INHIBITORS AND PROMOTERS OF STONE FORMATION*

H. Fleisch

Department of Pathophysiology
University of Berne
Berne (Switzerland)

Currently, three main mechanisms are thought to be important in the formation of urinary stones: 1) the relationship between the concentration of the precipitating substances in urine and the solubility of the mineral phase formed, 2) the role of promoters of crystallization and aggregation, and 3) the part played by inhibitors of crystal formation and aggregation (Fig. 1).

SATURATION OF URINE

It is now widely accepted that even in normal people, urine is ordinarily supersaturated with respect to calcium oxalate (1-6), octocalcium phosphate (2, 3), hydroxyapatite (1, 2), and sometimes with respect to brushite (1, 7, 8). The degree of supersaturation is usually higher in patients with urinary stones (2-4, 7-10). This is due mainly because these patients tend to excrete more calcium (10-12), but also because urinary oxalate can be increased (10, 13). Urine is also often supersaturated with respect to sodium urate and ammonium urate (14, 15). Supersaturation with regard to magnesium ammonium phosphate is restricted to the cases where the urine becomes alkaline because of ammonium production by bacteria.

SUPERSATURATED SOLUTION

Homogenous/heterogenous nucleation and

Crystal growth

SMALL CRYSTALS

Crystal growth

LARGE CRYSTALS

Crystal aggregation

CRYSTAL AGGREGATES

Fig. 1. Mechanisms of mineral formation. Inhibition of crystal growth is denoted by open arrows; inhibition of crystal aggregation is denoted by the large closed arrows.

Supersaturation can vary in degree. It can be in the metastable range where precipitation may occur only when induced by epitaxy or heterogenous nucleation, or it can be in the unstable region where rapid spontaneous precipitation does occur. The limit between the two ranges, which can be called the spontaneous formation product, is not a fixed number but will depend upon the duration of incubation.

These theoretical considerations are relevant to what occurs in vivo. It was found that when the urinary saturation measured chemically is above the spontaneous formation product required for a rapid induction of precipitation in inorganic solutions, crystals can usually be detected in the voided urine specimen (3). On the other hand, when the ion product is below this product, crystals are absent.

CRYSTAL GROWTH AND CRYSTAL AGGREGATION

In the past, attention was devoted mostly to the formation and growth of crystals. Recently, interest has been directed to an area which, until now, had been neglected: the crystal aggregation. This term describes the process of crystals binding one to another, resulting in the formation of larger clusters. In vitro, aggregation of both calcium oxalate (16, 17) and calcium phosphate crystals (18).