Salt in the Wound

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Aldosterone activates the epithelial sodium channel (ENaC) in principal cells of the collecting duct to regulate salt excretion, extracellular volume, and BP. Seminal studies by Hostetter and colleagues demonstrated that aldosterone also contributes to glomerular sclerosis in a remnant kidney model. Treatment of rats with aldosterone and salt induces an inflammatory response, characterized by perivascular leukocyte infiltration and increased expression of proinflammatory genes through a MR-dependent mechanism. Not surprising, MR activation by aldosterone stimulates the expression of proinflammatory and profibrotic genes through MR-dependent activation of NF-κB in the cortical collecting duct.5 It would be interesting to know whether increased oxidative stress contributes to the MR-dependent activation of NF-κB in the cortical collecting duct during low salt intake.

Aldosterone or MR activation causes both tubulointerstitial fibrosis and glomerulosclerosis in animal models. Thus, the MR antagonists spironolactone and eplerenone decrease interstitial inflammation and glomerular injury in rats with radia-

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tion injury, unilateral ureteral obstruction, diabetes, and aldo-
sterone infusion.\textsuperscript{3,12} MR inhibition even reverses preexisting
glomerulosclerosis in a five-sixths nephrectomy model.\textsuperscript{13} The
to extent to which increased expression of NF-\(\kappa\)B-targeted genes
contribute to aldosterone-induced renal injury may be de-
duced from studies in genetically deficient mice. Obese (\textit{db/db})
mice genetically deficient in MCP-1 are protected against protein-
uria, inflammation, and glomerulosclerosis\textsuperscript{14,15}; whether MCP-1
deficiency protects against aldosterone-induced renal injury \textit{per se}
has not been reported, but obesity is associated with increased
circulating aldosterone concentrations. PAI-1–deficient mice are
also protected from aldosterone/salt-induced glomerulosclero-
sis\textsuperscript{16}; in contrast, PAI-1 deficiency does not protect against inter-
stitial inflammation in response to aldosterone and salt treatment.

What implications do these studies have for the treatment of
patients? Activation of the renin-angiotensin-aldosterone
system increases whereas MR antagonism decreases circulating
IL-6 and PAI-1 concentrations in humans.\textsuperscript{16} Whether MR ac-
tivation decreases renal cytokine or PAI-1 expression in hu-
man IL-6 and PAI-1 concentrations in humans.\textsuperscript{16} Whether MR ac-
tivation decreases renal cytokine or PAI-1 expression in hu-
man. Our understanding of the pathophysiologic role of aldoste-
rona has progressed during the past 15 yr, and the clinical use
of MR antagonists has seen resurgence. We often contrast the
proinflammatory/profibrictic effects of aldosterone in nonepi-
thelial cells to the classic physiologic role of aldosterone in
promoting epithelial sodium transport. The studies of Leroy \textit{et al.}
suggest that, in the kidney, these two effects are more inti-
mately linked than previously appreciated.

DISCLOSURES
None.

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See related article, “Aldosterone Activates NF-\(\kappa\)B in the Collecting Duct,” on
pages 131–144.

Unified Ultrasonographic Diagnostic Criteria for
Polycystic Kidney Disease

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Autosomal dominant polycystic kidney disease (ADPKD) is
the most common life-threatening hereditary disease in the

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