

MANAGEMENT OF URINARY TRACT INFECTIONS

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In recent years, pronounced progress in the management of urinary tract infections has been made primarily because of three factors:

1. A more complete investigation of the urinary tract to rule out the presence of coexisting pathological conditions. The ease with which this may be accomplished has been facilitated greatly since the introduction of intravenous urography.

2. A thorough bacteriological study, including a stained smear of the sediment and such cultural investigations as are deemed necessary to classify the organism. In certain instances, additional cultural studies should be made to determine certain properties which may be possessed by the various organisms, such as the power of splitting urea.

3. The introduction of the newer chemotherapeutic agents. Since sulfanilamide and mandelic acid have been made available, numerous drugs which have been employed in the treatment of urinary tract infections in the past have been discarded and the management of such infections has been placed on a strictly scientific basis.

Although the type of organism present definitely influences the choice of drug to be prescribed, additional conditions merit consideration before mandelic acid or sulfanilamide are used. In the aged, the blood urea and carbon dioxide should be studied frequently as acidosis may result from the administration of mandelic acid. The use of sulfanilamide may produce a similar result, but with the simultaneous administration of sodium bicarbonate, it occurs to a lesser degree.

With impairment of renal function, further depression of function may follow the use of either drug, and concentration of the drugs in the urine may not be sufficient to exert bacteriocidal effects. Lack of tolerance or an idiosyncrasy to either of the drugs may prevent its use for the time needed to secure satisfactory results.

Occasionally, recurrent infections of the bladder in men fail to respond to the use of mandelic acid, usually because a persistent infection in the prostate and seminal vesicles continues to reinfect the bladder. In such cases, sulfanilamide is prescribed for its bacteriostatic action.

Mandelic acid therapy may be utilized when *Escherichia coli*, *Aerobacter aerogenes*, and *Streptococcus fecalis* are isolated from the urine. Members of the genera *Salmonella*, *Pseudomonas*, and *Shigella* may respond to this therapy. The ammonium salt in the elixir form, containing approximately 28 per cent of the salt, is usually administered in three fluid drachms (12 cc.) after meals and at bedtime. Approximately 12 gm. of the pure acid are required a day for satisfactory results.

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Certain conditions must exist in order to eradicate the infection: (1) The pH of the urine must be maintained between 5.3 and 5.5, (2) the concentration of the drug in the urine must be between 0.9 and 1.0 per cent, and (3) the fluid intake must be restricted to between 1,000 and 1,200 cc. a day.

If mandelic acid alone does not maintain the pH of the urine at the desired level, acidifying agents such as ammonium chloride or ammonium nitrate may be prescribed. As mandelic acid is eliminated almost entirely in the urine, the concentration of the drug in the urine may be determined readily from the output of urine in a twenty-four hour period, and the amount of the drug taken daily. The medication may be continued over a period of ten days to two weeks unless a toxic reaction or an idiosyncrasy to the drug is evident. If after an interval of a week or ten days the culture of the urine is positive, a second course of treatment is indicated. Mandelic acid therapy will be efficacious in eradicating approximately 85 to 90 per cent of uncomplicated infections of the kidney and bladder.

Sulfanilamide may be used when the organisms are *Escherichia coli* and *Aerobacter aerogenes*. It also exerts a bacteriocidal effect in alkaline urine, and thus has a distinct advantage over mandelic acid which acts efficaciously only in the presence of strongly acid urine. Sulfanilamide, therefore, may be used in the presence of urea splitting organisms which form ammonia and render the urine strongly alkaline. Accordingly, certain cases of uncomplicated infections caused by the proteus organism may respond to this medication. However, in the coccal group of infections, our results from the use of sulfanilamide have not been striking.

The prescribed dosage of sulfanilamide varies with the authors advocating this drug. In treating urinary tract infections in adults, I prefer the following dosage: 60 gr. (4 gm.) a day for a period of three days, to be taken after each meal and at bedtime; for the next two days a total dosage of 40 gr. (2.65 gm.) if given. After this period, a maintenance dosage of 30 to 40 gr. (2.0 gm.-2.65 gm.) a day for a total period of ten to fourteen days is prescribed. In infants, 5 to 10 gr. are given daily; in children from two to five years of age, 15 gr. daily; from five to ten years of age, 15 to 20 gr. daily; and over fifteen years of age to young adults, 20 to 25 gr. daily.

Equal doses of sodium bicarbonate are given with the sulfanilamide. There is some indication that better results are secured when the drug is administered at regular intervals both day and night. By doing so, it is possible to maintain in the blood a constant free sulfanilamide level of approximately 9 to 10 mg. per 100 cc.

Neoprontosil, which forms sulfanilamide in the body by a process of reduction, also may be prescribed. As has been indicated by other

authors, neoprontosil apparently has a more pronounced therapeutic effect in some instances than can be explained by its sulfanilamide content, and may be employed when the patient does not tolerate sulfanilamide. Forty to 60 gr. (2.65 to 4 gm.) may be given daily.

If sulfanilamide or neoprontosil cannot be administered by mouth because of nausea and vomiting, subcutaneous or intramuscular injections of prontosil are advisable. In an adult, 2 cc. of a 2.5 per cent solution of neoprontosil per pound of body weight to 110 or 120 pounds may be administered daily, one-sixth of the calculated dose being injected every four hours. Careful check of the sulfanilamide content of the blood and repeated blood studies always should accompany the administration of sulfanilamide, and with the appearance of idiosyncrasies or toxic manifestations, the use of the drug should be discontinued.

Nearsphenamine is an extremely useful drug in the presence of coccal infections and eliminates the cocci from the urine in from 40 to 50 per cent of uncomplicated cases. In many instances, however, it does not render the urine sterile.

Sulfathiazol and sulfamethylthiazol* in which the thiazol radical has been substituted for a hydrogen radical in sulfanilamide have been produced recently. Insufficient time has elapsed in my experience for me to make definite statements regarding these drugs.

With the introduction of any new medication, the possibility of complications should be kept in mind, and overenthusiasm about results secured in a small series of cases should be avoided. Pool and Cook¹ in citing a series of fifty patients treated with these drugs state that, in their opinion, these two new derivatives of sulfanilamide are less toxic than either sulfanilamide or sulfapyridine.

Of five patients, in whom *Staphylococcus aureus* was isolated in the urinary tract, four received sulfamethylthiazol and one, sulfathiazol. The urine in all these patients became sterile and remained so. The dosage of both these drugs is usually 15 gr. (1 gm.) four times a day.

Although sulfapyridine may be used to combat infections of the urinary tract, it appears to be no more efficacious for eradicating the infection than sulfanilamide. Signs of renal irritation may accompany its use over the period of time needed to eliminate the organisms from the urine, and renal calculi may be produced. Moreover, the cost of the drug is almost prohibitory to the majority of patients.

In patients in whom a mixed infection is present, successful eradication of the infection in the uncomplicated case depends upon a careful bacteriologic study. One or more drugs may be necessary to render the urine sterile. This is especially true in the presence of chronic pyelonephritis in which a mixed infection is present in over 10 to 12 per cent of

*Since the writing of this article, sulfamethylthiazol has been withdrawn from the market.

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cases. When colon bacilli and staphylococcus are coexistent, mandelic acid may be utilized to eliminate the bacilli from the urine and sulfanilamide or nearsphenamine to eradicate the coccal infection.

Today, the majority of uncomplicated infections of the urinary tract can be eradicated by a scientific approach to the problem. Incomplete bacteriologic studies will be attended by persistence of the renal infection, which will continue to exert a deleterious effect upon the renal parenchyma, accompanied by impairment of renal function and perhaps even death attributed to renal disease.

REFERENCE

1. Pool, T. L. and Cook, E. N.: Sulfathiazol and sulfamethylthiazol in the treatment of infections of the urinary tract, Proc. Staff Meet. Mayo Clin., 15:113-116, (February 21) 1940.