several neutral end point standards independently and have them match each other. As a substitute the neutral red indicator solution is diluted 5 times with water and 1 drop added to the alkaline filtrate to serve as standard. One drop of 0.01% phenol red is added and then 1.0 N HCl to neutrality, followed by 5 drops in excess The pH is then 1-2 and the color matches that of the stronger neutral red solution at pH 7. The urine filtrate may be used for this standard since the solution is acid in reaction. It replaces the Northrop neutral standard containing phosphate.

In a series of 63 determinations in triplicate, the variation has averaged 0.02 ml. with a maximum of 0.07 ml. In comparisons with titrations after distillation *in vacuo* the variation has been 0.04 ml. which is the error to be expected from duplicates by that method. Much of the variation is probably caused by inequality in size of drops of indicator solutions so that titrations carried out with independently made standards will vary more than those made with the same standards.

9569

Hydrogen-Ion Concentration of the Gall Bladder Bile of the Dog.

FRANCES F. BECK,* JOHN C. KRANTZ, JR., MAURICE FELDMAN AND C. JELLEFF CARR.

From the Department of Pharmacology and Research Division of the Department of Gastroenterology, School of Medicine, University of Maryland.

An experimental study was reported[1] on the hydrogen-ion concentration of the bile of the guinea pig. In this series of experiments, effort has been made to determine which constituents of the dog's gall bladder bile are responsible for the fluctuating pH in normal dogs and also upon medication with Extract of Ox Bile, U.S.P.

The hydrogen-ion concentration of the gall bladder bile of normal dogs was determined by means of the glass electrode at 25° and an analysis of the principal constituents was carried out according to Douglas-Sauermann's[2] method. The results on 8 dogs are shown in Table I.

* Emerson Fellow in Pharmacology.

1 Krantz, J. C., Jr., Feldman, M., Morrison, S., and Carr, C. J., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 48.

2 Douglas-Sauermann, A. G., *Z. Physiol. Chem.*, 1935, **231**, 92.

TABLE I.
Constituents of Normal Dog Bile.

	pH	Total Solids, %	Ash, %	Alkalinity of Ash, % as Na_2CO_3	Bile Acids Cholic and Desoxycholic %
Aver.	6.15	23.00	1.78	.71	6.75
Low	5.78	21.85	1.66	.58	3.72
High	6.93	24.40	1.88	.86	8.37

A series of 21 dogs were fed 1.5 and 8.0 gm. of extract of ox bile per day for varying periods of time. This produced a cholagogue effect in direct proportion to the quantity of ox bile administered and the time of medication. Thus the bile becomes less acidic and lower in total solids when ox bile is fed. The bile constituents are recorded in Table II.

TABLE II.
Constituents of Dog Bile After Ox Bile Feeding.

	pH	Total Solids, %	Ash, %	Alkalinity of Ash, % as Na_2CO_3	Bile Acids Cholic and Desoxycholic %
		1.5 gm. Ox Bile Daily (25 to 72 days).			
Aver.	6.66	21.67	1.67	.69	6.09
Low	6.20	18.94	1.38	.51	3.63
High	7.35	23.86	2.08	.83	7.87
		8.0 gm. Ox Bile Daily (11 to 67 days).			
Aver.	7.24	17.56	1.66	.60	5.35
Low	6.06	8.61	1.08	.40	3.49
High	8.02	25.22	2.08	.85	7.25

In these 29 determinations the correlation coefficient between the pH and total solids is –0.83, P.E. ±0.04. The correlation coefficient between the pH and ash is –0.46, P.E. ±0.14; that between the pH and the alkalinity of the ash is –0.60, P.E. ±0.12; and that between the pH and the bile acids is –0.46, P.E. ±0.14.

These data indicate that a concentrated bile is likely to exhibit a low pH despite wide variations in its constituents, such as bile acids and ash. Kjeldahl determinations on the residue of several specimens of bile showed that the nitrogen content varied directly as the total solids. It is likely, therefore, that bile protein buffers the potential hydroxyl ions of bile and permits the acidity of the bile acids to become manifest. This concept is in accordance with the work of Aronsohn and Andrews.[3]

Conclusion. The correlation between total solids and pH of

[3] Aronsohn, H. G., and Andrews, E., PROC. SOC. EXP. BIOL. AND MED., 1935, **33**, 89.

dog's gall bladder bile, normal or ox bile fed dogs, is high indicating with a certainty of approximately 45% greater than sheer chance that concentrated biles will possess a greater hydrogen-ion concentration than those which are more diluted.

9570 P

Effect of Metrazol Convulsions on Brain Metabolism.*

HAROLD E. HIMWICH, KARL M. BOWMAN, JOSEPH F. FAZEKAS AND LEO L. ORENSTEIN.

From the Department of Physiology and Pharmacology, Albany Medical College, Union University, and Bellevue Hospital, Department of Psychiatry, New York University Medical College.

The wide use of metrazol in the treatment of schizophrenia has made it advisable to study the physiological changes produced by metrazol convulsions.[1] Twelve observations were made on 7 patients with schizophrenia. As seen in Table I, 7 samples of blood were collected from the femoral artery during various stages of the convulsions, 4 pairs of samples were collected simultaneously by 2 observers from the femoral artery and internal jugular vein immediately after the seizure had ceased, as was one additional sample of arterial blood. Breathing was greatly diminished during the convulsions and this was reflected in the analyses of the arterial blood, which disclosed a retention of CO_2 as well as a diminished O_2 content. Even during the first part of the seizure, as seen in Wi, 9/13, the O_2 content was diminished so that the Hb saturation $\left(\frac{O_2 \text{ content}}{O_2 \text{ capacity}}\right)$ was reduced from a theoretical normal of 95% to 84%. As the convulsions progress, the Hb saturation continues to fall so that towards the end of the seizure the saturation of Hb may be below 50% (M., 9/7). During these convulsions the patient's face is at first a dark red color. When the convulsion is completed, the anoxemia is evidenced by a leaden cyanosis. Nevertheless, as soon as unimpeded breathing is reëstablished the Hb saturation, though still reduced, is found rapidly rising towards a normal value (last 5 observations of Table I). The anoxemia, as well as the severe

* This investigation was made possible by a grant from the Child Neurology Research.

1 von Meduna, L., *Z. f. d. ges. Neur. u. Psychiat.*, 1935, **152**, 235.