TEST ID: SAT24
SUPERSATURATION PROFILE, 24 HOUR, URINE

USEFUL FOR

Diagnosis and management of patients with renal lithiasis:

- In patients who have a radiopaque stone, for whom stone analysis is not available, the supersaturation data can be used to predict the likely composition of the stone. This may help in designing a treatment program.
- Individual components of the supersaturation profile can identify specific risk factors for stones.
- During follow-up, changes in the urine supersaturation can be used to monitor the effectiveness of therapy by confirming that the crystallization potential has indeed decreased.
- Urine ammonium can be used to evaluate renal excretion of acid and urine pH.
- The protein catabolic rate, calculated from the urine urea nitrogen, can be used to estimate a patient’s protein intake.

CLINICAL INFORMATION

Urine is often supersaturated, which favors precipitation of several crystalline phases such as calcium oxalate, calcium phosphate, and uric acid. However, crystals do not always form in supersaturated urine because supersaturation is balanced by crystallization inhibitors that are also present in urine. Urinary inhibitors include ions (eg, citrate) and macromolecules but remain poorly understood.

Urine supersaturation is calculated by measuring the concentration of all the ions that can interact (potassium, calcium, phosphorus, oxalate, uric acid, citrate, magnesium, sodium, chloride, sulfate, and pH). Once the concentrations of all the relevant urinary ions are known, a computer program can calculate the theoretical supersaturation with respect to the important crystalline phases (eg, calcium oxalate).

Since the supersaturation of urine has been shown to correlate with stone type, therapy is often targeted towards decreasing those urinary supersaturations that are identified. Treatment strategies include alterations in diet and fluid intake as well as drug therapy, all designed to decrease the urine supersaturation.
**INTERPRETATION**

Delta G (DG), the Gibbs free energy of transfer from a supersaturated to a saturated solution is negative for undersaturated solutions and positive for supersaturated solutions. In most cases the supersaturation levels are slightly positive even in normal individuals but are balanced by an inhibitor activity.

While the DG of urine is often positive, even in the urine of nonstone formers, on average, the DG is even more positive in those individuals who do form kidney stones. The “normal” values were simply derived by comparing urinary DG values for the important stone-forming crystalline phases between a population of stone formers and a population of nonstone formers. Those DG values that are outside the expected range in a population of nonstone formers are marked “abnormal.”

If the urine citrate is low, secondary causes should be excluded including hypokalemia, renal tubular acidosis, gastrointestinal bicarbonate losses (e.g., diarrhea or malabsorption), or an exogenous acid load (e.g., excessive consumption of meat protein).

A normal or increased citrate value suggests that potassium citrate may be a less effective choice for treatment of a patient with calcium oxalate or calcium phosphate stones.

An increased urinary oxalate value may prompt a search for genetic abnormalities of oxalate production (i.e., primary hyperoxaluria). Secondary hyperoxaluria can result from diverse gastrointestinal disorders that result in malabsorption. Milder hyperoxaluria could result from excess dietary oxalate consumption, or reduced calcium (dairy) intake, perhaps even in the absence of gastrointestinal disease. High urine ammonium and low urinary pH suggests ongoing gastrointestinal losses. Such patients are at risk of uric acid and calcium oxalate stones.

Low urine ammonium and high urine pH suggests renal tubular acidosis. Such patients are at risk of calcium phosphate stones.

Patients with calcium oxalate and calcium phosphate stones are often treated with citrate to raise the urine citrate (a natural inhibitor of calcium oxalate and calcium phosphate crystal growth). However, since citrate is metabolized to bicarbonate (a base) this drug can also increase the urine pH. If the urine pH gets too high with citrate treatment, one may unintentionally increase the risk of calcium phosphate stones. Monitoring the urine ammonium is one way to titrate the citrate dose and avoid this problem. A good starting citrate dose is about one-half of the urine ammonium excretion (in mEq of each). One can monitor the effect of this dose on urine ammonium, citrate, and pH values, and adjust the citrate dose based upon the response. A fall in urine ammonium should indicate whether the current citrate is enough to partially (but not completely) counteract the daily acid load of that given patient.

The protein catabolic rate is calculated from urine urea. Under routine conditions, the required protein intake is often estimated as 0.8 g/ kg body weight.

The results can be used to determine the likely effect of a therapeutic intervention on stone-forming risk. For example, taking oral potassium citrate will raise the urinary citrate excretion, which should reduce calcium phosphate supersaturation (by reducing free ionic calcium), but citrate administration also increases urinary pH (because it represents an alkali load) and a higher urine pH promotes calcium phosphate crystallization. The net result of this or any therapeutic manipulation could be assessed by collecting a 24-hour urine and comparing the supersaturation calculation for calcium phosphate before and after therapy.

Important stone-specific factors:

- **Calcium oxalate stones:** urine volume, calcium, oxalate, citrate, and uric acid excretion are all risk factors that are possible targets for therapeutic intervention.
- **Calcium phosphate stones** (apatite or brushite): urinary volume, calcium, pH, and citrate significantly influence the supersaturation for calcium phosphate. Of note, a urine pH <6 may help reduce the tendency for these stones to form.
- **Uric acid stones:** urine pH, volume, and uric acid excretion levels influence the supersaturation. Urine pH is especially critical, in that uric acid is unlikely to crystalize if the pH is >6.
- **Sodium urate stones:** alkaline pH and high uric acid excretion promote stone formation.

A low urine volume is a universal risk factor for all types of kidney stones.