Treatment of Cardiac Arrest and Slow Ventricular Rates in Complete A-V Heart Block

Use of Molar and Half Molar Sodium Lactate: A Clinical Study

By Samuel Bellet, M.D., Fred Wasserman, M.D. and Jerome I. Brody, M.D.

Molar and half-molar sodium lactate was efficacious (a) in restoring the heart beat following episodes of cardiac arrest, (b) ventricular standstill occurring during repeated Stokes-Adams seizures and (c) in increasing the idioventricular rate in the presence of complete A-V heart block. The increase in rate was related to the rapidity and amount of injection. These effects were associated with an increase in blood pressure and other evidences of improvement in the clinical state. No ventricular extrasystoles or other dangerous types of ectopic rhythms were observed in these subjects. The possible mechanisms by which the sodium lactate produces these effects are discussed.

There are few dependable drugs available for increasing the ventricular rate in complete A-V heart block, during prolonged sinus pauses, and following periods of cardiac arrest occurring in association with anesthesia and other states. Epinephrine1, 4, 19-20 (and occasionally other sympathomimetic drugs) and Isuprel19 are used to increase the idioventricular rate, but are not always dependable and may, at times, manifest serious untoward effects. In states where the slow heart rates are associated with increased vagal tone, a wider spectrum of drugs are available; i.e., parasympatholytic drugs (atropine,6 Banthine14 and sympathomimetic drugs (ephedrine,8 Paredrine5 and others). The cardiac slowing that occurs under many conditions (medical and surgical) may, however, be the result of a combination of several factors: namely, depression of the conducting tissue in the cardiac muscle, varying degrees of increased vagal tone, or a combination of both factors. In such cases, the drugs mentioned above will be either ineffectual or only partially effective.

Although sodium lactate (molar, half molar and sixth molar) has been used for the treatment of acidosis of various etiologies,10, 11, 12, 13, 22, 23, 24 the direct cardiac effect in the intact animal and human subject has not been little studied. Some of these, we feel, are of considerable practical importance and are the subject of this report.

The object of this presentation is to report the effects of sodium lactate (molar and half molar) solutions: (a) in restoring ventricular beating during repeated episodes of cardiac standstill of Stokes-Adams seizures; (b) during episodes of cardiac arrest of other etiologies; (c) in increasing the ventricular rates in states accompanied by slow heart rates; e.g., varying grades of partial A-V heart block and sinus bradycardia; and (d) in increasing the rate of ventricular beating in complete A-V heart block. These effects have, insofar as we know, not been previously reported.

Effect of Sodium Lactate Upon Episodes of Cardiac Standstill During a Stokes-Adams Attack

Case 1. A. T., a 71-year-old white male, was admitted to the Graduate Hospital of the University of Pennsylvania on the General Service on Thursday, May 16, 1955.
Fig. 1. Case 1. A—Control tracing, lead II, taken at 3:30 p.m. Note complete A-V heart block: auricular rate, 115; ventricular rate, 55 per minute. B—Effect of pounding on chest in presence of ventricular standstill. Pounding on chest started at X. Note beginning of ventricular beats at X1 and restoration of cardiac beating with complete A-V heart block at X2. This sequence of events was typical in restoration of the heart beat following many episodes of ventricular standstill. C—Effect of electrical stimulation. Electrical stimulation was applied at X. Note the resumption of ventricular beating at X1. The idioventricular rate is 61 per minute and is slightly more rapid than the control (rate 55 per minute) and the ventricular complexes are more aberrant. D—Following a period of ventricular standstill at X, sodium lactate was started (see text). Note the beginning of idioventrie-
of Pennsylvania on Oct. 15, 1954 following a syncopeal attack. While attending the outpatient clinic on Oct. 15, 1954, he suddenly lost consciousness at 11:30 a.m. During the approximate 30 second interval of unconsciousness, no pulse could be felt and no heart sounds were audible. Breathing ceased and he developed a cadaveric pallor. Pounding on the chest restored the heart beat and this was followed by resumption of respiration. He was admitted to the medical ward at about 12:30 p.m. An electrocardiogram on admission showed a complete A-V heart block (fig. 1A). The blood pressure was 124/60, the heart was top normal in size; no murmurs were audible, the apical rate was 32 per minute and slightly irregular. No congestive phenomena were present.

At about 4:15 p.m., four hours after admission, the patient became cyanotic and his heart stopped beating again. Vigorous pounding on the precordium restored the heart beat and a few seconds later, respiration began. The patient was cold and clammy and the blood pressure was 80/50. He was given nasal oxygen and ephedrine sulphate, 25 mg. (grain $\frac{3}{4}$) hypodermically, at this time. At about 4:30 p.m., an intravenous infusion consisting of 4 cc. of Levophed in 5 per cent dextrose in water (1000 cc.) was started. The above measures were apparently not efficacious in preventing further seizures, since the heart again stopped beating at about 5:00 p.m. Thumping on the precordium again restored the heart beat. At this time, the intravenous infusion was changed to 1000 cc. of 5 per cent dextrose in water with 10 mg. of Neosynephrine. In spite of this treatment, the heart beat stopped after about 20 minutes and was again restored by a vigorous thump over the precordium. Because the patient's condition was gradually deteriorating and the cyanosis becoming more marked, at 8:30 p.m. an electric stimulator (Burdiick) with DC current was used to restore the heart beat. This was successful in initiating ventricular beating in much the same manner as precordial thumping (fig. 1C). In spite of these measures, however, the periods of asystole became more frequent and the patient's clinical state gradually deteriorated. Up to this time (9 p.m.) Neosynephrine solution and atropine, 2.4 mg. (grain $\frac{1}{2}$) had been ineffectual in maintaining the heart beat. The only procedures of value, but of temporary efficacy, had been pounding over the precordium and electrical stimulation to the chest wall.

At 9 p.m., 120 cc. of molar sodium lactate was added to the 250 cc. of intravenous fluid (making about a third molar solution). This was infused in about 30 minutes and the heart beat was restored almost immediately (in one to two minutes) after the administration of the fluid. With more rapid infusion, the ventricular beating became more rapid and increased to 78 per minute. The complete A-V heart block was maintained (fig. 1D). From 9:30 p.m. to 10:50 p.m., 250 cc. of half molar sodium lactate was given by slow drip. During this period, when the lactate was stopped the ventricular beating also stopped. To satisfy ourselves that the lactate was the sole cause of restoration of the ventricular beats, this procedure was repeated 10 times during this period of one hour and 20 minutes. The ventricular beats regularly ceased about two to five minutes after the lactate was stopped, and were immediately restored by the administration of the sodium lactate solution. At about 10:55 p.m., however, when the solution was stopped, the patient's heart rate was maintained spontaneously at about 40 per minute for approximately one hour. The patient's condition at this time was good. There was no cyanosis and the blood pressure was 150/100. At 11:55 p.m., ventricular beating ceased again and was restored by the sodium lactate solution. The same sequence of events recurrent at 2:00 a.m. on October 16 with a similar result. The ventricular beating was then maintained by the administration at intervals of the sodium lactate solution until 6:05 a.m. At approximately 6:10 a.m. on Oct. 16, 1954, the patient suddenly expired. He was not receiving sodium lactate at the time of death. During the night of October 15 and 16, the following laboratory studies were obtained:

<table>
<thead>
<tr>
<th>Time</th>
<th>CO$_2$</th>
<th>Na</th>
<th>K</th>
<th>Cl</th>
<th>Ca</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:55 a.m.</td>
<td>38</td>
<td>130</td>
<td>5.2</td>
<td>97</td>
<td>—</td>
</tr>
<tr>
<td>1:00 a.m.</td>
<td>38</td>
<td>128</td>
<td>6.0</td>
<td>96</td>
<td>10</td>
</tr>
</tbody>
</table>

Comment. Ephedrine sulphate, Neosynephrine, and atropine had no apparent effect in preventing or alleviating the attacks of ventricular standstill occurring in this patient. Because this patient's condition deteriorated rapidly, thumping on the chest was tried and
successfully restored cardiac contraction. Thumping on the chest wall was a consistently successful method of therapy but the response was brief and the procedure had to be repeated at increasingly shorter intervals (from 15 to 5 minutes). The same success and shortcomings were present with electrical stimulation. Furthermore, this was always accompanied by a transient, tonic convulsive seizure. Half molar lactate consistently restored ventricular beating on 10 different trials and uniformly tended to increase the idioventricular rate when administered. The increase in rate depended on the amount and rapidity of administration. In the initial phase of its effect, the heart rate was maintained only during the administration of sodium lactate. After the first two hours, the heart rate was maintained for one to four hours even after cessation of the medication. This patient experienced numerous periods of cardiac standstill during the 18 hours of observation with resultant damage to the vital centers and heart during these episodes. The latter were undoubtedly contributory factors to his final demise.

**Effect in Terminal Cardiac Arrest: Restoration of Cardiac Beating with Sodium Lactate**

Case 2. B. C. was a 57-year-old Negro woman who was admitted to the Graduate Hospital of the University of Pennsylvania in a comatose state on Nov. 3, 1954. The patient had been followed in the Hypertension Clinic of this hospital for several years because of headache attributed to benign essential hypertension. The blood pressure had ranged from 200/90 to 250/120. The patient had complained of severe headache in the right frontal area of the skull approximately 24 to 36 hours prior to admission. Two hours before admission, she suddenly lost consciousness and at the same time developed involuntary movements of her right arm and leg and urinary incontinence.

On admission, blood pressure was 180/100; pulse was 100 per minute (regular) and respiration was 30 per minute. The patient had a left hemiplegia and was deeply comatose, failing to respond to even painful stimuli. The heart was slightly enlarged to the left. A diagnostic spinal puncture yielded grossly bloody cerebrospinal fluid with an opening pressure of 260 mm. H₂O. The hemoglobin and red blood cell count were normal. Urinalysis revealed a 3 plus albuminuria, a 4 plus glycosuria and a positive test for ketone bodies. The fasting blood sugar was 265 mg. per 100 cc.; Carbon dioxide, 50 volumes per 100 cc. and blood urea nitrogen 14 mg. per 100 cc. The patient was started on oxygen, antibiotics and parenteral fluids. The blood sugar promptly dropped to 132 mg. per cent without insulin and remained at about that level until she died. The clinical diagnosis was hypertension with cardiac enlargement, left ventricular hypertrophy and cerebral hemorrhage.

On Nov. 5, 1954, sodium was 137 mEq. per liter, potassium 3.4 mEq. per liter, chlorides 100 mEq. per liter, carbon dioxide 52 volumes per 100 cc. and the blood urea nitrogen 18 mg. per 100 cc. The patient’s temperature slowly rose from 100.8 F. rectally on admission to 102 F. on Nov. 5, 1954 and her respiratory difficulty increased. She was digitalized intravenously with a lanatoside-C preparation without improvement and at 12:30 a.m. on Nov. 6, 1954 an emergency tracheotomy was performed. Her blood pressure had dropped to 80/40 prior to tracheotomy and intravenous Levophed was necessary to maintain a blood pressure of 100–110/80–70. At 2:05 p.m. on Nov. 6, 1954, the patient’s respiration ceased and the heart sounds, blood pressure and pulse were unobtainable. Thirty seconds later, 17 cc. molar sodium lactate was injected intravenously over a period of about one minute. Toward the end of this period, the heart sounds became audible and the electrocardiogram recorded a rate of 150 per minute (fig. 2A). Manual respiration was then begun and several minutes later, positive pressure respiration was instituted. The heart rate remained constant at 150 beats per minute with a blood pressure of 80/60 (fig. 2A). It appeared that this rate would be maintained indefinitely without further administration of sodium lactate; 12 minutes after artificial respiration was stopped. At 2:47 p.m., the grade of block increased to 2 to 1 with a ventricular rate of 36 per minute (fig. 2D). Sodium lactate was started soon afterwards when complete A-V heart block ensued (2F). There was a gradual increase in the idioventricular rate to 60 per minute after about 50 cc. of the molar sodium lactate solution had been given. The complete A-V heart block persisted although the ventricular complexes assumed a more normal configuration (fig. 2F). After 70 cc. of molar sodium lactate, the ventricular rate increased to 70 per minute. Since the heart rate was maintained at this time, further sodium lactate was stopped. (Two minutes prior to fig. 2G.) At about 3:00 p.m., artificial respirations were stopped and a slower idioventricular rate developed (fig. 2G). The Neophor was started again (3:10 p.m.) and the sodium lactate given (fig. 2H). This resulted in a gradual increase of the idioventricular rate (fig. 2I). The heart rate again maintained itself at 36 per minute even after the sodium lactate had been stopped for five minutes. Artificial respiration was then stopped and the heart rate again slowed. Administration of sodium lactate without artificial
Fig. 2. Case 2. Effect of molar lactate following episode of cardiac arrest (see text). A—One minute after cardiac standstill occurred, 17 cc. of molar sodium lactate was administered in 30 seconds. (Tracing taken 2 minutes after lactate). Note return of ventricular beating at a rate of 150 per minute. This rate appeared to continue indefinitely during the maintenance of artificial respiration. B—After artificial respiration stopped for two minutes. Note the slowing of the ventricular rate and the appearance of a coronary sinus rhythm. C—Five minutes after artificial respiration stopped. Note further cardiac slowing; ventricular rate is now 68 per minute. D—Seven minutes after respiration stopped. Note still further slowing of the heart. A 2:1 A-V heart block is present. The ventricular rate is 36 per minute; auricular rate is 72 per minute. E—After sodium lactate started. Note the increase in the ventricular rate to 45 per minute with complete A-V heart block. F—Note further increase in ventricular rate to 68 per minute. Complete A-V heart block is still present. G—After lactate was stopped. Note progressive decrease in heart rate. The auricular complexes are of small amplitude. H—Shows a slow idioventricular rhythm. Sodium lactate was started at X. I—Two minutes after lactate was started in conjunction with artificial respiration. Note increase in ventricular rate to 12 per minute (strip 2). Strip 3. Ventricular rate now 35 per minute. The heart continued to beat for five minutes longer during lactate administration and stopped soon after its cessation.
respiration resulted in a speeding of the rate. There was sudden stoppage of the heart beat at 3:50 p.m.

Comment. After a period of cardiac arrest lasting about 30 seconds, the heart beating was restored following the intravenous administration of 17 cc. of molar sodium lactate. When the heart beat had been restored and artificial respiration started, the heart appeared to continue to beat indefinitely with a systolic blood pressure 80 mm. Hg. Inasmuch as complete recovery was impossible due to extensive and irreversible brain damage, the effect of sodium lactate administration was, therefore, studied following the anoxia induced by respiratory arrest. Sodium lactate was efficacious in increasing the rate of ventricular beating after three successive periods of anoxia which occurred when the artificial respirations were stopped. Each successive episode required larger amounts of lactate and, after the third episode, a slow idioventricular rhythm occurred from which the patient did not recover. Although the lactate increased the rate to 68 per minute, there was no change in the inherent rhythm, (complete A-V heart block). The ventricular complexes became increasingly widened with the third episode of anoxia and, although the sodium lactate speeded up the rate, death ensued with sudden cardiac standstill.

CARDIAC ARREST: TEMPORARY RESUMPTION OF CARDIAC BEATING FOLLOWING INTRACARDIAC INJECTION OF MOLAR SODIUM LACTATE

Case 3. W. J. was a 47-year-old Negro man who was admitted to the Graduate Hospital of the University of Pennsylvania with carcinomatosis on Nov. 12, 1954. Toward the terminal part of his illness he manifested a marked degree of cachexia with ascites, pleural effusion, hepatomegaly and splenomegaly and was in a state of shock for 24 hours before death. His respiration stopped at 11:40 a.m. on Dec. 2, 1954. The heart continued to beat for a few minutes as noted in the continuous strips of figure 3A and B. At X2, cardiac standstill was recorded. At X3, a needle was inserted into the left ventricle. Since this procedure yielded two ectopic beats, no sodium lactate was infused until the tracing showed continuous cardiac standstill. At X4, 40 cc. of molar sodium lactate was injected slowly. Note the appearance of aberrant ventricular beats, in figure 3F; after a second intracardiac injection of 20 cc. of molar sodium lactate, these became more frequent in strips G and H. Ventricular fibrillation occurred shortly thereafter. The patient did not receive any form of artificial respiration during the period of observation. The mechanical effects of the intracardiac injection cannot be ruled out as an explanation for the restoration of the ventricular contractions.

Comment. In this, as well as in two other cases, sodium lactate was given by intracardiac injection several minutes after the respirations had ceased (none of these three patients received positive pressure artificial respiration) and cardiac beating had stopped. Although there was temporary restoration of the heart beat, there was no effect on the blood pressure or other evidence of consistent or sustained improvement. We have not had the opportunity to study the effects of intracardiac injection under more favorable circumstances.

EFFECT OF LACTATE IN COMPLETE A-V HEART BLOCK

Effect in Presence of An Extremely Slow Heart Rate (15 per minute) accompanied by a State of Shock

Case 4. J. B., age 59, a truck driver, was admitted to the Philadelphia General Hospital on Dec. 9, 1954 with the chief complaint of "heart trouble." The patient had experienced shortness of breath and episodes of distress in the chest following exertion for the past two years. During the past 18 months, these had become particularly severe. Treatment consisted of digitoxin, aminophylline and other diuretics. For three days prior to admission, the patient experienced several attacks of syncope followed by palpitation, anorexia and generalized weakness. He had vomited "a little." The past medical history, social history and family history were unobtainable.

Examination revealed a normally-developed, pale, sweating white man who was restless, dyspneic, in shock and obvious acute distress. The temperature was 98.6 F. The blood pressure was unobtainable. There was a bruise over the right forehead, probably the result of a fall. Venous distension and pulsations were noted in the neck vessels. Decreased fremitus was present at the right base posteriorly and bilateral moist rales were heard below the seventh intercostal space posteriorly. The point of maximum impulse was located in the sixth intercostal space at the anterior axillary line. A grade III to IV rough systolic murmur was heard at the base of the heart which was transmitted into the right side of the neck. A short, soft, aortic diastolic murmur was heard best at the second left intercostal space. The aortic second sound was markedly diminished in
The infusion was then given continuously from 12:30 p.m. to 5:30 p.m. at which time, it was discontinued. A total of 960 cc. of sodium lactate (360 cc. molar and 600 cc. half molar) was given in a period of five and one-half hours. At 5:30 p.m., the patient developed normal sinus rhythm with first degree A-V heart block (fig. 5). The patient appeared to be markedly improved; the blood pressure was sustained at about 140/95. The patient's urinary output was fairly constant at about 50 cc. per hour. Because of the hyperpotassemia (the serum potassium drawn shortly after admission was reported later in the day as 7.3 mEq. per liter) he was also given 1000 cc. of 5 per cent glucose in water with 15 units of insulin at 6:00 p.m. In addition, he received 2 Gm. of calcium gluconate by vein at 6:00 p.m. and 15 Gm. of cation-exchange resin orally. At 7:30 p.m., on Dec. 9, 1954, the patient's blood pressure was 146/52, the pulse rate was 72 per minute and of good volume.

On Dec. 10, 1954 the patient's urinary output decreased to 4 cc. per hour, the pulse dropped to 40 per minute and the patient became dyspneic. The blood pressure was 158/76. The electrocardiogram at this time revealed very bizarre complexes followed by ventricular flutter and ventricular fibrillation. Death ensued within a few minutes thereafter. Intracardiac epinephrine (1 cc. of 1:1000 solution) was given without effect. The patient was pronounced dead at 2:45 p.m.
TREATMENT OF CARDIAC ARREST AND SLOW VENTRICULAR RATES

**Fig. 4. Case 4.** A—Control electrocardiogram (read II), taken at 11:35 A.M. Ventricular rate is 15 per minute, auricular rate is 80 per minute. Note the QRS complexes (0.18 second). Lactate infusion began at X1. Strips taken from continuous electrocardiographic tracing. B—Thirty six seconds after lactate was started, approximately at 11:40 A.M. C—One minute and 12 seconds after lactate was started. D—Two minutes after lactate was started. E—Two minutes and 36 seconds after lactate was started. F—Three minutes and 12 seconds after lactate was started. G—Three minutes and 48 seconds after lactate was started. H—Four minutes and 36 seconds after lactate was started. Note that the ventricular rate has increased from 15 in A to 38 in H, that the auricular rate has increased from 80 in A to 100 in H, and that the QRS width has decreased from 0.18 to 0.14 second. Complete A-V heart block is still present.

The results of the laboratory studies made on December 9 and 10 follow:

<table>
<thead>
<tr>
<th></th>
<th>12-9-54 (After 120 cc of molar sodium lactate)</th>
<th>12-10-54 (No sodium lactate for 15½ hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN mg./%</td>
<td>72</td>
<td>108</td>
</tr>
<tr>
<td>Blood sugar mg./%</td>
<td>86</td>
<td>—</td>
</tr>
<tr>
<td>NA mEq/L</td>
<td>137</td>
<td>138</td>
</tr>
<tr>
<td>K mEq/L</td>
<td>7.5</td>
<td>3.4</td>
</tr>
<tr>
<td>Cl mEq/L</td>
<td>90.9</td>
<td>94.0</td>
</tr>
<tr>
<td>Ca mg./%</td>
<td>7.2</td>
<td>8.6</td>
</tr>
<tr>
<td>CO₂ vol. %</td>
<td>25</td>
<td>63</td>
</tr>
</tbody>
</table>

**Necropsy.** The findings of interest were referable to the heart and lungs. The heart weighed 1000 Gm. and showed evidence of both right and left ventricular hypertrophy. The aortic valves were thickened, rigid and calcified and indicated the presence of aortic stenosis. In the right auricle an organized mural thrombus was present. The right lung showed evidence of an acute infarction and the main branch of the right pulmonary artery showed a fresh embolus. The pathologic diagnoses were rheumatic heart disease, aortic stenosis and insufficiency, right and left ventricular hypertrophy and acute cor pulmonale. Death was apparently caused by acute pulmonary embolism arising from the thrombus in the right auricle.
FIG. 5. Case 4. A—Lactate was then stopped (at approximately 12:15 p.m.). A total of 240 cc. molar sodium lactate given. Note return of ventricular rate to its original low figure (15 per minute) and the return of widened QRS complexes, similar to that of the control (fig. 4A.). B—Half molar sodium lactate started at X1. (approximately 12:30 p.m.). C—Forty eight seconds after sodium lactate infusion was begun. Note increase of ventricular rate to 33 per minute and the narrowing of the QRS complexes. D—One minute and 12 seconds after lactate infusion had been started. Ventricular rate 33 per minute. E—Two minutes and 12 seconds after lactate infusion started. Ventricular rate 38 per minute. F—Lactate infusion slowed to 20 drops per minute in attempt to titrate speed of administrations against patient's heart rate. Note once again the return to slow ventricular rate (15 per minute) and widened QRS complexes (0.18 second). QRS width 0.18 sec. G—Subsequent to titration attempt, lactate was again speeded up. This tracing taken approximately three hours after continuous sodium lactate infusion. Note the more rapid ventricular rate and the narrowed QRS complexes. Ventricular rate 38 per minute. H—Three hours and five minutes after continuous sodium lactate administration. Ventricular rate, 45 per minute; auricular rate, 100 per minute. I—Five hours after lactate administration. Note more rapid ventricular rate, 48 per minute, auricular rate 110 per minute. J—Five and one-half hours after continuous sodium lactate administration. Patient now has normal sinus rhythm with a first degree A-V heart block. Sodium lactate was subsequently discontinued. The ventricular rate is 100 per minute. The QRS complexes have changed somewhat in configuration. The QRS width is 0.14 second, the P-R interval is 0.28 second. K—Two hours after cessation of sodium lactate infusion. The patient remains in normal sinus rhythm. The ventricular rate is 75 per minute; P-R is 0.28 second.
Comment. This patient, when first seen, showed a ventricular rate of 15 per minute with complete A-V heart block and bundle branch block (QRS 0.18 second). In addition, he was in a state of shock and the blood pressure was unobtainable. Within several minutes after the sodium lactate was started ventricular rates increased and the QRS complexes narrowed (fig. 4D to H). During continued administration the ventricular rate increased to 38 per minute and the auricular to 100 per minute and the QRS width narrowed to 0.14 second. Atropine sulphate, 0.8 mg. (grains \(\frac{1}{75}\)) given intravenously, resulted in no significant effect on the heart rate.

The sodium lactate solution was instrumental in increasing the idioventricular rate, narrowing the QRS complexes, elevating the blood pressure, and reversing the state of shock. That the sodium lactate solution was responsible for this improvement was indicated by the fact that on three successive occasions, cessation of administration or marked slowing of the rate of infusion resulted in a return to the control tracing; that is, a decrease of the ventricular rate to 15 per minute, widened QRS complexes and a fall in blood pressure (fig. 5A). On resumption of sodium lactate administration, the process was reversed. Following five hours of continuous sodium lactate administration, the increased heart rate and blood pressure were subsequently maintained without additional lactate infusion. Indeed, the heart rate tended to gradually increase spontaneously and at 5:30 p.m. normal sinus rhythm appeared associated with a partial A-V heart block (fig. 5).

It is of some interest to consider the mode of action of the sodium lactate in this patient. The decrease in acidosis, increase in the idioventricular rate and increase in blood pressure were accompanied by an improvement in the clinical state. These factors were probably also instrumental in improving the hyperpotassemia. The serum potassium the following day was normal (3.4 mEq. per liter).

Effect of Sodium Lactate Upon the Auricular and Ventricular Rates in a Case of Asymptomatic Complete A-V Heart Block

Case 5. M. F., a 38-year-old white woman, was admitted to the Philadelphia General Hospital on Oct. 14, 1954 with the diagnosis of rheumatic heart disease, aortic valvular disease and complete A-V heart block. The auricular and ventricular rates preceding and following sodium lactate are shown in

![Fig. 6. Case 6. Effect of lactate on the auricular and ventricular rate in complete A-V heart block. A—Control tracing. Note complete A-V heart block. Ventricular rate 71 per minute; auricular, 100 per minute. B—Note slight increase in auricular and ventricular rates. Ventricular rate 79 per minute; auricular 107 per minute. C—After 25 minutes an additional 30 cc. of molar sodium lactate had been given. Note the ventricular rate of 100 per minute and auricular rate of 150 per minute. D—After sodium lactate administration was slowed. Note decrease in auricular and ventricular rates. E—Fifty-five minutes after the initial infusion had been started. Ninety cc. of additional molar sodium lactate given.](http://circ.ahajournals.org/doi/abs/10.1161/01.CIR.18.3.694)
It should be noted that the control rates of the auricles and ventricles were 100 and 71 per minute, respectively (fig. 6A). Ten minutes after the administration of half molar sodium lactate (initial infusion) and immediately following the administration of 30 cc. of molar sodium lactate (second infusion), the auricular and ventricular rates speeded up to 150 and 107 per minute, respectively. This maximum rate was attained when the solution was infused rapidly at a rate of 150 drops per minute (fig. 6C). As the rate of infusion was slowed, the ventricular rate slowed correspondingly (fig. 6D). Ten minutes after the end of the infusion, the atrial and ventricular rates had returned to 115 and 78 per minute, respectively, or to a figure slightly above the control values. There was no effect on the inherent or basic rhythm (complete A-V heart block). This patient experienced paresthesias (numbness and tingling of the hands and feet and about the mouth) at the height of the lactate effect. These manifestations could have been the result of the alkalosis and slight hypocalcemia that resulted during the infusion.

**Effect in Complete A-V Heart Block, with Occasional Cycles of Normal A-V Conduction: Conversion to 2:1 A-V Heart Block by Molar Sodium Lactate**

**Case 6.** L. W., a 69-year-old Negro woman, was admitted to the Philadelphia General Hospital on October 26, 1954 with the diagnosis of arteriosclerotic heart disease. The control electrocardiogram showed complete A-V heart block with a ventricular rate of 42 per minute, consisting of idioventricular beats and occasional QRS complexes which appeared to be normally conducted (fig. 7A, complex X). Serum electrolytes (sodium, potassium, chloride and carbon dioxide combining power) were normal.

After 100 cc. of molar sodium lactate the complete A-V heart block and idioventricular heart beats were entirely replaced by normally conducted ventricular complexes and a 2:1 A-V heart block ensued (fig. 7B). About 15 minutes after the sodium lactate was stopped, the electrocardiogram returned to the control tracing: namely, complete A-V heart block with idioventricular beats.

**Effects of Sodium Lactate in Other Arrhythmias and Conduction Disturbances**

The effects of sodium lactate have been studied in patients with partial A-V heart block, in the presence of sinus bradycardia with nodal escape, in the slow heart rate accom-

---

**Table 1.** Effect of Sodium Lactate on the Auricular and Ventricular Rate in Complete A-V Heart Block (Case 6)

<table>
<thead>
<tr>
<th>Sodium Lactate Given</th>
<th>No. of cc.</th>
<th>Time (p.m.)</th>
<th>Rate per Min.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>—</td>
<td>2:15</td>
<td>100 71</td>
</tr>
<tr>
<td>0.5 molar solution</td>
<td>120</td>
<td>2:25</td>
<td>107 70</td>
</tr>
<tr>
<td>0.2 molar solution</td>
<td>120</td>
<td>2:35</td>
<td>115 83</td>
</tr>
<tr>
<td>Total</td>
<td>240</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.0 molar solution</td>
<td>20</td>
<td>2:40</td>
<td>140 88</td>
</tr>
<tr>
<td>1.0 molar solution</td>
<td>30</td>
<td>2:45</td>
<td>150 100</td>
</tr>
<tr>
<td>1.0 molar solution</td>
<td>20</td>
<td>2:55</td>
<td>134 100</td>
</tr>
<tr>
<td>1.0 molar solution</td>
<td>20</td>
<td>3:10</td>
<td>124 88</td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
<td></td>
<td>115 78</td>
</tr>
</tbody>
</table>

**Fig. 7.** Case 6. Effect of molar sodium lactate on complete A-V heart block with occasional normally conducted beats. A—Control. Note presence of complete A-V heart block, auricular rate 73 per minute; ventricular rate 42 per minute. An occasional normally conducted beat is seen at X. B—After the administration of 100 cc. of molar sodium lactate. Note the occurrence only of conducted beats with the presence of 2:1 A-V heart block.
panying hyperpotassemia, bundle branch block and in patients with extrasystoles.

In addition, the effects on the electrocardiogram, blood pressure and serum electrolytes have been studied in normal human subjects. This data will form the basis of a subsequent report.8

Discussion
Method of Administration and Dose of Molar and Half Molar Sodium Lactate

Although sixth molar sodium lactate (isotonic solution) has been rather commonly employed in the therapy of acidosis, the use of molar or half molar sodium lactate has been rather infrequent. The latter solutions have been used by Hartman,16, 11, 12 Neubauer22, 23, 24 and others for the treatment of acidosis in the human subject due to various factors; diabetic acidosis, the acidosis of renal origin, acidosis due to diarrhea, and acidosis accompanying severe infections. Hartman15 (1938) injected 3.2 to 8.1 cc. of molar sodium lactate per kilogram of body weight intravenously in a period of 18 to 27 minutes; 0.125 per cent calcium chloride was added to prevent tetany. Neubauer used 120 to 240 cc. of sodium lactate, administered as molar or half molar solution over a period of 1 to 2 hours in the treatment of acidosis associated with azotemia; 2 to 6 Gm. of calcium gluconate was given within three to four hours after the lactate to prevent tetany secondary to the alkalosis. Sodium lactate, especially prepared for oral administration, has also been employed for mild cases in conscious patients.22

We employed a dose ranging from 15 cc. of molar sodium lactate* administered in about one minute, to a total of 960 cc. (molar and half molar solution) administered within a period of five hours. The rapidity of injection depended upon the urgency of restoring the heart rate. For example, in case 1, the initial dose of 250 cc. of third molar sodium lactate solution was injected rapidly within about 30 minutes. In case 2, 15 cc. was injected in one minute; in case 4, 240 cc. in four minutes was required to increase the heart rate from 15 to 60 beats per minute. After the rate had been restored the infusion was given more slowly, at the rate of 50 to 100 drops a minute, to maintain the heart rate close to a normal figure. It is interesting that in these cases the rapidity of the heart rate varied directly with the speed of infusion and could be regulated by it. In case 1, after an infusion period of approximately two hours, the heart was maintained for long periods of time (four to five hours) without further administration during the period; in case 4, after an injection period of five hours, the heart rate was maintained without further sodium lactate administration.

Electrolyte Alterations and Fate of Sodium Lactate

When given in a dose of 7 cc. of the molar sodium lactate solution per kilogram over one-half hour, it has been demonstrated22 that sodium r-lactate is completely metabolized within a period of from one to two hours by normal individuals. A portion of the lactate radical is oxidized and the remainder converted into glycogen.

The lactic acid concentration increases in the blood and reaches a concentration of 120 mg. per 100 cc. in one hour after the injection of 220 cc. of molar sodium lactate12 and usually returns to a normal level within one to two hours after the injection is started. In the treatment of acidosis, even though lactic acid may be abnormally high before the sodium r-lactate injection, normal values are usually seen two or three hours after the injection. This has been explained as being due to the effect of the increased blood flow on the utilization of lactic acid.

Abramson and coworkers pointed out that injected lactate acts like an easily oxidizable substrate which replaces other food stuffs in metabolism. A point of considerable interest is the fact that the metabolism of sodium lactate may be accomplished up to the point of death. In a case reported by Hartmann and Senn,23 although the patient died about four hours after the administration of sodium lactate, the plasma carbon dioxide content had

* Each 100 cc. of the solution as supplied contained sodium lactate, 11.2 Gm., representing 11.2 per cent (w/v). In terms of potential alkali it equals 8.4 Gm. (approximately 130 grains) sodium bicarbonate.
increased from 27.5 to 44.6 volumes per 100 cc. during the first half of this period. Similar cases have been documented by these authors.

The sodium ion, liberated during the oxidation of lactate or its conversion into glycogen, is transported to the kidneys for excretion largely as the bicarbonate salt. There exists, therefore, a state of alkalosis of the base bicarbonate excess type for several hours after the injection with commensurate increase in the hydrogen ion concentration of the blood. Within four hours, more than half of the injected sodium is excreted. Serum chloride levels show a reciprocal drop with the elevated carbon dioxide combining power.

An increase of from 25 per cent to 50 per cent above the basal rate of oxygen consumption follows the intravenous administration of the racemic sodium lactate to normal human subjects when given at a rate of 7 cc. per kilogram of bodyweight. This increase is apparently the result of the oxidation of the d-isomer. The blood sugar increases slightly and then sinks to slightly hypoglycemic levels. The intravenous administration of sodium lactate results in a significant increase in maximum tubular excretory capacity for para-aminohippuric acid in man. The average maximum increase amounted to about 30 per cent of the preinjection levels.

Mechanism of the Cardiac Effect

Theoretical Considerations. The mechanism of the observed cardiac effects of sodium lactate are not entirely established. Nevertheless, there are certain actions of the solution and its breakdown products that have been well documented and which merit discussion. These actions will be discussed under the following headings: effect of the lactate; effect of the alkalosis or reduction in degree of acidosis; the action of the sodium ion; the sympathomimetic effect and the vagolytic effect.

Effect of the Lactate. The lactate which is relatively rapidly utilized serves as a fuel which can be readily utilized by the heart. There results an increase of 20 per cent to 50 per cent in the basal rate of oxygen consumption. There is some evidence that the heart muscle can utilize lactate for direct provision of energy. Bing found that the isolated dog's heart removed from the circulating blood more lactic acid than any other substance and that lactate is utilized for direct combustion. An increase in arterial lactate levels caused an increase in myocardial lactate extraction. However, compared with glucose, the myocardial lactate extraction and usage were usually significantly lower. The lactate may act directly as added substrate to the Krebs cycle and may be converted to pyruvate via the coenzyme diphosphopyridine nucleotide, circumventing the intermediate steps of conversion of glucose to pyruvate. This may, in effect, serve to act directly in the oxidative metabolic mill of the Krebs cycle and to more efficiently utilize and conserve the energy of the cell.

Effect of the Alkalosis. There is considerable evidence which indicates that alkalosis has a profound effect on maintaining and accelerating the heart beat: i.e., that acidosis tends to retard and alkalosis tends to accelerate conduction. Ringer (1882-83), in the isolated perfused heart, observed that when a ventricle had lost its contractility it could be restored for a short time by adding to the dose of saline 5 cc. of sodium bicarbonate solution. That the sodium bicarbonate acted by virtue of its alkalinity and not as a sodium salt was indicated by the fact that the addition of calcium hydrate or ammonium carbonate produced the same restoration of beats. Ringer felt that sodium bicarbonate exerted little, if any, influence over the cardiac contractions; this was regulated by the action of calcium and potassium salts. The effect of sodium bicarbonate was that of neutralizing the acid reaction produced by the contraction; without this neutralizing effect the tissue and blood would become acid resulting in cessation of function. Mines (1912), working on the isolated terrapin and the mammalian heart, observed that electrical and mechanical excitation decreased with an acid pH and the A-V intervals were lengthened and disappeared with a pH of 7.0. Shifting to a high pH reversed this process. He was of the opinion that with a fall in pH, the total excitatory processes develop more slowly and that a rise
in pH results in a more rapid development of the excitatory process, acceleration rhythm and increase in conductivity.

Andrus and Carter\(^4\) (1924) reported effects on the P-R interval in a perfused terrapin heart similar to that reported by Mines. The rate at which the excitation was transmitted in auricular muscle was dependent upon the hydrogen ion concentration of the perfusate; it was increased by more alkaline and decreased by more acid pH. The administration of sodium lactate is accompanied by relatively rapid alterations in pH. This probably occurs earlier in the region of the heart even before it is reflected in the peripheral blood. As a result, any local changes characterized by acidosis in the heart would tend to become less marked and the balance would proceed towards the alkalotic state. Since anoxic states are frequently accompanied by acidosis, these local changes in the heart would tend to speed up the rate. That alkalosis is an important factor of itself is indicated not only by the experiments performed in the isolated heart, but also by the fact that changes of a similar type were obtained by the use of sodium bicarbonate during the complete heart block produced by obstructive asphyxia in dogs.\(^6\)

**Effect of Sodium.** Injection of molar sodium lactate results in an increase in the serum sodium concentration. The sodium liberated from the lactate is excreted by the kidneys as the bicarbonate salt. Within four hours, more than half of the sodium is excreted in this way. That the increased sodium content of the extracellular fluid effects the conductivity in the cell is supported by many observations.\(^15, 16, 21\) Hodgkin and Katz\(^15\) (1949), using the giant axon of the squid, showed that the action potential was abolished by sodium-free solutions and that a decrease in the sodium concentration decreased the height of the action potential. The height of the action potential was increased by a hypertonic solution containing additional sodium chloride. The rate of rise of the action potential was directly proportional to the external concentration of sodium. The conduction velocity undergoes a substantial decrease in solutions of low sodium content. Increasing the external potassium causes a depression of both acting and resting potential. Natsuk and Hodgkin\(^21\) stated that the reversed potential difference across that active membrane was related in linear fashion to the logarithm of the sodium concentration in the external fluid.

Hoffman, Siebens and Brooks\(^16\) determined the effect of alterations in sodium on the excitability of cardiac tissue before and after vagal stimulation. When the sodium concentration was decreased, both the magnitude and rate of rise of the action potential are diminished. It has been suggested on the basis of these effects that acetylcholine, by decreasing the sodium entry, causes a slower heart rate and decreased rhythmicity at a time when repolarization is accelerated.

**Sympathomimetic Effects.** There is considerable evidence to suggest that molar or half molar sodium lactate does not possess typical sympathomimetic effects. The lack of these effects is suggested by the failure of lactate to increase the blood pressure or the heart rate in the normal human subject in the doses given and even in large doses in the dog. Rapid administration of sodium lactate in the dog results in a fall in blood pressure.\(^5\) There was no significant increase in the heart rate in the normal experimental animals. Although sodium lactate restored the heart rate in cardiac arrest and increased the ventricular rate in complete A-V heart block, it did not produce extrasystoles and other dangerous types of ectopic rhythm as are frequently observed with epinephrine.

**Vagolytic Effect.** That sodium lactate may have at least a partial vagolytic effect is suggested by (a) the increase in the auricular rate in the complete and partial A-V block,\(^5a\) (b) decrease in the P-R interval; (c) increase in the ventricular rate in partial A-V heart block.\(^5a\) Although preliminary experiments suggest that its vagolytic effects in doses of 100 cc. to 200 cc. in the human subjects are not particularly marked, evidences of some vagolytic effect have been shown in the dog.\(^5\)

**Summary of Mode of Action.** We cannot state with certainty at this time the mechanism by which the molar or half molar sodium lactate produces the effects noted. At the present time
we are attempting to more definitely localize the site of action in increasing the heart rate (cases 1 to 4) and in narrowing the QRS complex in the cases studied (cases 4 and 6). Preliminary observations in the human subject and in dogs suggest that the chief effects are due to alkalosis, to the direct effect of the sodium ion and probably the lactate ion on cardiac muscle. Preliminary studies in the dog would lead us to believe that the alkalosis is the most important factor. An increase in the rhythmicity of the cardiac pacemaker and/or the conductivity of the impulse within the heart muscle may also result from a change in any of the factors compromising these properties. The mode of action would explain (a) restoration of the heart beat after cardiac arrest and ventricular standstill; (b) change of the widened QRS complexes to those that are narrower (cases 4 and 11); and (c) the increase in idioventricular rate in complete A-V heart block, the increase depending upon the amount and rapidity of the sodium lactate administration.

**Summary**

The therapy of episodes of cardiac arrest, ventricular standstill during Stokes-Adams seizures, the slow idioventricular rhythm of complete A-V heart block, the slow ventricular rates of partial A-V heart block and sinus bradycardia by the administration of molar and half molar sodium lactate is reported.

After epinephrine, Neosynephrine and atropine were without effect in restoring the ventricular beating during repeated, prolonged periods of ventricular standstill in a case of Stokes-Adams syndrome, molar and half molar sodium lactate, administered intravenously, restored the heart beat on 10 separate occasions. After two hours the heart continued to beat spontaneously for several hours. In the case of terminal cardiac arrest the intracardiac injection of sodium lactate temporarily restored ventricular beating.

Sodium lactate was administered to three cases of complete A-V heart block. In one of these the patient presented a ventricular rate of 15 per minute, widened QRS complexes and a state of shock. Sodium lactate increased the ventricular rate to 60 per minute and increased the blood pressure to 120 to 140 systolic with resultant marked improvement in the patient's clinical state. The widened QRS complexes were significantly narrowed. Decrease in the rate of administration or cessation of administration of the lactate solution on two separate occasions resulted in a return of the electrocardiogram to the control rate of 15 per minute. After five hours of administration the ventricular rate had increased to 60 per minute and was maintained without further lactate administration. About one hour later normal sinus rhythm was restored.

In a second case of complete A-V heart block (case 5), the ventricular and atrial rates were significantly increased following the administration of sodium lactate. In a third case of complete A-V heart block, with occasional normally conducted beats (case 6), the complete A-V heart block was abolished and the idioventricular beats were entirely replaced by normally conducted beats.

Sodium lactate appears to have marked qualities of increasing cardiac rhythmicity while possessing little or no pressor action. Our observations in the human subject and in the experimental animal suggest that this solution possesses qualities that should be of help in the prevention and therapy of sudden cardiac standstill. In addition, it did not produce dangerous ectopic rhythms.

The dose, method of administration and fate of the sodium lactate in the body is discussed.

The possible mechanisms by which the sodium lactate produces the effects described are outlined.

**Summario in Interlingua**

Es reportate le uso de solutiones molar e semi-molar de lactato de natrium in le tractamento de episodios de arresto cardiac, de inhibition ventricular in accessos del syndrome de Stokes-Adams, del lente rhythmio idioventricular in complete bloco atrio-ventricular, de reducete frequentia ventricular in partial bloco cardiac, e de bradycardia sinusal.

Post que, in un caso del syndrome de Stokes-Adams, epinephrina, Neosynephrina, e atropina
non habeva succedite, in le curso de repetite e prolongate accessos de inhibition ventricular, a restaurar le pulso ventricular, le administration intravenose de lactato de natrium in solutiones molar e semi-molar resultava in le restaura tion del pulso cardiac in dece episodios separate. Post duo horas le corde comenciava batter spontaneamente lo que continuava durante plure horas. In le caso de arresto cardiac terminal, le injection intracardiac de lactato de natrium restaurava le pulso ventricular al minus temporarimente.

Lactato de natrium eseva administrate in tres casos de complete bloco atrio-ventricular. In un de illos, le patiente presentava un frequen tia ventricular de 15 per minuta, allargate complexos QRS, e un stato de choc. Lactato de natrium augmentava le frequen tia ventricular a 60 per minuta e le systolic pression sanguinee a 120 o 140 mm Hg, con resultante marcate melioration del stato clinic del patiente. Le allargamento del complexos QRS eseva reducite significativamente. In duo episodios le reduction o cessation del administration de lactato de natrium resultava in un retorno al previe frequen tia ventricular de 15 per minuta. Post cinque horas de administration de lactato de natrium le frequen tia ventricular attingeva 60 per minuta e manteneva iste valor sin admini stration additional del solution. Circa un hora plus tarde le normal rhythm sinusual eseva restaurate.

In un seconde caso de complete bloco atrio-ventricular, le frequentias ventricular e atrial se augmentava significativamente post le ad ministration de lactato de natrium. In un terte caso de complete bloco atrio-ventricular, caracterisate per le occurrentia sporadic de complexos QRS apparentemente a conduction normal, le complete bloco atrio-ventricular eseva eliminata e le pulso idioventricular eseva complete mente reimplaciate per pulso a conduction normal.

Lactato de natrium pare haber un marcate capacitata a augmentar le rhythmicitate cardiac sin exercer multe o mesmo ulle action pressorial. Nostre observationes in subjectos human e in animales experimental pare indicar que le solution de lactato de natrium ha qualitates que promitte esser utile in le prevention e le therapia de subite inhibitiones cardiac. In plus, illo non producere periculose rhythmos ectopic.

Es discutite le dosages, le methodos de administration, e le destino ulterior de lactato de natrium in le corpore.

Le possibile mechanismos per que lactato de natrium produce le effectos describite es analy sate in lineas general.

ACKNOWLEDGMENTS

We wish to thank Drs. Henry L. Bockus and Joseph C. Yaskin of the Graduate Hospital of the University of Pennsylvania, and Dr. D. N. Kremer of the Philadelphia General Hospital for permission to study the cases on their services.

REFERENCES

26 RINGER, S.: A further contribution regarding the influence of the different constituents of the blood on the contraction of the heart. J. Physiol. 4: 29, 1883.
27 —: A Third contribution regarding the influence of the inorganic constituents of the blood on the ventricular contraction. J. Physiol. 4: 222, 1883.
28 —: Concerning the influence exerted by each of the constituents of the blood on the contraction of the ventricle. J. Physiol. 3: 380, 1882.
Treatment of Cardiac Arrest and Slow Ventricular Rates in Complete A-V Heart Block: Use of Molar and Half Molar Sodium Lactate: A Clinical Study
SAMUEL BELLET, FRED WASSERMAN and JEROME I. BRODY

Circulation. 1955;11:685-701
doi: 10.1161/01.CIR.11.5.685

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1955 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/11/5/685

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/