, was admitted to the same hospital, May 8; having been taken ill three days previously with headache, fever and vomiting. The blood-count, May 8, showed 16,400 leukocytes, 82 per cent. poly-

nuclears. A blood examination showed: the leukocytes 12,400, polynuclears 76 per cent. When seen on the day following admission the patient looked very ill, frequently groaning as though in pain and with irritability alternating with apathy. Her condition markedly resembled typhoid fever at its height. Her headache was intense, and the rash was similar in appearance and extent to that of her brother. A physical examination, May 15, showed no abnormality other than a somewhat enlarged and tender spleen. The rash was fading and the patient had a slight cough. It was noted that her head was full of vermin. She made an uneventful recovery without other symptoms than those which usually accompany an infectious fever. Examination of the spinal fluid gave the following results: 8 c.c. of bloody fluid under very light pressure. Cytology: many red blood-cells, few leukocytes and polymorphonuclears; also brown crystals. There were no bacteria in either smear or culture. Albumin +. Globulin +.

The blood examination of these patients gave the results noted in the histories. In the father and two children the polymorphonuclear leukocytes showed the

inclusion bodies described by Döhle and others as occurring in scarlet fever and other diseases. The mother's blood was not examined for this condition. The treatment was purely symptomatic. Measures against the spread of this disease to physicians and nurses consisted in shaving the hair and the free use of parasitocides; the clothes were disinfected by steam.

We believe that there can be no reasonable doubt that these four patients were infected with the same virus, that of typhus fever.

#### RESULTS OF INOCULATIONS

Israel K.: Blood was drawn May 9, and 2 c.c. directly injected intraperitoneally into Guinea-Pigs 462 and 468 at the bedside. The remaining 4 c.c. were partially defibrinated. At the laboratory the clot was broken up in citrate solution and this added to the defibrinated blood and injected into Monkey A. This monkey at the same time received 1 c.c. of citrated blood from the next patient, Lena K.

Result: Monkey A. On the eleventh day the temperature rose to between 104 and 105 F. for twenty-four hours. This may or may not have been an abortive reaction, which, however, could be proved only by showing that the monkey is or is not immune.

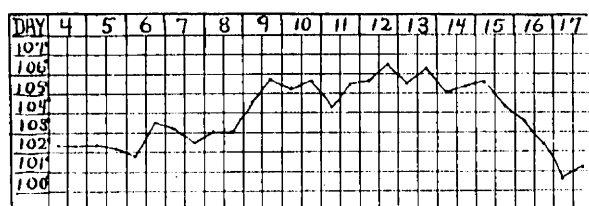


Chart 3.—Temperature of Monkey E.

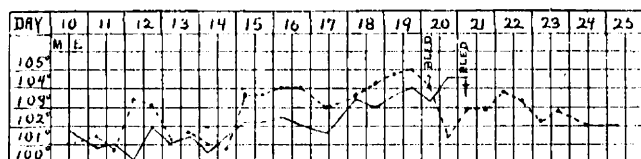


Chart 4.—Temperature of Guinea-Pigs 462 (solid line) and 468 (line of dashes).

Guinea-Pig 462: Positive. There was a definite rising temperature from the fifteenth to the twenty-first day when the animal died as a result of bleeding from the heart.

Guinea-Pig 468: Positive. Except for a transient rise on the twelfth day there was a definite rise starting on the fifteenth day.

Although the inoculation of Monkey A was apparently negative, the results in the guinea-pigs must be considered positive as evidenced by the reaction of the monkey inoculated with their blood.

Monkey E, inoculated with blood from Guinea-Pigs 462 and 468. A chart of the temperature showed a typical typhus temperature curve. Examination of blood-smears on the twelfth day showed the presence of the same inclusion bodies in the leukocytes as were found in the clinical cases.

Lena K.: May 9, 1912, 1 c.c. of citrated blood was injected into Monkey A, as already mentioned. On the next day, May 10, 10 c.c. of defibrinated blood was obtained and injected into Monkey B. May 11, 3 c.c. of cerebrospinal fluid was injected into Guinea-Pig 437.

Results: All the animals were negative.

Harry K.: May 11, 3 c.c. of cerebrospinal fluid was injected into Guinea-Pig 423.

Results: Negative.

One case, therefore, that of Israel K., gave positive, results in two guinea-pigs whose blood, injected into a monkey, caused a typical typhus temperature reaction.

This, then, is a verification of the inoculability of so-called "Brill's disease" or endemic typhus into monkeys. It also shows that it is possible to infect guinea-pigs directly with this disease. This, as far as we know, is the first time that the endemic type of typhus as it occurs in New York has been directly transmitted to guinea-pigs, and is an additional point of similarity to the epidemic type as it occurs elsewhere.

The negative results following the inoculation of cerebrospinal fluid was to be expected as previous workers have not found it infective.

The negative results of inoculation in the case of Lena K., are probably due to the variation in susceptibility of the animals. The doubtful reaction in Monkey A is attributed to the same cause.

We wish to express our thanks to Dr. Leo Stieglitz, attending physician to the Har Moriah Hospital on whose service the cases occurred, for permission to study and report these cases, and to Dr. H. Steinmetz, the house physician, for his aid.

NOTE.—Since the above was written it has been brought to our attention that Dr. Warren Coleman of New York City reported at a meeting of the Academy of Medicine, Feb. 15, 1910, four cases of so-called Brill's disease in one family. No details were given.

## THE PRESERVATION OF TISSUES AND ITS APPLICATIONS IN SURGERY\*

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### I. INTRODUCTION

Six years ago, at the Rockefeller Institute, I began to investigate how tissues isolated from the organism could be preserved and used after a few days or weeks as grafts. I wished to find a method by which tissues, extirpated from the amputated limb of a living animal or a fresh cadaver, could be stored during the period which elapses between their extirpation and their transplantation on the patient. It would be very convenient for the surgeon to keep in store pieces of skin, periosteum, bone, cartilage, blood-vessels, peritoneum, omentum and fat, ready to be used.

I attempted to preserve the tissues outside of the organism in a condition of latent or active life.

A tissue is in latent life when its metabolism becomes so slight that it can hardly be detected, and also when its metabolism is completely suspended. Latent life means, therefore, two different conditions—unmanifested actual life and potential life. Unmanifested actual life is a normal stage of the evolution of all organisms, when they progress from general death toward elemental death. As the metabolism is still going on, although very slowly, it is a temporary condition. Sooner or later cadaveric lesions develop which bring about the complete disintegration of the protoplasm. Potential life consists of a suspension of all actual vital processes. The metabolism being suppressed, no cadaveric changes would take place in the protoplasm. Tissues in a condition of potential life could be preserved outside of the body for an indefinite period of time.

Latent life was discovered two centuries ago by Loewenhoeck, who obtained the resurrection of *Milnesium tardigradum*, which had been completely dried for a long time, by moistening it with water. In 1840,

\* Read in the Section on Surgery of the American Medical Association, at the Sixty-Third Annual Session, held at Atlantic City, June, 1912.

\* From the Rockefeller Institute for Medical Research.