Report on the St. Louis outbreak of encephalitis / prepared by direction of the surgeon general.

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REPORT ON THE ST. LOUIS OUTBREAK OF ENCEPHALITIS

U. S. TREASURY DEPARTMENT
PUBLIC HEALTH SERVICE
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REPORT ON THE ST. LOUIS OUTBREAK OF ENCEPHALITIS

PREPARED BY DIRECTION OF THE SURGEON GENERAL

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FOREWORD

As will be seen in the pages of this bulletin, the 1933 epidemic of encephalitis was unique in several respects. The isolation of the virus and the thorough and continuing study of the circumstances under which the disease occurred, and its effects, were definitely furthered by the plan of cooperation adopted. St. Louis as a community may well be proud of her record in this respect. Not all the value which may result from such work is immediately apparent. To one who was on the ground several times during the epidemic two things stand out which are not heralded as widely as some of the more unusual aspects: the human suffering which such a visitation entails, and the faithfulness with which those who looked after the sick—the physicians, the nurses, and all the personnel of modern medicine—carried on their duties, at great self-sacrifice, but with the abundant satisfaction of a task well done. It is to be hoped that in the future the results of such studies as those here set forth may help to lighten those tasks and relieve that suffering.

H. S. Cumming,
Surgeon General.

REPORT ON THE ST. LOUIS OUTBREAK OF ENCEPHALITIS

INTRODUCTION

The study of a new disease is thrilling. When the disease threatens the lives of many in the community, public interest may then lend a dramatic emphasis which can be a complication rather than a benefit. The accuracy of any study depends on adequate control of methods. The control of enthusiasm is likewise important. Next to a logical attitude nothing can control enthusiasm as well as conference between diverse workers. The romance of medical investigation is not hampered by control. The greatest thrill lies in the greatest accuracy of results.

In the study of epidemic encephalitis which was a disease new to the United States in epidemic form, and which occurred chiefly in the St. Louis area in the late summer of 1933, all of the features requisite for controlled study were present. An unusual gathering of workers from many specialized fields was assembled, and all were filled with enthusiastic energy. Here was a situation calling for the discovery of a cause, and the protection of a helpless public. In the work which was planned there were available, experts in epidemiology, bacteriology, pathology, animal experimentation, and clinical medicine. Two universities combined their efforts with those of the United States Public Health Service and the United States Army under the direction of the newly formed Metropolitan Health Council. The pages which follow are, after all, but a small expression of the labor which was given to the cause of public health. Out of the study has come many new and important pieces of information. Many undiscovered facts stand out with disquieting clearness, and call for further and more determined effort. There is no doubt that this effort is being made at the present time, and that the desired information will be acquired eventually.

The ideals of medical research have been served, and the ideal of the doctor—the preservation of the public health—has once more been demonstrated. The list of authors does not contain the names of all who worked without recognition during the epidemic. Internes and house physicians, directors of laboratories and technicians, were all moved by the enthusiasm which prevailed at the time, and their work was probably just as indispensable as the work of those who directed them. The enterprise will no doubt stand as a model in coordinated effort in the controlled study of disease.

The report here presented is assembled as a summary of the contribution of St. Louis to the knowledge of the epidemic encephalitis of 1933. More complete reports on various phases here outlined will be made in appropriate publications.

OTHER OUTBREAKS OF ENCEPHALITIS

The sudden and explosive appearance of an acute form of encephalitis in the St. Louis metropolitan area in the summer of 1933 was a most unusual and unexpected phenomenon. It is generally believed in St. Louis that the disease observed here was a new entity and led to an extensive epidemic for the first time in the history of encephalitis on the Western Hemisphere. It is almost inconceivable that such a disease should appear without any precedents and without certain definite factors preparing the ground for the explosion. It is only common sense to reason, and it seems to be in perfect harmony with similar observations in epidemiology, that the virus of this disease must have been present in this area for a considerable length of time, and that some factors conspired to produce finally the 1933 epidemic.

It is not the purpose of the present discussion to give a complete and detailed history of encephalitis, as this has been done more satisfactorily in many places previously. For the thoroughness of this monograph, on the other hand, it seems to be desirable to include a brief review of the history of encephalitis, mainly because the clinical experiences, the epidemiologic and laboratory investigations in the St. Louis epidemic, have changed our concepts of the various forms of encephalitis.

This change in point of view is probably reflected in this review of the history more clearly than in some of the previous discussions on the same topic. The more recent history of encephalitis is at the same time an interesting and depressing illustration of how an infectious process affecting the human race can develop before our very eyes. From the knowledge gathered up to the present time we may safely assume that in the recently observed phenomena we were actually witnessing a most undesirable acquisition of the human race. It seems that one of the many curses accompanying the march of civilization will be an increased liability of the human central nervous system to frequent and diversified infections. While a great many of the other contagious and epidemic diseases are gradually retreating, encephalitis and similar affections of the central nervous system are not only holding their own, but apparently are taking on new forms and are tending to invade territories heretofore untouched.

The older history of encephalitis is more or less shrouded in uncertainty. It is safe to assume that the infective agent, whatever its nature may be, might have been in symbiosis with the human race for many hundreds or even thousands of years. It is even possible

that minor or major epidemics of the kind that we experienced in our midst may have occurred here and there in the past, and may have been classified under some other name, as, for instance, brain fever, grip, flu, meningitis, etc. Outbreaks somewhat similar to epidemic encephalitis seem to have been associated with the pandemics of influenza which occur from time to time. The epidemic in northern Italy following the influenza of 1889–91 was known under the name of Nona, and from the contemporary reports it appears to have resembled the disease prevalent in 1915–25. The first definite reports on this more recent prevalence came from Economo during the winter of 1916–17 from Vienna. Almost at the same time similar reports were published by Cruchet in France, although the identity of this early prevalence of encephalitis in France is questioned by Economo. Very shortly after these first reports the epidemic appeared in many other parts of the world, and has since been present almost all over the world.

It does not seem to be limited to the white race. It is known in China, Mongolia, and Japan. The dark races in Africa are free from reported outbreaks up to the present time.

This Economo, or "lethargic", type of encephalitis (type A) may be considered for the present as more or less endemic in all civilized countries. It has produced almost no explosive outbreaks, and the total number of cases reported amounts to less than 10 per 100,000 population every year in the larger countries. Its clinical form, its varieties, and the frequent sequelae mark this disease as a definite entity, distinguishable from other types of infections involving the central nervous system. More or less contemporaneously with the Economo type of encephalitis, other forms of encephalitis appeared in different parts of the world. In chronological order, the oldest one is the Japanese encephalitis which scientists of that country report under the name of type B as differentiated from the type A discussed above.

In Japan, up to 1929, 13 epidemics have been recorded. A brief history of these repeated outbreaks will be rather illuminating for our present problem.

The first epidemic occurred during the summer and fall of 1871 and affected mostly older people. The second epidemic appeared in the early fall of 1873. This was a small epidemic but with a high fatality rate, up to 90 percent. The third epidemic was in July to October 1901; this was a rather large one with a high fatality rate, affecting mostly older people. Another epidemic predominently meningeal occurred from August to November 1903; a fifth in August to November 1907; in September 1909 Tokyo witnessed the sixth outbreak. The seventh epidemic occurred from August to October 1912. This was again a large epidemic with high fatality, chiefly affecting older people. The next epidemic occurred in 1916 with a fatality rate of 61.5 percent. Next year they had a small epidemic, but in

this only younger people were affected, between 15 and 20 years of age. The fatality rate in this epidemic was only 10 percent. Up to this time Japanese investigators believed that the disease was akin to meningococcic or epidemic meningitis, but in no case could they find or culture the causative agent. In the next epidemic, which occurred in the summer and fall of 1919, they came finally to the definite conclusion that they were dealing with a meningo-encephalitis of a special kind.

The largest outbreak of this disease occurred in the summer and fall of 1924. That summer was unusually dry and hot, the weather turning somewhat cooler about the middle of August. The outbreak of the epidemic, which came when the heat began to abate, was quite sudden, producing a large number of cases in widely separated areas almost at the same time. This suddenness and the lack of connection between the cases led the writers to speak of the cause as seemingly rained from the skies. They call it a stormlike or lightninglike epidemic. The total number of cases reported in this outbreak reached almost 7,000, with a fatality rate of 60 percent. The age distribution was such that 76 percent of the patients were over 40 years of age and only 24 percent under 40. Since this epidemic, Japan has been visited by two more epidemics: smaller ones in the summers of 1926 and 1927 and a large one producing over 2,000 cases in the summer of 1929. This last epidemic had again a high fatality rate, the average for the whole country being 65 percent. The case fatality rate in this last epidemic, as one might expect, was particularly high in the older age groups. It was 43 percent for the age group between 1 and 10 years and 83 percent over 70 years, the other age groups occupying a middle position between these two extremes.

The conclusion of Japanese scientists was that in these repeated outbreaks of the epidemics they were dealing with a definite entity different from the Economo type of encephalitis, which they classify as type A. The fact that encephalitis type B has been endemic in Japan for over 60 years would speak for the independence of this disease from the so-called European type.

In Australia in January to April 1917 (the late summer in the southern hemisphere) and again in the same season of 1918 a disease appeared quite suddenly which was called the "Mysterious" disease or "X" disease. These two epidemics produced a hundred odd cases with the unusually high fatality rate of 70 percent. Backwoods, out-of-the-way places, districts hundreds of miles remote from the metropolis and far removed from one another, but all alike in possession of a dry climate, were chiefly affected. Nearly 50 percent of the cases were under 5 years and 25 percent over 25 years of age. More males than females were affected. The clinical picture was suggestive of the Japanese type B encephalitis. The pathological

findings were thought by Dr. Flexner to resemble poliomyelitis. The source of the infection seemed to be quite mysterious, but the Australian authors definitely stated that there was no apparent connection with insects and no nonhuman carriers could be established. The most likely mode of transmission seemed to be through human contacts. A similar epidemic of somewhat smaller proportions visited Australia in 1925.

In Europe no outbreaks of this or any similar disease have been reported up to the present time.

In Spokane, Wash., we have on record a fall and winter outbreak of an acute type of encephalitis in 1919–21. Seventy-eight cases were reported in 22 months in a population exceeding 100,000.

In Indianapolis, Ind., during the cooler months of 1930, 1931, and 1932, a curious outbreak is reported by Kempf and others which they describe by the name of meningo-encephalopathy. There was also an epidemic of meningococcus meningitis more or less overlapping this outbreak. From the reports published it is impossible to obtain a clear picture of the exact type of the disease, but it may have been that some of the cases were similar to the St. Louis type.

Through the courtesy of the Illinois State Department of Health we have on hand the official reports on the outbreak of epidemic encephalitis at Paris, Edgar County, Ill., in the summer of 1932. The first patient mentioned in these reports developed his initial symptoms July 29, 1932, and the last one on September 12, 1932. In all there were 27 cases reported, but only in 19 was the State investigator able to concur in the diagnosis. Cases were found in the best and poorest types of families. Mostly older people were affected. There were about as many males as females. "These patients were from all ranks of life, lived in different parts of Paris. Also it so happened that very few had any social contacts whatever, neither was there more than one case in a family. Three cases were under 35 years of age; in all others the age varied from 46 to 82 years." Ten of the twenty-seven patients died.

This Paris epidemic of encephalitis on the surface appears to be similar to the St. Louis epidemic. Whether it is fully identical as to etiology will have to be decided by further investigations, particularly through immunological studies.

In the St. Louis area various interesting phenomena were observed and put on record preceding the outbreak of the encephalitis epidemic in 1933. It is quite natural that these observations remained unnoticed until after the epidemic started, when our attention was focused on them only in retrospect. A few of these phenomena are mentioned here without the least intention of specifically connecting them with the epidemic.

It is important to emphasize that preceding the 1933 epidemic there has been little attempt made, with the exception of Japanese reports, to differentiate between the various forms of "epidemic" encephalitis. Almost all cases reported in this country are classified as "lethargic" encephalitis, this name, descriptive of only a fraction of the cases, being strongly entrenched at present in medical terminology. The incidence of encephalitis cannot be truly gaged in any community due to the fact that cases are often diagnosed incorrectly, and even if they are diagnosed, usually reporting remains incomplete and unsatisfactory. Due allowances have to be made for the above facts when we make any statements concerning the incidence of encephalitis in the St. Louis metropolitan area. It seems to be well established, at least from the observations of some of the hospitals, that the Von Economo type of encephalitis has almost completely disappeared in St. Louis in the last few years. In the St. Louis Children's Hospital the last case which was authentically diagnosed was one in 1926. In spite of this fact the number of cases of encephalitis has increased during the past 6 or 8 years. This increase naturally includes all forms of encephalitis, but an interesting fact was brought out in an analysis of cases of encephalitis admitted to the St. Louis Children's Hospital. This analysis was made by Dr. Alexis F. Hartmann who found that in the period between 1919 and 1932, that is, in 14 years, the incidence of cases of encephalitis of unknown etiology, those which were not associated with any primary infection, and were not classified as "lethargic" or Von Economo type of encephalitis, had shown a definite seasonal distribution. The increase begins in June, reaches its peak in July and August, and begins to decline in August and September. This curve curiously parallels the incidence of epidemic encephalitis as observed in 1933. This is again recorded here without any attempt to interpret it in any definite form.

During the 2 or 3 years preceding the 1933 epidemic there have been several reports by physicians in St. Louis on a form of meningeal involvement which is described as lymphocytic meningitis. The clinical picture of this disease seems to be suggestive of some of the milder cases of meningo-encephalitis seen in the 1933 epidemic.

It is mentioned as a curious coincidence that during the past few years an epizootic of encephalomyelitis prevailed in horses. This epizootic was especially prevalent in California and then in Utah. A similar or identical disease has since prevailed in the Midwest, and lately in the Eastern States. It is of some interest to note that in a few instances this same disease was contracted by human beings and also that the virus of the St. Louis epidemic was possibly slightly pathogenic to two mules. It is far from our intention to attempt to connect the two diseases.

In the early part of 1933 the incidence of other virus diseases in St. Louis in many respects was unusually high. A very severe rabies

epidemic started in the early winter and late spring, extending far into the summer. In May of that year a measles epidemic broke out, an unusual feature being that it occurred out of season.

Febrile conditions observed in human beings must have been decidedly on the increase in June and July of the same year. This is concluded from the fact that the requests for Widal tests reaching the public health laboratories of the division of health of the city showed an increase of almost 100 percent over the average for the preceding 2 years. The only proper interpretation for this can be found in the fact that many obscure clinical cases with high temperature must have been seen by physicians and that they must have been puzzled as to the diagnoses. After the outbreak of the epidemic questionnaires were sent to the physicians who had requested these laboratory tests in order to clarify the situation. Altogether, inquiry was made regarding about 119 patients and replies were received concerning 80 patients. Of this group 20, or one-fourth, suggest that the febrile conditions may have been a mild form of epidemic encephalitis.

All in all, these observations seem to support our statement made above that the virus of encephalitis must have been present and more or less active in this area for a considerable length of time. The appearance and disappearance of epidemics are among the most puzzling problems of epidemiology and medical science.

For the completeness of the monograph we feel that a classification of the various forms of nonpurulent encephalitis should be given here. On the basis of our present knowledge idiopathic human encephalitis may be classified in the following manner:

I. Infectious encephalitis.
   1. Type A or Economo or lethargic type, chiefly sporadic.
   2. Type B, chiefly epidemic.
      (*a*) Japanese form.
      (*b*) St. Louis form.
   3. Other types.

II. Post or parainfectious encephalitis.

HISTORY OF THE EPIDEMIC

For those who may not be fully conversant with the facts concerning the Public Health jurisdiction of St. Louis and St. Louis County, a few words of explanation might be in order. St. Louis City constitutes a county in itself with an approximate population of 830,000. St. Louis County, which surrounds St. Louis, has a population of approximately 210,000. The populations of the city of St. Louis and of St. Louis County merge into each other. The daily intercourse between the county and city is considerable since many people living in the county work in the city. In St. Louis County there are a number of small incorporated villages, towns, and cities. There are health officers in

these administrative units and in addition there is a full-time county health officer. Across the Mississippi River in the State of Illinois there are two counties with a large industrial population which have continuous contact with the city of St. Louis. These two are St. Clair and Madison Counties in Illinois. It is important to have this picture in mind in order to understand the possibilities in the control of communicable diseases in the St. Louis metropolitan area.

There were certain preliminary conditions which are of interest and which occurred before the outbreak of the encephalitis epidemic. Climatic conditions in the St. Louis metropolitan area for the three summer months of June, July, and August in 1933 were very unusual. According to the official weather bureau records the rainfall in St. Louis for these 3 months was the lowest in its history, a cloud burst which fell over a very small portion of the city represented almost the entire rainfall. In St. Louis County the rainfall for these same 3 months was the lowest since 1837 when the first official Weather Bureau records were compiled. The drainage and sewage problem in St. Louis County (with many open drainage ditches for sewage disposal) was favorable to the breeding of unusually large numbers of mosquitoes in areas commonly infested. With the dry season the flow in these open ditches was small and practically consisted of sewage only, and the odors that emanated from these places were quite offensive.

The first information that the health division of St. Louis received of the epidemic of encephalitis was on August 8, 1933. On this date the health commissioner of St. Louis was informed by the superintendent of the St. Louis Isolation Hospital that 16 cases of an unusual type of encephalitis had been admitted which had previously been admitted to and diagnosed at the St. Louis County Hospital. On the morning of August 9 these cases were examined by the assistant health commissioner in consultation with staff members of the Isolation Hospital. After reviewing the histories, making physical examinations of the patients, and gathering the laboratory data, a meeting was held in the health commissioner's office. Although no cases had been reported in St. Louis it was promptly appreciated that these cases represented an unusual disease, and one which was obviously spreading rapidly. It was felt furthermore that there were possibly many more cases which were not reported. Because of the intimate contact of the county with the city it was believed that this disease would shortly be a problem for the city of St. Louis. Immediate steps were taken to advise the medical profession and the public that an unusual epidemic of encephalitis was existant. It was important that this information reach the public as well as the medical profession so that prompt and satisfactory reporting of cases might

be assured. The daily press of St. Louis was very cooperative in carrying this news to the general public and in disseminating other information as it accumulated.

On August 10 additional cases were reported from the county, and the first impressions were strengthened, namely, that the city of St. Louis could not escape this epidemic. With the excellent cooperation of the county health officer plans were made for field investigations, and a beginning was made in gathering epidemiological facts in the county since at this time there were no cases reported in the city of St. Louis. On August 12 a telegram was received from the Surgeon-General of the United States Public Health Service offering any assistance that might be needed. The health division of St. Louis wired back requesting an epidemiologist. Dr. James P. Leake, senior surgeon, United States Public Health Service, arrived on the morning of August 14. At the time of his arrival there were no reported cases in St. Louis so that all investigations, covering some 25 cases, were related to patients in St. Louis County.

On August 12 the health division of St. Louis was much concerned as regards the mode of handling the epidemic, and appreciated fully that unless they had the cooperation of all the health officers in the surrounding territory little progress could be made. Letters were sent out to all of these health officers notifying them of a meeting in the health commissioner's office in St. Louis on August 14, 1933. At this meeting there was a free discussion of the situation as it existed, and proposals were made and adopted for general plans for handling the epidemic, including a uniform questionnaire to be sent to the health officers representing the various units in St. Louis County and others from St. Clair and Madison Counties in Illinois. It was suggested at this time that the Metropolitan Health Council be formed, to be composed of all health officers in St. Louis County, St. Louis proper, and the two counties in Illinois, St. Clair and Madison Counties.

The Metropolitan Health Council was to be a cooperative body, consisting of the health commissioner of St. Louis, the health commissioner of St. Louis County, the various other health officers of St. Louis County, and the health officers of St. Clair and Madison Counties of Illinois; in addition the hospital commissioner of St. Louis, superintendent of the St. Louis County Hospital, and the superintendent of the Isolation Hospital of St. Louis; other physicians and public health workers who might be interested were also invited.

The purposes of this Metropolitan Health Council were to coordinate the public-health activities in the Metropolitan area for the handling of emergencies; to adopt uniform rules and regulations as far as possible for the handling of communicable diseases; and to formulate uniform rules and regulations as to isolation and quaran-

tine. While the idea of a Metropolitan Health Council had been considered for some months previous to the epidemic, it was felt that this immediate emergency warranted prompt action. All of the health officers in the St. Louis metropolitan area were of the same opinion, and the splendid cooperation made it possible in every way to work out a satisfactory program. The Metropolitan Health Council was, therefore, organized on August 17, 1933, and at this meeting two standing committees were appointed; namely, a committee on rules and regulations and a committee on scientific research.

St. Louis was fortunate in having two excellent medical schools and also adequate hospital facilities. Because of the obscure nature of the disease it was immediately apparent that the cases should be hospitalized, and that autopsies were imperative. In order that no autopsy material should be lost, and that all of it should be used to the greatest advantage, the scientific research committee centralized all of its work at Washington University Medical School where the laboratory facilities and personnel were thought to be particularly suited for this problem. The splendid cooperation given the research committee made it possible to have all autopsy material available to this personnel. This avoided waste of valuable material and permitted the centralization and coordination of research. It was felt that autopsy material might be difficult to obtain, and that the number of autopsies would be restricted. It was most important that nothing should be wasted which might aid any possible investigations. The uniform questionnaires which were used throughout the Metropolitan area made it possible to gather all statistics on epidemiology in a manner so that they might be analyzed in relation to the epidemic as a whole, and not solely in relation to any one particular section of the area involved.

The early field investigations led to the belief that a disease was present which was similar in its spread to poliomyelitis. The cases were rather widely scattered, and were occurring in the suburban areas of St. Louis County. It was apparent immediately that it was rare for more than one individual member of a family to be affected, and furthermore, that the older age groups were affected more frequently than the younger individuals. Because of the nature of the disease itself it was necessary to decide promptly on a hospital program. It was evident that the St. Louis isolation hospital for communicable diseases would not be able to handle all of the cases. It was, therefore, necessary to throw open all of the hospitals in St. Louis for the care of these patients. Rules and regulations concerning the care and isolation of patients were promptly promulgated. It was felt that it was relatively safe to handle these cases in general hospitals, provided that sections of the hospitals were set aside where routine isolation could be enforced as with any other communicable

disease. The cooperation of every hospital in St. Louis was prompt and whole hearted, and it was a relief to know that the patients could have the advantages of hospitalization and the best conditions for lumbar puncture, an important procedure in early diagnosis and treatment.

Physicians and the public were thoroughly informed as to the measures advised in the presence of the epidemic. This publicity was most helpful as evidenced by the fact that approximately 95 percent of the cases were hospitalized. The frequent delay in diagnosis in cases with a fever of obscure origin cannot be criticized. Many of these encephalitis patients had no early localizing symptoms. Early lumbar puncture as a diagnostic procedure was urgent. The hospital was the only satisfactory place where this could be done routinely with the minimum amount of risk. Besides this the clinical symptoms and complications that arose during the course of the disease made it almost impossible to care for these patients in the average home without a day and night nurse. Urinary disturbances, the tendency to bedsores, and feeding problems all required expert nursing attention, and patients with delirium demanding various amounts of restraint would be a difficult problem for home treatment. Hospitalization further gave an opportunity for more accurate and more uniform clinical and laboratory studies.

Since the epidemic is over, the value of these uniform records has been appreciated more than ever. Today it is possible to gather clinical and laboratory data of a nature that would never have been available had these cases been scattered through the homes. In this way there has been avoided, to a great extent, the lack of detailed information.

Daily bulletins were issued and with the aid of the newspaper and radio, the medical profession, as well as the general public, were constantly kept informed. The cooperation received was beyond all expectation. The information issued early was fairly complete from the clinical point of view and served to minimize the difficulties in recognizing the significance of fever, headache, and other early symptoms so prominent in this disease. The response from the profession and the public was almost dramatic. Cases came in from all sources for consultation, and hospitalization was made routine. It was urged that the isolation in hospitals should be maintained for at least 3 weeks from the date of onset of the disease.

Reports of all new cases were sent by the physicians to the local health officers, who in turn telephoned them to the secretary of the Metropolitan Health Council. Daily bulletins on all new cases and their addresses were mailed to all the health officers and other members of the Metropolitan Health Council. Reports of cases in the city of St. Louis were first received on August 17. Shortly there-

after physicians commenced to review in their own minds some obscure cases of illness which they had attended in previous weeks or months. A friendly rivalry existed among the profession as to who had the distinction of recognizing the first cases. The records now disclose that sporadic cases had existed for some time previous to the onset of the epidemic. The first case according to the official records dates to July 7, 1933. The first case was reported in St. Louis County on July 11. Another interesting feature in checking laboratory records in the St. Louis City Health Division was the fact that an unusually large number of blood specimens were sent in for Widal tests for typhoid.

The early investigations led to the strong belief that the disease in question was a virus disease similar in its spread to poliomyelitis, and possibly transmitted through nasal secretions. The seasonal occurrence, the wide distribution, beginning in the suburban points and traveling toward the denser population, were factors in leading to these beliefs. Every mode of transmission had to be studied, and one of the first was the water supply. That water could be a carrier of this infection was promptly dismissed. Milk was also excluded since about 95 percent of the supply of St. Louis County comes from dairies which supply the same milk to the residents of the city of St. Louis. There were no common sources of food which could be considered so that foods were also ruled out.

The first week of the epidemic had not elapsed before the health division was overwhelmed with many opinions as to the cause of the disease, and there was a revival of many of the ancient theories associated with past epidemics. Even the old miasmatic theory was revived since many felt that the odors from the sewers and open drainage ditches were responsible for the epidemic. Because the term "sleeping sickness" had been applied in the daily press, it was thought by less well-informed people to have been transmitted by flies. By a strange coincidence a missionary and his family had visited one of the smaller subdivisions of St. Louis County, after returning from a visit to Africa; within 30 days of this visit the epidemic of encephalitis started. Even the purchase of certain species of animals for the zoo were thought to have brought the disease to the city. Another theory was based on the fact that elsewhere in the State a number of hogs died of an "unusual" disease, and that possibly some of the meat of these animals had reached the city and caused the epidemic. Investigation showed that these hogs died of hog cholera. Many of these suggestions, of course, were dismissed without any serious consideration, but they are mentioned here because they are but a few of the many fanciful suggestions that a health officer receives.

The field investigations did not prove any definite history of contact of the patients with other known cases yet the infection was widespread and the carrier factor became an important part of the epidemiologic investigations. With the large number of mosquitoes in the areas involved, naturally many felt that mosquito transmission was likely. It was not felt that mosquitoes played an important part in the spread of the disease. However, it was believed that the mosquito theory should be studied very thoroughly if for no other reason than to obtain some information even though in the negative sense. As a result the United States Public Health Service and also scientists of the Army Medical School Laboratories carried on this tedious work of studying the possible role of mosquitoes in the transmission of this disease.

The laboratory work progressed during the course of the epidemic; the susceptibility of many species of animals was tested in order to isolate the virus. The early laboratory work gave negative results from a bacteriological standpoint, therefore the investigations were soon directed toward the virus theory. The difficulty in transmitting the virus to susceptible animals was early appreciated. Even the laboratory workers received many suggestions from all quarters as to how they should proceed. A rule was made that results of all research work should be submitted to the Scientific Research Committee in order to avoid the publication or dissemination of statements which were not warranted by the actual status of the studies. The research work necessarily had to proceed cautiously and announcement of results therefore was delayed. The research workers were continually bombarded with impatient questioning. However, the committee was able to carry on the work without interruption, and the Metropolitan Health Council did everything in its power to prevent all unnecessary interruptions. The citizens of St. Louis County and St. Louis were very cooperative, and sufficient autopsy material was obtained to carry on the necessarily tedious and extensive laboratory investigations.

The value of centralizing the authority for handling the entire epidemic in the Metropolitan Health Council soon became apparent. The personnel of both universities, the hospitals, the health officers, and the public worked together very smoothly. With conflicting views and suggestions coming in from all directions the Metropolitan Health Council stood firmly on the principle that no regulations should be made without careful consideration of all the facts which were obtainable. Theories have their place only when based on facts. The best professional minds were mobilized locally and they cooperated with the State health department and with the United States Public Health Service. All worked side by side in perfect harmony, and no words can express the deep appreciation that the local health

authorities felt toward those who came to aid in the local situation. The steadying influence of the United States Public Health Service served to concentrate efforts and to give backing to the regulations adopted.

Toward the end of August a pressing problem in the minds of many people arose as to whether the schools should be opened. The health officers, therefore, had to take a stand on this important issue which occurs almost in every epidemic. It was felt that with the information on hand there was no valid reason why the schools should not be opened. Health officers are continually and insistently urged by the public and sometimes by professional men to close the schools when anything unusual happens. The health division and the Metropolitan Health Council felt very strongly that this was a time for educating the public, and took the firm stand that the schools should open; public opinion should be created and not merely accepted in a situation of this nature. There were many who doubted the wisdom of this recommendation, but almost simultaneously with the opening of the schools the epidemic had reached its peak and continued to subside thereafter. Because of the offensive odors of many of the sewers, the health officers were tempted to call out the fire department to flush them out. This was another revival of the miasmatic theory. However, no water was wasted and the epidemic subsided.

Many of the difficulties with which the health officers had to contend came through exaggerated statements concerning the epidemic, particularly in newspapers outside the city of St. Louis. The Metropolitan Health Council did everything possible to keep the press from making sensational statements. On the other hand the health council felt that the press very materially aided in securing cooperation from all sides. People who were away from St. Louis for vacations were frightened by some of the articles they had read in papers outside of St. Louis. They were afraid to send their children back to schools and colleges. They had even been warned later by health officers in various cities that they would not be permitted to send their children back to colleges and schools because they were living in St. Louis. This was done in spite of the fact that the Metropolitan Health Council had made clear and definite statements as to the safety of sending these children back to school, and that in St. Louis itself the schools were not closed. Official statements were made by Federal, State, and local health authorities cautioning the people against many of these exaggerated statements.

During the course of the epidemic, the Metropolitan Health Council appreciated the necessity for a systematic follow-up of all patients who had had encephalitis, for at least 2 years following the epidemic. Only in this way could there be gathered data of real value as to the

after effects in individuals who had been attacked by this disease. Again a uniform questionnaire was adopted in the metropolitan area, and at present the cases are being followed for the second year. Earlier results are mentioned on pages 58, 63, 73, and 80. Another committee was formed to take up the question of publishing this monograph on this unusual disease so that there might be available the information gathered in St. Louis and so that any community might be on guard should they have an unpleasant visitation similar to that which St. Louis has experienced. By gathering together the men who were actively engaged in the epidemic, it was hoped to present authoritative facts.

The Metropolitan Health Council felt a deep responsibility in handling this epidemic because of its possible recurrence locally as well as in other areas of the United States. The council tried to demonstrate modern public health methods in handling this epidemic while conflicting opinions arose from all sides. All regulations that were issued were based on the simple principles of handling any communicable disease: "Early diagnosis, hospitalization, and isolation of all fever cases until an accurate diagnosis can be established." The practical handling of the problem naturally could not wait for laboratory confirmation. Many problems arose that might involve months or even years to solve. The principle that served as a guide was, that one was dealing with a virus disease spread by human carriers and by mild cases. Because of the widespread infection one also felt that immunity of the general population must be quite high. The rarity with which more than one member of a family was involved made one feel that quarantine of other members of the family was not advisable. The health council did not want to impress anyone with the idea that it was doing more than it was possible to do. The public as well as the medical profession was frankly informed at all times about the actual facts occurring in the epidemic, and concerning the reasons why certain precautions were taken, and why many other procedures were not advocated.

That the measures taken in emphasizing hospitalization and isolation were effective can only be measured by the fact that 95 percent of the reported cases were hospitalized. How successful these measures were in checking the disease will always remain a matter of speculation. There is no yardstick whereby one can evaluate the effectiveness of such measures. These are, however, the methods that have been recognized as effective in the control of all communicable diseases of the contact group. The greatest satisfaction has been that the most complete cooperation that could be expected anywhere was given throughout the epidemic, and no regulations which were not based on sound public health practice were issued at any time. Until more fundamental knowledge is forthcoming one

could not advocate anything further today than when the epidemic was handled last year; possibly one would not have to change a single item in this procedure, in a similar situation in the future.

EPIDEMIOLOGY

Just as in laboratory studies of the virus, a final opinion as to the exact nature of the disease, its pathogenesis, and method of spread, so far as these may be traced from epidemiological studies, must await more complete analyses and confirmation. Nevertheless enough is apparent to give definite trends to our estimation of these points.

A word might be said about the reliability of the fundamental epidemiological data, that is, the accuracy with which the disease was reported. In the St. Louis area this was believed to be fairly good, especially for a disease in which lack of a definite clinical criterion, and lack of uniformity in symptoms, made personal opinion a large factor in diagnosis. It would be hard to find actual conditions in which this accuracy could be improved upon. Elsewhere in this report note is made of the remarkable spirit of cooperation which prevailed. Confidence in the medical profession and in the health authorities was general. The fact that the homes where the disease occurred were not placarded, and that no unreasonable restrictions were imposed, made the public free to call in medical advice when the illness was severe enough to constitute a definite case of this disease; and the physicians, on their part, saw no harm to the interests of their patients in reporting the cases. General insistence on hospitalization was conceded to be wise, and since all hospitals, as a rule, were persuaded to admit cases of the disease, any class of treatment and of medical attention was available. The population of St. Louis is more stable than that of most other American cities of its size, and it has a corresponding degree of neighborliness. Cases would therefore not be so easily concealed, and in fact many rumors of individual cases supposedly concealed or not reported, when traced down, were found to refer to cases already known to the health department. Satisfactory treatment facilities were available for all economic conditions and there is no indication in the geographical distribution of the reported cases that any tendency existed for one group of the population to show a disproportionate number of cases. Many of the patients lived in the more expensive neighborhoods; some were very wealthy; yet the suburban district which had the highest incidence was the one with probably the most crowded though widely scattered homes; on the other hand, in the city the older and poorer sections had somewhat lower incidence than other parts. A check-up at the close of the epidemic of homes not known to have been infected, covering sample neighborhoods in all parts of the city and suburbs, revealed no unreported cases.

Two questions in this connection deserve further consideration: Did many mild cases occur, so mild that they could not be diagnosed as encephalitis by any of the ordinary standards? From the random fashion in which the frank cases of the disease occurred in the community, it might be reasonable to suppose that this was the case. Yet actual search failed to reveal them in any significant numbers, either in other members of households where a frank case existed or in households in which no case had been reported. It is true that in a disease like poliomyelitis or encephalitis occurring in communities as densely populated as the St. Louis area, the numbers of such "abortive" cases do not appear to be large even in the presence of an epidemic, while in smaller or more rural settlements histories of such cases are more much frequently obtained. Several of the St. Louis physicians whose practice carried them into homes of the well-to-do believed that they saw during the summer an unusual number of mild indeterminate illnesses, particularly among children, but the total number of such reports was not great.

As will be noted in the clinical sections, the cases in this epidemic, while lacking a single definite and unifying pathognomic sign, were in general less varied in their symptomatology than the cases previously described under the term "epidemic encephalitis." The fact that hospitalization was the rule also made for more uniform and more accurate diagnoses. But a further question arises: Did the practice of using an increased cell count in the spinal fluid to determine the diagnosis tend to cause the inclusion of illnesses due to other causes, or to exclude cases which should have been considered part of the epidemic? It is not believed that any notable error crept in on either side from this practice, in spite of the errors in sampling involved in the count of a small number of cells. The cases which corresponded to the disease in general symptomatology did have in almost all instances an increase in cell count at some stage of their course, and there was no considerable group of cases diagnosed as encephalitis on the basis of the spinal cell count which failed to fall in with the clinical picture of some one of the types of the disease. Cell counts higher than normal were much more uniformly found in this epidemic than in "epidemic encephalitis" in general. It is none the less to be recognized that the spinal fluid in typhoid fever, for example, and in some other diseases with pronounced cerebral symptoms, may show pleocytosis independent of any ideopathic encephalitis.

In recent years encephalitis has been always present, and at every season, in communities of large size. A survey of the more important cities of the United States, made since the St. Louis outbreak, reveals what might have been expected, that many of the cases currently being reported as epidemic or lethargic encephalitis lack the characteristics either of the disease as seen in St. Louis in 1933, or of the

disease as originally called lethargic encephalitis by Von Economo, or epidemic encephalitis since Economo's first description. These current cases frequently turn out in their further course to be some other condition. In other instances, on account of early fatality after being first brought to clinical attention or for some other reason, observation has been too limited to point definitely toward the diagnosis of encephalitis. Other cases are diagnosed epidemic encephalitis on the basis of behavior disorders or juvenile Parkinsonism without any clear history of an attack of encephalitis itself.

Fatal cases of encephalitis are reported in the death certificate, according to the 1930 International List of Causes of Death, either under number 17, lethargic or epidemic encephalitis, an infectious disease, or under number 78, encephalitis (nonepidemic), a disease of the nervous system. In view of the difficulty experienced in concluding from the reported number of cases that there were anything like that number of cases of the Economo disease, and the actual impossibility of diagnosis in many of the sporadic cases, it might seem wise to replace number 17 with the name "Infectious encephalitis", leaving the further subdivision into the various kinds of infectious encephalitis to be made at a time when or in places where such subdivisions can be made with a reasonable degree of definiteness. Number 78 would thus be left to include only noninfectious encephalitis. It seems a misnomer to label the Economo disease "epidemic encephalitis" when it has not been epidemic at all as compared with the Japanese and St. Louis forms.

Of the forms of infectious encephalitis which come into consideration in connection with this epidemic there may be considered first, and dismissed, the encephalitis due to the virus of acute anterior poliomyelitis. This is an exceedingly rare form of poliomyelitic infection when not combined clinically with a myelitis; so far as known, with the very questionable exception of the Australian epidemic of 1917 and 1918, it has never appeared by itself with epidemic prevalence.

The post-infection encephalomyelitis which is characterized, as Perdrau has shown, by a patchy demyelination, occurs typically (but rarely) after measles, vaccinia, variola, and varicella, and at a fairly definite period in the evolution of these diseases. The meningoencephalitis occurring after mumps appears to be different from this, running a more uniformly mild course, and due to the mumps virus itself. Individual cases of post-infection encephalitis might be confused with the disease in St. Louis.

In comparing this epidemic with the form of infectious encephalitis which goes by Economo's name (lethargic or "epidemic" encephalitis) and in comparing it with the Japanese form of the disease (type B) a distinction might well be made in each case between the descriptions

of the disease given when prevalence was at its height—1917–1923 for the Economo type, and 1924 for the Japanese form—and the more recent descriptions, which in general are less clean-cut. Such a comparison might be made, for example, between Achard's monograph of 1921 and Stern's of 1928, or, for the Japanese form, between Kanako's article of 1925 and his longer one with Aoki in 1928. In each instance it is the former description, unclouded by the inclusion of "sporadic" cases, which comes nearer to the St. Louis findings. And in both instances individual cases might not be distinguishable from the disease as it occurred in St. Louis. A group of cases of the Economo form does offer differences from the St. Louis cases, but even in the mass, the Japanese form shows great similarity to the St. Louis form.

The outbreak which occurred in the summer of 1932 in Paris, Ill., and to which reference has previously been made in this report, is more nearly precedent for the St. Louis outbreak; clinically and epidemiologically they might be regarded as identical. Through the courtesy of the Illinois State Department of Health, the Paris physicians, and particularly the local health officer, Dr. W. E. Conklin, opportunity was afforded to search for cases in that city. Thirty-eight cases, similar in all respects to the St. Louis cases, were found to have occurred during the summer of 1932, 75 percent of them during the 3 weeks from August 2 to 22. This was an incidence of 433 per 100,000 population, over four times the rate in St. Louis City and County in the following year, greater than the rate in any subdivision of the St. Louis area of comparable size, and 60 percent more than the rate in Kagawa, the most severely affected province of Japan in the heaviest epidemic year, 1924. Thirty-seven percent of the Paris cases were fatal, as compared with 20 percent in the St. Louis epidemic, 60 percent in the Japanese 1924 epidemic and 63 percent in the Japanese 1929 outbreak of 2,000 cases. As in St. Louis and Japan, there was a great preponderance of cases in the older age-groups in Paris, 82 percent being in persons over 50 years of age. As to sequelae, also, there was a notable lack of the distressing after-effects which subsequent to the Economo type of the disease are so frequent that their occurrence in a considerable proportion of the cases is almost characteristic. In spite of the advanced age of many of the patients who had had a severe febrile attack with temperature exceeding 104° and with marked cerebral involvement, very little increase of the deterioration to be expected with age was found in these Paris patients 15 months afterwards. In less than 2 percent of the Japanese cases were aftereffects detectable, 1 year following the 1924 epidemic.

The number of cases of encephalitis reported by weeks during the 1933 epidemic in St. Louis City and County is shown by the two

curves in figure 1. The epidemic practically ended with October. A few straggling cases were reported from time to time during the winter months, none during the spring months. As has been previously noted, individual cases on the basis of signs and clinical course are often impossible of definite assignment to one or the other of the groups of infectious encephalitides, and a few may be considered endemic. It is seen from the figure that the epidemic began in the county and subsided there first. The intercensal estimated population of the city for 1933 was 836,979, and that of the county 244,850. About 575 cases occurred in the former and 520 in the latter, making a rate of approximately 100 cases per 100,000 population for the entire area, or 69 per 100,000 for the city and 212 per 100,000 for the

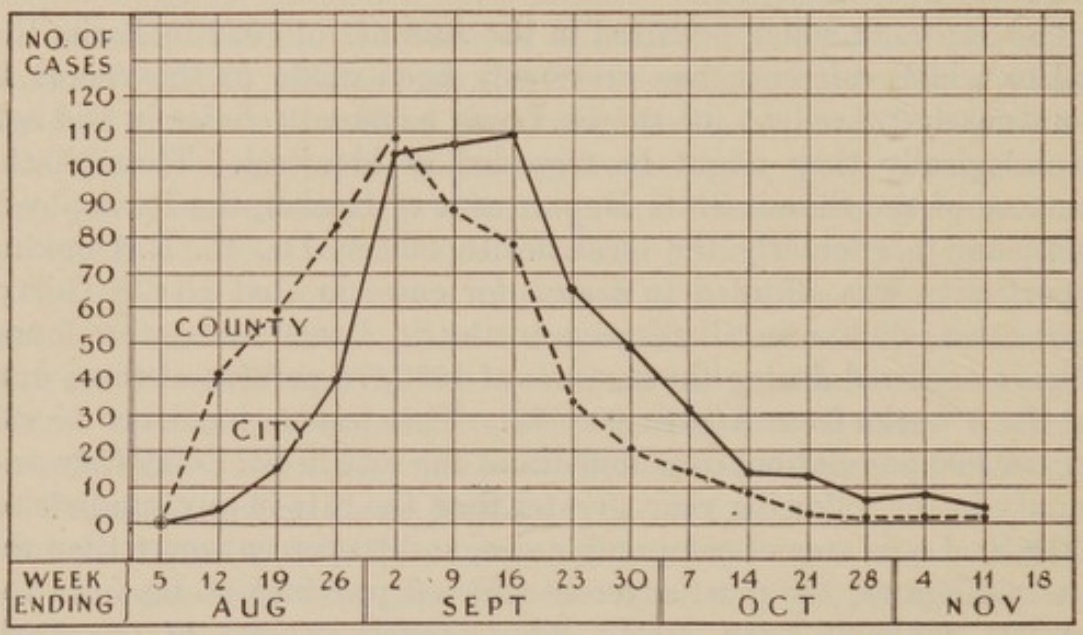

FIGURE 1.—Cases reported by weeks, St. Louis City and St. Louis County.

county. The chronology of the cases occurring in the city of St. Louis, by dates of onset, is shown in figure 2.

Counting the city and county together, the percentage of cases that occurred in males was the same, 50.9 percent, as the percentage of males in the total population. As to color 9.9 percent of the cases were reported as occurring in colored persons, who form 10.1 percent of the total population. The disease, therefore, showed no preference as to sex or color.

As stated previously, the case mortality rate for all ages was approximately 20 percent, and the incidence for the area 100 cases per 100,000. Table 1 shows specific case and death rates per 100,000, and the case mortality rate for decennial age groups in city and county together.

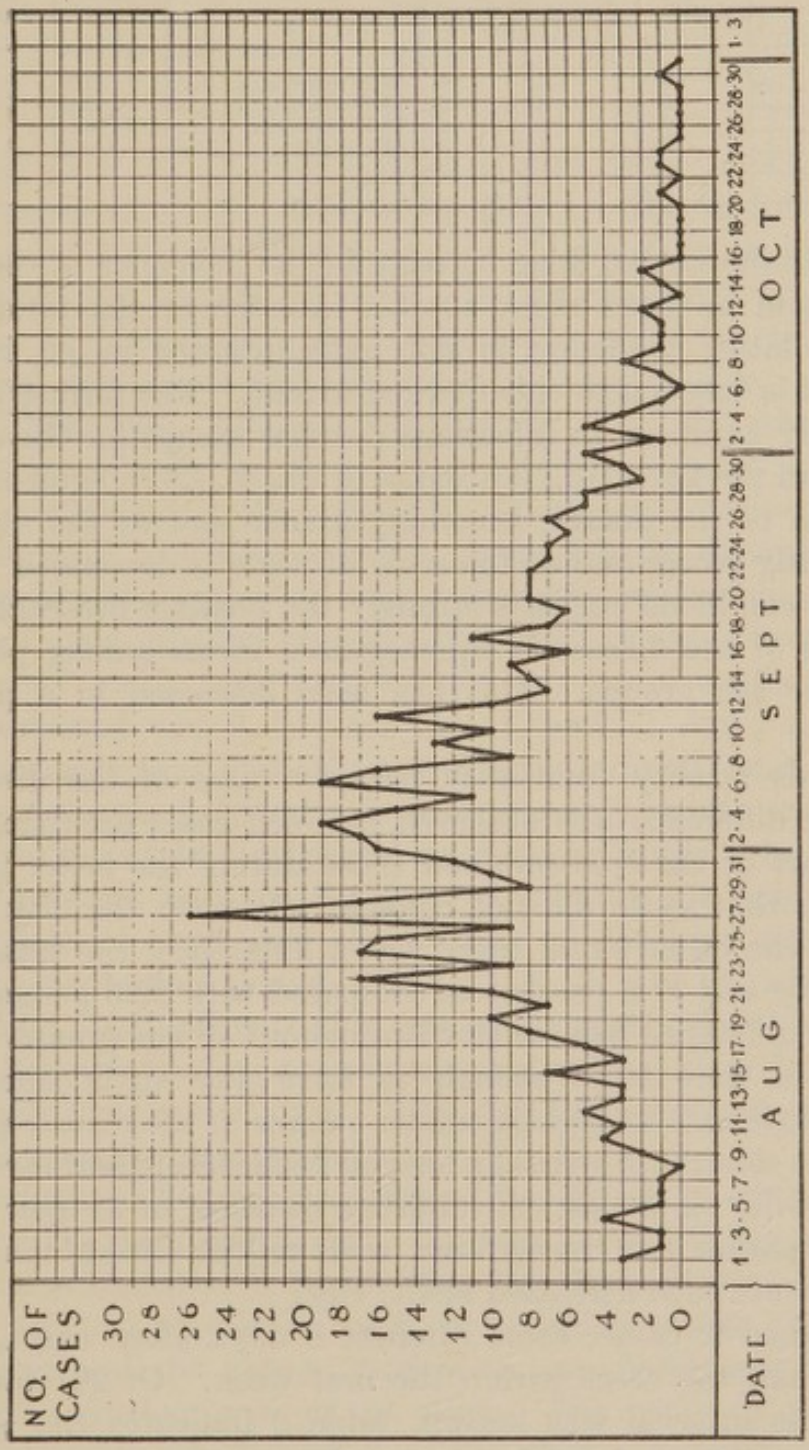

FIGURE 2.—Cases in St. Louis City, by date of onset.

TABLE 1.—*Case incidence and death rates by age groups in the St. Louis City and County encephalitis epidemic of 1933*

Age group	Cases per 100,000 population in each decade	Deaths per 100,000 population in each decade	Case fatality (per-cent)	Age group	Cases per 100,000 population in each decade	Deaths per 100,000 population in each decade	Case fatality (per-cent)
0–9 years	54	4	8	50–59 years	169	36	21
10–19 years	64	3	5	60–69 years	285	109	38
20–29 years	68	3	4	70–79 years	364	204	56
30–39 years	73	6	8	80–89 years	419	335	80
40–49 years	119	14	12				

This table shows a striking increase in the incidence of the disease with age, and an even more notable increase in the fatality with age. This latter tendency is not extraordinary in an infectious disease, but is unusual to this marked extent. The former tendency is practically unknown in infectious diseases except for the Japanese epidemic and the Paris, Ill., prototype of the St. Louis epidemic. The combination of the disease becoming milder and at the same time less frequently recognized as the scale of years is descended from old age toward childhood suggests strongly the possible presence of very many cases of the disease in unrecognized forms among persons in the younger age groups. This has been discussed in a preceding paragraph.

As regards fatality (mortality per 100 cases of the disease) no noteworthy difference was observed between cases occurring during the first part of the epidemic and those during the latter part; the virulence in that sense did not change. Between the city and the county, on the other hand, there was a difference; the fatality rate in the county was 17.5 percent as compared with 22.5 percent in the city. This difference was evident throughout all age groups in which the numbers were large enough to have any significance. This might be attributed to slightly milder strains of the disease predominating in the suburbs in spite of a heavier incidence, to better resistance against lethality on the part of suburban dwellers, or to their securing medical attention and recognition with milder illness than would generally secure such attention in the city.

Death, when it came, came oftenest 6 days after onset, and in more than half the cases within the first week. Of 201 fatal cases in which this interval was known, table 2 indicates the length of survival.

TABLE 2.—*Survival after onset in 201 fatal cases 1933 encephalitis, St. Louis area*

Interval between onset and death	Number of cases	Interval between onset and death	Number of cases
1 day	2	1–2 weeks	62
2 days	10	2–3 weeks	10
3 days	11	3–4 weeks	8
4 days	23	4–5 weeks	5
5 days	24	5–12 weeks	5
6 days	25		
7 days	16	Total	201

Reliable data on the incubation period of a prevalent disease in urban communities are difficult to obtain. The multitude of possible opportunities for infection makes uncertain any conclusion from apparently connected cases. In this epidemic it was ascertained by a subsequent survey that only cities in the St. Louis section of the country showed any appreciable amount of infection with this form of encephalitis. It was thus possible to assign boundaries to the infected region. Persons who entered this region without previous contact with infected territory and who later contracted the disease might reasonably be assumed to have had an incubation period no longer than the interval between their coming into the infected area and the onset of the disease. In the 6 such cases which were recorded the maximum incubation period thus ascertained was 9, 12, 14, 14, 14, and 21 days, respectively. Other persons would have their first symptoms at some time after going from the St. Louis area into presumably uninfected surroundings. Here the incubation period we should suppose to be not shorter than the interval between the date of entering the uninfected area and the date of onset. In the 7 cases of this kind the presumed minimum incubation period was 4, 7, 8, 9, 11, 13, and 14 days, respectively. According to this, one would expect about half a dozen cases to have incubation periods ranging at least from 9 to 14 days, and possibly from 4 to 21 days. Among a thousand cases a somewhat wider range might be expected.

The earlier and heavier incidence of the disease in the county than in the city has been mentioned. An even more striking tendency in this direction is noticeable (fig. 3) when the city is divided into sections of about 120,000 population each, in accordance with their relation to the river and the oldest districts on one hand, and the county border and suburban area on the other. The two such sections containing the wards which border on the river only, without touching the county, had only 31 cases per 100,000 population. The wards in the southern part of the midcity region, touching neither the river nor the county boundary, had a rate of 46. The northern midcity wards had a rate of 51. The wards at the northern and southern extremities of the city, which border both river and county, had a

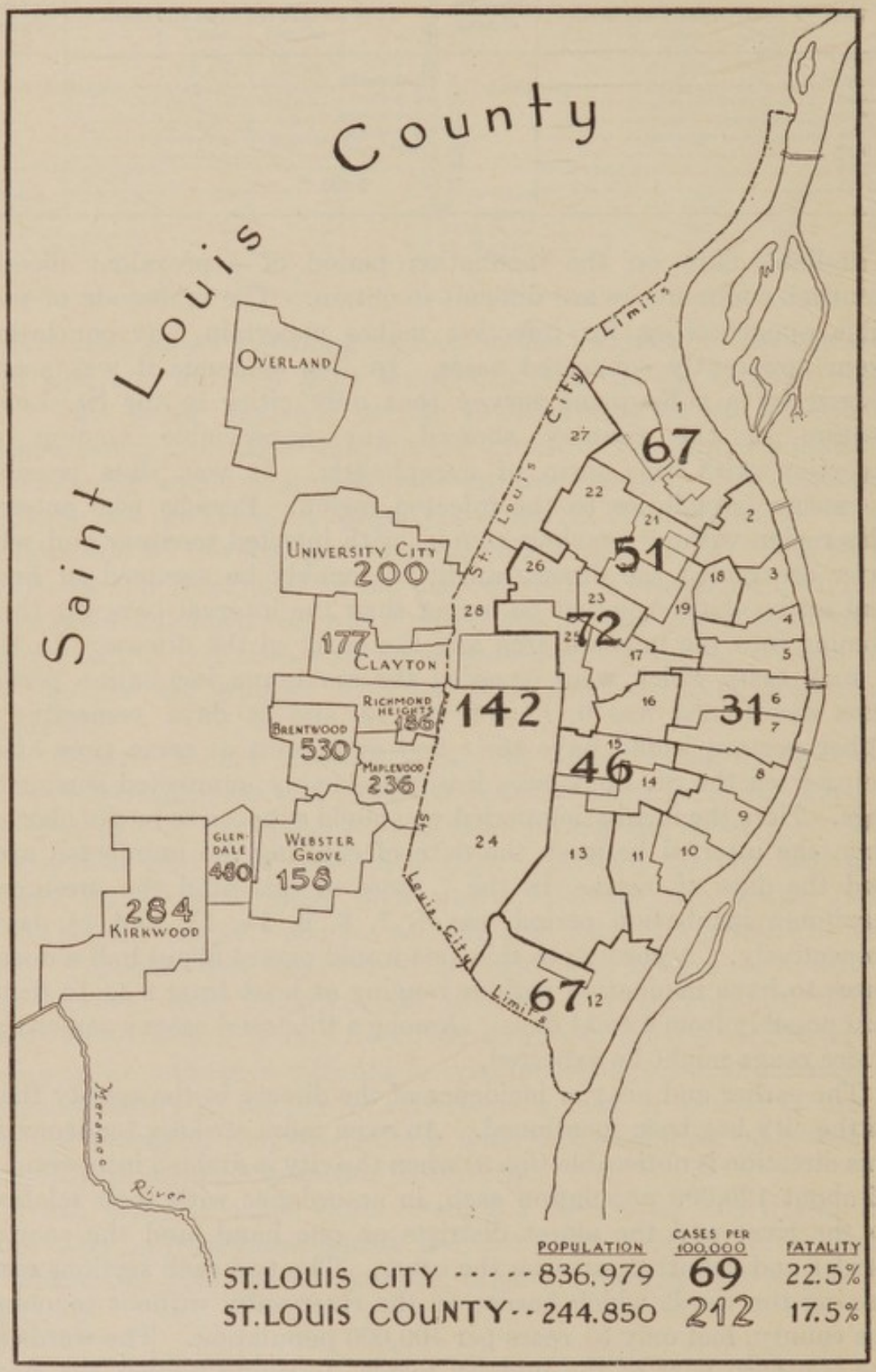

FIGURE 3.—Incidence of encephalitis per 100,000 population in the different sections of St. Louis City and St. Louis County.

rate of 67 per 100,000. The central midcity wards, the old west end, had a rate of 72, while the extreme western wards, along the county line, had 142 cases per 100,000. Out in the county, the city of Webster Groves, along the railroad, had a rate of 158; Clayton, 177; Richmond Heights, 186; University City, 200; and Maplewood, 236; all these were close to the city line. Somewhat farther out were Kirkwood with a rate of 284, Glendale with 480, and Brentwood with 530 per 100,000.

The epidemic centered in St. Louis County, and did not radiate far. About 150 cases occurred in Illinois, including the satellite cities across the Mississippi River from St. Louis, but the disease did not spread to Chicago, 250 miles away; two definite foci did occur 75 and 100 miles from St. Louis, and about twice as far from the Paris focus of 1932. Louisville, 250 miles from St. Louis, was the only other locality to the east to have any considerable number of cases.

To the west, scattered cases in excess of the normal occurred in Missouri and Kansas, with foci in Columbia, in and around Kansas City, and in St. Joseph, respectively, 100, 230, and 250 miles from St. Louis. In the larger of these foci, namely the Kansas City area, Louisville, and St. Joseph, the same tendency was evident that was noted in St. Louis, for the cases to be more numerous in the outlying sections than toward the center of the cities. In the Kansas City area there were 181 cases and in St. Joseph 45, with fatality rates of 23 percent and 30 percent respectively. As to age distribution, a tendency toward selecting the older persons was noticeable, and the curve of the Kansas City outbreak, as to dates, was similar to that of the St. Louis cases.

In all places were the disease has appeared, there has been a notable freedom from multiple cases in the same family, or from other obvious contagion between cases. This is even more striking than in outbreaks of poliomyelitis, and some difference in that direction would be expected between a disease primarily of children and one of old people. As regards communities, the spread by contagion, in the broadest sense of the word, presumably by human transfer, is obvious, but as regards individuals, the reverse is true. Once the disease is established in a community the matter of individual susceptibility, in which age played a part, appeared to be a much more important determining factor in the contracting of the disease than did contagion. In many of the households affected the least mobile member, and the one least in contact with the outside world, was the one stricken. The sharp seasonal limitation of the disease in its typical form is also noteworthy. In none of the places to which the affection spread did the outbreak prolong itself beyond the season during which it prevailed in St. Louis.

There were no instances of two attacks in the same individual, but persons who had had an attack of poliomyelitis, even within a few years, were not spared from this disease.

The possibility of spread by drinking water came early to attention in St. Louis. The city of St. Louis derives its water supply from the Mississippi and Missouri Rivers, through pumping stations well above the city. The water supply for the various municipalities of the county is from a pumping station on the Missouri River some distance from the city station which supplements the Mississippi River supply. This sharp division between the two water supplies which exists at the city limits suggested a possible reason for the outbreak being largely a county affair, especially during the first few weeks, and for its wide dissemination over the county. Fortunately this matter could be promptly settled by investigation of the cases occurring in the city of Kirkwood. This city derived its water supply from a system entirely different from that of the rest of the county, and has its pumping station on the Meramec River, a tributary of the Mississippi. As may be seen from Figure 3, the incidence of the disease in Kirkwood was even higher than in the other parts of the county, and the patients were found in almost all instances to have taken their drinking water chiefly from the Kirkwood supply, and not at all from the county supply.

The milk supply of the cases throughout the city and county was found to be distributed among the different milk dealers roughly in proportion to the total amount of milk which each handled, without any dealer or dealers having a disproportionate number of cases among patrons.

The sharp limitation of the epidemic to the warm season of the year and the lack of obvious connection between the cases as to contagion, water supply, food supply, or milk supply, suggested at once one of the major objectives of the epidemiological inquiry—the possibility of transmission by insects. Entomological investigation of the circumstances under which the disease was occurring pointed to the mosquito as being the most probable vector if there was an insect vector. No other biting insect, not even *Stomoxys calcitrans*, the biting stable fly, was likely to have a range long enough and breeding places so situated, as to account for the wide and fairly rapid spread of the disease. The summer was an exceptionally dry one, and though replies to specific inquiries varied, it was generally believed that mosquitoes were worse than usual.

Aside from the studies on the virus and clinical studies, entomological investigation was the first laboratory phase of the joint inquiry which was taken up. It was carried on by a corps of workers of the United States Public Health Service greatly aided by laboratory facilities provided by the Oscar Johnson Institute of Washington

University, and by special humidity and temperature rooms placed at our disposal by the Missouri Botanical Gardens. Later, work was also carried on by a group from the United States Army with special facilities for *Aedes* experiments.

Attempts were made to inoculate monkeys and mice by the bite of mosquitoes which had been allowed to feed on encephalitis patients at various stages of the disease, and allowed to bite the experimental animals at various periods, after the initial feedings. Initial feedings were also made on inoculated monkeys and mice. Parts of the lots of presumably infected insects were also ground up at various times and inoculated into monkeys and mice. The three species of mosquitoes on which chief stress was laid in the experiments were *Aedes aegypti* on account of the ease with which this insect may be handled experimentally, *Anopheles quadrimaculatus*, on account of the presence of malaria clinically and this host having been found in the district concerned, and *Culex pipiens*, which was the common mosquito of the region and in spite of the difficulty in handling for experimental purposes was the only species which could reasonably be incriminated as the possible vector in nature for this outbreak.

All the tests were negative.

On account of the relatively low percentage of success with monkey intracerebral inoculations (only 40 percent) under the most favorable experimental conditions, it was believed that only human experiments would show the possibility of contracting the disease through the bite of a mosquito under natural conditions. For this purpose the Governors and the health commissioners of the States of Mississippi and Virginia allowed certain of the convicts in the State penitentiaries to volunteer to submit themselves to the bites of presumably infected mosquitoes. All three species of mosquitoes were used, and various periods of the disease were used for the initial feedings and various intervals for the attempted human inoculations.

Here again all tests were negative.

Our results therefore speak against mosquito transmission in this form of encephalitis. In spite of entire failure under a wide variety of experimental conditions we cannot say that the possibility of transmission of encephalitis by mosquitoes in nature is finally disproved. It would, however, be extremely difficult to account for the rather uniform diffusion of the disease over a wide metropolitan area on the basis of such transmission being operative as the major factor in the spread of the disease. At any one time there was no concentration in any sharply localized section of the city and suburbs, and no section was definitely spared, considering the distribution of the population. In other words, even on the basis of insect transmission one would think of individual susceptibility as more of a

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determining factor than the bite of an infected mosquito in the acquiring of the disease.

It is interesting that there is on record a report of an investigation of the 1878 yellow fever epidemic in St. Louis. There were 151 cases in St. Louis with 71 deaths, of which 31 (23 fatal) were of indigenous origin. These were practically all in groups closely connected geographically, without any diffusion over the city.

In view of the trend of the insect experiments, the diffuse fashion in which poliomyelitis, except in the most intense epidemics, spreads through a community without apparent contact between cases, and in view of the radial spread of this epidemic of encephalitis by communities, but not by individual cases, it appears likely that human contact, chiefly through unrecognized carriers, is the method of infection here, but that susceptibility, in which age is an important factor, determines who will contract the disease in an infected community.

STUDIES OF THE VIRUS

The etiology of epidemic encephalitis has been extensively studied in many laboratories since 1917, and the literature is comprehensively reviewed and a complete bibliography given in the Reports of the Matheson Commission. (*1*) (*2*) [1] The lack of specific diagnostic criteria, and the probability that several unrelated etiological agents may cause similar clinical syndromes, make a comparison of work in different laboratories extremely perplexing.

In view of these difficulties, this report deals only with the disease which occurred in epidemic form in St. Louis in the summer of 1933. Encephalitis, as it appeared in this epidemic, differed in so many respects from the disease described by von Economo that it seems wise to consider it a separate entity. This disease is apparently quite similar to the form of encephalitis which has occurred in Japan and which has been designated type B by Kaneko and Aoki (*3*).

In this article the general aspects of studies concerning etiology will be briefly described with a résumé of the results and a discussion of their significance. Only essential technical details are presented.

Bacteriological

Cultures of blood and spinal fluid.—From the outset of the epidemic, cultures of blood and spinal fluid were made routinely. This was done in the different hospitals accepting cases of the disease, and, although certain routine media were employed throughout, a number of other culture media were also used. The outcome of such studies was consistently negative, indicating beyond any reasonable doubt that the presence of ordinary bacteria in the blood or spinal fluid played no etiological role.

[1] Italic figures in parentheses refer to Bibliography of this section, p. 35.

Cultures of brain tissue.—At autopsy, the skull plate was removed, leaving the dura intact. The dura was then wiped off with an alcohol sponge, and opened with sterile instruments. Pieces of brain tissue were removed with a second set of sterile instruments and placed in Petri dishes and in bottles of 50 percent glycerine for transportation to the laboratory.

Bits of brain removed in this manner were triturated without sand in a sterile mortar under a hood, emulsified in Locke's solution, and cultured. A variety of culture media were used, always including broth and blood agar which were incubated both aerobically and anaerobically. Egg medium, potato medium, and dextrose-cystine-blood agar were used in many cases. Fifteen brains, which were also used for animal inoculation, were cultured in this way, and in eight no growth occurred. Some growth took place in one or more of the tubes of inoculated media from the other seven brains, but the bacteria were few in number and of various types, consisting largely of diphtheroids, staphylococci, and molds. The collection and handling of the tissue was of necessity done in such a manner that some contamination was unavoidable, and the small number and variety of bacteria encountered seemed to justify excluding them from further consideration. It seems evident, therefore, that invasion of the brain by ordinary bacteria did not explain the etiology of the disease. In further confirmation of this conclusion, stained sections of brain tissue failed except in a few cases to reveal the presence of bacteria.

Transmission to Animals

The early unpromising results of attempts to culture bacteria from tissues that were presumably infected made a search for a filterable virus imperative, and with this object in view a large number of animals were inoculated. For some of this work, blood and spinal fluid collected early in the disease was used, but, since these experiments gave negative results, they will not be described. Filtered nasal washings, concentrated in vacuo, were also used a few times with negative results. The outcome of these attempts is, however, probably of no significance, since the washings were made with Locke's solution, and the virus that was later established in animals does not pass through a Berkefeld filter under the conditions employed in our laboratory when suspended in this solution.

Emulsified brain tissue, prepared as described for culture, was inoculated intracranially with failure to produce any disease in rabbits, guinea pigs, cats, dogs, rats, vitamin-deficient rats (secured through the courtesy of Dr. Cowdry), chickens, sheep, pigs, and ferrets.

The negative results secured with rabbits are significant, since rabbits are susceptible to herpes virus, which has been considered by

many, notably Levaditi (*4*), and Gay and Holden (*5*), to be the probable cause of epidemic encephalitis.

Seven rabbits were inoculated intracranially with brain emulsions (from two of these brains a virus which will later be described was established in monkeys), 6 with spinal fluid, 3 with blood, and 1 with a mixture of blood and spinal fluid. A number of rabbits were also inoculated by other routes. If a virus had not been demonstrated in monkeys and mice these negative results would not be extensive enough to be conclusive, but since from several of the brain emulsions used, a virus that reacted specifically with the serum of convalescent individuals was isolated, the findings reported here seem to exclude herpes virus from consideration as the cause of the epidemic of encephalitis occurring in St. Louis in 1933. Eight cebus monkeys also failed to show signs of illness after the inoculation of brain tissue, or of passage virus from macacus rhesus monkeys.

Monkeys.—Macacus rhesus monkeys were shown to be susceptible by Muckenfuss, Armstrong, and McCordock (*6*) when inoculated intracerebrally with brain emulsions. At the outset approximately a 10-percent brain emulsion was inoculated in a single dose of 0.25 cc but none of the inoculated monkeys developed any evidence of illness. The density of the emulsions (in Locke's solution) was therefore increased to about 15–20 percent and the amount injected intracranially to 2.0 cc, in addition about 4–5 cc of the same emulsion was injected into the peritoneal cavity. After 4 or 5 days this double inoculation was repeated, utilizing the opposite hemisphere. In all, emulsions from 15 brains were inoculated, with the development of disease in monkeys inoculated with seven of these. After periods varying from 8 to 15 days from the first inoculation, the temperatures of the animals began to rise gradually, and at the same time they became weak and listless, usually sitting quietly in the cage when undisturbed. When aroused, tremors were observed, and were most marked in the legs when the animals climbed up the sides of the cage; tremors of the arms were also present. Incoordination was evidenced when the animals were disturbed with a rod; in attempting to grasp it, they would often find it necessary to make two or three attempts before it was finally seized in their hands. Lumbar puncture at this time usually showed 50 to 150 cells in the spinal fluid.

Most of the animals were sacrificed, either at the height of illness or just as the temperature was beginning to decline. A few were permitted to recover. Since, as a rule, the disease was not allowed to run its course, it is impossible to predict the usual outcome in monkeys, but in a few instances the illness seemed severe enough to lead one to expect a fatal termination.

When the brains of monkeys killed by chloroform or ether were exposed, hyperemia was usually observed. Some of the inoculated

material could usually be found in the hemisphere of the brain, but cultures of this material were uniformly sterile, and bacteria could not be demonstrated in smears or in sections of tissue. Microscopically the changes seen were similar to those observed in fatal cases of human encephalitis. Vessels in the cortex, the base of the brain, and the upper levels of the cord were surrounded by collars of lymphocytes (fig. 4), and occasional nerve cells were seen to be dead and surrounded by phagocytic cells. These lesions usually tended to be more numerous in the region of the base of the brain and of the medulla, although they were present throughout the central nervous system.

Passage of the virus in monkeys was attended with considerable difficulty. Not all monkeys were susceptible (approximately 60 percent were refractory), and it was necessary to continue the large inoculation, and usually the second inoculation was also made. In spite of these procedures, several strains were lost, although four strains were carried through five monkey passages before the use of monkeys was largely discontinued.

Mice.—During the course of this work, Dr. L. T. Webster, of the Rockefeller Institute for Medical Research, inoculated a strain of mice, bred in his laboratory and peculiarly susceptible to neurotropic viruses, with material shipped to him in glycerin from St. Louis. Using these animals, Webster and Fite were able to establish four strains of a virus which was uniformly fatal, and which produced no disease in rabbits or guinea pigs (7). Dr. Webster informed us of these results.

Brain tissue of our monkeys showing illness in the second animal passage was removed aseptically and emulsified as previously described. We inoculated these emulsions intracranially into stock mice in quantities of 0.025 to 0.03 cc. In the first experiment 5 mice were inoculated, and 2 of them died, the other 3 showing no sign of illness. Passage from the brain of 1 of these into 4 other mice resulted in the death of all of them after an incubation period varying from 5 to 7 days, and further passage was readily accomplished. Three strains of virus being carried in monkeys were established in mice in this manner. The stock mice available in St. Louis were found to be susceptible uniformly, although on the first inoculation the incubation period was quite variable and only a few of the mice would succumb. Mice usually became ill rather suddenly after the expiration of the incubation period (ordinarily 4 to 8 days), and many were hyperirritable, and showed convulsions, incoordinated movements when attempting to walk, and tremors. After a short time they became quiescent, and respiration was barely perceptible. In a few hours death occurred, and frequently the entire illness occupied only 5 or 6 hours, although some mice lived for 24 hours or even for several

days after the onset, when the inoculating dose was small; a few recovered after showing characteristic illness.

Strains of virus isolated in St. Louis and strains isolated by Dr. Webster were exchanged, and their identity compared. These viruses had similar incubation periods, caused the same clinical picture, the same pathological changes in mice (fig. 5), and were similar immunologically. The results of these studies seem to indicate unquestionably that the strains compared were the same virus.

Immunological relationship of the virus to encephalitis.—Neutralization of this virus by the serum of individuals convalescent from encephalitis has been reported by Webster and Fite (7). This observation has been confirmed. The technic employed in the majority of such experiments has been as follows:

A mouse showing characteristic symptons of encephalitis was killed by ether. After being pinned to an autopsy board, alcohol was dropped over the head and back, and the skin reflected back with sterile instruments. Alcohol was then dropped over the exposed surface and a second set of sterile instruments was used to remove the top of the skull. The brain was then removed either with scissors or a small spatula, and placed into a sterile container, and a small piece removed for culture. The brain was then triturated in a small sterile mortar without sand and emulsified in 3 cc of Locke's solution, making an emulsion of approximately 10 percent. This emulsion was cultured. Serial dilutions were then made in Locke's solution, changing the pipette with each dilution. Dilutions of 1–10,000 and 1–100,000 were pipetted into small sterile tubes to which an aliquot portion of aseptically collected serum was added. These mixtures of serum and virus were incubated for 2 hours at 37° C. and then injected intracranially into mice, 4 mice being used for each tube. In making these injections a tuberculin syringe of 0.25 cc capacity was used. The mouse was lightly etherized, and held upon the table with its head between the thumb and forefinger of the left hand, after which alcohol was dropped upon its head and the small hypodermic needle forced through the skull to make the injection into the brain tissue. Such inoculations were readily made.

Table 3, copied from the report of Webster and Fite (7), shows the characteristic result of such an experiment. Neutralization of the virus by the serum of convalescents drawn from a few weeks to 3 months after recovery has been consistently observed, although there have been a few exceptions to this rule.

Susceptibility of animals.—The disease produced in mice and monkeys has been described. Rabbits, guinea pigs, and ferrets have

FIGURE 4.—BRAIN OF MONKEY SHOWING PERIVASCULAR LYMPHOCYTIC INFILTRATION.

FIGURE 5.—BRAIN OF MOUSE, SHOWING PERIVASCULAR CUFFING.

not been found susceptible by intracranial inoculation. Six horses and mules were inoculated intracerebrally. One mule showed a slight rise of temperature of a few days' duration about 10 days after

TABLE 3.—*Protection test*

Sera	Virus-serum dilution			
	10^{-3}	10^{-4}	10^{-5}	10^{-6}
J., normal New York	5,[1] 5, 6, 8	7, 7, 8	8	
K., normal New York	4, 5, 5, 8	5, 5, 5, 6	7, 7, 7	
R., normal New York	5, 5, 5, 7	5, 5, 5, 7		
No. 10, St. Louis convalescent	6			
No. 9, St. Louis convalescent	7, 9, 10			
No. 33, St. Louis convalescent	8, 10	8		

[1] Duration of life of mouse in days. Blanks indicate mice remained healthy.

inoculation. Another mule, inoculated with a monkey brain, showed an elevation of temperature and other signs of illness about 10 days after inoculation. This animal was sacrificed, and the brain showed perivascular cuffing with round cells. Passage to another animal was not successful. Although no disease was established, the results of this work seem to indicate that some degree of susceptibility may exist in the mule.

Pathological lesions in mice are similar to those seen in monkeys, namely perivascular accumulations of round cells, scattered foci of round cells apparently unrelated to blood vessels, and degeneration of nerve cells.

Preservation of the virus in glycerine at ordinary ice-box temperature is of rather short duration. A mouse brain, originally causing the death of all of the inoculated mice, was placed in the refrigerator in a bottle of 50 percent glycerine. After 5 weeks an emulsion of this brain caused the death of only 2 out of 6 mice inoculated, and these died after prolonged incubation periods. A number of fresh brains in small test tubes were stored frozen by placing them in the freezing coils of the refrigerator. Under these conditions deterioration seemed to be slow, and in the course of a week or ten days no loss of potency could be detected.

Deterioration of emulsions at room temperature occurs fairly rapidly as shown by the following experiment:

An emulsion of fresh brain was diluted serially and inoculated immediately. All of the mice given a dilution of 1–1,000,000 died. After standing for 5 hours at room temperature, only the dilutions up to 1–1,000 caused the death of all inoculated animals; and after

24 hours at room temperature this occurred only with the 1–10 dilution. (Table 4.)

TABLE 4.—*Deterioration of virus suspensions on standing*

	Immediate inoculation	After 5 hours room temperature	After 24 hours room temperature		Immediate inoculation	After 5 hours room temperature	After 24 hours room temperature
1–10	[1] 3/3	3/3	3/3	1–10,000	3/3	1/3	0/3
1–100	3/3	3/3	2/3	1–100,000	3/3	0/3	0/3
1–1,000	3/3	3/3	1/3	1–1,000,000	3/3	0/3	0/3

[1] These fractions indicate the number of mice dying over the number inoculated.

Filtration when the brain emulsion is made in Locke's solution has not been successful in our hands. When, however, the brain is emulsified in nutrient broth pH 7.6, the virus is readily filterable through a Berkefeld N candle. Filtration had also been reported by Webster and Fite (*7*).

Routes of inoculation.—Intracerebral and intranasal inoculations have infected mice regularly in our hands, as was also reported by Webster and Fite (*7*). Other routes of inoculation have not proved satisfactory.

Comparison with other viruses.—The infectivity for various animals is different from any other virus ordinarily encountered and having neurotropic properties. Webster and Fite (*7*) (*8*), and Cox and Fite (*9*) have reported that the virus of encephalitis is immunologically unrelated to the viruses of herpes, poliomyelitis, equine encephalomyelitis, and vesicular stomatitis. Webster and Fite (*8*) have also reported that the virus is not neutralized by the serum of individuals who have had lethargic encephalitis (v. Economo). Similar observations have been made in the laboratories of Washington University and of the National Institute of Health. However, the interval from the attack to the securing of the sera was usually considerably longer than in the St. Louis epidemic. Webster and Fite (*10*) have recently reported that the virus is not neutralized by serum of individuals convalescent from encephalitis in Japan.

DISCUSSION

The successful establishment in animals of a number of strains of a virus, identical insofar as comparative tests have been completed and different from previously known viruses, is in itself strong indication of the etiological relationship of this virus to encephalitis occurring in St. Louis in the summer of 1933. The pathological lesions in the affected animals are consistent with the disease as observed at autopsies during the epidemic. The specific neutralization of the virus by the serum of individuals convalescent from encephalitis makes the

evidence seem conclusive that this virus was the etiological agent of encephalitis in this epidemic. The bacteria that were encountered at times and in small numbers seem undoubtedly to be either contaminants or secondary invaders.

The susceptibility of monkeys is in accord with the results reported by McIntosh (*11*), but, since his virus could not be maintained, the identity of the virus isolated in St. Louis cannot be compared with his.

The failure of sera from cases of lethargic encephalitis (v. Economo) to neutralize the virus isolated in the St. Louis epidemic is strong indication that the disease occurring in this epidemic was different from that described by v. Economo.

Conclusions

1. The etiological agent of the St. Louis epidemic of encephalitis was a filterable virus.
2. Several strains of this virus, identical insofar as comparisons have been carried out, have been established in animals.
3. Mice and monkeys are susceptible to the action of this virus.
4. This virus is neutralized specifically by the serum of individuals convalescent from encephalitis.
5. Lethargic encephalitis appears to be immunologically unrelated to the type of encephalitis occurring in this epidemic.

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STUDIES OF THE RELATION OF STREPTOCOCCI TO THE DISEASE

In the extensive literature on encephalitis numerous references may be found to the occasional cultivation of streptococci or diplococci from materials supposedly containing the causative agent of the disease.[2] Organisms of this kind have been encountered more frequently than any other variety of cultivable bacteria. Very few investigators, however, have seriously considered the streptococci

[2] A summary will be found in the first report (1929) of the Matheson Commission.

as the primary cause of infectious encephalitis. On the contrary, the majority of workers have regarded them merely as secondary invaders, or accidental contaminants.[3]

Rosenow, however, on the basis of extensive work upon the etiology of encephalitis has claimed that a certain variety of streptococcus represents the true causative agent of this disease.[4] Employing the same technique as in the past, Rosenow studied the outbreak of epidemic encephalitis in St. Louis and secured evidence similar to that previously brought forward by him concerning the etiological importance of streptococci.[5] His principal findings were (1) that diplococci or streptococci were present and often could be recovered in pure culture from the spinal fluid, blood, and glycerinated brain specimens from encephalitis cases; (2) that the great majority of the streptococci secured in primary brain broth cultures from the nasopharynx of encephalitis patients showed a cataphoretic velocity which he regards as characteristic of neurotropic strains, whereas only a small proportion of the organisms in similar cultures from well persons, especially from those living outside the epidemic area, showed this velocity; (3) that intracerebral inoculations into rabbits of the primary brain broth cultures from the nasopharynx, or spinal fluid, of encephalitis patients, or injections of pure cultures of green colony streptococci recovered from inoculated rabbits, reproduced in these animals "the more important clinical and pathological manifestations" of encephalitis as seen in human cases; (4) that cultures from the nasopharynx of normal individuals, inoculated in the same way, caused symptoms and death, with "less marked" lesions, in a much smaller percentage of rabbits; (5) that Rosenow's encephalitis antistreptococcus serum agglutinated "markedly, and in high dilution" streptococci isolated from human cases, and (6) that the serum of convalescent encephalitis patients agglutinated specifically the "more sensitive" strains of streptococci isolated from St. Louis patients.

We are reporting below the results obtained in an independent study of the etiological significance of streptococci in the St. Louis epidemic. In view of the fact that Rosenow uses in his studies a particular culture medium and certain technical procedures not ordinarily employed by other bacteriologists, and lays great stress upon the value of these features of his work, we made a special effort to learn the details of his technique and to follow them exactly. In

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this we had the full cooperation of Dr. Rosenow, who was kind enough to visit our laboratory and to give us a personal demonstration. He furnished us a generous supply of his encephalitis antistreptococcus serum and later he sent us, as examples of typical strains, several cultures of streptococci which he had isolated from cases of encephalitis in St. Louis.

In order to learn the details of the method used by Rosenow for the determination of cataphoretic velocity we visited his laboratory at Rochester, Minn., and on return set up an apparatus duplicating in every essential respect the technical arrangements employed there. All of our cataphoretic velocity determinations were made by a single individual and, as in Rosenow's laboratory, without knowledge of either the source of the culture, or the purpose for which it was being used.

Our principal findings may be summarized as follows:

There was nothing distinctive about the nasopharyngeal flora of encephalitis patients. Green colony streptococci were present in primary blood agar plate cultures from the nasopharynx of 86 percent of 29 encephalitis patients and 75 percent of 21 normal persons; they were apparently the predominating bacteria in approximately half of the cultures in both groups. Included among the cultures from well persons were nine obtained from residents of Washington, D.C., having had no contact with St. Louis residents. In these the relative number of green colony streptococci was at least as high as in the cultures made in St. Louis.

Primary cultures from the nasopharynx in glucose brain broth, whether from patients or well persons, always showed in smears many Gram positive diplococci and streptococci and rarely organisms of other morphology, apparently due to the selective effect of the medium. However, plating showed that these cultures were nearly always mixtures of streptococci and other cocci or diphtheroids.

When these primary cultures were inoculated intracerebrally into albino rabbits, most of the animals developed symptoms like those shown by the rabbits injected by Dr. Rosenow in our laboratory. Of 23 rabbits inoculated intracerebrally with dilutions of the primary brain broth cultures from the nasopharynx of 21 encephalitis patients 5 showed no symptoms, while 18 (78 percent) died. Of these, 13 died within 48 hours, and the remainder in from 3 to 5 days after inoculation. Autopsies were done on 15 of the rabbits and from the brain of 12 of them green colony streptococci were recovered, in 7 cases in pure culture, while heart's blood cultures were sterile, except in 3 instances. Several of the pure strains of streptococci obtained in this way were passed at once through a series of rabbits and an intracerebral dose of 0.1 cc of a 1–1,000 dilution of a young brain broth culture was invariably fatal, usually within less than 48 hours.

Similar inoculations of the primary cultures from the nasopharynx of normal persons, including those from six of the individuals living in Washington, D.C., caused identical symptoms in rabbits. Of 10 animals so inoculated 7 (70 percent) died, in an average time of about 40 hours, and 2 other rabbits developed mild choreiform symptoms which have persisted for 2 months. Green colony streptococci were recovered from the brain of 6 of the rabbits (4 times in pure culture), and from the heart's blood also in 3 instances. These pure strains produced the same train of symptoms in rabbits as the streptococci recovered by animal passage from encephalitis patients, but they appeared to be somewhat less virulent, since intracerebral injections of the usual dose (0.1 cc of a 1–1,000 dilution) caused death in only a third of the animals.

The effects produced in rabbits by these inoculations were indistinguishable from those observed in the rabbits demonstrated to us by Dr. Rosenow, and in the animals inoculated by us with the supposedly typical strains of encephalitis streptococci which Dr. Rosenow sent us. So far as they are outlined above our findings closely agree with those of Rosenow. However, it seems entirely unwarranted to assume that the brain infection produced in rabbits by inoculations of these streptococcus cultures is a reproduction of human encephalitis.

All our rabbits exhibited a fairly uniform set of symptoms, including the early development of acute respiratory embarrassment, a cerebellar gait, with choreiform movements and later moderate retraction, twisting, or drooping of the head, edema of the eyes and sometimes nystagmus, weakness or flaccid paralysis of the legs, and body tremors, but the course of the illness was not appreciably different whether the inoculum was a pure streptococcus or a mixture of organisms, and further, it was the same whether the inoculated culture was obtained from an encephalitis patient or a normal person. The extremely brief incubation period and rapidly fatal issue of this rabbit infection does not parallel the clinical course of human encephalitis.

The principal gross pathologic change seen in the brains of over two-thirds of the 71 rabbits examined, consisted in a marked engorgement of the vessels of the leptomeninges. Visible meningeal exudate was observed in about one-third of the cases, and multiple petechiae in the medulla, pons, or upper part of the cord in about 15 percent. About half of the rabbits showed hemorrhagic edema of the lungs, and softening of the spleen, and the majority showed a congestion of the kidneys. Neither the appearance of a visible meningeal exudate, nor the other changes mentioned could be correlated with the source of the inoculum. Microscopically, brain sections showed an infiltration of the pia-arachnoid by polymorphonuclear leucocytes and large lymphocytes. Most of the sections revealed an exudate also in the ventricular cavities. The vessels of the arachnoid were dilated and

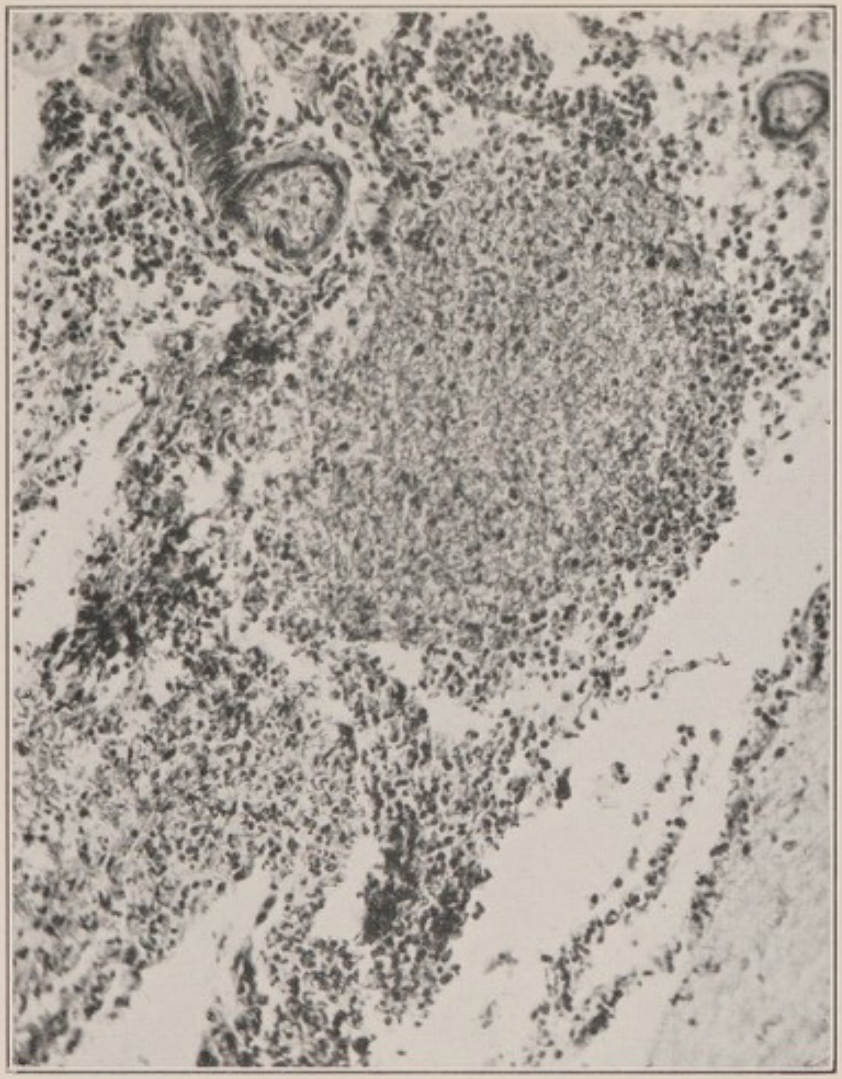

FIGURE 6.—MENINGITIS IN INOCULATED RABBIT.

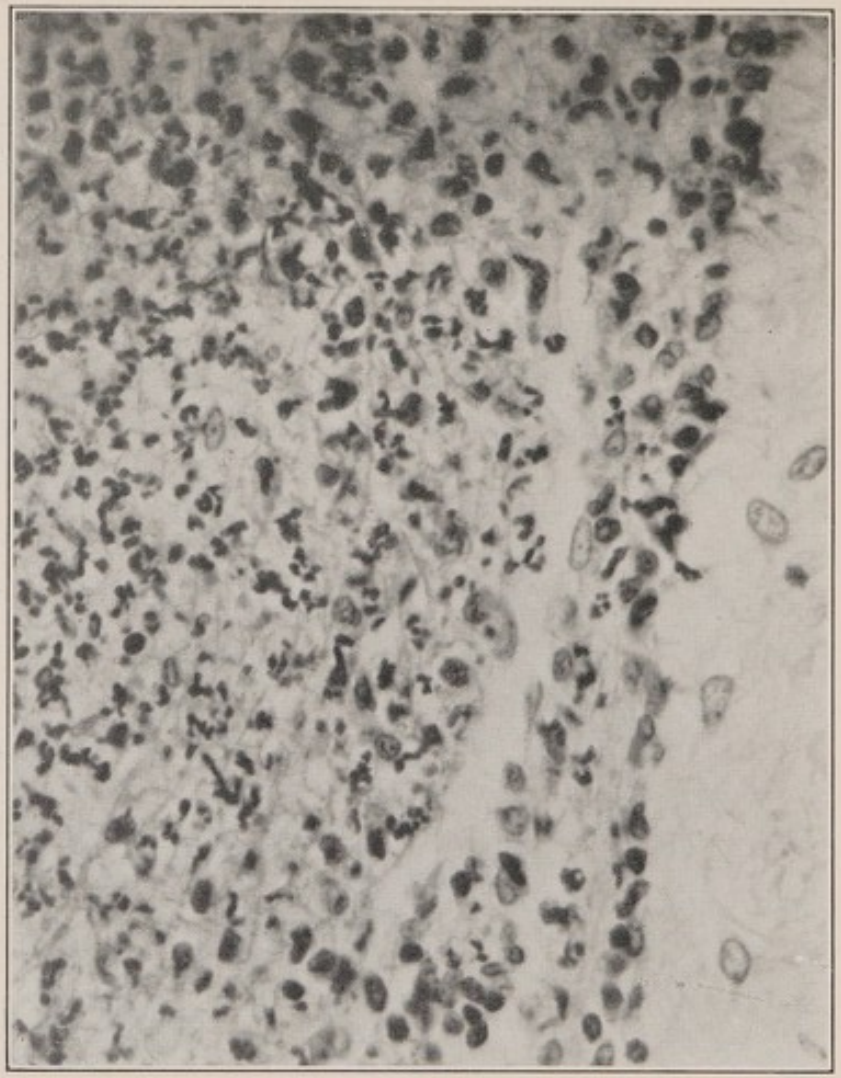

FIGURE 7.—MENINGITIS IN INOCULATED RABBIT.
(Higher magnifications.)

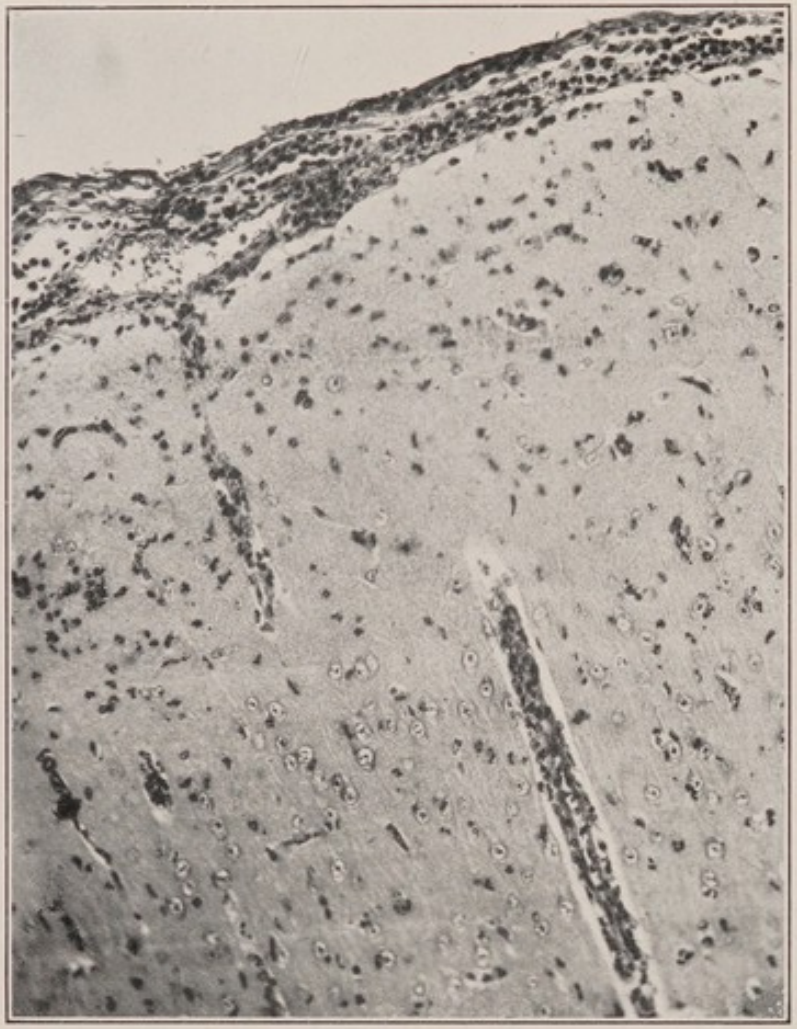

FIGURE 8.—BRAIN OF RABBIT, SHOWING SUPERFICIAL INFILTRATION.

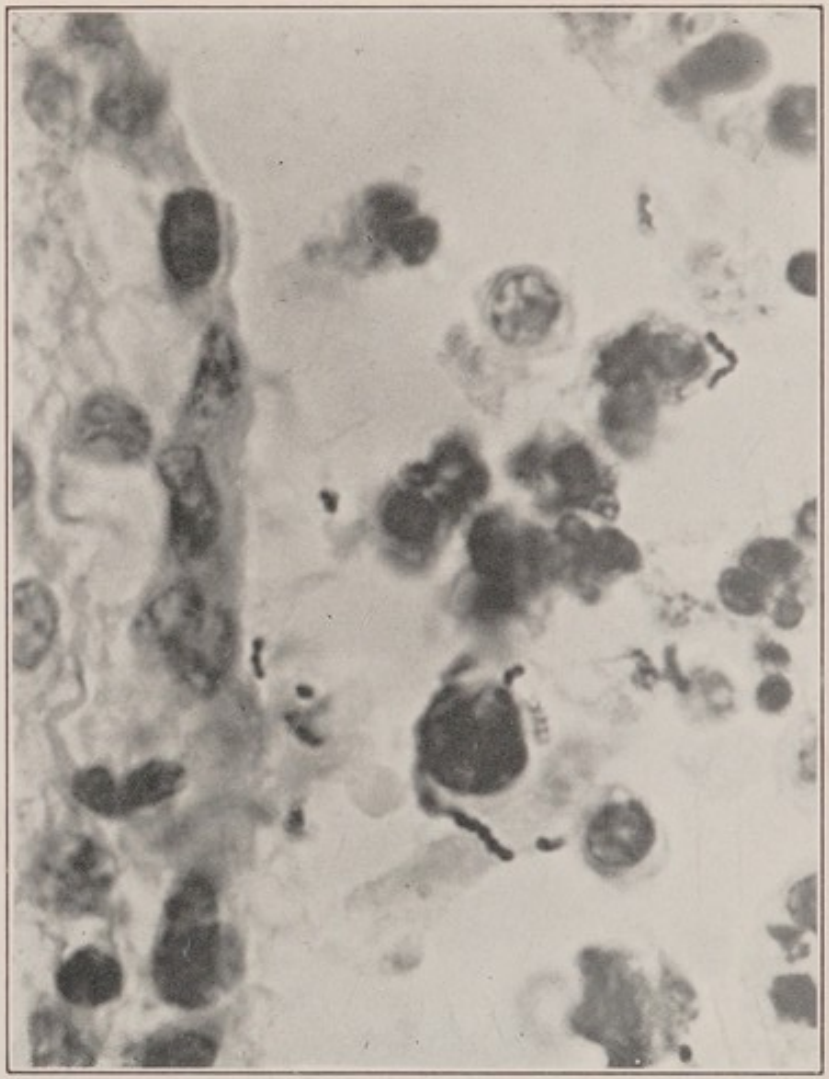

FIGURE 9.—STREPTOCOCCI IN MENINGES OF RABBIT.

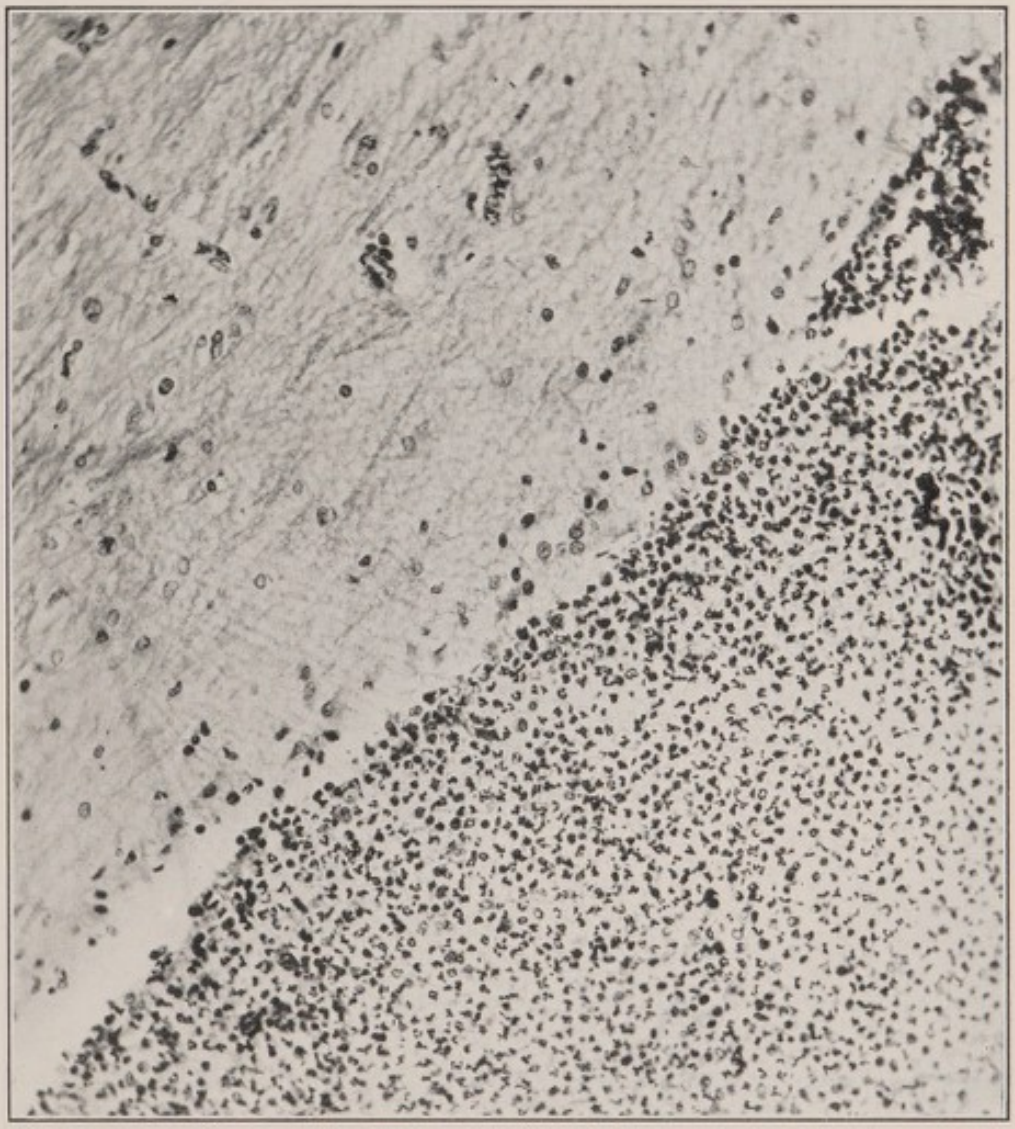

FIGURE 10.—MENINGITIS IN RABBIT INOCULATED BY DR. ROSENOW.

occasionally small hemorrhages were seen (figs. 6 and 7). In about half of the cases the vessels of the *superficial* cortical layers were surrounded by "cuffs" of polymorphonuclear leucocytes and large lymphocytes, and there was a diffuse infiltration of the peripheral layers of the cortex and subependymal tissue (fig. 8). Pathologic changes in the nerve cells were not found. Streptococci were stained in the brain sections of several animals, lying in the pia-arachnoid, or in the subependymal tissues (fig. 9). In brief, the principal pathological changes found in the brains of all rabbits examined, including those inoculated by Dr. Rosenow in our laboratory (fig. 10), were those of a purulent meningo-encephalitis. No relationship could be detected between the extent or severity of the lesions and the origin of the strain of infecting organisms. These lesions evidently do not correspond in character or distribution with those observed in cases of human epidemic encephalitis.[6]

We could not discover any consistent correlation between the cataphoretic velocity of the organisms in primary nasopharyngeal cultures, or the streptococci in pure cultures, and their source, or their relative virulence for rabbits. Measurements of the cataphoretic time of the bacteria in the mixed primary brain broth cultures from the nasopharynx seemed of doubtful significance in any event, since the observer could not be certain that all the organisms in the field were in fact streptococci, and not other organisms. Rosenow's encephalitis anti-streptococcus serum agglutinated all of 44 pure strains of streptococci isolated during the study, including 14 from normal persons. The streptococci from encephalitis patients were more often agglutinated in higher dilutions than those from healthy subjects. However, the difference was slight, since only 7 out of 30 cultures from patients were agglutinated in a dilution beyond 1–640, while 2 out of the 14 cultures from well persons were agglutinated in at least that dilution. All of 42 streptococcus cultures tested were found to be insoluble in bile; they developed green colonies on blood agar and showed the usual fermentation reactions of *Streptococcus viridans*.

In order to test in the fairest way the possible agglutinating power of encephalitis convalescent serum, a number of sera were specially chosen, 4 from patients whom we had cultured, and from whom we had isolated streptococci with the characteristic virulence for rabbits, 5 from other convalescent patients, and 5 from monkeys previously inoculated with the virus isolated from St. Louis cases by Muckenfuss, Armstrong, and McCordock,[7] and convalescent after a definite attack. All these sera had been shown to possess distinct protective power against the virus in mice in experiments conducted by Smadel and Muckenfuss. In addition, as controls, 6 specimens of normal sera

[6] See chapter on Pathology.

[7] Pub. Health Rep., *48*, 1341, 1933.

were tested. As test organisms we selected 12 pure strains of streptococci, including 3 of Rosenow's strains, one strain from a well person which was agglutinated highly by Rosenow's serum and 8 of the most typical strains from encephalitis patients. No sign of specific agglutinating power for these organisms was shown by any of the convalescent sera.

A series of controlled experiments were performed to test the protective capacity of convalescent sera, and of Rosenow's serum. Rabbits were inoculated intracerebrally with one of the strains of streptococci sent us by Dr. Rosenow or with a typical strain freshly isolated by us from an acutely ill encephalitis patient, after mixture of the culture with the various sera, according to the recommendations of Rosenow. Four of the seven sera used had been tested and found to have marked protective power against the virus in mice. The results showed that Rosenow's serum had a definite, though partial protective effect (as would be expected since it is an antistreptococcus serum), but none of the convalescent sera gave any protection whatever.

It is concluded that while virulent green colony streptococci are apparently abundant in the nasopharynx of encephalitis patients, no significant evidence has been adduced which would support the view that these organisms are the primary etiologic agents in human epidemic encephalitis or have any specific relationship to the virus isolated from St. Louis cases.

PATHOLOGY

During the epidemic ample material for a complete study was secured at 63 autopsies performed by various members of the committee. In the majority of instances the thoracic and abdominal organs and portions of the spinal cord were examined in addition to the brain. All of this material has not yet been studied but a sufficient number of sections from each case have been examined to gain a fair understanding of the pathological changes in this form of encephalitis. The essential pathological process is an acute nonpurulent inflammation of the central nervous system characterized by intense vascular congestion with petechial hemorrhages, cellular infiltration of both nervous tissue and meninges with various types of mononuclear cells, and evidences of toxic degeneration in the nerve cells.

Vascular congestion is the one constant change found in all cases. In severe examples of the disease the inflammatory lesions are widespread throughout the brain and cord. In milder cases, even though the vascular congestion is universal, the inflammatory collections of mononuclear cells may be restricted to one portion of the brain, and such cellular infiltration is most likely to be found in the pons, medulla or midbrain.

PATHOLOGICAL CHANGES IN FATAL CASES

Gross changes.—Vascular congestion of varying degree was the only consistent pathological alteration in the central nervous system, that could be observed by a naked-eye examination at the time of autopsy. Every one of the 63 brains examined showed obvious congestion of the meningeal and intracerebral vessels. In addition to extreme congestion, small hemorrhages were present in the meshes of the pia-arachnoid in about one-quarter of the cases. These were usually situated in the space formed by the junction of two or more sulci. Cross-sections through the fresh brain revealed about the same degree of congestion in the intracerebral vessels as was present in those upon the surface. Most of the cut vessels oozed blood under slight pressure. It was difficult to distinguish grossly between petechial hemorrhages and these dilated veins. In every instance in which there was marked vascular congestion the gray substance was prone to show a light salmon-pink color, which microscopic examination later proved to be due to intense capillary congestion. In several cases the entire cerebral cortex, as well as the gray substance of the cerebellum, midbrain, brain stem and spinal cord, was pink instead of being of the normal gray color. With the exception of these extreme examples, this pinkish discoloration of the gray substance was blotchy in distribution. In some brains the blotches were found scattered throughout the cerebral cortex and in the basal nuclei and brain stem; in others, the change was restricted to the basal nuclei, the pons and medulla.

The cerebrospinal fluid was noticeably increased in amount at 20 autopsies. In almost every instance the clinical records showed that in these cases repeated spinal punctures had not been performed during life. The most marked increase in cerebrospinal fluid observed during the epidemic was in one of the early acute cases in which the patient died a few days after the onset of symptoms without a spinal puncture having been done. The fluid was always clear and this was consistent with the absence of exudate in the meninges.

An increased softness of the brain tissue due to edema was evident in many of the more acute cases (fig. 17).

Thrombosis of the venous sinuses or of the cortical vessels was never encountered.

Microscopical changes.—The microscopical lesions in the brain were those of an acute inflammation, the three most important changes being: Vascular congestion and hemorrhage, cellular infiltration, and nerve cell degeneration.

Congestion and hemorrhage.—In every case congestion of the blood vessels of the meninges or brain substance could be found in some of the sections. Each of the 20 cases in which the vascular congestion was extreme also showed small subarachnoid hemorrhages, as well as

extravasations of blood into the perivascular speces (fig. 13), and in some places petechial hemorrhages in the brain substance (fig. 14). The pink areas in the gray substance that were apparent to the naked eye showed, under the microscope, a most intense congestion affecting all the vessels down to the smallest capillaries (fig. 12).

Cellular infiltration.—Three types of cellular infiltration were observed; namely, perivascular round-cell infiltration, focal collections of mononuclear cells, and areas of diffuse cellular infiltration. All but three of the brains examined revealed the characteristic perivascular collections of mononuclear cells, forming the typical cuffs around the vessels that so commonly are found in diseases of the nervous system (figs. 23 and 24). These cells were usually limited to the Virchow-Robin space, but in the case of some vessels they invaded the perivascular space of His and occasionally extended for a short distance into the surrounding brain tissue.

Most of the mononuclear cells in the perivascular spaces revealed all the morphological characteristics of lymphocytes. There were, however, in addition a small number of plasma cells and occasionally a few polymorphonuclear leucocytes and large mononuclear phagocytes.

A very striking feature in about two-thirds of the cases was the presence of small foci of mononuclear cells that did not bear any apparent relation to blood vessels (figs. 15 and 16). In 10 instances these foci were so numerous that several were often included in a low-power field, and they could be found in sections from many regions of the brain. When viewed with a low-power objective these cellular foci somewhat resembled small foci of infection or fresh miliary tubercles. Under higher magnification two types of cells predominated in these nodules. One was a small cell with scant cytoplasm and a darkly staining nucleus, which in most respects resembled a lymphocyte in hematoxylin and eosin preparations, but some of them were probably glial cells (oligodendroglia). The second type of cell was somewhat larger and showed a pleomorphic nucleus which was often elongated and curved (fig. 21). Sections impregnated with silver revealed a few fibers projecting from the cell body. Because of these characteristics this cell was regarded as a glia cell probably derived from the microglia.

Polymorphonuclear leucocytes and large mononuclear phagocytes were occasionally found in small numbers intermingled with these glia cells. Degenerated nerve cells could sometimes be seen within these focal collections of cells.

Varying degrees of diffuse infiltration of large areas of brain tissue with cells simi ar to those comprising the focal collections were found in about one-half of the cases. This general infiltration varied from a slight obvious increase in cellular constituents (figs. 15 and 20) to

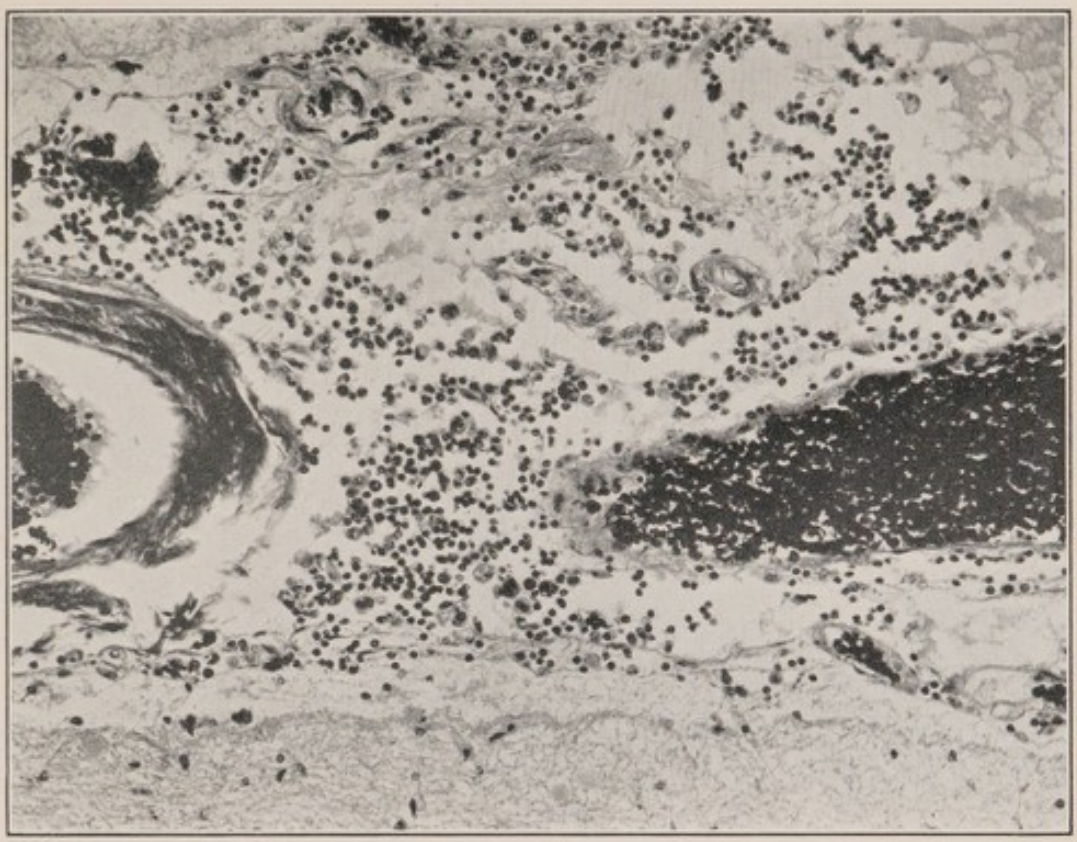

FIGURE 11.—MONONUCLEAR MENINGEAL EXUDATE, CASE I.

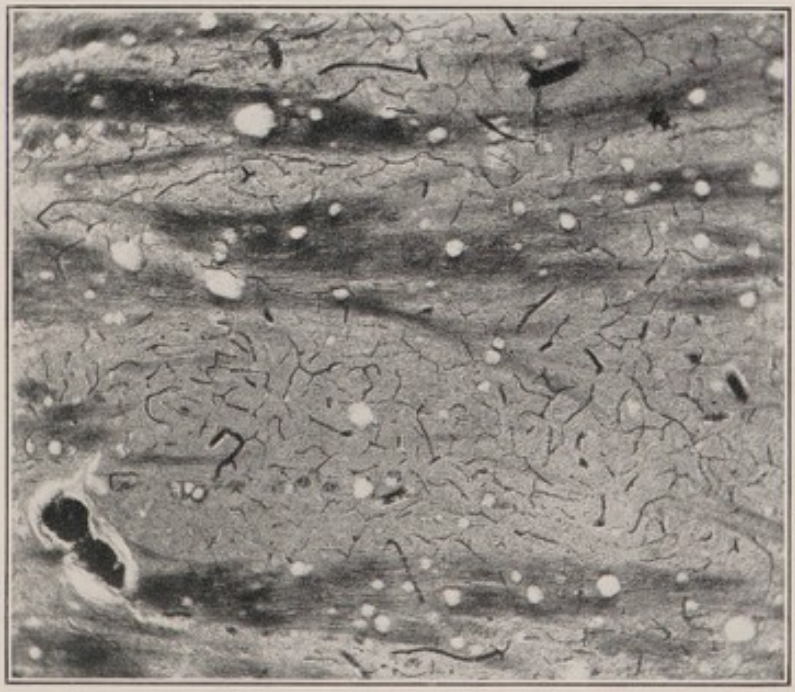

FIGURE 12.—CONGESTION OF CAPILLARIES IN PONS, CASE III.

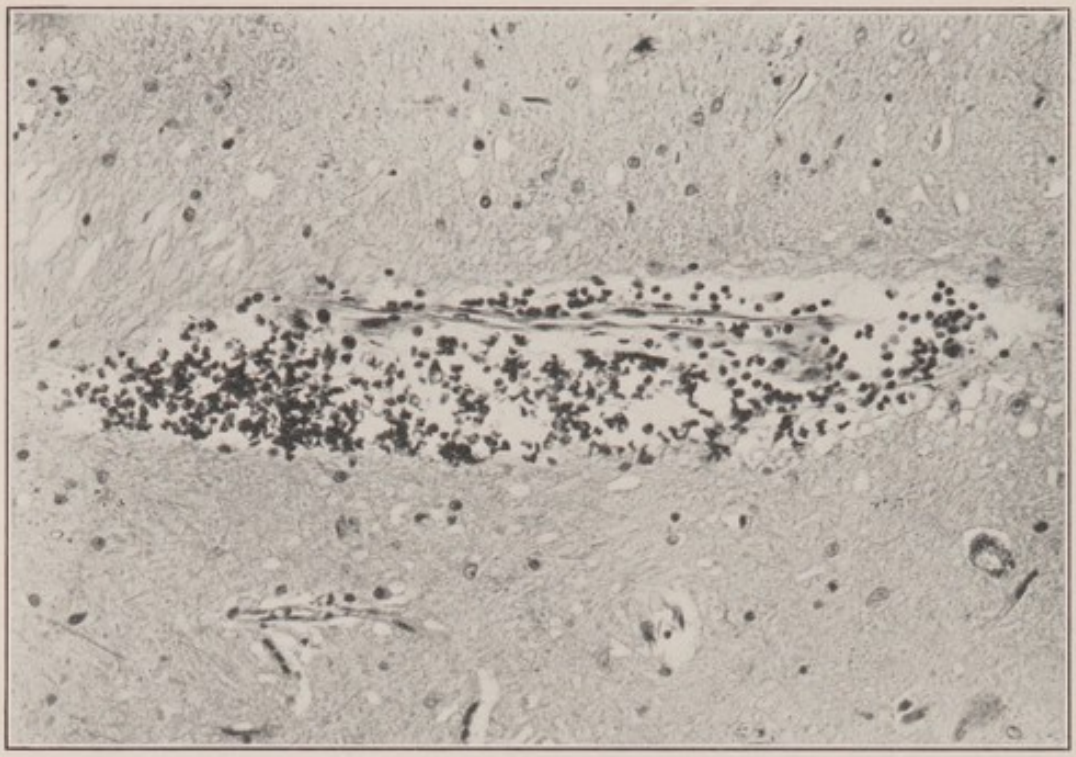

FIGURE 13.—HEMORRHAGE INTO PERIVASCULAR SPACE IN CAUDATE NUCLEUS, CASE II.

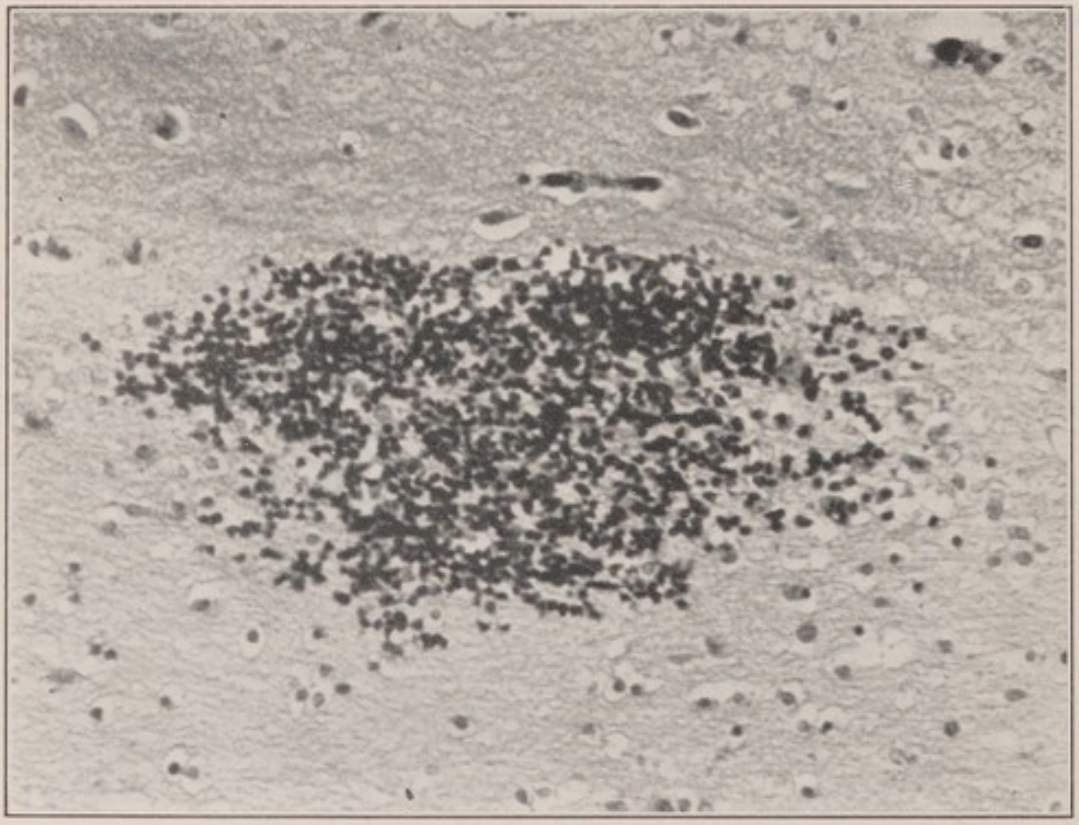

FIGURE 14.—PETECHIAL HEMORRHAGE IN BRAIN.

FIGURE 15.—CELLULAR FOCI AND DIFFUSE INFILTRATION IN CORTEX, CASE I.

FIGURE 16.—FOCUS OF MONONUCLEAR INFILTRATION IN CORTEX, CASE I.

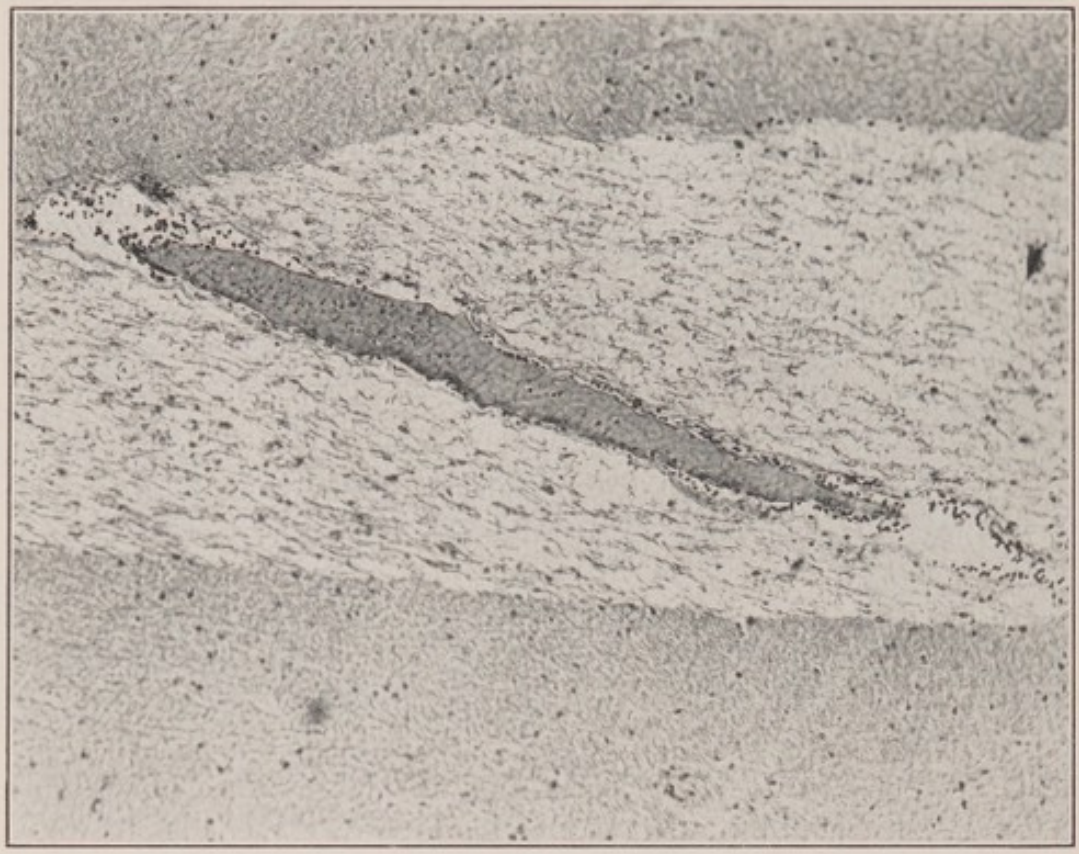

FIGURE 17.—EDEMA OF BRAIN.

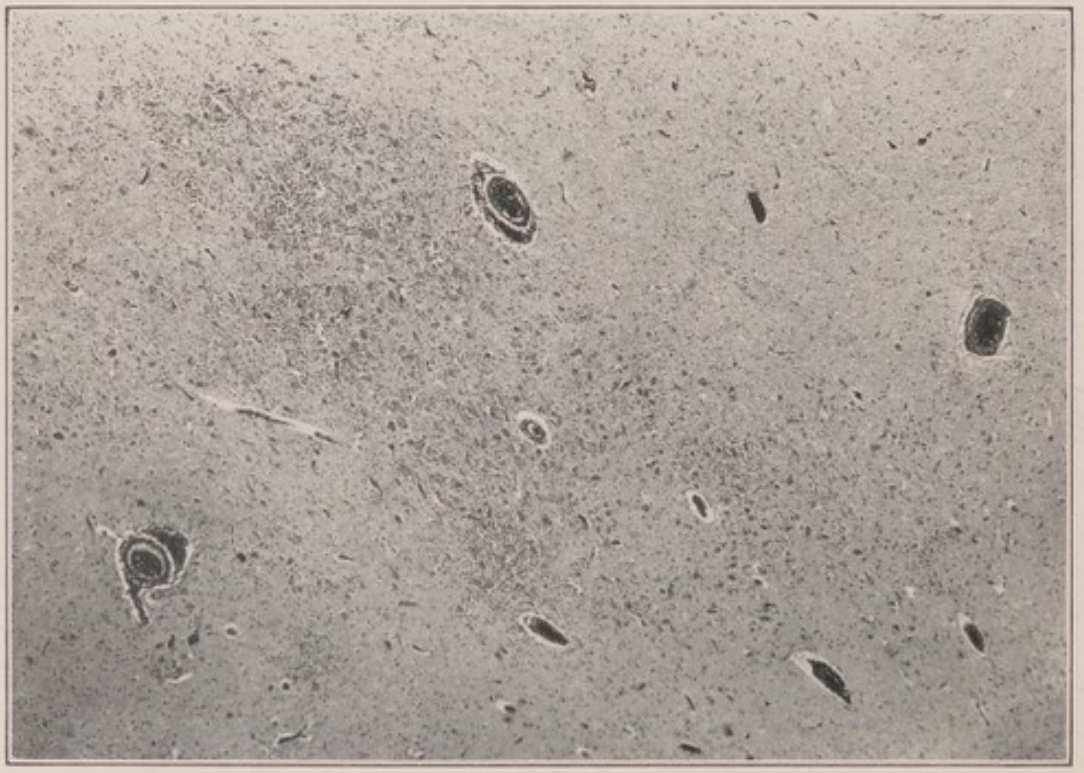

FIGURE 18.—DENSE CELLULAR INFILTRATION IN MIDBRAIN, CASE III.

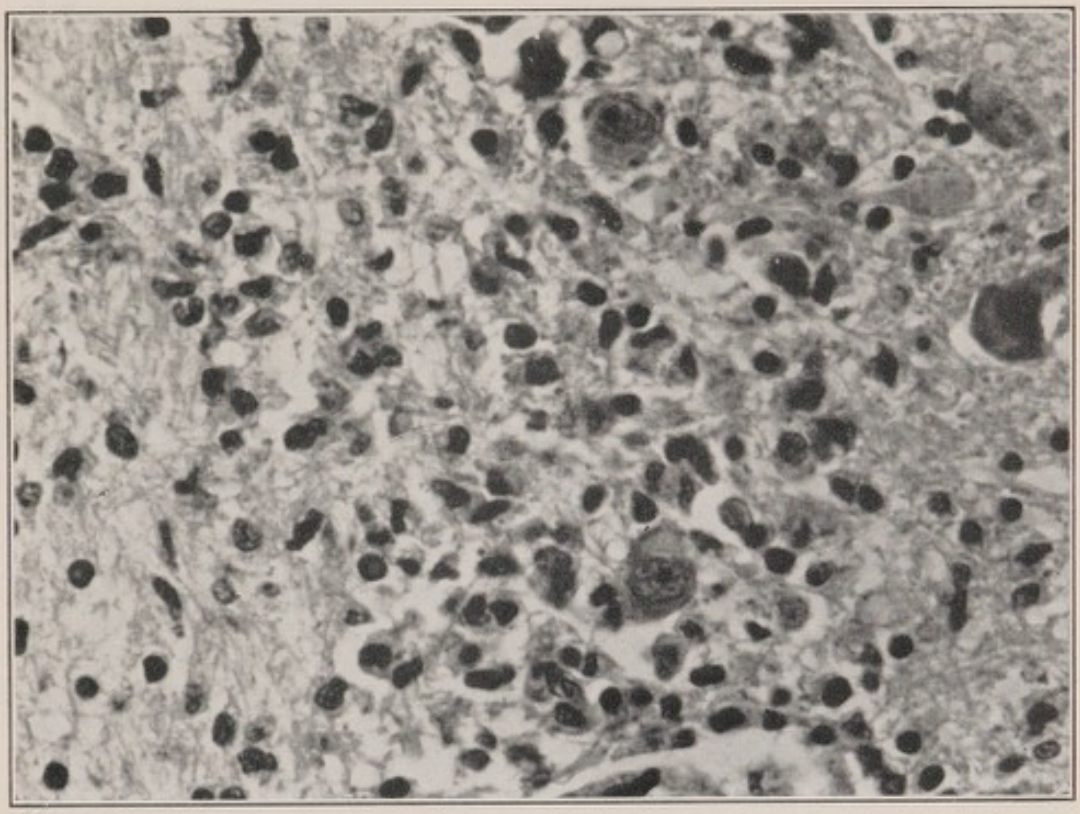

FIGURE 19.—DENSE CELLULAR INFILTRATION AND DEGENERATION OF NERVE CELLS.

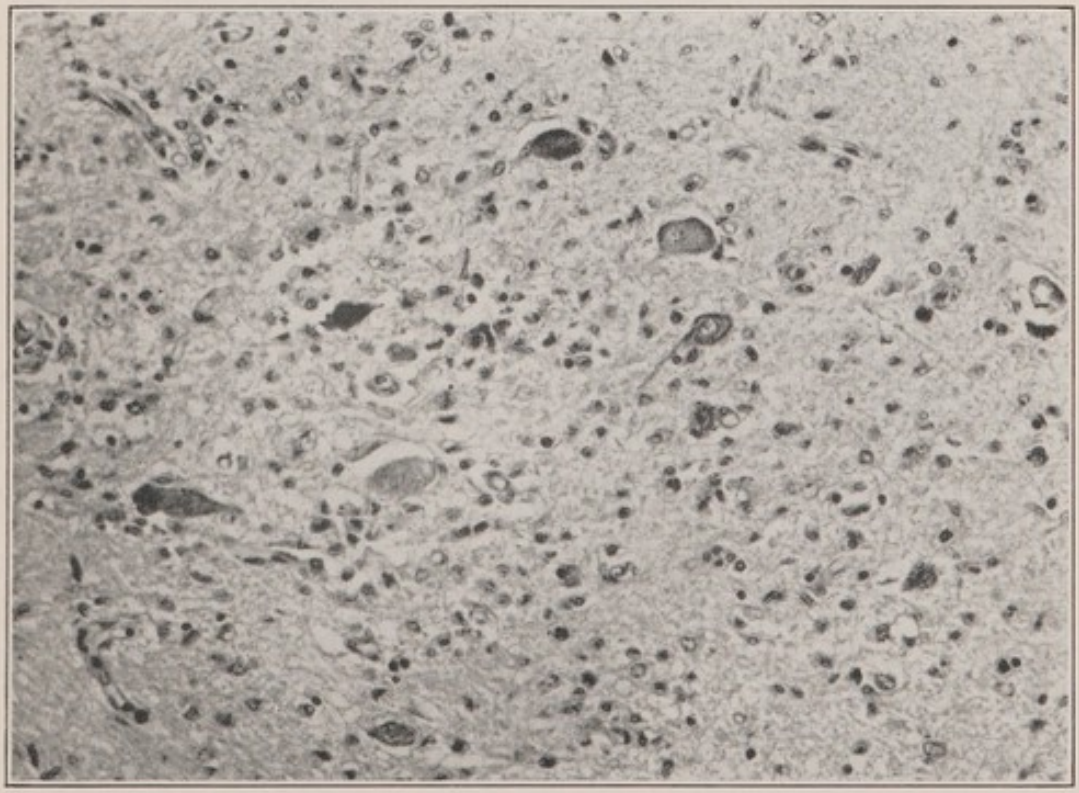

FIGURE 20.—DIFFUSE CELLULAR INFILTRATION WITH DEGENERATIVE CHANGES IN NERVE CELLS.

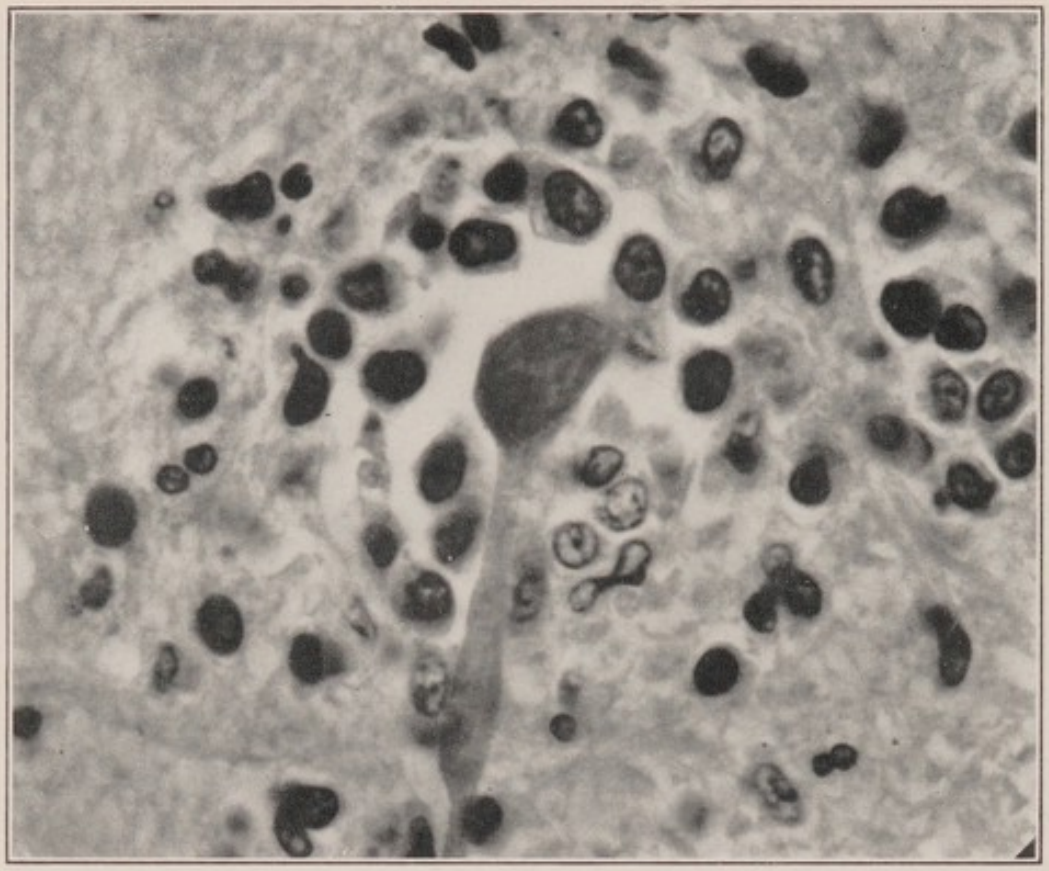

FIGURE 21.—COLLECTION OF CELLS HAVING PLEOMORPHIC NUCLEI AROUND DEGENERATED NERVE CELL; SWELLING OF AXIS CYLINDER PROCESS. PONS. CASE 1.

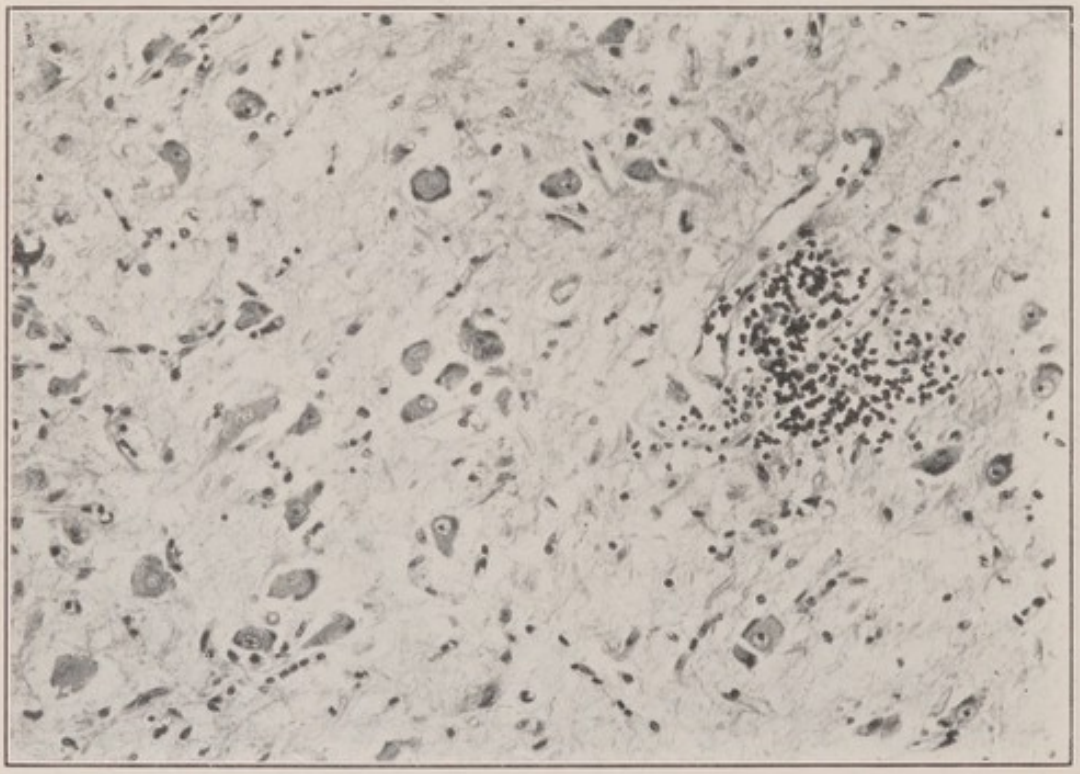

FIGURE 22.—FOCUS OF MONONUCLEAR INFILTRATION WITH NUCLEAR CHANGES IN NERVE CELLS.

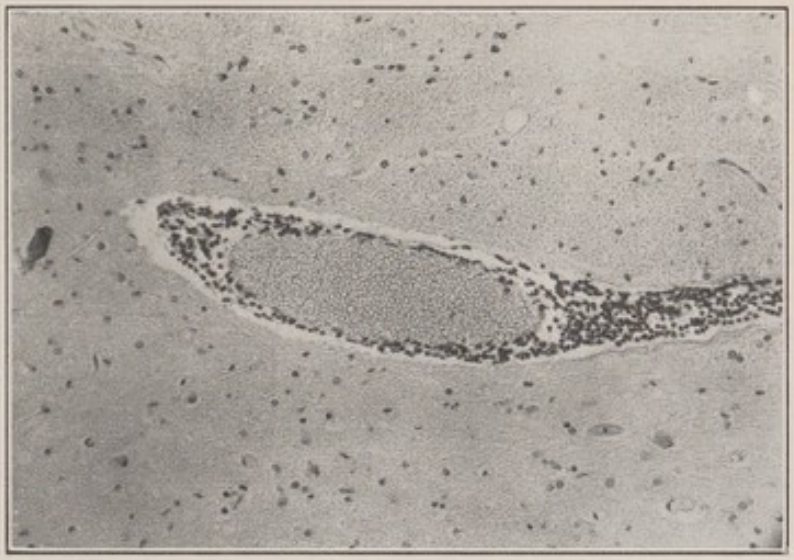

FIGURE 23.—PERIVASCULAR CUFFING IN PONS, CASE I.

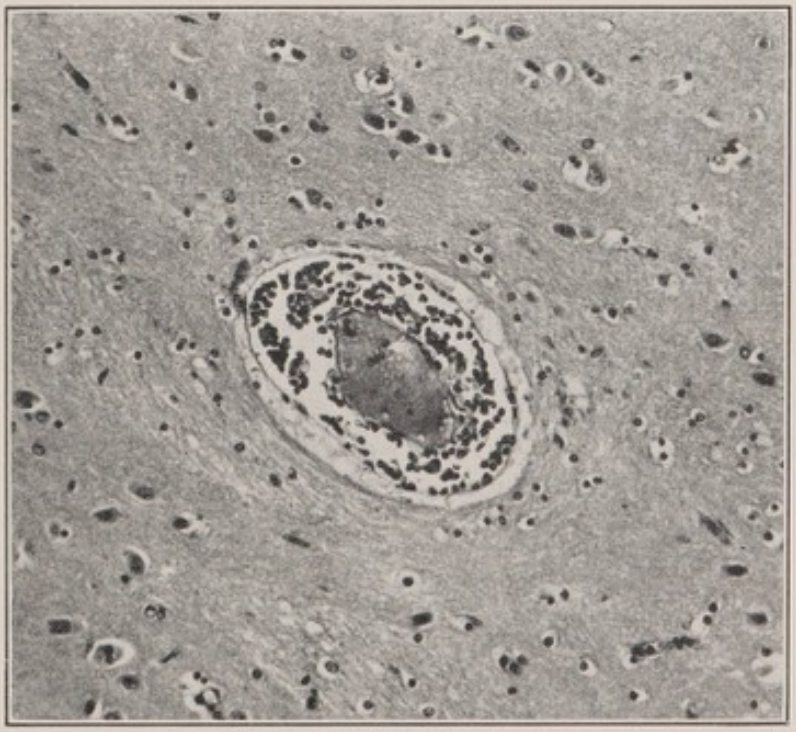

FIGURE 24.—MONONUCLEAR PERIVASCULAR CUFFING IN PONS, CASE I.

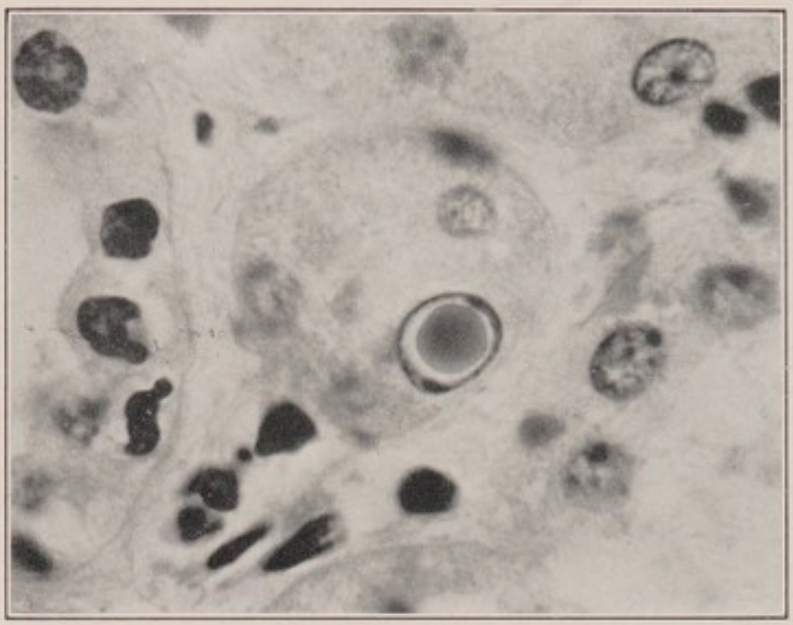

FIGURE 25.—EOSINOPHILIC INTRANUCLEAR INCLUSION IN CELL OF HENLE'S LOOP, CASE II.

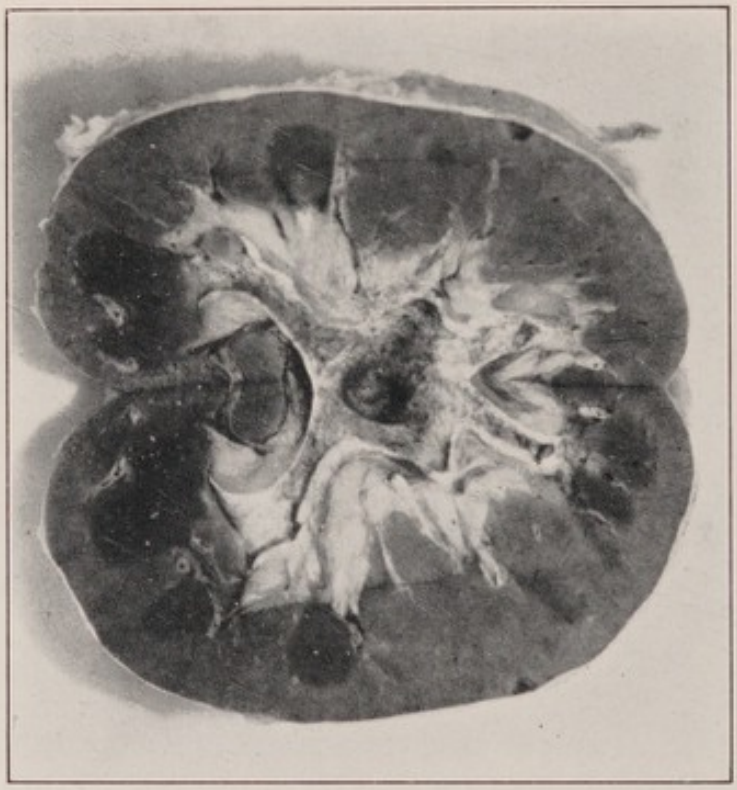

FIGURE 26.—CONGESTION OF KIDNEY, WITH PETECHIAE OF PELVIC MUCOSA, CASE II.

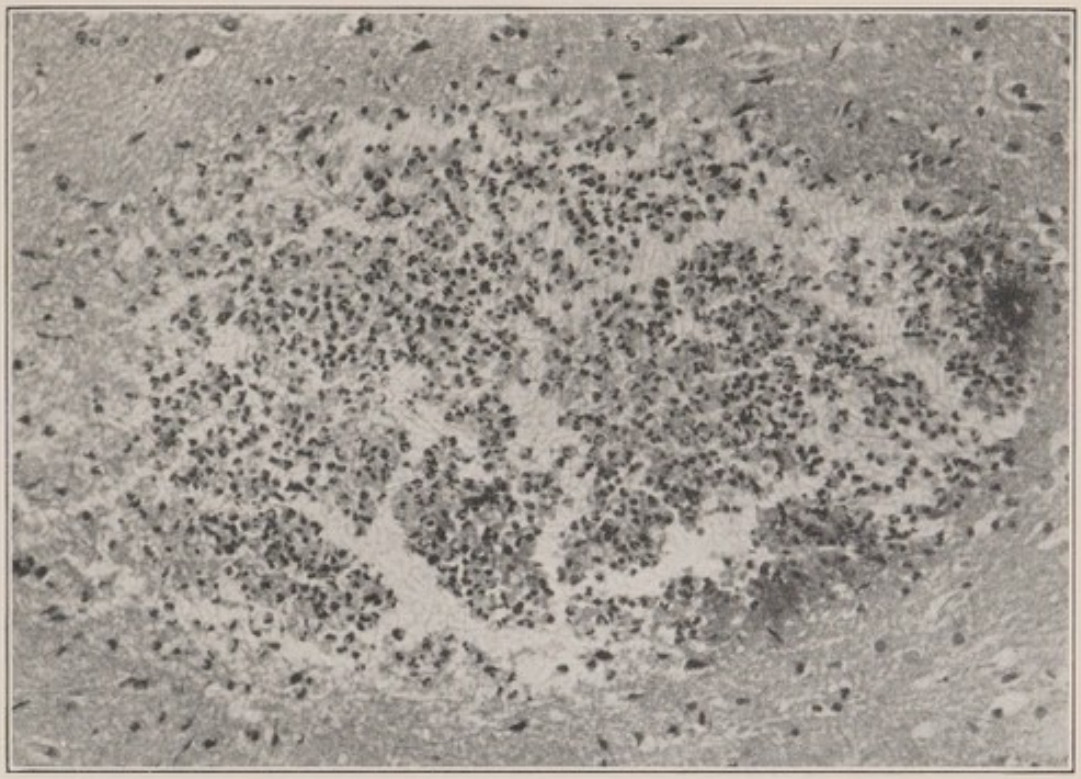

FIGURE 27.—SMALL ABSCESS OF BRAIN.

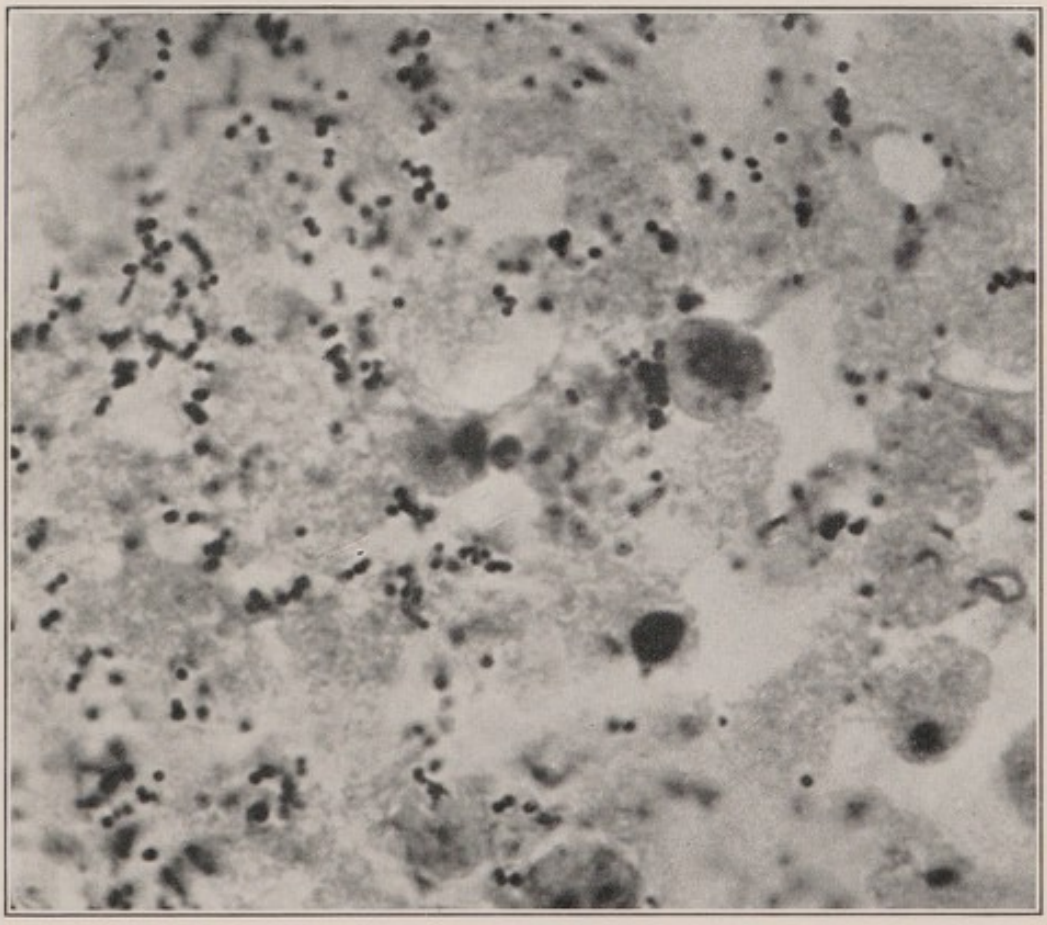

FIGURE 28.—COCCI IN BRAIN ABSCESS.

dense collections that obscured the architecture of the area involved (figs. 18 and 19).

Nerve cell degeneration.—Some degree of pathological changes in the nerve cells was found in almost every case. Slight alterations, such as perinuclear chromatolysis, eccentricity of the nucleus, excess of pigment and swelling of the nucleolus were common (fig. 22). Marked degenerative changes in the nerve cells were present in all cases showing extensive cellular infiltration (figs. 19 and 20). Some of these damaged cells showed shrinkage of the cell body with darkly staining cytoplasm, some pycnosis of the nucleus, and others partial liquefaction of the cytoplasm with hyperchromatic nuclei. In some sections all that could be seen of a nerve cell was a faint pink, shadow-like remnant in which only the outline of the nucleus was visible.

Clusters of inflammatory cells of glial or mesoblastic origin were found encircling many of the degenerated nerve cells (fig. 21). This process of neuronophagia was quite marked in every case where nerve cell degeneration was extensive.

Typical inclusion bodies such as are associated with many virus diseases were never seen in nerve cells, although swollen nucleoli frequently stained red with eosin or fuchsin.

Cellular infiltration of the meninges.—A purulent exudate was never encountered in the lepto-meninges, but increased numbers of mononuclear cells were found in about three-quarters of all the brains examined (fig. 11).

In 25 cases these cells were very numerous and were seen in every section that contained meninges. The meninges about the cord were densely infiltrated in two instances. Most of these cells were lymphocytes, but plasma cells, large mononuclear phagocytes and occasionally a few polymorphonuclear leucocytes were also seen.

Other changes in the nervous system.—In studies of lethargic encephalitis, (*1*)[8] amyloid bodies have been described in brains from young individuals, similar to those found in the posterior columns in tabes dorsalis as well as in other degenerative lesions of the nervous system and in the aged. These were frequently found in several of the brains from older individuals, but only once, and then in small numbers, in sections from the brain of a young adult.

Sclerosis of the cerebral arteries and hyaline thickening of the arterioles was evident in about 65 percent of cases. Areas of encephalomalacia and small foci of old hemorrhagic softening were present in 24 cases.

Perivascular patches of demyelination so characteristic of post-vaccinial and post-measles encephalitis were never found.

[8] Italic figures in parentheses refer to Bibliography of this section, p. 49.

Sections have been prepared from the proximal ends of the cranial nerves in five cases. The only change found in any of these has been a slight superficial infiltration with lymphocytes, which was usually seen in the optic and trigeminal nerves.

No alterations have been observed in the dorsal root ganglia, from various levels, that were obtained from eight different cases.

Distribution of inflammatory lesions in nervous system.—The subarachnoid hemorrhages were usually situated somewhere over the lateral surfaces of the cerebral hemispheres, but they were not found consistently in any particular location. Hemorrhage was very infrequently observed over the base of the brain or about the pons and medulla. Petechial hemorrhages were occasionally visible in the walls of the lateral ventricles or upon the floor of the fourth ventricle. Gross hemorrhage into the ventricles was never observed. Areas showing intense capillary congestion were likely to be found in any region of the brain but were most numerous in the cerebral cortex or in the pons and medulla. In two of the cases in which the entire spinal cord was removed the anterior and posterior horns were bright pink at all levels. Microscopically, this color change proved to be due to universal distention of the capillaries in the gray matter of the cord.

When lymphocytes were present in large numbers in the leptomeninges, the greatest concentration was usually observed at the base of the brain.

The intensity and distribution of the cellular infiltrations presented great variation in the different cases. The most severe and the most wide-spread reactions were found in the brains from those individuals who died early in the epidemic. In these cases the foci of inflammatory cells were evident in every region of the brain, and were often numerous in the cerebral cortex and in the pons and medulla. The large areas of intense, diffuse, cellular infiltration were seen only in these early, severe cases. They were never observed in the cerebrum, but usually were found in the midbrain, basal nuclei, or pons. Milder degrees of diffuse cellular infiltration occasionally were obvious in many different parts of the brain during the entire epidemic.

Perivascular cuffs of round cells, which were present in all but three cases, were always found in the pons even when not apparent in other localities. When numerous, they also might be present in the midbrain, basal nuclei, and occasionally in the white matter of the cerebrum, both horns of the spinal cord, or in the cerebellum in the neighborhood of the dentate nucleus.

The degenerative changes in the nerve cells were not consistently restricted to any particular group, nor did the extent or severity of this change bear any definite relation to the vascular congestion or to the cellular infiltration. Of course, in areas of dense cellular infiltra-

tion most of the nerve cells were either destroyed or showed severe degenerative changes, but sections from other regions of the same brain often revealed fewer damaged nerve cells than were present in other brains in which the cellular infiltration was an inconspicuous feature. Damaged nerve cells were present in the cortex, but were more frequent in the pons, basal nuclei, and medulla. Individual cells and not groups of cells usually displayed degenerative changes. One or two cells in a field might show alterations, and yet those on either side of the damaged ones appeared normal. The cells of the nuclei of the cranial nerves were seldom affected, although signs of degeneration were seen in the cells of the third, sixth, and seventh nuclei in two cases in which the inflammatory lesions were unusually extensive.

Two cases showed severe lesions in both the cervical and lumbar regions of the spinal cord. These alterations consisted of hyperemia, cellular infiltration, and degenerative changes in the nerve cells. Both horns were equally involved but the pyramidal cells of the anterior horns did not show the selective destruction that is characteristic of anterior poliomyelitis.

Changes in other organs.—Since the majority of necropsies were performed upon the bodies of individuals from the upper age groups, it is not surprising that chronic changes in the heart and kidneys, as well as the inevitable vascular alterations that accompany old age, should have been found in a high percentage of the cases. About 65 percent of all the autopsies revealed arteriosclerosis or hyaline thickening of the arterioles. The kidneys were scarred or showed evidence of chronic nephritis in about 25 percent of the cases. Fibrous-tissue replacement of muscle fibers (fibrous myocarditis) was observed in about 15 percent of all the hearts examined. Bronchopneumonia was the most frequent terminal process. This was present in more than one-half of the autopsied cases. Usually the penumonia was the ordinary lobular type. In a few instances, however, the lungs showed an acute hemorrhagic and edematous consolidation resembling that seen during epidemic influenza in the lungs of individuals dying a few days after the onset of symptoms. Microscopically, also, the picture resembled that of acute hemorrhagic influenzal pneumonia, with destruction of bronchial epithelium, thickening, and hyperemia of the bronchial wall, and a hemorrhagic alveolar exudate, with small areas of necrosis of lung tissue.

Dural endothelioma occurred in two cases, and pyelonephritis with abscesses in the kidneys was observed three times.

About one-third of all the cases showed an acute change in the kidneys that was apparently related to the disease itself and not due to some antecedent condition nor to chronic changes in the organs. This consisted of swelling and intense congestion of the blood vessels with petechial hemorrhages in the pelvic mucusa (fig.26).

Cortical flecks, such as accompany acute nephritis, were not observed. Microscopically, the most striking feature in these kidneys was marked distention of the intertubular vessels and of the glomerular capillaries. A small quantity of blood was occasionally found in the glomerular space and in the tubules. Cloudy swelling and necrosis of the tubular epithelium was also observed but was not always marked. This kidney damage was observed, many times in young individuals whose clinical records did not suggest any previous alteration in kidney function.

Intranuclear inclusions have been observed in the epithelial cells of the convoluted tubules and of Henle's loops in about one-quarter of the 25 kidneys that up to now have been thoroughly examined. (fig. 25.) Their possible significance and relation to this type of encephalitis has yet to be determined. The results of other studies, however, make it obvious that these inclusions are not present in routine autopsy material from other diseases.

About 10 percent of the cases showed petechial hemorrhages in the serous surfaces and in the mucosae similar to those seen in acute infectious processes or in acute leukemia.

Comparison with other types of infectious encephalitis.—The first few cases that came to autopsy showed the most intense inflammatory lesions in many different parts of the brain. A comparison of the pathological changes with those specimens from fatal cases of encephalitis lethargica of the Von Economo type, that had occurred in St. Louis some years previously, as well as with published descriptions of this condition, revealed several striking differences.

Qualitatively the lesions in these two types of encephalitis are similar. The differences are those of degree and of distribution and may be briefly summarized. Severe cases of the St. Louis type differ from the lethargic type in the following respects:

1. The meninges show more intense infiltration with mononuclear cells than is usually found in the lethargic type.
2. The inflammatory foci are more widespread throughout the brain, often occurring in great numbers in the cerebral cortex, and are not restricted to the midbrain or basal ganglia.
3. Degenerative changes in the nerve cells are more frequent, and neuronophagia is more marked.
4. The nerve cells in the nuclei of the cranial nerves, especially the third, rarely show degenerative changes.
5. There is more extensive involvement of the spinal cord.

As the epidemic progressed the lesions became less intense and not so widely scattered throughout the nervous system. Many of these milder cases show about the same degree of intensity and of restriction of the inflammatory lesions to the midbrain, basal nuclei, and pons, as is seen in lethargic encephalitis. As far as the milder cases of the

St. Louis type are concerned, it therefore seems impossible to differentiate them with any degree of certainty from the lethargic type upon the basis of pathological lesions alone.

The pathological lesions in severe examples of the St. Louis type are similar to the descriptions of the Japanese type B as reported by Kaneko and Aoki (*2*). The intensity of the meningeal infiltration, the distribution of the focal collections of cells, the absence of involvement of the cranial nuclei, and the frequent presence of lesions in the spinal cord as reported by the Japanese in their type B resemble the St. Louis type. The small areas of softening which they describe as being especially characteristic were not a conspicuous feature in our material. Whenever present they could be explained by advanced arteriosclerosis of the blood vessels and were not unlike similar areas of softening often seen in the aged. Retrogressive changes in the glial nodules were also infrequent in our cases, but this may perhaps be explained by the fact that most of our autopsies were upon individuals dying soon after the onset of symptoms.

Bacteria in nervous tissue.—Multiple small abscesses in the brain tissue were found in three cases (fig. 27). When small they resembled the focal collections of mononuclear cells associated with the encephalitis, and seen elsewhere in the same brains, except that they were composed of polymorphonuclear leucocytes. Bacteria were demonstrated by Gram stain in these abscesses in each of the three cases. In two instances cocci were present in groups, pairs, or short chains (fig. 28). The organisms in the third case were Gram negative bacilli, possibly B. coli. These were the only three instances in which bacteria were found in the nervous system with any sign of cellular response to their presence. These abscesses were amply explained by the presence of pyelonephritis in two cases, one of which showed similar abscess formation in the liver; and by extensive bronchopneumonia, fibrinous pleurisy and lung abscesses in the third.

Bacteria were found as the result of postmortem invasion in several cases. The organisms usually were seen in cases in which the autopsy was deferred until long after death or in tissue that was transported from a distant hospital before fixing. The brains were always cut immediately after removal and portions from selected regions fixed at once. The remaining pieces usually were placed in formalin, but if this was not available several hours often elapsed before fixation. Bacteria of various kinds including cocci in chains were seen in this poorly fixed material, but they were situated most often near the surface and in no instance was there any sign of cellular reaction about them. In several instances sections of the same brain from blocks of tissue fixed immediately after removal failed to show these postmortem invaders.

Bacteria or other microorganisms although searched for in every case were not consistently found, and this corresponds to the negative character of cultures from the spinal fluid during life and from the brain emulsion used for experimental purposes.

ANALYSIS OF AUTOPSY MATERIAL

TABLE 5.—*Sex and race distribution*

Total number of autopsies	63	Colored	8
Males	31	White	55
Females	32		

TABLE 6.—*Age group, distribution of cases*

1–10 years	2	60–70 years	25
10–20 years	0	70–80 years	13
20–30 years	3	80–90 years	4
30–40 years	2		
40–50 years	7	Total	63
50–60 years	7		

TABLE 7.—*Number of cases showing various lesions*

Meninges:	
Congestion (100 percent)	63
Hemorrhages	30
Mononuclear-cell infiltration	46
Brain:	
Congestion of blood vessels	61
Perivascular hemorrhages	40
Hemorrhages in tissue	26
Perivascular lymphocytic infiltration (cuffing)	60
Focal collections of inflammatory cells	60
Diffuse cellular infiltration	7
Degenerative changes in the nerve cells	49

TABLE 8.—*Number of cases showing lesions in various parts of the nervous system*

Cerebral cortex	33
Basal nuclei	47
Mid brain	51
Pons and medulla	59
Spinal cord (out of 24 cases in which the cord was examined)	19
Ammon's horn (out of 15 cases so far examined)	10

TABLE 9.—*Number of cases in which frequent changes were found in other organs*

Arteriosclerosis or hyaline thickening of arterioles	40
Areas of cerebral softening	[1] 24
Congestion of kidneys and pelvic hemorrhages	23
Bronchopneumonia	34

[1] In one group of 24 autopsies areas of encephalomalacia were encountered 19 times. In another group of 39 cases this change was seen 5 times.

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APPENDIX

Abstracts from Autopsy Protocols of Typical Cases

Case 1. C.D.: A white woman 55 years of age was admitted to the hospital August 8. The symptoms which first appeared 3 days previously were sore throat, diarrhea, and vomiting. Two days prior to entry she became semicomatose. Examination revealed nystagmus, pinpoint pupils, marked rigidity of the neck and coarse tremors. Babinski and ankle clonus were negative. Temperature was 103.8°. The spinal fluid was under increased pressure and contained 195 cells per cubic millimeter; the majority of the cells were lymphocytes. Cultures of the spinal fluid were negative. The blood pressure was 170/90. Respiration became more difficult, cyanosis developed and the patient died August 9, one day after admission.

Abstract of autopsy protocol.—This was the first autopsy performed within the city of St. Louis.

The blood vessels of the meninges are intensely congested. Even the finer branches stand out distinctly. The cerebrospinal fluid is increased in amount but clear. Several small hemorrhages are seen in the meninges over each cerebral hemisphere. Sections of the brain show all of the intra-cerebral blood vessels to be markedly distended, and slight pressure upon the brain tissue produces oozing from these cut vessels. Small petechial hemorrhages are present upon the walls of both lateral ventricles and a few are seen in the floor of the fourth ventricle. The arteries at the base of the brain show considerable calcification and many areas of yellow intimal thickening.

Microscopical examination reveals the most extreme vascular congestion, with extravastation of blood into the perivascular spaces about many of the blood vessels and small petechical hemorrhages in the brain tissue. Congestion is seen in sections from all regions of the brain.

Cortex.—Sections from various regions of the cerebral cortex show striking changes. There is a diffuse infiltration of the meninges with mononuclear cells (fig. 11). For the most part these are lymphocytes, but a few polymorphonuclear leucocytes, plasma cells, and large mononuclear phagocytes are also present. Small cellular foci are scattered throughout the gray matter (figs. 15 and 16). Many of

these are situated close to the meningeal surface; others are deep in the substance of the cortex. Under low power they resemble small abscesses or recently formed miliary tubercles. Under higher power, however, the cells are mostly mononuclears, but an occasional polymorphonuclear leucocyte is seen. The mononuclear cells are lymphocytes and glial cells with bandlike nuclei which often are curved. In silver preparation fine fibers extend from these cells, and they are therefore considered to be glial cells derived from the microglia. These glial nodules are present in great numbers in many of the sections. In the white matter of these cortical sections several of the medium-sized blood vessels are surrounded by cuffs of mononuclear cells.

Basal nuclei.—Sections through the caudate and lenticular nuclei show changes similar to those of the cortex but much less intense. There is less perivascular cuffing, but the most conspicuous alteration is the presence of numerous foci of inflammatory cells. Slight degenerative changes are seen in many of the nerve cells.

Midbrain.—Sections from this region show a few areas of diffuse cellular infiltration with mild degrees of degeneration in some of the nerve cells. The perivascular cuffing is not marked nor are the glial nodules numerous. The meninges in this region show an infiltration with mononuclear cells. No changes are noted in the cells of the nucleus of the third cranial nerve.

Pons.—The intensity of the inflammatory lesions in the pons is about as great as was observed in the cortex. Most of the vessels are surrounded with typical cuffs of mononuclear cells (figs. 23 and 24). Vascular congestion is extreme. The nerve cells show advanced degenerative changes. Focal nodules of proliferated glial cells and lymphocytes are present in many areas. More advanced changes are observed in the nerve cells in this region than in those of any other portion of the brain. Chromatolysis is frequent and severe. The nucleus often occupies an eccentric position and the Nissl granules are situated at the extreme periphery of the cell. Clusters of mononuclear cells are often seen about degenerated nerve cells. This process of neuronophagia (fig. 21) is marked in all sections of the pons. Slight degenerative changes are seen in a few cells in the nuclei of the sixth and seventh cranial nerves.

Medulla.—Many leucocytes are present in the meninges and a few can be found in the fibers of the twelfth nerve as they emerge from the medulla. There is considerable perivascular cuffing in the region of the floor of the fourth ventricle. Neuronophagia is marked about some of the smaller nerve cells. No degenerative changes are seen in the nerve cells of the nucleus of the twelfth cranial nerve, although some of the blood vessels in the immediate

neighborhood of this nucleus are surrounded by thick cuffs of lymphocytes.

Cerebral blood vessels.—The cerebral vessels show calcification and fibrous thickening of the intima. Many of the arterioles have a thickened and hyalinized wall. This is especially true of some of those in the pons, medulla, and cerebral cortex. One small area of softening is found in the corpus striatum. This is old and partly filled with large compound granular cells.

Spinal cord—Cervical region.—The blood vessels of both horns are intensely congested and small petechial hemorrhages are especially numerous in the anterior horns. Perivascular cuffing is marked in both horns and focal collections of cells are present, not only in the gray matter, but also in the white substance. Selective degeneration of the pyramidal cells of the anterior horn is not apparent, but various degenerative changes are seen in the cells of both anterior and posterior groups.

Other organs.—The lungs show microscopical patches of lobular pneumonia. There are a few superficial cortical scars in the kidney.

Case II. V. F.: White girl, aged 21, was admitted to the hospital August 20. The onset of the disease was 3 days previous to this date, with headache, vomiting, and fever.

No abnormal reflexes were present and the neck was not rigid. The temperature was 102.8°. A lumbar puncture was not done. The patient was alert and uneasy and had to be restrained. Signs of pneumonia developed, and she died of respiratory failure on August 21.

A strain of virus was obtained from this brain by intracerebral inoculation into a monkey.

Abstract of protocol.—Extreme vascular congestion is apparent in all the meningeal and intracerebral blood vessels. The spinal fluid is noticeably increased but clear. The brain tissue seems to be softer in consistency than normal, due to edema. Changes in other organs consist of a broncho-pneumonia and a congestion of both kidneys with petechial hemorrhages in the pelvic mucosa.

Microscopical notes—Cortex.—There are a few lymphocytes in the subarachnoid space. No changes are observed in the nerve cells in the cortex from several regions. Cellular foci similar to those so abundantly present in the first case are found in a few of the sections from the cortex, but they are not numerous. A few of the blood vessels in the white substance show small numbers of lymphocytes in the adventitial spaces. There is a moderate increase in the small, round, darkly staining cells along the course of some of the capillaries.

Midbrain.—Focal collections of cells are found in the midbrain but vascular cuffing is not apparent. Few degenerative changes are observed in the nerve cells.

Pons.—Here there are scattered focal collections of mononuclear cells. Degenerated ganglion cells can be seen in the centers of some of these foci. A few of the smaller veins show distinct perivascular cuffing. Slight degenerative changes are observed in many of the nerve cells.

Optic thalamus and basal nuclei.—Sections from these regions show no obvious increase in inflammatory cells. A few of the larger nerve cells show degenerative changes and some of these are surrounded by a small number of phagocytic cells. In the caudate nucleus the vascular congestion is extreme and there are small extravasations of blood into the perivascular lymphatic spaces (fig. 13). In a few places red blood cells can be found in the brain tissue about the distended vessels.

Spinal cord.—The only change in the spinal-cord sections from the cervical region is marked vascular congestion with small petechial hemorrhages, especially in the anterior horns.

Lungs.—There is a marked broncho-pneumonia in both lower lobes. The exudate is hemorrhagic in character. In many places the epithelial lining of the bronchi has been destroyed. The blood vessels of the bronchial walls are intensely congested and the surrounding alveoli are filled with blood, a small amount of fibrin, polymorphonuclear leucocytes and a few large mononuclear phagocytes.

Kidneys.—Both kidneys are congested, and there are hemorrhages in the pelvic mucosa (fig. 26). Intranuclear inclusions are found in the epithelial cells of the Henle's loop (fig. 25).

Case III. R. R.: A white male child, 3 years of age, was admitted to the hospital on August 20. The parents gave a history of headache, stiffness of the neck, vomiting, and fever. Examination revealed stupor, neck rigidity, and a temperature of 103°. The child died a few hours after entering the hospital.

Abstract of autopsy protocol.—The autopsy was performed about 45 minutes after death. The venous sinuses contain fluid blood. All the meningeal blood vessels are intensely congested. One is able to trace even the finest branches of the cerebral vessels. The blood vessels about the base of the brain are also distended. Small hemorrhages are present over both cerebral hemispheres, at the base of the brain and over the pons. On section most of the intracerebral vessels are very prominent. The gray substance of the cortex shows pink blotches in many regions. This salmon-pink coloring of the gray substance is also seen in the pons (fig. 12), basal ganglia, and spinal cord.

Microscopical examination—Cortex and meninges.—Large collections of red blood cells are seen in the meshes of the meninges in several places. In other regions there is a moderate increase in the number of mononuclear cells. There is an extreme degree of infiltration of the

cortex with mononuclear cells. Sections from many regions show a great number of focal cellular collections. In addition to these foci, in many areas there is also a diffuse infiltration of large patches of tissue with mononuclear cells. Small hemorrhages are seen in the perivascular spaces. There is a good deal of vascular cuffing in the white substance. A few of the nerve cells in the cortex show degenerative changes. In many of these cells the Nissl substance is no longer visible. In others various degrees of chromatolysis can be seen. Neuronophagia is quite marked in the lower layers of the cortex.

Basal ganglia.—In this region there is an intense cellular infiltration. Large areas of tissue are so densely infiltrated with mononuclear cells that the normal architecture of the region is obscured. The nerve cells show the most extreme degenerative changes. Perivascular cuffing is extensive and there are numerous focal collections of mononuclear cells. Petechial hemorrhages are seen in the brain tissue and extravasations of blood are common in the perivascular lymphatic spaces.

Midbrain and pons.—The cellular infiltration in these regions is about as marked as in the basal nuclei (fig. 18). The majority of the vessels are surrounded by large collars of mononuclear cells. Both nerve-cell degeneration and neuronophagia are marked in all of the sections from these regions. Lymphocytes are seen infiltrating the superficial layers of the proximal end of the oculomotor nerve.

Medulla.—There is extensive patchy infiltration of the medulla with inflammatory cells. No degenerative changes are seen in the nerve cells of the twelfth nucleus. There is, however, a general infiltration in the region around the floor of the fourth ventricle. Several of the veins in this locality are surrounded by thick masses of lymphocytes. Many of the cells in the olivary nucleus show degenerative changes, and focal collections of cells are found in many portions of the olivary body.

CLINICAL ASPECTS: SYMPTOMS, DIAGNOSIS, IMMEDIATE PROGNOSIS, TREATMENT

In attempting to evaluate the importance and significance of the various symptoms encountered in the 1933 epidemic of encephalitis, a tabulation was made from the records of the five hospitals which cared for the largest number of cases. These hospitals were the St. Louis Isolation Hospital, the St. Louis County Hospital, the Firmin Desloge Hospital, St. Mary's Hospital, and the Jewish Hospital. In addition, because it seemed advisable to devote a separate chapter to the manifestations of the disease as they occurred in children, the records of the St. Louis Children's Hospital were included, although the number of cases treated there was small. The total number of cases thus tabulated was 786, of which 106 were children under 16

years of age. Of the entire number of cases in this study, the St. Louis Isolation Hospital furnished records on 348; the Firmin Desloge Hospital, 127; the St. Louis County Hospital, 122; St. Mary's Hospital, 100; the Jewish Hospital, 72; and the St. Louis Children's Hospital, 17 cases. In each institution the records were compiled by the clinicians who had come in active contact with the patients and were, therefore, in a position to discriminate as to the probable correctness of the information supplied. Many unavoidable discrepancies appear in the records, due to the fact that the epidemic developed with dramatic suddenness, in the middle of summer, when many of the hospital staffs were undermanned, and the immediate need was the isolation and care of large numbers of desperately sick patients suffering from a disease about which little was known. In consequence, considerable difference of opinion existed as to the frequency and importance of some of the findings, although there was a remarkable agreement as to the general characteristics of the disease. For this reason, it seemed inadvisable at this time to give a detailed statistical study of the symptomatology, but instead, an attempt will be made to present a fairly comprehensive description of the clinical course, based on actual observation, and the facts as set down in the tabulation of this large group of cases.

Even a brief study of the records reveals that there was a wide variation in the clinical picture observed, especially as regards intensity of the infection, general constitutional response to its presence, and the reaction of the nervous system. Further consideration, however, suggests that there are certain basic symptoms which, from their frequency, seem especially characteristic of the disease, and about which may be built up a complete picture of the affection as observed during the 1933 epidemic. With an understanding of such main features of the condition, variations in symptomatology can usually be explained by differences in the severity of the infection, or degree of involvement and localization of lesions in the central nervous system. Moreover, in many instances, particularly in the aged, existing pathology at the time of the onset of the illness so modified the clinical aspects as materially to increase the difficulty of diagnosis. The clinical symptoms which came to be looked for as especially significant of this disease may be enumerated as follows: Abrupt onset of fever; headache; nausea or vomiting; mental confusion or disorientation; tremors of hands, tongue, or lips; difficulty in speech; drowsiness; stiff neck or spine; and positive Kernig and Brudzinski signs. Lumbar puncture in such a suspected case was relied upon to verify the diagnosis by revealing clear spinal fluid with increased mononuclear cell count and no diminution in sugar content.

Before engaging in a more detailed description of the individual symptoms, it seems essential to have some impression of the clinical

course of the disease as most commonly observed. In the main, the significant symptoms are referable to the lesions of the central nervous system, but in addition there are others which seem rather to be called forth by the toxemia or systemic reaction to a more or less general infection.

In the latter group may be placed, for example, such complaints as pronounced malaise, extreme lassitude, chills or chilly sensations, grippy aches in back or limbs, nausea and abdominal pains, and in occasional instances, slight conjunctivitis with photophobia, sore throat, or other signs of a mild upper respiratory infection. Accompanying these manifestations, there were usually fever and a certain amount of headache. Physical examination, however, reveals no abnormality indicative of participation of the brain or meninges in the infection, and hence it is not surprising to find a tentative diagnosis of grippe or influenza made at this time. In occasional instances, even at this early stage, patients will complain of pain in the neck muscles, and a more careful examination may arouse some suspicion of slight cervical rigidity. In the type of case without neurological symptoms at the start, this *stage of invasion*, if it may be called such, lasts from 1 to 4 days, or even longer, and during this time not infrequently a marked amelioration of symptoms occurs, the temperature ranging lower and the headache subsiding. Suddenly, however, the temperature again rises abruptly to 103°, 104°, or even 105° F., the headache becomes much more severe, and the typical picture of encephalitis develops, with definitely stiff neck, mental confusion, and tremors. From this point on, the clinical course is indistinguishable from the second or purely encephalitic type of the disease. The graphic temperature curve of such a case is reminiscent of the so-called "two-humped type" of fever in certain cases of acute poliomyelitis. The number of patients exhibiting prodromata of this sort, however, is apparently distinctly smaller than the number belonging in the second group in which such symptoms are either absent or so mild as to be entirely overlooked.

A more usual type of the disease, then, is that in which the characteristic encephalitic or meningeal symptoms appear at the very outset of the infection. The disease is ushered in abruptly with headache and fever, and without prodromal manifestations of any sort. Less frequently, the onset is gradual. The temperature is ordinarily high, at least 102° or 103° F. and at times 105° or 106° F., and nausea or vomiting are frequent. Chills or chilly sensations, lassitude, weakness, myalgias and abdominal pain may occur, but are less frequent than in the first group discussed. Occasionally, especially in children, convulsions may take the place of chills. In general, neck rigidity, often accompanied or even preceded by stiffness of the spine below the cervical region, was perhaps the commonest objective finding.

In the majority of instances, the Kernig sign was positive at some time during the course of the disease, but not always in the early phase. In some cases, however, despite marked head retraction, the Kernig remained absent throughout the entire illness. As regards the other reflexes, the most constant finding was an absence of the abdominals, even in the first few days of the illness. Occasionally, however, especially in children, they remained unchanged despite other obvious evidence of serious invasion of the central nervous system. The knee jerks and other tendon reflexes were inconstant, being exaggerated oftener than diminished. The Oppenheim, Gordon, Chaddock, and Babinski tests varied not only in different patients, but at different times in the same patient. As a rule, no reliance could be placed on abnormal plantar reflexes or ankle clonus in arriving at a diagnosis of encephalitis, although almost all combinations of such pathological signs were observed. The pupils, as a rule, were small, but equal, and reacted to accommodation. Reaction to light was occasionally sluggish.

Coincidently with the development of the above-mentioned symptoms, or at least within 1 or 2 days of the onset of the illness, many patients showed definite evidences of mental impairment. Some were completely disoriented as to time and place, others remembered their own names and ages, but could not recall where they lived; many during convalescence had no recollection of lumbar punctures, the early part of their illness, or how they had come to the hospital. Despite the popular name of "sleeping sickness", drowsiness was by no means always present. In fact excitment or mild delirium were not uncommon, and a few patients actually suffered from insomnia. Nevertheless the majority of individuals with moderately severe encephalitis showed a tendency to drowsiness or mental apathy, and some went into real coma. Rarely, however, was the drowsiness so pronounced that the patient could not be aroused at least momentarily to answer a few simple questions, following which he usually lapsed again into a peaceful sleep. At the height of the symptoms there was often great difficulty in speaking, ranging from complete aphasia in a few, to thick or slurred speech, running words together, etc. Unquestionably, in certain instances such speech difficulty was due, at least in part, to tremors of the lips and tongue, but true aphasia occurred as well as dysarthria.

As soon as it became apparent that these patients were suffering from encephalitis in epidemic form, especial attention was directed to possible ocular manifestations. In contrast to previously observed epidemics, ophthalmoplegias were found to be conspicuous by their absence. Occasional instances of transient double vision and mild strabismus were observed, usually disappearing within a few days. Complaints of slightly blurred vision early in the disease were con-

siderably more frequent, but ordinarily lasted only for a day or two. Ptosis was so rare that its presence was noted only a few times in this tabulation of 786 cases, and then it was of mild degree and persisted only a few days. When one considers the nature and distribution of the pathological lesions which were found at autopsy, it is rather surprising that ptosis and other ocular manifestations were not more prominent in this epidemic. Nystagmus, both lateral and vertical, was observed in a few cases, but disappeared within a few days. Ophthalmoscopic examinations, by competent ophthalmologists, failed to reveal any striking abnormality of the fundi. In fine, such ocular symptoms as were observed, occurred early in the disease and were transient in character, no residuals of this nature being recorded.

Among the other symptoms noted in our records, one of the most important is vertigo. This was mentioned as occurring in about one-fourth of the cases, almost always at the onset of the disease and disappearing within a day or two. The dizziness as a rule was so mild that its presence was revealed only upon definite inquiry. A very few instances of real ataxia suggesting a cerebellar origin were observed, but these, too, cleared up rapidly. Mild degrees of exophthalmos were observed a number of times, but it seems probable that, in at least a certain percentage of the cases, this symptom antedated the encephalitis and was not related to it, since slight exophthalmos is not uncommon in adults and is often overlooked by relatives and friends. However, several patients with a history of a previous attack of toxic goitre showed a definite increase in the prominence of the eyes during the attack of encephalitis, and as convalescence was established, there was a regression of this symptom. In one patient who had been operated upon several years previously for exophthalmic goitre, there was such an extreme increase of the exophthalmos following the onset of the encephalitis that there was a complete forward dislocation of the globes out of the orbits, the eyes being fixed and immovable, the cornea dry and clouded, and the conjunctiva intensely congested. This patient died on the day of her admission to the hospital, and unfortunately no autopsy was obtained. In a very few cases transient deafness or tinnitus was observed.

Fever in the typical encephalitis case was highest in the first 2 or 3 days of the infection, and then, in most instances, fell by rapid lysis, so that the normal was reached within a week or 10 days of the onset. Somewhat less frequently, the temperature fell by crisis, and in general, it was uncommon to have any subsequent exacerbation of the fever except when complications developed. Occasionally, however, the febrile course, even in uncomplicated cases, was very much more prolonged, even up to a month or 6 weeks. As a rule, the patient's general condition improved as the temperature returned to

normal, but exceptions were observed in which the fever disappeared although the patient remained confused and disoriented, or had tremors even as long as 3 or 4 weeks later. The pulse was ordinarily proportional to the temperature, but it was not at all infrequent to find a marked bradycardia, and less commonly, a tachycardia. The blood pressure was unchanged except in those individuals with preexisting arteriosclerosis, nephritis, or cardiac conditions.

Mention has been made of the frequency with which nausea and vomiting occurred in the early stages of the disease. It should be emphasized, however, that this was rarely of the forceful type seen in meningitis or other conditions in which there is associated a marked increase in intracranial pressure. As might be expected under the circumstances, the spinal fluid in most cases was not under greatly increased pressure, and reaccumulated slowly after lumbar puncture. Constipation was very common, probably due in part to reduction in the ingestion of solid food, but a small number of patients had severe diarrhea, occasionally with a considerable amount of blood in the stools. Retention of urine was common and in some instances incontinence of feces and urine occurred, the latter at times as an overflow phenomenon when the bladder was distended. (The possible relationship of such bladder and rectal involvement with cord lesions will be discussed in the section on neurological symptoms.)

It is important, too, to record the fact that in a few cases paralyses developed during the course of the acute illness, before the febrile period had ended. When these involved the extremities, monoplegias, hemiplegias, and diplegias were observed, usually of the spastic type. Facial paralysis was occasionally a somewhat later complication, occurring toward the end of the second week. As a rule, however, all such manifestations had disappeared by the end of the third or fourth week of the disease. Despite this generally favorable course, in a few cases there was marked mental deterioration and spasticity of all four extremities persisting long after the usual isolation period of 3 weeks had passed. (See section on neurological symptoms.) At the first follow-up examination, however, 3 months from the onset of the disease, practically all of these patients had shown such remarkable improvement as to encourage the hope and belief that there was still a good chance of their ultimate complete recovery.

Finally, in discussing the clinical types of encephalitis as observed in the 1933 epidemic, it is important to mention a third group, made up of *mild* or *abortive* cases, in which the symptoms were so mild and atypical as to make diagnosis exceedingly difficult. In many instances the only symptoms these patients presented were headache and fever of unexplained origin, the usual manifestations of the disease which had come to be looked upon as characteristic being entirely absent. Only the presence of an epidemic justified the suspicion of encephalitis

and diagnostic lumbar puncture. It seems probable that more cases of this type were overlooked than were discovered. As a rule, however, careful examination and history revealed at least some suggestive symptoms, as, for example, slight tremors of tongue and hands, mild transient vertigo or blurring of vision at the onset of the disease, and nausea, chilly sensations, or extreme lassitude at the same period. Moreover, the majority of such patients had some suggestion of spinal or neck rigidity in the early phases, many had absent abdominal reflexes, and a few showed other abnormalities such as changes in the knee jerks and plantar reflexes. With such vague and indefinite symptoms, it is not surprising to find a diagnosis of malaria or typhoid fever made, especially in those cases having an associated leucopenia. Disorientation and other mental symptoms, however, were almost always entirely absent, and drowsiness was infrequent and not pronounced when present. The temperature, which rose to 102° or 103° in the early stages, had usually returned to normal within 5 to 7 days, with coincident improvement in all the symptoms. The spinal fluid, even in such mild cases, usually revealed the typical increase in mononuclear cells and helped establish the diagnosis. There is indication, too, that these patients subsequently have immune substances in their bloods, as seems to be the rule in the more typical cases.

Discussion of Individual Symptoms

Since encephalitis as it was seen in the 1933 epidemic in St. Louis apparently differs materially from the disease usually seen in this country, it seems justifiable to offer a brief recapitulation of some of the more important symptoms. The neurological manifestations are discussed elsewhere in this monograph, hence these features of the disease will not be detailed here.

Systemic reaction.—Prostration, malaise, and extreme lassitude were often forerunners of the disease, or accompanied the earliest appearance of the neurological symptoms. Chilly sensations were present in perhaps half the patients, at times replaced by real chills, but usually not repeated after the first few days of the illness. Convulsions occurred in a small number of adults and a larger proportion of children, usually at the onset, but occasionally later in the course of the disease. In general, convulsions were indicative of a severe infection. Neuromuscular pains referred to the back, joints, and muscles of the extremities were exceedingly common, associated at times with marked hyperesthesia, so that patients complained of all examinations. These disappeared as the fever subsided and other evidences of improvement were manifest. Abdominal pain was sometimes produced by gaseous distention of the intestines, over-

filled bladder, tender abdominal muscles, and, occasionally, quite independently of all of these.

The onset of the disease was oftener sudden than gradual, the characteristic and fully developed picture of encephalitis requiring 2 or 3 days to develop in those with slow progression of symptoms. A definite period of invasion or prodromal stage was occasionally observed, during which the symptoms were suggestive of an influenzal infection.

Symptoms referable to the upper respiratory tract occurred often enough to make it appear improbable that this was due entirely to coincidence. Cough, except during a complicating pneumonia, was very rare, but mild rhinitis was observed a number of times. Complaints of sore throat, however, were more frequent, and mild pharyngitis was observed even oftener. In most instances, the throat showed a dusky red color involving the lateral pharyngeal walls, the pillars of the soft palate, and to a lesser extent the posterior wall. A few throats exhibited a blotchy appearance of the soft palate somewhat similar to that observed in measles. At least 3 cases of acute follicular tonsillitis were discovered at the first examination, and 4 others in which shallow, grayish oval ulcers appeared on the anterior pillars. No particular studies of the bacteriology of these throat infections were attempted. Acute catarrhal conjunctivitis was seen in a small percentage of cases, often accompanied by a surprising amount of photophobia. The tongue was usually heavily coated with a brownish fur, and thick tenacious mucus of offensive odor appeared in the throats especially of such patients as were unconscious or markedly dehydrated.

Headache.—This was rarely absent in the acute phase of the infection. No particular localization was favored, although frontal and occipital headache was perhaps more frequently complained of than parietal. It was often very severe, but usually relieved at least in part by spinal puncture, and disappeared entirely with improvement in the general condition.

Nausea and vomiting.—Nausea and vomiting were common in the early part of the illness, but rarely persistent or frequently repeated. Projectile vomiting was exceptional.

Fever.—With the onset of the encephalitic symptoms, and occasionally during the period of invasion, the temperature rose abruptly to 101° or 102° F. in the mild cases, 103°–104° F. in those of moderate severity, and perhaps to 105° or 106° F. in the worst cases. In the average case the temperature reached normal by the end of the eighth or tenth day, falling by lysis oftener than by crisis. Improvement in the general condition was noticed as the fever subsided, but exceptions to this occurred in which mental confusion, tremors, etc., persisted long after the temperature had returned to normal. Occa-

sional prolonged febrile courses were observed, lasting 4 to 6 weeks or more, but as a rule, return of fever or prolongation of its course was due to complications. In some instances, the fever was elevated at the onset of the prodromal symptoms, ranging lower in the next few days, and returning abruptly to a high peak with the development of the typical encephalitic syndrome.

Pulse.—As a rule the pulse was of good volume and the rate proportional to the temperature. In a large number of patients, however, marked bradycardia occurred, and less frequently tachycardia. No dicrotism or other change was noted. Blood pressure was unaffected.

The disease in children.—Relatively few children were affected by the disease. Of the 786 cases comprising this report, 106 were children, the youngest being 6 weeks. The symptoms were less typical, and usually milder in children, the death rate being much lower than at any other age period. Occasional exceptions were noted, in which the symptoms were unusually severe and prolonged. Convulsions were more common in children than in adults, and absent abdominal reflexes were the exception rather than the rule. As might be expected, vomiting and diarrhea was somewhat more common in the young. Other symptoms were quite similar to those seen in adults. Recovery was rapid in most cases.

Complications.—Most of the complications observed were due to pathological conditions which existed before the onset of the encephalitis. The commonest were senility, arteriosclerosis, chronic nephritis, chronic cardiac disease, and hypertension. Concomitant diabetes was observed several times, and in these the routine administration of intravenous glucose solution was omitted. Pregnancy was diagnosed in a few cases, and was not interrupted by the disease, except in three instances where the fetus was near term. These children survived and were apparently well. Retention of urine, cystitis, and pyelitis were all observed, the first quite frequently. Pneumonia, both lobar and more commonly broncho-pneumonia, was the one complication which seemed not solely dependent upon previous pathology. It was probably the commonest direct cause of death.

Diagnosis.—In the early or prodromal stage of encephalitis, when the symptoms consist largely of moderate headache, fever, chilly sensations, grippy pains, photophobia, and possibly other upper respiratory symptoms, the similarity to *influenza* may be striking. The subsequent course, stiff neck, and neurological findings, however, will usually justify diagnostic lumbar puncture and reveal the proper diagnosis.

Malaria may be suggested when, in addition, there are definite chills and absence of leucocytosis. The spleen in encephalitis is occasionally palpable, but rarely as large and hard as in malaria, and search for

malaria plasmodia in the blood, together with the observation of the subsequent course, serves to differentiate the two. The malarial patient feels relatively well on the days when he has no chills or fever, the chills are repeated, and the fever may be characteristic, whereas the encephalitis patient rarely has chills except in the early phase, reaches the height of his symptoms as a rule within a few days, and then presents neurological signs and rapid improvement.

Typhoid fever may be simulated by encephalitis, especially if a leucopenia is present, but the more gradual onset in typhoid, with palpable, soft spleen, rose spots, positive blood culture or Widal, and absence of stiff neck, of Kernig sign, etc., help clarify the diagnosis. *Delirium tremens* may be ruled out only with the greatest difficulty in certain patients with excitement and delirium. Hallucinations are much less frequent in encephalitis, and the fever and neurological signs in encephalitis usually lead to lumbar puncture, when a high cell count is found. The two diseases may be associated, however, and a very confusing picture results.

Encephalitis and *tuberculous meningitis* may present symptoms that are so similar as to make differentiation possible only with the aid of the laboratory or by observation of the subsequent course. In tuberculous meningitis, however, irregular respiration, especially of the Biot type, is much more common. Tuberculin test, and roentgenograms of the chest may give valuable aid, and examination of the spinal fluid reveals a diminution of the sugar content, marked increase of globulin, pellicle formation, and tubercle bacilli. In encephalitis, on the other hand, the spinal fluid sugar is not reduced, globulin is only slightly increased, and the pressure is not so great. Moreover, the temperature is apt to be higher in encephalitis in the early stages; mental confusion, drowsiness, speech difficulty, and tremors are all early symptoms in encephalitis, and occur less frequently and later in tuberculous meningitis. Fundus examination shows no abnormality in encephalitis, and in tuberculous meningitis may reveal choroidal tubercles or evidence of increased intracranial pressure. The course in tuberculous meningitis is progressively downward, with slight remissions, to a fatal termination in about 3 weeks, whereas the encephalitis patient is usually well by that time.

Acute anterior poliomyelitis may start abruptly with headache, convulsions, fever, neck and spine rigidity, tremors and coma, and the spinal fluid showing an increase in mononuclear cells. However, cases of poliomyelitis of such severity are almost always followed by paralysis of certain muscle groups which is characteristic. The sensorium is usually clear in poliomyelitis and there is no disorientation or mental confusion. Abnormal toe signs, vertigo, and blurred vision are also relatively common in encephalitis and very rare in polio-

myelitis. The spinal fluid globulin is often markedly increased in poliomyelitis, and usually only slightly so in encephalitis.

Finally, differentiation from *other forms of encephalitis* may present difficulties. The type of encephalitis observed in this epidemic differed markedly from the usual or ordinary case of encephalitis of the so-called "lethargic" type. The onset in our cases was more often abrupt, the fever higher, ophthalmoplegias rare and transient, there was no progression of the disease with the development of new symptoms months after the onset, and recovery was rapid, usually without sequelae. The acute disseminated encephalomyelitis, or so-called "post-infectious" myelitis, associated with measles, varicella, vaccinia, etc., may be so similar to the present disease as to make differentiation impossible except by the history, or, in fatal cases, by autopsy. It seems probable from preliminary studies on the blood of recovered patients and the neutralizing effects of such blood against the encephalitic virus, St. Louis type, that we may ultimately be enabled to draw a sharp distinction between these two diseases, at least after recovery.

Prognosis.—Recovery in the typical case of encephalitis was surprisingly rapid and complete. In the vast majority of cases, the temperature was normal within 10 or 12 days of onset, and the patient at this time obviously well on the road to recovery. Headache was often relieved by the first lumbar puncture, and drowsiness, mental confusion, and tremors decreased as the temperature returned to normal. In some instances, to be sure, some disorientation or difficulty in speech persisted well into the second week, and tremors were found to last even longer than the other symptoms mentioned. But, with few exceptions, the patients who survived the acute phase of the disease, and had no serious preexisting complications, were entirely well at the end of the arbitrarily fixed isolation period of 3 weeks.

Mention has been made in the chapter on Epidemiology that the general mortality figure was 20 percent, and that the mortality was much higher in the older individuals than in the young. Some of the deaths were unquestionably the direct result of the toxemia and intensity of the infection, but many more were caused by the fact that the encephalitis affected individuals who were already handicapped by the existence of other serious pathological conditions.

The only complaints, with few exceptions, that one heard when patients left the hospital were of nervousness, weakness, fatigue, and apprehensiveness as to the future.

Treatment.—No efficacious specific treatment was developed during the epidemic, although many things were tried. Among these may be mentioned arsphenamine, quinine, mercurochrome intravenously, and Rosenow's antistreptococcic serum. In most hospitals it was more

or less the routine to force fluids by mouth and subcutaneously, and often repeated injections of intravenous glucose solution were used. The latter two procedures were life-saving measures in certain collapsed or dehydrated individuals, but in many others no apparent effect on the encephalitic symptoms was observed. Lumbar puncture was used for the relief of headache, and for studying the characteristics of the spinal fluid. As patients appeared to recover from the disease, the thought occurred to many clinicians to use blood or serum from these convalescent patients. Since it has now been fairly definitely established that such blood actually contains neutralizing substances for the virus of the disease, such a procedure appears to be rational. However, it must be remembered that convalescent serum may be quite ineffective in therapy, as is convalescent measles serum during the course of measles. Its use prophylactically is hardly warranted unless future epidemics embrace larger numbers or show a greater tendency to produce multiple infection in the same family. In most of the cases recovery was so rapid and apparently complete as to make anything beyond symptomatic treatment seem unnecessary.

Typical Case Histories

Case 1 (see fig. 29). A. M.: Male, aged 40 years. Admitted to the hospital August 11, 1933, with temperature 103° and without history of onset or previous illness. He was apparently in a semicomatose condition, from which he could be aroused momentarily to answer simple questions. His complaints were severe headache and photophobia, but he was quite irrational and confused, and had difficulty in enunciating. There was a tremor of the hands and tongue. Heart and lungs were normal, his pharynx and soft palate were injected and a dusky red color, the tongue heavily coated, his abdomen negative. His pupils were small, equal, and reacted to light and accommodation. His neck was very stiff, but he had a negative Kernig; there were no abdominal, plantar or other reflexes. Fundus examination was negative, and blood pressure 130/75. Lumbar puncture revealed clear spinal fluid under slightly increased pressure, with a cell count of 76 per cubic millimeter, predominantly mononuclears, with slightly positive Pandy and positive sugar. His white blood count was 7,000 per cubic millimeter and the Schilling differentiation showed a slight left shift. On August 14 the neck was less stiff, and though he was still somewhat disoriented, he was less drowsy and definitely improved. The spinal fluid on August 13 showed 192 cells, 98 percent of which were mononuclear cells. By August 18 he was no longer somnolent, was well oriented, but had no recollection of how he had come to the hospital, or of lumbar punc-

tures and intravenous glucose injections. He was discharged August 27, apparently entirely recovered, with no residual manifestations.

CASE 2 (fig. 30). *Typical case, moderate severity, bradycardia.* P.R.: White male, 44 years old. Taken sick August 26, 1933, with fever and malaise, but no headache, dizziness, or lethargy. On August 27 had headache; temperature ranged between 103° and 105° F. and he became irrational and confused. W.B.C., 20,000; spinal fluid, 58 mononuclear cells. Admitted to hospital August 30 with temperature 104.4°, drowsy, confused, mumbling, with thick speech, very rigid neck, positive Kernig, and negative abdominal reflexes. Other reflexes hyperactive, but no abnormal plantar reflexes. Slight exophthalmos present. Throat was very red, with blotchy appearance of

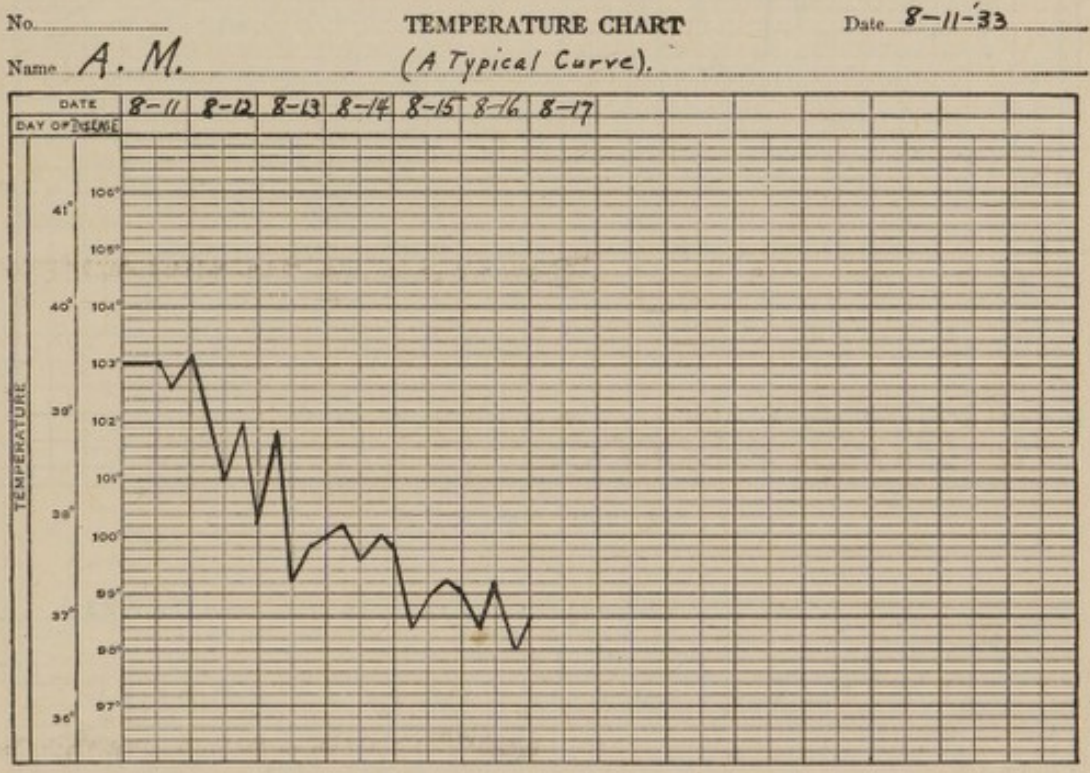

FIGURE 29.—Male, aged 40, no history or onset.

soft palate and anterior pillars of fauces. W.B.C., 21,800. Spinal fluid showed 31 cells, of which 23 were mononuclears. Pulse 100–110 with temperature of 105° F. On September 9, 1933, speech, which could hardly be understood the first few days in the hospital, was quite good. Tremors of face and hands were practically absent, but were noticeable in tongue. Abdominal reflexes still absent. Neck much less stiff. Still some disorientation present. Discharged September 17 entirely recovered, without residuals. Exophthalmos no longer visible.

CASE 3 (fig. 31). *Well marked period of invasion and prodromal symptoms.* Mrs. M. S.: White female, 33 years. Became ill day of July 29, 1933, with headache of moderate degree, chilly sensations, grippy pains in back and limbs, and temperature 101° F. Suspicion

No..... TEMPERATURE CHART Date 8-30-33

Name P. R. (Note Bradycardia)

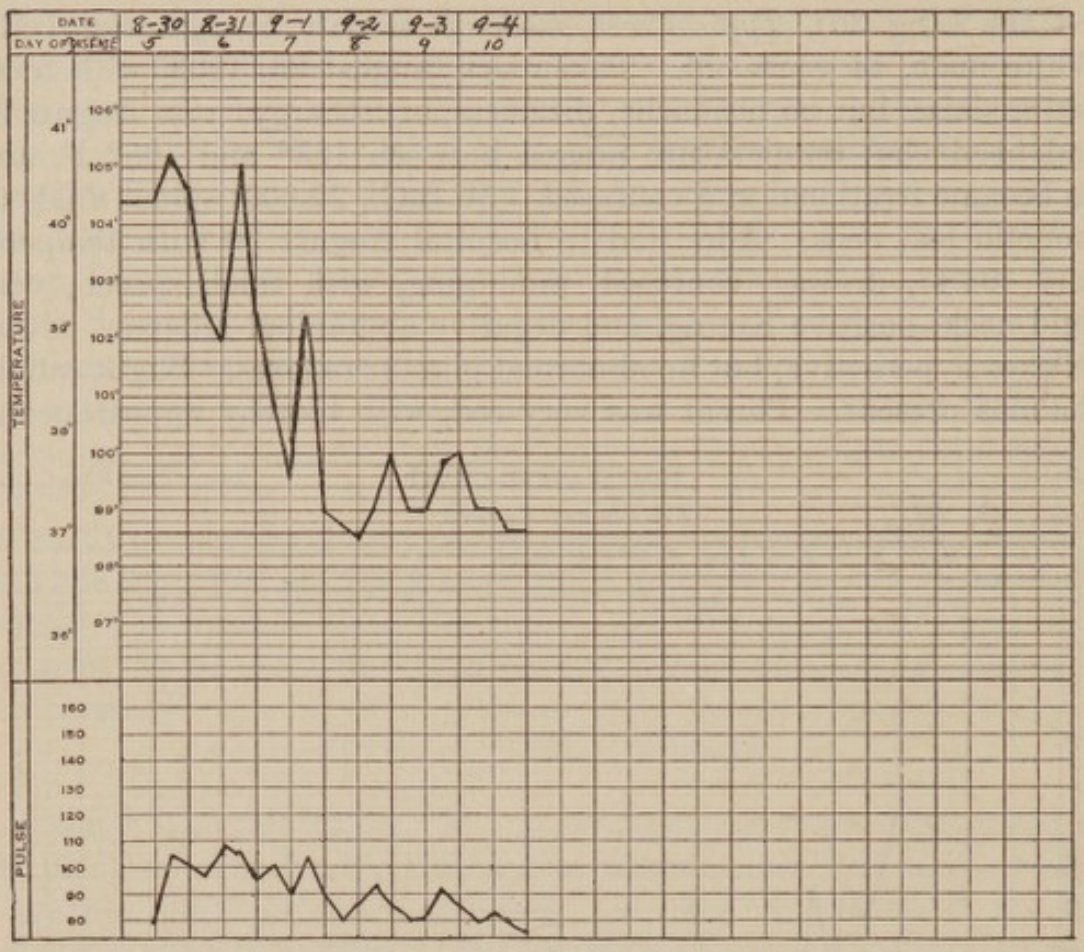

FIGURE 30.—Male, aged 44.

No..... TEMPERATURE CHART Date 7-29-33

Name Mrs. M. S. (Period of Invasion).

FIGURE 31.—Female, aged 33.

of very slight neck rigidity present. July 30 and 31 temperature around 102°, headache still quite severe but malaise less pronounced. August 1 temperature 102.8°, headache less severe. August 2 patient very much improved, headache gone, temperature down to normal in evening. No abnormal neurological findings. August 3 temperature still normal, patient in good humor, considers herself well. August 4 severe headache and delirium. August 5 went into coma, temperature 102°, neck very stiff, Kernig positive, spinal fluid showed 67 cells, almost all mononuclears. Very drowsy for several days, then rapid recovery. No residuals. Still normal 8 months later.

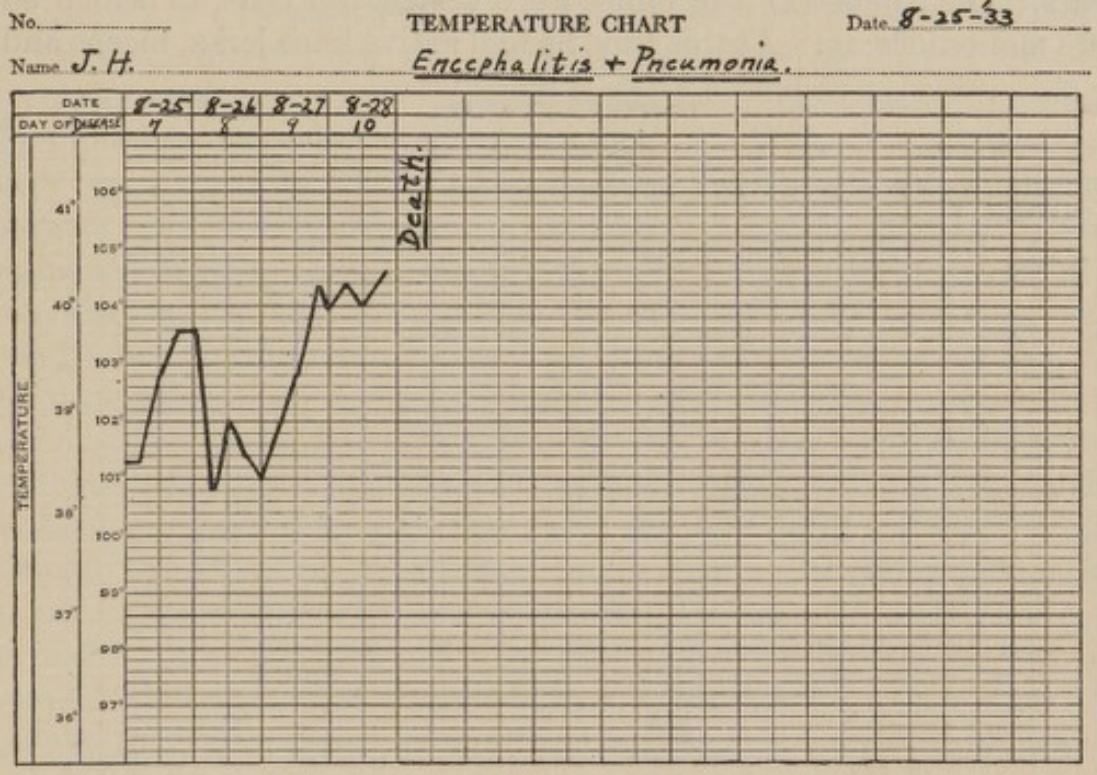

FIGURE 32.—Male, aged 56.

CASE 4 (fig. 32). *Death from complicating pneumonia.* H. J.: White male, aged 56 years. Became ill on August 19, 1933, with anorexia and malaise, and he slept more than usual. On August 21 he had severe headache, abdominal pain and stiff neck. He entered the hospital on August 24, with the diagnosis of encephalitis and bronchopneumonia. On entrance he had a very stiff neck, positive Kernig, and absent abdominal reflexes. He slept a great part of the time, but at other times was boisterous though fairly rational, and either would not or could not answer questions. Although his temperature rose to 103.6° F., his W.B.C. was only 8,250, and his Schilling count showed 14 stab forms, 66 segmented, 17 lymphocytes, and 3 monocytes. Lumbar puncture revealed clear fluid under moderately increased pressure with 134 lymphocytes and 21 polynuclears. On August 28 the spinal fluid had 195 cells, of which 177 were lymphocytes. He grew progressively worse, and died August 28, 1933. Autopsy.

CASE 5 (fig. 33). *Typical case, with cystitis.* T. M.: White male, aged 68. Entered the hospital on August 20, 1933, with a history of having had vertigo on August 12, 1933, which was not severe, though present to some extent for several days. By August 16 he had so much headache, malaise, and weakness that he went to bed, and on August 17 became unconscious. When admitted to the hospital 3 days later, he was extremely stuporous, had a rectal temperature of 103.4° F., very stiff neck, positive Kernig sign, and absent abdominal reflexes. His W.B.C. was 11,600 and the urine showed a large amount of pus. His spinal fluid had 160 cells, mostly mononuclears. On August 21 the puncture revealed 105 cells, of which 83 were mononuclears. At this time he had active knee jerks, biceps and

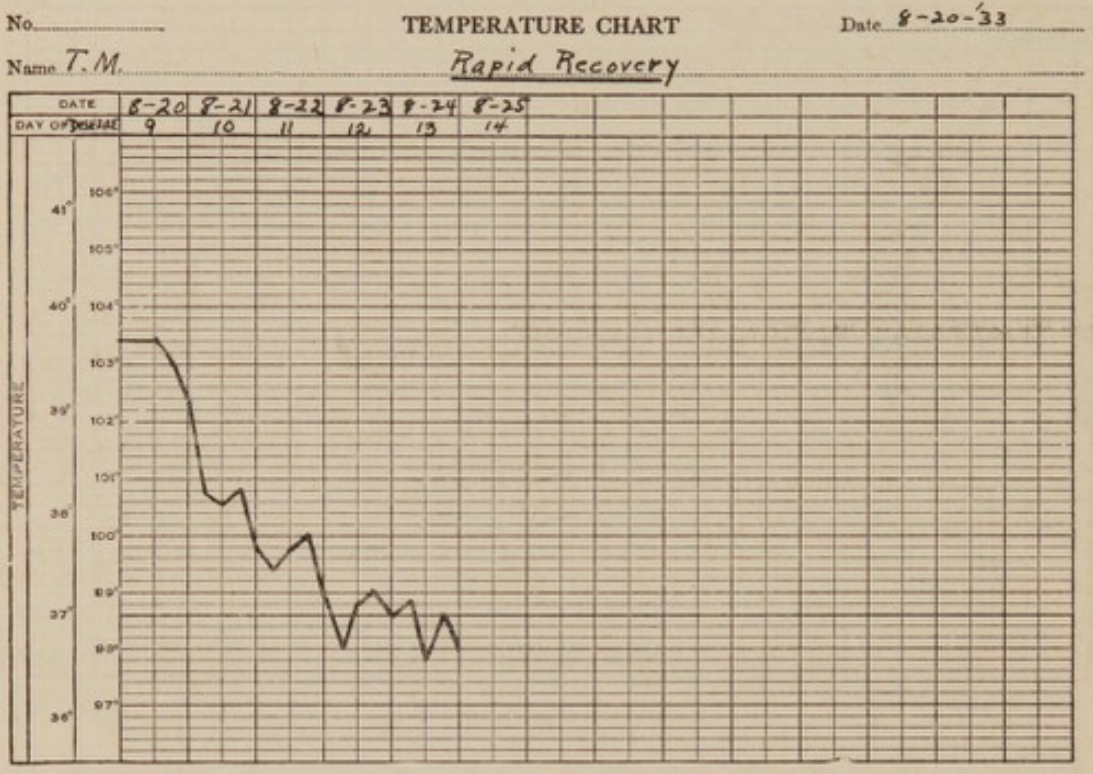

FIGURE 33.—Male, aged 68.

triceps reflexes, positive bilateral Oppenheim and negative Gordon and Babinski signs. The Kernig sign was positive and the neck less stiff. Except for persistence of the pyuria, he improved rapidly from this time on, so that on August 28, 1933 he was no longer drowsy, though still slightly disoriented. He had apparently recovered fully by August 31, 1933 and was discharged on September 2, 1933.

CASE 6. *Mild or abortive encephalitis.* E.D.: White female, 19 years, in good health up to 6 days before admission. Since then has had moderate amount of headache, some fever and pronounced photophobia. On admission she was found to have a temperature of 103°

F., was clear mentally, not drowsy, had no tremors nor speech difficulty, and did not look very sick. The Kernig sign was negative, but there was no abdominal reflex. However, her neck was very slightly stiff, and the headache persisted, though not severely. There had been no vomiting or nausea. The W.B.C. was 13,000. Lumbar puncture revealed 107 cells, almost all mononuclears. Three days later the temperature was normal, headache gone, and the patient said she felt fine. No further symptoms developed.

NEUROLOGICAL ASPECTS, INCLUDING LATE RESULTS

Interest in encephalitis B in St. Louis has arisen only recently due to the epidemic of 1933. There have been observed here in the past 5 years a series of sporadic cases of meningitis differentiated by spinal fluid findings; the cell counts were as high as 700, chiefly lymphocytes, with comparatively little increase in globulin, the sugar content normal, and bacteriological examination entirely negative. These cases, called lymphocytic meningitis, resembled the early picture of a tuberculous meningitis, but they became well and rarely showed involvement of the cranial nerves as found in tuberculous meningitis. Also in the summer and fall of 1932, there occurred cases resembling poliomyelitis, with signs of acute infection, altered reflexes, increased lymphocytes in the spinal fluid, without paralysis, and recovering without residuals. In December and January 1932 and 1933, there came to the attention of one of us, four patients who showed evidence of an acute meningitis with severe prostration and spinal fluid findings as in these previous cases. In the three cases which failed to recover, apoplectiform manifestations occurred. Therefore one is inclined to believe that the present type of encephalitis may have been with us previously.

The attempt of Kaneko and Aoki in their comprehensive discussion of encephalitis B to group the cases in several ways is justifiable inasmuch as the range of clinical manifestation is wide. This disease may run a period as short as 12 hours with recovery, or as long as one-half year. The average duration is about 2 weeks. The points to remember are first, that we are dealing with a constitutional disease occurring for the most part in older individuals, and secondly, that the relative vulnerability of the nervous system to this infection varies considerably. This neurotropic variation can be better understood when we consider the relatively small incidence of encephalomyelitis in pertussis, scarlet fever, measles, and vaccinia. Another point worthy of consideration is that part of the clinical picture may be patho-physiological, a predominantly toxic invasion. We know that this reaction depends upon two factors, namely the virulence of the infection and the constitutional reaction pattern of the patient.

Therefore, it will be of considerable help to consider the various schemes of classification suggested.

TYPES

1. *Classification of Yamada:*
   - Comatose.
   - Lethargic.
   - Hemiplegic.
   - Delirious—hyperkinetic.
2. *Classification of Kaneko and Aoki:*
   - Comatose.
   - Delirious—hyperkinetic.
   - Apoplectic—hemiplegic.
   - Somnolent—lethargic (seldom).
   - Choreiform.
3. *Classification based on localized pathology:*
   - Cerebral.
   - Basal-ganglionic.
   - Bulbar.
   - Spinal.
   - Meningeal.
4. *Classification based on course of illness:*
   - Foudroyant (fulminating).
   - Acute.
   - Subacute.
   - Chronic (few).
5. *Classification based on intensity of illness:*
   - Very severe.
   - Severe.
   - Moderately severe.
   - Light.
   - Abortive.

Probably the easiest and most logical approach to the present discussion of neurological manifestations is to ascertain when the family physician or internist who first sees the case feels a need to call the neurologist in consultation.

The onset of headache, severe, more or less persistent, usually over the brow, in the parietal regions, or in the occiput, occurs on about the second to seventh day of illness. It is so severe that any active or passive motion elicits acute pain, not only in the head but in the neck as well, and the patient on examination shows in most cases rigidity of his neck and a Kernig sign, although one feels the Kernig is of less value in the older patient as there may be present a certain amount of joint pathology that invalidates this finding. One finding of particular aid is the rigidity of the spine on having the patient sit up. At this time, further neurological examination may show nothing more than pupils which are smaller than normal for age, and which react slowly to light. Abdominal reflexes are usually absent. Deep reflexes may be unaltered or increased at first and then diminished. These findings warrant examination of the spinal fluid which shows

moderately increased pressure, little increase in globulin, a variably increased cell count with a relative lymphocytosis. The headache is remarkably relieved by the lumbar puncture and in a large percentage of cases, the patient begins to convalesce slowly.

In another group of individuals, we find in addition to the above symptoms and findings, paraesthesia, backache, and myalgic pains throughout the body especially in the abdominal muscles and calves. There are, likewise, motor disturbances, namely a moderately coarse, irregular intention tremor of the tongue, lips, and outstretched fingers associated with generalized weakness and poor muscle coordination. In a few instances, this may be erroneously called ataxia. Because of the tremors of the lips and tongue, the speech becomes thick, "sloppy", "sticky", and akin to that found in delirious patients.

With the disappearance of the abdominal and cremasteric reflexes, come the vesical and rectal disturbances. The clinical data given by Kaneko and Aoki may be of interest. In 115 cases, 15 showed urinary retention and 46 showed incontinence. They also noted some slowness in expelling the feces, but in only one instance was there incontinence. One feels that the incontinence is an overflow phenomenon. In the cases seen during the St. Louis epidemic, urinary retention was a very common finding. Constipation was also present and neither condition showed improvement until the return of the abdominal reflexes. This almost constant finding raises the question as to whether one dealt with a cord lesion.

Involvement of the cranial nerves is rarely seen at this stage of the illness. The patients sometimes complain of blurred vision, but only very occasionally do they complain of double vision, in contrast to patients with lethargic encephalitis. Careful and repeated testing fails to reveal any paresis of the extra-ocular muscles, indicating a very transient condition. Very few cases of optic neuritis or of nystagmus have been reported. Also, it is exceptional that one may note involvement of the auditory nerve.

At this stage of the illness, the most common manifestations are an increase in motor restlessness, apprehension, confusion, and somnolence. The picture is essentially that of toxic delirium and may lead to coma from which the patient can usually be aroused. When so aroused the patient will cooperate in a confused way; but during the course of examination, if his attention is not actively held he will fall back to sleep. It is at this time that his intention tremors are conspicuously present. The coma may last from a few days to several weeks. An unsuccessful attempt was made to correlate these findings with a previous use of alcohol.

Contrasting this with lethargic encephalitis (Von Economo), it will be remembered that at some time during his illness the typical patient with the Economo type of disease seemed to be quietly asleep,

resting comfortably and not appearing particularly ill. When aroused he seemed clear, cooperated nicely and when his attention was no longer held, he resumed his peaceful sleep. The motor restlessness was characteristically choreiform or athetoid. There was no confusion or bewilderment. The patient with lethargic encephalitis did not impress one as sick, either physically or mentally—quite in contrast to patients seen in the present epidemic.

Acute fulminating cases with severe prostration and high fever showed absence of all reflexes. The longer the duration of delirium and coma, the more likely one is to find further neurological signs. For example, such a pyramidal-tract sign as the Babinski may be elicited. The striking fact is that such findings vary, not only from day to day but in the half hour during the course of a ward walk. Later, they may persist showing that one no longer deals with irritative phenomena but with definitely localized pathology. Other signs of a pyramidal-tract lesion may be present such as the Oppenheim, Gordon, Chaddock, or Rossolimo, but no one sign is consistently present.

In numerous instances of the less acute types, one finds that after these signs disappear, a well-sustained ankle clonus is present without further evidence of pyramidal-tract involvement. This may persist for weeks despite the patient's general improvement.

While the pyramidal-tract signs appear in the lower extremities for the most part, there is occasionally some involvement in the upper extremities. In a very few instances, this is evidenced by weakness and then spasticity and rigidity of the arm, which varies from time to time. This is quite understandable when the pathological lesion is considered in its various stages. One may find a Hoffmann sign, a Meyer or a Leri, but an absence of these does not exclude pyramidal-tract involvement as these signs appear only in fully developed lesions of this motor system.

Although transient cranial nerve palsies are seen early in the disease, there is a certain small group of subacute cases in which involvement appears late. Delirium and coma were prominent features of these cases. In three instances peripheral paralysis of the facial nerve occurred long after the subsidence of fever. Tremors of the face were common. Paralyses of the twelfth nerve are also seen occasionally but usually cause no difficulty. In a few cases speech difficulties other than those typical of delirium arise. In a child of three, there was no speech except crying and screaming when restless and annoyed. In an elderly patient who had a hemiplegia following a fractured skull and who subsequently developed encephalitis, it was noted that he spoke less well, motor coordination was poorer, he became bed-ridden and incontinence appeared.

In the more chronic cases, although the patient may have no fever or may have only an occasional rise in temperature, drowsiness, befuddlement, confusion and motor restlessness may continue. One patient had complete amnesia for the entire period of hospitalization. This suggests Korsakow's syndrome, characterized by confabulation and disorientation, chiefly nocturnal, of long duration.

Much attention has been given to residual symptoms which were found so frequently in encephalitis lethargica. While Kaneko and Aoki found 1.8 percent residuals in some 2,000 cases of the 1924 Japanese epidemic, further data are unavailable. The findings in their 35 cases are as follows:

	Percent
Paresis such as hemiplegia (7)	20
Memory disturbance (6)	17. 1
Psychic disturbance (5)	14. 3
Hearing disturbance (4)	11. 4
Head pains—headache (3)	8. 6
Vertigo (2)	5. 7
Speech disturbance (2)	5. 7
Spasms of extremities (2)	5. 7
Contractures of leg (2)	5. 7
Visual disturbances (1)	2. 9

It is difficult in the present monograph to talk at length of residuals and sequelae in the St. Louis epidemic. Patients with neurological or mental conditions have long since been afebrile and showed general and progressive improvement. Quite a few show excessive physical and mental fatigue. When the latter type of fatigue occurs, one finds irritablity and difficulty in concentration which may be called by them a memory disturbance. A few have insomnia. Three patients seen by one of us have complained of a deep, burning type of pain in the shoulders and arms—pain which did not respond to heat or anodynes and which subsided slowly. One woman spoke of feeling that she was wearing a constricting iron band under her corset. These pains are very probably of central origin. Some of the children have shown hemiplegias and monoplegias. One of these developed a Jacksonian epilepsy.

It should again be emphasized that such patients had not fully convalesced from their illness, but after they were on the road toward recovery, developed the above symptoms. Apparently they were developing pathological lesions provocative of the above clinical findings. This view is borne out by the finding that in some of these cases spinal fluid examination still shows increased cells and globulin. Further examinations are planned in these cases. Behavior problems in children have been observed in two cases; one where lying, stealing, and running away occurs, and another where the child is destructive and belligerent and has a Jacksonian epilepsy. It is, however, too

early to discuss the extent and frequency of chronic symptoms and residuals. Thus far not many have been seen.

An attempt to give some sequence of development of neurological signs and symptoms is recorded in the following table. While no rule of thumb is feasible, moderately severe cases are apt to develop the first eight findings. The more severe types progress so that the other findings enumerated may occur.

1. Headache—Parietal, occipital, intense; paresthesia, myalgia.
2. Rigidity of neck, immobility of cervical and dorsal spine; Kernig sign.
3. Deep reflexes at first increased and then slightly diminished or unaltered.
4. Tremor—moderately coarse, irregular—of intention type, in fingers, lips, and tongue in about half the cases.
5. Pupils somewhat contracted with diminished reaction to light.
6. Coma, stupor, delirium, *essentially a toxic picture.*
7. Abdominal reflexes absent.
8. Sphincter disturbance, urinary incontinence or retention, constipation.
9. Pyramidal tract signs, pathological toe signs, signs in upper extremities, tendency to change at first but as lesions organize persist.
10. Cranial nerve involvement; rare. *Early:* Exophthalmos, external rectus palsies, facial weakness, nerve deafness, paresis of tongue. *Late:* Bell's palsy, external rectus palsies, speech defects.
11. Late results—Paresis and paralysis of the extremities; paresthesia, spontaneous pain; fatigue, physical and mental. Mental disturbances—irritability, concentration difficulty, confusion akin to Korsakow's syndrome, behavior problems.

The typical case presents no great diagnostic problem. The abortive or mild forms which the family physician and internist see may, as in all epidemics, pass unrecognized. The severe cases in which one finds a multiplicity of symptoms and signs are our concern and were seen by the neurologist. Differential diagnoses were: Tuberculous menigitis, encephalitis lethargica, cerebral hemorrhage, typhoid fever, and drug poisoning.

The following severe chronic cases are presented in extenso because of the *unusual* findings.

Case 1. M.J.M.: Female, age 3. Admitted September 23, 1933, with a complaint of fever, stiffness and pain in the neck, and general malaise and lassitude for the past 3 days and vomiting for the past 2 days.

The present illness began in the afternoon of September 20, 1933, with stiffness and pain in the neck which diminished the next morning. It recurred in the afternoon at which time fever and malaise set in. As her temperature rose, she had generalized convulsions, lasting for a few minutes. It was noted she rolled her eyes and was semicomatose. The family physician found a white count of 16,000 and the spinal fluid showed 170 cells and a trace of globulin.

On admission to the hospital she seemed conscious, was very drowsy, cross and irritable. The pupils were small, reacting to light; tonsils and pharanyx were slightly injected. The neck was somewhat rigid; abdominal reflexes absent; bilateral Kernig; Babinski, bilateral, more marked on right than left.

On the 26th she was stuporous, had to be tube-fed but could be aroused. On the 28th, her legs were rigid, her stupor increased and she began to have convulsions which were characterized as follows: Pupils varying in size; at one time, the right was dilated; her head was turned to the right and drawn back; convulsions began in the right hand, spreading to the face and right leg and then later to the left side of the face. Tuberculous meningitis was suspected but the spinal fluid sugar was found to be 97.

September 29, 1933, her temperature fell, the stiffness of the neck decreased but the patient was still stuporous. She became more alert and on October 6 developed a left otitis media. October 9 she again had localized convulsions and examination showed bilateral Babinskis. Shortly thereafter she showed clonic movements of the left arm, leg, and face. She had the cry ascribed to meningitis and gradually became more stuporous, rigid but very restless. Examination showed stiff neck, Kernig, absent abdominals, hyperactive deep reflexes and bilateral Babinski.

On October 24, 1933, the knee jerks disappeared, returning in the next 3 days. November 2 she seemed slightly improved, squirming and kicking under any attention. November 9, she began to talk some, saying "daddy", "ball", and an over-reaction to any attention was experienced, an extreme restlessness, so that examinations were impossible. Her pupils now showed paradoxical reaction to light.

Spinal fluid examinations were as follows:

Date	Pressure	Sugar	Globulin	Cell count	Differential	
					Poly-nuclears	Lympho-cytes
					Percent	*Percent*
Sept. 23, 1933			1 plus	170		
Sept. 26, 1933	4 plus	97 mgm	do	151	10	90
Oct. 3, 1933	do	1 plus	3 plus	125	60	40
Oct. 6, 1933	Bloody tap					
Oct. 9, 1933	2 plus	1 plus	2 plus	79	12	88
Oct. 12, 1933	Normal	do	3 plus	54	8	92

Examination made March 27, 1934, showed the child to be extremely restless and irritable. She showed weakness of the right arm and leg, with increased deep reflexes on the right and Babinski right. The convulsions are becoming less severe both in frequency and intensity. She walks fairly well, dragging her right foot.

The interest in this case lies in the prolonged course, marked irritative meningeal signs with Jacksonian convulsions, and resultant hemiplegic picture. Whether one is dealing with a progressive picture can only be determined by time and further examination.

Case 2. O.D.: Female, age 22, single. This patient when first hospitalized complained of severe frontal headache of 3 days' duration, fever for 2 days, and vomiting during the past day.

Examination showed transitory spasticity of all extremities and hyperactive reflexes; the white count was 15,500 with a differential of 20 stab forms, 58 segmented and 28 lymphocytes. Spinal fluid examination showed 115 cells per mm, 89 of which were lymphocytes, globulin 3 plus, sugar 93 mgm.

On admission the patient was rational, but rapidly became noisy, restless, screaming loudly, and delirious. This necessitated removal to the Isolation Hospital September 27, 1933, where she showed similar behavior, constantly throwing herself about in bed. When quiet, she lay with her head turned to the left, eyes deviating back and to the right; with passive motion of her head, her eyes remained in the same position; left facial weakness was only slight. Abdominal reflexes were active. She was incontinent of urine. While the lower extremities were rigid, this rigidity seemed to be of a voluntary type. Her arms and hands were flexed and as time elapsed, this posture became more characteristic so that at the end of a few months, her hands could hardly be forced open. At no time did she talk but vigorous protest to attention was registered in screaming; insomnia was marked and responded little to any hypnotics or sedatives.

Spinal fluid findings:

Date	Pressure	Sugar	Globulin	Cell count
Sept. 28, 1933	2 plus	Trace	Negative	25
Oct. 7, 1933	do	do	do	18
Oct. 2, 1933	3 plus	57 mgm	do	15
Oct. 26, 1933	1 plus			8
Jan. 10, 1934			Negative	33

On discharge from the hospital March 7, 1934, she showed marked spontaneous lateral nystagmus, marked tremor and incoordination. There were periods of cyanosis and the pulse was rapid. She was beginning to walk and talk.

This case was of unusual interest; unlike the other prolonged cases, it showed: (1) *Peculiar posture:* The head was at first constantly turned

to the left and backward; the eyes remaining fixed as the head was turned; the arms were flexed at the elbows and wrists and held stiffly, although no postural reflexes could be elicited. The condition suggested decerebrate rigidity; no pyramidal tract signs were present. (2) *Speech:* Absent until recently; any attention, particularly if unpleasant, caused a violent to and fro motion of the head and crying out. (3) *Absence of gross alterations in reflexes.* (4) *Mental state:* Characterized by restlessness, excessive incoordinated motor activity although the patient remained in a fixed posture; irritability, noisiness, and insomnia are present. Although the patient is generally improved and shows few neurological signs, one feels that there is involvement of the brain stem.

Case 3. M.M. Female, age 47, single, admitted September 13, 1933, complaining of headache of 2 to 3 months' duration but in the past 3 days developing pain in the back of the neck and head with fever and extreme drowsiness. The latter had increased. She seemed delirious and extremely tremulous. Examination showed her to be delirious; her speech was thick and the content rambling; pupils were small but reacted to light; she had a mild conjunctivitis, and coarse irregular tremors of tongue, lips, and outstretched fingers; her neck was stiff; Kernig positive; abdominal reflexes active; all deep reflexes were hyperactive and equal; there were no pathological toe signs.

She rapidly went into a coma, having to be tube-fed and catheterized. September 22, 1933, she came out of this coma but showed a lateral rectus palsy on the left; facial weakness on the left, and her tongue deviated to the left. October 4, 1933, she gradually slipped back into her previous comatose state, showing much nocturnal disorientation and restlessness.

November 4, 1933, she had a Babinski on the right and since this time had a well sustained ankle clonus on the right without other pyramidal tract signs.

Examination done March 18, 1934, showed marked digital and oral tremors; hyperactive reflexes; absent abdominals and bilateral clonus, more marked on the right.

Spinal fluid findings:

Date	Pressure	Sugar	Globulin	Cells	
				Polynuclears	Lymphocytes
Sept. 13, 1933	3 plus	40 mgm	Negative	80	98
Sept. 20, 1933	2 plus	Trace	do		10

The predominating features of this case were: Intermittent coma of long duration, after which time the patient showed involvement of the sixth, seventh, and twelfth cranial nerves; urinary and rectal

retention; pyramidal-tract signs on the right which persist. She also has complete amnesia for her entire hospital stay.

Again, it should be emphasized that these cases were atypical, presenting unusual and lingering features, and that improvement seemed to be taking place.

SEQUELAE AND RESIDUAL SYMPTOMS AS ASCERTAINED BY QUESTIONNAIRE

Within a few weeks after the nature of the St. Louis epidemic was determined the importance of a detailed study of the sequelae occurring in recovered patients was realized and plans were laid for following up each patient.

The following guiding principles were decided upon: (1) Every patient should be seen at least twice during the first year following recovery from epidemic encephalitis, and (2) whenever possible the patients should be seen by the physicians who originally treated them.

The first periodic survey was started early in December 1933 and completed the first of March 1934, about 4 months after onset. The patients naturally fell into two groups; first, those treated in institutions and, second, those treated by their private physicians. Notifications were sent by the Metropolitan Health Council to the surviving patients who had been in the local hospitals requesting each patient to be present for a follow-up clinic on a specified day when all interested physicians could attend. So far as possible follow-up on the second group was carried on through the attending physicians who were sent a follow-up questionnaire for each patient reported. Reports were received from the clinicians of the hospitals and institutions on 102 patients. The public health nurses called on 193 to obtain the desired information. Of the 379 questionnaires which were returned 4 were incomplete and therefore were not included in the statistical analysis, leaving 375 surviving cases to be studied.

Following is a summary of the city cases reported and of the follow-up reports:

Cases reported during summer and fall	577	
Deaths reported during summer and fall	130	
		447
Additional cases reported since fall	8	
		455
Mistaken diagnoses or death from other causes	15	
		440
Not found or no complete report submitted	65	
Follow-up reports received		375

It was found that in 35.5 percent of the cases complete recovery had been made according to the examining physicians' statement or that no residual effects were noted on the report. A classification by age does not show any significant distribution of complete recovery except in the age group under 10 years; here the recovery is higher than the general average.

Age group	Total follow-up reports	Complete recovery or no residuals noted		Age group	Total follow-up reports	Complete recovery or no residuals noted	
		Number	Percent			Number	Percent
Up to 9 years	42	20	47.6	60–69 years	49	15	30.6
10–19 years	43	16	37.2	70–79 years	17	6	35.3
20–29 years	60	20	33.3	80–89 years	3	1	
30–39 years	38	13	34.2	Unknown	1	1	
40–49 years	61	18	29.5				
50–59 years	61	23	37.3	Total	375	133	35.5

Some of the reports were not clear as to whether the symptoms of the patients were really after-effects of the encephalitis or whether they had been present in the same degree before the illness; in some instances it was evident that symptoms during the acute stage of the disease were included in the report and in other instances it was not entirely clear as to whether the symptoms noted were observed during the acute stage or at the time of the follow-up examination. The tabulations would therefore tend to represent the maximum rather than the minimum.

Number of cases	Symptoms noted in follow-up reports
100	Headaches.
90	Pains in various parts of the body.
86	Restlessness in sleep or sleepless.
72	Tremor of hands or other part of body.
69	Nervousness.
66	Impaired vision, or pain or burning of eyes.
56	Dizziness.
54	Forgetfulness or confusion.
48	Reflexes hyperactive or sluggish.
45	Personality changes; more excitable or irritable, or more sullen or melancholy.
29	Loss of strength, weakness.
24	Easily fatigued.
23	Speech affected—slower, or stammering, or jerky.
22	Droswy, lethargic.
21	Paralysis of face or other part of body.
19	Increased perspiration.
14	Diminution of hearing.

Symptoms noted ih follow-up reports—Continued

Number of cases	
13	Impairment of ability to concentrate.
4	Withdrawal from social contact.
3	Ptosis of eyelid.
1	Rapid decay of teeth.
1	Difference in size of two legs.
1	Knee bending habit.
1	Weakness in legs.
1	Fits.
1	Post-encephalitis involvement of cerebrum, "out of head most of time."

The symptoms varied from being occasional and slight in degree to being continuous and of considerable severity. About half a dozen physicians stated that the patient was in better health than before the attack of encephalitis and about the same number stated that the personality of the patient was quite changed, usually for the worse. In a good many instances, the symptoms noted were stated to have been much more severe and to be gradually improving. It is obvious that most of the residual symtoms, no matter what their actual cause, would fall into a neurasthenic grouping. Other summaries of the sequelae will be found on pages 58, 63 (first, second, and fourth paragraphs), and 73.

CLINICAL PATHOLOGY

No attempt will be made to present this study as more than a statistical compilation. The large number of individuals who made these tests, the variety of methods and interpretations and the extra work thrown upon the interne staffs by the sudden influx of many patients made these figures amenable to gross analysis only. Selected groups of cases in which some of the factors have been more satisfactorily controlled may be studied later. It will be found, however, that the tables below give a more or less accurate picture of the clinical pathology in this epidemic of encephalitis.

BLOOD

Cultures.—The cultures, usually in plain or enriched broth or on blood agar plates, were uniformly negative.

Chemistry.—No deviation from the normal range of blood sugar and nonprotein nitrogen (the only tests made) was found that could not be accounted for upon some basis other than the encephalitic syndrome.

Red blood cells.—The total erythrocyte count was within normal limits.

White blood cells.—In table 10, the total leucocyte counts are grouped in parallel columns, figures being given for all cases and for those cases that died. In the 20 percent of all cases in which the leucocytosis was 15,000 cells or more, pneumonia, cystitis, pharyngitis, and other

infections were frequent concomitants. In a few cases, however, no explanation was found for excessive leucocytosis other than encephalitis. The slightly (6 percent) higher percentage of cases having a total count of 15,000 or more white blood corpuscles in the fatal cases was probably due to the increased incidence of complications in these instances. One can say that there was usually a mild to moderate leucocytosis in the uncomplicated cases of encephalitis.

TABLE 10.—*White blood cells*

Number of cells	All patients		Patients that died		Number of cells	All patients		Patients that died	
	Number of cases	Percent of cases	Number of cases	Percent of cases		Number of cases	Percent of cases	Number of cases	Percent of cases
Below 5,000	19	3.4	3	3.4	12,000–15,000	98	17.4	14	16
5,000–7,000	50	8.9	7	8	15,000–18,000	54	9.6	11	12.6
7,000–9,000	89	15.8	12	13.7	18,000 plus	57	10.1	12	13.7
9,000–12,000	194	34.5	28	32.3					

DIFFERENTIAL (SCHILLING) COUNT

Monocytes.—On the average, the monocytes were between 2 and 3 percent, ranging almost always between zero and 5 percent. A very few cases showed higher values.

Lymphocytes.—In table 11, the lymphocyte counts are enumerated. Eighty-five percent of all cases had lymphocyte counts of less than 30 percent. In the cases that died, the decrease in lymphocytes was even more marked, as over 76 percent of these had lymphocyte counts of less than 20 percent.

TABLE 11.—*Lymphocytes*

Percent of lymphocytes	All patients		Patients that died		Percent of lymphocytes	All patients		Patients that died	
	Number of cases	Percent of cases	Number of cases	Percent of cases		Number of cases	Percent of cases	Number of cases	Percent of cases
1–9	32	9.4	6	12.7	40–49	12	3.5	0	0
10–19	135	39.8	30	63.8	50–59	4	1.2	0	0
20–29	121	35.7	7	14.9	60–69	2	.6	0	0
30–39	29	8.6	2	4.3	70 plus	4	1.2	2	4.3

MYELOCYTIC SERIES

In table 12 are the tabulations of the segmented neutrophiles. A great percentage of cases showed an increase in neutrophilic segmented leucocytes.

TABLE 12.—*Segmenters*

Percent of segmentors	All patients		Patients that died		Percent of segmentors	All patients		Patients that died	
	Number of cases	Percent of cases	Number of cases	Percent of cases		Number of cases	Percent of cases	Number of cases	Percent of cases
1–9	3	0.9	1	2.1	50–59	65	19.1	7	14.9
10–19	2	.6	0	0	60–69	127	37.2	12	25.6
20–29	8	2.3	1	2.1	70–79	82	24.1	18	38.3
30–39	5	1.5	0	0	80–89	17	4.9	5	10.6
40–49	31	9.1	2	4.3	90 plus	1	.3	1	2.1

The "stabkernige", "stabs", or band forms were increased, 76.5 percent of all cases having more than 6 percent "stabs", as noted in table 13.

TABLE 13.—*Stabs*

Percent of stabs	All patients		Patients that died		Percent of stabs	All patients		Patients that died	
	Number of cases	Percent of cases	Number of cases	Percent of cases		Number of cases	Percent of cases	Number of cases	Percent of cases
1–3	27	7.9	3	6.3	16–20	34	10.0	7	14.8
4–6	53	15.6	7	14.8	20–25	18	5.3	1	2.1
7–10	112	33.1	15	31.9	25–30	6	1.7	1	2.1
11–15	85	25.1	12	25.5	30 plus	3	.8	0	0

No juvenile forms were recorded in about 40 percent of all cases. In the remainder, these cells ranged between 1 and 6 percent with very few above 10 percent.

Eosinophiles, myelocytes, and basophiles occurred rarely.

The hemogram, as a whole, can be interpreted as a moderate relative and absolute neutrophilic leucocytosis with a slight to moderate shift to the left in the Schilling differential count. The differences in the hemograms of those patients that recovered and of those that died were not marked enough to be of prognostic significance.

SPINAL FLUID

Gross appearance.—Variations from clear to moderately turbid fluids were recorded.

Pressure.—The pressure was usually increased, although not always so. The different methods used in the several hospitals for estimation of pressure made it difficult to tabulate the results. Manometric readings were rarely made and, because of this, the results were not very useful. The symbols used to record pressure were quite variable, some used "O" for normal and "plus" for increased pressure; others graded the pressure from "O" to "four plus (++++)." The designations "slight" and "moderate" were also used. In table

14, "plus" (+) includes those cases where the pressure was designated "slightly increased" as well as those that were graded "+." Many of these cases may have been "several plus" if they had been evaluated upon a graduated scale.

TABLE 14.—*Spinal fluid pressure*

Degree of pressure	All patients		Patients that died		Degree of pressure	All patients		Patients that died	
	Number of cases	Percent of cases	Number of cases	Percent of cases		Number of cases	Percent of cases	Number of cases	Percent of cases
0	79	15.5	7	7.8	++	152	29.9	30	33.3
±	7	1.3	0	0	+++	69	13.5	19	21.1
+	175	34.4	27	30	++++	26	5.1	7	7.8

Microscopic appearance.—The total cell count (see table 15) varied over a considerable range, as many as 500 or more cells per cubic millimeter having been reported. The preponderance of cases showed only a moderate increase in the number of cells. It is interesting that the percentage figures in the fatal cases parallel those of the series as a whole. Cell counts on patients at the time of discharge were variable, some being higher and others lower than the cell counts during the active stages of the disease.

TABLE 15.—*Spinal fluid counts*

Number of cells per mm ^{3}	All patients		Patients that died		Number of cells per mm ^{3}	All patients		Patients that died	
	Number of cases	Percent of cases	Number of cases	Percent of cases		Number of cases	Percent of cases	Number of cases	Percent of cases
1-20	86	13	19	16.6	120-200	99	15	16	14
20-40	102	15.4	18	15.7	200-500	92	13.9	21	18.4
40-80	169	25.6	24	21	500 plus	24	3.6	4	3.4
80-120	88	13.3	12	10.5					

The differential cell count showed a predominance of lymphocytes, the average being approximately 80 to 90 percent lymphocytes. It was noted by some observers that some of these mononuclear cells did not have the appearance of true lymphocytes, in that they were larger and tended to be polygonal in shape. The true nature of these cells was not determined.

Chemistry.—The presence of protein was estimated qualitatively in almost all instances. The Pandy test was the one almost exclusively used, although the Ross-Jones test was also mentioned. The various designations used in recording results were "negative", "increased", and a variable number of pluses. The results tabulated in table 16 show that most of the cases had an increased amount of protein.

TABLE 16.—*Spinal fluid (Pandy)*

Reading	All patients		Patients that died		Reading	All patients		Patients that died	
	Number of cases	Percent of cases	Number of cases	Percent of cases		Number of cases	Percent of cases	Number of cases	Percent of cases
0	234	40.1	27	28.4	++	30	5.1	5	5.2
±	50	8.5	0	0	+++	6	1.0	0	0
+	261	44.7	61	64.2	++++	2	.3	2	2.1

The Lange colloidal gold test was not carried out in all instances. Marked variations in the type of curve obtained were noted. It is interesting that in some institutions entirely normal curves were reported, whereas in others a "tabetic" curve was predominant.

The results of the sugar determination varied, the greater number being within the range considered as normal. The reported figures should be considered with reservations because the method of determination was not stated and simultaneous blood sugars were not performed. Table 17 shows those cases in which spinal fluid sugars were reported.

TABLE 17.—*Spinal fluid sugar*

Mg percent of sugar	All patients		Patients that died		Mg percent of sugar	All patients		Patients that died	
	Number of cases	Percent of cases	Number of cases	Percent of cases		Number of cases	Percent of cases	Number of cases	Percent of cases
Below 60	94	36.3	5	18.5	90–99	16	6.2	2	7.4
60–69	76	29.7	6	22.2	100–119	11	4.3	3	11.1
70–79	40	15.6	5	18.5	120 and above	4	1.6	2	7.4
80–89	15	5.9	4	14.8					

URINE

Examinations of the urine showed nothing significant in uncomplicated cases.

PUBLICITY AND COMMUNITY COOPERATION

The encephalitis epidemic did not cease without leaving for St. Louis a heritage of good results. As one looks back upon the days of August and September 1933, one cannot but feel that the experiences through which the community has passed were far from being an unmixed evil. We expect to review in this chapter the results of more or less permanent value left by the epidemic in three separate sections dealing with—

I. Public Information.
II. Cooperation and Reactions of the Public.
III. Lessons for the Community.

Before undertaking a detailed study of each of these three heads, it might be well to point out the conclusions, the evidence for which will become apparent in the course of our discussion. With regard to public information it must be said, to the credit of the press of St. Louis and of all the agencies which contributed to public information, that at no time during the period of the epidemic was there the slightest evidence of a psychological panic and at no time did the people of the Metropolitan area lose confidence in the capability, the earnestness, and the diligence of its health leaders. More striking still, it must be insisted, that at no time during the period was there voiced a suggestion of criticism of the health authorities. Finally, what must be regarded as even more striking, at no time during the epidemic, despite the fact that the public clamored more and more for details concerning the researches and the clinical studies which were known to be in progress, did the public lose confidence in the value of the scientific procedures which were being openly and frankly discussed. The public felt that it received the full confidence of the scientific investigators, of the physicians who were conducting the clinical studies and of the other workers who were devoting themselves to research in special scientific or social or economic or hygienic phases of the investigations. That all of this is directly or indirectly traceable to the manner in which the daily press and those responsible for other modes of public information were handling their subject there can be no reasonable doubt.

Concerning the spirit of cooperation and mutual understanding engendered in the community by the epidemic, excellent results of the highest importance are traceable even after almost a year. The boundary sharply enough drawn between the county and city was temporarily and it may be hoped to some extent permanently effaced. What had seemed quite difficult of achievement was created almost overnight, namely, the Metropolitan Health Council. The differences between private and public health agencies, hospitals, outpatient departments, welfare organizations, were almost suddenly obliterated and the mutual understanding which was effected bids fair to persist if not in its fullness, at least sufficiently to form a solid foundation upon which further building may result in permanent and effective cooperation.

Lastly, with respect to the lessons for the community, these are so obvious that anyone who has known St. Louis over a long period of years can note the change in public thinking. A large interest was created in science, particularly in scientific investigation; respect for the science and art of medicine has increased; a strong interest in public health has been created; an appreciation has been developed for standards in public health and for the personnel of health agencies and, finally, but by no means least, a most eloquent and effective lesson

was given to the community at large in community planning, community organization, and community cooperation.

We propose in the following pages to supply the data upon which the generalizations here summarized are based.

I. Public Information

To write a complete history of the modes by which public information concerning the encephalitis epidemic was diffused would lead us much farther than is possible within the confines of the concluding chapter of this monograph. These agencies of diffusion included the press, radio talks, public lectures, the bulletins of public and private agencies and, to be sure, conversation, as the most effective even if perhaps the most fallible mode of diffusion.

1. *The press*

(*a*) *The local press.*--To the daily press of St. Louis must be attributed to no small extent the fact that the public's attitude toward the epidemic was largely one of deep interest in the scientific aspects of encephalitis rather than an attitude of panic or self-pity. A rapid review of the headlines reveals three distinct types of captions; first, those that were purely factual, stating the number of new cases, the number of deaths, the number of patients in individual hospitals, etc.; secondly, those which announced the progress made by the investigators or announced comments by persons of prominence upon the progress of scientific investigations; and thirdly, those which stressed the safeguards against the spread of infection. Of these three classes of headlines only the first obviously would have a tendency to arouse a feeling of dread or alarm in the public mind. The other two types of headlines had a tendency to awaken interest in the scientific aspects and to create confidence in the effectiveness of the procedures which had been adopted. It is true that occasionally a misleading article did appear in the daily press. So effectively had the propaganda of the press achieved the desired results that the public was watching the laboratories and the examination rooms in which the investigators and physicians worked with an interest never before equaled in this community. To be sure, the "mysterious character" of the disease was of itself largely responsible for this profound interest. The contrasts between the St. Louis epidemic and other epidemics of encephalitis such as the Japanese epidemic were featured rather than the similarities with other epidemics known to have been particularly virulent and lethal. To what extent this trend in the publicity was conscious no one can say, but the fact of itself speaks volumes for the spirit in which the entire subject was approached by the press. Moreover, the investigators by a conscious or subconscious use of psychology appreciated the public interest. They

disseminated rapidly and effectively such scraps of information as could be safely distributed. It is true that now and again information reached the press which on closer investigation proved less accurate or premature or in some cases even false in its implications, but all of this seemingly was taken rather as an evidence of the difficulty of the problem which confronted the investigators than as an evidence of their incapacity to cope with the question. It is noteworthy too that either by reason of the press activity or for some other undiscoverable reason, the interest of the public centered rather in the investigations which were going on than in the virulence of the epidemic. This fact might be attributable to the relatively low mortality, as well as to the fact that relatively few sequellae of a disquieting nature seemed to follow immediately upon convalescence. The progress of the epidemic, therefore, was watched by the public very much as a group of public health experts might watch and study it. These attitudes proved to be of enormous importance to the maintenance of equilibrium and soundness in the public psychology.

Another factor which was no less significant was this, that for reasons not as yet fully understood, the incidence of the disease was restricted apparently almost universally to one person in a family, only a few cases having been found in which more than one member of the family was stricken. Similarly, the "spotty" character of the incidence played a considerable role in the maintenance of the public's peace of mind. Very few cases, if any, were on record in which persons living in contiguous or closely neighboring houses took sick. The press made the most of these pacifying facts and contributed thereby to the general peace of mind.

It would be difficult to give a fair estimate of the amount of space devoted to the epidemic by the local press. An estimate of a daily average during the period of 6 to 8 weeks as a column and a half for one of the papers, a column and a quarter for another and three quarters of a column for the third, would probably come very close to the facts. In addition, occasional pictures of local physicians or visitors to the city in connection with the epidemic as well as of various meetings were carried in the pictorial or news sections. These pictures always aroused very considerable interest and their influence in creating and molding public opinion must not be overlooked. Constantly keeping before the mind of the public the men and women who were engaged in safeguarding the city was a not insignificant factor in the creation of the public psychology.

Another feature of the newspaper activity must be mentioned even if only in passing. We refer to the editorials. These were uniformly appreciative of the efforts which were being made. They were laudatory of the individuals engaged in fighting the epidemic and

freely distributed recognition of the achievements of the scientific workers.

If in retrospect one might now desire that something might have been changed in the publicity, it might be pointed out that too little attention was devoted in the press both in the news columns as well as in the editorials to those institutions and agencies which were carrying on the routine labors of combating the epidemic while attention was devoted too exclusively to what might be called the potentially sensational aspects of the disease. Almost all of the institutions which cared for these sick patients could tell volumes of human interest stories, some of them of the finest publicity value which were overlooked amidst the wealth of more striking news, but perhaps this only means that there was so much of news value available that the newspapers had to choose only what was presumably most impressive. The press was also probably most effective in aiding in recognition and isolation. This desirable result was achieved through the publication of tempered, well considered and casually worded warnings. The character of the warnings was most "common sensible", emphasizing the need of consulting a physician promptly at the earliest instance of some of the well-established premonitory symptoms. Apparently, the press was anxious to get interviews which stressed this phase of the epidemic and it must be said to the credit of the St. Louis medical profession that such interviews were gladly and generously supplied. The press also deserves credit for understressing rather than overstressing occasional controversies with respect to the scientific investigations as well as with respect to the diagnosis and therapeutics of the disease, although probably in some cases these controversies would have made excellent copy at least from the viewpoint of the reporter.

(*b*) *The press outside of St. Louis.*—If all of the above must be accepted in justice and fairness to the St. Louis press, it is to be regretted that one's account of the publicity activities of the press outside of St. Louis cannot be as gratifying. This perhaps is not unexpected. Scare headlines announcing A Mysterious Death Stalking Through St. Louis and the claims of a Mysterious Malady Overhanging Missouri Metropolis were common enough during the period of the epidemic. The outside press somehow did not share the optimism of the St. Louis press. The suspicion had been engendered in the minds of the country's newspapermen that the St. Louis press was in some way suppressing or at least minimizing the gravity of the epidemic. Apparently even aspersions were cast upon the veracity and reliability of the incidence and mortality statistics. There was traceable in the press outside of the city something of the desire to "scare head" noticeable in a roadway sign near one of the cross-roads approximately 35 miles outside of St. Louis. The sign read:

"Detour here and drive around St. Louis. Avoid danger to your life." It must not be thought that this attitude was universal. Some papers carried accounts of the epidemic in relatively inconspicuous locations. The writer had the experience of studying the daily press accounts in approximately 35 newspapers during a 1,200 mile automobile drive shortly after the peak of the epidemic. The editorials in the newspapers of the larger centers were still suggestive of threats and menace even though the copy was sufficiently guarded. In the smaller population centers, however, the newspaper accounts were progressively inconspicuous and less harmful, the farther one withdrew from St. Louis. There is ample evidence that this form of publicity was not without its effect. An attitude of fear on approaching St. Louis was distinctly traceable. The Chamber of Commerce was besieged with letters as were also the schools which drew their student body from other localities. We shall have to come back to this point when we discuss the publication of bulletins by private and public agencies. The fact is mentioned here, however, only to suggest the effect of the press in creating public opinion in the Nation. Authenticated instances are on record in which people in other cities avoided contact with recent visitors from St. Louis for fear of contracting encephalitis.

(*c*) *Periodical press.*—The periodical press, largely the weekly and monthly reviews, all carried articles of more or less significance during the period of the epidemic and shortly after. These articles were largely factual in character and attempted for the most part to report carefully the situation as it existed in the St. Louis area. Interest seemed to center largely in two phases of the epidemic, in the disease itself and in the investigations which were taking place concerning the nature of this illness. The announcement of the various characteristics of the disease, the further announcement of the transmissability to lower mammals, the various suggestions which were made and tested concerning insects or other carriers, made copy which was deemed sufficiently interesting to the readers of these periodicals to merit not a little space. Pictures also proved popular. Secondly, but still quite extensively, the symptomatology of the disease and statistics concerning incidence and the mode of propagation were deemed not without their appeal to the general reader and it might be questioned whether any disease in recent years has been as fully or as extensively described in the semipopular press as was encephalitis.

The effect of this type of publicity was probably good, centering the interest of the reader upon those features in which an educative publicity program could best serve the social purposes of the periodical press. It is noteworthy that there has not come to the attention of the writer a single instance of criticism of health authorities or the public officials of the city. As far as is known, such reviews expressed

appreciation of the cooperative efforts of various agencies engaged in combating the disease.

(*d*) *The scientific and technical press.*—It would lead us too far afield from the immediate purposes of this review to present here even in summary the activities of the scientific and technical press. A large number of research papers have emanated from St. Louis as a result of the epidemic. These papers again pertain to both the strictly scientific and the clinical phases of encephalitis. Obviously, no attempt need here be made to evaluate their merit or to point out the sequence in thought about encephalitis of which these papers give evidence. This entire monograph is in reality a summary of what has been accomplished and while much that is herein contained has been previously unpublished, it is also true that a large percentage of it has already found its way into scientific literature. From the viewpoint of significance in future encephalitis epidemics, these publications form one of the most valuable results of the St. Louis epidemic. The study of encephalitis has been materially advanced. Interest in the disease has been intensified. Medical societies throughout the country have had special programs devoted to symposia on this subject. Papers have also been presented at the national meetings of associations of specialists and special papers by invitation were presented at the 1934 convention of the American Medical Association.

2. *Radio talks*

The radio proved to be one of the most effective factors in informing the public of the epidemic. Practically all of the local radio stations cooperated most generously in placing time at the disposal of the health authorities, the physicians and others who made radio addresses. The local health department was most zealous in its use of the radio, several members of the personnel making addresses as developments occurred. The general trend of these addresses was very much of the same tenor as that of the press. We quote from one of the addresses which emanated from the health department. "We feel that the best weapon in the hands of any modern health department is an unreserved and full publicity of everything that pertains to public health. In the last analysis, public-health work is primarily educational and the wider the circles it can reach through publicity the more will it accomplish. * * * The public had to know about this disease. The attention of the medical profession had to be centered upon this unusual epidemic. The country at large and medical science universally had to be notified of its appearance here. We have been told that the publicity accompanying this epidemic damaged St. Louis business by keeping many fearful people away. That may have been the case and it is possible that a few dollars that might

have come to St. Louis were lost, but we feel that the health of the people of this city is more valuable than a few dollars." Radio addresses were made not only by the health department but by physicians and welfare workers as well. Some of the titles of these addresses might be deemed interesting: One was called "Encephalitis and the Business Man"; another "The Mystery of Encephalitis", a third, "The Epidemiological Features of Encephalitis." One of the addresses dealt with the suggested causation of the disease, another with the strictly scientific aspects, particularly the pathological ones; another with research phases and still another with the cooperating agencies. In addition to these formal addresses, however, the countless incidental references may be thought as having had no little importance in shaping the public attitude. References were made to the epidemic in sermons, in business and advertising talks, in economic and political discussions and in health talks which dealt with other forms of illness. As is so often noticeable, the radio is perhaps one of the best barometers of public thinking and in this case also the popular mind was well mirrored by the number of casual references to the health conditions existing in the St. Louis metropolitan area.

As for the activities and the effectiveness of the national chains, very little could be learned. It is known that occasional references to the encephalitis epidemic were made in addresses on national hook-ups. There is record, moreover, of at least one whole address on a national hook-up. The manager of one of the networks writes, "It appears that on the matter to which you refer we only presented one program under the auspices of the New York Academy of Medicine on the subject of sleeping sickness during the time of the epidemic in St. Louis." The manager of one of the national companies writes, "I know that I did not book anything on sleeping sickness. I wanted to, but nobody would speak about it. They thought they knew too little about the subject to discuss it."

One of the local stations writes as follows: "The principal activity of this station in the dissemination of information regarding the encephalitis epidemic took place during our 'Mr. Fix-It' periods and was in the nature of the reports of new cases and advisory matter regarding precautions to minimize likelihood of infection. In other words, we handled the situation much as the newspapers handled it and were guided very largely by an attitude of trying not needlessly to alarm our listeners."

Another local station writes, "For your information, the health department of this city presents a weekly address over our station every Thursday evening, 5 to 5:10, and during the encephalitis epidemic numerous talks were given relative to this epidemic."

3. *Public lectures*

Concerning public lectures on the encephalitis epidemic, much the same comments must be made as have been made with reference to radio addresses. Almost all of the investigators and the physicians prominently connected with the care of the encephalitis patients received numerous invitations from social-service agencies, women's clubs, men's luncheon clubs, and fraternal organizations to give talks on the epidemic, upon the nature of encephalitis, upon the preventive measures and on similar points of public interest. The public mind was again expressed on these occasions through the uniformly large attendance which these lectures attracted. It was found to be quite impossible to accede to the numerous requests for talks which were received by the available lecturers. Occasional reports indicate that in almost all cases the desire was expressed to discuss the lecture, after it was given, and as might be expected the lecturers were often confronted with naive and sometimes startling theories and attitudes concerning the causation of the disease, suggested cures, and the popular fear of consequences.

In addition to these popular presentations, many other meetings of a scientific character were addressed by research workers. The St. Louis Medical Society scheduled at least two symposia on the subject. Several of medical specialists devoted one or more meetings to the discussion of special phases of the disease. Outside of the city the local medical societies invited speakers from St. Louis to present papers on the epidemic or some one of its special phases. Welfare organizations also outside of the city extended welcome to special lecturers from St. Louis.

4. *The bulletins of public and private organizations*

(*a*) *Organizations and agencies.*—The number of bulletins on the epidemic issued by the various public and private agencies and organizations are so numerous that it would be quite impossible without extensive research to describe them adequately. An effort, however, must be made to select types in the interest of securing a fairly complete presentation. The publicity director of the St. Louis Chamber of Commerce writes as follows: "The part that the St. Louis Chamber of Commerce played in the sleeping-sickness epidemic was designed largely to protect the good name of St. Louis. Letters that we had received indicated the public on the outside had a rather exaggerated opinion of the encephalitis outbreak in St. Louis. In many cases students and visitors hesitated to come to St. Louis due to the impression that prevailed from the large amount of publicity given to it that there was serious danger that they might contract the disease while visiting the city."

The statements here made and the opinions expressed are found to be quite common among the executive personnel of business

houses. It seems to be a fairly well established fact that salesmen were afraid to come to the city. Other business visitors to the city occasionally manifested similar fear. To what extent business was really influenced during this period by this dread disease of encephalitis it is not our purpose or aim here to estimate even if we could. It is doubtful whether reliable figures could be assembled upon this point. It is equally certain, however, that it is popularly believed that business did suffer rather extensively by the misconceptions engendered in the mind of the general public outside of St. Louis concerning the virulence and danger of the disease.

(*b*) *Schools.*—There are in St. Louis a number of schools, among them two universities, which recruit their student body largely from nonresidents of the metropolitan area. Some of these schools had the experience of receiving letters from former students and new students with inquiries concerning the safety of returning to the city during the period of the epidemic. It was somewhat unfortunate for these schools that the opening of the classes for the session 1933–34 coincided with the period of pronounced activity in the epidemic, even though its peak had passed by the middle of September. One of the schools solved its problem by sending a letter to each of its nonresident students, from which we quote: "Some of our students and their parents and relatives are disturbed concerning the epidemic of encephalitis. Apparently this epidemic is thought of much more seriously outside of the city than it is here. While the situation should not be minimized, nevertheless, it has not caused serious alarm concerning the health conditions in this city. None of the schools, public or private, have thus far announced any postponement of their opening dates. While it is true that up to date (Sept. 4, 1933) 424 cases of the disease have been reported for the St. Louis district, city and county included, it is obvious that this incidence in a population of more than 1,200,000 and that, too, over a period of more than 3 weeks, cannot justify radical measures." It would be easy but perhaps useless to quote the letters of anxious parents and of anxious students concerning their return to school.

As may be noticed in this quotation, reference is made to the action of the board of education. The board refused to be swept off its feet by over-cautious or over-zealous individuals who demanded that the opening of the public schools be deferred. The action of the school board met with unanimous and general approval of the citizens of St. Louis, since the conditions certainly did not warrant an action as radical and as significant as a delay in the opening date. As a matter of fact, events proved the wisdom of the school board's decision, since so far as is known, no new cases developed as a result of the opening of the schools.

(*c*) *The foreign non-American press.*—An effort was made to secure data from the foreign consulates in this city concerning the treatment of the epidemic in the foreign press and by other publicity channels in foreign countries. The effort, however, did not yield significant results. The foreign consulates all replied to the inquiries. The Swiss consulate, for example, records the following: "Numerous accounts, some of an alarming nature, have been published abroad concerning the epidemic. For this reason and in order to appease the anxiety of relatives in Switzerland of Swiss residents in this city, I deemed it advisable to send a report of actual conditions to my Government." The German consul writes as follows: "The encephalitis epidemic in St. Louis has been extensively discussed in the German press. Not only were individual phases of the epidemic and the incidence and mortality of the disease referred to in the German press, but extensive articles written by local correspondents were published. * * * The president of the Bureau of Health of the Reich presented a report to the Minister of the Interior concerning the encephalitis epidemic." Incidentally, the report to which the German consul refers is a well-considered and carefully compiled article, cautious and accurate, and must be deemed an excellent résumé of the local situation. The consulates of Ecuador, Great Britain, Austria, Mexico, Latvia, and Spain surmise that accounts of the epidemic have been published in their various countries but did not have details available. The Italian consul calls attention to the news service of the local Italian paper and of the New York Italian papers in which accounts of the epidemic appeared. The Netherlands consulate records the fact that several leading papers in Holland carried notices concerning the epidemic and also accounts published in medical journals. The Pan American Sanitary Bureau forwarded a copy of the Boletin de la Oficina Sanitaria Panamericana in which an extensive review of seven pages is published.

(*d*) *Reports of insurance companies.*—It was thought that the bulletins of life insurance companies might reveal the extent of interest in the epidemic among the insurance companies. The inquiry yielded relatively little information of value. One of the companies writes: "Encephalitis is placed in a group which includes other diseases of the brain and nervous system such as meningitis", and there is therefore "no way of determining how many of the encephalitis cases came from St. Louis without getting up a large number of death claims and investigating them all." Another one of the insurance companies points out unpublished data concerning death claims based on encephalitis deaths. While in 1932 this particular company settled 153 death claims for encephalitis, only 2 of which occurred in St. Louis, it settled in 1933 a total of 248 claims, 47 of which occurred in St. Louis. For the 153 encephalitis deaths in 1932 the

company paid benefits aggregating $47,474; it paid for the 248 encephalitis deaths in 1933, $94,988. The 2 encephalitis deaths in St. Louis in 1932 cost the company in benefits only $578, whereas the 47 encephalitis deaths in St. Louis in 1933 demanded the payment of $22,908 in insurance benefits.

(*e*) *Popular conversation.*—With all the agencies for the dissemination of information at our disposal, it is probably still true that the most effective one is still ordinary human converse. This phase of the question must not be overlooked and in the recent epidemic it formed a most effective factor in the maintenance of public confidence. Whether the well-known conservatism of St. Louis influenced the situation or whether the public confidence in the health leaders was so solidly founded that nothing short of catastrophe could shake it, the fact remains that while the epidemic was discussed in household and club, over bridge table and in amusement places constantly throughout the entire 2 months of the city's trial, there seems to be little evidence that could be assembled from extensive inquiry concerning any large fear in the minds of St. Louisans. The activities of the Metropolitan Health Council and of the various research laboratories as well as the activities of the hospitals and physicians elicited extensive popular interest and even now more than half a year after the cessation of the epidemic almost daily references are made to the period of the epidemic. It is evident, however, that people "kept their heads." There were few, if any, demagogic manifestations, not uncommon in other epidemics. Curiosity concerning the nature of the disease was common enough and was fostered by the attitude of the press as we have already pointed out. It must, however, be considered as evidence of the common-sense attitude of St. Louisans that the exaggerated reports which reached the city through contact with visitors concerning the epidemic were treated largely as jokes and furnished the cause for not a little amusement on the part of the local citizenry. There was even noticeable an absence of resentment concerning these exaggerations, one of the best signs of the good humor with which these exaggerations were regarded. The warnings to detour around St. Louis discovered by the St. Louis tourists in other sections of the country were sent back home as evidences of an almost superstitious gullibility on the part of the people at large. It was significant furthermore, that there was little dread of visiting hospitals in which the sick were treated or undertaking establishments where the remains of the victims of the epidemic were kept. While it is true that a rigorous isolation was maintained in the hospitals, yet the public did not regard such rigor as definitely indicated and it yielded to the situation only after the health department had made it clear by interviews and radio addresses that precautionary measures were adopted largely because

of the unknown mechanism of the transmission. It was not found necessary to forbid public attendance at wakes and funerals. All of this "saneness" in the face of a disquieting situation was indicative of strong mental hygiene.

II. Cooperation and Reactions of the Public

1. A large number of symptoms might be enumerated and discussed at great length to show to what extent the encephalitis epidemic affected and developed a spirit of community cooperation and a desire for community planning. The first and foremost of these symptoms is the development of the Metropolitan Health Council. It is obvious that the location of the city of St. Louis with a population of over 800,000 amidst immediate environs to the north, south, and west comprising 32 different municipalities with a combined population of well over 1,000,000 must necessarily present special problems of the most complicated nature arising out of the interrelationship between these various political units. If we add to this the fact that east of the city we find East St. Louis across the Mississippi River and to the north and south again a series of 8 to 10 different municipalities, it becomes clear that the problems are decidedly multiplied. Most active interchange of personnel and goods takes place between these various population units. Between St. Louis and East St. Louis, for example, it is estimated that more than 50,000 persons cross the various bridges each day and a similar active intercommunication is maintained between the outlying towns and cities and the city itself.

It is not our purpose here to enter into an explanation for a situation which becomes more complex each succeeding year. Suffice it to say that those who have studied the matter are fully assured that not only political but also local difficulties of the highest intricacy must be solved before this very anomalous situation can be cleared and the activities of the metropolitan area be unified.

In the matter of health it is obvious that the interests of St. Louis and those of the adjoining cities and villages are very closely interlocked. The health director of St. Louis must constantly lean upon the assistance of the health officers of the county and of East St. Louis and must in turn give them such assistance as a particular problem would seem to indicate.

It is unnecessary, furthermore, to stress the thought that understanding between these various communities and most intimate cooperation is not only desirable but at times absolutely essential for the preservation of the community's health and safety. The constant migration of this large population amounting to one million and a quarter makes it necessary to effect a considerable measure of uniformity of regulations if the health and safety of any fraction of this geographical area are not to be sacrificed. Streets are continuous;

drainage sheds are not confined within geographical lines; water supply, in certain areas at least, is more or less the same; food and milk supplies are identical; and in effect, the political subdivisions of the area are in reality only so many artificial lines drawn through what is essentially a fairly homogeneous community.

Many efforts have been made in the past to effect an understanding between these different communities and to organize a Metropolitan Health Council. As often happens in such instances, one difficulty after another is raised, not the least significant of which is the attitude of this or that special group of citizens who believe their interests endangered or who suffer some vague psychological trauma through such unified arrangements. The authority of the State health board has in the past never been sought to effect what mutual understanding has failed to bring about. As a matter of fact, there are some who question whether the State health department possesses such legal authority to enforce an arrangement except in the face of a general emergency.

The encephalitis epidemic, as a matter of fact, began in the county and was first recognized as a menace by the county health officers. It was soon found, however, at first in relation to the purely practical matter of hospitalization that the county could not alone cope with the problem. Within a few days after the county hospital first received patients and the menacing character of the illness was recognized, an appeal was made to one of the hospitals in the city to take county cases. A floor was immediately set aside in the newly organized Firmin Desloge Hospital and without raising the question of authority and assuming that the emergency demanded immediate action, patients were received. From this beginning the hospitalization program spread rapidly to other institutions, and before long the City Isolation Hospital was receiving patients irrespective of their geographical origin. There might have been an occasion for a considerable number of sharp conflicts between health authorities. As a matter of fact if there were such differences, they were submerged in the presence of the common need and it must be said to the honor of St. Louis and of the county, that no one thought for one moment of expressing differences but rather sought ways of effecting unified action. At the instigation of the St. Louis authorities, preliminary meetings were called for the organization of the Metropolitan Health Council and almost before the citizens realized it, the council was established and was functioning. Programs were adopted by mutual cooperation of all parties interested and concerned; information blanks of various kinds were agreed upon in rapid succession; the method of reporting the various phases of the epidemic were determined; the hospitals were called upon to modify whatever special forms they had been accustomed to use in order that the data might thus become

more valuable from unified recording; frequent meetings of the health council were held, in each of which progress was marked. The investigative and the clinical fields were carefully surveyed and responsibility for different aspects was allotted; all this, with only one consideration in mind, the selection of the best person to undertake a particular "job."

No one is surprised that such an understanding was effected amongst physicians, health administrators, social workers, and others who approached the problem from a professional viewpoint, but it is surprising that all of this was possible with the complete understanding of the people at large. The press was in complete accord with what was being done, and the people took their cue from editorial comment and the tone of the news items.

Relations with the United States Public Health Service.—Another phase of the epidemic which has elicited words of commendation is the relation between the local health authorities and the United States Public Health Service. Quite unlike experiences on other occasions, the people of St. Louis cordially approved the action of the St. Louis Health Department in inviting the United States Public Health Service to take part in the study and control of the epidemic. It was fortunate also that the character of the persons sent here by the Public Health Service was such that they immediately were taken into the community as welcome guests and their activities were looked upon with favor largely as a result of their cooperative spirit. As a matter of fact, they were excluded from none of the executive meetings which took place with such frequency throughout the epidemic. They had free access to all the institutions in which patients were hospitalized, and to all local laboratories. They were given opportunities to pursue their own researches with the utmost freedom and the leadership of the United States Public Health Service officials was accepted unquestionably and whole-heartedly. This is all the more remarkable since it is clear that St. Louis could probably itself have coped with the situation if it had drafted all of the local talent which could have been made available in facing the disease. The fact that this was not done, however, is another illustration of the spirit which actuated the people of the city.

We have repeatedly referred to the fact that throughout the epidemic evidences of panic were noteworthy by their absence. The acceptance of the Public Health officers was, therefore, not inspired by fear, but rather by the appreciation of the necessity and value of using all means at the disposal of the health officials to bring about a speedy solution of the difficulties confronting the city. The completeness of the cooperation given by the United States Public Health Service deserves the warmest commendation and appreciation of the citizens of the St. Louis area. Not content with sending a director,

the Federal officials put at the disposal of the health authorities enough capable and specially trained personnel to assist the local officials with practically every phase of the scientific and clinical study and of the control of the epidemic.

Private and public health agencies.—One of the most striking social phenomena which emerged from the public need was the manner in which the private and public agencies threw themselves into the work of combating and controlling the disease. Historically a fairly sharp line had always been drawn between the public and private agencies and while there has always been considerable understanding between the two groups, nevertheless, the prerogatives of each were carefully safeguarded, sometimes to such an extent as to prevent action when such action might have been very conducive to the public good. During the time of the epidemic, these differences were rapidly effaced. The private and the public hospitals were used indiscriminately for the care of public and private patients. Understandings were rapidly effected for the payment of services given by private institutions to public patients. The arguments, political and otherwise, against such allocation of funds were dealt with summarily and the services rendered by the private institutions was freely recognized. The epidemic had a pronounced leveling effect upon the undesirable features of an exaggerated individualism in some of the institutions. This was due largely to the broad manner in which the directors of these private institutions conceived their public duty. Time was not taken to draw elaborate and fine distinctions, but when work was allotted, it was freely and generously performed.

The universities.—Another striking feature very noticeable during the epidemic was the spirit of unanimous cooperation given to the public health authorities and the official health agencies by the two universities. A division of labor between the two universities was quickly and almost automatically effected. Washington University was able to place its extensive laboratories at the disposal of the health authorities and St. Louis University found itself in a position to open its extensive hospital facilities for the hospitalization of the patients. St. Louis University's share in the clinical care of these patients was made possible largely through the generous and unselfish manner in which the Sisters of St. Mary, maintaining their honorable history in previous epidemics, extended their activities in meeting the present one. These facts determined the allotment of responsibility between the two institutions. The scientific investigation was left largely to Washington University and the clinical investigation of the disease to St. Louis University. It must not be assumed that this line was drawn so sharply that a sense of possession of the two fields was developed in the personnel of the two schools. As a matter of fact, both universities contributed not a little to the clinical care and to

the scientific work. As a result of this division of work the "sensational" aspects of the epidemic fell largely to the lot of one of the schools. Both of the institutions carried their combined responsibilities in a spirit of self-effacement, in a manner entirely worthy of university faculties. The personnel of both universities acted in practically equal numbers on the various committees which were established and in the allotment of directional duties it was clear that the committees were actuated by one thought only, the selection of the most available and capable person, irrespective of his school affiliation.

Hospitals and out-patient departments.—The work of the hospitals and out-patient departments throughout the epidemic has been described in other sections of this monograph. The purpose here is merely to point out the fact that not only did the hospitals and out-patient departments take a large share in the public responsibility, but they did so with a most remarkable spirit of cooperation. The City Isolation Hospital and the Firmin Desloge Hospital accepted by far the largest number of encephalitis patients. St. Mary's Hospital and the Jewish Hospital taxed their resources to take care of their allotments. Many of the other hospitals had a scattered number of patients, but even these small numbers of patients implied that the officials of those institutions were willing to take upon themselves the extensive additional burden of maintaining proper contacts with the official health agencies and the directors of the encephalitis study and to maintain those relations with the public which at a time such as the period of the epidemic are particularly important. Two of the hospitals, keenly aware of the mental anxiety caused by the disease to the relatives of the patients, are reported as having made special efforts to allay any popular misgivings. The fact that this was done must be regarded as a very large factor in the maintenance of public confidence. Information given out over the desk or telephone to relatives was most carefully couched in reassuring terms. One of the hospitals issued orders that the answers to be given to inquiries were to be detailed and that general descriptions of the patients, as frequently emanate from a hospital and especially over the hospital telephone, such as "The patient is improving" or "The patient had a good night", were not to be used in the present instance. Rather, the relatives were to be given a factual statement authorized by the physician in charge of the case. In this same institution, while isolation was rigorously maintained, a relative of the patient was allowed to visit at the door of the sick room for not more than 5 minutes each day. The time limit was carefully adhered to by the nurse in charge. It must be admitted that this procedure took away from the public mind much of the dread of the disease and had a pronounced and very valuable reassuring effect. The work of the

hospitals during this period must be regarded as a very gratifying phase of the epidemic and as very creditable to the St. Louis institutions.

The cooperation extended by the nursing profession in the face of the epidemic was such as might have been taken for granted. The visiting nurses and the municipal nurses reported that they came into frequent contact with relatives of the patients and that their ministrations as mediators, counsellors and friends were most acceptable. The nurses, both lay and religious, who gave nursing care to the encephalitis patients did so with the fullest confidence that the professional safeguards which had been adopted were fully adequate to combat the dangers of infection. As a matter of fact, not a single nurse is known to have contracted the disease in the line of her professional activity. It speaks well also for the public spirit and broadmindedness of the nursing profession that so many of the nurses gave liberally of their time without compensation in at least one of the institutions in which encephalitis patients were cared for. When the call went out for volunteers to take care of the indigent patients, there was a general response from the alumni of this institution. Gradually other nurses volunteered their services and during a not inconsiderable part of the epidemic a number of the patients were being cared for on an individual basis by nurses who had contributed their services with no other remuneration than their board and lodging in the hospital during their period of service.

The record of the medical profession during the epidemic will probably bear remembrance for many a year to come. There was a noteworthy absence of those differences of opinion which can so easily develop under the stresses of a public emergency. The profession followed the scientific researches with extreme eagerness, diligently studied the publications on the clinical findings and symptomatology, was prompt in the reporting of cases and in carrying the responsibility for executing the directions of the health department. The St. Louis Medical Society organized two meetings bearing directly upon encephalitis and its members contributed greatly through personal conversation, lectures and in other ways towards the formation of public opinion with respect to the epidemic. A great many radio talks were sponsored by the St. Louis Medical Society.

LESSONS FOR THE COMMUNITY

In addition to the spirit of cooperation which was engendered in the community by the encephalitis epidemic, there have been other gains, some of them so important that it may be hoped that their memory will continue to live among our people. Among these it is important to stress, first of all, an increasing understanding of the aims and methods of medicine and of scientific research.

We have already pointed out the reactions of the people to the newspaper publicity. This publicity since it was largely concerned with the methods of caring for the encephalitis cases, the epidemiology and the scientific research, served as one of the most effective educational campaigns ever developed in St. Louis. Thoughts and terms which are common enough in the medical lecture hall almost over night became household words and clamors were eloquent for other sources of information to satisfy the public demand for information upon these points. It was quite illuminating to see how the daily press grew in its use of technical terms as the epidemic progressed. Even the ordinary news item towards the end of the epidemic used entirely cursively and incidentally the complicated terminology associated with the sciences of immunity, bacteriology, physical diagnosis, pathology, etc. Certainly to distinguish between a virus disease and a bacterial disease is no small task for a newspaper writer to undertake and yet articles bearing upon this point were not at all uncommon. The discussion of inclusion bodies as alleged indicators of virus disease was another point which elicited abundant comment. The relation between the micro-organisms in disease, the diagnostic indications for bacterial classification, serum reactions—all of these and many other similar topics found their way into everyday newspaper reading and into conversation.

More significant, however, than positive indication upon the nature of infection was the gain of the public through its education in viewpoints. It is true that at the beginning of the epidemic considerable doubt was expressed concerning the adequacy of medicine to cope with the epidemic and not a little fear was voiced in certain limited quarters, though not at all generally, that the disease would get ahead of medical science unless a "cure" were speedily discovered. It was only gradually that the public began to learn the meaning of a "cure." Not that all misunderstanding concerning specific cures for specific diseases was erased from the public mind, but it is clear, nevertheless, that with the progress of the disease the public began more and more to understand the complex physiological and pathological interrelationships and thus developed an understanding sympathy for the methods of the laboratory. As one person put it, the public was receiving an intensive graduate course in the methods of medical research. Each new phase of progress was heralded with considerable enthusiasm and the public was thrilled no less than the laboratory worker himself often is with the ups and downs of his work, with the momentary successes which alternate with prolonged setbacks. The best evidence of the public's reaction lies in the fact that when the epidemic closed without a definite solution to the problem of prevention or cure, the sympathy was entirely on the side of medicine and none of the frequently heard criticisms of research workers were voiced, at least in educated circles.

A third gain under this head was the development of public understanding regarding the methods and aims of public health. So true is this that many individuals in the community became anxious to contribute their own observations or suspicions to the general discussion. Letters poured in from all sides from entirely sincere persons, some of whom were unquestionably highly educated and others of whom probably bordered on illiteracy, suggesting an endless number of causations for the disease. Encephalitis was blamed upon first of all a vast number of insects—mosquitoes, the house fly, butterflies, lice, bedbugs, cockroaches, water beetles, grasshoppers—these and many other insect forms were blamed as carriers. Among the vertebrates—chickens, rats, mice, cats, dogs, cows, horses—were blamed. Inorganic etiological factors were not neglected; rain-washings, dry dust, etc., were frequently mentioned, though it is not clear whether the authors of these theories attributed the fact to the organic content of the water and dust or to the water and dust themselves. The sewage system or the lack of it was most commonly accused, especially in the early days when the epidemic was confined largely to St. Louis County. Letters of this kind were received in such large numbers by the Health Department of St. Louis that a form answer was drafted, but almost all the physicians engaged in research upon the disease were the recipients of numerous suggestions as were also the officials of the two universities and the administrators of the hospitals. From one point of view, to be sure, these suggestions were naive enough, but they gave so much evidence of an understanding of the problems in the transmission of disease that the suggestions cannot be treated except as evidence of the growing understanding of the problems of science. It certainly impressed upon the writer that such letters could not have been written 15 years ago, let us say, before the conclusions of scientific medicine had become the commonplaces of popular thinking. The writer would not be understood as reporting, of course, that there were not some evidences of gross misconception in these letters, but the fact remains that in practically every case there was enough of a kernel of truth to indicate some familiarity with the science of today. It is clear, therefore, from all of the above that a growing interest in scientific medicine was one of the outstanding results of the epidemic.

A second interest in health activities was the interest of which the epidemic was the occasion in personal and public hygiene. For the most part it is probably true of all of our large cities that the normal function of a health department is a matter of concern to relatively few of the citizens. It is only in moments of catastrophe that the activities of a health department come into the foreground against the strong background of the common and general public sorrow, the incidence of a contagious disease, an accelerated death rate, or some

similar public calamity. The officials of the health department of the city and of its environs were shrewd enough to grasp the public psychology. The radio addresses and other lectures frequently took the form of discussions on matters of general hygiene and the immediate lessons of the encephalitis incidence served as many a useful wedge for the influx of new enlightenment and knowledge. The importance of diet, of exercise, of sleep, the preservation of general fitness, the avoidance of psychological as well as physical strain, the maintenance of balance in the face of family or personal difficulties—these and the many other lessons were inculcated with an effectiveness that could not have been secured except under equally thought-provoking conditions.

There was noted also a growing sympathy for the intracacies and trials of medical practice. The physician was promoted into the focal point of popular interest. His education, his knowledge, his difficulties in the face of illness, his limitations, the importance of his professional progress by reason of the progress of medicine—these and many other phases of the physician's life became better understood, were more sympathetically viewed, and were more adequately explained to the public, frequently enough, by speakers outside of the profession.

Another product of this popular interest in science was the growing interest in the significance of autopsies and the public's readiness to grant permission for them. In relatively few cases only was permission for autopsy refused during the entire period of the epidemic once the physician had explained the reasons for the request which he was making. The autopsies yielded a large harvest of information about the disease and the public appreciated the change of attitude in the medical profession which in the beginning of the epidemic regarded the disease as largely one of the nervous system and with the progress of the sickness came to regard it as a general disease affecting practically every organ system.

Lastly, considerable progress was made in the public's understanding of the importance of community organization for health. The place of the physician and the nurse and of the medical social worker, of the public and the private hospitals and the out-patient departments, and the relation of all of these to the welfare agencies and in turn the relation of the health activities of the welfare agencies and of other organizations to the official health department—all of these are today better understood in St. Louis than before perhaps and those who are interested in these activities find that they need no longer begin their discussions even before less instructed groups by appealing to the A B C of medical science. It may be questioned, of course, how deeply this interest and this education really penetrated into the minds of the people. The public at large is notoriously vacillating

in its interest, but it may be confidently said that even though the intensity of the interest has passed, enough, no doubt, remains to have made the epidemic a worth-while experience for the citizens of St. Louis.

It must not be thought from the above that there was a general helter-skelter and uncorrelated educational campaign, volcanic in its intensity, during the period of the epidemic. Much of this work was done quietly and unobtrusively but yet with a persistence and a continuity that yielded excellent results. There was no hurry and skurry about these educative programs and no crusading frenzy. It is to the credit of those who undertook these activities that all of this was done deliberately and quietly with a full conviction of its value, but also with a full realization of the slowness and the inertia of the public mind.

Taking all of these desirable results into consideration, the encephalitis epidemic brought with it not a little gain for the metropolitan area of St. Louis. If the price paid for these gains was excessive in the loss of life and in the anxieties and worries created by the disease, it is still good to bear in mind that even so severe a visitation is not devoid of results which it may be confidently hoped have improved the city and its surrounding territory in many important phases of community activity.

Appendix A

RECOMMENDATION OF COMMITTEE ON CORRELATING METROPOLITAN PUBLIC HEALTH ACTIVITIES

1. A cooperative consultative body shall be formed called the Metropolitan Health Council.

Members of this Council shall be—

(*a*) All constituted health commissioners of the St. Louis metropolitan area, including St. Louis County and the suburban municipalities, St. Clair and Madison Counties (Ill.), and subdivisions.

(*b*) The hospital commissioner of St. Louis, the superintendent of St. Louis County Hospital, the superintendent of City Isolation Hospital.

(*c*) Other physicians and public health workers who may be invited from time to time.

2. The purpose of this Council shall be—

(*a*) To coordinate all public health activities in the metropolitan area for the handling of emergencies.

(*b*) To adopt uniform rules and regulations as far as possible for handling patients with contagious diseases.

(*c*) To adopt uniform rules and regulations as to isolation and quarantine.

3. A secretary shall be selected to organize and handle activities of the Council.

Duties of secretary shall be—

(*a*) To keep summarizing records and statistics of developments in epidemics.

(*b*) To organize and handle mutual exchange of reports and information between the different health departments and hospitals.

(*c*) His office to act as a clearing house for communications and various information between members of health council.

4. The Council shall meet as need arises on call by the secretary. Meetings shall be at headquarters of health commissioners in rotating order. Chairman of meeting shall be one of health commissioners in rotating order.

5. Two standing committees shall be appointed:

(*a*) Committee on rules and regulations.

(*b*) Committee on research.

Appendix B

RULES AND REGULATIONS CONCERNING THE HANDLING OF CASES OF EPIDEMIC ENCEPHALITIS IN ST. LOUIS METROPOLITAN AREA

1. All cases to be reported immediately to the respective health departments.

2. All hospitals to be requested to report cases also to respective health departments.

3. Daily list of reported cases to be sent by health departments to secretary of Metropolitan Health Council (No. 1 Municipal Courts Building, St. Louis, Mo.—Dr. P. J. Zentay).

4. In case of death, complete post-mortem examination shall be urged. Autopsies to be done under cooperation of research committee. (Call Dr. Zentay's office.)

5. Patients are to be kept in the hospital isolated for 3 weeks from date of onset; discharge from the hospital before this period should be done only with permission of the health division.

6. Contacts need not be quarantined.

7. Homes not to be placarded. "Warning" signs optional.

8. Every case to be investigated carefully by representatives of respective health departments by using the questionnaire suggested by the committee.

9. Closing of schools not considered at present.

10. Food handlers coming in contact with patients to be restricted in the same manner as in case of poliomyelitis.

11. All hospitals to treat patients in separate rooms or wards. No special nurses required, but strict routine of isolation with the use of face masks mandatory. (All hospitals are permitted to keep patients who are diagnosed as cases of epidemic encephalitis for treatment.)

12. No visitors permitted in isolation wards, and it is suggested that the visiting in the hospital generally should be limited to the minimum.

13. Funerals shall be private, only immediate family attending. Services in church permitted.

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Appendix C

QUESTIONNAIRES FOR EPIDEMIOLOGIC INVESTIGATION

1. Metropolitan Health Council (Cases)

Case No. _____

Patient's name _____

Address _____

Color: W., Y., B. Sex: M., F. Social condition: M. W., S. Age _____

Occupation _____ { Employer _____ / Address _____

Patient's physician: Dr. _____ Address _____

First seen by _____ Date _____

Hospitalized: Yes. No. Hospital, and date _____

Date and hour first symptoms and the course and severity _____

_____

In case of death was there a post mortem? _____ When _____

Other members of family:

Name _____ Age _____

Address _____

Occupation _____ Present health _____

Contacts made by patient with known case or the immediate family of one _____

Contacts made by patient's family with known case or the family of one _____

Visits, or meals by the patient, away from home (dates) _____

Visits, or meals by patient's family, away from home (dates) _____

Visitors to the family, with residence, and date of visit _____

Sources of water supply _____

Dairy products:

Milk _____ Cream _____

Butter _____ Ice cream _____

Uncooked food _____ Grocer _____

Address _____

Sanitation _____ Screens? _____ Local stables? _____

PAST HISTORY

Any affection of nervous system before? _____

Childhood diseases: Measles? _____ Mumps? _____ Whooping cough? _____

Scarlet fever? _____ Flu? _____ Pneumonia? _____ Typhoid? _____

Nervous? _____ Diphtheria? _____ Venereal? _____

(Check those which patient has had.) Operations? _____

If female: Married _____ Children? _____

General health _____

Remarks _____

Reported by _____ Date _____

2. United States Public Health Service (Cases)

Case No.---- State---- County----
City---- Town---- District----
Dates unconscious---- Date of fatality----
Name---- Color---- Sex---- Age----
S.M.W.D. date reported.
Address---- house (R) (L) between----
and----
Date first symptom----Date fever----Date in bed---- Date recovery----
First physician---- Date first visit---- Second physician----
Other residences or visits within 3 weeks of onset, with dates----
---
Hospitalization or moves after onset, with dates----
Visitors within 3 weeks of onset, where from, dates----

Places of employment or school, dates----

Church or Sunday School, dates----Stores, dates----
Picnics, etc., dates----
Theaters, etc., dates----
Swimming, places, dates----
Other visits, meals, or contacts outside household, dates----
---
Assigned cause----
Direct contact with case, number, dates----
Connection with other cases, numbers, dates----

Other illnesses or injuries of patient within 3 weeks of onset, dates----
---
Other members of household, from oldest down, designating head of household:

Sex	Age	Name	Relation to case	Number in household

Brief description of illnesses of other members of household, by name, within 3 weeks of onset of case----
---
Contacts of other members of household with known case or possible source of infection, places and dates----
---
Did other members of household mingle freely with population of previously infected territory?----
If not, how restricted was their contact?----
Drinking water: Main source---- Other sources----

Milk and cream, daily average for patient before onset---- Main source----
Other sources----
Ice cream, weekly average---- Main source----
Other sources----
Reported presence of flies before onset----
Mosquitoes---- At dusk----
Other biting insects----

2. United States Public Health Service (Cases)—Continued

Artificial containers of water, location, character (cisterns, rain barrels, etc.)____

Natural exposed water, distance, direction, character_____

Patient bitten by mosquitoes at home_____
Elsewhere, dates_____
Animals on premises, pets_____
Rodents_____ General cleanliness_____ Economic status_____
Age of patient at infection with Measles_____ Chicken pox_____ Mumps_____
Whooping cough_____ German measles_____ Scarlet fever_____ Diphtheria_____ Pneumonia_____ Tuberculosis_____ Typhoid_____ Dysentery _____ Poliomyelitis_____ Meningitis_____ Chorea_____ Rheumatic fever _____ Encephalitis types_____ Influenza_____
Other previous history, especially nervous diseases and infections_____

Hay fever_____ Asthma _____ Hives_____
Vaccinated against smallpox?_____ Dates successful vaccinations_____
Dates unsuccessful vaccinations_____
Other inoculations, with dates: Diphtheria_____ Typhoid_____
Scarlet fever_____ Colds_____ Other_____
Date, hour, and character of first symptom of this attack of encephalitis_____
Further course of disease_____

Headache_____ Other pains_____Sore throat_____
Fever? Degree_____ Chills_____Chilliness_____
Vomiting_____ Diarrhea_____Constipation_____
Unusual sleepiness_____ Dullness_____Excitement_____
Paralysis_____
Tremors_____ Other irregular motions_____
Stiff neck_____
Sources of information_____
Dates of investigation_____ Investigator_____

3. UNITED STATES PUBLIC HEALTH SERVICE

Survey of Noninfected Homes, St. Louis Encephalitis Epidemic, 1933

Street_____ Number_____ City or town_____

Water supply _____ Milk supply _____

Members of household (place head of family first)	Relation to head of house	Sex	Age	Occupation	Place of employment	Contact with case or suspect: Direct	Contact with case or suspect: Indirect	Visits away from home	Church or theater	Picnics	Swimming	Meals away from home	Milk or cream: Beverage	Milk or cream: Coffee or cereal	Bitten by mosquitoes	Poliomyelitis	Encephalitis	Meningitis	Smallpox vaccination	Chronic illness or other conditions
1	✓																			
2																				
3																				
4																				
5																				
6																				
7																				
8																				
9																				
10																				

Visitors in home from epidemic areas: None, rarely, frequently. Cleanliness of home: Poor, fair, good. Economic status: Poor, fair, good.

Description of acute illnesses in members of household (indicate by number)_____

Description of contact with case (name case)_____

NOTE.—A check mark indicates a positive finding. A dash indicates a negative finding. A question mark indicates questionable information.

Appendix D

OUTLINE FOR CLINICAL RECORD

I

Last name_____No_____
First name_____
Hospital_____
Record No_____ Race and sex_____
Age_____ Date admitted_____ Date terminated_____
Duration illness before admission_____
Duration of illness prior to onset encephalitis symptoms_____

Contributing Causes and Mode of Onset

Symbols: + = Yes.
O = No.

Previous illness_____ Sore throat (early symptom)_____
Other respiratory infections (early symptom)_____
Other diseases present (at onset)_____
Unusual fatigue or exposure to elements_____ Alcoholism_____
Exposure to encephalitis or other predisposing factors_____
Onset gradual; sudden (G., over 3 days) (S., 3 days)_____
Chill or chilly sensation_____ Convulsions_____

II

Headache symbols: F = frontal; O = occipital; P = parietal; D = diffuse

Name of hospital_____Record No._____
Headache: Character, duration, severity, type_____
Prodromal, lassitude (use + and O)_____
Pains: Back, muscles, limbs_____
Vomiting_____ Constipation_____ Diarrhea_____
Skin eruption character_____ Vertigo_____ Abdominal pain_____
Fever prior to admission_____ Fever on admission_____
Type fever in hospital, fall by lysis or crisis_____
Total duration fever and maximum temperature_____
Pulse: O = proportion to temperature; B = bradycardia; T = tachycardia_____
Urinary retention or incontinence: Use R and I_____
Pupils: Regular____ React to L. and A_____
Blurred vision when noticed, duration_____
Diplopia: When developed_____ Duration_____
Strabismus, type and duration_____
Nystagmus, type and duration_____
Ptosis, duration_____
Photophobia and conjunctivitis_____
Eye grounds_____
Disturbance of hearing: Type____ Duration_____
Facial weakness_____ Pain in neck muscles_____
Neck rigidity_____ Spine rigidity_____

General spasticity_____ Muscle weakness or paralysis_____
Coarse jerking movements_____ Choreiform movements_____
Muscular twitching_____ Tremors, type and location_____ Tongue protrusion_____

III

Name of hospital_____Record No_____
Aphasia: Duration, completeness_____
Other speech difficulty, type and duration_____
Difficulty in swallowing_____ Hiccough_____
Herpes, during illness_____
Dyspnea and cyanosis, cause_____
Cardiac abnormality_____ Pulmonary abnormality_____
Arteriosclerosis_____
Abdominal reflexes (+ or O)_____ Ankle clonus_____
Knee jerks_____ Other abnormal deep reflexes_____ Cremasteric reflex____
Abnormal plantar reflex: O=normal; B=Babinski; C=Chaddock; G=Gordon; Opp=Oppenheim.
Brudzinski_____ Kernig_____
Drowsiness_____ Stupor_____ Irritability_____
Mental confusion_____ Delirium mild, severe, noisy_____
Blood pressure_____
Spinal fluid: Cell count, total and percent lymphocytes and polynuclears (use L. and P.)_____
Spinal fluid pressure (if not measured, use + to ++++)_____
Spinal fluid: Pandy_____ Spinal fluid sugar (amount) _____ Blood sugar_____
Spinal fluid Wassermann (or Kahn, etc.)_____
Blood W.R_____
Spinal fluid colloidal gold (N=normal curve; O=not made)_____
Blood N.P.N._____ Abnormal urinary findings_____
Blood platelets_____

IV

Name of hospital_____ Record No_____
Total W.B.C_____
Schilling shift_____
Percent juveniles_____
Stabs_____ Segmented_____ Lymphocytes_____
Monocytes_____ Eosinophiles_____ Basophiles_____
Encephalitis diagnosis: Positive or questionable (+=yes; O=questionable.)
Final outcome: R=recovery; I=improved; X=death_____
Residuals? (+ or O, describe) note interesting or unusual findings_____
Transferred to another hospital: Name_____

Preexisting Complications

Name of hospital_____ Record No_____ F.D.H_____
Arterial hypertension_____ Nephro-sclerosis_____ Syphilis_____
Tuberculosis_____ Chronic bronchitis_____ Asthma_____
Chronic cholecystitis_____ Diabetes_____ Toxic goitre_____
Poliomyelitic paralysis_____ Pregnancy_____ Chronic arthritis_____
Cancer_____ Deafness_____ Chronic myocarditis_____

V

Complications Developing in Course of Disease

Name of hospital_____ Case No_____
Cystitis_____ Urinary incontinence_____
Urinary retention_____ Pylelitis_____
Pneumonia interstitial_____ Pneumonia purulent_____
Pharyngitis_____ Hypotension_____
Early Parkinsonism_____
Acute otitis media_____
Paralysis of muscles deglutition_____
Passive congestion of lungs_____ Nephritis_____
Cardiac failure_____ Phlebitis_____
Results_____

Appendix E

QUESTIONNAIRES FOR FOLLOW-UP OF CASES OF ENCEPHALITIS

1. By Query

Series---------- Case No--------
Name----------
Street No---------- District----------
Age---------- Date of reporting----------
Name of doctor----------

A. Is the above patient still living?----------
If not, please give date and cause of death----------

B. Has any circumstance arisen which makes you doubt the correctness of the original diagnosis of epidemic encephalitis type B?----------
If so, please give particulars----------

C. Has the patient recovered? If so—
1. Has he/she returned to his/her previous work?----------
2. Is he/she able to do any work at all?----------
3. If of school age has he/she returned to school?----------

D. If not completely recovered, what is the general nature of the disability?
---
1. Is he/she confined to bed?----------
2. Are there any ocular disturbances?----------
   (*a*) Failure of vision.
   (*b*) Nystagmus.
   (*c*) Squint.
   (*d*) Unequal pupils.
   (*e*) Loss of pupillary reactions.
   (*f*) Ptosis.
   (*g*) Changes in blinking reflex.
   (*h*) Other visual disorders.
3. Is speech affected?----------
4. Are there any dizzy spells?----------
5. Is there any headache?---------- In what part? (frontal or occipital)----------
6. Is there any pain elsewhere?-------- In what part?----------
7. Is there any paralysis?---------- If so, where?----------
8. Is there any tremor or shaking?---------- If so, in what part of body?----------
9. Is there any lethargy or somnolence?----------
10. Is there any nocturnal insomnia or restlessness?----------
    If so, is it improving?----------
11. Is there any delirium?----------
12. Is there any change in personality or moral character?----------
    If so, please give particulars----------

1. By Query—Continued

13. Are there any changes in mentality?..... Memory?.....
If so, please give particulars.....
14. Are there any fits?..... If so, what is there nature?.....
15. Are there any attacks of disorderly breathing?.....
If so, please give particulars.....
16. Is there any cough at night?.....
17. Is there any evidence of Parkinsonism?.....
What parts are affected?.....
When did it begin?.....
Is it getting worse?.....

E. Is there any objection to a neurological consultation?.....
(*a*) By family?.....
(*b*) By physician?.....

---

2. By Examination

Series..... Case No. .....
Name.....
Street..... District.....
New Address.....

GENERAL

Date of onset.....
How long was patient confined to bed?.....
Duration of convalescence.....
Has patient returned to previous occupation?.....
Is there any incapacitation to work?.....
If school age, has patient returned to school?.....
Is there any doubt about the correctness of the original diagnosis of epidemic encephalitis?.....

SPECIAL DISABILITIES OR COMPLAINTS

A. Mental:
Delirium.
Confusion.
Lethargy or somnolence.
Sleep disturbances, restlessness.
Disturbances of memory.
Impairment of intelligence.
Habits of eating.
Other habit problems.
Behavior problems.
Personality changes.
Moral character.

B. Nervous:
Headaches—location, type.
Dizziness.
Fits, spasms—type and location.
Pains—location, type.
Sensory changes—location, type; paresthesias.

Visual disturbances:
- Double vision.
- Other difficulties (fatigue, etc.).

Hearing disturbances.
Speech disturbances.
- Reading difficulties.

Motor disturbances:
- Paralysis, parosis.
- Hyperkinesis, hypokinesis.
- Tremor, shaking—location, type.
- Tics—location, type.
- Gait.

Coordination, balance.
Respiration.
Autonomous nervous system:
- Perspiration.
- Sebaceous secretions.
- Other disorders.

PHYSICAL AND NEUROLOGICAL FINDINGS

A. General physical status:
- Respiratory system.
- Circulatory system.
- G.I. system.
- G.U. system.

B. Neurological status:
- Cranial nerves.
  - Sensory.
  - Motor.
- Spinal nerves.
  - Sensory.
  - Motor.
- Muscle tonus:
  - Spasticity.
  - Hypotonicity.
- Muscle paralysis.
- Reflexes:
  - Superficial.
  - Deep.
  - Pathological reflexes.
- Autonomous nervous system.

Other remarks----------
