in sensitivity for a given period of dark adaptation, and the sensitivity at the end of this period. This would seem to give the most important information needed; namely, the light sensitivity of the light-adapted eye, the sensitivity that may be attained after a selected period of dark adaptation and the speed of dark adaptation. This information would enable the examiner to exclude eyes defective in power to see at low illumination when either light-adapted or dark-adapted (hemeralopia, avitaminosis, etc.) and to select the best of the normal eyes.

In our thinking as to the comparative importance of pilot fitness as a safety factor in aviation, it is well to keep in mind a statement made by Major-General James E. Fechet (Ret.), formerly chief of the U. S. Army Air Corps.[4] Discussing the causes of airplane crashes, he says that in more than half the number of cases these crashes are due to personnel error or to undetermined causes. In the personnel group he includes the pilot, the weather man, the airline operations manager and the mechanic. A small per cent. of these crashes—less than five, he says—is due to mechanical failure—engine malfunctions, breakage of some part of the plane or its essential accessories. From this it seems that not the plane but its operation is chiefly at fault.

C. E. FERREE
G. RAND

SPECIAL ARTICLES

HUMAN TOXOPLASMOSIS: OCCURRENCE IN INFANTS AS AN ENCEPHALOMYELITIS VERIFICATION BY TRANSMISSION TO ANIMALS*

A PROTOZOAN encephalomyelitis in infants, described in recent years,[1,2] has been experimentally transmitted to animals and shown to be due to a Toxoplasma. The latter is a Protozoan which in smears appears of crescentic shape, measures 4–6 microns in length and 2–3 microns in width. It is pointed at both ends or has one blunt end and has a central chromatin body. Although it is of uncertain classification, it is characterized by an affinity for many tissues, especially the central nervous system, wide-spread geographic distribution and pathogenicity for a wide variety of hosts. In spite of the last, human infection has not hitherto been established, one report being very doubtful.[3] Its occurrence is now proved by the recent transmission of the infection to animals from an infant.

The child became ill at three days of age and developed convulsive seizures, disturbances in respiration and symptoms of involvement of the spinal cord. Terminally, irregular reddish-brown areas were observed ophthalmoscopically in each macular region. The infant died at the age of 31 days. Autopsy, limited to the nervous system, revealed a wide-spread encephalomyelitis, characterized by focal areas of inflammation and necrosis, and disseminated miliary granulomas. The right eye showed a localized chorioretinitis. A Protozoan morphologically identical with Toxoplasma was present in all the lesions.

Fresh tissue removed from lesions in the cerebral cortex and cervical spinal cord five hours postmortem was emulsified in sterile physiological saline. Four rabbits, 26 infant mice and 9 rats were inoculated with the emulsion intracerebrally. Eighteen infant mice were cannibalized by the mothers, but of the remaining 8, 6 showed the following evidence of having been infected: (1) They became ill and were sacrificed or died in from 18 to 40 days. (2) They showed lesions in the central nervous system resembling those seen in the human case. (3) Protozoa like those in the nervous system of the infant were present in the lesions. (4) Transmission to rabbits and mice was attempted from 4 of these mice and was successful in each instance, using brain tissue for intracerebral inoculation with the production of similar lesions containing parasites, and further successful serial passages. The other mice showed a meningo-encephalitis but no parasites.

Three of the rabbits died in from 9 to 13 days and showed a meningo-encephalitis. Parasites were found in the lesions in 2 and successful transmission of the infection to rabbits and adult mice by intracerebral inoculation of emulsified brain was carried out from each of the 3. The fourth rabbit and the 9 rats showed neither clinical nor pathological evidence of infection. Excluding 18 cannibalized infant mice and 6 rats dying shortly after inoculation apparently of cerebral trauma, one finds that 9 or three-fifths of the remaining 15 animals became infected. That this was not a spontaneous infection activated by the inoculations is evidenced by (1) the high percentage of infection following the inoculation of the human material, (2) the fact that toxoplasmosis has not been described in rabbits or mice in North America and (3) the absence of similar infection in many animals of the same stock similarly inoculated with other materials.

* Investigation aided by a grant from the Friedsam Foundation.

[1] A. Wolf and D. Cowen, *Bull. Neur. Inst. N. Y.*, 6: 306, 1937.

[2] A. Wolf and D. Cowen, *Ibid.*, 7: 266, 1938.

[3] J. O. W. Bland, *Lancet*, 219: 52, 1930. *Brit. Jour. Exper. Path.*, 12: 311, 1931.

[4] J. E. Fechet, *Flight Surgeon Topics*, School of Aviation Medicine, Randolph Field, Texas, 1: No. 2, 44–48, 1937.

In the first 6 months, 24 serial passages in rabbits and 22 in irregularly alternating rabbits and mice have been carried out by intracerebral or combined intracerebral and intraperitoneal injection of infected brain emulsion. Filtrates of emulsions passed through Berkefeld "N" filters proved non-infective. Of 148 rabbits inoculated, 131, and of 105 mice, all but 2, succumbed, the majority in from 5 to 9 days. Of 98 infant mice inoculated intracerebrally, 52 or four-fifths of the non-cannibalized succumbed, the majority in from 2 to 3 weeks. In most of the animals, symptoms did not appear until the last day of life. These included sluggishness, pareses, tremors, convulsions and respiratory difficulties. A rise in temperature beginning on the second or third day was noted in the rabbits.

In every instance, there was a severe disseminated encephalomyelitis marked by focal inflammation and necrosis. The exudate included lymphocytes, plasma cells, mononuclear leucocytes and fewer neutrophiles and eosinophiles. Granulomas like those in the infant's brain were often observed. Focal inflammatory lesions were less frequently encountered in the lungs, striated muscles, heart, spleen and liver. Parasites identical with those in the human case were found in large numbers in the lesions. Attempts to cultivate the Protozoan on a variety of media free of living cells failed.

In addition to rabbits and mice, chicks from 1 to 11 days old and guinea pigs were inoculated intracerebrally. These species proved susceptible as evidenced by the development of typical histologic lesions containing parasites. A rhesus monkey injected intracerebrally and subcutaneously remained well and its temperature continued normal. The susceptibility of this species to this strain of Toxoplasma is being investigated further.

Six rabbits which did not succumb to an initial inoculation were re-inoculated intracerebrally from 1 to 3 times within 3 weeks to 3 months and all proved to be immune. Eight control rabbits and 3 mice injected with the same material by the same route succumbed. Four mice which did not succumb to an initial inoculation were also re-inoculated intracerebrally and intraperitoneally within 2½ to 4½ months. All survived, while 2 rabbits and 11 mice used as controls succumbed.

That the microorganism isolated from the human case is a Toxoplasma is indicated by the following: (1) Its morphology corresponds to that of Toxoplasma of animal origin. (2) The course of the disease and the lesions produced in the animals inoculated with it are very similar to those noted in the same species by inoculation of a Toxoplasma of animal origin. (3) The susceptibility of the rabbit, mouse, guinea pig and chick to this Toxoplasma corresponds to the wide host range of Toxoplasma of animal origin. (4) Convincing evidence of the nature of the microorganism was obtained by cross-immunity experiments. Toxoplasma from a guinea pig passaged through mice was kindly furnished us by Sabin and Olitsky.[4] The 6 rabbits and 4 mice, noted above to be immune to the human strain of Toxoplasma, were re-inoculated respectively intracerebrally, and intracerebrally and intraperitoneally with the Sabin-Olitsky strain using infected mouse or rabbit brain emulsion. All 10 animals proved to be immune. Seven control rabbits and 6 control mice succumbed. Conversely, 2 rabbits immunized against the Sabin-Olitsky strain proved to be immune to the human strain, while two controls succumbed. Working with the same strains of Toxoplasma, Sabin and Olitsky, using other methods, have confirmed this cross-immunity and will report their results in the near future. The Protozoan found in the infant might be called *Toxoplasma hominis,* with the reservation that it may later prove to be identical with one or all of the animal strains.

Four other cases[1,2,5,6] (respectively from New York City, Chicago, Prague and Rio de Janeiro), very similar clinically and pathologically to the present case, have been shown by two of us to constitute a distinct disease entity marked by encephalomyelitis. In one of these reports,[6] the author mentioned focal inflammatory lesions in the heart, striated muscles and subcutaneous tissue as well. The lesions in each infant contained a parasite morphologically indistinguishable from that in the present case. There is little doubt then that they too were cases of toxoplasmic encephalomyelitis, although experimental evidence is lacking. That there may be other forms of human toxoplasmosis is very probable.

In conclusion, toxoplasmosis has been demonstrated in man. It has been shown to occur as a characteristic disease of young infants involving the central nervous system. The first experimental transmission of a human toxoplasmosis to animals is described.

ABNER WOLF
DAVID COWEN
BERYL PAIGE
COLLEGE OF PHYSICIANS AND SURGEONS,
COLUMBIA UNIVERSITY

THE LOCALIZATION OF MINERALS IN ANIMAL TISSUES BY THE ELECTRON MICROSCOPE[1]

IN recent years there have appeared a number of articles on the electron microscope with reference to its use in biological investigations. Most of these papers

[4] A. B. Sabin and P. K. Olitsky, SCIENCE, 85: 336, 1937.
[5] J. Jankû, *Casopis lekarew ceskyck,* 62: 1021, 1923.
[6] C. M. Torres, *C. R. Soc. de Biol.,* 97: 1778, 1927.

[1] Aided by grants from the Rockefeller Foundation and the Josiah Macy, Jr., Foundation.