**Review**

**Aldosterone-Induced Organ Damage: Plasma Aldosterone Level and Inappropriate Salt Status**

Atsuhisa Sato and Takao Saruta

In recent years, it has been clarified that aldosterone can directly damage various organs, such as the heart, blood vessel, and kidneys, via non-epithelial mineralocorticoid receptors, independent of changes in blood pressure. Anti-aldosterone drugs have been clinically reported to be useful for their organ-protecting effects. The fact that these effects have been considered important for almost 10 years seems to indicate that aldosterone-induced organ damage can develop as a consequence of plasma aldosterone levels being in disproportion to salt status. In a previous study, cardiac fibrosis could not be induced in an experimental model of hyperaldosteronism with a low-salt diet. It is, therefore, extremely important to understand the relationship between plasma aldosterone level and inappropriate salt balance when considering diseases or states for which an anti-aldosterone drug is called for. In this paper, we review the fundamental and clinical studies reported to date, mainly to investigate the pathology of organ damage induced by aldosterone and excess salt. Aldosterone-induced direct organ damage mediated through vasculitis essentially requires salt, which is inappropriate for plasma aldosterone level, and studies performed from this standpoint may provide a clue to the clarification of the involvement of salt in the actions of aldosterone via non-epithelial mineralocorticoid receptors. In humans, it is also strongly suggested that organ damage may occur, even at a plasma aldosterone level within a normal range, if salt intake is imbalanced to the aldosterone level. This means that the new aldosterone blocker eplerenone may also have significance as a drug inhibiting inflammation, possibly serving as a trigger of organ damage. (Hypertens Res 2004; 27: 303–310)

**Key Words:** aldosterone, mineralocorticoids, high-salt diet, mineralocorticoid receptors, vasculitis

---

**Introduction**

It is known that the effects of aldosterone on unidirectional electrolyte transport are triggered by the expression of serum and glucocorticoid inducible kinase 1 (sgk-1) via epithelial mineralocorticoid receptors (MR), whose selectivity to aldosterone is protected by the enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2). Although MR are also present in non-epithelial tissues, over 90% of such MR are thought to be occupied by cortisol and corticosterone because of the lack of expression of 11β-HSD2 in these non-epithelial tissues and the much higher (100–1000 fold) circulating free levels of the physiologic glucocorticoids (1). In recent years, it has been clarified that aldosterone can directly injure various organs, such as the heart, blood vessel, and kidneys, via non-epithelial MR, independent of changes in blood pressure, and anti-aldosterone drugs have been clinically reported to be useful because of their organ-protecting effects (2–5).

Almost 10 years have passed since Weber et al. (6, 7) and Young et al. (8) (1992–1994) reported aldosterone-induced cardiac fibrosis (interstitial and perivascular region) in their pioneer studies on the direct organ-damaging effects of aldosterone via non-epithelial MR. The fact that this effect has been said to be of importance seems to indicate that aldosterone-induced organ damage can develop as the result of plasma aldosterone levels that are inappropriate for salt sta-
tus. No cardiac fibrosis develops in experimental models of
eraldosterone with a low-salt diet. By contrast, it may be possible that the organ-damaging effect of aldosterone is clinically observed, even with so-called normal plasma aldosterone levels, if salt intake is inappropriate for the aldosterone level. In consideration of our dietary lives, in which salt intake cannot be reduced to zero, we should always keep in mind that aldosterone at a normal level can injure organs as a consequence of excess salt intake inappropriate for the aldosterone level.

Just before the introduction of eplerenone, a new aldosterone blocker with markedly-increased selectivity to MR as compared with spironolactone, it is extremely important to understand the relationship between plasma aldosterone levels and inappropriate salt balance. In this paper we review the fundamental and clinical studies reported to date, mainly to investigate the pathology of organ damage induced by aldosterone and excess salt.

**Aldosterone-Induced Cardiac Fibrosis Cannot Be Observed without High-Salt Diet**

In 1992, Weber *et al.* reported that blood pressure elevation and cardiac fibrosis were observed in uninephrectomized rats receiving the mineralocorticoid aldosterone or deoxycorticosterone along with 1% saline for 8 weeks (6, 7). In a subsequent study, Young *et al.* extended their experimental design and observed similar cardiac changes (8). Particular attention was given to the fact that neither blood pressure elevation nor cardiac fibrosis was observed in these experimental models even in a hyperaldosteronism state (similar result was obtained in hyper-deoxycorticosterone state), if the rats were fed with a low-salt diet. This strongly suggests the possibility that excess salt has particular importance for non-epithelial MR-mediated effects of aldosterone. In these experiments, Brilla confirmed that rats receiving aldosterone with a low-salt diet had a significantly higher plasma aldosterone level that those receiving aldosterone with a high-salt diet, but these hyperaldosteronism animals developed no cardiac fibrosis (6).

Furthermore, Young *et al.* (8) could not observe blood pressure elevation or cardiac fibrosis in rats by administering corticosterone, a physiologic glucocorticoid for rats, even at a high concentration. On the other hand, perivascular fibrosis was induced with RU486, a glucocorticoid receptor (GR) antagonist, proving that the effect of inducing cardiac fibrosis in the presence of a high-salt diet is mediated via classical MR. The data on RU486 have revealed that effects via cardiac GR are constantly exerted as antagonistic effects against fibrosis in the heart. Although Selye *et al.* reported in the 1940s that severe hypertension and vascular damage in the heart, kidneys, and brain were observed in rats receiving mineralocorticoid and a high-salt diet (9), they did not discuss the relationship between mineralocorticoids and excess salt.

In later studies, it was disclosed that the effect of aldosterone in inducing cardiac fibrosis is not directly exerted on cardiac fibroblasts, and blood vessels are the primary target organ of aldosterone among non-epithelial tissues. From these results, aldosterone-induced vasculitis (aldosterone-induced vasculopathy) was thought to serve as a trigger for subsequent cardiac fibrosis. Moreover, it was revealed that a high-salt diet is also required by these experimental models of aldosterone-induced vasculitis. It has been determined that inflammatory cell infiltration and expression of proinflammatory molecules, such as monocyte chemotactic protein-1 (MCP-1) and osteopontin, are increased prior to the occurrence of fibrosis by aldosterone and excess salt.

Rocha *et al.* observed inflammatory cell infiltration (monocytes and macrophages) and fibrinoid necrosis around coronary arteries in an experimental model receiving aldosterone with a high-salt diet within an early period (about 4 weeks) before the occurrence of cardiac fibrosis (8 weeks). They also observed the expression of proinflammatory molecules, such as vascular cell adhesion molecule-1 (VCAM-1), cyclooxygenase-2 (COX-2), MCP-1, and osteopontin, within a much earlier period (1–2 weeks) (10). This experimental model was also determined to require concomitant administration of a 1% salt diet. In their model, there was very little possibility that the salt-dependent effect of aldosterone was mediated by circulating angiotensin II (Ang II), because of the extremely low plasma Ang II levels. Hartner *et al.* (11),
Fig. 2. Given the fact that, under a physiological situation, 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2), an enzyme protecting the mineralocorticoid receptors (MR) selectivity of aldosterone, is absent in non-epithelial tissues, and the fact that circulating concentrations of glucocorticoids (GCs) are commonly three orders of magnitude higher than those of aldosterone, 90% or more of the MR may be occupied by even nadir levels of GCs. Therefore, it is assumed that the harmful actions of aldosterone via cardiac MR may be blocked by GCs combining with most of the MR. On the other hand, under a pathologic condition, aldosterone actions through cardiac MR occur by various possible mechanisms, including increased sensitivity of aldosterone in combining with MR, the induction of 11β-HSD2, or the up-regulation of MR. It is plausible that in non-epithelial tissues, only a slightly increased connectivity to MR is sufficient for the harmful actions of aldosterone to appear. Thus, even under such a situation, GCs apparently bind to cardiac MR to a greater extent than aldosterone. MCs, mineralocorticoids.

<table>
<thead>
<tr>
<th>Physiological</th>
<th>Aldosterone levels that are inappropriate for salt status</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCs → GR → MR → cardioprotection (?)</td>
<td>GCs → 11β-HSD2 induction (?) → MCs → up-regulation (?)</td>
</tr>
<tr>
<td>non epithelial unprotected</td>
<td></td>
</tr>
</tbody>
</table>

Beswick et al. (12), and Blasi et al. (13) observed aldosterone-induced inflammatory cell infiltration and vasculitis in the kidneys, and they all recognized the necessity of 1% saline. As for the relationship between aldosterone and salt that initially attracted attention because of the essential requirement of salt for aldosterone-induced cardiac fibrosis, current interests have focused on the question of why inflammatory cells cannot be activated without excess salt, and why genes of proinflammatory molecules cannot be expressed without excess salt. By contrast, studies from this standpoint may provide the clue needed to clarify how salt is involved in the non-epithelial MR-mediated effect of aldosterone. Furthermore, we also should keep in mind that uninephrectomy is needed for these experimental models. We summarize the information on aldosterone-induced target organ damage, especially in cardiovascular systems, via nonepithelial MR in Figs. 1 and 2.

Effects of Angiotensin II in Inducing Organ Damage in the Presence of Excess Salt May Be Mediated in Part by Aldosterone

From the results of the fundamental and clinical studies reported to date, it is inferred that aldosterone and Ang II have their own direct effects of inducing organ damage, and several differences in their actions have been reported. However, both Ang II and aldosterone may be involved together in organ damage in a complex manner in some circumstances. Robert et al. reported that cardiac fibrosis induced by aldosterone with a high-salt diet can be inhibited not only by the MR antagonist, but also by an Ang II type 1 (AT1) receptor antagonist (ARB), suggesting the possible involvement of Ang II via the AT1 receptor in aldosterone actions via non-epithelial MR (14).

However, the results obtained from a series of studies performed by Rocha et al. strongly suggested that Ang II-induced organ damage with excess salt are in part mediated by aldosterone. When they administered Ang II and Nω-nitro-L-arginine methyl ester (L-NAME; nitric oxide synthesis inhibitor) to rats along with 1% saline (under these conditions, it has been reported that organ damage is dependent on Ang II), severe fibrinoid necrosis in the kidneys and proteinuria were observed (15). The organ damage thought to be induced by Ang II was found to be inhibited by eplerenone, a selective MR antagonist. They also reported that organ damage was inhibited even by total adrenalectomy. Moreover, renal damage was reproduced by “systemic” administration of aldosterone following total adrenalectomy, which strongly suggested that the renal damage induced by Ang II with 1% saline was in part mediated by the effect of “circulating” aldosterone on the kidneys. Based on the results of their series of experiments, it was also suggested that the effects of Ang II on the heart under the same experimental conditions may possibly be mediated by the effects of “circulating” aldosterone (16).

Katayama et al. reported that blood pressure elevation and cardiac hypertrophy were observed in rats receiving Ang II and 0.7% saline for 8 weeks. The Ang II-induced organ damage in this experimental model was inhibited by spironolactone (17). Plasma aldosterone levels in Ang II-treated rats were about 5.4 times higher than those seen in control rats, suggesting the intervention of the effects of aldosterone with excess salt, although these plasma aldosterone levels were markedly lower than those seen in former experimental models (6–8). However, interestingly, the interaction between Ang II and aldosterone in the heart may differ from that in the kidneys because renal hypertrophy (increase in renal weight/body weight ratio) induced by Ang II was not inhibi-
ed by spironolactone (17).

These reports strongly suggest that the “circulating” aldosterone is closely related, at least in part, to the organ damage directly induced by Ang II under salt loading, although the details remain obscure due to the lack of comparison with experiments under low-salt intake.

Studies with Transgenic Mice

The MR belongs to the family of steroid/thyroid/retinoid/orphan receptors and a ligand-dependent transcription factor whose receptor itself exists in the cytoplasm. Organ damage induced by aldosterone with excess salt results from the effects mediated via classical MR in non-epithelial tissues. This leads to the question: what organ damage appears in transgenic mice with overexpression of classical MR.

Menuet et al. examined organ damage using transgenic mice with overexpression of human MR under P1 promoter control (18). In these mice, the human MR was overexpressed in all mineralocorticoid target tissues, and it was determined that so-called dilated cardiomyopathy developed because of an increase in left ventricular end-systolic diameter, a decrease in left ventricular fractional shortening ratio, and an increase in pulse rate. Blood pressure remained normal; therefore, these were not hemodynamic changes through blood pressure. In the heart, atrial natriuretic peptide (ANP), sgk-1, and early growth response gene 1 were also induced. It was interesting that no cardiac fibrosis was observed in these mice. The cardiac changes observed are clearly different from those induced by aldosterone with excess salt as previously reported (6-8). Although the plasma aldosterone level in these transgenic mice was only about 1.4 times higher than that seen in wild-type mice (with statistical significance), it is assumed that aldosterone has a greater chance to bind MR in the transgenic mice due to overexpression of human MR, compared with wild-type mice; however, it is thought that aldosterone may exert totally different effects on the heart in the absence of salt.

It should be noted that the classical MR has an equal affinity for aldosterone, glucocorticoid cortisol, or corticosterone. Thus the enzyme 11β-HSD2 must exist in aldosterone target tissues, in addition to the regional expression of MR, to make aldosterone selectively bind to the classical MR in those tissues (1). MR selectivity to aldosterone cannot be protected in tissues with abundant MR, but insufficient expression of 11β-HSD2, results in the dominance of effects of glucocorticoids. 11β-HSD2 is present at a very low level in almost all non-epithelial cells, including cardiomyocytes. Sheppard and Autelitano reported that 11β-HSD2 mRNA was not expressed in rat heart homogenates, cardiomyocytes, or cardiac fibroblasts, when examined by a nuclease protection assay method (19). Therefore, it is important to discuss to what extent aldosterone can bind to the classical MR in the heart of this transgenic mouse with overexpression of human MR that shows a plasma aldosterone level only about 1.4 times higher than that seen in the wild-type mouse.

Provided that aldosterone can selectively and excessively bind to the classical MR in the heart, can aldosterone manifest the same cardiac effects without excess salt as observed in the presence of salt? Qin et al. performed experiments in transgenic mice with overexpression of 11β-HSD2 in cardiomyocytes using the mouse α-myosin heavy chain promoter (20). These transgenic mice developed cardiac hypertrophy and cardiac fibrosis, and they died by heart failure in an immature state, despite their normal blood pressure and standard salt intake, and the changes observed were all inhibited by eplerenone. From these results, it is thought that classical MR in the heart are usually (physiologically) occupied by glucocorticoids (because of the almost complete lack of expression of 11β-HSD2), providing the antagonistic effects against MR-mediated adverse effects of aldosterone. Moreover, it is strongly suggested that the adverse effects of aldosterone on the heart can appear due to increased binding or sensitivity of aldosterone to the classical MR in the heart under some pathologic conditions, although not to a level as high as that seen in these transgenic mice.

One extremely important finding in these transgenic mice is that cardiac fibrosis does exist, but only in the interstitium, and no perivascular fibrosis is observed. This is definitely different from the cardiac changes induced by aldosterone with excess salt. Namely, it is determined that vasculitis due to predominant perivascular infiltration of inflammatory cells and associated perivascular fibrosis cannot occur in the absence of salt. In other words, aldosterone-induced vasculitis cannot be observed in the absence of salt, even if the binding capacity of aldosterone to the classical MR is increased as much as possible in the heart through overexpression of 11β-HSD2. Therefore, the entity of the organ-damaging actions of aldosterone is “vasculitis,” when salt intake is improper to the plasma aldosterone level. This means that eplerenone, a new aldosterone blocker, has great significance as a drug inhibiting vascular inflammation and possibly triggering organ damage.

Young et al. reported that interstitial fibrosis induced in the heart by aldosterone with excess salt has different responses to various steroid hormones compared with those of perivascular fibros (8). Fujisawa et al. reported that interstitial fibrosis showed a different time course from that of perivascular fibrosis in a model receiving deoxycorticosterone (acute bolus injection) with excess salt (21). Given that vasculitis essentially requires salt for its formation whereas interstitial fibrosis can occur without salt, what factors are involved in interstitial fibrosis? Pu et al. observed blood pressure elevation, increased heart weight, and vascular hypertrophy in an experimental rat model receiving a standard amount of salt with aldosterone (22). These histological changes were inhibited by spironolactone, and also by the endothelin receptor (ET-A) antagonist. This indicates a possible intervention of endothelin-1 secreted from vascular endothelial cells and smooth muscle cells as a consequence of oxidation.
stress due to increased active oxygen species (ROS) through aldosterone. It has been reported that endothelin-1 appears in clinical cases during relatively long-term administration of an angiotensin-converting enzyme (ACE) inhibitor, and this factor is involved in aldosterone-induced organ damage occurring after aldosterone breakthrough (23). In the future, non-salt-mediated interaction between aldosterone and endothelin-1 should be further studied.

In contrast, Beggah et al. reported the unexpected finding that down-regulation of endogenous MR mRNA expression leads to cardiac fibrosis and severe heart failure (24). Although they did not show any data in terms of the relationship between mineralocorticoids and salt, their findings raise new questions about the role of cardiac MR.

**Plasma Aldosterone Level and Salt Balance: Clinical Studies**

To date, there have been no clinical studies performed to directly investigate the extent to which organ damage differs according to the balance between plasma aldosterone level and salt intake. Schlaich et al. compared baseline levels of various parameters with those after salt loading in young normotensive and mild hypertensive subjects to investigate the effects of aldosterone on the heart in relation to salt (25).

After salt loading, the aldosterone levels in 24-h urine significantly decreased in normotensive subjects (10.98 ± 7.44 µg/day; p < 0.02), whereas the urinary aldosterone levels remained unchanged in hypertensive patients (9.34 ± 10.51 µg/day; p < n.s.; lack of aldosterone suppression by salt loading). They observed a significant positive correlation between urinary aldosterone levels after salt loading and heart weights calculated via echocardiography (r = 0.43; p < 0.01), revealing that the less the decrease in urinary aldosterone levels after salt loading, the severer the cardiac dysfunction. There were no intergroup differences in plasma (152 ± 22 pg/ml in normotensive group; 145 ± 33 pg/ml in hypertensive group) or urinary (showed above) aldosterone levels before salt loading, nor was there a correlation between heart weight and cardiac function.

Some previous clinical studies disclosed a significant correlation between baseline plasma aldosterone levels and the severity of organ damage, such as cardiac hypertrophy, whereas some other studies did not reveal such a correlation. In these studies, certain consistent results would have been obtained, if the investigation had been performed using the same condition for salt balance, such as after salt loading. From the results of the study of Schlaich et al. (25), it is strongly suggested that aldosterone-induced organ damage may occur in humans, even at a plasma aldosterone level within a normal range, if the aldosterone level and salt intake are imbalanced.

Moreover, an effect of sodium restriction on the circadian blood pressure rhythm in patients with primary aldosteronism has been reported (26, 27). Uzu et al. reported that the circadian rhythm of blood pressure was disturbed in patients with primary aldosteronism who maintained a relatively high sodium intake. Both adrenalectomy and sodium restriction restored a nocturnal dip in blood pressure in primary aldosteronism (27). In the patients with primary aldosteronism, the balance between plasma aldosterone levels and salt intake also seems to be important.

**Mechanisms**

Although it has not been clarified in large part why salt is needed for the direct effect of aldosterone on each organ that is mediated through aldosterone-induced vasculitis, and what imbalance acts with what messenger, possible mechanisms will be summarized in the following section.

**Enhancement of the Tissue Renin-Angiotensin-Aldosterone (RAA) System**

When Gu et al. cultured rat myoblasts and vascular smooth muscle cells for 5 days in media containing Na at a normal concentration (146 mEq/l) and high concentrations (152, 160, and 180 mEq/l), they found that the cell diameter, cell volume, and protein synthesis increased in an Na-concentration-dependent manner. Thus they reported that salt may have a direct hypertrophic effect in the heart and vascular wall (28). However, it was not determined whether a similar direct effect was also observed in inflammatory cells or cardiac fibroblasts. Recently, it has been reported that the tissue RAA system may be enhanced by a high-salt diet. When Boddí et al. gave a high-salt diet to normotensive subjects, they observed increased production of Ang I and Ang II in the vascular tissue of the forearm. The plasma renin activity decreased, proving the dissociation between circulatory and tissue RAA systems. Thus they revealed the possibility that salt may reinforce the regional effect of Ang II in the blood vessel (29).

On the other hand, the concept of “tissue aldosterone,” considered as an autocrine/paracrine substance that is produced locally and acts locally, has attracted increasing attention. It has been pointed out that this “tissue aldosterone” synthesis is also increased by a high-salt diet, leading to the involvement in organ damage. When Takeda et al. gave a high-salt diet to rats for 8 weeks, they observed cardiac hypertrophy although blood pressure remained unchanged (30). In these rats, up-regulation at the level of aldosterone synthase (CYP11B2) mRNA and increased aldosterone synthesis were observed in the heart, although the circulatory RA system was suppressed. Lal et al. gave an 8% salt diet to rats for 4–8 weeks, in combination with spironolactone to investigate the effects on the heart, on the assumption that the concomitant use of an MR antagonist should be useful if aldosterone production from the heart is involved in organ damage (31). These rats developed cardiac hypertrophy after 4 weeks and then interstitial and perivascular fibrosis after 8...
weeks, but these changes were all inhibited by spironolactone. Although it is unclear exactly where spironolactone exerts its effects, it may act locally in the heart, since its effect on the kidney seems to be weak due to salt loading.

Influences on the Sodium-Hydrogen (Na/H) Exchanger

The Na/H exchanger is known to be important to maintain physiological pH in cardiovascular cells. In recent years, it has been confirmed that increased activity of the Na/H exchanger is involved in hypertrophy of experimental postinfarction myocardial cells (32), the heart in spontaneously hypertensive rat (SHR) (33), and cardiomyocytes in mice with overexpression of β2-adrenergic receptor (34), and that inhibition of the activity of the Na/H exchanger can reduce cardiac hypertrophy. Navarro-Lopez et al. clinically revealed that the severity of cardiac hypertrophy was positively correlated with the degree of activity of the Na/H exchanger in patients with essential hypertension (35). In the experimental model receiving aldosterone with excess salt, the activity of the Na/H exchanger was also confirmed to increase, suggesting that organ damage may arise from vasculitis via the exchanger.

Fujisawa et al. observed an increase in Na/H exchanger isoform 1 protein, and collagen deposition in perivascular and interstitial regions in the heart at 8 days after the start of administration of deoxycorticosterone with 0.9% saline (36). The collagen deposition was inhibited by spironolactone, and also by the Na/H exchanger isoform 1 inhibitor, proving the involvement of the Na/H exchanger in organ damage induced by mineralocorticoid with salt. To date, an aldosterone-induced increase at the level of Na/H exchanger mRNA or its increased activity has been reported in vitro in myocardial cells (37) and vascular smooth muscle cells (38), and these findings are confirmed in relation to salt by the results of the study of Fujisawa et al. (36).

Young and Funder observed inflammatory cell infiltration, increased expression of proinflammatory molecules, and interstitial fibrosis after administration of deoxycorticosterone with 0.9% saline. These changes were found to be inhibited by early administration of a Na/H exchanger isoform 1 antagonist (39). It is much more important that the rapid nongenomic action of aldosterone is involved in part in the effect of aldosterone on the activity of the Na/H exchanger (40), suggesting that the rapid nongenomic action of aldosterone may serve as a trigger for the subsequent actions of aldosterone via transcription activity (genomic actions, which can be blocked by spironolactone or eplerenone). This would seem to provide the first interesting interpretation of the rapid action of aldosterone.

However, further studies are required because it remains completely obscure how salt influences the Na/H exchanger, and why aldosterone and salt balance influence the activities of the Na/H exchanger.

Others

Although it is not a direct evidence, it may provide a clue to the mechanisms of organ damage induced by aldosterone with excess salt that up-regulation is observed at the classical MR mRNA level in the heart (41), and there are both proinflammatory molecules whose expression is increased by aldosterone with salt and those whose expression is not significantly increased by aldosterone with salt (clarification of each gene upstream region and regulatory mechanisms may provide new evidence).

Conclusion

Aldosterone-induced direct organ damage mediated through vasculitis essentially requires salt, which is inappropriate for plasma aldosterone level. Thus the entity of the organ-damaging effects of aldosterone can be considered “vasculitis.” Neither infiltration of inflammatory cells nor increased expression of proinflammatory molecules occurs in the absence of salt, indicating a process largely different from that of interstitial fibrosis. Salt is needed for the actions of aldosterone from the standpoint of vasculitis, and studies performed from this standpoint may provide a clue to the involvement of salt in the actions of aldosterone via non-epithelial MR.

In humans, it is also strongly suggested that organ damage may occur, even when the plasma aldosterone level is within a normal range, if salt intake is imbalanced to the aldosterone level. This means that the new aldosterone blocker eplerenone may also have significance as a drug inhibiting inflammation, and possibly serving as a trigger of organ damage.

Acknowledgements

We would like to express our profound gratitude to Professor John W. Funder (Prince Henry’s Institute of Medical Research, Clayton, Australia) for his valuable advice on this review.

References

Hypertension 2003; 41: 64–68.


