

centration, and 1 in a 0.02% concentration. In every instance growth was luxuriant. When the 8 sulfanilamide-tolerant strains were introduced into broth containing sulfathiazole in concentrations of 0.005%, 0.01%, and 0.025%, no growth occurred.

Discussion. The results of this study are striking in that the strains of the gonococcus studied acquired only slight, if any, tolerance for sulfathiazole, although resistance to sulfanilamide was readily established. Even though attempts were made repeatedly over a period of 3 months to establish growth in a medium containing sulfathiazole, success was attained at only the lowest concentrations, *i. e.*, 0.0005 to 0.002%. It is apparent that sulfathiazole exerts a more marked bacteriostatic and bactericidal action on the gonococcus than either sulfapyridine or sulfanilamide. Lawrence⁴ has reported that a 0.001% concentration of the drug inhibits the development of the gonococcus in 5 hours.

These *in vitro* studies are in accord with clinical observations of the superior chemotherapeutic action of sulfathiazole in gonococcal infection. The failure of the gonococcus to develop resistance to sulfathiazole *in vitro* suggests that sulfathiazole-fast strains of the organism are less likely to become established in the population at large than are sulfanilamide- or sulfapyridine-fast strains.

Summary. Ten strains of *Neisseria gonorrhoeae* developed little, if any, tolerance for sulfathiazole when grown for approximately 3 months in a blood broth containing concentrations of the drug varying from 0.0005% to 0.005%.

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Changes in Blood Urea Following Hypothalamic Lesions.

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The following observations are reported as part of a study of the influence of diencephalic lesions upon the nitrogenous constituents of the blood.

Methods and Material. Eight cats received lesions in the pre-

⁴ Lawrence, C. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1940, **43**, 92.

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optic region and the anterior hypothalamic area; 11 cats, lesions in the posterior hypothalamic, tuberal or subthalamie regions; and 11 were controls. All animals received daily about 150 g kidney or beef and 75 cc milk. Blood samples obtained by heart puncture without anesthesia were examined for albumin, globulin, urea, N.P.N., creatinine, cholesterol, chlorides, and sugar; also estimations were made of the hemoglobin, erythrocytes, leucocytes, platelets, and differential counts; in a few instances the blood volume was measured but with results too inconclusive to merit reporting.

Under intraperitoneal nembutal anesthesia, supplemented when necessary by light ether anesthesia, bilateral lesions, symmetrical as nearly as possible, were placed by means of a modified Horsley-Clarke apparatus.¹ Blood studies were made preoperatively and continued from the first postoperative day, in some cases from the second or later days. A majority of the animals reacted badly to the operation, refusing food and drink and losing weight sharply. After 5-7 days they began to improve and regain weight. Withdrawing blood at too frequent intervals produced a marked anemia, this disappeared when the bleedings were discontinued.

Results. A rise in blood urea was noted in 7 of 8 cats with lesions of the anterior hypothalamic and the preoptic area (Table I). The exception, cat No. 16, proved to have widely asymmetric lesions. The rise in urea was paralleled by a rise in N.P.N., the latter representing exactly the increase of urea N. All other substances tested in the blood remained at *normal levels*. Cat No. 13 was of particular interest. Daily blood urea figures, normal for several weeks before operation, became abnormally increased during the 31-89th postoperative days. The animal appeared to be in excellent health although it grew very fat (confirmed at autopsy). The urine was

TABLE I.
Blood Urea of Cats with Anterior Hypothalamic and Preoptic Lesions.

Cat	Pre-op. urea	Post-op. urea	Post-op. days survival
7	23.0	62 (4); 46 (11); 34.4 (16); 22.5 (23)	27
9	25.8	15.6 (1); 44 (4); 58.2 (7)	8
10	25.6	11.5 (1); 100 (3)	5
11	22.1	20.4 (1); 28.0 (5); 49.3 (6); 28.4 (7); 24.1 (8)	18
13	22.7	Normal (1-9); 46.6-55.0 (31-87); 29.0 (108)	113
15	19.0	11.6 (2); 18.1 (9); 38.3 (14); 62.0 (15)	15
16	28.3	14.3 (1); 11.8 (5)	6
19	19.8	34.0 (2); 72.0 (3)	3.5

Figures in () designate number of post-operative days.

¹ Spiegel, E. A., and Miller, H. R., *J. Lab. and Clin. Med.*, 1941, **26**, 1657.

TABLE II.
Blood Urea of Cats with Lesions in

Cat	Pre-op. urea	Post-op. urea	Post-op. days survival
(a) Posterior Hypothalamus.			
5	25.4	27.2 (2); 27.2 (86)	92
12	20.4	25.4 (2); 29.6 (5)	6
15A	22.0	15.0 (2); 19.0 (39)	59
17	14.1	15.0 (2)	2
20	23.0	22.7 (2); 19.6 (19)	19
(b) Subthalamus.			
2	40.1	20.8 (4); 24.0 (17)	32
5A	28.8	26.4 (3); 27.2 (53)	64
12A	20.4	24.0 (2); 23.4 (32)	41
(c) Tuberal Region.			
1	24.8	20.1 (2); 34.4 (18)	24
4	26.1	28.0 (9); 38.2 (28)	30
21	25.0	22.5 (2); 22.0 (4)	4

Figures in () designate number of post-operative days.

normal. Blood urea fell to normal on the 108th day. On the 113th day the cat was accidentally killed during cardiac puncture. Macroscopically the kidneys were unusually pale and fatty in appearance with fine irregular surface and marked lobulations. Microscopic studies of the kidneys and other organs are in progress. Marked obesity developed also in one cat (with tuberal lesion) with normal urea level observed for 30 days after operation, indicating that development of obesity and rise of urea may be independent phenomena.

No rise in urea or in other blood elements thus far studied followed the lesions in the posterior hypothalamus, in the subthalamus, in the tuberal region, or in "combined" diencephalic lesions in the posterior hypothalamic and tuberal region (cats Nos. 5, 12, 15a). In 11 control experiments, *i. e.*, after starvation up to 10 days or anesthesia, anemia following frequent bleedings (hemoglobin 40%), unilateral lesions in the anterior or in other hypothalamic areas, or in the presence of purulent infection, the urea level remained normal. There was one instance of "spontaneous" increase in blood urea; the urea was 200 and 150 mg per 100 cc on 2 different days. This animal appeared to be fairly old and sick; it was not operated on. Autopsy disclosed a left shriveled, atrophic kidney, the right markedly hypertrophied.

Summary. 1. Lesions of the anterior hypothalamic area and pre-optic region were associated with a definite and apparently isolated rise in blood urea, no change being noted in the level of the other blood substances tested. 2. In 3 animals surviving beyond 18 days

the elevated blood urea returned to a normal level (Table I). 3. With one exception the kidneys of the operated animals were macroscopically normal. 4. No apparent interdependence was discerned between the level of blood urea and the state of severe anemia or between the former and body temperature or the development of obesity. The disturbance in the level of blood urea presumably is not associated with any discernible metabolic disorder.

The rise in blood urea may be due to an impairment of the ability of the kidney to clear urea at normal blood level; an increased blood urea may be a prerequisite for the adequate elimination of this substance when lesions are made in the anterior hypothalamic and preoptic regions.

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Precipitation of Active Influenza A Virus from Extra-Embryonic Fluids by Protamine.

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The allantoic and amniotic fluids of infected chick embryos have been found to contain large amounts of both active influenza virus and the complement fixation antigen^{1, 2} in spite of their low total protein content. These extra-embryonic fluids, either fresh or lyophilized, constitute a very adequate antigen for the diagnosis of influenza by complement fixation test, and the suggestion has been made by us that they should be superior to the usual tissue emulsions as vaccines because of the relatively small amount of cellular debris.

We have carried out a series of experiments to determine the degree of protection afforded to mice by intraperitoneal vaccination with infected extra-embryonic fluids. Five-week-old Swiss mice were inoculated once with 0.05 cc of pooled dialyzed fluids. The fluids used were infectious for mice in dilutions of 10^{-8} to 10^{-10} and

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¹ Henle, W., and Chambers, L. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1941, **46**, 713.

² Nigg, C., Crowley, J. H., and Wilson, D. E., *J. Immunol.*, 1941, **42**, 51.