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## **Pathophysiologic approach to metabolic acidosis**

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Metabolic acidosis is one of the most common complications of chronic kidney disease. It is related to progression of chronic kidney disease, and wide range of other functional impairments in patients. Until recently, only serum bicarbonate levels have been used for evaluation of acid-base disturbance in patients with reduced kidney function. However, recently emerging evidence may imply that nephrologists should re-think clinical approach to metabolic acidosis of patients with chronic kidney disease from two viewpoints, pH and anion gap. In the first place, textbooks of biochemistry or physiology clearly address that blood pH is the most important acid base parameter for cellular function. Therefore, we should know whether the prognostic impact of hypobicarbonatemia varies according to pH levels. A recent cohort study using chronic kidney disease patients revealed venous pH modified the association of low bicarbonate levels with progression of chronic kidney disease. And recently an acidosis with high anion gap has been recognized as an important prognosis factor, because veverimer, a non-absorbable hydrochloride binding polymer, has been shown to improve kidney function and decrease anion gap. Acidosis with high anion gap frequently develops in later stage of chronic kidney disease. Therefore, anion gap is time varying factor. Recent analyses using marginal structural models showed that acidosis with high anion gap was associated with high risk of chronic kidney disease. From these evidences, it may be necessary to re-consider clinical approach to metabolic acidosis of chronic kidney disease.