first 6 to 7 days. If the hemorrhage weight were not considered in the above, the level of progestin would be still higher since the hemorrhage which occurs in about 50% of the corpora lutea at this stage[3] increases the weight of the tissue. This high content of progestin correlates well with the active growth of the granulosa cell during this period.[3] It can be physiologically explained by the fact that a completely proliferated endometrium is necessary for implantation of the fertilized ovum when it reaches the uterus.

The oestrin content of the corpus luteum is more or less uniform suggesting saturation of tissue and not actual preparation of oestrin. The values found here are about half those obtained by D'Amour *et al.*[4]

7746 C

Results of Repeated Determinations of the Blood-Cerebrospinal Fluid Barrier.

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Investigations of the barrier between the blood and cerebrospinal fluid by the Walter method[1] and its modifications[2-5] have amply proved its value as an aid in the diagnosis and treatment of mental diseases. A number of variations from this generally accepted procedure have been suggested as the result of studies intended to show that the distribution of bromide between the blood and cerebrospinal fluid does not attain an equilibrium at the end of the 5-day period of bromide ingestion.[6] Recommendations have been made that would alter the method or even change it entirely.

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[3] Corner, G. W., *Am. J. Anat.*, 1919, **26**, 117.

[4] D'Amour, F. E., D'Amour, M. C., and Gustavson, R. G., *J. Pharm. and Exp. Therap.*, 1933, **49**, 141.

[1] Walter, F. K., *Z. f. d. ges. Neurol. u. Psychiat.*, 1925, **95**, 522.

[2] Hauptmann, A., *Z. f. d. ges. Neurol. u. Psychiat.*, 1926, **100**, 332.

[3] Malamud, W., and Mullins, B. M., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 871.

[4] Malamud, W., Mullins, B. M., and Brown, J. R., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 1084.

[5] Malamud, W., Brown, J. R., and Mullins, B. M., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 733.

[6] Fremont-Smith, F., Dailey, M. A., and Sloan, D. H., *Trans. Am. Neurol. Assn.*, in press.

The chief purpose of this study is to set forth the results obtained in a series of patients who received from 2 to 6 spinal punctures at 3-day intervals following the administration of varying amounts of bromide. The test employed, including the correction for the

TABLE I.
Bromide Content of Blood (Mg. per 100 cc.).

Patient	Days after starting bromide (Five-day bromide test)							
	6	9	12	15	18	19	21	22
1	81.5	84.7	80.2	76.1	75.7		73.2	
2	71.4	62.5	60.0*	54.7		50.8		44.8
3	65.2	67.3	55.5					
4	75.0	62.5	57.7	50.0		42.9		37.5
5	142.8†	147.8	121.0	90.9		76.9		65.2
6	150.0†	103.4	93.8	82.4				
7	100.0†	100.0	88.2	87.2*	86.2		84.7	
8	147.0†	132.5	97.4		81.5		67.3	
9	73.2	61.2						
10	68.8	61.7			48.4			
11	82.9	67.9						
12	65.8	55.5	50.0					
13	77.3	64.6	56.6	57.5	47.0*		47.0*	
14	87.7	90.4	78.9	70.4	68.2		60.0	
15	285.7‡	265.5	219.0*	193.6	174.4		150.0	
16	300.0‡	270.7	230.8	196.0	174.4		135.2	
17	68.2	54.5	58.8	57.0	50.0		50.0	
18	61.7	53.6	50.0		37.5			
19	72.1	62.5	50.0	50.0				
20	78.9	64.6	60.0					

*Corresponding cerebrospinal fluid specimens discarded; bloody.
†Patients previously receiving bromide; test bromide given.
‡Patients with bromide intoxication; test bromide not given.

TABLE II.
Permeability Quotients.

Patient	Days after starting bromide							
	6	9	12	15	18	19	21	22.
1	3.08	2.87	2.86	2.94	2.88		2.86	
2	3.09	3.13		2.70		3.28		2.85
3	2.72	2.39	2.78					
4	3.05	3.00	3.16	3.21		3.32		3.09
5	2.74	2.88	3.12	3.29		3.43		3.19
6	2.38	2.52	3.14	3.10				
7	2.32	2.38	2.45		2.73		2.76	
8	2.49	2.51	2.98		2.94		3.00	
9	2.86	2.71						
10	2.63	2.79			2.72			
11	3.15	3.00						
12	3.04	2.95	2.60					
13	2.73	2.46	2.60	2.79				
14	2.58	2.51	1.86	2.90	2.97		3.04	
15	2.02	1.95		1.85	1.91		2.07	
16	2.10	2.03	1.98	1.89	1.98		2.14	
17	2.92	2.91	2.64	3.13	3.04		2.96	
18	2.49	2.44	2.58		1.99			
19	2.08	2.51	2.60	2.66				
20	2.50	2.46	2.68					

difference between the chloride content of the blood and cerebrospinal fluid,[5] has been described.[3, 7] The data obtained are recorded in Tables I and II.

Patients 5, 6, 7, and 8 had ingested bromide before the study was made but not in sufficient quantity to mitigate their receiving the test dose. Patients 15 and 16 on admission to the hospital were toxic from prolonged bromide sedation and were therefore included in the series without receiving the test dose. The latter patients and experience with others suffice to vitiate the use of large doses of bromide, or, because of its cumulative effect, smaller doses given over a longer period of time. Toxic symptoms are not infrequently manifested when the bromide content of the blood reaches 150 mg. per 100 cc., and conversely, toxic patients as a rule do not show significant improvement until the blood bromide content has fallen to approximately 150 mg. Patients in whom the bromide content of the blood is unusually high (cases 15 and 16), have extremely low permeability quotients which, as long as the blood bromide is in excess of 150 mg. per 100 cc., vary insignificantly one from the other during a series of examinations. It is inferred therefore that a high concentration of bromide in the blood damages the blood-cerebrospinal fluid barrier permitting an excess of bromide to enter the cerebrospinal fluid, or that the cerebrospinal fluid is capable of absorbing a relatively high proportion of bromide from the blood which it releases almost proportionately with the blood until the blood concentration falls to approximately 150 mg. per 100 cc., when the cerebrospinal fluid increases disproportionately its release of bromide and thereby again makes possible significant variations in the permeability quotients obtained on successive examinations. The latter is substantiated by the fact that the average permeability quotient increases with the passage of time. The lower limit of drug dosage is governed by the technical unreliability of the colorimetric method when the bromide concentration falls below 50 mg. per 100 cc. of blood.

The average permeability quotient was calculated for each group of examinations made and the mean variation from the average quotient determined. The figures of 0.289 for the examinations made on the sixth day and 0.264 on the ninth day vary insignificantly, whereas those obtained on subsequent days vary widely except for that obtained on the sixth puncture. However, because the amount of bromide contained in the blood of test patients 18 or 19 days

[7] Malamud, W., Fuchs, D. M., and Malamud, N., *Arch. Neurol. and Psychiat.*, 1928, **20**, 780.

after discontinuing the drug is too low often for accurate study, the results obtained for this group are less reliable than those obtained on earlier punctures.

Individual permeability quotients obtained on successive punctures varied widely from their corresponding initial quotients except for those obtained on the second puncture or ninth day, Similarly the average variation of 0.127 for the second group from the initial average quotient was markedly less than that for subsequent groups. But 4 cases deviated in their quotients on the ninth day by more than 0.20 which is the probable error of the colorimetric method itself.[7] Since one of these varied only 0.21 we may consider that but 3 or 15% of the cases varied significantly from their initial quotients while 11 or 55% of the cases varied less than 0.10. Average and especially individual quotient variations after the ninth day were wide and inconsistent.

With a majority of 13 cases on the ninth day showing a negative variation from their initial quotients (and with the average quotient slightly though insignificantly lower), the inference is that the cerebrospinal fluid continues to absorb additional bromide following the first puncture. In some instances an increase in the blood bromide content on the ninth day is associated with an increased permeability quotient and *vice versa*. There is no significant correlation, however, and the variations are relatively small. Our deduction, then, is that at the end of the 5-day bromide ingestion period a state of equilibrium between the bromide of the blood and that of the cerebrospinal fluid has been reached which is maintained until the ninth day. After the ninth day the percentage of cases showing positive quotient variations, as well as wide individual variations, increases markedly which accounts for the gradual average quotient increase resulting from the relatively rapid release of bromide from the cerebrospinal fluid.

Summary. 1. Twenty patients were given repeated spinal punctures after ingesting varying amounts of bromide. 2. A state of equilibrium between the bromide of the blood and that of the cerebrospinal fluid is maintained from the end of the 5-day bromide ingestion period to the ninth day. 3. The permeability quotient tends to rise with the passage of time indicating that after the drug has been discontinued the return of bromide from the cerebrospinal fluid to the blood is relatively more rapid than the elimination of bromide from the blood. 4. Permeability quotients do not vary widely when the bromide concentration of the blood is high; significant variations are detected when the bromide content of the blood is

maintained between 50 and 150 mg. per 100 cc. 5. The method employed is practicable and provides an ideal concentration of bromide in the blood.

7747 P

Concentrated Fouadin in Treatment of Schistosomiasis Japonica in Rabbits.

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Khalil *et al.*[1] and Khalil[2] found that fouadin—antimony III-pyrocatechin-disulphate of sodium—was very efficacious against bilharziasis. Lee[3] and Lee and Chung,[4] however, did not obtain the same result in *Schistosomiasis japonica*. For treatment of this disease, a related compound of calcium salt called "Concentrated Fouadin", has been manufactured. Apart from its composition, the new drug is said to differ from fouadin in being more concentrated and less irritating. It contains 11% of antimony III-pyrocatechin-disulphate of sodium and calcium and is issued in ampoules. Each cc. of the solution has 14.3 mg. of Sb. III and 7 mg. of calcium.

To obtain experimental subjects, young rabbits of 1.5 to 2 kg. in weight were infected with the fork-tailed cercariae of *S. japonicum*. On the discovery of the ova in the feces, the animals were given 6 weekly intramuscular injections of Concentrated Fouadin until the eggs disappeared or died as determined by the hatching test. During treatment, particular attention was paid to the daily weights and to the appearance of toxic symptoms as a guide to the regulation of dosage. Thus it was found that the following scheme of administrations was well tolerated: an initial dose of 0.15 cc. followed by 0.25 cc. and 0.3 cc. for the second, third and subsequent injections respectively.

The effects of the drugs were judged from the findings at autopsy when the condition of the lungs, the liver and intestine was noted

[1] Khalil, M., Nazmi, M., Peter, F. M., El Din, M., Salach and El Betash, M. H., *Deutsch. med. Woch.*, 1929, **55**, 1125.

[2] Khalil, M., and Betasche, M. H., *Lancet*, 1930, **1**, 234.

[3] Lee, C. U., *Chinese Med. J.*, 1932, **46**, 1169.

[4] Lee, C. U., and Chung, H. L., *Chinese Med. J.*, 1933, **47**, 1411.