Quantitative Excretion of Water and Sodium Load by Isolated Dog Kidney: Autonomous Renal Response to Blood Dilution Factors

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Received July 16, 1968

Summary. Totally isolated dog kidneys of the same pairs are perfused with heparinized blood under identical conditions, one of the kidneys being submitted to a supplementary isotonic or hypotonic saline load. Excess sodium is excreted quantitatively as well as excess solute-free water. Autonomous renal response depends on blood dilution, changes in blood pressure being excluded as well as influence of volume expansion or of extrarenal hormonal factors. The experiments demonstrate kidney ability to control quantitatively fast changes in saline balance by autonomous mechanisms in the sense of intrarenal feedback type relation to blood composition. Dilution factors (plasma sodium, potassium, proteins) control excretion primarily by adjustment of tubular reabsorption to filtration. Moreover, the absence of relation between basal control excretion and response to saline loading in the present experiments suggest that different mechanisms could insure long duration adjustment of the kidney to a definite blood composition and saline balance. It is demonstrated that many effects attributed to volume expansion can be caused by blood dilution; moreover, interference between dilution effects and specific hormonal control by eventual natriuretic factor should be avoided.

Key-Words: Sodium Excretion — Water Excretion — Isolated Kidney.

Schlüsselwörter: Na-Exkretion — Wasserexkretion — Isolierte Niere.

Two fundamental mechanisms are susceptible to control renal excretory response after saline and water loading, depending respectively on volume changes and on composition changes of blood and extracellular fluid. An increase of blood volume may result in a concomitant increase of water and sodium excretion by the way of reflex mechanisms involving receptors sensitive to volume variations and controlling the secretion of antidiuretic hormone and of a possible natriuretic factor (Lichardus [23]; Lichardus and Pearce [23]; Cott [6]; Pannier, Seroussi, Martineaud, Vassilikos, and Durand [35]). Modifications of blood composition caused by saline loading as, for example, decreased

* This work has been performed with the help of the Fonds National de la Recherche Scientifique (Belgium).
plasma protein concentration and lowered haematocrit may induce sodium and water elimination by the kidney; the importance of such physical factors has recently been emphasized again [25]. It is difficult to dissociate the role played by either volume changes or blood dilution in the response of kidneys in situ; isolation of these mechanisms and study of autonomous renal controls can be best performed on totally isolated kidneys; under such experimental conditions, blood pressure can be kept constant, extrarenal hormonal factors are ruled out, and renal response depends only on changes of blood composition related to water and sodium loading.

We have previously described a technique for the perfusion of isolated dog kidneys with heparinized blood [10,28]; this technique has been applied to the study of autonomous renal control of water and sodium excretion. The previous results showed an increase of sodium rejection by kidneys taken from dogs submitted to a high sodium diet for 3 weeks prior to isolation of kidneys [32]. Sodium rejection is at the highest during the first hour of artificial perfusion by heparinized blood; this observation is compatible with the presence of a natriuretic factor of short life. A large increase of sodium rejection is also observed after infusion of saline either to the animal 1/2 hour before isolation of the kidney [32] or during the artificial perfusion. In the last case, interference of extrarenal factors other than blood dilution is avoided [27, 32]. In order to reduce individual differences of animals, further series of experiments have involved comparative and simultaneous perfusion of both kidneys of the same pair by two identical equipments with unilateral modification of the blood. It was demonstrated that sodium and water rejection by isolated kidney working at a constant blood pressure is not only related to changes in glomerular filtration, but primarily to reduced tubular reabsorption; decrease of haematocrit and increase of total renal blood flow are not the only factors involved [29]. Important parameters are plasma protein concentration and oncotic pressure: the addition of serumalbumin (or of dextran) reduces sodium and water excretion by isolated kidneys submitted to a saline load; the response is chiefly related to increased tubular reabsorption [31]. Other factors are ionic disequilibrium. Dilution of plasma by saline induces hypokalaemia which in turn reduces tubular reabsorption of sodium without changes in filtration [30]. Moreover, tubular sodium reabsorption is also controlled by plasma sodium concentration; autonomous rejection of hypertonic saline depends on reduced reabsorption as an immediate consequence of increased plasma sodium concentration [33].

It appears from these results that the kidney is able to eliminate a saline load by purely autonomous mechanisms; kidney response depends on cumulative factors bound to blood dilution [34].

The fundamental question is therefore raised to know to what extent autonomous renal response to blood dilution is capable of insuring a quantitative excretion of the extra load and, as a consequence, of keeping constant the composition of blood and extracellular fluid. The purpose of the experiments described in the present paper is to answer this question. Two kidneys of the same pair are perfused in identical basic conditions: one of the kidneys is submitted to an extra water and sodium load and the perfusion is prolonged until urine flow comes back to an identical