Radcliffe Infirmary. Reis *et al.* (1950), whose good results have already been mentioned, consider that the blood sugar in the infant of a diabetic mother tends to fall more rapidly, to reach lower levels, and to return to normal more slowly than in the normal infant, a marked fall in the first hour being characteristic. They advocate giving 50% glucose solution by mouth from the first half-hour of life, but changing to 5% glucose solution after two hours. Peel and Oakley (1950) have studied a few cases and confirm this very rapid fall in blood-sugar levels immediately after birth. As the results at the Radcliffe Infirmary are satisfactory we are continuing to give 5% solution in ½- to 1-oz. (14- to 28-ml.) feeds every two to four hours during the first one or two days.

We have had no experience of the effect of repeated gastric aspirations for infants delivered by caesarean section as advocated by Gellis, White, and Pfeffer (1949) with a view to minimizing the risk of regurgitation and inhalation of vomit.

Lactation may be difficult to establish in the diabetic woman, and this, together with the lethargy and poor condition of the infant, leads to failure in breast-feeding in a proportion of cases. As a rule nothing is to be gained by putting the infant to the breast early; the mother expresses the milk until the stage of engorgement is over, by which time the infant is likely to be more vigorous and able to suck from the breast. Ten mothers in the present series breast-fed their babies satisfactorily.

If the close co-operation of the obstetrician and the physician can reduce stillbirths and intrauterine deaths, allowing the well-controlled diabetic mother to be delivered of a live baby, then the infant should stand a good chance of survival even when it is born at the 36th week. After birth the skill of the nursing staff is the most important factor in reducing neonatal deaths.

### Summary and Conclusions

A series of 25 consecutive diabetic pregnancies beyond the 28th week (1947 to 1950) is presented. No mother died and 23 babies are living. Although this series is small it shows that good results have been obtained by adopting the principles of (1) working as a team with a definite policy; (2) careful diabetic control; (3) induction of labour not later than the 36th week of pregnancy; and (4) careful neonatal control but without overtreatment of the baby.

We acknowledge our thanks to Dr. A. M. Cooke, head of the Radcliffe Infirmary Diabetic Clinic, to Dr. D. C. Lewin (registrar, Diabetic Clinic, 1947–8), and to Professor J. Chassar Moir and Mr. J. Stallworthy for allowing us to publish details of their patients. We thank Sister Ware, who has been in charge of the nurseries in the maternity department for the last four years, for her invaluable help.

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# LYMPHOCYTIC CHORIOMENINGITIS

## ASSOCIATED HUMAN AND MOUSE INFECTIONS

BY

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Lymphocytic choriomeningitis (L.C.M.) was first differentiated from other types of aseptic meningitis by Rivers and Scott (1935), the causative virus having been described by Armstrong and Lillie (1934). The main reservoir of infection occurs in the house mouse (*Mus musculus*), but laboratory experiments have suggested that bed bugs, mosquitoes, lice, and trichinella larvae may be implicated in the spread of the disease (see van Rooyen and Rhodes, 1948).

In investigations of houses in areas in which human infection occurred, Armstrong (1940) found that approximately 40% harboured infected mice, and about 50% of the mice trapped in such premises were found to be carriers of active virus, which they may excrete in saliva and nasal secretions, urine, and faeces. Transmission to man probably takes place via contaminated food or by the inhalation of dust infected from mouse excreta, with possibly occasional arthropod transmission. It has not been proved that man-to-man transmissions may occur. Mice infected naturally may carry the virus throughout life and the female may transmit it to her offspring.

Wooley *et al.* (1937) reported that up to 12% of samples of serum from persons not suffering from the disease possessed neutralizing antibodies against L.C.M. virus, but this has not been confirmed in recent years in U.S.A. or elsewhere. MacCallum (1949, 1950) has found that only 3 to 5% of two series of cases of lymphocytic meningitis investigated in England in 1947–9 had had a recent infection with this virus.

Final diagnosis depends on laboratory methods. The virus has been isolated from blood, cerebrospinal fluid, and nasopharyngeal secretions during the febrile period by intraperitoneal inoculation into guinea-pigs or intracerebral inoculation into mice. Complement-fixing antibodies develop in the serum three to four weeks, and neutralizing antibodies usually six to eight weeks, after the onset of illness.

After exposure to the virus an incubation period of 5–10 days may be followed by an influenza-like attack of 7–20 days' duration. Recovery may ensue or, after some days' remission, meningeal symptoms may appear. These persist for 7–30 days, gradually recede, and are followed by recovery. Few fatal cases of proved infection have been reported (Smadel *et al.*, 1942). Sometimes the attack is initiated by meningeal symptoms and in severe cases there may be somnolence, disturbed deep reflexes, and paralysis. The cerebrospinal fluid is sterile bacteriologically, and cell counts range from a few hundred to 3,500, mainly lymphocytes.

The differential diagnosis includes other forms of meningitis, encephalitis, and anterior poliomyelitis.

## Two Recent Cases

Lymphocytic choriomeningitis is not a notifiable disease, and few cases have been reported in this country. Below are given details of two cases occurring, nearly 16 months apart, in houses in the same road separated by only a few yards. As mice in this area were found to be infected with L.C.M. virus, the record may be of public health interest.

### Case 1

This case has been previously reported by MacCallum (1949). A labourer aged 52, of No. 50, Z Road, suffered from headaches of increasing severity for three weeks until on November 16, 1948, he was confined to bed. He felt better on November 22 and returned to work, but he collapsed the next day and was taken home. On the 24th he was admitted to the Park Hospital, Lewisham, complaining of vomiting, pains in the back and limbs, with some neck stiffness and drowsiness. There was marked photophobia and a positive Kernig sign. The cerebrospinal fluid was opalescent and contained 1,800 cells per c.mm., 50% being polymorphonuclear leucocytes, and L.C.M. virus was isolated from it by guinea-pig inoculation. The diagnosis was confirmed serologically by complement-fixation tests with the following results: (1) serum taken on the 41st day of illness, titre 1/8; (2) serum taken on the 61st day of illness, titre 1/8; (3) serum taken five months after onset, titre 1/2; (4) serum taken one year after onset, negative. The titres refer to the initial dilutions of serum in which complement fixation occurred.

On being questioned, the patient said that there were large numbers of mice in his rooms. He had been trapping them and clearing out the traps afterwards. Attempts were made to trap mice, but only one was caught about two months after the probable time of infection. No virus was isolated from its brain or spleen.

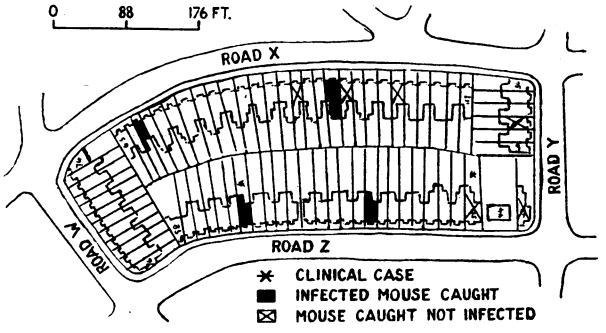
### Case 2

A married woman aged 69, of No. 86, Z Road, had been treated at home by her doctor for bronchopneumonia since February 8, 1950. Her condition improved rapidly until February 23, when she was admitted to Lewisham Hospital in a drowsy, dehydrated, flushed state with some neck rigidity. The cerebrospinal fluid was cloudy and under pressure, containing 400 lymphocytes and 200 large mononuclear cells per c.mm. She rapidly improved until by March 1 she was symptom-free apart from slight headaches, and was discharged on March 29. The cerebrospinal fluid was not examined for virus. A presumptive diagnosis of lymphocytic choriomeningitis was made serologically by complement-fixation test with the following results: (1) serum taken on the 20th day of illness, titre 1/8; (2) serum taken on the 28th day of illness, titre 1/8; (3) serum taken on the 49th day of illness, titre 1/16; (4) serum taken nine and a half months after onset, negative.

In view of the diagnosis, arrangements were made to trap mice at the house. Three mice were caught, and, from the pooled brains of these, L.C.M. virus was isolated after inoculation into guinea-pigs and mice.

## Investigation into the Cause

Owing to the proximity of the houses of these two patients it was decided to visit each of the 73 houses comprising the block made by the four roads (see diagram) to inquire specifically for the presence of mice and to set traps if possible. About a dozen houses at a time were visited, and the purpose was explained. For various reasons traps were set in only 34 of the 73 houses. Ten more mice were caught and examined for virus. A 2% suspension of each mouse brain was inoculated intracerebrally into six mice. These were examined daily. Where virus was present, the mice showed ruffled coats, had laboured respiration, and developed convulsions with terminal spasm six to nine days after inoculation. Where no signs of illness were noted the mice were further tested intracerebrally, 14–21 days after the original inoculation,




with a known strain of virus to detect any immunity which might have developed from a subclinical infection. Details of the results are as follows:

| Address | Caught | No. of Mice | Result |
|---|---|---|---|
| 50, Z Road .. | 9/12/48 | 1 | No virus isolated |
| 86, Z ,, .. | 31/3/50 | 3 | Virus isolated from pooled mouse brains |
| | 1/4/50 | | |
| | 4/4/50 | | |
| 42, Z ,, .. | 4/5/50 | 1 | No virus isolated |
| 66, Z ,, .. | 3/5/50 | 1 | Virus isolated |
| 36, Y ,, .. | 26/5/50 | 1 | No virus isolated |
| 67, X ,, .. | 26/5/50 | 1 | Virus isolated |
| | 27/5/50 | 1 | No virus isolated |
| 91, X ,, .. | 14/7/50 | 1 | ,, ,, ,, |
| 97, X ,, .. | 12/7/50 | 1 | Virus isolated |
| | 13/7/50 | 1 | No virus isolated |
| 99, X ,, .. | 11/7/50 | 1 | ,, ,, ,, |
| 107, X ,, .. | 14/7/50 | 1 | ,, ,, ,, |

Sera from three inhabitants of No. 66, Z road, in which an infected mouse had been trapped on May 3, contained no complement-fixing antibody against L.C.M. virus when tested 29 weeks later. It is apparent that they had not been infected with L.C.M. virus during the preceding six months. The back gardens of the houses in Z and X roads are separated by an old low brick wall or a wooden fence. The main structures of the two sets of houses are 80–90 ft. (24.4–27.4 m.) apart. Many of the gardens contain sheds which mice might inhabit, but in fact mice were trapped only in the houses.

From unpublished observations (Southern, personal communication, 1950) it appears that the movement of house mice is limited and may be confined to contiguous rooms. If they migrate it is thought most likely that they will move to near-by houses, less likely that they will move into gardens and thence into houses opposite, and least likely that they will move across moderately wide metalled roads to houses on the opposite side. From time to time movement wider afield takes place, but its extent is unknown.

An inquiry into the possible occurrence of further cases in Lewisham was carried out. Over 200 doctors were circularized, but no other cases, suspected or confirmed, were reported. Similarly, seven of the eight M.O.H.s of surrounding districts stated that no cases had occurred in their areas during the preceding two years. The other M.O.H. reported a case which occurred in February, 1950, in a house 3½ miles (5.6 km.) from the block of houses containing the two reported cases. No mice were caught in the rooms occupied by the patient, but two were trapped in the flat below, and from these L.C.M. virus was isolated at

Colindale. These boroughs, with Lewisham, cover an area of 66 square miles (171 km.²) with a population of 950,000.

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# A CASE OF CHRONIC NEUTROPENIA TREATED BY SPLENECTOMY

BY

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In view of the reports of chronic neutropenia which have recently appeared in the literature, the following case seems worthy of record.

## Case Report

A motor-lorry driver aged 45 was admitted to hospital in March, 1947, suffering from an abscess in the perineum. His temperature was 100° F. (37.8° C.), pulse 82, and respirations 20. He was pale and sallow and had no symptoms beyond pain at the site of the abscess. This was incised, and, because of its failure to heal, he came under medical observation, when a chronic ulcer was found in the perineum, lying anteriorly to the rectum; the edges were hard and undermined, the base was unhealthy, and there was surrounding induration. A biopsy examination of the ulcer tissue did not reveal any specific characteristics. The Wassermann reaction test was negative. On May 27 the liver was enlarged three fingerbreadths below the costal margin and the spleen was also palpable. The blood showed a severe leucopenia, with a marked diminution in the number of neutrophil cells.

From May 9 to the end of June fever continued and the white corpuscles varied from 900 to 1,000 per c.mm., and a considerable reduction in the percentage of neutrophil cells was noticed. Most of the cells were very primitive, and some of these contained nucleoli and showed monocytoid features. During June the liver and spleen were considerably enlarged and the patient developed an ischio-rectal abscess. The white cells varied between 1,200 and 2,000 per c.mm. Treatment with penicillin and pentnucleotide was given, and on June 13 the white cells numbered 2,000, but no granular leucocytes were seen in the film. Four weeks later the leucocytes still numbered only 1,000, and a blood film showed only one or two granulocytes. Nearly all the white cells were of the monocyte series. The ulcer in the perineum had by this time healed, and the patient was allowed to return home but was instructed to remain under observation.

In spite of treatment the white-cell count had failed to improve, and the patient left hospital with a leucopenia, hypochromic normocytic anaemia, and thrombocytopenia, and a normal bone marrow. His condition was thought to be due to hypersplenism, and it was decided that, if improvement did not occur or if deterioration should take place, he should return for splenectomy. On September 13 the white cells were 3,850, haemoglobin 100%, platelets 188,000, bleeding-time 2 minutes, and the coagulation time 4 minutes. Splenectomy was performed on September 25. On the 27th the white cells numbered 12,600 (polymorphs 80%, lymphocytes 14%, monocytes 6%) and platelets 300,000 per c.mm. After the operation the patient developed a left-sided basal pneumonia, but eventually made a satisfactory recovery and returned home on December 17. A histological report on the spleen did not indicate any changes characteristic of any particular disease.

From December, 1947, until October, 1948, the patient remained in good health, but was then readmitted to hospital on account of a streptococcal sore throat. A blood examination at this time showed: red cells, 5,370,000; white cells, 4,600 (neutrophils 5%, lymphocytes 78%, eosinophils 1%, basophils 3%, Türk cells 4%, monocytes 9%); colour index 1. The erythrocytes were normocytic and normochromic. The platelets were numerous and large, but there was a marked neutropenia, and sternal puncture revealed a moderately cellular normal marrow. The myeloid series of cells consisted mainly of myelocytes and metamyelocytes and a few scanty myeloblasts. The blood uric acid at this time was 3.4 mg. per 100 ml. (serum). Blood counts gave the following results, along with occasional myelocytes:

| | November, 1948 | | | | December, 1948 | | | January, 1949 | |
|---|---|---|---|---|---|---|---|---|---|
| | 10th | 14th | 21st | 29th | 9th | 13th | 23rd | 5th | 13th |
| W.B.C... | 4,800 | 5,100 | 5,500 | 4,500 | 5,500 | 9,000 | 8,800 | 4,300 | 4,200 |
| Neutrophils.. | 7% | 6% | 2% | 13% | 33% | 49% | 4% | 3% | 2% |
| Lymphocytes.. | 71% | 70% | 79% | 66% | 53% | 38% | 78% | 80% | 86% |
| Monocytes | 20% | 17% | 11% | 14% | 12% | 13% | 15% | 13% | 10% |
| Eosinophils.. | 2% | 6% | 7% | 5% | 1% | — | — | 1% | — |
| Basophils | 0% | 1% | 1% | 2% | 1% | — | 3% | 3% | 2% |

On November 9 the patient developed an irritable erythematous rash on his arms and legs, but this cleared up satisfactorily. On November 29 nodular inflammatory areas appeared in both buttocks, and on December 13 two abscesses were opened and drained. He was finally discharged from hospital in good health on January 13, 1949; the white cells at this time numbered 4,280, with 20% neutrophils.

When examined on January 10, 1950, he was found to be in good health and weighed 14 stone (88.9 kg.). He had completely recovered from his illness, but there was still a relative neutropenia, the figures of the blood count being: red cells, 5,320,000; white cells, 7,000 (neutrophils 33%, lymphocytes 59%, monocytes 4.5%, eosinophils 1.5%, basophils 2%); P.C.V., 52%; C.I., 0.85; M.C.V., 98$\mu^3$; M.C.H.C., 28%. The red blood cells were of good size and shape, but hypochromic. Platelets were numerous. A relative neutropenia with a shift to the left was noted.

## Discussion

In this case a diagnosis of hypersplenism was made and the patient underwent splenectomy. It is interesting to note that after the operation, whilst his general condition improved, the white-cell count remained for a long time at a low level and at the last blood examination there was still a relative neutropenia. Furthermore, histological examination of the spleen did not show any abnormality.

Many cases of neutropenia have recently been recorded. Primary splenic neutropenia was originally described by Wiseman and Doan (1939, 1942), who emphasize the following characteristics: profound granulocytopenia, hyperplasia of the bone marrow, splenomegaly, and the curative effect of splenectomy.

At no time did my patient show any evidence of haemolytic anaemia, and, although the spleen was