Ventricular Arrhythmias after Intravenous Sodium Lactate in Heart Block

By John F. Murray, M.D., and S. H. Boyer IV, M.D.

Molar sodium lactate has been described as a safe and effective agent in the treatment of bradycardia accompanying complete heart block. However, in 12 patients with heart block, hypertonic lactate infusions produced ventricular tachycardia in 6 and an increased idioventricular rate in only 4. Isopropylnorepinephrine was more effective and without such hazard. The effects of alkaloisis from molar lactate, 5 per cent sodium bicarbonate, and hyperventilation are compared. Of these 3, lactate was productive of the greatest ventricular acceleration.

SODIUM lactate has recently been advocated in the treatment of bradycardia and asystole associated with complete heart block. Bellet, Wasserman, and Brody reported that 13 out of 16 such patients responded with an increased ventricular rate following the intravenous administration of .5 or 1.0 M sodium lactate. The coincident appearance of ectopic beats was noted in only 1 patient of this group. These authors concluded that intravenously administered sodium lactate was more effective and less toxic than the more commonly used sympathomimetic and vagolytic drugs in the treatment of atrioventricular block.

This report describes the effects of .5 and of 1.0 M sodium lactate given to 12 patients with heart block. Contrary to previous studies, ectopic beats and ventricular tachycardia were often produced. Only 4 patients exhibited increased ventricular rate. Hypertonic sodium bicarbonate solution was given to 3 patients, and the effect is compared with that obtained with lactate. The effects of isopropylnorepinephrine and lactate are also compared. Other studies performed in an attempt to elucidate the mechanism of increase in the ventricular rate are included.

Materials and Methods

Eleven patients with complete atrioventricular dissociation and 1 patient with 2:1 block were given .5 and 1.0 M sodium lactate intravenously on 22 occasions. Age, sex, and presence or absence of syncope at the time of treatment are given in table 1.

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With the exception of patient 9 during his second trial of lactate, none of the patients was in overt heart failure when studied. All but 2 patients (8 and 9) are alive at the time of this report. Every patient except 4, 5, and 10 had experienced Adams-Stokes attacks prior to hospitalization. Slow idioventricular rhythm and asystole were mechanisms of syncope in patients 3, 7-9, 11, and 12. Patient 12 was the only one exhibiting a paroxysm of ventricular tachycardia in the control tracing.

Control electrocardiograms were obtained in all cases before lactate infusion. Nearly continuous recordings were made during and in most cases intermittently for at least half an hour after infusion.

Ten patients (1-3, 5, 7-12) received isopropyl-norepinephrine (Isuprel) sublingually. Patients 2, 5, and 7 were given 1 or 2 20 mg. doses of the drug. Patient 9 received 20 mg. every 1 to 2 hours when symptomatic; patient 10, 20 mg. every hour with gradual discontinuance the following week; patients 1, 3, 8, 11, and 12, 20 mg. every 3 hours.

Sodium bicarbonate as a 5 per cent solution was administered intravenously on 4 occasions to 3 patients (7, 8, and 11) who had previously received sodium lactate. The amounts given are shown in table 2.

Patients 9, 10, and 12 required external electric stimulation* of the heart, as described by Zoll and co-workers.7

Case Reports

Case 1. A 67-year-old white woman with known heart block of 4 years’ duration and repeated Adams-Stokes attacks, treated by ephedrine, experienced 4 attacks on the day of hospital admission.

An electrocardiogram on the day of entry showed complete heart block, idioventricular rhythm, and a

* The pacemaker used for this purpose was Model PM-65 of the Electrodyne Company, Norwood, Mass. This device has a monitor of ventricular rate that may be used automatically to signal an asystole of predetermined length and to start external stimulation.
TABLE 1.—Results with Lactate

<table>
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<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Syncope when treated</th>
<th>Ectopic beats/min. control</th>
<th>Hospital day</th>
<th>Lactate</th>
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<td></td>
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* Brief paroxysmal ventricular tachycardia.

Following a second infusion of 90 ml. of .5 M lactate, given in 7 minutes and begun 14 minutes after the end of the first infusion, ventricular tachycardia promptly developed. The ectopic beats disappeared within 5 minutes of stopping the infusion. With a final infusion of 80 ml. of .5 M lactate, given in 7 minutes and begun 10 minutes after the end of the second infusion, ventricular tachycardia reappeared within 4 minutes and persisted, on 1 occasion, for 30 seconds. At no time, with any of the infusions, was there an increase in basic ventricular rate.

The patient was given 20 mg. of isopropynoradrenaline every 3 hours during the remainder of her hospitalization and experienced no further syncopal attacks.

Case 2. A 65-year-old white woman with a history of bradycardia for 11 years, a myocardial infarction 3 years ago, and syncopal attacks for the last 3

TABLE 2.—Results with Five Per Cent Bicarbonate

<table>
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<th>Case no.</th>
<th>Vent. rate</th>
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paroxysm of 5 ectopic beats. The following day about 10 ectopic beats per minute (fig. 1A) were present just before the administration of 160 ml. of .5 M sodium lactate in 8 minutes. Three minutes after beginning this infusion paroxysms of ventricular tachycardia appeared (fig. 1B) that ended about 5 minutes after stopping the infusion (fig. 1D). Thereafter an occasional ectopic beat occurred.
years, was admitted to the hospital in a semistuporous condition and with congestive heart failure.

Complete heart block, atrial fibrillation, and an atrioventricular nodal rhythm of about 44 beats per minute were demonstrated by an electrocardiogram.

The patient was treated by phlebotomy, diuretics, and oxygen with moderate improvement. Intravenous atropine, 0.3 mg., produced vomiting and an increase in heart rate from 44 to 56 nodal beats per minute; 20 mg. of isopropylnorepinephrine had little effect.

On the second hospital day repeated electrocardiograms showed a nodal rate of 41 to 43 per minute and very rare ectopic beats. Three hundred milliliters of .5 M sodium lactate were given intravenously in 10 minutes. Although there was no change in nodal rate during or in 40 minutes following administration, ventricular ectopic beats, often bigeminal, appeared in the fourth minute of infusion and persisted for the next 4 minutes.

Two days later signs of a left cerebral vascular accident were noted. After 2 weeks' hospitalization the patient was discharged to her home without specific therapy for heart block.

Case 3. A 63-year-old white woman, known to have a slow pulse rate without syncope for the preceding 2 years, had repeated Adams-Stokes attacks on the day of hospital entry.

An electrocardiogram showed complete heart block without ectopic beats and an idioventricular rate of about 24 per minute, frequently interrupted by periods of asystole (fig. 2A) as long as 12 seconds in duration during which she convulsed. She was given 250 ml. of .5 M sodium lactate in 84½ minutes. Periods of asystole (fig. 2B) up to 24 seconds' duration continued to occur until the fifth minute of infusion. Thereafter ventricular ectopic beats appeared and steadily increased in frequency until the majority of beats were extrasystoles, often forming runs of ventricular tachycardia (figs. 2C and 2D). Sixteen minutes after completion of the lactate infusion and 5 minutes after receiving 20 mg. of isopropylnorepinephrine, the ventricular rate was 44 per minute with a varying R-R interval (fig. 2E).

The patient received 20 mg. of isopropylnorepinephrine every 3 to 4 hours and had no further Adams-Stokes during a 1-month period of observation.

Case 4. A 63-year-old white man, known to have had a myocardial infarction 12 years ago and complete heart block without syncope for 4 years, entered the hospital with congestive heart failure. He became essentially asymptomatic after treatment with digitalis, diuretics, salt restriction, and rest.

On the seventh hospital day an electrocardiogram showed complete heart block, an idioventricular rate of about 44 per minute, 3 different forms of QRS, and at the most 1 ectopic beat per minute. An infusion of 140 ml. of .5 M sodium lactate was given in 3 minutes. Within 2 minutes of beginning the infusion the majority of beats were ectopic and the patient complained of retrosternal pain. Seven minutes after stopping the infusion the number of ectopic beats had decreased to 8 per minute. The idioventricular rate, as calculated from the R-R
Case 5. A 40-year-old white woman was admitted to the hospital complaining of chest pain and mild breathlessness of 5 days' duration. She had received digitalis before admission.

Repeated electrocardiograms showed a ventricular rate of 30 to 50 per minute and varying, but always with second degree heart block. No consistent change in degree of block or ventricular rate was observed after oral potassium chloride, 1.0 mg. of subcutaneous atropine, 25 mg. of oral ephedrine, or 20 mg. of isopropylnorepinephrine. Following 0.5 mg. of intravenous epinephrine atrioventricular block changed from 4:1 to 2:1.

Patient became asymptomatic in the hospital and was discharged to her home. No definite diagnosis of underlying heart disease was made.

Three weeks after discharge she was given 160 ml. of 1.0 M sodium lactate in 8 minutes. A control electrocardiogram showed 2:1 atrioventricular block, with a ventricular rate of 41 per minute and no ectopic beats (fig. 3A). The 2:1 block 7½ minutes after beginning infusion persisted, but ventricular response had increased to 47 per minute. Almost immediately thereafter atrioventricular block became complete and a slow idioventricular rhythm appeared (figs. 3B and C). The lactate was stopped, but within a few seconds a paroxysm of ventricular tachycardia occurred (fig. 3D) and the patient complained of nausea and lightheadedness. The ectopic beats stopped and 2:1 block reappeared about 6 minutes after the end of the lactate (fig. 3E and F).

Case 6. An 80-year-old white man with known complete heart block for several years entered the hospital with mild congestive heart failure. Two episodes of syncope occurred in the preceding 5 years. Congestive failure responded fairly well to diuretics, salt restriction, and rest.

Just before the administration of molar sodium lactate on the fourth hospital day an electrocardiogram showed complete heart block, an idioventricular rate of about 46 per minute, with QRS of 2 different forms, and no ectopic beats. Administration of 140 ml. of molar lactate in 6½ minutes had no effect on the heart rate. No other cardioacceleratory drugs were given.

Case 7. A 75-year-old white man entered the hospital in a semicomatose condition, having had repeated convulsions on the day of entry.

An electrocardiogram showed complete heart block with many ventricular ectopic beats and an idioventricular rate of 36 per minute. Subsequently runs of asystole lasting as long as 1½ minutes appeared. Thereafter a variety of agents, including an unknown amount of molar sodium lactate, procaine amide, isopropylnorepinephrine, and potassium chloride, were given. Sixteen hours after entry the patient was conscious, the heart rate was 50 per minute, and Adams-Stokes attacks had stopped.

Fig. 3. Case 5. A. Control tracing showing 2:1 atrioventricular block and ventricular rate of 41 per minute. B. Seven minutes and 33 seconds after starting molar lactate at 20 ml. per minute. Note 2:1 block still present in first 2 ventricular complexes (ventricular rate 47 per minute); thereafter atrioventricular block increased and a slow idioventricular rhythm developed (third, sixth, and seventh beats). The fourth and fifth complexes are probably supraventricular in origin. C. and D. Continuous tracing beginning 7 minutes and 53 seconds after starting lactate. Note slowing of ventricular rate, ventricular ectopic beats, and paroxysm of ventricular tachycardia. The bar marks completion of 160 ml. molar lactate, given in 8 minutes. E. Six minutes after stopping lactate. Note reappearance of 2:1 atrioventricular block interrupted briefly by complete block and 2 idioventricular beats (third and fourth complexes). Ventricular rate, at end of strip, 48 per minute. F. One hour after E. Ventricular rate 42 per minute (first 2 complexes). Arrow marks held inspiration. The resultant equal slowing of atria and ventricles indicates 2:1 rather than complete atrioventricular block.

interval, at no time changed more than 2 beats per minute.

Half an hour after stopping the first infusion a second infusion of .5 M lactate was begun. Eighty milliliters were given in 3 minutes with a prompt increase in ectopic beats from about 10 to 15 to 23 per minute and reappearance of chest pain. Frequent ectopic beats persisted for half an hour.

On the eleventh hospital day a control electrocardiogram showed an idioventricular rate of 50 per minute and about 10 ectopic beats per minute. Two hundred and forty milliliters of .5 M lactate were given in 9½ minutes. At the end of this time ectopic beats were 2 per minute and idioventricular rate 43 per minute. Five minutes after stopping the infusion the patient had a brief paroxysm of 5 ectopic beats and complained of retrosternal pain. Thirty minutes after stopping the infusion ventricular rate had gradually increased to 46 per minute and ectopic beats had disappeared.

Throughout hospitalization chest pain was only experienced during lactate infusion. No other cardioacceleratory drugs were given.
At that time all medication was discontinued. A monitor-pacemaker was attached but no electric stimulation was given.

On the third hospital day 100 ml of molar sodium lactate were given in 10 minutes. A control electrocardiogram showed an idioventricular rate of 39 per minute and no ectopic beats (fig. 4A) during a 4-minute period. Four minutes after starting the infusion the ventricular rate, as calculated from the R-R interval, had slightly decreased (fig. 4B). Lactate was stopped upon the appearance of ventricular tachycardia (fig. 4C). Ectopic beats disappeared about 7 minutes after end of the infusion (fig. 4D and E). With recovery from ventricular tachycardia the ventricular rate increased to 44 per minute (fig. 4F).

The patient vomited blood on the twelfth hospital day, and a few hours later asystole developed. The heart beat was restored by a slap on the chest. Several blood transfusions were given during the next 24 hours.

On the fourteenth hospital day 200 ml of 5 per cent sodium bicarbonate were given in 13 minutes (table 2). The ventricular rate increased from 38 to 40 per minute. No ectopic beats appeared.

On the twenty-second hospital day 200 ml of molar sodium lactate were given in 10 minutes. The heart rate increased from 38 to 46 ventricular beats per minute. Only 2 ectopic beats were observed. Serial electrolyte and pH determinations were made (table 3).

When last seen on the thirtieth hospital day the patient had been transferred to the surgical service with a partial large bowel obstruction of unknown etiology. He remained free of syncopal attacks.

Case 8. A 67-year-old white man, known to have complete heart block for 3½ years and Adams-Stokes attacks for 6 months, entered the hospital because of increased frequency of syncopal attacks.

Isopropyl norepinephrine, 20 mg every 3 hours during waking hours, markedly diminished the frequency and severity of attacks.

On the fifth hospital day an electrocardiogram showed complete heart block, an idioventricular rate of 38 to 40 per minute, and 1 to 3 ectopic beats per minute. Half-molar sodium lactate, 325 ml, was given in 18 minutes. A maximum ventricular rate of 43 to 44 per minute appeared 5 minutes after the end of infusion and 1 ectopic beat per minute was present. Twenty-three minutes after completion of the infusion the rate had returned to 38 to 39 per minute.

On the seventh hospital day isopropyl norepinephrine was withheld for 4 hours. The ventricular rate was 15 to 17 per minute with periods of asystole up to 6 seconds in duration. No ectopic beats were present. The patient was conscious but very weak and faint. Then 120 ml of .5 M sodium lactate were given in 7 minutes. Within 3 minutes the ventricular rate was 29 per minute and the patient felt stronger. A maximum rate of 37 per minute appeared 3 minutes after stopping the infusion. Ten minutes later the rate had fallen to 32 to 33 per minute, at which time an additional 200 ml of .5 M sodium lactate were given in 12 minutes. A maximum rate of 41 per minute was attained 6 minutes after starting the infusion.

On several occasions administration of 20 mg of isopropyl norepinephrine increased ventricular rate by amounts varying from about 18 per minute to 30 per minute, within 3 to 4 minutes.

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**TABLE 3.—Electrolyte Studies in Case 7**

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<th>Time (min.)</th>
<th>pH</th>
<th>CO₂ (mEq./L.)</th>
<th>Na (mEq./L.)</th>
<th>K (mEq./L.)</th>
<th>Cl (mEq./L.)</th>
<th>Vent. rate per min.</th>
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**FIG. 4. Case 7. A. Control tracing. Ventricular rate 39 per minute. B. After nearly 50 ml molar sodium lactate in 4 minutes 45 seconds. Note ventricular rate, exclusive of ectopic beats, is slower than in control. C. Thirty seconds after completion of 100 ml molar sodium lactate in 10 minutes. Note paroxysms of ventricular tachycardia. D. Three minutes after completing infusion. New ventricular pacemaker 37 per minute. E. Eleven minutes after completing infusion. Note original pacemaker has returned at 38 per minute. F. Sixteen minutes after infusion. Ventricular rate 44 per minute.**
The patient was discharged from the hospital and was essentially asymptomatic while taking 20 mg. isopropylnorepinephrine every 3 hours.

He returned to the hospital for further study. Hyperventilation at 12 respirations per minute was performed for 3 minutes. Within a minute of starting this maneuver the ventricular rate increased from about 29 per minute to 37 per minute. Upon discontinuing hyperventilation the increased rate persisted for 9 seconds then was followed by a marked slowing of ventricular rate to 4 beats, with a new QRS form in the next 21 seconds, during which he had an Adams-Stokes attack. During this attack, at a time when ventricular rate was 15 per minute, an infusion of 185 ml. of 5 per cent sodium bicarbonate solution was begun that required 10 minutes for completion (table 2). Within 1½ minutes after beginning the infusion the original QRS form returned at 29 beats per minute. A maximum rate of 42 per minute appeared 3 minutes after completing the infusion and persisted for at least half an hour.

On another occasion intravenous administration of 250 ml. of 5 per cent sodium bicarbonate solution in 23 minutes caused the ventricular rate to increase from a control rate of 33 per minute to 42 per minute 18 minutes after starting the infusion.

Subsequently, on the same day 2 trials of hyperventilation at 12 respirations per minute caused prompt increase in ventricular rate from 31 to 36 and from 32 to 37 per minute. These effects disappeared within 2 to 5 minutes after stopping overbreathing and the rate returned to about 32 per minute.

Several months after these studies the patient died under circumstances unknown to us. At autopsy, coronary vessels were reported to be nearly normal.

**Case 9. A 71-year-old white man first developed complete heart block and Adams-Stokes attacks 1 year before the present entry. Following treatment with epinephrine and isopropylnorepinephrine his rhythm reverted to a sinoatrial pacemaker. He remained well until the day of his last entry, when he again had a syncopal attack and was found to have complete heart block. He was treated with 10 to 20 mg. of isopropylnorepinephrine every 1 to 2 hours and 0.3 mg. of atropine subcutaneously every 4 hours.

The rhythm included a period of complete heart block with a ventricular rate of 40 per minute, 2:1 block, and sinus rhythm. No ectopic beats were observed.

On the fifth hospital day isopropylnorepinephrine was omitted and 2½ hours later, during a syncopal episode, he was given 130 ml. of molar lactate, with an increase in ventricular rate from 27 to 43 per minute and an accompanying disappearance of symptoms. No ectopic beats were present. Twenty-nine minutes after the end of infusion the ventricular rate had decreased to 35 per minute. On the seventh hospital day acute pulmonary edema developed and was successfully treated by morphine, oxygen, and phlebotomy. On the eighth hospital day a long period of cardiac arrest appeared, and 200 ml. of molar sodium lactate, begun at once, was given intravenously in a 15-minute period. The external electric pacemaker was used at the same time as the lactate in order to facilitate circulation of the infused material. In spite of the infusion, discontinuance of the electric pacemaker resulted in asystole; pulmonary congestion that was present before the infusion increased.

The external pacemaker was employed almost continuously for the next 24 hours. Intravenous epinephrine was administered and 2:1 heart block reappeared. On the ninth hospital day asystole again appeared that was unresponsive to external stimulation and epinephrine. Permission for autopsy was refused.

**Case 10. A 42-year-old Negro with a history of paroxysmal tachycardia for 5 years entered the hospital with persistent tachycardia of several days' duration. More than 2.0 Gm. of digitalis leaf had been given in the 3 days before admission and 0.2 mg. of lanatoside C (Cedilanid) was given in the emergency room.

Electrocardiograms showed ventricular tachycardia of about 220 beats per minute. With the administration of a total of 1.0 Gm. of procaine amide intravenously the heart rate gradually slowed to 150 per minute. One hour later the patient suddenly convulsed and the electrocardiogram showed ventricular asystole. Repeated blows to the chest restored the heart beat momentarily. When this became ineffective direct stimulation of the myocardium with a needle with and without epinephrine produced ventricular contractions. A ventricular rate of 30 to 60 per minute was maintained by an infusion of about 2 to 4 µg. of epinephrine per minute. Complete heart block alternating with varying second degree block was present. The patient was conscious and comfortable. A pacemaker-monitor was attached.

Three hours after the development of asystole epinephrine was slowly discontinued and complete heart block became constant. Atropine, 1 mg. intravenously, had no effect. In the next 45 minutes the ventricular rate gradually decreased; when it was 19 per minute with the patient semiconscious, 130 ml. of molar sodium lactate were given in 9 minutes. During the infusion the ventricular rate continued to slow, and long asystoles, together with convulsions, developed. The external electric cardiac pacemaker was employed almost continuously for the next 15 minutes. Twenty milligrams of isopropylnorepinephrine were given; within 7 minutes the ventricular rate was 50 per minute.
TABLE 4.—Electrolyte Studies in Case 11

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Complete heart block, second degree block, and normal sinus rhythm were variously present for the next 4 days. Several episodes of asystole occurred during this time. Twenty milligrams of isopropyl-norepinephrine every hour were necessary for the first few days in order to prevent periods of asystole. The drug was gradually discontinued when normal sinus rhythm was persistent.

The patient was discharged after 3 weeks' hospitalization, asymptomatic and without medication.

Case 11. A 67-year-old man with known heart block and Adams-Stokes attacks for at least 3 years entered the hospital because of increasing frequency of syncope. Shortly after entry isopropyl-norepinephrine, 20 mg. every 3 hours, was begun; the ventricular rate increased from 36 to 40 per minute to 44 to 48 per minute and no further attacks appeared.

On the fourth hospital day 170 ml. of molar sodium lactate were given in 14 minutes. No other medication had been given in the preceding 3 hours. A control electrocardiogram showed complete heart block with an idioventricular rate of about 38 per minute and no ectopic beats. Ten minutes after stopping the infusion the ventricular rate had reached a maximum of 44 per minute. No ectopic beats appeared. Eighty-four minutes after beginning the infusion, heart rate had returned to control levels. Serial electrolyte and pH determinations were obtained (table 4).

The following day 185 ml. of 5 per cent sodium bicarbonate were given in 20 minutes (table 2). No other medication had been given in the preceding 6 hours. A control electrocardiogram showed an idioventricular rate of 36 per minute. The rate increased to 38 per minute 2 minutes after stopping the infusion.

Case 12*. A 73-year-old white woman with known complete heart block and repeated Adams-Stokes

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* We wish to thank Dr. George Schwartz, Brooklyn, N. Y., for allowing us to study this patient.
Cardia persisted but gradually decreased in frequency during the following 28 minutes. Suddenly the frequency and duration of the paroxysms increased and for the first time were associated with convulsions. It was then noted that the infusion was again flowing and that 75 ml. of molar lactate had inadvertently been administered to the patient in the preceding 7 to 10 minutes. For 20 minutes there were continued paroxysms of ventricular tachycardia and numerous accompanying convulsions. External cardiac stimulation with the electric pacemaker was applied during a brief period when idioventricular rate was about 48 per minute. Stimulation was continued for 2½ minutes at 60 beats per minute following which there were no further paroxysms for the next half hour. Several paroxysms without convulsions were noted over the next 13 hours but external stimulation was not required.

During the remainder of her hospitalization the patient received 20 mg. of isopropylnorepinephrine every 3 hours. The ventricular rate remained between 33 and 50 per minute with only occasional ectopic beats and no further Adams-Stokes attacks.

**Results**

**Lactate**

The results together with the amount and rate of lactate administration are listed in table 1. The responses may be conveniently divided into 4 categories, as listed below. Three patients (4, 7, and 9) exhibited a different response on successive occasions and therefore appear in 2 categories.

*Increased Ventricular Rate without Ectopic Beats.* Four patients are included in this group (8, all trials; 9, first trial; 7, second trial; and 11). Patients 8 and 9 were treated during syncopal episodes and responded with increased ventricular rates and cessation of symptoms; both had made equally prompt and satisfactory recoveries with isopropylnorepinephrine on previous occasions. Patient 9 was subsequently treated with 200 ml. of molar sodium lactate during bouts of prolonged asystole and failed to respond until stimulated with an external electric cardiac pacemaker. He is therefore also included in the last group.

*Increased Frequency of Ectopic Beats.* Two patients, 2 and 4 (first and second trials), had ventricular ectopic beats in the control electrocardiograms that increased in frequency and became multifocal. Ventricular tachycardia did not appear.

*Paroxysmal Ventricular Tachycardia.* The most striking effect was the production of frequent paroxysms of ventricular tachycardia in 5 patients (1, 3, 5, 7, and 12) on 9 occasions. Patient 4, who had previously manifested an increased frequency of ectopic beats (on 2 occasions) following lactate infusion, on the third trial had an initial decrease in ectopic activity and in the idioventricular rate followed by a single paroxysm of ventricular tachycardia 5 minutes after the completion of the infusion.

Patients 1 (fig. 1) and 12 (figs. 5 and 6) had ventricular ectopic beats in control tracings that increased in frequency during the infusion and were followed by ventricular tachycardia on 3 trials in both patients. Patients 5 (fig. 3) and 7 (fig. 4) showed no ventricular ectopic beats in control electrocardiograms taken for at least 4 minutes. Patient 3 (fig. 2) was having syncopal attacks and the control tracing was limited to 1½ minutes during which no ectopic beats were observed.

In 2 patients (1 and 12) there was no change in the ventricular rate, as calculated from the R-R interval and exclusive of ectopic beats, prior to the onset of ventricular tachycardia. In 3 patients (4, 5, and 7) there was a slowing in the idioventricular rate before the appearance of ventricular tachycardia. Patient 4 had a decrease from 50 to 42 beats per minute. Patient 5 (fig. 3) had an initial increase in the sinoatrial rate with a resultant change from 41 to 47 ventricular responses per minute; at the end of the infusion the existing 2:1 block suddenly became complete and a slow idioventricular rate developed that was rapidly followed by multifocal ectopic beats and short paroxysms of ventricular tachycardia.

Patient 7 (fig. 4) was given lactate on the third hospital day and responded initially with a decreased idioventricular rate followed by multifocal ectopic beats and ventricular tachycardia. Nineteen days later he was given twice as much lactate at twice the rate and responded with an increase in ventricular rate from 38 to 46 contractions per minute without the appearance of ectopic beats.

Only 1 (patient 3) of this group had an increase in idioventricular rate before developing ventricular tachycardia; however,
long asystoles continued to occur in this patient (figs. 2B and D).

In every patient except 12 (figs. 5 and 6) ventricular tachycardia disappeared within a few minutes of stopping the infusion. Patient 12 continued to have paroxysms of ventricular tachycardia and syncope for at least 13 hours after discontinuing the lactate therapy. Prior to this hospitalization, the mechanism of the Adams-Stokes attacks was thought to be asystole.

No Change or Slowing. Patient 6 showed no increase in the rate of ventricular contractions originating in 2 foci of nearly similar rate and seen in the control records. Patient 9 failed to respond on his second trial during bouts of asystole until external stimulation was applied as already described. Pulmonary congestion was present in this case and became worse following 200 ml. of molar sodium lactate. Patient 10 had a gradual fall in ventricular rate from 24 to 19 per minute during a 45 minute control period. Then 130 ml. of molar sodium lactate were given in 9 minutes to this patient. While the infusion was running, he had a prolonged period of asystole and a convulsion that lasted until external cardiac stimulation was applied.

Isopropylnorepinephrine

Isopropylnorepinephrine was without effect on the ventricular rate in patients 2 and 5. The drug was given in combination with too many other agents in patient 7 to be properly evaluated. Patient 9 had decreased frequency of Adams-Stokes attacks while receiving this drug. Patients 1, 3, 8, and 10–12 were completely free of syncopal episodes while receiving isopropylnorepinephrine in effective dosage.

In most cases where the drug was effective, 20 mg. every 3 hours by day was sufficient. In patient 8 administration before arising for nocturnal urination was necessary to prevent a syncopal attack that frequently occurred at that time.

In no case was an increased frequency of ectopic beats observed after the administration of isopropylnorepinephrine.

When compared with intravenous lactate, sublingual isopropylnorepinephrine was found equally effective in increasing ventricular rate in patients 8 and 11. In 4 patients (1, 3, 10, and 12) having no response or increased ectopic activity after lactate, isopropylnorepinephrine abolished Adams-Stokes attacks. In 2 patients (2 and 5) both drugs were ineffective. In no case where the 2 drugs could be compared was lactate effective and isopropylnorepinephrine ineffective.

Bicarbonate

Three patients (7, 8, and 11) received hypertonic sodium bicarbonate. The results are shown in table 2. Only in patient 8 was the increase in ventricular rate comparable to the change after hypertonic lactate. No ectopic beats were noted in any of the trials with bicarbonate.

Other Studies

Hyperventilation. A single patient (8) hyperventilated by increasing the depth of respiration, not the rate, for 3-minute periods. On 3 occasions, there was an increase in ventricular rate from 29 to 37, 31 to 36, and 32 to 37 per minute. However, 9 seconds after completion of the first hyperventilation period there was an abrupt slowing of ventricular rate to about 15 contractions per minute and syncope occurred. This phenomenon was not seen on the 2 subsequent trials following which the increased ventricular rate gradually returned to control levels in 2 to 5 minutes.

Electrolyte and pH Determinations. Arterial blood samples were obtained in cases 7 and 11 for determination of serial changes in carbon dioxide, sodium, potassium, chloride, and pH.* The results together with ventricular rates at appropriate intervals are presented in tables 3 and 4.

Discussion

The data presented show clearly that sodium lactate may cause undesirable ventricular

* Carbon dioxide was determined by the manometric method of Van Slyke and Neill; sodium and potassium were measured by flame photometry with an internal lithium standard; chloride was measured by the method of Schales and Schales; pH was obtained by Beckman glass electrode pH meter, model H-2.
ectopic activity ranging from increased frequency of ectopic beats to paroxysms of ventricular tachycardia. These deleterious effects were found on 13 occasions in 7 patients, and could not be uniformly related to the presence or absence of ectopic activity seen in records obtained prior to the administration of sodium lactate. Four of the 5 patients with ventricular premature contractions in control electrocardiograms exhibited an increase in ectopic beats. However, of the 7 patients without ventricular premature contractions before treatment, 3 showed the prompt appearance of multifocal ectopic beats and paroxysms of ventricular tachycardia.

In some instances, there was a relationship between the amount of sodium lactate given and the rate of infusion to the development of ventricular arrhythmias. Bellet, Wasserman, and Brody recommended that 20 to 80 ml. of molar sodium lactate be given in 1/2 to 2 minutes to patients having Adams-Stokes attacks; to asymptomatic patients, doses of 100 to 160 ml. of sodium lactate were to be given in 10 to 15 minutes. The reasons for a maximal rate of infusion were not discussed. Five of our patients (4, first trial; 5-7, second trial; and 12, first trial) were given lactate in excess of these recommendations. Three of the 5 persons exhibited transient increases in ectopic activity. Patient 12, however, revealed an equal tendency to develop ventricular tachycardia on 2 subsequent trials despite a decrease in the rate of infusion (figs. 5 and 6).

In patient 4, decreasing the rate of infusion decreased the frequency of ectopic activity. In patient 6, no change from control electrocardiograms was noted in spite of infusing molar sodium lactate at 22 ml. per minute.

Patient 7 clearly demonstrates that the rate and amount of molar lactate administered are not the sole factors responsible for the production of ectopic ventricular rhythms. Shortly before the time of initial study, intermittent syncopal attacks occurred. He responded to the administration of 100 ml. of molar sodium lactate with multifocal ventricular ectopic beats and paroxysms of ventricular tachycardia (fig. 4). The patient became asymptomatic after treatment with salt restriction and bed rest and was restudied after 19 days of this therapy. He was given twice as much molar sodium lactate (200 ml.) at twice the infusion rate as in the initial test, distinctly in excess of recommended dosage, and his heart rate increased from 38 to 46 beats per minute with only 2 ectopic beats noted early in the trial. It is obvious that reversible factors, probably originating within the myocardium, may profoundly alter the response to the lactate ion. It is not known what these factors are.

Four patients (3, and 8-10) were treated on 5 occasions during syncopal episodes associated with prolonged asystole or very slow idioventricular rates. In patient 3, ectopic beats appeared 5 minutes after beginning an infusion of .5 M lactate at nearly 30 ml. per minute; she was still asymptomatic at that point, having had a 24-second period of asystole in the minute preceding the ectopic beats. When given molar lactate at rates of flow and dosage greater than in patient 3, patient 9, in his first trial, had a prompt increase in rate of contractions without ectopic activity. Patient 9 on another occasion and patient 10 when initially treated failed to respond to the equivalent amounts and rates of infusion that produced ventricular tachycardia in patient 4. Patients 9 and 10 required external cardiac stimulation to maintain circulation. Perhaps the rates of infusion were inadequate in the latter cases to produce the desired effect; but it can be seen that equal amounts and rates of administration produce inconstant and possibly hazardous effects in different patients.

We have no explanation for the marked contrast between our results and those reported by Bellet, Wasserman, and Brody. Of their 16 patients with complete heart block, 13 had an increase in ventricular rate following lactate infusion and only 1 developed ventricular extrasystoles. No instances of paroxysmal tachycardia were noted in 30 additional patients with a variety of other types of cardiac rhythm. Ventricular ectopic beats appeared only 6 times in the total of more than 46 patients tested.

These authors contrasted the relative safety and efficacy of molar lactate with the dangerous effects produced by sympathomimetic agents,
particularly epinephrine. Ten of our patients received isopropylnorepinephrine, often in large doses; 7 of these responded with increased ventricular rate and without the development of ventricular arrhythmias.

Arterial blood samples obtained before, during, and after administration of molar sodium lactate demonstrated alkalosis and electrolyte shifts that are in no way different from those reported by Singer\(^8\) using hypertonic sodium bicarbonate and are in accord with the reports of others\(^4\) using molar sodium lactate. These results establish that there is nothing unique in the over-all effects of sodium lactate. An increase in heart rate was found on several occasions after hyperventilation in 1 patient and in 2 instances in the same patient following the administration of 5 per cent sodium bicarbonate. These limited observations suggest that alkalosis is the determining factor in producing the cardiac effects. However, mole for mole, bicarbonate does not affect the heart as strikingly as lactate. The latter is no better buffer or alkalinizing agent than sodium bicarbonate until metabolized to provide base and raise the pH. Since the myocardium has a very high capacity to utilize lactate,\(^10\) sodium lactate must alter its pH far more than equimolar doses of sodium bicarbonate, with a correspondingly greater change in cardiac irritability and rhythmicity.

**Summary**

Twelve patients with heart block and bradycardia or asystole were given .5 or 1.0 M sodium lactate on 22 occasions. Contrary to previous reports, molar sodium lactate was found to be much less efficacious and far more hazardous than isopropylnorepinephrine. Increased frequency of ectopic beats developed in 7 patients, of whom 6 developed ventricular tachycardia on 10 occasions. Many of these patients had idioventricular slowing before the appearance of tachycardia. Only 4 patients on 6 occasions had an increase in ventricular rate without developing ectopic beats.

The effects of hypertonic bicarbonate and hyperventilation were compared with the results of lactate infusion in a few patients. The greater magnitude of ventricular rate increase after lactate suggests that its rapid uptake and utilization by the myocardium promotes greater myocardial alkalosis and altered irritability.

**Summario in Interlingua**

Dece-duo patientes con bloco cardiac e bradycardia o asystole recipieva a 22 occasions administrationes intravenose de lactato de natrium de 0,5 o 1,0 M. In contrasto con previe reportos, lactato de natrium in solution molar se monstrava mucho minus efficace e mucho plus risose que isopropylnorepinephrina. Augmentate frequentias de pulsos ectopic se disveloppava in 7 patientes. Sex de istes disveloppava tachycardia ventricular a 10 occasions. Multes de iste patientes habeva retardation idioventricular ante le apparition del tachycardia. Solmente 4 patientes mostravara a 6 occasions un acceleration ventricular sin le disvelppamento de pulsos ectopic.

Le effectos de bicarbonato hypertonic e de hyperventillation eseva comparete in un certe numero de patientes con le resultatos del infusión de lactato. Le plus grande acceleration ventricular post lactato pare reflecter que su rapide acception e utilisation per le myocardio produce plus alte grades de alcalose myocardial e un alterate irritabilitate.

**REFERENCES**

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Medical Eponyms

By Robert W. Buck, M.D.

Durozlez' Sign. Paul Louis Durozlez (1826–1897) of Paris wrote of “The Intermittent Crural Double Murmur as a Sign of Aortic Insufficiency” (Du double souffle intermittent crural, comme signe de l'insuffisance aortique) in the Archives générales de Médecine, 5th series, 17: 417–443 (April), and 588–605 (May), 1861.

“The intermittent crural murmur always accompanies aortic insufficiency, and betrays it in difficult and complicated cases. It is the pathognomonic sign of this condition. Since this has never been said before by any author, I shall proceed to demonstrate the fact.... When the crural artery is compressed, the hand perceives a shock, or trembling; with the ear may be heard a bruit which may be represented by the sound toc or a peculiar murmur, the intermittent simple murmur.... If, after having compressed the artery for some little time, one slowly lessens the amount of compression, a splendid murmur will appear, especially in chlorotic subjects.... This is the continuous double murmur.

“But there is another murmur called the intermittent double murmur which is met in certain cases, to which we shall now give special study.... There are two methods of producing this double murmur, that is, with the stethoscope or with the hand. One presses gradually with the instrument until the artery is obliterated, and with a certain degree of pressure the double murmur appears... or one may apply pressure with the hand alternately both proximal and distal to the instrument with which no pressure is exerted. The proximal pressure produces the first murmur, and distal pressure produces the second murmur. This, however, can only be done when the second murmur is produced with unusual ease.”
Ventricular Arrhythmias after Intravenous Sodium Lactate in Heart Block

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