SULFATHIAZOLE THERAPY OF GONORRHŒA

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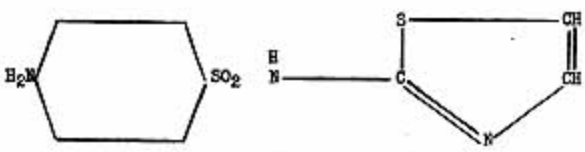
THE various sulfanilamide compounds used in the treatment of gonorrhœa have been highly effective in clearing up active symptoms of the disease. Not long after the discovery of the anti-bacterial properties of sulfanilamide, numerous related sulfanilamide compounds made their appearance. Each compound underwent exhaustive laboratory and clinical tests, and most were cast aside as not measuring up to the present day clinical standards.

Out of this vast array of compounds first came sulfapyridine, which is known all over the world for its therapeutic value in pneumococcal and gonococcal infections. The search for a chemotherapeutic agent of greater effectiveness and less toxicity than those now available continued. The most recent addition to this list is sulfathiazole, a sulfanilamide derivative, which appears to possess advantages over sulfapyridine.

Sulfathiazole is the thiazole analogue of sulfapyridine. It has the following structural formula.



Sulfathiazole was first described by Fosbinder and Water[5] in 1939. Long, Haviland, Edwards and Bliss[9] enumerated the clinical applications of sulfanilamide, sulfapyridine and sulfathiazole in March, 1940. They stated that sulfathiazole was effective against the streptococcus, pneumococcus, staphylococcus and colon bacillus infections.

The pharmacology of sulfathiazole has been carefully investigated by Van Dyke, Greep, Rake, and McKee[15] by Long, Haviland and Edwards[10] and by Barlow and Homburger.[2] These investigators often used sulfanilamide or sulfapyridine for comparison. Its chief advantages compared to sulfapyridine are believed to be: (1) more uniform absorption; (2) less conjugation after absorption so that a higher proportion of the total drug in the body-fluids is chemotherapeutically active; (3) less tendency to cause serious nausea or vomiting; and (4) greater effectiveness against the staphylococcus.

Pool and Cook,[13] in their paper on urinary tract infections, presented one case of gonorrhœa which was cured by the administration of sulfathiazole. Recent clinical reports indicate that sulfathiazole is particularly effective in the treatment of this disease. Excellent results have been presented by Stirling[14]; by Lloyd and Erskine[8]; by Mahoney, Wolcott and Van Slyke[11]; by Culp[4]; by Ballenger, McDonald and Coleman[1]; by Burkholder and Bang[3]; by Knight, Uhle and Latowsky[7]; and by Mitchell, Greig and Uren.[12]

The object of this report is to describe the experiences and results with sulfathiazole obtained in the treatment of gonorrhœa at the Toronto General Hospital. One hundred and twenty cases of gonorrhœal urethritis in the male are the basis for this report. In addition,

38 cases of non-specific urethritis cases in the male are presented.

The 120 male cases of gonorrhœa treated with sulfathiazole were obtained from routine admissions to the out-patient clinic. No selection of patients was made in this series. Cases of both acute and chronic gonorrhœa were included in the group. The duration of the urethral discharge varied from 1 day to 4 months, with 85 per cent confined to 7 days or less. The average age of the 120 cases was 25 years, but their ages varied from 14 to 65 years.

Of the 120 cases 96 had had no previous treatment with any chemotherapeutic agent. Twenty-four cases had previously failed to respond to one or more courses of sulfanilamide or sulfapyridine.

A positive diagnosis of gonorrhœa was obtained before sulfathiazole was started. A positive smear or culture of the urethral exudate was obtained in every case. Gonococci were demonstrated in the smears of those cases failing to have positive cultures.

Each patient in the early stages of treatment was seen at intervals of 2 days, and later at weekly intervals. On each return visit a careful urological examination was made, and urethral smears and cultures were obtained at appropriate intervals.

The patients were instructed to avoid alcohol, fatigue, heavy work, and abstain from sexual activity. The fluid intake was not limited.

The criteria of cure required that there be a complete absence of clinical evidence of the disease, that repeated smear and culture examinations be negative, and that the two-glass test of urine be free of pus and shreds. Patients were observed for a period of 6 weeks following cessation of chemotherapy.

Dosage.—The routine consisted of: 1st day—1 gram, 3 times a day after meals; 2nd and 3rd days—1 gram, 3 times a day after meals, and 1 gram on retiring; 4th and 5th days—1 gram, 3 times a day after meals.

It was decided to keep the dosage uniform, and not to administer the drug beyond the 5-day period if possible. The dosage can be prolonged, if so desired, although this is unnecessary in most instances. The reasons for not extending the drug beyond the 5-day period were: (1) it was apparent that if sulfathiazole was to be effective the patient was usually gonococcus-negative in an average of 3 days. (2) As we were dealing with ambulatory patients it was decided to give a dosage of the drug compatible with the normal activity of the patient. (3) Toxic reactions are rare before 5 days.

Of the 120 cases treated with sulfathiazole the majority received a total dosage of 17 grams in all. In some cases the amount administered varied considerably. In resistant cases the above course of treatment was either repeated or supplemented by the addition of 1.5 grams per day for an additional 7 to 10 days. The maximum amount given any patient was 51 grams.

RESULTS

The results of treatment of gonorrhœal urethritis in the male with sulfathiazole are summarized in Table I. Cures were obtained in 111 of 120 cases, indicating a gross cure rate of 92.5 per cent. Of this group of 120 cases, 24 had previously failed to respond to courses of sulfanilamide or sulfapyridine, and 22 (90.6 per cent) were cured with sulfathiazole. The remaining 96 cases had not been treated previously with any chemotherapeutic agent, and 89 (92.7 per cent) responded favourably.

TABLE I.

SUMMARY OF TREATMENT OF 120 CASES OF GONORRHŒAL URETHRITIS IN THE MALE TREATED WITH SULFATHIAZOLE.

Type of case	*Number of cases*	*Cured cases*		*Failures*	
		No.	*Percentage*	*No.*	*Percentage*
Total cases...	120	111	92.5	9	7.5
Previously untreated cases.	96	89	92.7	7	7.3
Previous sulfanilamide or sulfapyridine failures.....	24	22	90.6	2	9.4

Nine cases were failures. In 3 of these there was evidence that failure was due to re-infection, as they indulged in coitus during the early period of treatment. In 3 other cases the discharge recurred after an asymptomatic stage of the infection which lasted from 4 to 10 days after the drug was discontinued. Some of the failures were encountered in individuals who failed to co-operate in their treatment, or in those who indulged in excessive manual labour during the treatment.

In the cured cases the time-interval between the beginning of sulfathiazole therapy and the disappearance of discharge averaged 3 days and ranged from 1 to 7 days. No complications such as prostatitis or epididymitis developed in any of the cases during the period of treatment.

TOXIC MANIFESTATIONS

In 110 of the total number of 120 patients who were given a full course of sulfathiazole there were no symptoms of toxicity. In the remaining 10 patients, 3 complained of slight headache, 3 experienced vertigo, 2 suffered nausea, and 2 noticed slight drowsiness. The incidence of toxic reactions was 8.0 per cent. These symptoms were invariably mild, and did not in any way interfere with the normal daily activities of the patient.

Other toxic manifestations, sometimes mentioned, such as fever, rash, hæmaturia, injection of scleræ and conjunctivæ, anuria with azotæmia, leukopenia, granulocytopenia, and painful joints were not encountered in the present series.

NON-SPECIFIC URETHRITIS

The results of treatment of non-specific urethritis cases in the male with sulfathiazole are summarized in Table II. The dosage routine in these cases was the same as for the gonorrhœal cases, except that the above course was supplemented by the continued administration of 1.5 grams per day for a variable period of time. Of the 38 cases treated with sulfathiazole, the majority received a total dosage of 30 grams.

TABLE II.

SUMMARY OF TREATMENT OF 38 CASES OF NON-SPECIFIC URETHRITIS IN THE MALE TREATED WITH SULFATHIAZOLE.

Type of case	*Number of cases*		*Cured cases*		*Improved cases*		*Failures*	
	No.	*Per-centage*	*No.*	*Per-centage*	*No.*	*Per-centage*	*No.*	*Per-centage*
Non-specific urethritis.	38		21	55.3	9	23.7	8	21.0

Cures were obtained in 21 of 38 cases, indicating a gross cure rate of 55.3 per cent. Improvement was noticed in 9 cases, or 23.7 per cent. Eight cases (21.0 per cent) were failures.

In the cured cases the time-interval between the beginning of sulfathiazole therapy and the disappearance of discharge averaged 8 days.

TABLE III.

SUMMARY OF THE RESULTS OF TREATMENT OF GONORRHŒA BY CHEMOTHERAPEUTIC AGENTS AT THE TORONTO GENERAL HOSPITAL

Drug	*Total cases*	*Cured cases (percentage)*
Sulfanilamide.....	500	36 (77% improved)
Sulfapyridine.....	252	87
Sulfamethylthiazole.....	65	84
Sulfathiazole.....	120	92.5

SUMMARY AND CONCLUSIONS

1. The results in the treatment of 120 cases of gonorrhœal urethritis in the male treated with sulfathiazole are presented. The gross cure rate was 92.5 per cent. In the patients who had had no previous form of therapy the cure rate was 92.7 per cent. The group that had failed to respond to previous forms of chemotherapy did not show an appreciable fall in the cure rate.

The majority received an average of 17 grams of sulfathiazole and were cured within 3 days.

2. The use of sulfathiazole is associated with an unusual freedom from complications, so frequently encountered with gonorrhœa.

3. The occurrence of toxic reactions to sulfathiazole in the dosages recommended is slight.

4. Sulfathiazole appears to be a most efficient drug in the treatment of gonorrhœa. Its use is accompanied by a higher percentage of cures and a lower incidence of toxic effects than with any other chemotherapeutic agent.

5. A summary of the treatment of 38 cases of non-specific urethritis in the male treated with sulfathiazole is also presented. The cure rate in this group was lowered to 55.7 per cent, but an additional 23.7 per cent were greatly improved.

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