However, when the individual curves are examined it is seen that at the *0.245% calcium level the largest rats were raised at a Ca/P ratio of 0.5. When the calcium level was 0.490%, the Ca/P ratio at which the largest rats were raised, was 1.0.* The results of such examination can be tabulated as follows:

% Ca in diet	Largest Young Raised at Ca/P ratio of	Average wt. at 21 days
0.245	0.50	43.3
0.490	1.00	46.7
0.735	1.50	44.4
1.225	1.66	45.4
2.450	2.00	37.3

It is, we believe, fair to consider the average weight of the young raised during 10 reproductive cycles as a criterion for the suitability of the Ca/P ratio of the diet. As stated previously, if an *average* curve for the 4 lowest levels of calcium were constructed, the optimum ratio would be at, or very near to, 1.0, but inasmuch as *each* level of calcium used showed a maximum weight of young at a different Ca/P ratio we must conclude that no one optimum ratio can be stated unless at the same time the amount of calcium is known. The level of calcium in a diet, therefore, determines what level of phosphorus, *i. e.*, what Ca/P ratio, is optimal.

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Nature of the Blood-Cerebrospinal Fluid Barrier Permeability Revealed by Isohemagglutinin Tests.

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It has been stated that blood-cerebrospinal fluid barrier permeability is capricious. This is possibly a confession that the meaning and mechanism of permeability are yet incompletely understood. It is not surprising that this is so for careful study of standard texts and original papers since 1910 leads one to conclude the theories of origin, function and fate of cerebrospinal fluid are far from agreed upon.

Studies of variations in the permeability of the barrier have been prosecuted from two points of view. Foreign substances have been introduced, more commonly into the blood stream, occasionally into the subarachnoidal space, and their fate traced. Such substances have been crystalloids, as bromide; colloids, colored and uncolored, and McKinley and Holden[1] utilized the bacteriophage. Again, study has been made of blood elements not normally found in the cerebrospinal fluid whose presence there may be taken as evidence of increased permeability. Of these may be mentioned induced antibodies and naturally occurring antibodies such as hemolysins and isohemagglutinins. Three references exist dealing with this last indicator of permeability.

Weil and Wall[2] found no isohemagglutinins in 12 cerebrospinal fluids from such conditions as syphilis of the central nervous system, hemiplegia, brain tumor and myoclonic encephalitis. On the other hand Herman and Halber[3] found isohemagglutinins in 11 of 80 fluids examined. These fluids came from more than 30 widely different types of pathology, although most involved the central nervous system either organically or functionally. In 6 of 22 cases of bacterial meningitis the cerebrospinal fluids contained isohemagglutinins but the 6 cases of tuberculous meningitis included were all negative. Two of 3 cases of cord tumor, 2 of 4 cases of sclerosis, and 1 of 3 cases of chorea accounted for the remaining 5 positives. Parr[4] examined 104 cerebrospinal fluids at Beirut and found 6 containing isohemagglutinins.

These suggestive but far from conclusive results led the present authors to further investigate the problem. The cerebrospinal fluids examined came from the services of the Worcester City Hospital and represent material from cases of all ages and both sexes. They were forwarded to Washington for examination. All found colored, contaminated, or otherwise unfit for use were discarded. Tests were carried out on 156 different cerebrospinal fluids by mixing small quantities of the fluid under test with equal volumes of 5% saline suspensions of (1) known type A red blood cells, and (2) known type B red blood cells. The mixtures were sealed in well slides by means of vaselined coverslips and incubated from one to 2 hours. The preparations were then uncovered, agitated and ex-

[1] McKinley, E. B., and Holden, M., PROC. SOC. EXP. BIOL. AND MED., 1927, **24**, 595.

[2] Weil, P. E., and Wall, P. I., *Compt. Rend. Soc. Biol.*, 1923, **88**, 173.

[3] Herman, E., and Halber, W., *Compt. Rend. Soc. Biol.*, 1924, **91**, 959.

[4] Parr, L. W., *J. Lab. and Clin. Med.*, 1932, **17**, 333.

amined, readings being made as one would make them in typing unknown blood sera by the use of known red blood cells. The patients from whom the fluids were taken were blood typed in Worcester and these data together with clinical and pathological information were made a part of the record.*

It should be recalled that persons of blood type AB (Jansky 4) have no isohemagglutinins in their blood and in such cases one would not find isohemagglutinins in the cerebrospinal fluid even with a highly permeable barrier. Such persons, however, number less than 5% of our population and do not materially complicate the picture.

In 21 of the 156 specimens typed isohemagglutinins were found. These positive specimens were from cases of skull fracture, multiple sclerosis, lues, cerebral hemorrhage, post-operative and post-partum symptomatology, epilepsy, pneumonia, sinus infection, bronchitis, influenzal meningitis and concussion. Negatives derived from these same conditions and also from poliomyelitis, encephalitis, uremia, brain tumor, tuberculous meningitis, hypertension, pulmonary tuberculosis, anemia, senile dementia, psychoneurosis, convulsions, hydrocephalus, alcoholism, diabetes, mastoiditis, Korsakoff's syndrome, endometritis, Adams-Stokes syndrome, myelitis, pyelitis, influenza, nephritis, paresis, tabes dorsalis, rheumatism, gas and also barbital poisoning, neoplasm, cholecystitis, general trauma, and amebic dysentery.

Our experience corroborates the impression previously held that such permeability of the blood-cerebrospinal fluid barrier may exist as to permit passage of isohemagglutinins from the blood. However, we have not been able to demonstrate that the passage of these natural antibodies occurs with constancy in any given pathological condition, nor were the positives obtained correlated with age, sex, or racial stock.

The test for isohemagglutinins in the cerebrospinal fluid is slow and fresh red blood cells of 2 types are needed to carry it out. It seems unlikely that such a procedure has much practical value either in the understanding of permeability *per se* or in clinical laboratory diagnosis. Lastly, from the point of view of the occurrence of isohemagglutinins in cerebrospinal fluid barrier permeability is capricious.

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