

ment induced us to use the auto-serum test, the result of which was positive.

Further, the negative reactions obtained in the allergic cases have only borne out the opinion that these individuals had no active tuberculosis and were accepted as favorable rather than as disparaging results.

Aside from this recapitulation of cases, we do not care to draw any conclusions or make any definite statements as to the value of the reaction, and we feel that this attitude will be readily comprehended in view of the small number of cases that we have completed, as compared with the several hundred reported by Wildbolz and his associates.

In conclusion, however, we do desire to call attention to the following statement, which we consider of exceptional interest, made by Lanz in his original article after he had observed the auto-urine and autoserum reactions in more than 300 cases:

In all clinically positive cases of tuberculosis, both reactions give positive results. In all nontuberculous cases both reactions are negative. If the reaction turns out positive contrary to expectation, then there is positively an undemonstrable but still active tuberculous process in the body. The reactions are the finest diagnostic medium for the discovery of an active tuberculous focus.

IODIN IN THE CEREBROSPINAL FLUID

WITH SPECIAL REFERENCE TO IODID THERAPY

EARL D. OSBORNE, M.D.

Assistant in Section on Dermatology and Syphilology, and Fellow in Dermatology, the Mayo Foundation
ROCHESTER, MINN.

The presence of iodine in the cerebrospinal fluid of normal individuals or of patients receiving iodids therapeutically has hitherto not been demonstrated. Catton,¹ in 1916, reported a series of tests in patients receiving from 15 to 45 grains of potassium iodid by mouth three times a day. He concluded that, regardless of the amount of iodine administered by mouth, no iodine or compounds of iodine can be found in the spinal fluid, and that either iodine compounds do not pass the ependymal cells of the choroid plexus in any measurable quantity, or such iodine as reaches the spinal fluid is very rapidly fixed in the tissues. These conclusions were based on a method less delicate than that devised by Kendall, which I have employed in this study. This method has enabled me to show that there is iodine in the normal cerebrospinal fluid, and that iodine is found in the fluid in increased amounts following its administration by mouth, by rectum and intravenously. A brief outline of Kendall's method is as follows:

The material is placed in a nickel crucible and evaporated to dryness with sodium hydroxid. It is then fused with solid sodium hydroxid, with the addition of potassium nitrate to assist in the oxidation of the organic matter. The fused mass is poured on the crucible cover, and after cooling is dissolved in boiling water on a hot plate. The solution is transferred to a 500 c.c. Erlenmeyer flask and cooled. Five cubic centimeters of a 20 per cent. solution of sodium bisulphite and two drops of a 2 per cent. solution of methyl orange are added. Eighty-five per cent. phosphoric acid is added slowly, with constant shaking until the indicator turns pink. Then 5 c.c. of a 20 per cent. solution of phosphoric acid is added. This solution is made up to about 250 c.c.; and after a small piece of hard coal has been placed in it to prevent bumping, it is boiled for

at least ten minutes, and then cooled. From five to ten drops of bromine are added, and the flask is shaken until the contents assume a definite yellowish color. It is again boiled for just five minutes after the solution becomes colorless. A small amount, from 1 to 2 mg., of salicylic acid is added and the solution cooled. Five cubic centimeters of a reduced 20 per cent. solution of phosphoric acid, and a few crystals of pure potassium iodid are added. The free iodine liberated is titrated with two hundredth normal sodium thiosulphate with starch as an indicator. For the numerous details of Kendall's method the reader is referred to his original articles.²

In Table 1 the results obtained with normal spinal fluid are recorded. From 5 to 10 c.c. of spinal fluid was

TABLE 1.—IODIN IN NORMAL SPINAL FLUID

Spinal Fluid, C.c.	Iodin, Mg. 100 C.c. Spinal Fluid
100.....	0.002
100.....	0.022
100.....	0.019
75.....	0.024
100.....	0.019
100.....	0.018
100.....	0.020
100.....	0.021
100.....	0.019
Average.....	0.018

withdrawn from each patient besides the ordinary amount for routine laboratory tests. A mixed spinal fluid from ten to twenty patients was used in each determination. Each patient was carefully questioned with regard to previous therapy, and specimens from those who admitted having had medication by mouth at any time during the preceding three or four months were rejected. Kendall and Richardson found the average iodine content of the blood to be 0.013 mg. per hundred cubic centimeters of blood. My figure of 0.018 for the same amount of spinal fluid is slightly higher (Table 1). This difference, 0.005 mg., is within the range of experimental error, and is equivalent to one drop of two hundredth normal sodium thiosulphate.

POTASSIUM IODID BY MOUTH

In Table 2 are recorded the results obtained after administration of potassium iodid by mouth. In all of the six determinations iodine was found. Necessarily,

TABLE 2.—IODIN IN SPINAL FLUID AFTER ORAL ADMINISTRATION OF POTASSIUM IODID

Spinal Fluid, C.c.	Potassium Iodid Three Times a Day	Iodin, Mg. 100 C.c. Spinal Fluid
10	50 grains, last dose 3 hours before.....	Faint trace*
10	50 grains, last dose 12 hours before.....	Faint trace*
10	100 grains, last dose 2 hours before.....	Faint trace*
7	50 grains, last dose 2 hours before.....	0.367
15	50 grains, last dose 72 hours before.....	Faint trace*
15	70 grains, last dose 3 hours before.....	0.335

* Amount too small to be accurately titrated.

specimens of spinal fluid from individual cases were in much smaller amounts than 100 c.c. A faint trace was recorded in four cases, because in the final titration the amount of two hundredth normal sodium thiosulphate used was so small that, if computed on a scale of 100 c.c. of spinal fluid, the margin of error would be very great. In the other two cases, amounts of iodine sufficiently large to be correctly determined were found. These two determinations were made at two and three

2. Kendall, E. C.: The Determination of Iodine in the Presence of Other Halogens and Organic Matter, *J. Am. Chem. Soc.* **34**: 894-909, 1912; The Determination of Iodine in Connection with Studies in Thyroid Activity, *J. Biol. Chem.* **19**: 251-256, 1914; The Determination of Iodine in Connection with Studies in Thyroid Activity, *ibid.* **43**: 149-159 (Aug.) 1920. Kendall, E. C., and Richardson, F. S.: Determination of Iodine in Blood and in Animal Tissues, *ibid.* **43**: 161-170 (Aug.) 1920.

1. Catton, J. H.: Studies of the Spinal Fluid During Iodid Medication by Mouth, *J. A. M. A.* **67**: 1369-1370 (Nov. 4) 1916.

hour intervals, respectively, following the administration of the drug. Buchholtz,³ in 1918, showed that the blood concentration of iodine after administration by mouth was highest from two to three hours after administration. The foregoing determinations suggest a parallelism between the concentration in the blood and the cerebrospinal fluid. Further study with larger dosages is now in progress.

POTASSIUM IODID BY RECTUM

Two determinations were made on patients receiving potassium iodid by rectum only. The results are recorded in Table 3. Both patients showed appreciable

TABLE 3.—IODIN IN SPINAL FLUID AFTER RECTAL ADMINISTRATION OF POTASSIUM IODID

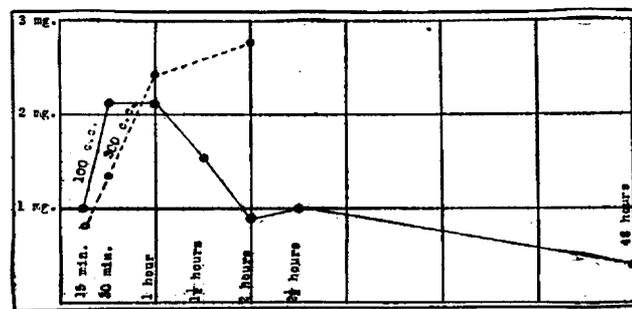
Spinal Fluid, C.c.	Potassium Iodid Three Times a Day	Iodin, Mg. 100 C.c. Spinal Fluid
5	125 grains, last dose 1 hour before.....	1.808
10	*350 grains, last dose 12 hours before.....	0.381

* Impossible to estimate exact amount retained; probably not more than 50 per cent.

amounts of iodine in the spinal fluid, in the first case 1.808 mg. per hundred cubic centimeters (100 times the normal), one hour after the last administration of the iodid, and in the second case 0.381 mg. per hundred cubic centimeters (twenty times the normal), twelve hours after the last administration.

SODIUM IODID INTRAVENOUSLY

The results obtained at varying intervals following an intravenous injection of 10 per cent. sodium iodid solution are shown in Table 4. Iodin in appreciable quantity appears in the spinal fluid within fifteen minutes after the intravenous injection of sodium iodid solution, as shown in the accompanying chart. With the injection of 100 c.c. of a 10 per cent. solution, the peak of the curve of increased iodine content of the spinal fluid



Iodin in spinal fluid following sodium iodid intravenously (10 per cent. solution).

TABLE 4.—IODIN IN NORMAL SPINAL FLUID AFTER INTRAVENOUS ADMINISTRATION OF 10 PER CENT. SODIUM IODID SOLUTION

Spinal Fluid, C.c.	Sodium Iodid, C.c.	Hours Before Spinal Puncture	Iodin, Mg. 100 C.c. Spinal Fluid
15	100	1/4	1.00
15	100	1/2	2.133
15	100	1	1.533
15	100	1 1/2	0.900
15	100	2	1.032
15	100	2 1/2	0.400
10	200	1/4	0.804
15	200	1/2	1.341
10	200	1	2.414
15	200	2	2.784
8	200	24	0.303

is reached from one-half to one hour after injection. This amount, 2.133 mg. per hundred cubic centimeters, falls rapidly during the next hour, approximately to the same amount as that obtained for the fifteen minute interval. The decline in iodine content is then very gradual, until at the end of forty-eight hours

0.4 mg. per hundred cubic centimeters, or approximately twenty times the normal content, was found. With the injection of 200 c.c. of a 10 per cent. solution of sodium iodid, the iodine content of the spinal fluid at the end of the one hour interval is only 0.3 mg. per hundred cubic centimeters of spinal fluid, higher than with 100 c.c. However, instead of dropping at this point, the curve continues to rise, and at the two hour interval the amount of 2.784 mg. per hundred cubic centimeters of spinal fluid is reached. Of necessity, these determinations were made by observations on successive patients and not by successive punctures on a single patient.

With large dosages of sodium iodid intravenously, the question of a cumulative increase in the amount of the drug must be considered. Very little such increase was observed. One patient received daily intravenous injections of 100 c.c. of a 10 per cent. sodium iodid solution for ten days. On the eleventh day he received 200 c.c., and two hours later showed 3.180 mg. of iodine per hundred cubic centimeters of spinal fluid. This amount is approximately only 0.4 mg. higher than that recorded in Table 4 for the iodine content of the spinal fluid two hours after the intravenous injection of 200 c.c. of a 10 per cent. solution of sodium iodid in the normal patient.

During the course of the study, several observations of especial interest were made which are summarized in Table 5:

Patient 1 presented a high grade meningeal involvement. His cerebrospinal fluid showed a positive Wassermann reaction, a positive Nonne reaction, and 306 lymphocytes. He was placed on 10 per cent. sodium iodid solution intravenously in amounts up to 450 c.c. daily (45 gm.). Twenty-four hours after the last injection

the spinal fluid contained 4.851 mg. of iodine per hundred cubic centimeters, which is approximately from fifteen to twenty times the amount (0.303 mg.) in 100 c.c. of spinal fluid of a normal patient twenty-four hours after the injection of 200 c.c. of sodium iodid solution (Table 4).

TABLE 5.—SPECIAL OBSERVATIONS

Case	Diagnosis	Following 10 per Cent. Sodium Iodid	Amt. of Last In-jection, Spinal C.c.	Hours Before Spinal Puncture	Iodin, Mg. 100 C.c. Spinal Fluid
1 (298829)	Neurosyphilis; marked meningeal involvement	200 to 400 c.c. daily for two weeks	450	24	4.851
2 (316584)	Neurosyphilis; advanced tabes dorsalis	100 c.c. daily for two weeks	100	8	4.600
3 (250805)	Neurosyphilis; marked meningeal involvement	100 to 250 c.c. daily for two weeks	250	1/2	42.308
4 (334068)	Neurosyphilis; advanced tabes dorsalis	None	200	8	4.377

Patient 2 had advanced tabes dorsalis with moderate meningeal involvement which had resisted all efforts at treatment. The Wassermann reaction on the cerebrospinal fluid was positive, the Nonne reaction was negative, and there was one lymphocyte per cubic millimeter. The patient had received 100 c.c. of 10 per cent. sodium iodid solution daily for two weeks. Three hours after the last injection he had 4.6 mg.

3. Buchholtz, J.: The Pharmacology of the Iodides, Ugesk. f. Læg. 80: 139-146 (Jan. 24) 1918.

of iodine per hundred cubic centimeters of spinal fluid. As shown in Table 4, the normal amount would have been about 1.0 mg. per hundred cubic centimeters.

Patient 3 had an even more marked meningeal syphilis. In spite of all treatment, the cell count on the spinal fluid varied from 149 lymphocytes at the time of examination to 110 lymphocytes and 306 polymorphonuclears at the time of the test. He had received daily injections of from 100 to 250 c.c. of the sodium iodid solution. His spinal fluid contained 42.3 mg. of iodine per hundred cubic centimeters. This amount is about thirty times more than would be expected under similar conditions in a patient without evidence of neurosyphilis.

Patient 4 presented a well advanced *tabes dorsalis* with very slight meningeal involvement. The spinal fluid Wassermann reaction and the Nonne reaction were positive; there was one lymphocyte. Two hours after an intravenous injection of 200 c.c. of a 10 per cent. solution of sodium iodid, the spinal fluid contained 4.377 mg. per hundred cubic centimeters as compared with the normal amount of 2.784 mg. under the same conditions.

These four observations point to one or both of two possibilities: Either the meninges are more permeable to iodine compounds when there is meningitis, or tissue actively involved by syphilis takes up more iodine than normal tissue. Loeb,⁴ in 1912-1913, found that iodids accumulated in greater concentrations in syphilitic glands than elsewhere in the body, suggesting a selective affinity for syphilitic processes. Fujisawa,⁵ in 1919, made the statement that all syphilitic tissue takes up more iodine than other organs. My observations tend to support the latter possibility. In Patient 1, moreover, the determination was made twenty-four hours after the last intravenous injection, which indicates that the iodine had been fixed in the syphilitic tissue, thus causing an increased concentration in the spinal fluid. In Patient 2 there was only a mild meningeal involvement. Neurologic examination revealed a far advanced parenchymatous degeneration of the posterior columns. This suggests that the large amount of syphilitic tissue had fixed a correspondingly large amount of iodine. In Patient 3, however, the process was predominantly meningeal, pointing to an increased permeability of the meninges. Patient 4 presented essentially the same condition as Patient 2, except that he had practically no active meningeal involvement. These data suggest the possibility that the iodine content of the cerebrospinal fluid following iodid administration may be of diagnostic importance in the study of diseases of the central nervous system.

CONCLUSIONS

1. Iodine is present in the cerebrospinal fluid of normal individuals.
2. Iodine, in increased amounts, is present in the cerebrospinal fluid following the administration of iodids by mouth, by rectum and intravenously.
3. The iodine content of the cerebrospinal fluid following administration of iodid by mouth or by rectum is small compared with that following the administration intravenously.
4. The iodine content of the cerebrospinal fluid following the administration of iodid intravenously plots a definite curve, depending on the amount administered.
5. Certain observations made in the course of this study suggest the possibility that (a) neurosyphilitic tissue takes up more iodine than normal nervous tissue, and (b) the presence of a meningitis increases the permeability of the meninges to iodine compounds in the blood.

4. Loeb, O.: Ueber Jodverteilung im syphilitischen Gewebe. Arch. f. exper. Path. u. Pharmacol. 69: 108-113, 1912-1913.

5. Fujisawa, K.: Distribution of Iodine in Animal Body, Mitt. a. d. med. Fakult. d. k. Univ. au Tokyo 19: 389, 1918.

TREATMENT OF THE SUBNORMAL AND PSYCHOPATHIC CHILD

A NEW AVENUE OF APPROACH *

LOUIS A. LURIE, M.A., M.D.

Physician in Charge, Psychopathic Institute; Junior Neurologist,
Jewish Hospital

CINCINNATI

Psychiatry may be broadly defined as the study of the conduct reactions of an individual in his attempted adjustment to his environment. As long as an individual is adjusted to his environment, as long as his conduct reactions are in harmony with those of the particular group in which he finds himself, so long is he considered normal from the psychiatric standpoint. If, however, his actions become bizarre or different from those commonly accepted as proper by the particular group of which he forms an integral part, he becomes the subject for psychiatric study.

From this it follows that conduct reactions that are considered normal in one environment may be definitely abnormal in another. For example, it may be perfectly normal for a Fiji Islander to consider himself fully dressed when bedecked in a loin cloth or in a fig leaf. However, any one assaying such a feat in this country would rightly be taken into immediate custody and his sanity investigated.

Again, we see individuals who, although apparently perfectly adjusted to their environment, fail miserably when called on to do tasks or to struggle with situations which require a degree of mental ability greater than that which they possess. This was only too well demonstrated in the recent war. A large proportion of the "war neuroses" or so-called "shell shock" cases was composed of boys who had led perfectly adjusted lives in, it is true, possibly sheltered environments. However, when called upon to meet unusual stresses and strains, they succumbed.

The nature of an individual's conduct reaction and the possibility of a successful adjustment will depend on two fundamental factors: heredity and environment.

Through the former the individual is endowed with a certain capacity for reacting; through the latter this capacity is either permitted full sway or stifled.

VARIOUS POSSIBILITIES

The interplay of these two factors permits of various possibilities.

1. An individual may be born without capacity for reacting or adjusting, no matter how simple the environment—for example, an idiot.
2. An individual may be born with only a partial capacity for reacting, one insufficient for his environment but amply sufficient if he be placed in a different environment. For example, a moron placed in a highly complex situation will ultimately be submerged, but if removed from such a situation and placed in a simpler one, he will, without doubt, be able to adjust himself and become a useful member of society. A comparable example is the child born of tuberculous parents, who in all probability will die if permitted to live in squalor, filth, and dirt, but will live in spite of the handicap of bad heredity, if placed in proper hygienic surroundings and given plenty of fresh air and nourishing food.
3. An individual may be well born as far as his capacity for reacting is concerned; but his environment

* Read before the Academy of Medicine, Feb. 2, 1921.