STUDIES IN THE METABOLISM OF SODIUM *r*-LACTATE. III. RESPONSE OF HUMAN SUBJECTS WITH LIVER DAMAGE, DISTURBED WATER AND MINERAL BALANCE, AND RENAL INSUFFICIENCY TO THE INTRAVENOUS INJECTION OF SODIUM *r*-LACTATE

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Since the complete metabolism of sodium *r*-lactate involves to such a great extent hepatic and renal activity, it should naturally be of interest and importance to study the response of subjects with liver and kidney damage.

Acute catarrhal jaundice

Up to the present time we have been able to study four cases of *acute hepatitis* of the type more commonly known as acute catarrhal jaundice. As may be noted from Table 1 and Chart 1, the rate of disappearance of lactate from the blood was considerably delayed in the subjects with jaundice as compared with the normal. Increase in glucose in the blood was less rapid and less marked. A slight delay in the rise of the carbon dioxide content of the blood was also noted, the peak coming at the end of the second hour in two instances, and at the end of the fourth hour in one. In order to compare these data graphically with the normal, the results of Cases H-1130, F-2131 and H-925 were averaged because of their more complete data and because the dose of molar sodium *r*-lactate was approximately the same in each instance, averaging almost exactly 7 cc. per kilogram of body weight. For the graphic presentation of the normal subjects Cases G-336, G-1982, F-2131 and H-925 were selected for similar reasons. The average dose of molar sodium *r*-lactate in this group was 6.75 cc. per kilogram of body weight.

Hemolytic jaundice

The response of Case G-2473 (Table 2) resembled that of the patients with acute hepatitis in the delayed blood carbon dioxide content peak. This patient had just recovered from a "crisis" of abdominal pain, fever and vomiting. The liver was enlarged, its edge reaching the level of the umbilicus. In all probability some impairment of liver function was present.

TABLE 1
Acute hepatitis

Case number and date	Age	Weight	Molar sodium <i>r</i> -lactate		Blood							Urine			Remarks
			Dose and diluent*	Per kgm. body weight	Min-utes after in-jection	Type of blood sample†	CO ₂ con-tent	Lactic acid	Glucose		Inor-ganic phos-phorus	Time of urine collec-tion†	CO ₂ con-tent	Vol-ume	
G-2144 October 21, 1930	year 9	kgm. 24.6	cc. 110 + 180 W	cc. 4.5			vol-umes per cent	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.		vol-umes per cent	cc.	Onset of jaun-dice October 18, 1930
					0	S	71.6	21.4	126.0	126.0					
					15	S	70.0	42.8	151.0	151.0					
					30	S	72.7	31.5	172.0	172.0					
					60	S	73.7	21.3	126.0	126.0					
					120	S	73.2	16.3	99.0	99.0					
October 24, 1930					180	S	72.6	11.3	93.0	93.0					Jaundice still present, di-minishing rapidly
					0	WB	53.7	17.6	74.0	100.0					
					15	WB	59.4	29.7	71.0	87.0					
					30	WB	59.9	23.9	71.0	87.0					
November 17, 1930					60	WB	62.8	15.1	86.0	87.0					Completely re-covered clin-ically
					120	WB	58.1	12.6	80.0	87.0					
					0	WB	53.7	24.5	107.0	112.0		0	4.1		
					15	WB	57.6	41.6	122.0	125.0		30	45.4		
					30	WB	57.0	23.0	110.0	112.0		60	359.0		
					60	WB	58.6	16.4	70.0	73.0		120	309.0		
H-1130 May 16, 1931	3	16.7	115 + 120 R	6.9	120	WB	57.1	11.5	62.0	64.0					Onset of jaun-dice May 14, 1931
					0	WB	59.2	20.2	52.0	58.0	4.8	0	8.2	120	
					50	WB	68.2	76.7	126.0	133.0	4.5	60	172.0	100	
					120	WB	75.2	25.2	111.0	119.0	3.9	150	250.0	100	
					240	WB	67.8					240	288.0	70	

TABLE 1 (continued)

Case number and date	Age	Weight	Molar sodium <i>r</i> -lactate		Blood							Urine			Remarks
			Dose and diluent*	Per kgm. body weight	Minutes after injection	Type of blood sample†	CO ₂ content	Lactic acid	Glucose		Inorganic phosphorus	Time of urine collection†	CO ₂ content	Volume	
									True	Apparent					
F-2131 January 10, 1931	years 7	kgm. 22.7	cc. 170 + 200 R	cc. 7.5				mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.			vol-umes per cent	cc.	Onset of jaundice January 1, 1930
					0	WB	42.5	14.5	86.0	113.0	0	2.6			
					30	WB	58.1	75.6	93.0	118.0	30	2.6			
					60	WB	61.2	44.0	101.0	126.0	105	130.0			
					120	WB	63.1	13.9	90.0	93.0	240	104.0			
January 29, 1931			170 + 200 R	7.5	0	WB	49.8	22.6	76.0	83.0		0	240.0	Subject completely recovered clinically	
	30	WB	63.6	32.4	93.0	95.0	60	308.0							
	60	WB	61.0	18.0	79.0	90.0	120	254.0							
	120	WB	59.9	15.1	85.0	90.0	240	241.0							
	240	WB	59.4	17.6	90.0	103.0									
H-925 May 4, 1931	12	35.5	240 + 200 R	6.8	0	P	58.7	26.5	60.0	63.0	4.0	0	22.6	pH of last blood sample = 7.67 Calcium = 10.0 mgm. per 100 cc.	
					0	WB	69.8	60.0	110.0	112.0	2.0				
					30	P									
					60	P	73.5	51.0	130.0	132.0	2.0	60	49.8		485
					120	P	78.9	25.5	114.0	117.0	1.5	120	303.0		85
					240	P	70.5				240	466.0	150		

TABLE 1 (continued)

Case number and date	Age	Weight	Molar sodium <i>r</i> -lactate		Blood							Urine		Remarks												
			Dose and diluent*	Per kgm. body weight	Minutes after injection	Type of blood sample†	CO ₂ content	Lactic acid	Glucose		Inorganic phosphorus	Time of urine collection ‡	CO ₂ content		Volume											
June 25, 1931		kgm.	cc.	cc.	6.8	0	P	57.6	25.2	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	vol-umes per cent	cc.	Completely re- covered clin- ically										
																	240 + 250 R	0	WB	70.0	58.2	76.0	89.0	2.8	0	22.1
240	30	WB	86.0	46.6	67.0	80.0	2.5	30	99.6	430																
60	60	WB	84.3	18.7	114.0	124.0	2.5	105	311.0	240																
120	240	WB	82.8					240	498.0	210																

* Diluent = Ringer's solution (R) or distilled water (W).

† S = Serum.

WB = Oxalated whole blood.

P = Oxalated plasma.

‡ Indicates the end of the interval (in minutes) during which urine was collected.

TABLE 2
Miscellaneous cases

Case number	Age	Weight	Molar sodium r-lactate		Whole blood				Urine		Remarks
			Dosage and diluent*	Per kgm. of body weight	Min-utes after in-jection	CO ₂ con-tent	Lactic acid	Glucose	Time of urine collec-tion†	CO ₂ con-tent	
						vol-umes per cent	mgm. per 100 cc.	True	Apparent	minutes	
G-2473	5 years	18.2 kgm.	cc. 130	7.2	0	52.7	11.0	73.0	99.0	0	11.0
					30	61.6	47.8	113.0	125.0	30	65.0
					60	60.7	20.1	103.0	132.0	60	310.0
					120	64.3	17.5	83.0	93.0	120	350.0
					240	56.0	21.5				
G-2099	15	32.7	160 + 275 R	4.9	0	48.5	27.1	60.0	67.0		
					15	48.5	37.8	99.0	100.0		
					30	66.5	31.5	105.0	113.0		
					60	67.6	15.8	102.0	113.0		
					120	63.7	12.6	90.0	93.0		
											Diagnosis: Unilateral tuberculosis of kidney

* Diluent = Ringer's solution (R).

† Indicates the end of the interval during which urine was collected.

CHART 1. COMPARISON OF RESPONSE OF NORMAL SUBJECTS AND SUBJECTS WITH ACUTE HEPATITIS TO THE INTRAVENOUS INJECTION OF SODIUM *r*-LACTATE

Anhydremia and hypochloridemia secondary to acute pyelonephritis

In Case H-695 (L.H.) we were able to study a rather severe urinary tract infection of the acute pyelonephritic variety with a secondary disturbance of water and mineral balance. At the beginning of the study on March 18, 1931, the patient was dehydrated from previous vomiting and fever and showed the effects of loss of gastric juice in the diminished serum chloride content (491 mgm. per 100 cc.). The nonprotein nitrogen was markedly elevated (160 mgm. per 100 cc.), and the standard urea clearance (Van Slyke) was 64 per cent of the normal. The carbon dioxide content was at the upper limits of normal (63 volumes per cent). The urine was entirely free from chloride, bicarbonate and lactic acid. We predicted in this case that the injection of the usual amount of sodium *r*-lactate would be followed by a persistent alkalosis with continued acid urine, because of the initially low electrolyte content of the blood (due to loss of chloride) and that later by giving chloride the bicarbonate could be made to enter the urine and alkalinize the latter.

As may be noted from Table 3, the first half of our prediction was realized; the carbon dioxide content rose and was still 100 volumes per cent 16 hours after the administration of the lactate. The urine in the meantime remained acid, the highest carbon dioxide content being but 13 volumes per cent.

The following day, after the intravenous administration of 900 cc. of Ringer's solution, the plasma carbon dioxide content began to fall, as expected. In its excretion into the urine, however, base must have been claimed by acids other than bicarbonate, as the bicarbonate content of the urine remained practically at zero. It does not seem improbable, since nonprotein nitrogen was falling rapidly in concentration in the blood, that acid radicals were also being excreted, claiming the base released by bicarbonate.

Renal insufficiency secondary to chronic pyelonephritis

In Case G-198 (Table 4) we had the opportunity to study the response of a patient with marked renal insufficiency secondary to long standing cystitis and obstruction of the bladder neck. As discussed previously, it is easy to relieve the acidosis of this type of case by administering properly a calculated dose of sodium *r*-lactate. After this was accomplished on February 6, 1931, we repeated the administration of the lactate. Theoretically the initial carbon dioxide content of 43.1 volumes per cent should have been raised to 71.1 volumes per cent. Actually, this exact concentration was reached after one hour and maintained during the second hour. After four hours, however, the carbon dioxide content had diminished to 61.0 volumes per cent. This fall was not attended by any increased alkalinity of the urine. It is interesting to note that a somewhat similar late fall in the carbon dioxide content of the blood occurred

TABLE 3
Acute pyelonephritis with anhydremia and hypochloridemia
(Case H-695. Female, age 8 years, weight 23 kgm.)

		Blood							Urine			
Date and time relative to injection	Type of blood sample*	CO ₂ content	NaCl	Lactic acid	Inorganic phosphorus	Protein	Calcium	Non-protein nitrogen	Time§ relative to injection	CO ₂ content	NaCl	Lactic acid
minutes		vol-umes per cent	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	grams per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	minutes	vol-umes per cent	mgm. per 100 cc.	mgm. per 100 cc.
March 18, 1931												
Before 270'	S	63.0	491		6.5	7.12	12.4	160.0	Before.....	1.0	0.0	0.0
Just before injection I †	P	53.7		53.5		6.09		150.0	After 120'	13.0	0.0	92.3
After 30'	P	75.6		78.4								
After 70'	P	86.7	421					145.0				
After 70'	WB	76.0		41.6	5.0			140.0				
After 135'	S	90.4		45.3	5.4							
March 19, 1931												
Injection II †									March 19, 1931			
Just after.....	S	100.3	450	31.5					Before.....	4.7	0.0	18.0
After 60'	S	91.2	533	35.2				123.0	After 60'	8.8	170	
After 120'	S	88.8	567	32.8					After 120'	5.2	350	
After 240'	S	79.8	527						After 240'	7.8	350	
March 20, 1931												
Early A.M.....	S	90.0	538					100.0				
Noon.....	S	84.0	515					68.0				

* S = Serum.

WB = Oxalated whole blood.

P = Oxalated plasma.

† 161 cc. molar sodium γ -lactate plus 800 cc. distilled H₂O given intravenously.

‡ NaCl 15.0 grams, KCl 0.5 gram, CaCl₂·2H₂O 0.25 gram in 900 cc. distilled water given intravenously.

§ Indicates the end of the interval (in minutes) during which urine was collected.

TABLE 4
Chronic pyelonephritis with renal insufficiency
 (Case G-198. Male, age 7 years, weight 16.8 kgm.)

Date	Molar sodium r-lactate		Blood						Urine		Remarks	
	Dose and diluent*	Per kgm. of body weight	Min- utes after in- jection	Type of blood sample†	CO ₂ con- tent	Lactic acid	Glucose		Time of urine collec- tion‡	CO ₂ con- tent		
							True	Apparent				
October 30, 1930...	cc.	cc.			vol- umes per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.		vol- umes per cent		Whole blood N. P. N. = 87 mgm. per 100 cc. P. S. P. output = 1 per cent in 2 hours. Maximum urinary concentration = 1.010
	110	6.5	0	WB	33.1	18.9	127	151	0	13.1		
			15	WB	35.2	41.1	158	185	15	11.0		
			15	P	39.3							
			30	WB	40.8	30.9	158	185	30	10.2		
			30	P	46.1				60	13.1		
February 6, 1931...			60	WB	41.1	22.7	97	118	60	13.1		Maximum urea clearance (Van Slyke) = 10 per cent
			120	WB	39.8	12.6	62	87	120	12.9		
	100 +	6.0	0	WB	30.1	27.5	49	70	0	15.3		
	100 R		30	WB	41.9	56.7	90	102	45	15.3		
			60	WB	48.4	39.7	76	96				
			120	WB	48.4	27.0	65	83	120	23.0		
			240	WB	40.4	16.0	60		300	38.9		

TABLE 4 (continued)

Date	Molar sodium γ -lactate		Blood						Urine		Remarks
	Dose and diluent*	Per kgm. of body weight	Min-utes after in-jection	Type of blood sample†	CO ₂ con- tent	Lactic acid	Glucose		Time of urine collec- tion‡	CO ₂ con- tent	
							True	Apparent			
February 7, 1931...	cc.	cc.			sol- umes per cent	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.		sol- umes per cent	
	150	9.0	0	WB	43.1	12.6		89	0	46.0	Whole blood N. P. N. = 87 mgm. per 100 cc.
	+		30	WB	64.3	80.7		121			
	100 R		60	WB	71.1	41.0		128	60	36.0	
			120	WB	71.6	30.5		121			
			240	WB	61.0	19.0			180	36.5	

* Diluent = Ringer's solution (R).

† WB = Oxalated whole blood.

P = Oxalated plasma.

‡ Indicates the end of interval during which urine was collected.

in the two previous instances of lactate administration in this case, even though the carbon dioxide content had not been brought into the zone of alkali excess. Complete mineral balance experiments will have to be done before we can be certain as to the mechanism by which such excess base disappears from the blood of such subjects.

SUMMARY AND CONCLUSIONS

The response to the intravenous injection of sodium *r*-lactate of patients with acute hepatitis, acute and chronic pyelonephritis and miscellaneous diseases was studied, with the following results:

1. In the four cases of acute catarrhal jaundice studied there was a slight, but definite *delay* in the complete metabolism of the lactate.
2. In the case of anhydremia and hypochloridemia secondary to acute pyelonephritis because of initial low electrolyte concentration of the body fluids the base released from lactate was held as bicarbonate, causing persistent alkalosis, which was then relieved by administration of chloride.
3. In a single case of marked renal insufficiency secondary to chronic pyelonephritis, alkalosis was of no greater duration than in the normal subject.