INTRODUCTION

In the past decade, two major developments have focused research interest on the cell membrane for the role it may play in the pathogenesis of hypertension. One development is based on the finding that the sensitivity of vascular smooth muscle increases in experimental hypertension. This increase is due to an altered membrane function of this tissue [1]. It may be responsible for the increase in total peripheral resistance that causes the arterial pressure elevation. The second development is the evidence that the membrane abnormality in hypertension is present in many tissues [2, 3]. The membrane of the red blood cell has been mostly studied as a readily available marker for the disease and as a tool for study of the characteristics of the membrane malfunction.

This manuscript will present evidence supplementing both of these developments. It will conclude with arguments supporting the hypothesis that the membrane malfunction that really initiates hypertension is in a pressure-regulating center in the hypothalamus. Evidence will be drawn from each of the three common forms of experimental hypertension: genetic, renal, and mineralocorticoid. Cell membrane abnormalities, although they may differ with the form of hypertension, have been described for each. However, one defect that may be common to all is an abnormal relationship between the membrane and the calcium ion.

METHODS

Blood pressures

Blood pressures were measured indirectly by the tail cuff method. To do this, a Narco Pneumatic pulse transducer was recorded on a Grass polygraph. Triplicate readings were taken and averaged for each rat.
Red blood cells

Rats were anesthetized with 50 mg/kg of sodium pentobarbital i.p. The abdominal aorta was cannulated, and 10 cc of blood were drawn into a syringe containing 100 units of sodium heparin. It was centrifuged for 10 minutes at 1000 × g, and the plasma and buffy coats were removed. Red blood cells were washed three times at room temperature in physiological salt solution (PSS) containing (mM): NaCl, 140; KCl, 5; MgSO₄ · H₂O, 1.22; NaH₂PO₄ · 7H₂O, 1.19; CaCl₂ · H₂O, 1.6; dextrose, 11.1; morpholino propane sulphonic acid, 20; fraction V bovine albumin (0.25%). The pH was adjusted at room temperature to 7.4. After each wash, the cells were centrifuged and the PSS discarded. Packed red blood cells, 1 or 1.5 ml, were resuspended in an equal volume of PSS in a 25-ml siliconized glass Erlenmeyer flask and incubated with gentle shaking to prevent sedimentation. Before and after incubation, hematocrit values were measured for each sample. After incubation, the samples were centrifuged and the incubation PSS separated for final Na⁺ and K⁺ concentration determinations. Final hemoglobin concentrations were also measured in the PSS. Ionic flux was measured as a change in the ion concentration (expressed as mEq/L packed cells/unit time) in the PSS and adjusted for red blood cell volume shifts as measured by hematocrit changes. The following formula was used:

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\text{IONIC FLUX} = \frac{[\text{ion}]_a (1 - H_a) - [\text{ion}]_b (1 - H_b)}{H_b}
\]

where \([\text{ion}]_a\) = ion concentration in the PSS after incubation

\([\text{ion}]_b\) = ion concentration in the PSS before incubation

and \(H_a\) = value of hematocrit after incubation

\(H_b\) = value of hematocrit before incubation.

Hematocrits were determined using microhematocrit tubes centrifuged at 4500 × g for 2 minutes.

Albumin and dextrose were added to the PSS to minimize hemolysis during the washing and incubation. The percentage of lysis was calculated by dividing the concentration of hemoglobin in the PSS after incubation by the hemoglobin concentration of the erythrocyte suspension in PSS before incubation. Hemoglobin concentrations were measured by the cyanohemoglobin method. Hemolysis rarely exceeded 1.3% and never exceeded 2.0%.

Vascular smooth muscle

Two-kidney one-clip (2K-1C) renal hypertensive rats were prepared with a silver block (0.2-mm slit) on one renal artery. Rats were used 3 to 4 months after this