The Royal Society of Medicine

International Congress and Symposium
Series · Number 44

ARRHYTHMIAS AND MYOCARDIAL INFARCTION

THE ROLE OF POTASSIUM

Published by The Royal Society of Medicine
1 Wimpole Street London
Academic Press · London · Toronto · Sydney
Grune & Stratton · New York · San Francisco

Royal Society of Medicine

International Congress and Symposium Series

Number 44

Arrhythmias and Myocardial Infarction: The Role of Potassium

Edited by
CLIVE WOOD AND WALTER SOMERVILLE
Assistant Editor YVONNE RUE

1981

Published jointly by
THE ROYAL SOCIETY OF MEDICINE
1 Wimpole Street London
ACADEMIC PRESS
London Toronto Sydney
GRUNE & STRATTON
New York San Francisco

ROYAL SOCIETY OF MEDICINE
1 Wimpole Street, London W1M 8AE

ACADEMIC PRESS INC. (LONDON) LTD.
24/28 Oval Road, London NW1 7DX

United States Edition published and distributed by
GRUNE & STRATTON INC.
111 Fifth Avenue, New York, New York 10013

Library of Congress Catalog Card Number: 80–42099
ISBN (Academic Press): 0–12–794911–9
ISBN (Grune & Stratton): 0–8089–1374–3

British Library Cataloguing in Publication Data

Arrhythmias and myocardial infarction. –
(International congress and symposium series/
Royal Society of Medicine, ISSN 0142–2367; no. 44)
1. Heart – Infarction – Congresses
2. Arrhythmia – Congresses
I. Wood, Clive II. Rue, Yvonne III. Royal Society of Medicine IV. Series
616.1′2 RC685.I6 80–42099

Printed in Great Britain at the Alden Press, Oxford

Contributors

T. R. Dyckner
Department of Internal Medicine, University of Umeå, Sweden

J. W. Hollifield
Specialized Center for Research in Hypertension, Vanderbilt University, Nashville, Tennessee, USA

D. E. Hyams
Merck Sharp & Dohme Research Laboratories, Rahway, New Jersey, USA

D. M. Krikler
Division of Cardiovascular Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London, UK

S. T. McCarthy
Department of Geriatric Medicine, Radcliffe Infirmary, Oxford, UK

J. C. Melby
Section of Endocrinology and Metabolism, Boston University School of Medicine, Boston, Massachusetts, USA

D. B. Morgan
University Department of Chemical Pathology, General Infirmary, Leeds, UK

T. O. Morgan
Division of Clinical Practice, Faculty of Medicine, University of Newcastle, New South Wales, Australia

J. E. Nordrehaug
Diakonissehjemmets Sykehus, Bergen, Norway

P. A. Poole-Wilson
Cardiothoracic Institute and National Heart Hospital, London, UK

L. E. Ramsay
Department of Therapeutics, The Royal Hallamshire Hospital, Sheffield, UK

R. J. Solomon
Division of Nephrology, Department of Medicine, Roger Williams General Hospital and Veterans Administration Medical Center, Providence, Rhode Island, USA

W. Somerville
Department of Cardiology, Middlesex Hospital, London, UK

Contents

Chairman's Introduction

W. SOMERVILLE

Department of Cardiology,
Middlesex Hospital, London, UK

This Symposium has been designed to focus attention on a single facet of myocardial infarction, disturbances of cardiac rhythm. Readers may well ask what more is there to say in the light of the vast amount of material written and discussed within the past decade. Yet the fact that the routine management of the acute attack differs so widely from centre to centre indicates clearly that no ideal standard drill exists. Uncertainty remains even at basic levels of prevention. Should prophylactic anti-arrhythmic drug treatment be given at the onset of the attack? Every affirmative opinion is counterbalanced by a negative. Are arrhythmias commoner at home or in the Coronary Unit? The very question triggers emotional answers from the ayes and nos.

The Organizers of this Symposium had the bright idea of singling out one thread of the tangled knot, potassium, for individual scrutiny. Popular attitudes towards potassium behaviour in normal and diseased states have swung widely since the writer was first involved with this mysterious element. In the early 1950s at the Peter Bent Brigham Hospital in Boston, a recrudescence of interest in potassium behaviour coincided with Professor George Thorn's researches in Addison's Disease and Dr J.P. Merrill's work on haemodialysis (Merrill *et al.*, 1950). A number of communications emerged of which the writer was a co-author, discussing the mechanisms whereby potassium excess or deficiency initiated a wide variety of ventricular and supraventricular arrhythmias (Levine *et al.*, 1951; Somerville *et al.*, 1951). Many of these concepts are still current, but the pathophysiology of potassium in myocardial ischaemia, the main focus of this Symposium, is now more firmly based. By the end of this Meeting, it may well be that some of its ramifications will still be obscure, but those who hear and subsequently read what has been said will certainly be more enlightened. With characteristic breadth of vision, the Sponsors have not concerned themselves with commercial interests. They have given free rein to a coterie of national and international experts and have not spared themselves in their efforts to throw light on the role of a lowered potassium in the genesis and aetiology of arrhythmias, both after an acute myocardial infarction and during the treatment of hypertension.

References

Levine, H. D., Merrill, J. P. and Somerville, W. (1951). *Circulation* **3,** 889.
Merrill, J. P., Levine, H. D., Somerville, W. and Smith, S. (1950). *Annals of Internal Medicine* **33,** 797.
Somerville, W., Levine, H. D. and Thorn, G. W. (1951). *Medicine* **30,** 43.

Arrhythmias and Myocardial Infarction: The Role of Potassium. Royal Society of Medicine International Congress and Symposium Series No. 44, published jointly by Academic Press Inc. (London) Ltd., and the Royal Society of Medicine.

Hypokalaemia and Diuretics

D. B. MORGAN

University Department of Chemical Pathology, General Infirmary, Leeds, UK

Hypokalaemia is without doubt the most widely recognized complication arising from the use of potent diuretics. It is regarded as an important complication because hypokalaemia, at least when severe, brings the risk of serious events such as cardiac arrhythmias, renal damage and muscular weakness. It is these risks which have led to the view that such hypokalaemia should certainly be corrected when it is detected and should preferably be avoided, either by the choice of diuretic or by adding some other treatment, such as potassium supplements. Hypokalaemia as a complication of diuretic therapy is defined as any plasma potassium level less than the lower limit of normal (say $< 3{\cdot}6$ mmol/l), whereas patients with the complications of hypokalaemia already mentioned usually have a much lower plasma potassium concentration, often $< 2{\cdot}5$ mmol/l.

There was a great deal of quantitative information on the effects of diuretics on plasma potassium available but it had not been collected and analysed before we attempted to do so (Morgan and Davidson, 1980). Table 1 shows our major conclusions and Table 2 gives the average fall in the plasma potassium level and the frequency of hypokalaemia after administering the commonly used diuretics frusemide and thiazides in patients with hypertension or chronic heart failure. In chronic heart failure, the plasma potassium level was higher before treatment, so that although it fell by the same amounts after treatment, treated patients with heart failure did not have such low plasma potassium levels as treated patients with hypertension. The values in treated patients with hypertension in Table 2 will be used as reference data for some of the arguments to be made in this presentation.

From these findings I would emphasize that the average fall in plasma potassium due to diuretics is small; that values less than 3·0 mmol/l are unusual, and there is not a linear relationship between the fall in the mean plasma potassium and the frequency of low values.

The fall in plasma potassium after thiazides is twice that after frusemide, whereas the frequency of hypokalaemia is three times greater. This relationship is discussed further by Morgan and Davidson (1980).

It can be argued that many of the data we have collected are not relevant to actual clinical practice. Many of the observations were made in "experimental situations" with regard to blood taking and most of them were in chronically ill patients in a "steady state" and not in patients in acute situations such as myocardial infarction. In addition, we did not take account of the effects of sex and age on the hypokalaemic influence of diuretics or of the effect of variation in plasma potassium on the assessment of changes in the plasma potassium levels in the individual. In relation to treatment, we assumed that prevention and correction of hypokalaemia were not

Arrhythmias and Myocardial Infarction: The Role of Potassium. Royal Society of Medicine International Congress and Symposium Series No. 44, published jointly by Academic Press Inc. (London) Ltd., and the Royal Society of Medicine.

Table 1

Conclusions from a survey of published data on diuretics and hypokalaemia (Morgan and Davidson, 1980)

Little information exists on diuretics other than frusemide and thiazides
Flat dose response curves are found for frusemide and thiazides
The plasma potassium falls in the first week of treatment with diuretics and then remains constant but low while treatment is continued
The fall in plasma potassium is greater after thiazides than after frusemide (in the commonly used dose)
The fall in the plasma potassium level is the same in hypertension as in cardiac failure but the pre-treatment and therefore the post-treatment values are higher in cardiac failure
Potassium supplements are relatively ineffective in correcting hypokalaemia

Table 2

Plasma potassium level (mmol/l) and frequency of hypokalaemia in patients with cardiac failure and hypertension before and after frusemide or thiazide diuretics (summarized from Morgan and Davidson, 1980)

	Cardiac failure			Hypertension		
	Before diuretics	Frusemide	Thiazide	Before diuretics	Frusemide	Thiazide
Mean potassium concentration	4·4	4·2	3·8	4·2	3·7	3·5
Fall in potassium concentration		0·2	0·6		0·5	0·7
% less than 3·6 mmol/l		5	25		25	48
% less than 3·0 mmol/l		0·2	4		2	7

basically different, but there is evidence that they might be. This presentation gives a brief review of the importance of some of these variables to our concepts of the relation between hypokalaemia and diuretics.

Effects of Sex and Age

It has been suggested recently in several reports that hypokalaemia is more common in women than men. This difference was noted in severe clinical hypokalaemia by Surawicz *et al.*, (1957) and Lawson *et al.*, (1979) in patients with hypokalaemia and myocardial infarction (Dyckner *et al.*, 1975) and it was seen to a striking degree in elderly patients given diuretics (Krakauer and Lauritzen, 1978).

We have recently completed a survey in Leeds (the *High Royds Survey*) of the

Table 3

Comparison of the effect of diuretics on the mean plasma potassium levels in men and women (mmol/l)

	Men				Women			
	None	Any	Fruse-mide	Thia-zide	None	Any	Fruse-mide	Thia-zide
Krakauer and Lauritzen (1978)	4·2	4·1			4·2	3·9		
High Royds Survey	4·1	4·0	4·0	4·0	4·1	3·8	3·9	306
Davidson *et al.* (1976)	4·2	4·1	4·2	3·9	4·1	3·9	4·0	3·7

nutritional state and drug toxicity in 1200 patients in a long stay mental hospital. As part of that survey we measured the plasma potassium levels in fasting patients, not given their morning tablets, and collected details of their drug treatments. Some of these data have been analysed and compared with those reported by Krakauer and Lauritzen (1978, Table 3). Most of the patients in both of these studies were elderly. The results are strikingly similar in the two studies and indicate that the fall in plasma potassium in patients given diuretics is much greater in women than men. Indeed, the fall in men is clinically negligible in both studies.

Most of the patients studied by Krakauer and Lauritzen were taking thiazides rather than frusemide but the results were not analysed separately for the two diuretics. We have done this for the High Royds Survey and the preliminary results suggest that the larger fall in plasma potassium after diuretics in women was almost entirely in those given thiazides, whereas frusemide had a smaller effect which was similar in women and men. The plasma potassium in the elderly women given thiazides was similar to that found in our previous review (3·6 mmol/l). In contrast, the fall in plasma potassium in men after diuretics was much less than was expected from our previous survey. The question which arises is whether the difference between men and women occurs only in the elderly, as most of the patients in the High Royds Survey are more than 60 years old. The results obtained so far indicate that this difference between the men and women is the same at all ages from 50–80 years.

Nevertheless, we were surprised by the result and have therefore looked in more detail at a previous survey we had performed on younger patients attending a cardiological outpatient clinic (Davidson *et al.*, 1976). We had noted that the plasma potassium level was lower in patients taking thiazides than in patients taking frusemide but we did not examine the results separately in men and women. When this is done (Table 3) the results agree closely with those from the High Royds Survey and suggest that the difference between men and women is in their response to thiazides. This sex difference is clearly important as it suggests that prevention of hypokalaemia is unnecessary in men, although it might simply indicate that men do not take their tablets as regularly as women.

The influence of age on the relation between diuretics and hypokalaemia will be discussed later in this Conference. But in the High Royds Survey, our results suggest that the plasma potassium increases with age and that the effect of diuretics on the plasma potassium does not change with age.

Individual Variation

There is little doubt that in the experimental and clinical situation the obtained value is usually regarded as the patient's "real" value. The implication is that any but the smallest change is a real and significant change in the patient's steady state. However, it is equally clear that there is considerable variation in the plasma potassium level within the individual (Morgan, 1978). There is not only variation during the day, but also from day to day. In our patients with heart failure, the average within-person standard deviation was 0·4 mmol/l, which is greater than that reported in healthy persons.

Factors which could contribute to this increased variation include greater difficulty in taking the blood sample, and greater variation in the plasma potassium level because of the acute effect of each diuretic tablet (Hang, 1976). One consequence of this variation is that only when the difference between two values on different days is of the order of 1 mmol/l is there an acceptable probability that the patient has changed, for example, as a result of treatment. The other consequence of this large within-person variation is that although a group has an average plasma potassium level which is low and similar on two occasions, this does not mean that the same patients will be hypokalaemic at these two moments (Morgan, 1978). The frequency of hypokalaemia in a group of patients is therefore an indication of the shift from normal in the group, but the presence of hypokalaemia in the individual is not a reliable guide to the drop in plasma potassium in that individual himself.

Correction versus Prevention

The general view has been that hypokalaemia should be prevented if possible, and corrected when it is found. However, the question of what value justifies treatment is one of the major issues of this Meeting. In the past it has often been any value less than the generally agreed lower limit of normal (3·6 mmol/l). Prevention and correction have been regarded as equivalent, in terms of what is required for success, even though prevention was thought preferable. There is a view, however, that correction is more difficult to achieve than prevention, and in particular that it requires higher doses of the chosen treatment and more time than would be expected. For example, Schwartz and Swartz (1974) found it difficult to correct the hypokalaemia in hypertensive patients who were taking chlorthalidone. Even 100 mmol of potassium/day was not adequate in some cases, whereas much smaller doses of potassium are regarded as adequate to prevent hypokalaemia if given from the beginning of treatment.

One reason for such a difference would be that hypokalaemia itself leads to a change in the renal handling of potassium, with a tendency towards a renal leak. Thus, a larger load of potassium is needed to achieve a particular plasma potassium level until the leak is repaired. This change certainly happens in severe hypokalaemia (Dickinson and Swaminathan, 1978) but it is not known whether it also happens in the lesser degrees of hypokalaemia due to diuretics.

Another possible explanation for a difference between prevention and correction of hypokalaemia after diuretics lies in the selection of patients. Prevention is applied to all patients given diuretics, whatever their plasma potassium levels, and the aim would be to prevent any change in the plasma potassium. This is quite different from the correction of hypokalaemia, where obviously the treatment is applied only to a sub-group of the population, i.e. those with a plasma potassium level less than some chosen value.

What is rarely discussed is what should be the expected result of treatment in this sub-group. The aim would presumably be to return these patients to the values they

had before treatment. What seems to be attempted and/or expected is that as a group they should have the same mean plasma potassium levels as untreated patients. Such an approach assumes that the sub-group before treatment had values throughout the whole normal range of plasma potassium, and that they have particularly low values as a result of variable falls in the plasma potassium level. However, a more detailed analysis of the available data suggests that those patients who have the lowest plasma potassium levels after diuretics do so because they start off in the lower part of the reference range, and not because they have a greater fall in the plasma values. In this case the aim should be to return them to the lower part of the normal range. Our preliminary observations suggest that this is where patients admitted to hospital with hypokalaemia, not necessarily due to diuretics, end up when the cause of the hypokalaemia is treated.

The other possible reason why correction of hypokalaemia may be more difficult than prevention is that the doses of the various treatments are more or less standard. Thus, the increase in the plasma potassium is more or less the same after a particular treatment. The lower the plasma potassium before treatment, the less successfully will it be corrected with this standard treatment which might nevertheless adequately prevent hypokalaemia.

The Concept of Acute Hypokalaemia

A further difference between prevention and correction is that acute correction might exert effects of its own. For example, the correction of arrhythmias by potassium in patients with hypokalaemia could be due to a non-specific effect of potassium on the cardiac arrhythmias themselves. Hypokalaemia is undoubtedly common among patients admitted with myocardial infarction. The frequency has been reported to vary from 15% (Dyckner *et al.*, 1975) to 9% (Beck and Hockrein, 1978) whereas in our own series of acutely admitted patients it was 21%.

A frequency of hypokalaemia of 21% in patients with myocardial infarction compares with frequencies in patients with other causes of acute admission of 20–40%. The overall frequency of hypokalaemia among patients investigated "out of hours" was 41% compared with 25% among general inpatients and 15% in general outpatients. In all of these situations, as in patients with myocardial infarction, most of the values of plasma potassium below 3·6 mmol/l were still above 3·0 mmol/l.

These results suggest that there is a condition of *acute hypokalaemia* which occurs in a wide variety of acute disorders. It may well be transient, and due to a redistribution of potassium from the plasma to the cells rather than to a loss of potassium from the body.

The question which then arises is whether diuretics make a contribution to this acute hypokalaemia, particularly in patients with myocardial infarction. The answer depends to some extent on how the data are analysed. In the study of Dyckner *et al.*, (1975), diuretic treatment was more common in those with hypokalaemia than in those without (43% compared with 27%), which suggests a major (and expected) role for diuretics. On the other hand, the frequency of hypokalaemia was 12% in patients not on diuretics and only 15% in the whole group (22% in the diuretic group). The overall effect of diuretics on the frequency of hypokalaemia was therefore small, and the surprising finding was the high frequency of hypokalaemia which was not due to diuretics and which could be regarded as *acute* hypokalaemia. A similar analysis suggests that the influence of hypokalaemia on arrhythmias after myocardial infarction is also small, since although the frequency of arrhythmias is higher in patients with hypokalaemia, relatively few such patients were hypokalaemic.

Summary

Most of the available evidence suggests that the fall in the plasma potassium level is greater in women than in men. The results indicate that this difference is due to a greater effect of thiazides in women. The effects of frusemide and thiazides are so small in men that regular prevention of hypokalaemia in men may be unnecessary.

The within-patient variability in the plasma potassium level is large enough to make it difficult to follow up the individual and means that a patient may be hypokalaemic on one occasion but not on another.

The correction of hypokalaemia may be more difficult than its prevention.

Hypokalaemia is common in many acute conditions requiring urgent admission to hospital. This *acute hypokalaemia* may be a non-specific response to acute illness.

Much of the hypokalaemia associated with myocardial infarction may be of this acute variety, and the results suggest that the role of diuretics in the hypokalaemia of myocardial infarction has been exaggerated.

References

Beck, O. A. and Hochrein, H. (1978). *Zeitschrift für Kardiologie* **66,** 187.

Davidson, C., Burkinshaw, L., MacLachlan, M. S. F. and Morgan, D. B. (1976). *Lancet* **2,** 1044.

Dickinson, R. J. and Swaminathan, R. (1975). *Postgraduate Medical Journal* **54,** 836.

Dyckner, T., Helmers, C., Lundman, T. and Wester, P. O. (1975). *Acta Medica Scandinavica* **197,** 207.

Hang, T. (1976). *British Medical Journal* **2,** 622.

Krakauer, R. and Lauritzen, M. (1978). *Danish Medical Bulletin* **25,** 126.

Lawson, D. H., Henry, D. A., Lowe, Julia M., Gray, J. M. and Gemmell Morgan, H. (1979). *Archives of Internal Medicine* **139,** 978.

Morgan, D. B. (1978). *Annals of Clinical Biochemistry* **15,** 49.

Morgan, D. B. and Davidson, C. (1980). *British Medical Journal* **1,** 905.

Schwartz, A. B. and Swartz, C. D. (1974). *Journal of the American Medical Association* **230,** 702.

Surawicz, B., Braun, H. A., Crum, W. B., Kemp, R. L., Wagner, S. and Bellet, S. (1957). *American Journal of the Medical Sciences* **233,** 603.

The Myocardial Cell Membrane: The Effect of Diuretics

P. A. POOLE-WILSON

Cardiothoracic Institute and National Heart Hospital, London, UK

Thiazide and loop diuretics are widely used in the treatment of patients with heart disease or hypertension and a common side-effect is hypokalaemia. Amongst patients treated with thiazides for hypertension and not given any form of potassium therapy, as many as 50% will have a plasma potassium below 3·5 mmol/l and 7% below 3·0 mmol/l (Morgan and Davidson, 1980). In patients with heart failure given frusemide, the figures are 5% and 0·2% respectively. Hypokalaemia is also common in the elderly. In a recent report, 37% of elderly patients admitted to hospital were taking diuretics and of these 20% had a plasma potassium level below 3·5 mmol/l (Hamdy *et al.*, 1980). Since one million, and possibly in the future four million, people in this country are considered to require treatment for hypertension (Editorial, 1980) and since thiazide diuretics are commonly prescribed, the size of the problem is immense. Without some form of potassium therapy 70,000 patients would be expected to have a plasma potassium level below 3·0 mmol/l and half a million below 3·5 mmol/l.

Hypokalaemia may cause lethargy, neuromuscular weakness, postural hypotension and proximal renal tubular damage, but the major consequence is the risk of serious cardiac arrhythmias. It is common knowledge that an arrhythmia frequently responds to elevation of an even marginally reduced plasma potassium concentration in patients with myocardial infarction or after cardiac surgery. Likewise in studies with isolated cardiac muscle preparations, spontaneous ectopic activity can readily be suppressed by increase of the perfusate potassium. Arrhythmias appear to be more frequent in those with heart disease, and in hypertensive patients unsuspected coronary artery disease may coexist. Thus, there is a logical argument for supposing that patients with cardiovascular disease and hypokalaemia caused by diuretic treatment are at risk of dangerous arrhythmias.

Evidence for the occurrence of such arrhythmias or even sudden death in a small percentage of the large number of patients on diuretics is difficult, perhaps impossible, to obtain and is complicated by the fact that most patients are given some form of potassium therapy by their physicians despite advice to the contrary (Editorial, 1974; Editorial, 1977; Kassirer and Harrington, 1977; Beeley, 1980). This lack of evidence should not be taken as justification for the questionable view that potassium therapy is not indicated in otherwise healthy hypertensive patients.

An important problem relevant to this debate is the mechanism by which hypokalaemia causes arrhythmias and whether diuretics have any direct effect on the myocardial cell membrane. Donaldson *et al.*, (1976) suggested that potassium sparing diuretics might preserve cellular potassium by some mechanism other than elevation of the plasma or extracellular potassium. Weber (1972) showed that triamterene prevents glycoside toxicity and Seller (1975a,b) proposed that this was due to inhibition of

Arrhythmias and Myocardial Infarction: The Role of Potassium. Royal Society of Medicine International Congress and Symposium Series No. 44, published jointly by Academic Press Inc. (London) Ltd., and the Royal Society of Medicine.

potassium efflux from the myocardium. The claim that these results showed an inhibition of potassium efflux by diuretics in the absence of glycosides has been disputed (Walter, 1976). Coronary flow was not measured and arterial potassium concentrations altered by up to 2·6 mmol/l in 10 min, making the interpretation of changes in the arterio-venous difference of potassium almost impossible. In the experiments of Weber (1972) acid-base changes were substantial and are known to affect potassium exchange in the myocardium (Poole-Wilson and Langer, 1975).

Other evidence suggests that diuretics do not affect potassium exchange in the myocardium. Studies on myocardial microsomal Na^+, K^+ ATPase show inhibition only at high concentrations (above 10^{-3} mol/l) of frusemide, amiloride and triamterene (Gibson and Harris, 1970; Erdmann and Krawietz, 1976). The binding of ouabain to the myocardial membrane is only reduced by high concentrations of diuretics and the effect appears to be non-specific (Erdmann and Krawietz, 1976). The electrophysiological changes induced by cardiac glycosides are reversed only by high concentrations of amiloride (10^{-2} mol/l, De Azevedo *et al.*, 1973). Chronic administration of frusemide and ethacrynic acid to animals does not alter the Na^+, K^+ ATPase activity (Gibson and Harris, 1970) and chronic administration of frusemide (Hall and Cameron, 1977) or thiazides (Tobian *et al.*, 1962; Weller and Haight, 1963; Irvine, 1968; Kusumoto *et al.*, 1974) or dietary depletion of potassium (Ward and Cameron, 1980) does not reduce myocardial potassium content, despite a reduction of the potassium content of skeletal muscle and the presence of hypokalaemia.

Since the evidence is conflicting, an investigation was undertaken of the effect of diuretics on developed tension, the action potential and potassium fluxes in isolated cardiac muscle (Poole-Wilson *et al.*, 1978).

Methods and Results

Experimental

Experiments were performed on the isolated but arterially perfused interventricular septum of the rabbit heart (Poole-Wilson and Langer, 1975). The details have been published (Poole-Wilson *et al.*, 1978). The uptake of potassium was followed by adding the isotope ^{42}K to the perfusate and recording with a Geiger-Muller probe the counts in the muscle. When equilibration was complete the effect of an intervention on total tissue potassium was followed. A net change of 0·5% could be detected, which represents approximately 0·2 mmol/kg wet tissue. The efflux of potassium was determined by labelling the muscle with ^{42}K and at time zero perfusing with a solution containing no isotope (Fig. 1). During the washout, drugs were introduced and a loss greater than 0·2 mmol/kg wet tissue could be detected. The washout of potassium was recorded as a decrease in the counts in the muscle and as the appearance of counts in the effluent (Fig. 1). Since the two lines plotted on a logarithmic scale in Fig. 1 are straight and parallel, potassium in this preparation follows first-order kinetics and the efflux is as if from a single homogeneous compartment.

The results obtained in 4 septa for each diuretic showed that frusemide (400 mg/l), amiloride (4 mg/l) and triamterene (30 mg/l) did not alter potassium efflux or net tissue potassium. Potassium influx, therefore, was unchanged, In separate experiments, the action potential was recorded from papillary muscles excised from the right ventricle of rabbit hearts. All 3 diuretics after 20–30 min had no effect on the resting membrane potential or the configuration and duration of the action potential (Fig. 2). During the initial exposure to triamterene, a small shortening of the action potential was apparent. Developed tension was not changed by any diuretic in the septal preparation.

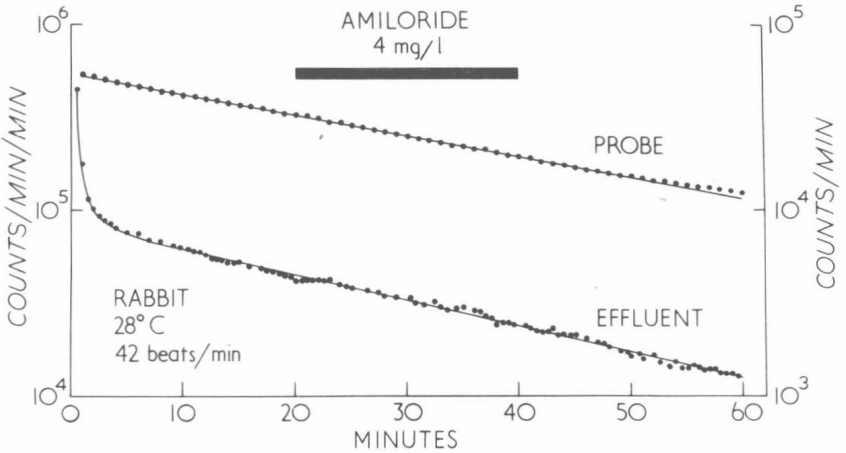

Figure 1. Washout of ^{42}K from the interventricular septum of the rabbit heart. The line marked PROBE is the tissue counts recorded each minute. The line marked EFFLUENT is the effluent counts (counts/min/min, corrected for any small changes in perfusate flow). Amiloride (4 mg/l) had no effect on potassium efflux.

Amiloride caused a small fall in developed tension (< 5%) in 2 out of 3 papillary muscles.

Clinical

Ten years ago the importance of potassium in the genesis of arrhythmias was apparent. In the intensive care unit at St Thomas' Hospital, London, the initial plasma potassium

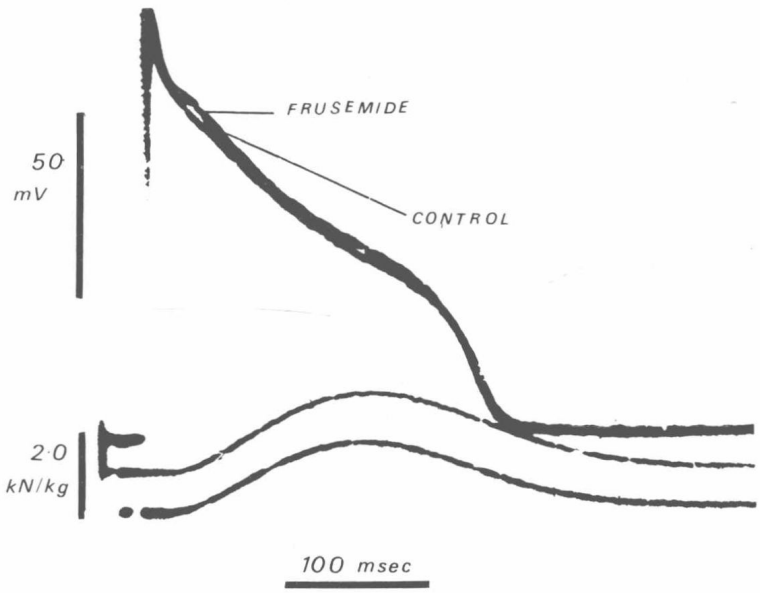

Figure 2. Action potential from right ventricular papillary muscle of the rabbit at 37°C. Frusemide (400 mg/l) had no effect on the action potential or developed tension. The tension records have been displaced so that both control and experimental traces can be seen.

Table 1

Distribution of plasma potassium concentrations in 158 patients admitted to an intensive care unit with myocardial infarction (1969–1970)

	Reason for admission				
	Prophylaxis	Arrhythmia	Pump failure	Post-resuscitation	Total
No. patients with plasma potassium >3·5 mmol/l	19	36	32	22	109
No. patients with plasma potassium <3·5 mmol/l	6	10	9	24	49
Total	25	46	41	46	158

and blood gas levels were recorded in 158 patients admitted consecutively with myocardial infarction. The reasons for admission are given in Table 1. Of the total, 31% had a plasma potassium below 3·5 mmol/l and 52% of those who had had cardiac resuscitation were hypokalaemic.

Factors predisposing to hypokalaemia were equally common in those who had undergone resuscitation and those who had not (Table 2). An additional factor in patients after resuscitation was metabolic alkalosis which was presumed to be secondary to the administration of bicarbonate. In 8 patients post-resuscitation with a plasma potassium of 3·1–3·5 mmol/l, the pH was $7{\cdot}42 \pm 0{\cdot}03$; $PCO_2 = 36$ mm Hg and $HCO_3^- = 23{\cdot}6 \pm 2{\cdot}2$ mmol/l (mean ± SEM). In 11 patients post-resuscitation with a plasma potassium below 3·0 mmol/l, the pH was $7{\cdot}49 \pm 0{\cdot}03$; $PCO_2 = 30{\cdot}7$ mm Hg and

Table 2

Patients admitted to intensive care with myocardial infarction and plasma potassium <3·5 mmol/l

	Post-resuscitation	Others
No. patients	24	25
No predisposing cause for low potassium	10	12
Predisposing cause for low potasium	14	13
Diuretics	11	10
Hypertension	5	3
Diabetes	2	1
Steroids	0	1
Traceable gas tension	19	14
pH (±SEM)	7·46±0·02	7·40±0·02
PCO_2 (mm Hg)	38·6	38·4
HCO_3^- (mmol/l±SEM)	27·4±1·7	23·3±0·8
Plasma potassium (mmol/l±SEM)	2·90±0·02	3·29±0·01