Rapid changes in plasma potassium during a game of squash

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SUMMARY
1. The game of squash has recently been associated with a high incidence of ventricular arrhythmias and sudden death. To investigate this further, plasma catecholamines and potassium (K+) were monitored during a game of squash in six normal volunteers.
2. No cardiac arrhythmias were seen in this study despite the subjects reaching maximum heart rates of 181 ± 5 beats/min (mean ± SEM).
3. During exercise, plasma K+ rose from 3.82 ± 0.16 to 4.29 ± 0.2 mmol/l and after 90 s rest this fell to 3.68 ± 0.28 mmol/l and after 180 s to 3.44 ± 0.17 mmol/l. This rapid K+ shift could not be accounted for by generalized changes in venous acid-base status or by changes in venous plasma catecholamines. Although pretreatment with a β-antagonist caused the overall plasma K+ levels to be higher, it had no significant effect on the fall in plasma K+ after exercise.
4. Such rapid K+ shifts after exercise might contribute to arrhythmogenesis in susceptible individuals. The precise mechanism of the fall in K+ after exercise remains undetermined, but it seems not to involve catecholamines stimulating β1-adrenoceptors and is more likely to be due to increased skeletal muscle blood flow and/or intracellular acidosis.

Key words: adrenaline, arrhythmia, noradrenaline, potassium.

Abbreviations: ECG, electrocardiogram.

INTRODUCTION
The game of squash has become increasingly popular over the last few years. With this, however, has come a disturbing growth in the number of sudden deaths associated with this sport [1]. In addition, Northcote et al. [2] have recently documented a high incidence of ventricular arrhythmias in healthy volunteers during a game of squash.

One possible mechanism for such an effect relates to plasma adrenaline, which is known to be elevated during physical exercise. Adrenaline is not only arrhythmogenic per se but also causes profound hypokalaemia, which could be arrhythmogenic [3]. This latter effect is, however, complex in that adrenaline causes potassium (K+) influx in skeletal muscle by stimulating β2-adrenoceptors while also causing K+ efflux from cardiac muscle [4–6].

It is well known that skeletal muscle itself releases considerable amounts of K+ into the circulation during exercise [7]. It is quite possible that adrenaline-induced K+ influx in skeletal muscle is a mechanism which has evolved to replenish skeletal muscle K+ content and/or to prevent life-threatening hyperkalaemia during prolonged exercise. However, it may be that one price to pay for these considerable exercise-induced K+ shifts is electrical instability of the heart. We have therefore now performed a study to examine the inter-relations between K+, catecholamines and electrocardiogram (ECG) abnormalities in squash players and have examined the effect of blocking adrenaline-induced hypokalaemia with a β2-antagonist on these metabolic effects.

METHODS
Six normal male non-smoking volunteers were recruited from staff of the Royal Postgraduate Medical School. They were aged 27–45 years (mean 33 years) and had no family history of premature sudden death. They had normal biochemistry, haematology, chest X-rays and resting ECG. They had all played squash regularly at least twice monthly for 1 year. None of the players was receiving drugs. The study was approved by the local research and ethical committee and written informed consent was obtained from each volunteer.

Each subject was studied on two occasions and on both occasions the squash game began at 14.30 hours after a light lunch with no caffeine-containing drinks. One hour
before commencement of the game, they were given 25 mg of ICI 118551 (a specific β₂-adrenoceptor antagonist) in syrup form or a matching placebo syrup in a randomized double-blind fashion. An intravenous cannula (Venflon) was then inserted into a superficial vein in the mid to distal forearm of the non-playing arm and was secured in place with elastoplast. A superficial vein was chosen to minimize the effect of K⁺ extraction by deep tissues. Ambulatory ECG monitoring was performed with a Medilog-1 system which was firmly taped to the anterior chest wall. Recording began at least 10 min before the squash game and continued for at least 30 min after each game.

At 14.30 hours, the subject under study had a pre-game blood sample taken and immediately thereafter began a 10 min warm-up period in the squash court of Hammersmith hospital. On each occasion, his opponent was of similar ability and each subject played the same opponent on his 2 study days. A third person (investigator) stood at the back of the court in order to take rapid blood samples without interfering with the overall game. At the end of each set (nine winning points), a blood sample was taken as soon as possible. The delay at this stage was of the order 3 s. The game was deliberately halted for 3 min and further blood samples were taken 90 s and 180 s after exercise. The procedure was repeated after each set of nine winning points so that three to four groups of three blood samples were collected from each subject on each study day. Each set of nine winning points lasted for approximately 3

Plasma K⁺ from the end of exercise to 90 and 180 s after exercise were also analysed by analysis of variance to look for a significant trend with time and a significant difference between drug treatments.

RESULTS

Fig. 1 shows the peripheral plasma K⁺ measurements. A burst of physical exercise was associated with an increase in plasma K⁺ which was rapidly reversed within 90 s after exercise. On the ICI 118551 study day, the overall K⁺ profile was set significantly higher (\( P < 0.01 \), analysis of variance). The change in plasma K⁺ after exercise showed the expected significant change (\( P < 0.01 \), analysis of variance) over time but no significant difference between the two drug pretreatments.

As expected, plasma noradrenaline and adrenaline were above the normal range during exercise (Table 1).

Venous blood gases showed that acid-base status changed little in the crucial 90 s after the end of exercise (Table 1). Although oxygenation of the blood increased at this time, this had little effect on blood pH, which in this situation appears to be successfully buffered. Pretreatment with ICI 118551 had no effect on venous blood gases.

The maximum heart rate reached during exercise was 181 ± 5 beats/min (mean ± S.E.M) on the placebo study day and 175 ± 5 beats/min on the ICI 118551 study day. Since maximum heart rates during exercise are normally taken to be (200 minus age) beats/min, these subjects were exercising close to their own individual physical limits. This suggests that ICI 118551 was producing no discernible β₂-adrenoceptor blockade although this dose has previously been shown to produce β₂-adrenoceptor blockade [9]. The ambulatory ECG monitoring showed that sinus tachycardia was the only heart rhythm found in

![](Plasma_K_+_response_mean_+_SEM_to_a_game_of_squash_with_(X)_and_without_(•)_pretreatment_withICI_118551_in_six_normal_male_volunteers.png)

**Fig. 1.** Plasma K⁺ response (mean ± S.E.M) to a game of squash with (×) and without (•) pretreatment with ICI 118551 in six normal male volunteers.
this study. No extrasystoles either of ventricular or supraventricular origin were detected in this study.

**DISCUSSION**

There are a great deal of previous data on the haemodynamic, acid–base and plasma K⁺ changes during bicycle exercise where muscular activity is constant throughout [10–12]. In many sports, including squash, the situation is very different and muscular activity is highly intermittent with bursts of fervent activity interspersed with relative immobility. This highly intermittent muscular activity is liable to be accompanied by equally intermittent periods of muscular K⁺ efflux, but all previous data on this topic relate to the constant muscular activity of bicycle exercise. In addition, these two forms of exercise differ in that, unlike squash, ventricular arrhythmias have not been found in short-term constant bicycle exercise.

This study has shown that during a competitive game of squash, there is a rapid fluctuation in plasma K⁺ in the 180 s after each burst of exercise. It is worth remembering that these fluctuations in plasma K⁺ will be repeated throughout the game due to the very intermittent nature of the muscular activity. Therefore in the 180 s after exercise, the circulating level of K⁺ fell from 4.29 ± 0.20 to 3.44 ± 0.17 mmol/l. It is also possible that our blood sampling missed the absolute minimum value of plasma K⁺. However, the fall which we observed represents the immediate loss of 20% of circulating K⁺ and indicates an extremely avid re-uptake mechanism. From measurements of arteriovenous K⁺ gradients after bicycle exercise, this avid re-uptake seems to occur mainly in skeletal muscle [13].

We found no arrhythmias during ambulatory monitoring in this study. This contrasts with Northcote et al. [2], who found ventricular arrhythmias in eight out of 27 subjects either during play or in the immediate period after exercise. It is worth noting that of these eight subjects, two gave a history of early myocardial infarction and four smoked more than 10 cigarettes per day. None of our subjects had any such coronary artery disease risk factor. This would appear to be the only difference between the study groups as both age and heart rate achieved during exercise were similar in both groups. It is possible therefore, that the squash-induced ECG abnormalities found by Northcote et al. [2] represent 'silent' coronary artery disease, although this was apparently not detected by subsequent maximal exercise ECG on a treadmill. In a subsequent study, however, Northcote et al. [14] have noted a high frequency of cardiovascular risk factors and prodromal symptoms in a group of 60 sudden deaths associated with squash playing.

Could the K⁺ changes which we found during squash contribute to the arrhythmias noted by Northcote et al. [2]? In general, the mechanisms leading to arrhythmogenesis are very poorly understood [15]. An intravenous infusion of K⁺ rapidly produces ectopic activity and ventricular fibrillation, due probably to loss of resting membrane potential, shortening of the action potential duration and blocking of the fast inward Na⁺ channel [16]. Furthermore, hypokalaemia is also known to promote ventricular arrhythmias both in normal hearts and after myocardial infarction [17–19]. In our study, it is not the magnitude of either the increase or decrease in K⁺ which is striking but rather the extreme rapidity at which K⁺ fluctuates within the normal range. Such rapid fluctuations in extracellular K⁺ probably also cause rapid changes in myocardial resting membrane potential, which is a major determinant of arrhythmogenic potential. Certainly, during constant bicycle exercise, there are

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### Table 1. Plasma catecholamines, blood glucose and blood gases at the end of a burst of exercise during a game of squash

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<thead>
<tr>
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<th>End of exercise</th>
<th>After exercise</th>
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<tbody>
<tr>
<td></td>
<td>90 s</td>
<td>180 s</td>
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<tr>
<td><strong>Placebo</strong></td>
<td></td>
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<tr>
<td>Plasma noradrenaline (µg/l)</td>
<td>1.4 ± 0.2</td>
<td>1.4 ± 0.2</td>
</tr>
<tr>
<td>Plasma adrenaline (µg/l)</td>
<td>0.40 ± 0.16</td>
<td>0.28 ± 0.19</td>
</tr>
<tr>
<td>Blood pH</td>
<td>7.33 ± 0.02</td>
<td>7.34 ± 0.02</td>
</tr>
<tr>
<td>Blood Po₂(kPa)</td>
<td>6.84 ± 0.75</td>
<td>9.69 ± 0.71</td>
</tr>
<tr>
<td>Blood PCO₂(kPa)</td>
<td>5.74 ± 0.7</td>
<td>5.14 ± 0.16</td>
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<tr>
<td>Bicarbonate (mmol/l)</td>
<td>22.4 ± 0.7</td>
<td>20.7 ± 1.0</td>
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<tr>
<td>Blood glucose (mmol/l)</td>
<td>4.0 ± 0.1</td>
<td>4.2 ± 0.1</td>
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**ICI 118551**

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<tr>
<td>Plasma noradrenaline (µg/l)</td>
<td>1.6 ± 0.2</td>
<td>1.1 ± 0.2</td>
</tr>
<tr>
<td>Plasma adrenaline (µg/l)</td>
<td>0.28 ± 0.12</td>
<td>0.22 ± 0.14</td>
</tr>
<tr>
<td>Blood pH</td>
<td>7.35 ± 0.02</td>
<td>7.35 ± 0.02</td>
</tr>
<tr>
<td>Blood Po₂(kPa)</td>
<td>7.35 ± 0.78</td>
<td>9.96 ± 0.57</td>
</tr>
<tr>
<td>Blood PCO₂(kPa)</td>
<td>6.04 ± 0.26</td>
<td>5.35 ± 0.12</td>
</tr>
<tr>
<td>Bicarbonate (mmol/l)</td>
<td>23.5 ± 3.7</td>
<td>22.7 ± 3.3</td>
</tr>
<tr>
<td>Blood glucose (mmol/l)</td>
<td>3.8 ± 0.1</td>
<td>4.2 ± 0.1</td>
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For normal resting values in our laboratory for plasma noradrenaline are < 0.8 µg/l and for plasma adrenaline < 0.2 µg/l [8].
major transient changes in T wave amplitude which are related, albeit imperfectly, to coincidental K+ changes [20]. Therefore at this point in time, any link between these K+ changes and arrhythmias is entirely speculative, but they are at least an intriguing observation deserving of further study.

There are, nevertheless, major limitations in the use of peripheral venous K+ levels as in this study. If cardiac arrhythmias are related to plasma K+ at all, then it is the arterial plasma K+ concentration which is most relevant. In addition, plasma K+ levels do vary in different parts of the circulation with variable K+ release and extraction by different tissues [21]. However, it was not practically or ethically possible for our volunteers to play a fully active game of squash with either an intra-arterial line or an intravenous long line in site. We did place our intravenous cannula in a superficial vein rather than a deep vein in order to partially overcome the problem of deep tissue K+ release/extraction. We must therefore accept the above practical limitation and try to estimate what kind of K+ changes would be occurring in myocardial tissue in our study. The exercising leg skeletal muscles will cause a bolus of K+-rich blood to be released and this will mix with venous outflow from other regions. This means that our peripheral venous K+ measurements will tend to underestimate the corresponding increase in myocardial extracellular K+, since myocardial tissue is much closer to the site at which the K+ bolus was released into the circulation [22, 23]. By contrast, the fall in K+ after exercise may well be less in the myocardium than in our peripheral measurements. This is because non-exercising arm skeletal muscle is known to avidly extract K+ at a site proximal to our sampling venous cannula [13]. Overall, therefore, the myocardium is liable to have been subject to a greater increase in K+ but a lesser fall in K+ than our peripheral measurements. The actual fluctuation in extracellular K+ may therefore have been similar in myocardial tissue as in our peripheral measurements.

The mechanism of this K+ re-uptake by muscle after exercise remains elusive, but our study has shown that adrenaline, which was a likely candidate, cannot be responsible. This is because the fall in plasma K+ after exercise was little affected by prior β2-adrenoceptor antagonism while the same dose of the same β2-antagonist has previously been shown to completely inhibit adrenaline-induced hypokalaemia in man [9]. This contrasts with constant bicycle exercise for 5–7 min where β2-blockade does blunt the return to baseline K+ [12, 24]. In our study, β2-adrenoceptors may be involved in K+ homeostasis in the medium term since the K+ profile after ICI 118551 was higher overall, but they would appear not to be involved in the minute-to-minute variations of plasma K+ after exercise. Our rapid fall in K+ is unlikely to be due to insulin, since insulin normally decreases during physical exercise [25]. We were unable ethically to sample arterial blood during squash but the lack of any change in venous pH measurements make it unlikely that generalized changes in acid–base balanced mediate this effect [26]. This is further supported by the observation of Coester et al. that increasing inspired CO2 and decreasing arterial pH have no effect on the fall in plasma K+ after exercise [20]. It therefore seems likely that this re-uptake of K+ is due to other factors. It should also be appreciated that this uptake mechanism is unusually active in this situation, since after squash plasma K+ overshoots to below baseline within 90 s, whereas after an intravenous infusion of K+ to normal volunteers the plasma K+ did not return to baseline even after 120 min [27]. The different rate of clearance of K+ between exercise and a K+ infusion at rest is probably due to two factors. First, exercise increases cardiac output which subsequently increases delivery to and blood flow through tissues which are able to actively extract K+. Secondly, the skeletal muscle membrane probably becomes more responsive to K+ influx during exercise and this is most likely to be due to localized acidosis developing within skeletal muscle [28]. Increased exchange between extracellular K+ and intracellular H+ may help normalize the intracellular pH during squash.

In summary, at the end of a burst of exercise during a game of squash, there is a rapid fall in circulating plasma K+ but this does not appear to be due to adrenaline. Although the suggested high incidence of ventricular arrhythmias during squash is bound to be multifactorial in origin, this rapid K+ shift might be a contributory element although probably only in susceptible individuals with 'silent' coronary artery disease.

ACKNOWLEDGMENTS

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REFERENCES


