blood counts and drug levels in the blood were not determined. All infants in this group were observed in the hospital for at least one week after being cured. No complications or relapses were noted during this time or in the follow-up clinic. These cases are presented in table 1.

The results of the methods of treatment of the three groups of patients are compared in table 2.

SUMMARY AND CONCLUSIONS

1. The sulfonamides used in the treatment of gonococcic ophthalmia neonatorum have greatly decreased the duration of the disease and have practically eliminated complications.

2. Patients are now treated routinely at this hospital only with sulfathiazole by mouth. Local therapy and mechanical protection of the unaffected eye are apparently unnecessary.

3. Sulfathiazole in doses of 1 grain per pound of body weight daily cured our patients and prevented complications.

THE TREATMENT OF MENINGOCOCCIC INFECTIONS WITH SULFADIAZINE AND SULFAMERAZINE

(SULFAMETHYLDIAZINE, MONOMETHYLSULFADIAZINE)

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Many observers have attested the value of sulfadiazine in meningococcic infections.[1] A previous report from this hospital[2] on the treatment of meningitis with sulfadiazine included 24 patients with meningococcic meningitis. Since then we have continued to treat all patients admitted to the Gallinger Municipal Hospital with sulfadiazine[3] or, since March 1943, alternately with sulfamerazine and sulfadiazine. During this time there has been an increasing incidence of meningococcic infections in the District of Columbia as well as in the country as a whole. Through May 31, 1943 we had treated 118 patients with meningococcic meningitis (including the 24 cases already reported) and 3 patients with meningococcemia.

The present report includes a summary of the results obtained with sulfadiazine and sulfamerazine together with an analysis of the factors which influenced recovery or death. We have also studied the severity of the disease as the epidemic progressed and have attempted to correlate this with the results of therapy.

Miss Ruth Mayer rendered technical assistance.

From the George Washington Medical Division (Drs. Lepper and Dowling) and the Pediatric Service (Dr. Sweet), Gallinger Municipal Hospital, and the Departments of Medicine and Pediatrics, George Washington University School of Medicine.

1. Dingle, J. H.; Thomas, Lewis, and Morton, A. R.: Treatment of Meningococcic Meningitis and Meningococcemia with Sulfadiazine, J. A. M. A. **116**: 2666 (June 14) 1941. Trevett, G. I.; Nelson, R. A., and Long, P. H.: Studies on Sulfadiazine: II. The Clinical Use of Sulfadiazine in the Therapy of Bacterial Infections Other Than Pneumonia, Bull. Johns Hopkins Hosp. **49**: 314 (Oct.) 1941. Finland, Maxwell; Peterson, O. L., and Goodwin, R. A., Jr.: Sulfadiazine: Further Clinical Studies of Its Efficacy and Toxic Effects in 460 Patients, Ann. Int. Med. **17**: 920 (Dec.) 1942. Hodes and Strong.[8] Rundlett, Gnassi and Price.[9] Feldman, Sweet and Dowling.[2]

2. Feldman, H. A.; Sweet, L. K., and Dowling, H. F.: Sulfadiazine Therapy of Purulent Meningitis, War Med. **2**: 995 (Nov.) 1942.

3. Sulfadiazine and sulfamerazine for this study were supplied by the Lederle Laboratories, Inc.

PROCEDURE

Routine procedures in the diagnosis and treatment of these patients have been carried out as follows: As soon as a patient believed to have meningitis was admitted to the ward, a lumbar puncture was performed. On the specimen of spinal fluid obtained several examinations were made. A cell count and a Pandy test were done. Smears of the centrifuged sediment were made. They were stained with both methylene blue and Gram's stains. If organisms believed to be meningococci were seen, typing by means of the Neufeld technic was attempted. Cultures were planted in tryptose-phosphate or tryptose-phosphate-hemoglobin broth and on chocolate agar slants. A quantitative dextrose determination was made on the clear supernatant fluid by an application of Benedict's modification of the Folin-Wu method.[4] After this study had established a presumptive diagnosis of meningococcic meningitis, a blood culture was obtained and treatment was begun. An initial oral dose of 6 Gm. of sulfadiazine or sulfamerazine was followed by 1 Gm. every four hours in adults. A proportionately smaller dose was given to children. For severely ill patients, especially those too stuporous to swallow, or for those who were vomiting excessively, the initial dose and a varying number of following doses were given as a 0.5 to 1 per cent solution of the sodium salt of the drug intravenously or subcutaneously. The sulfonamide drug was continued until the patient was afebrile for approximately seven days unless some indication for stopping the drug developed sooner. Frequent hemograms, urinalyses and blood urea nitrogen and blood sulfonamide determinations were obtained during the period of drug administration. Follow-up lumbar punctures were done on the second hospital day and again when discharge was contemplated. If the cell count had not fallen to 30 cells per cubic millimeter the puncture was repeated at weekly intervals until that level was reached. At this time the patient was allowed out of bed and was subsequently discharged. Additional lumbar punctures were done only when recovery was not progressing satisfactorily. Each spinal fluid specimen was examined in the same way as the one obtained by the initial lumbar puncture.

Patients who responded poorly to this regimen in the first twenty-four to forty-eight hours were considered candidates for serum therapy. After reevaluation of the clinical status of the patient and the laboratory findings, serum was given intravenously if it was believed indicated.

RESULTS

There have been a total of 118 cases of meningitis treated here using this routine. The etiologic agent in every case was established by one or more of the following methods: (1) positive spinal fluid culture, (2) a positive blood culture, (3) a smear containing demonstrable typical gram negative intracellular or extracellular organisms. All cases not fulfilling these criteria were omitted from this series. Whenever possible the organisms were typed.[5] Seventy-three group I and 6 group II (alpha) organisms were found.

In addition there have been 3 cases of meningococcemia in which neither meningeal signs or symptoms nor any increase in cells in the spinal fluid occurred. Meningococci were cultured from the blood of all these patients.

4. Benedict, S. R.: The Determination of Blood Sugar, J. Biol. Chem. **64**: 207 (March) 1925.

5. Dr. Sara E. Branham of the National Institute of Health typed many organisms.

Among the 118 patients with meningitis 12 (10.1 per cent) died. Several clinical and laboratory features have been found to be related to prognosis. These factors include age, presence and duration of coma before treatment, number of organisms in spinal fluid and concentration of spinal fluid dextrose on admission and on the second day following therapy. We have measured the speed or recovery by the duration of coma, the duration of temperature elevation over 101 F. by rectum and the duration of a spinal fluid cell count over 30 cells per cubic millimeter from the beginning of treatment. For these comparisons only the patients receiving sulfadiazine have been studied.

The distribution of patients by age is shown in table 1. Sixteen (13.6 per cent) of the patients were under 10 years of age, 66 (55.9 per cent) from 10 to 39 and 36 (30.5 per cent) were 40 years or over. No one under 10 years died, whereas 4 (6.1 per cent) of the patients in the intermediate age group (10-39 years) and 8 (22.2 per cent) of the patients over 39 years succumbed. The difference between the youngest group and the intermediate group is not statistically significant but the death rate in the oldest group is significantly greater than the rate in either of the other two groups as well as these two groups combined. It is also of note that the average duration of coma, fever and pleocytosis is progressively longer in each group and significantly so in the oldest group.

The presence of coma on admission shows a high correlation with the outcome. Among the 44 patients admitted in coma 12 (27.3 per cent) died, whereas not 1 of the 74 patients not in coma on admission died. This is highly significant when tested statistically. The average duration of fever for patients who recovered after being admitted in coma was 4.4 days and for those not in coma was 2.6 days. Moreover, the average duration of lymphocytosis was 26.1 and 18.1 days for patients with and without coma respectively. Both of these differences are of definite statistical significance. On the first day of coma 2 (8.3 per cent) died, whereas of 20 patients admitted with coma of over 1 day's duration 10 (50 per cent) died. In addition, the average duration of illness before the onset of coma of the patients who died was 2 days, which is significantly greater than the average of 1.2 days for the patients who survived after being admitted in coma.

The number of organisms in the spinal fluid has been estimated from smears made in a uniform manner. "Many" organisms were reported when at least one organism was present in practically every field and several organisms were seen in most fields. "Few" organisms were said to be in a smear when approximately one half of the fields contained no organisms and relatively few organisms were present in any individual field. "Rare" organisms were said to be present when they could be demonstrated only after considerable search. When "many" organisms were present 9 patients among 42 (21.4 per cent) died, which is a significantly higher rate than for the patients with "few" organisms, among whom the rate was 5.2 per cent (3 deaths among 58 patients), and also higher than the group of 14 patients with "rare" or "no" organisms, among whom there were no deaths. The averages for the duration of coma, fever and elevated cell count again show a progressive increase the greater the number of organisms.

For the past year we have been doing immediate quantitative dextrose determinations in the spinal fluid. Forty of these patients had dextrose below 10 mg. per hundred cubic centimeters and 6 (15 per cent) died. One (3 per cent) patient among 35 with dextrose between 10 and 49.9 mg. per hundred cubic centimeters died, and 1 (14.3 per cent) out of 7 with dextrose over 49 mg. per hundred cubic centimeters died. Even though suggestive, these figures are not significant. The criteria of rapidity of recovery showed a slight but not significant trend in that the patients with higher dextrose levels responded more rapidly. Dextrose determinations were made on spinal fluids obtained on the second day. The results have been divided into three groups: first, those which decreased or did not increase, second, those which increased but not to 50 mg. per hundred cubic centimeters and, third, those which returned to 50 mg. per hundred cubic centimeters and above.

In the first group 1 out of 4 (25 per cent) died. In the second group 3 (9.7 per cent) among 31 died. In the third group 1 (2.9 per cent) of 34 died. None of these differences are statistically significant.

Other factors which were studied but showed no significant relationship to recovery were sex, race, duration of illness before treatment was begun, presence of

TABLE 1.—*Factors Influencing Prognosis of Patients with Meningococcic Meningitis Treated with Sulfadiazine and Sulfamerazine*

Factor	Group	Number of Patients	Died		Speed of Recovery *		
			Number	Per Cent	Average Duration of Coma	Average Duration of Fever †	Average Duration of Pleocytosis
All cases		118	12	10.1	0.48	2.7	20.6
Age	Less than 10	16	0	0	0.10	1.5	18.6
	10 to 39	66	4	6.1	0.67	2.6	21.9
	40 and over	36	8	22.2	0.89	4.4	22.1
Presence of coma on admission	Yes	44	12	27.3	....	2.6	26.1
	No	74	0	0.0	....	4.4	18.1
Number of organisms in initial spinal fluid	Many	42	9	21.4	0.74	3.4	23.2
	Few	58	3	5.2	0.27	3.1	20.5
	Rare or none	14	0	0.0	0.20	2.0	17.0
	Not recorded	4	0	0.0			
Initial spinal fluid dextrose	Less than 10 mg. per 100 cc.	40	6	15	0.46	3.5	25.7
	10 to 49.9 mg.	35	1	2.9	0.39	3.4	19.2
	50 mg. per 100 cc. and over	7	1	14.3	0.10	1.8	14.0
	Not done	36	4	11.1			
Second day spinal fluid dextrose	No change or decreased	4	1	25.5	2.6	6.4	38.6
	Increased but not normal	31	3	9.7	0.74	4.3	33.3
	Increased to normal	34	1	2.9	0.17	2.2	18.0
	Died before second day	3	3	10.0			
	Not done	48	4	8.3			

* Includes only patients treated with sulfadiazine. † Temperatures permanently below 101 F. by rectum.

neurologic complications on admission, extent of rash, height of initial spinal fluid cell count, group of organisms and the presence of positive blood cultures on admission. Of these, the presence of neurologic complications on admission and the height of the initial spinal fluid cell count show a trend that might become significant when more cases are collected. These trends are that the presence of neurologic complications or of cell counts over 10,000 per cubic millimeter indicates a slower recovery.

Among the patients who recovered, the most frequent complications related to the infection were nerve palsies. These occurred in 21 patients. The majority of them were present on admission or when they could be identified as a comatose patient regained consciousness. They involved both sensory and motor nerves. The only sensory change noted was deafness, which was present in some degree in 8 patients. The motor nerves involved were the cranial third (oculomotor), fourth (trochlear), sixth (abducens), seventh (facial), eleventh (spinal accessory) and twelfth (hypoglossal), which were involved in 14 patients. In 1 boy there was a temporary spinal nerve palsy resulting in a transitory foot drop. More than one nerve was frequently involved, the greatest number in any 1 patient being six. The follow-up on the patients with nerve palsies has been too short for an evaluation of the eventual outcome. However, there has been no appreciable recovery to date in 6 of 8 patients who become deaf, whereas there has been some recovery in 12 of 15 patients with motor nerve involvement.

The other complications that we have encountered include 3 patients who had arthritis, 3 with tenosynovitis and 1 with conjunctivitis from which a meningococcus was cultured. All of these complications were of short duration.

TABLE 2.—*Severity of Illness and Results of Treatment of Meningococcic Meningitis Treated with Sulfadiazine and Sulfamerazine*

Treatment	Number of Patients	Severity of Illness: Admitted in Coma, Number	Admitted in Coma, Per Cent	Dextrose Less Than 10 Mg. per 100 Cc., Number	Dextrose Less Than 10 Mg. per 100 Cc., Per Cent	Many Cocci in Initial Spinal Fluid, Number	Many Cocci in Initial Spinal Fluid, Per Cent	Results of Treatment: Died, Number	Died, Per Cent	Recovered: Average Duration of Coma	Average Duration of Fever *	Average Duration of Pleocytosis	Specific Serum Used
Sulfadiazine in series....	22	7	31.7	13	59.2	7	31.7	2	9.1	0.66	3.0	28.0	1
Sulfamerazine in series..	22	6	27.3	12	54.5	5	22.7	2	9.1	0.28	2.9	22.9	3
Sulfadiazine, all cases...	96	38	39.6	28	47.6†	37	39.4‡	10	10.4	0.48	2.7	20.6	8
Total of lines 2 and 3....	118	44	37.3	40	48.7§	42	36.8¶	12	10.2	0.44	2.8	21.0	11

* Temperatures permanently below 101 F. by rectum. † Determined in only 60 patients. § Determined in only 82 patients. ‡ Based on 94 patients. ¶ Based on 114 patients.

TREATMENT

As seen in the third line of table 2, the mainstay of treatment in 96 cases was sulfadiazine. There were ten (10.4 per cent) deaths in this group. One half of these deaths occurred within the first twenty-four hours after admission. Eight of these patients received serum in addition to sulfadiazine. Twenty-two cases have been treated with sulfamerazine. There were two deaths (9.1 per cent) in this group, neither within twenty-four hours. In 3 of these cases serum was administered in addition to chemotherapy.

The response to therapy in the sulfadiazine cases in which survival occurred has varied from dramatic to satisfactory. The time taken for the patient to become rational and the temperature to become normal has been spread over a wide range, the extremes being 0.25 to 6.75 and 0.0 to 12.0 days and the averages 0.48 and 2.7 days respectively.

The most significant complications of sulfadiazine therapy as well as the most common have been urinary in nature. The criteria which we recognize as diagnostic of urinary lithiasis are renal colic, gross hematuria and pronounced unexplained oliguria or anuria with or without azotemia or any combination of these. There have been 10 cases presenting one or more of these findings. In 6 of these cases symptoms developed at a time at which the drug could be discontinued safely. In all 6 cases an uneventful subsidence of symptoms occurred when this was done and fluids were forced. In cases in which further treatment of the infection was required the sulfonamide dosage was maintained, decreased or temporarily interrupted depending on the blood sulfadiazine level. Fluids were forced and attempts at alkalization were made with prompt and satisfactory recovery from renal symptoms. In only 1 case was cystoscopy needed. This was done on the third day of therapy and the drug was reinstituted in low dosage after a twenty-four hour interval.

Other toxicities from sulfadiazine have included 3 instances of rash with fever, 2 instances of fever alone and 1 instance of rash and conjunctivitis. One patient developed a transient leukopenia.

In addition to the foregoing patients, since March 1943 an attempt has been made to evaluate sulfamerazine by giving alternate patients this drug and sulfadiazine. To date this study is unfinished but, as seen in table 2, 22 cases have been treated with each drug with two (9.1 per cent) deaths in each series. The age distribution was approximately the same in the two groups. The severity of cases as measured by presence of coma, dextrose content of the fluid on admission and the number of organisms in the initial smear showed that those patients who received sulfadiazine were slightly more ill. The somewhat more rapid response in patients who survived after receiving sulfamerazine may be correlated with their being less seriously ill. Only 1 person in the sulfadiazine group received serum. Three sulfamerazine treated patients have also received serum.

Three sulfamerazine treated patients had kidney complications as defined. One required cystoscopy. The others responded favorably to conservative treatment. Two instances of rash and fever, 2 examples of fever alone and 1 instance of leukopenia have occurred with sulfamerazine.

SERUM

As shown in table 2, 11 patients received serum. The only patient in the entire series who received serum intraspinally did so in another hospital immediately after the diagnosis. One other patient also received serum before admission. The course of these 2 patients was not different from the course of those who received no

serum. One patient who was in diabetic acidosis was given serum as soon as the initial dose of sodium sulfadiazine was completed. However, the patient died within eight hours. Eight other patients received serum after having failed to respond to sulfonamide therapy in the first twenty-four to forty-eight hours. Four of these continued to fail and died. Four of these patients survived. In 2 it was felt that the recovery was definitely related to the administration of the serum in that a prompt improvement followed. In the other patients who recovered, the actual value of the part played by the serum in influencing the outcome is questionable. Four of the 6 surviving patients developed mild serum sickness.

Of the 3 cases of meningococcemia without evidence of meningitis, 1 presented an acute onset of petechial rash and high fever and the other 2 showed a maculopapular rash, joint pains and fever. The first patient was treated with sulfadiazine with rapid subsidence of symptoms and no complication. The other 2 patients had recovered spontaneously by the time the diagnosis was established. They were observed for a prolonged period and were discharged in good condition.

Table 3 shows the effect of time of onset of the diseases as the epidemic progressed on the incidence, severity and recovery. From Jan. 1, 1942 to June 30, 1942 there were 28 patients, from July 1, 1942 to Dec. 31, 1942 there were 22 patients and from Jan. 1, 1943 to May 31, 1943 there were 67 patients.

In the first time interval there were three (10.7 per cent) deaths, in the second interval three (13.6 per cent) deaths and in the third period six (8.5 per cent) deaths. It is seen, therefore, that no significant increase or decrease in mortality has occurred. On the other hand, the average duration of coma after treatment and of average time taken for temperature and cell count to return to the standards used have shown a prolongation in the more recent cases. The average duration of coma for the last two periods are both significantly greater than that for the initial interval, but the difference between these two compared with each other is not. The same statistical relationship holds for the average times for the temperature to return below 101 F. and the cell count to return below 30 cells per cubic millimeter. There has also been an increase in the percentage of patients admitted in coma. In the first six months 8 (28.6 per cent) patients were admitted in coma. In the next six months there were 10 (43.4 per cent) patients and in the last five months 31 (46.4 per cent).

COMMENT

We have reviewed our experience with two drugs, sulfadiazine and sulfamerazine, in the treatment of meningococcic meningitis and analyzed the clinical and laboratory factors which bore a relationship to the outcome.

Our experience with both sulfonamides to the present time has been favorable. The over-all death rate of twelve (10.2 per cent) deaths among 118 patients compares satisfactorily with those in the literature for sulfonamide therapy.[6]

The incidence of neurologic complications has not been high. Only a few have not cleared up, and the majority of these are nerve deafness. It is too early at this time to tell how many of these palsies will persist permanently. The incidence of toxicity, especially renal, but also rash and fever with or without conjunctivitis, is greater than generally reported for sulfadiazine. Four and two tenths per cent of the sulfadiazine treated patients had fever, rash and conjunctivitis. Ten and four-tenths per cent of patients developed kidney complications. The large doses used as well as the dehydrated state of many of these patients on admission undoubtedly accounted for this high incidence of complications. Certain things must always be done to guard against this danger. The most essential is to secure an adequate fluid intake. At least 3,000 cc. per day should be given. Excessively high doses of the drug should not be used unless necessary, and if the patient is showing satisfactory clinical progress in spite of a low blood sulfonamide level the dose should not be increased. Although we have attempted to keep the p_H of the urine at or above 7.5 in only a few cases, our results have been similar to those obtained by others and have convinced us that this should be done whenever large doses of the sulfonamides are being given.

It is impossible for us to reach any conclusions about serum therapy as an adjunct to sulfonamides, since we have treated too few cases. Occasional patients, however, do show definite benefit from the administration of serum and we feel that it should be available at all times in case the response to sulfonamides is not satisfactory.

TABLE 3.—*Relationship of the Date of Onset to Severity of Illness and Prognosis*

Date of Onset	Number of Patients	Admitted in Coma		Died		Average Duration of Coma*	Average Duration of Fever†	Average Duration of Pleocytosis
		Number	Per Cent	Number	Per Cent			
Jan. 1, 1942 to June 30, 1942.....	28	3	10.7	8	28.6	0.24	1.67	14.7
July 1, 1942 to Dec. 31, 1942.....	22	3	13.6	10	43.4	0.75	3.05	20.4
Jan. 1, 1943 to May 31, 1943.....	67	6	8.5	31	46.4	0.86	3.44	25.3

* Includes only patients who recovered after treatment with sulfadiazine.
† Temperatures permanently below 101 F. by rectum.

Several clinical factors have been found to be significant in prognosis following treatment with sulfadiazine.

Age is shown to be a most significant factor in mortality and in rate of recovery among surviving patients. Prior to the use of sulfonamides the prognosis of infants and elderly patients with meningococcic meningitis was extremely grave. Even with sulfonamide therapy results in these groups have been reported as still carrying higher death rates.[7] Although we have had relatively few infants in this series, the response in the few we have had has been highly satisfactory and our group under 10 years of age is the most favorable one. These results are in keeping with those reported by Hodes.[8] From our figures it would seem that by far the most unfavorable group to treat is that including patients of 40 years and over.

As stated, no significant differences or definite trends could be brought out relating recovery to duration of illness before therapy. This is almost certainly caused by the pleomorphism of the disease and should not encourage delay in diagnosis and treatment. In any individual case we feel sure that time is an important item. We have data that relate duration in the indi-

6. The references given in footnotes, 1, 7 and 10.

7. Beeson, P. B., and Westerman, Ethel: Cerebrospinal Fever: Analysis of 3,575 Case Reports with Special Reference to Sulfonamide Therapy, Brit. M. J. **1**: 497 (April 24) 1943.

8. Hodes, H. L., and Strong, P. S.: Treatment of Meningococcic Meningitis with Sulfonamides, J. A. M. A. **119**: 691 (June 27) 1942.

vidual case to outcome. Coma has been shown to be definitely detrimental, and any case which is delayed until coma is established certainly has been delayed too long. Furthermore, we have shown that the duration of coma before treatment is started as well as the duration of the illness before coma occurred are both significant in the outcome of the case. We have had several patients treatment of whom has been delayed, who have slowly gone into coma and been in coma for as long as two days before treatment was begun. These cases, we feel sure, would have been saved by earlier diagnosis and treatment. We feel, therefore, that early diagnosis and treatment are most essential.

Another laboratory manifestation which was found to be of significance in terms of mortality and duration of illness was the number of organisms in the spinal fluid. Apparently one can generalize and say that, the more organisms present, the more severe the illness is likely to be.

Prognostic value of spinal fluid dextrose has been emphasized recently by Rundlett, Gnassi and Price.[9] They feel that a rising spinal fluid dextrose is of utmost significance. We have evidence that, in general, relatively high initial spinal fluid dextrose or rising spinal fluid dextrose is a good prognostic sign. However, in the individual case we have found it not completely reliable. In 4 of our patients who died there was a higher spinal fluid dextrose on the second day of illness than on admission. In 1 of these it was over 70 mg. per hundred cubic centimeters. The duration of illness also did not follow spinal fluid dextrose levels more closely than the several other factors studied.

The time of onset in the epidemic was found to be important in speed of recovery but not in mortality. In considering this factor, all the morbidity measurements show a progressive increase in severity of the disease as the epidemic has progressed to the present time, and most of these trends are statistically significant. We feel safe in stating that there has been a definite increase in the severity of the illness in these cases although it has not been reflected in the mortality rate.

For some time it has been apparent that sulfonamides are effective in the treatment of meningococcic meningitis. However, it is well known that this disease is an extremely variable one in its severity, mortality rates varying from 20 to 90 per cent.[10] It is very difficult, therefore, to evaluate a new therapy without accurately controlled experiments. On the other hand, increasing severity and mortality has been the rule in epidemic times until the peak is reached, and if an agent is effective throughout an epidemic its therapeutic value can be accepted. In our experience the mortality in meningitis treated with sulfadiazine has been both low and stable in a time of increased incidence when the virulence of the disease was increasing. We feel that this gives definite proof of the value of this drug in this disease.

We have begun to evaluate the efficacy of treatment with sulfamerazine as compared with sulfadiazine. Up to the present time the mortality rate is exactly the same in the two groups. The duration of illness and complications in relation to the virulence of the infection have been the same with the two drugs. Sulfamerazine seems to be as effective as sulfadiazine. In our hands it has been slightly more toxic, but the difference is not great.

9. Rundlett, Emilie; Gnassi, A. M., and Price, Preston: Meningococcic Meningitis, J. A. M. A. **119**: 695 (June 27) 1942.
10. Dingle, J. H., and Finland, Maxwell: Diagnosis, Treatment and Prevention of Meningococcic Meningitis, War. Med. **2**: 1 (Jan.) 1942.

SUMMARY

1. We have given sulfadiazine to 96 patients who had meningococcic meningitis, of whom 10 died, and sulfamerazine to 22 patients, of whom 2 died.

2. The presence of coma on admission and the age of the patient were the two most important factors in prognosis. One fourth of all patients admitted in coma died. If coma had been present longer than one day, one half of the patients died. No patients not in coma on admission died. Almost one fourth of patients over 40 years of age died.

3. The presence of numerous organisms or of a very low dextrose level in the initial spinal fluid are other unfavorable prognostic signs.

4. The incidence and severity of the disease treated by us has increased as expected in epidemic times, but the mortality rate has been kept constant.

5. Sulfadiazine is an effective agent in the treatment of meningococcic meningitis.

6. Sulfamerazine is apparently as good a therapeutic agent as sulfadiazine.

TREATMENT OF EPIDEMIC NEONATAL DIARRHEA WITH SUCCINYL-SULFATHIAZOLE

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Outbreaks of epidemic diarrhea of newborn infants occurred in the fall of 1942 in Cleveland, Carlisle, Pa., Detroit, Toledo, Ohio, Dayton, Ohio, and Indianapolis.[1] The disease is now appearing again in various parts of the Midwest. The disease is not new. It has occurred many times in the past in Europe as well as in this country.[2] Infants afflicted are usually less than 1 month of age. Those weighing over 7 pounds (3.2 Kg.) are victims as well as smaller and premature infants. The latter suffer the greatest death rate. The onset of the disease may be sudden or insidious. In the former case the baby begins to pass frequent, watery, greenish yellow stools, vomits and has fever. It may be drowsy or irritable. The weight loss may be alarming, and dehydration within a few hours may be severe. Fluid replacement, blood transfusions, changes of feeding formulas or the addition of pectin agar to the formulas have no satisfactory effect on the outcome of the disease. The mortality rate is usually near 50 per cent.[3]

A milder type of the disease has been described.[2] In this the stools are less frequent, the vomiting is not severe, loss of weight is slight or absent, and dehydration and fever may not be present. The recovery usually occurs in a week or ten days.

During the past several months we have observed diarrheal, neonatal deaths the cause for which we could not ascribe to parenteral infection, improper feeding or specific infection of the gastrointestinal tract, such as the colon-typhoid group of organisms. In our hospital the strictest of preventive medicine is being employed. Throat and stool cultures as well as complete physical examination of all nursery employees reveal no positive

From the pediatric service of Dr. Louis H. Segar.
1. Medical News (Ohio), J. A. M. A. **120**: 853 (Nov. 14) 1942.
2. Ormiston, G.: Epidemic Neonatal Diarrhea in Maternity Hospitals: Clinical Aspect, Lancet **2**: 588-590 (Nov. 15) 1941.
3. Holt, L. Emmett, Jr., and McIntosh, R.: Diseases of Infancy and Childhood, ed. 11, New York, D. Appleton-Century Company, Inc., 1940.