and the unpalatability of the substance will also militate against its general acceptance in practical dietetics.

REFERENCES.

- ¹ Knoop: *Beiträge z. Chem. Physiol. u. Path.*, 1904, vi, 150.
- ² Dakin, H. D.: *Journ. Biol. Chem.*, 1907, iii, 57. *Ibid.*, 1908, iv, 77, 91, 221, 227, 419.
- ³ Höckendorf: Quoted by Dakin.
- ⁴ Embden, G., and Kalberlak: *Beiträge z. Chem. Physiol. u. Path.*, 1906, viii, 121. Embden, Salernoni, and Schmidt: *Ibid.*, 1905, viii, 129. Embden and Marx: *Ibid.*, 1908, xi, 318.
- ⁵ Ringer and Jonas: *Journ. Biol. Chem.*, 1913, xiv, 43.
- ⁶ Kahn: *Proc. Soc. Exper. Bact. and Med.*, 1923, xxi, 31.
- ⁷ Idem, *ibid.*, 1921-22, xix, 265-266.
- ⁸ Kahn: *Amer. Journ. Med. Sci.*, 1923, clxvi, 824.
- ⁹ Joslin, C. P.: *Treatment of Diabetes Mellitus*, 1923, 463-465.
- ¹⁰ Desgrez, Bierry, et Rathes: *Compt. rend. de l'Acad. des Sci.*, 1924, 178, 1771-1775.
- ¹¹ Sevringhaus, E.: *Scientific Proc. Soc. Biol. Chem.*, xviii, xix. *Journ. Biol. Chem.*, lix, 1924.
- ¹² Allen, F. M.: *Amer. Journ. Med. Sci.*, 1924, clxvii, 557.
- ¹³ Cowie and Hoag: *Journ. Amer. Med. Assoc.*, 1921, lxxvii, 493.
- ¹⁴ Pybus and Lyon: *BRITISH MEDICAL JOURNAL*, August 23rd, 1924, p. 328.

THE PERMEABILITY OF MENINGES TO URANIN AS A METHOD IN THE DIAGNOSIS OF MENINGITIS.

(Preliminary Communication.)

BY

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A METHOD whereby it is possible to decide simply by lumbar puncture whether meningitis is present or not may possibly be of interest. The normal meninges and plexus choroides have the power of preventing a number of substances that are foreign to the organism from passing into the spinal fluid; diseased meninges have lost this power. Especially in meningitis this permeability of the meninges to chemical substances is greatly increased, and it is thus natural to investigate whether the determination of the latter can be of assistance in diagnostic difficulties. The substance must be easily found in the spinal fluid and be non-poisonous. Such a substance is uranin (sodium fluorescein), a red colouring matter very readily soluble in water; a weak solution gives an intensely light-greenish fluorescence which strongly recalls the fluorescence seen in a positive Schlesinger reaction. The fluorescence does not disappear until the solution is weakened to 1 in 10,000,000. Weaker solutions have a dirty greenish colour, without fluorescence.

A series of investigations carried out by Kafka,¹ Schönfeld,² Jörgensen,³ and others have established that uranin, in doses of 6 to 8 grams by the mouth, passes into the spinal fluid in about 30 per cent. of healthy individuals, but in small quantities only. In dementia paralytica, and also in syphilitic persons, uranin was found more frequently in the spinal fluid, especially if it was altered. These authors do not appear to have made any determination of the permeability of the meninges in meningitis.

Uranin given in larger doses enters the spinal fluid where the meninges are not infected, and the patient's skin becomes intensely yellow. After several experiments we decided upon 2 grams of uranin for an adult, or about 0.03 per kilogram of body weight. One or two hours after such a dose the patient turns yellow, but the coloration is not stronger than in icterus, and the yellow colour of the skin and mucous membrane disappears comparatively quickly, as a rule after five to six hours. Uranin has no poisonous effects, and according to C. Jörgensen's investigations does not irritate the meninges. It can be administered by the mouth or by intramuscular injection in a 20 per cent. solution, but not subcutaneously, as a strong solution produces a sensitive infiltrate. After half an hour to an hour the blood serum gives a greenish fluorescence, which in the great majority of cases does not disappear until the serum is weakened to 1 in 64. The concentration of uranin in the blood is strongest two to three hours after it has been given, and it is at that time, therefore, that the lumbar puncture should be performed. We employ the following technique:

The patient is given 2 grams of uranin by the mouth (preferably in wafers) or by intramuscular injection (20 per cent. solution) if he is not quite conscious. Three hours later lumbar puncture is undertaken in the usual manner. In order to ascertain whether

the spinal fluid is fluorescent or not, the test tube must be held against a dark background. In meningitis the fluid gives off a distinct greenish fluorescence. No importance should be attached to a doubtful fluorescence. The presence of blood may confuse the reaction, since the blood contains great quantities of uranin. Investigations made at this section prove, however, that at least 1/3 c.cm. of blood must be mixed with 10 c.cm. of spinal fluid in order that the latter shall become fluorescent.

We have employed this simple method with 74 patients, 18 of whom were suffering from various forms of meningitis. The spinal fluid (from, in all, 22 lumbar punctures) taken from patients suffering from meningitis was in all cases fluorescent, in some quite strongly, like a markedly positive Schlesinger reaction. It is true that the fluorescence was weak in three instances, but nevertheless distinct. The method used in these cases, however, differed somewhat from the technique usually employed, the lumbar puncture being performed within one hour after the patient had received the uranin. In addition, the dose of uranin given to two of the patients was too small (1 gram). The spinal fluid in 38 of 56 non-meningitic cases was as clear as water. In 8 cases the fluid was of a dirty green colour without fluorescence; this shows that minimum quantities of uranin had entered the spinal fluid. In 10 cases the spinal fluid was faintly fluorescent, but in 7 of these there was an admixture of blood, which, as mentioned above, makes the results uncertain. Three of the non-meningitic cases, on the other hand, exhibited a faintly fluorescent spinal fluid three hours after 2 grams of uranin. The fluorescence disappeared, however, in a dilution of 1 in 2, whilst the spinal fluid from patients with meningitis showed fluorescence in a dilution of 1 in 8 and up to 1 in 30. (For this determination we employed small test tubes 11 mm. in width, and observed the fluorescence in a dark box, where the light at a distance of 15 cm. enters through a 20 dioptric biconvex lens.)

Conclusions.

Uranin in doses of 0.03 gram per kilo of body weight does not enter the cerebro-spinal fluid, or does so only in small quantities if the meninges are not infected. In meningitis the colouring matter enters the fluid in easily demonstrable quantities. If, therefore, by lumbar puncture three hours after uranin has been given in the doses stated, the spinal fluid shows a distinct greenish fluorescence, we can with great probability diagnose meningitis without making other investigations of the spinal fluid. If the spinal fluid shows no fluorescence, meningitis can with certainty be excluded.

It is not possible to decide what form of meningitis, if any, is present. The passing of the colouring matter into the spinal fluid merely indicates the greater or lesser permeability of the meninges. In meningitis comitans, circumscripta, etc., the uranin does not enter the fluid, or does so in relatively small quantities, even when pleocytosis is present. Opinions differ as to whether it is correct to designate these conditions meningitis, but this is doubtless chiefly a dispute about words.

REFERENCES.

- ¹ Kafka: Untersuchungen zur Frage der Entstehung, Zirkulation und Funktion der Cerebrospinalflüssigkeit. *Zeit. f. d. ges. Neurolog. u. Psych.*, 13, 192, 1912, and 15, 482, 1913.
- ² W. Schönfeld: Versuche am Lebenden über den Übergang von Farbstoffe aus dem Blut. *Arch. f. Dermatol. u. Syph.*, 132, 152, 1921.
- ³ C. Jörgensen: Uraninets Udskillelse i Spinalvaedskken, Neurologisk Selskaps forhandling, 1920-21, p. 25, *Hospitalstidende*, 1921.

A WEAK POINT IN STERILIZING METHODS.*

BY

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ONE of the problems of the operating theatre is to ascertain the temperature reached in the centre of a packet, tin, or drum of dressings in a sterilizer. It is very different from that of the steam around the outer side of the packet or tin, but the latter alone is registered by a thermometer projecting into the sterilizer and capable of being read from the outside, or, more commonly, by means of a pressure gauge. I made tests with a specially prepared thermometer, similar to a clinical thermometer

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