braziliensis, Trichophyton mentagrophytes, Epidermophyton floccosum, Aspergillus fumigatus, and a species of *Scopulariopsis. Microsporon canis* required 1.2 mg/ml for complete inhibition. 2. Six-week-old white mice could tolerate a single intraperitoneal or subcutaneous inoculation of Synkayvite up to 0.4 mg/g of weight but not 0.45 mg. Mice could also tolerate up to 0.15 mg/g daily for 28 days. 3. Mice infected with *H. capsulatum* could not tolerate non-toxic doses (to normal mice) of Synkayvite. This effect was particularly apparent between 7 to 21 days, but not 10 weeks, after infection. 4. The possibility that this type of medication in acute histoplasmosis could aggravate the disease is suggested.

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Importance of Anemia in Artificially Induced Metabolic Acidosis. (22625)

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It has been established that the plasma carbonic acid-sodium bicarbonate buffer group is the important buffer system in overcoming metabolic acidosis induced by accumulation of organic and inorganic acids. On the other hand, while the erythrocyte with its hemoglobin buffers as much as 92% of the endogenous carbonic acid, its effectiveness against fixed acids is uncertain.

In a given clinical situation acidosis and anemia may co-exist as in the anemic phase of glomerulonephritis, an occasional case of diabetic acidosis and the late stage of pyelonephritis. Bland(1) feels that hemoglobin as administered by transfusion of whole blood or red cell mass is fully as important a buffer as bicarbonate. This study was undertaken to determine whether the presence of anemia in itself had any adverse effect on the body's ability to overcome an artificially induced metabolic acidosis.

Materials and methods. Three volunteer patients suffering from severe blood loss anemia due to bleeding peptic ulcer were studied. These patients had no evidence of cardiac, pulmonary, or renal disease. All tests were performed in the postabsorptive state. At 8:00 a. m. the morning of the test, the bladder was catheterized and the catheter left indwelling. Initial blood serum bicarbonate, chloride, sodium, potassium, non-protein nitrogen, total and fractional proteins, and pH (Beckman pH meter) were determined along with red blood count and hemoglobin determination. (Sahli). An aqueous ammonium chloride* solution was infused intravenously at a constant rate so that 200 mEq. of ammonium chloride would be administered in exactly a 4-hour period.

At hourly intervals for the next 8 hours venous blood samples were obtained for pH and bicarbonate determination. At the same time the urinary catheter was opened and the urine collected under oil for determination of pH and total titratable acidity using 0.1 N NaOH and phenol red as an indicator. The pH of whole blood was determined at 25°C by transfer of the sample from a heparinized 5 cc syringe to the Beckman electrode cup and

* Ammonium chloride 400 mEq./1., furnished through the courtesy of Abbott Laboratories, North Chicago, Ill.

TABLE I. Changes in Blood pH and Blood Bicarbonate in Anemic and Normochromic Phase.

Patient	Hb (g/100 cc)	RBC (million)	Serum	mEq NH_4Cl 0	50	100	150	200	After 233, mEq $NaHCO_3$
I	4.75	2.84	CO_2	22.0	19.0	16.9	14.3	14.0	—
			pH	7.52	7.48	7.48	7.42	7.37	—
	13.0	5.42	CO_2	22.9	20.7	19.0	17.3	16.0	—
			pH	7.50	7.43	7.45	7.42	7.40	—
II	6.0	3.22	CO_2	25.0	21.2	19.0	16.9	17.3	30.6
			pH	7.48	7.48	7.42	7.40	7.38	7.58
	14.0	5.36	CO_2	26.4	22.9	19.9	18.6	17.7	28.5
			pH	7.52	7.50	7.50	7.38	7.38	7.58
III	7.5	2.53	CO_2	23.0	19.5	18.2	17.4	18.2	28.5
			pH	7.55	7.44	7.42	7.42	7.41	7.52
	13.0	4.50	CO_2	22.3	20.3	17.7	20.3	17.7	27.5
			pH	7.52	7.45	7.42	7.45	7.38	7.56

reading within a few seconds after transfer. Total serum carbon dioxide-bicarbonate was determined by the method of Van Slyke-Cullen and was expressed as mEq./Liter of sodium bicarbonate.

Red cell mass was given intravenously during the next week until hemoglobin and red count values were at normal levels and the above procedure was repeated exactly as outlined.

The procedure was varied in the last 2 patients so that 233 mEq. of sodium bicarbonate were administered intravenously in one hour at the end of the seventh hour and the procedure continued to determine the effect of infusion of sodium bicarbonate on blood pH, serum bicarbonate, urinary pH, and titratable acidity.

Results. Infusion intravenously with 50 mEq. of ammonium chloride per hour for 4 hours causes a progressive drop in the blood pH to the end of the fourth hour, with a subsequent rise to initial levels at the end of 8 hours. At the same time, the blood bicarbonate falls reaching its lowest level at the end of the fourth hour, rising slightly and continuing at low levels for the remainder of the 8-hour period—the last 4 hours representing a state of compensated metabolic acidosis (Table I). The urinary pH rises and titratable acidity falls during the ammonium chloride infusion; then the urine becomes very acid the last 4 hours and titratable acidity rises.

Repeating the above test on the same patient one week later with red blood count normal and hemoglobin at least 13 g per 100 cc shows essentially no change from the blood and urinary pattern induced in the patient during the period of anemia. The last 4 hours of both procedures represent a state of compensated metabolic acidosis and although in one patient the bicarbonate was 14 mEq. during the anemic phase and 16 mEq. during the normochromic and normocytic phase, these small variations can hardly be considered significant.

The second part of the procedure shows the effect of an infusion of 233 mEq. of sodium bicarbonate during the state of compensated metabolic acidosis induced in the same manner. During the period of anemia there is a prompt rise in blood pH and blood bicarbonate which rapidly goes to and exceeds normal limits during the next 3 hours. One week later following restoration of blood count and hemoglobin the test was performed again. Note identical response to infusion of bicarbonate as during the anemic phase (Table I).

There is a little difference in the blood pH or bicarbonate during infusion with ammonium chloride in the anemic phase as compared with the normochromic phase. Further, the response of this patient to correction of the acidosis with intravenous sodium bicarbonate is identical whether the patient is anemic or has a normal amount of hemoglobin. Table I shows changes in blood pH and blood bicarbonate in patients in the anemic and the normochromic phase during ammonium chloride induced acidosis and cor-

TABLE II. Urine Changes.

	Hb (g/100 cc)		Total*	1 hr	2 hr	3 hr	4 hr	5 hr	6 hr	7 hr	After 233, mEq $NaHCO_3$
				— NH_4Cl infusion —							
I	4.75	mEq acid excreted	8.76	.78	1.25	1.19	1.00	1.61	.69	2.24	—
		Urine pH		6.22	5.96	5.90	5.72	5.40	5.28	5.10	—
	13.0	mEq acid excreted	8.28	.41	.88	.94	.95	1.53	1.32	2.30	—
		Urine pH		6.04	6.18	6.10	6.00	5.40	5.00	5.00	—
II	6.0	mEq acid excreted	6.45	1.50	.49	.61	.31	1.30	.79	1.45	0
		Urine pH		6.20	6.35	6.10	6.00	5.70	5.20	5.30	7.50
	14.0	mEq acid excreted	5.60	.18	.32	.63	.57	.87	.98	1.05	.21
		Urine pH		7.20	6.75	6.50	6.30	5.83	5.60	5.50	7.38
III	7.5	mEq acid excreted	6.75	1.20	1.12	.86	.92	.99	.78	.88	.36
		Urine pH		6.2	6.1	6.0	5.9	5.7	5.7	5.5	6.9
	13.0	mEq acid excreted	5.60	.87	1.02	.77	.92	.69	.53	.80	.28
		Urine pH		6.4	6.5	6.3	6.1	5.9	5.8	5.8	7.0

* Total titrable acidity of urine during and following administration of NH_4Cl before administration of sodium bicarbonate.

rection with sodium bicarbonate. Note the nearly identical response regardless of hemoglobin levels. The non-protein nitrogen, sodium, potassium and total protein were all within the normal range for this hospital and are essentially unchanged in the anemic and transfused subject.

Discussion. The body response to an acid load would depend upon and involve the (1) base bound bicarbonate, (2) serum protein, (3) the tissues which release base, and (4) the kidney acidification process. While it is possible that the erythrocyte with its base and hemoglobin buffer would normally play a minor role in combatting acidosis induced by NH_4Cl, the value of correction of severe anemia in overcoming metabolic acidosis has to our knowledge not been previously assessed(2). Administration of ammonia chloride to a patient would be equivalent to adding hydrochloric acid since the ammonium is readily converted to urea. In this study the factors which make up the bulk of the total base of the body are held constant. Serum sodium, potassium, bicarbonate and protein concentrations are not appreciably altered by transfusion of the cell mass. The possibility that the plasma volume is expanded making the *total* base greater in anemia has not been excluded. Nevertheless, infusion of large quantities of red cell mass did not appear to offer any advantage in overcoming acidosis. The renal acidification mechanism is not accelerated following transfusion as is reflected in the same low total acid excreted in the urine (Table II). The erythrocyte does not appear significantly to resist acidosis directly or by transport of electrolytes to the kidneys or other tissues during the 8-hour period following onset of infusion of ammonium chloride. It would therefore appear that the height of the erythrocyte count and hemoglobin level of the blood has little, if anything, to do with overcoming the acidosis induced by ammonium chloride. Similarity of the blood and urinary pattern is striking and nearly identical in the same patient when anemic and when having a normal blood count and hemoglobin level. Furthermore, response to correcting compensated metabolic acidosis with sodium bicarbonate is identical whether hemoglobin and red blood count are normal or subnormal.

If these studies can be translated into clinical terms, it is suggested that in the anemias associated with uremic acidosis or diabetic acidosis, correcting blood count and hemoglobin levels would probably have very little effect on the accompanying acidosis. Although it may be important to have the red blood cell count normal because of the increased oxygen carrying capacity of the blood to vital organs, it is questionable whether the increased hemoglobin and red blood cell count would significantly combat the accompanying acidosis.

Conclusion. 1. Patients were made acidotic with intravenous ammonium chloride during a period when they were anemic and again during a period when the red blood count and hemoglobin values were normal. 2. No significant change in range of blood pH, bicarbonate, urinary pH or titratable acidity was demonstrated during and following infused ammonium chloride during the period of anemia as compared with the period of normal red blood count and hemoglobin levels. 3. No difference in response to infusion of sodium bicarbonate during the state of compensated metabolic acidosis was noted when the patients were anemic as compared with a normal red blood count and hemoglobin level. 4. Correction of a severe anemia is not important in overcoming ammonium chloride-induced metabolic acidosis or in the correction of the ammonium chloride-induced metabolic acidosis with sodium bicarbonate.

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Serum Transaminase Levels in Experimental Pericardial Injury.* (22626)

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Because of recent interest in serum glutamic oxalacetic (SGO) transaminase determinations in the differential diagnosis of myocardial infarction, measurements of the level of this enzyme were carried out after experimental production of acute pericarditis.†

Method. Thirteen dogs were studied. Pericardial injury was produced in 9 animals, and the remaining 4 animals were used as controls. After the dogs were anesthetized with pentobarbital sodium, the chest was entered by splitting the distal 3 inches of the sternum. The following substances were placed in the pericardial sac: (1) one cc of sterile sand was used in 3 dogs; (2) one cc of sterile talc in one dog; (3) one cc of a virulent culture of alpha streptococci obtained from human blood cultures in 5 dogs; 2 of these were treated with penicillin and streptomycin to reduce the severity of the infection. The pericardial sac was then sutured with 5-0 silk and the chest was closed. The 4 control animals underwent a sham operation but without manipulation or incision of the pericardium. Twelve-lead electrocardiograms and SGO transaminase samples were taken on all dogs before operation and at 24-hour intervals over a period of 5 days after operation. The animals were then autopsied and color photographs were taken of the visceral and parietal pericardia. Tissue sections were obtained from representative areas of the pericardium and myocardium. The severity of pericarditis was estimated at autopsy and was correlated with the color photographs, microscopic pathology, and electrocardiographic findings. The severity of the pericardial changes by electrocardiogram were estimated on the basis of the amount of elevation of the ST segments. One mm elevation of the ST segments was classified as mild, while an elevation of 5 mm or more in multiple leads was classified as severe

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