THE SULPHONAMIDES IN OPHTHALMIA NEONATORUM

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In an earlier communication (Sorsby, Hoffa, and Smellie, 1942) an account was given of the value of the administration of sulphapyridine in 273 cases of ophthalmia neonatorum treated at White Oak Hospital from towards the end of 1939 till Dec. 31, 1941. By comparison with 46 cases treated by the classical local methods, it was concluded that the results obtained with sulphapyridine justified the description of the new method of treatment as a revolutionary advance and that the classical methods of local therapy no longer had any place in the treatment of ophthalmia neonatorum. It was also shown that sulphapyridine proved as effective in non-gonococcal ophthalmia as in the gonococcal variety. The present paper deals with a further 258 cases (out of a total of 269) seen between Jan. 1, 1942, and Dec. 31, 1943. Of the 258 cases, 133 were treated with sulphapyridine, 43 with sulphathiazole, 28 with sulphamezathine, 31 with sulphadiazine, and in the residual group of 23 more than one of these sulphonamides were used as the cases proved resistant or intolerant to the drug employed initially. The results of treatment are set out in the following table.

TABLE I.—Comparative Results of Some Sulphonamides in Ophthalmia Neonatorum

Clinical Cure	Sulphapyridine			Sulphathiazole			Sulphamezathine			Sulphadiazine			Two or More of these Four			Total		
	Gonococci-positive	Gonococci-negative	Total	Gonococci-positive	Gonococci-negative	Total	Gonococci-positive	Gonococci-negative	Total	Gonococci-positive	Gonococci-negative	Total	Gonococci-positive	Gonococci-negative	Total	Gonococci-positive	Gonococci-negative	Total
1 to 3 days	15 (48.5%)	26 (25.5%)	41 (30.8%)	7	7	14 (32.5%)	3	8	11 (39.3%)	5	5	10 (32.3%)	1	—	1 (4.3%)	31 (51.7%)	46 (23.2%)	77 (29.9%)
4 " 8 "	13 (41.9%)	64 (62.7%)	77 (57.9%)	4	22	26 (60.5%)	2	13	15 (53.6%)	4	12	16 (51.6%)	10	10	20 (43.6%)	23 (38.3%)	121 (61.1%)	144 (55.8%)
9 " 30 "	3 (9.6%)	12 (11.8%)	15 (11.3%)	—	3	3 (7.0%)	—	2	2 (7.1%)	—	5	5 (16.1%)	2	7	9 (39.1%)	5 (8.3%)	29 (14.6%)	*34 (13.2%)
Over 30 "	—	—	—	—	—	—	—	—	—	—	—	—	1	2	3 (13.0%)	1 (1.7%)	2 (1.0%)	*3 (1.1%)
Totals	31	102	133	11	32	43	5	23	28	9	22	31	4	19	23	60	198	258

* Including relapses after an apparent clinical cure.

This table confirms the earlier findings as to the efficacy of sulphapyridine both in gonococcal and in non-gonococcal ophthalmia. As was indicated in the earlier study, the results there recorded had to be regarded as an understatement of the value of this drug, for many of the earlier cases received a dosage that later on was recognized as less than the optimum. For this reason it is possible to classify the present data, collected on the basis of uniform dosage, rather more finely than the earlier series: the clinical cures obtained within 8 days are now shown as those achieved within 1 to 3 days and those taking 4 to 8 days. It will be seen from Table I that 85.7% were cured within 8 days (as against 61.9% in the earlier series) and that no fewer than 29.9% were cured within 3 days.

Relative Value of the Different Sulphonamides

As to the relative value of the various sulphonamides, the only substantial study on the subject has come from Wong (1942), who found that on the average sulphanilamide effected a cure in 7.2 days in 20 cases of gonorrhoeal ophthalmia, while sulphapyridine was effective in 4.8 days in 10 cases and sulphathiazole in 3.4 days in a further series of 10 cases. The results recorded here do not cover a sufficiently large number of cases to allow fine distinctions to be drawn. However, it does not appear that any one of the four sulphonamides studied gives strikingly different end-results. Sulphadiazine has the advantage of being the best-tolerated of these four drugs, and sulphamezathine is probably as good. It is possible—but this requires confirmation—that sulphathiazole, while gratifyingly effective in such cases as respond

to it, is apt to be more selective in effect. Sulphapyridine is probably the least satisfactory owing to its greater tendency towards toxic manifestations; for the present, at any rate, its use as the routine drug has been discontinued.

Though the present series shows more favourable results than the previous one with its many early cases treated before a definite routine had been established, it is of some interest to summarize the findings in these two series, comprising together 531 cases (Table II).

TABLE II.—Results in 531 Cases of Ophthalmia Neonatorum treated by Sulphonamides (273 Cases published earlier and 258 in the Present Series) contrasted with the previously published 46 Control Cases treated locally by the Classical Methods

Clinical Cure	Local Treatment (Classical Methods)			General Sulphonamide Treatment		
	Gonococci-positive	Gonococci-negative	Total	Gonococci-positive	Gonococci-negative	Total
Well in 8 days	2	5	7 (15.2%)	97 (73.0%)	293 (73.6%)	390 (73.4%)
" 9 to 30 days	6	21	27 (58.7%)	26 (19.5%)	96 (24.1%)	122 (23.0%)
" more than 30 days	7	5	12 (26.1%)	10 (7.5%)	9 (2.3%)	19 (3.6%)
Totals	15	31	46	133	398	531

Gonococcal and Non-gonococcal Cases

In the previous series the incidence of gonococcal infection was 27.3% (89 cases in a consecutive series of 322). In the total present series of 269 cases it constituted 23.8% (64 cases).

The ophthalmia was confined to one eye in 89 instances, or 33.0%—a close approximation to the incidence of 30.5% observed in the previous series. The difference in unilateral incidence as between gonococcal and non-gonococcal ophthalmia is not great, being 28.1% (18 out of 64 cases) in gonococcal ophthalmia and 34.1% (70 out of 205 cases) in non-gonococcal ophthalmia.

The present evidence suggests that, while the sulphonamides are effective in non-gonococcal ophthalmia as well as in ophthalmia due to the gonococcus, rather quicker cures are obtained in the gonococcal variety. Cures within 3 days were obtained in 51.7% of gonococcal cases, against 23.2% in non-gonococcal cases (in 31 out of 60 cases and in 46 out of 198 cases respectively). In both groups the bulk of cases did not require treatment beyond 8 days, 90.0% of all gonococcal cases and 84.3% of all non-gonococcal cases, which included organismal, non-organismal, and the inclusion varieties of ophthalmia neonatorum, having become resolved by that time.

Delay in Initiating Treatment, and Protracted Cases

As in the earlier series, delay in starting sulphonamide therapy did not affect its efficacy: 85 cases first received sulphonamide treatment after the infection had been established for more than 8 days; these cases responded as well as the 173 less-established infections did. Seven cases had corneal ulcers (all unilateral) on admission. They all cleared quickly and well, leaving hardly perceptible or no scars, and in no case did a corneal ulcer develop while treatment was being given, though a number of infants had hazy cornea on admission.

In cases that take longer than 8 days for cure sulphonamide treatment is generally not needed, as the affection is no longer one of purulent ophthalmia but of a rather resistant conjunctivitis with some muco-pus. The proper treatment of such cases is still a matter of doubt; some, at any rate, are best left alone. In one case (non-gonorrhoeal) profuse purulent discharge continued for nearly a month in spite of intensive treatment with the various sulphonamides. In another, also non-gonococcal, a false membrane formed on the palpebral conjunctiva of the two lids of one eye, and is disappearing only now, three months later; all active treatment was suspended at the end of the first month, and at no time was there any apparent danger to the cornea.

Few relapses have been seen in the present series, and this is perhaps due to the greater initial dosage (0.25 g.) and maintenance dosages of 0.125 g. four-hourly, not only during the active phase of the affection but for three days after apparent clinical cure. Apart from minor toxic effects no untoward results were observed.

Causal Organisms

The 198 non-gonococcal cases in the present sulphonamide series included 50 in which pus cells only, but no organisms, were found, 52 with various bacilli (mostly diphtheroids), 88 with staphylococci, and 8 with other coccal organisms. Inclusion bodies were found 27 times; they occurred twice in association with organisms and 25 times in cases in which no organisms could be found. The actual distribution of the various organisms in this series, taken together with the 11 cases not treated by sulphonamides (but by newer methods of local therapy), is shown in Table III, which includes comparative figures from the previous series.

TABLE III.—*Differential Incidence of Organisms in 269 Consecutive Cases of Ophthalmia Neonatorum treated in the Period Jan. 1 1942, to Dec. 31, 1943, with Comparative Findings for 322 Cases seen during Sept., 1939, to Dec., 1941*

	Sept., '39, to Dec., '41	Jan., '42, to Dec., '43	Total
No organism found in smear or culture	53	51	104
Gonococcus	89	64	153
Staphylococcus:			
Staphylococci	55	48	92
and diphtheroids	25	20	
Staphylococcus albus	17	13	
aureus	13	11	203
Other coccal organisms:			
Gram-positive cocci	6	1	
Meningococci	4	2	9
Pneumococci	3	2	
Streptococcus haemolyticus	2	3	
viridans	1	—	29
Micrococcus catarrhalis	2	—	
tetragenus	2	1	
Bacilli:			
Diphtheroids	20	31	49
Koch-Weeks	8	2	
Coliform	6	2	
Gram-positive	3	1	53
Gram-negative	3	10	
Xerosis	3	—	
Morax-Axenfeld	3	3	102
Hoffmann	2	—	
Friedländer	1	4	
Total	322	269*	591

* Inclusion bodies found 27 times: twice in association with organisms and 25 times without organisms.

Summary

In the earlier series of 273 cases of ophthalmia neonatorum treated by the oral administration of sulphapyridine, 61.9% showed clinical cure within 8 days.

In the present series, in which a standard dosage was used in 258 cases, 133 were treated with sulphapyridine, 43 with sulphathiazole, 28 with sulphamezathine, and 31 with sulphadiazine; two or more sulphonamides were used in the remaining 23 cases, which were either resistant or intolerant to the sulphonamide used initially. In these 258 cases clinical cure was obtained within 8 days in 85.7%.

A high proportion of cases (29.9%) showed clinical cure within 3 days; 55.8% required from 4 to 8 days for clinical cure; and 14.3% showed a protracted course.

There was no appreciable difference in the action of the four sulphonamides used. Clinical cures within 8 days were obtained in 88.7% of cases treated with sulphapyridine, 93.0% of those treated with sulphathiazole, 92.9% of sulphamezathine cases, and 83.9% of

sulphadiazine cases. Sulphapyridine, because of its greater toxicity, appears to be the least desirable of these sulphonamides.

Gonococcal cases responded more rapidly to sulphonamide therapy than did the non-gonococcal cases; 51.7% of the 60 gonococcal cases showed clinical cure within 3 days, against 23.2% of the non-gonococcal cases. By the end of 8 days 90.0% of all gonococcal cases and 84.3% of non-gonococcal cases were clear.

In the present series inclusion bodies were found in 27 instances: twice in association with organisms and 25 times without such association. These cases responded well to sulphonamide therapy.

Only exceptionally is a case completely resistant to sulphonamide therapy. It is more a matter of sluggish response than of total resistance.

The routine at White Oak Hospital now includes administration of the sulphonamides for 3 days after clinical cure; fewer relapses are now observed.

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THE BLOOD PRESSURE IN MIDWIFERY

BY

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A study of the blood pressure during the later months of pregnancy is a recognized part of adequate ante-natal care, yet often it is neglected as soon as labour begins. This is all the more surprising since the value of blood-pressure records has been well established on the operation table and in the prevention and treatment of traumatic shock, and the same influences—drugs, haemorrhage, and trauma—are present to some extent in most labours.

The literature on this subject is very scanty; the most useful articles in the English language are those by Cook and Briggs (1903), Bailey (1911), Donaldson (1913), Schwarz (1923), Simons and Rasmussen (1925), and Matthews (1939). The subject is also practically ignored, apart from mentioning the blood pressure in eclampsia and toxæmia, in all the recent textbooks on midwifery that I have seen.

I have made records of the blood pressure, both systolic and diastolic, in all my midwifery for over two years, and I find them very instructive in assessing the effects of management and treatment, especially analgesia and anaesthesia. The technique is simple, and well within the scope of the general practitioner, even when working alone. The chief difficulty arises when the doctor is distracted from the mother to attend to urgent foetal asphyxia, for it is at this time during the third stage of the labour that the most important changes in blood pressure take place. I firmly believe that if more attention were paid to the blood pressure incipient shock would be recognized earlier while still amenable to simple treatment, and the lives of many of our mothers would be saved.

Types of Blood-pressure Curve

The first problem to be solved is that of the normal—that is to say, the blood-pressure curve in a straightforward delivery uninfluenced in any way by drugs or obstetric manipulations. It has been stated by Halls Dally (1936) that "during labour there is a progressive elevation of blood pressure, even to considerable heights as the pains become more intense, reaching a maximum as the head of the infant is expelled. After delivery the pressure rapidly falls." In my experience this description is very misleading, and there is far less disturbance of blood pressure than one would suppose.

Graph A is a typical blood-pressure curve, and probably approximates to the normal, even though nitrous oxide analgesia was given towards the end of the second stage. Exactly similar curves are recorded when no form of analgesia is given, and also when the agent used is weak chloroform or trichlorethylene. It will be seen that in labour there is a rise of about 20 mm. Hg, followed by a short-lived fall after delivery, partly due to reduced pulse pressure, but also shown in the diastolic pressure as well. In this particular case the blood pressure as the head was being born was not recorded, but I have rarely found it much higher. Soon