sidering all the facts we may conclude that while proliferation in the first phase depends upon the absence of the corpus luteum and upon the activity of another constituent of the ovaries, the proliferation which is found following the first period is in all probability due to substances secreted by the corpus luteum.[1] In the guinea pig, however, the effect of this substance becomes apparent only at a much later period than in the rabbit. The adaptive character of this phenomenon is clear if we remember that in the rabbit the functioning of the mammary gland is required at a much earlier period than in the guinea pig. Repeated intraperitoneal injections of corpus luteum of the cow does not produce a proliferation of the mammary gland in the guinea pig.

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The chlorides of the plasma in uremia.

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Previous investigations relating to the chlorid content of the blood or plasma in uremia have yielded conflicting results, some figures much lower than the lowest normal limit having been reported.[2] It is known that the chlorid content of nephritic plasma is usually somewhat higher than that of the average normal plasma, but the findings in uremia have apparently so far not been explained.

We have been able, in several cases, to make frequent observations of the chlorid content of the plasma of nephritic individuals during life, and up to the time of death in uremic coma. We have found a diminution of chlorids in the plasma to be the usual accompaniment of uremia, and we have found this decrease of chlorids in the plasma to accompany the increased H + ion concentration frequently observed in the blood of uremic patients shortly before death.

[1] The latter part of this conclusion depends in part at least upon the correctness of the observations of Bouin and Ancel and Frank and Unger.

[2] Strauss, H., "Die chronischen thieren entzündungen," Berlin, 1902, 51.

That increased acidity of the blood causes a diminution of the plasma chlorids, and an increase in the chlorid content of the cells had been shown experimentally both in vitro and in vivo by Hamburger.[1] That a similar change occurs with the increased acidity of the blood in uremia is illustrated by the following case of nephritis, terminating in uremia.

Case 1. P. W. M., male, age 44, chronic interstitial nephritis, uremia. Patient admitted June 17, suffering with chronic interstitial nephritis, hypertension and secondary cardiac failure with edema. With rest in bed the heart condition rapidly improved and the edema disappeared. Following this the patient felt well and the condition remained stationary, until October 12, when an impending uremia first became manifest by an increase in the blood urea and a diminished urea excretion. From June 17 to October 6 there were made twenty blood analyses, with simultaneous urine analyses, and the results showed very slight variation. The average of the figures for this period is shown below. The maximum concentration of NaCl in the plasma during this period was 6.53 grams per liter and the minimum was 6.06. The phthalein elimination, shortly after admission, was twice found to be 8 per cent. in two hours.[2]

It will be seen from the table that the diminished urea function, beginning about two weeks before symptoms of uremia appeared, was accompanied by a diminution in the reserve alkalinity of the plasma, as shown by Van Slyke's method. On October 29 an actual increase in acidity, as shown by the P_H of the blood, was present and there had been a sudden fall in the chlorid concentration of the plasma. This concentration remained low thereafter until death, and the change was far greater than could possibly be accounted for by the diminished diet. The change in NaCl concentration in the plasma is exactly that produced by intravenous injection of any acid, in quantities sufficient to change the P_H of the blood, and is accounted for by the increased acidity of the blood occurring during the disease.

[1] Hamburger, H., "Osmotischer Druck und Ionenlehre," Wiesbaden, 1902, I, 317.

[2] The observations on urea and chlorid elimination were made by the methods previously described by the author (*Jour. Exper. Med.*, 1915, XXII, 212 and 366). Plasma CO_2 was determined by the method of Van Slyke (PROC. SOC. EXP. BIOL. AND MED., 1915, XII, 165). For the determination of hydrogen ion concentration in the whole blood by the gas chain method, I am indebted to Mr. G. E. Cullen.

TABLE I.

Date, 1915.	Hour.	Blood Urea per Liter, Gm.	Index of Urea Excretion.	Plasma Sodium Chlorid per Liter.			Plasma CO_2 by Volume, %.	H+ Ion Concentration Whole Blood P_H.	Remarks
				Calculated, Gm.	Actual, Gm.	Difference, Gm.			
June 17 to Oct. 6		1.176	5.5	5.86	6.27	+0.41	49.1		
Oct. 12		1.542	2.9	5.86	6.25	+0.39			Patient feels quite well
Oct. 21		2.125	1.5	5.92	6.34	+0.42			Appetite slightly diminished
Oct. 26		3.005	0.7	5.84	6.28	+0.42	34.8		Complains of headache and muscular cramps
Oct. 27		3.285	0.4	5.84	5.89	+0.05	19.0		Nausea and vomiting
Oct. 28		3.430	0.27	5.78	5.83	+0.05	20.9		Severe headache; typical air hunger
Oct. 29		3.935	0.17	5.73	5.02	−0.71	17.6	6.86	Headache; stertorous breathing; mental condition good
Oct. 30	9 A.M.	4.580			5.53		15.2	6.93	Partial coma; muscle twitchings
	11:45 "				5.75		12.2		
	1-15 P.M.				5.30		32.8	7.44	After $NaHCO_3$, 30 gms. intravenously
	2:30 "	4.620			5.69		18.7	7.29	
	9 "				5.46		21.4		
	9:30 "				5.32		39.4		After $NaHCO_3$, 25 gms. intravenously
Oct. 31	10 "	5.020			5.31		33.3		Deep coma
Nov. 1		5.746							Died

Intravenous administration of sodium bicarbonate brought back the reaction of the blood temporarily to a normal point of 7.44 without influencing the course of the uremia. Both injections caused a still further lowering of the chlorids in the plasma. An identical effect is produced by intravenous administration of any salt and must be considered a salt action, rather than an alkali effect, as injection of strong alkalies increase the concentration of chlorids in the plasma.[1]

[1] Hamburger, H., loc. cit.