Interaction Between Plasma Potassium and Epinephrine in Coronary Thrombosis in Dogs

Huabao Lin, PhD; David B. Young, PhD

**Background** Both plasma potassium ([K]) and epinephrine concentrations have been known to increase during exercise and decrease rapidly shortly after exercise; in addition, it is also known that exercise can promote coronary thrombosis in human and animal subjects. Many studies have shown that epinephrine has a stimulatory effect on coronary thrombosis; however, little information is available concerning the effect of raising plasma [K] on coronary thrombosis. The present study was designed to investigate the effect of raising plasma [K] and its interaction with epinephrine infusion on coronary thrombosis.

**Methods and Results** A canine model of coronary thrombosis was used, and the frequency of cyclic blood flow reductions (CFRs) resulting from thrombus formation in the circumflex artery was analyzed in the study. By acutely raising plasma [K] to approximately 6.0 mEq/L, the frequency of CFs was reduced from 8.0±0.6 to 3.7±1.0 in 40 minutes (P<.01).

Epinephrine infusion (0.5 μg·kg⁻¹·min⁻¹) stimulated the frequency of CFs from 7.1±0.5 to 11.5±0.7 in 40 minutes (P<.01). However, if plasma [K] was raised to approximately 6.0 mEq/L while the epinephrine infusion was continued, the frequency fell from 11.5±0.7 to 7.7±1.1 in 40 minutes (P<.01).

**Conclusions** The present study demonstrated that acutely raising plasma [K] inhibited coronary thrombosis in dogs and also blocked the potentiating effect of epinephrine on coronary thrombosis. These findings may suggest that raising plasma [K] exerts a protective effect against coronary thrombosis and that a rapid decrease in plasma [K], such as that occurring shortly after exercise, facilitates coronary artery thrombosis when the artery has a preexisting pathological condition. (*Circulation, 1994;89:331-338.*)

**Key Words** • catecholamines • potassium • platelets • thrombosis

Exercise has been widely advocated and publicized because of its potential health benefits. However, sudden death during and shortly after exercise has repeatedly been reported.1-5 The precise mechanism of exercise-related sudden death is not fully understood, although ventricular arrhythmias are believed to be a major direct cause.6-9 It is well known from clinical observations and animal models that myocardial ischemia can trigger ventricular arrhythmias and that most myocardial ischemia is associated with atherosclerotic coronary heart disease. Data from previous reports have suggested that there was a strong relation between atherosclerotic coronary heart disease and exercise-related sudden death,3-6 particularly in those who were more than 30 years old at death. According to a study by Waller,3 69 of 72 subjects who died had evidence of atherosclerotic coronary heart disease, and the subjects had at least one of three major coronary arteries narrowed more than 75% by atherosclerotic plaque. Coronary thrombosis also plays a major role in sudden cardiac ischemic deaths. A study by Davies and Thomas10 found that among 100 subjects who died of ischemic heart disease, coronary artery thrombi were found in 74. In some cases of exercise-related sudden deaths as well, there is evidence to indicate that coronary thrombosis may play an important role.11,12 Ciampricotti and El Gamal11 suggested that physical exercise induced plaque rupture in the atherosclerotic narrowed coronary arteries, which could trigger coronary thrombosis. In addition, fresh thrombi in the coronary arteries were also found in some cases of exercise-related sudden death.5,12,13

Many physiological functions in the body undergo a great deal of change during exercise, and some of these may increase the risks of exercise-related sudden death. Several studies have demonstrated that plasma catecholamines can be elevated severalfold, including epinephrine and norepinephrine, and plasma potassium concentration ([K]) can be raised to a level from 5.5 to 7 mEq/L during vigorous exercise.14-20 After exercise, both plasma catecholamines and plasma [K] fall, with plasma [K] falling faster than the plasma catecholamine concentrations. Most of the increase in plasma [K] disappears within 2 to 3 minutes after exercise, although plasma catecholamine concentration has been reported to continue to rise further before returning to control levels.14,18 Such fluctuations can create a transient state in the first minutes after exercise in which high levels of plasma catecholamines concur with a relatively normal plasma [K]. It is well known that the period shortly after exercise is a vulnerable period for exercise-related sudden death.21 Goldschlager et al22 have found that ventricular arrhythmias in patients with coronary artery disease were much more common in the period shortly after exercise than during exercise, and most of the arrhythmias occurred within the first 3 minutes after exercise. It is possible that the transient state of elevated catecholamines with falling plasma [K] may increase the risks of sudden death in the postexercise period.

It is generally appreciated that increases in plasma catecholamines can stimulate platelet aggregation and

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coronary thrombosis. In several in vitro studies, catecholamines have been found to activate platelet aggregations. In vivo studies, Folts and Rowe found that epinephrine infusion could restore cyclic coronary blood flow reductions (CFRs), which were caused by periodic formations of coronary thrombi, after they were abolished by aspirin. Eidt et al demonstrated that treadmill exercise promoted CFRs in dogs with a critical stenosis of coronary artery and endothelial injury. They also found that the CFRs were associated with increases in plasma catecholamines. These findings strongly suggest that increases in plasma catecholamines have a stimulatory effect on coronary thrombosis. Yet, we are still uncertain of the importance of changes in plasma [K] and its interaction with plasma catecholamines in this event. Until now, little information has been available regarding the effects of increases in plasma [K] and interactions with catecholamines on coronary thrombosis. Therefore, the present study was designed to investigate the effects of acutely raising plasma [K] and epinephrine in controlled conditions to analyze their interaction on coronary thrombus formations.

Methods
The experiments were performed on mongrel dogs of either sex obtained from the research animal facilities of the University of Mississippi Medical Center (body weight, 19.6±0.6 kg; n=17). The animals were housed in the animal facilities before use and fed a standard laboratory diet. The food was removed from their cages 15 hours before surgery, but the dogs were given free access to water. The animals were initially sedated with 10 mg IM acepromazamine maleate. Ten minutes later they were anesthetized with approximately 30 mg/kg IV sodium pentobarbital.

Surgical Procedure and Experimental Measurements
After anesthesia, a respiratory pump was used to permit artificial ventilation through a trachea tube as needed to maintain normal blood gas values. Both femoral arteries and one femoral vein were cannulated with Tygon (Norton, Akron, Ohio) catheters. One arterial catheter reached the thoracic aorta and was used for measurement of arterial blood pressure. Other catheters were used for sampling arterial blood and for intravenous infusion. Blood pressure was determined by a pressure transducer (Cobe, Lakewood, Colo) that was placed at the same level as the dog's heart and connected to a polygraph (Grass Instrument Co, Quincy, Mass).

In the present study, a canine model with stenosed coronary circumflex artery plus damaged endothelium was used, which was initially described by Folts and coworkers. Folts et al also demonstrated that the CFRs in the model were abolished by aspirin but not by papaverine, nitroglycerin, and heparin. The cause of the CFRs in the model is generally recognized as cyclic formations of platelet thrombi in the coronary artery. This model has been widely used by others to study factors that can affect coronary thrombosis.

A left thoracotomy was performed through the fifth intercostal space, and the fifth rib was removed. The heart was exposed and suspended in a pericardial cradle. A catheter was inserted into the left atrium through the left auricle for the epinephrine or saline infusions. The coronary circumflex artery was gently isolated near its origin for 20 mm. An electromagnetic flowmeter (model FM-501, Carolina Medical Electronics, King, NC) was used to measure coronary blood flow. The flow probe was placed around the circumflex artery, and its size was appropriately selected so that it produced a tight fit on the artery. A section of the circumflex artery distal to the probe was compressed firmly to damage its endothelium, and a polished plexiglass constrictor was placed around the damaged section of the vessel. The constrictors were about 3 to 4 mm long and were made with a variety of internal diameters. The size of the constrictor was selected for each dog so that it produced a critical stenosis in the circumflex artery, but it usually did not reduce its resting flow. This maneuver abolished any increase in flow in response to the release of an upstream complete occlusion, ie, a reactive hyperemia. When an appropriate constrictor was placed on the damaged circumflex artery, a cyclic reduction in coronary blood flow occurred every 3 to 8 minutes, which indicated periodic formations of platelet thrombi in the coronary artery. After the blood flow reached near complete cessation, the thrombus was dislodged by gentle mechanical agitation and the flow immediately returned to the initial level. Then it started another cyclic reduction as a new thrombus formed. A portion of left anterior descending coronary artery (LAD) was also isolated. Another electromagnetic flow probe was placed around the vessel to measure normal coronary blood flow without a critical stenosis and damaged endothelium.

During the experiment, plasma sodium and potassium activities were measured by use of an ion-selective electrode Na-K analyzer (model Nova-1, NOVA Biomedical, Newton,

Table 1. Mean, SEM, and P Values for Comparison Between Control and KCl Infusion

<table>
<thead>
<tr>
<th></th>
<th>LAD, ml/min</th>
<th>Peak, ml/min</th>
<th>Hct, %</th>
<th>HR, bpm</th>
<th>BP, mm Hg</th>
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</thead>
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<tr>
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<tr>
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<td>53.0</td>
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<tr>
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<td><strong>KCl Infusion, mm Hg</strong></td>
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<td></td>
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<tr>
<td>Mean</td>
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<td>53.1</td>
<td>40.3</td>
<td>128</td>
<td>95.4</td>
</tr>
<tr>
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<tr>
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<td>NS</td>
<td>NS</td>
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</tr>
</tbody>
</table>

Control indicates control period; KCl infusion, KCl infusion period; LAD, coronary blood flow in the left anterior descending coronary artery; Peak, peak flow in the circumflex arteries; Hct, hematocrit; HR, heart rate; bpm, beats per minute; BP, arterial blood pressure; and NS, not significant.
Mass). The measurements were determined at approximately 5-minute intervals after KCl infusion. Blood gas measurements were also made with a pH/blood gas analyzer (model 1304, Instrumentation Laboratories, Lexington, Mass) to monitor the adequacy of artificial ventilation.

**Experimental Protocol**

Acute elevation of plasma [K]. The experiment was designed to investigate whether acutely raising plasma [K] has an effect on coronary thrombosis in dogs. In this experiment, each dog underwent two experimental periods, control and KCl infusion (n=10). After instrumentation of the circumflex artery, a stabilization period of approximately 20 minutes was observed before the start of a 40-minute control period during which the following variables were recorded: frequency of CFRs, maximum circumflex blood flow, heart rate, blood pressure, and plasma [K]. During the control period, a saline solution was continuously infused at a rate of 1.0 mL/min. At the completion of the control period, 12 mL of 1.0 mol/L KCl solution was slowly injected to raise plasma [K] to approximately 6.0 mEq/L, and then a continuous infusion of 250 mEq/L KCl solution was maintained so that the plasma [K] was kept at

![Graph showing arterial plasma potassium concentrations ([K]) of the control period, the epinephrine infusion period, and the epinephrine plus the KCl infusion period. As a result of the epinephrine (EPI) infusion, average plasma [K] was significantly reduced, from 3.52±0.06 (control period) to 2.73±0.04 mEq/L (epinephrine infusion period). Plasma [K] in the epinephrine plus KCl infusion period was raised to 5.94±0.15 mEq/L at the beginning of the experimental measurement.](image)
TABLE 2. Mean, SEM, and P Values for Control, Epinephrine Infusion, and Epinephrine+KCl Infusion Periods

<table>
<thead>
<tr>
<th></th>
<th>LAD, mL/min</th>
<th>Peak, mL/min</th>
<th>Hct, %</th>
<th>HR, bpm</th>
<th>BP, mm Hg</th>
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<td>Control</td>
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<tr>
<td></td>
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<td>Epi</td>
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<tr>
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<td>9</td>
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<tr>
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<td>45.3</td>
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<tr>
<td></td>
<td>(1:2) P</td>
<td>.01</td>
<td>NS</td>
<td>&lt;.01</td>
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<tr>
<td></td>
<td>(1:3) P</td>
<td>.01</td>
<td>NS</td>
<td>&lt;.01</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>(2:3) P</td>
<td>.05</td>
<td>NS</td>
<td>&lt;.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

Control indicates control period; Epi, epinephrine infusion period; Epi+KCI, epinephrine plus KCl infusion period; LAD, coronary blood flow in the left anterior descending coronary artery; Peak, peak flow in the circumflex arteries; Hct, hematocrit; HR, heart rate; bpm, beats per minute; BP, arterial blood pressure; and NS, not significant.

about 6.0 mEq/L throughout the experiment. After a stabilization of plasma [K], approximately 10 to 15 minutes, a second data collection of 40-minute duration was made with the same measurements as described above.

**Interaction between acutely raising plasma [K] and epinephrine infusion.** The experiment was designed to investigate the interactive effect between acutely raising plasma [K] and epinephrine on coronary thrombosis in dogs (n=7). In this experiment, a similar experiment was used as mentioned above, except three experimental periods were performed in each dog: control, epinephrine infusion, and epinephrine-plus-KCl infusion. In the epinephrine infusion period, epinephrine (Warner-Lambert Co, Morris Plains, NJ) infusion was given through a left atrial catheter at a rate of 0.5 μg/kg per minute. An infusion pump (Buchler Instrument, Inc, Fort Lee, NJ) was used for epinephrine infusion. In the epinephrine-plus-KCl infusion period, epinephrine infusion was also maintained at the rate of 0.5 μg/kg per minute, and meanwhile, KCl solution was administered through an intravenous infusion as previously described. Plasma [K] was maintained at a level of approximately 6.0 mEq/L.

**In vitro analysis of changes in [K] on platelet aggregation.** The experiment was designed to analyze the effect of changes in [K] on platelet aggregation in vitro. The experiment was conducted by using freshly collected human platelets from normal volunteers who had taken no medication or aspirin for 2 weeks (n=11). Ten-milliliter samples were drawn from the antecubital vein and placed immediately into a plastic centrifuge tube containing 10 mg EDTA and 25 U heparin. The blood was centrifuged at low speed (700g) for 5 minutes, and the supernatant platelet-rich plasma (PRP) was transferred to polypropylene tubes, which were held at room temperature until 2 minutes before addition of the agonist.

The platelet aggregational responses were determined in 500-μL volumes of mixtures of one part PRP and three parts buffer solution in siliconized cuvettes. The final platelet count was between 4×10^6 and 6×10^6. After 2 minutes in a heating block at 37°C, the cuvettes were transferred to the well of the aggregometer (Bio/Data aggregation profiler, model PAF-4), and 25 μL of agonist in buffer was added to them. Optical density was followed for 5 minutes or until a plateau was reached. The peak value as read by the machine was recorded. The 100% value was that read from a mixture of platelet-poor plasma from the subject and buffer solution.

The buffer solutions were designated K1, K2, and K3 and were identical except for the [K]. The solutions contained the following: sodium ion, 140 mEq/L; calcium ion, 1.4 mEq/L (Nova 2, Nova Biomedical, Newton, Mass); magnesium, 1 mEq/L; HEPES, 14.5 mEq/L; glucose, 6 mEq/L; apyrase, 1.0 U/L (grade VII, low ATP/ADP-ase activity ratio, Sigma Chemical, St. Louis, Mo); mannitol as needed to adjust osmolarity to 300 mOsM/L. The pH was adjusted to 7.30, and [K] was adjusted to 1.0, 6.0, and 10.0 mEq/L for K1, K2, and K3, respectively. When the buffer solutions were mixed with the PRP, the [K] levels for the mixtures were approximately 2.0, 5.5, and 8.0 mEq/L, respectively. The ion activities in the cuvettes were analyzed at the completion of the study. Bovine thrombin (thrombin reagent, Baxter Diagnostics, Inc, Deerfield, IL) was used as an agonist in experiments with platelets from 11 subjects.

**Data Analysis**

Group means and SEMs are presented in the text and in the figures. Statistical comparisons of all the data were performed with a single-factor ANOVA. The Dunnett test was used post hoc to determine the statistical probability of differences between the individual means. A value of P<.05 was accepted as indicating statistically significant differences. A value of P<.01 was also indicated in the results.

**Results**

**Effect of Acutely Raising Plasma [K] on Coronary Thrombosis**

In this experiment, plasma [K] was 3.53±0.05 mEq/L in the control period, and it was raised to approximately 6.10±0.09 mEq/L in the KCl infusion period. Plasma [K] was stable throughout the experiment (see Fig 1). Table 1 shows that heart rate, hematocrit, and arterial blood pressure were not different between the control period and KCl infusion period. Peak blood flow in the circumflex artery was also not significantly different between the two periods. Acutely raising plasma [K] usually caused a transient increase in blood flow in the LAD, but the increase did not last more than 5 minutes. During the period of measurement, blood flow in the LAD was 54.0±2.2 mL/min in the control period and 52.5±2.6 mL/min in the KCl infusion period (P>.05). A blood flow recording showing the CFRs in response to acutely raising plasma [K] is presented in Fig 2. As a result of the elevation in plasma [K], thrombus formation in the circumflex coronary artery was significantly inhibited. Frequency of the CFRs was decreased from 8.0±0.6 to 3.7±1.0 in 40 minutes (P<.01), a >50% reduction apparently caused by acutely raising plasma [K] (see Fig 3).

**Interaction Between Acutely Raising Plasma [K] and Epinephrine Infusion on Coronary Thrombosis**

Fig 4 shows plasma [K] in the three different periods. As a result of the epinephrine infusion, plasma [K] was significantly decreased, from 3.52±0.06 to 2.73±0.04 mEq/L (P<.01). Plasma [K] in the epinephrine-plus-KCl infusion period was elevated to approximately 5.94±0.15 mEq/L and was maintained throughout the experiment. Table 2 shows that blood flow in the LAD and the hematocrit were significantly elevated, but arterial blood
pressure was slightly reduced as a result of epinephrine administration. Blood flow in the LAD was further increased in the epinephrine-plus-KCl infusion period compared with that in the epinephrine period \((P<.05)\). The increase lasted throughout the experiment.

A blood flow recording showing the CFRs in response to epinephrine and epinephrine-plus-KCl infusions is presented in Fig 5. The data shown in Fig 6 demonstrate that epinephrine infusion significantly stimulated coronary thrombosis. The frequency of CFRs was increased by more than 60%, from 7.1±0.5 to 11.5±0.7 in 40 minutes after administration of epinephrine \((P<.01)\). However, as a result of raising plasma \([K]\) to approximately 6.0 mEq/L while epinephrine was continuously administered, the frequency of CFRs was significantly reduced, from 11.5±0.7 to 7.7±1.1 in 40 minutes \((P<.01)\). The frequency of CFRs was not significantly different between the control period and epinephrine-plus-KCl infusion period \((P>.05)\).

**Effect of Increases in \([K]\) on Platelet Sensitivity to Thrombin In Vitro**

In this experiment, thrombin was used as an agonist to determine the sensitivity of platelet aggregation in the three different levels of \([K]\). Six doses of thrombin from 2 to 12 U/mL were selected to perform the experiment. The mean and SEM for all 11 subjects are presented in Table 3. At 2.0 and 4.0 U/mL of thrombin, there was no effect of changing \([K]\) on the platelet aggregational response. However, at 6.0 and 8.0 U/mL, higher \([K]\) exerted an inhibitory effect on the platelet responses to thrombin. The greatest response was observed in the 6.0-U/mL group; the platelet response to the agonist in the K1 buffer was 52% greater than the response to the same level of agonist in the K3 buffer \((P<.01)\), and it was approximately 25% greater than the response in the K2 buffer \((P<.01)\).

**Discussion**

The present study has demonstrated that acutely raising plasma \([K]\) within a physiological range has an inhibitory effect on coronary thrombosis and blocks the potentiating effect of epinephrine on coronary thrombosis in dogs. The finding suggests that acute elevations in plasma \([K]\) may have a protective effect against coronary thrombosis in some conditions, such as strenuous exercise.

In the present study, plasma \([K]\) was raised to approximately 6.0 mEq/L from the normal \([K]\) level through an
intravenous system. This increase in plasma [K] is considered as a level within a physiological range and is observed in some human subjects during vigorous exercise.\(^{14,16,20}\) Our previous studies also showed that the increase in plasma [K] within this level in dogs and rabbits did not significantly alter major cardiovascular functions, such as heart rate and blood pressure.\(^{38,39}\) However, the present study demonstrated that it has a strong impact on coronary thrombosis. The frequency of CFRs was reduced more than 50% after plasma [K] was raised to approximately 6.0 mEq/L. This inhibitory effect on coronary thrombosis suggests that the acute elevation of plasma [K] during exercise may provide protection against arterial thrombosis. Although the importance of the inhibitory effect in physiological and pathological conditions is still uncertain, it appears that the effect may be important during and immediately after exercise. The present study did not directly deal with exercising subjects; however, the data are relevant to the mechanisms of thrombosis during exercise because elevations of plasma [K] and epinephrine concentration are commonly observed in exercise.

The present study also demonstrated that acutely raising plasma [K] not only inhibits coronary thrombosis but also blocks the potentiating effect of epinephrine on coronary thrombosis. The frequency of CFRs was increased more than 60% as a result of epinephrine infusion, but the increase was almost prevented by acutely raising plasma [K]. The stimulatory effect of epinephrine on coronary thrombosis in the present study is consistent with the results of previous studies.\(^{29,30}\) The effect of epinephrine is believed to be related to a direct action on the platelets.\(^{23-28}\) The results in this study showed that acutely raising plasma epinephrine significantly raised coronary blood flow in the LAD, by more than 20%, which suggests that increases in shear stress in the coronary artery may participate in stimulation of coronary thrombosis, because shear stress has been known to stimulate platelet aggregation.\(^{40}\)

Since acutely raising plasma [K] can block or impair the stimulatory effect of epinephrine on coronary thrombosis, the interactive effect may have a strong impact on exercise-related sudden death. Previous data have suggested that many victims of exercise-related sudden deaths had advanced atherosclerotic coronary heart disease,\(^{3-6}\) although often they experienced no prior symptoms. It is well documented that the patients with narrowed coronary arteries from atherosclerotic plaque can develop myocardial ischemia and trigger ventricular fibrillation during exercise by coronary spasm or coronary thrombosis or both.\(^{7,11,41,42}\) Ciampricotti et al.\(^{41}\) have hypothesized that active repeated coronary spasm during exercise could provoke fissuring or rupture of atherosclerotic plaques leading to coronary thrombosis and occlusion of the coronary artery. Postmortem studies have confirmed that coronary arterial thrombi are found in some victims of exercise-related sudden deaths.\(^{2,5,13}\) In an animal model, Eidt et al.\(^{43}\) also found that exercise promoted coronary thrombosis in dogs when the coronary artery was stenosed and the endothelial cells were damaged. Therefore, it is reasonable to believe that coronary thrombosis may play a significant role in exercise-related sudden death. During vigorous exercise, many factors, such as plasma catecholamines and shear stress, are elevated, and they may favor coronary thrombosis when the coronary artery has a preexisting pathological change. Because plasma [K] is increased during exercise, it may exhibit a protective effect against coronary thrombosis. This effect may offset those factors favoring thrombosis. How-

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**TABLE 3.** Mean, SEM, and P Values for the Effect of Changes in Potassium on Platelet Aggregation in Response to Thrombin

<table>
<thead>
<tr>
<th>Thrombin, U/mL</th>
<th>2.0</th>
<th>4.0</th>
<th>6.0</th>
<th>8.0</th>
<th>10.0</th>
<th>12.0</th>
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</thead>
<tbody>
<tr>
<td>Aggregation (100%)</td>
<td></td>
<td></td>
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<tr>
<td>K1</td>
<td>21.7±4.7</td>
<td>26.6±7.9</td>
<td>62.8±8.0</td>
<td>83.0±6.0</td>
<td>85.7±3.9</td>
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<tr>
<td>K2</td>
<td>19.0±4.5</td>
<td>25.8±7.9</td>
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<td>95.1±3.1</td>
</tr>
<tr>
<td>K3</td>
<td>22.0±5.0</td>
<td>25.0±7.0</td>
<td>41.2±9.0</td>
<td>70.7±6.9</td>
<td>81.7±5.4</td>
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<td>NS</td>
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<td>&lt;.01</td>
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<tr>
<td>P (K1:K3)</td>
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<td>NS</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
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<td>NS</td>
<td>&lt;.05</td>
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</tbody>
</table>

K indicates potassium concentration; K1, 1.92±0.04 mEq/L; K2, 5.47±0.04 mEq/L; and K3, 8.30±0.05 mEq/L.
ever, shortly after cessation of exercise, when plasma [K] falls more rapidly than catecholamines, the protective effect from high plasma [K] disappears and the stimulatory effects from catecholamines and other factors are further exposed, increasing the risks of coronary thrombosis.

The present study also found that acutely raising plasma [K] elevated coronary blood flow in the LAD, even though epinephrine infusion had already raised the blood flow. This may imply that a rapid fall in plasma [K] shortly after exercise not only facilitates coronary thrombosis but also may reduce coronary blood flow, thereby exacerbating cardiac ischemia.

To gain information concerning the mechanism of the observed inhibitory effect of elevation of plasma [K] on thrombus formation, we conducted a preliminary investigation of the effect of potassium concentration on platelet sensitivity. We chose the prototypical platelet agonist, thrombin, for our first study. Bovine thrombin was used in this first group, resulting in concentration-response relations to the right of those obtained by others using human thrombin. In addition, our use of EDTA rather than citrate to remove calcium from the blood sample shifted the relation further to the right. These aspects of our technique do not impair analysis of the effects of changes in potassium within the experiment, although they do complicate comparison of our results with those of others using different procedures. The initial results reported here suggest that increases in potassium concentration within the physiological range significantly reduce platelet sensitivity to thrombin. If sensitivity to other agonist is reduced by potassium elevation, the effect may be part of the mechanism involved in the reduction in thrombus formation observed in the present work.

In summary, the present study demonstrated that acutely raising plasma [K] inhibited coronary thrombosis in dogs. The inhibitory effect also could block or impair the potentiating effect of epinephrine on coronary thrombosis. In addition, acutely raising plasma [K] could further increase coronary blood flow in the presence of a high level of epinephrine. The findings suggest that the elevation of plasma [K] during exercise may provide protection against coronary thrombosis in a vigorous exercise condition. A rapid decrease in plasma [K] such as that occurring at the cessation of exercise may facilitate coronary thrombosis and contribute to cardiac ischemia. Because of these factors, avoiding sudden cessation of exercise can be beneficial for those engaging in vigorous exercise.

Acknowledgment

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References

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