natural samples is also omitted. There are some good sections in the book. The use of definite exercises facilitates the organization of a course. In general, the reaction of the reviewer toward this text is unenthusiastic.

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Ionic Equilibrium as Applied to Qualitative Analysis. By T. R. HOGNESS and WARREN C. JOHNSON, both at the University of Chicago. x + 306 pp., with 18 tables and 23 illustrations. New York: Henry Holt and Company. 1941. $2.00.

ACCORDING to the preface this book "consists of the revised edition of the complete text, 'Qualitative Analysis and Chemical Equilibrium.' It is designed to meet the needs of teachers who either prefer to use their own particular scheme of analytical procedure or want to include in their course supplementary materterial on chemical equilibrium in the form of problems and exercises."

Separate publication of Part I with minor additions and improvements over the 1937 edition should make this well-known exposition more attractive as a basis for class work. While the Brønsted theory is now included the authors still rightly maintain that its consistent and exclusive use is not advisable—*Cf. Jour. Chem. Education,* 14: 448, 1937.

BYRON A. SOULE

SPECIAL ARTICLES

TYPICAL URINARY CRYSTALS OF THREE SULFANILAMIDE DERIVATIVES PRODUCED IN VITRO[1]

FOLLOWING the administration of sulfapyridine, sulfathiazole or sulfadiazine to humans, corresponding crystals with characteristic shapes may appear in the urine (Fig. 1). These crystals were found to consist for the most part of the acetylated derivatives of the aforementioned compounds. Their appearance, however, is entirely different from the simple rectangular, rhomboid or trapezoid structures which can be obtained by crystallizing the pure acetyl derivatives from water.[1a] It seemed of interest, therefore, to investigate the influence of urine upon the crystal shape of acetylated sulfanilamide compounds.

Crystallization of the pure acetyl derivatives of sulfapyridine, sulfathiazole and sulfadiazine from *normal* human urine gave crystals identical with the simple forms obtained from water. This result remained uninfluenced by the addition of the free compounds to the urine. The presence of sugar and albumin in the specimen likewise had no effect upon the crystal forms. If, however, the urine of patients, receiving one of the above-named sulfanilamide derivatives, was used for crystallization of the acetyl compounds, the forms obtained in a large majority of experiments were identical with *urinary* crystals (Fig. 1), occurring naturally in such urines. The *in vitro* formation of these urinary crystals was not dependent upon the original presence of such forms in the patient's urine. The faculty of producing typical urinary crystals of sulfanilamide derivatives, apparently occurring exclusively in urines of patients receiving the compounds, suggests the presence of a certain substance in these urines responsible for the effect. Experiments on the nature of the crystal-forming reaction are in progress.

The structures of urinary crystals outlined in Fig. 1 are those most commonly encountered. They are

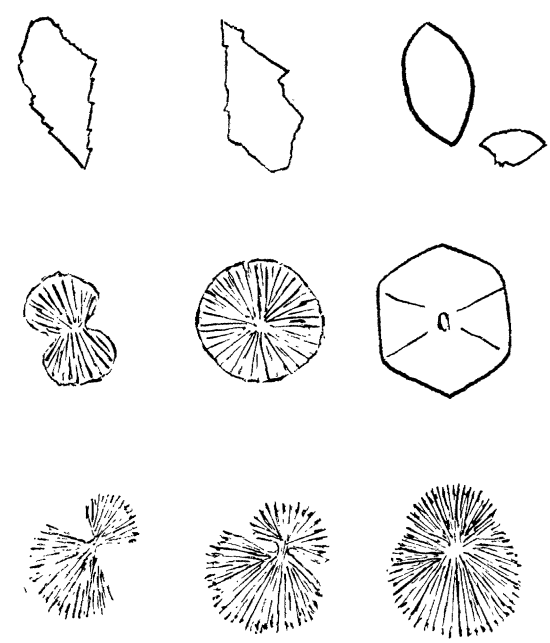

FIG. 1. Crystals appearing in human urine after administration of (top to bottom): *Sulfapyridine*—arrowheads and whetstones. *Sulfathiazole*—Striated dumb-bells (shocks of wheat with central binding), rosettes with radial striations and regular hexagonal platelets (all structures *symmetrical*). *Sulfadiazine*—Striated dumb-bells (shocks of wheat with excentric binding) and shell-forms with radial striations (all structures *asymmetrical*). It is apparent that the sulfathiazole rosettes and the sulfadiazine shells grow out of their respective dumb-bell forms. (Traced from micro-photographs of urinary sediment, enlargement 250×)

[1] Aided by a grant from the Sidney C. Keller Research Fund.

[1a] A saturated aqueous solution of any of these urinary crystals contained the acetyl derivative of the respective drug in a concentration which very significantly exceeded the solubility in water of the chemically pure acetylated compound. It was usually about twice as high.

based upon a follow-up study of crystal shapes in urines of 87 patients treated with sulfapyridine, sulfathiazole and sulfadiazine. Though varying in form from individual cases and sometimes even from the same patient on consecutive days, they were found to present forms specific for each of the three compounds investigated. Detailed data on physical and chemical analysis of these crystals will be published elsewhere. (Microphotographs of urinary crystals showing some of the typical sulfapyridine, sulfathiazole and sulfadiazine forms have been presented in several publications.[2, 3, 4, 5])

Crystallization experiments have been carried out with the urines of 51 patients receiving sulfapyridine, sulfathiazole and lately also sulfadiazine. In all specimens investigated, the *in vitro* formation of urinary crystals was attempted with acetylsulfapyridine as well as acetylsulfathiazole, regardless of which of the three compounds had been given to the patient. In recent experiments acetylsulfadiazine also was used.

For crystallization, an excess of the compound is added to the filtered and acidified urine, heated to boiling and immediately filtered. Crystals appear in the filtrate as it cools to room temperature.

It was found that urines of patients receiving sulfathiazole or sulfadiazine usually gave typical urinary crystals with both acetylsulfathiazole and acetylsulfadiazine, while with acetylsulfapyridine the forms obtained from these urines were atypical, although mostly different from crystals of the pure compound in water. Sulfapyridine urines, on the other hand, produced characteristic whetstones or arrowheads with acetylsulfapyridine, whereas the crystals formed with the acetyl products of sulfathiazole and sulfadiazine deviated more or less from their described typical appearance. In some instances sulfapyridine urines produced characteristic urinary crystals with the acetylated compounds of all 3 sulfanilamide derivatives.

Of the 51 urine specimens investigated, in 32 characteristic urinary crystals could be produced with at least one of the 3 compounds. The most typical form was always obtained with the acetyl-derivative of the drug which the patient had received. The shapes produced were identical with those shown in Fig. 1. Sixteen of the urines yielded more or less atypical crystals, while 3 gave negative results (forms as from water). These 3 urines had specific gravities between 1.010 and 1.014. In general it was observed that the production of characteristic urinary crystals may not succeed with highly diluted urines; it can, however, often be achieved with such specimens by concentrating them on the steam-bath before use for crystallization. On the other hand, urines can be depleted of their faculty to form urinary crystals by repeated supersaturation with an acetylated compound and removal of the crystals which appear on cooling. An alkaline reaction will inhibit the production of urinary crystals. The crystal-forming potency can be restored upon acidification. If urinary crystals are recrystallized from normal urine or water they assume the simple shapes which are obtained from water with the pure acetylated compounds. Urines of patients receiving sulfanilamide do not seem to possess the faculty of forming urinary crystals with the 3 compounds studied.

The artificial production of urinary crystals proves that the shapes outlined are specific for the individual compounds and are formed from their acetylated derivatives. The presence of such crystals in the urine, therefore, makes it possible to identify the particular sulfanilamide compound administered to the patient.

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A FILTERABLE VIRUS DEMONSTRATED TO BE THE INFECTIVE AGENT IN OVINE BALANO-POSTHITIS[1]

SO-CALLED venereal infection of sheep has been recognized in some sheep-raising areas of the United States and other countries for over thirty years. It is known in this country as foul sheath, sheath infection, balanitis, venereal form of lip and leg ulceration and, in Australia, it is called pizzle-rot. Filmer, in Australia, proposed the terms posthitis and balanoposthitis. Lesions are most commonly found at the prepucial orifice and on the lips of the vulva, and in the male the penis may be involved. The disease is characterized by ulceration with scab production. The more severe lesions have been noted on the prepuce and vulva. Severe sheath lesions usually result in phimosis or paraphimosis. The penis lesion is ordinarily a mild inflammation with ulceration unless accompanied by paraphimosis, which then results in a severe process with the more extensive ulceration and heavy scab formation such as is found on the prepuce.

Until late years, the disease has been classified as one of the many necrophorus infections. In a previous examination of two naturally infected rams

[1] Paper No. 155, Journal Series, Agricultural Experiment Station, Montana State College.