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Aetiology of Acute Bacterial Meningitis in Ibadan

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Alausa, K. O. and Osoba, A. O. (1974) *Nigerian Journal of Paediatrics*, 1 (2), 57. **Aetiology of Acute Meningitis in Ibadan.** A review of bacteriological records at the University College Hospital, Ibadan, Nigeria, has revealed that between January, 1970 and September, 1973, 366 pyogenic bacteria were isolated from the C.S.F. of 5,847 patients with a clinical diagnosis of meningitis. The results have also revealed that Gram-negative bacilli are the commonest causative organisms during the neonatal period and early childhood. The highest incidence of meningitis occurred in patients below two years of age.

The *in-vitro* anti-microbial sensitivity pattern of organisms isolated has revealed that the current 'blind' antimicrobial combinations, consisting of penicillin G, sulphadiazine and chloramphenicol, as the initial treatment in cases of clinically diagnosed pygenic meningitis in children, should be revised. Most of the organisms isolated in children below two years of age, showed high resistance to chloramphenicol and penicillin. The necessity for controlled clinical trials using a combination of ampicillin with gentamicin or kanamycin is suggested.

The bacteriological examination of cerebrospinal fluid (C.S.F.) is an essential investigation in the aetiological diagnosis of meningitis. However, the majority of medical institutions in developing countries, particularly those in the rural areas, are inadequately equipped to undertake full bacteriological diagnosis of infections. Only laboratories in big centres, such as University Teaching Hospitals and a few government hospitals, have facilities for the isolation, identification and sensitivity testing of pathogenic organisms.

The mortality from bacterial meningitis, particularly in children, appears to be related to the isolation rate and concurrent antibiotic testing of the causative organism recovered from the C.S.F. In many developing countries in Africa, where bacteria isolation rate is low, the mortality is reported to be between 24 and 37 per cent (MacGregor, 1958; Musoke, 1961; Audu, 1966; Seriki, 1966). It seems therefore, that for effective chemotherapy knowledge of the predominant organisms in different age groups and their sensitivity pattern is essential since the initial antibiotic management may be dependent on these factors. Howie (1962) has stressed the importance of accurate bacteriological diagnosis and specific treatment of infections.

The purpose of this communication is to present a retrospective review of the causative organisms cultured from the C.S.F. of patients with pyogenic meningitis at the University College Hospital, (UCH) Ibadan, between January 1970 and September 1973, and also to report on the antibiotic sensitivity pattern of

these organisms. It is hoped that the information obtained from this study will provide a rational regime for the management of acute pyogenic meningitis in areas where adequate laboratory services are either lacking or limited and where accurate aetiological diagnosis and sensitivity testing are unavailable.

Materials and Methods

The laboratory records of all patients with a clinical diagnosis of meningitis and whose C.S.F. were submitted for bacteriological examination between January 1970 and September 1973 were reviewed. Specimens of C.S.F. received in the department of Medical Microbiology were sent in sterile universal bottles. The uncentrifuged specimen was examined for colour, protein content, leucocytes and red cells. An aliquot amount of each specimen was centrifuged in a sterile tube. The deposit was then Gram-stained and cultured on blood and MacConkey agar plates for aerobic incubation at 37°C, and on chocolate agar plate for incubation in an atmosphere of 5–10 per cent Co_2. A loopful of the deposit was inoculated into glucose broth for aerobic incubation at 37°C. The cultures were incubated for a minimum of 48 hours unless growth was observed earlier. All isolates were identified using standard bacteriological methods (Cowan and Steel, 1965; Wilson and Miles, 1964). The *in-vitro* antibiogram of each isolate was determined by the multodisc method on Oxoid Dextrose sensitivity test agar, except in cases of *Neisseria meningitidis*, *Strept. pneumoniae* and *Haemophilus influenzae* which were determined on chocolate agar.

Results

The total number of patients from whom C.S.F. was obtained during the period under review was 5,847. Of these, 366 pyogenic bacteria were isolated; thus the overall bacteriological diagnostic rate was 6.3 per cent. Table I shows the number of positive C.S.F. cultures per year for the period of the study. It will be observed that the largest number of C.S.F. was examined in 1970 and the bacteriological diagnostic rate for that year was 7.8 per cent, being the highest for the four-year period.

TABLE I

Number of Positive C.S.F. Cultures Per Year (1970–73)

Year	*Total Number of C.S.F. Examined*	*Positive C.S.F. Cultures*	
		Number	*Bacteriological Diagnostic Rate (Per cent)*
1970 (Jan.–Dec.)	1,918	150	7.8
1971 (Jan.–Dec.)	1,510	71	4.7
1972 (Jan.–Dec.)	1,335	78	5.8
1973 (Jan.–Sept.)	1,084	67	6.2
Total	5,847	366	6.3

The specific causative organisms isolated per year are presented in Table II. The commonest organisms were *Streptococcus pneumoniae* (27 per cent), *Haemophilus influenzae* (15 per cent), *Neisseria meningitidis* (10.9 per cent), *Staph. pyogenes* (9.8 per cent), *Pseudomonas aeruginosa* (7.9 per cent), *Escherichia coli* (6.8 per cent), *Klebsiella spp.* (5.5 per cent), '*Coliforms*' (5.2 per cent) and *Salmonella spp.* (4.1 per cent). There were more organisms (41 .0 per cent) isolated in 1970 than in any other year. The highest incidence of *Neisseria meningitidis* also occurred in 1970. There was no significant seasonal variation in the incidence of any of the organisms.

The age distribution of the 366 patients with positive cultures are summarized in Table III. In the neonatal period, the commonest organisms were the Enterobacteriaceae (*Esch. coli*, 5; *Klebsiella spp.*, 4; Coliforms, 7; *Salmonella spp.*, 5; *Proteus spp.*, 4) accounting for 61.0 per cent (25 out of 41 cases) of all infections in this age group, and *Pseudomonas aeruginosa* (17.1 per cent). After

TABLE II

Organisms isolated from 366 Specimens of C.S.F. Per Year

Organism	*Year*				*Total*	*Per cent of Total*
	1970 Jan-Dec	*1971 Jan-Dec*	*1972 Jan-Dec*	*1973 Jan-Sept*		
Gram-positive						
Strept. pneumoniae	35	21	21	22	99	27.0
Staph. pyogenes	9	8	9	10	35	9.8
Strept. viridans	1	2	3	–	6	1.6
Non-haemolytic strept	2	1	1	–	4	1.1
Staph. epidermidis	2	–	1	1	4	1.1
Strept. faecalis	1	1	–	–	2	0.54
Strept. pyogenes	1	–	–	–	1	0.27
Gram-negative						
Haemophilus influenzae	21	7	14	13	55	15.0
Neisseria meningitidis	28	5	4		40	10.9
Pseudomonas aeruginosa	10	6	8	5	29	7.9
Esch. coli	12	6	5	2	25	6.8
Klebsiella spp.	6	4	6	4	20	5.5
Coliforms	15	4	–	–	19	5.2
Salmonella spp.	5	4	2	4	15	4.1
Proteus spp.	1	1	2	3	7	1.9
Alcaligenes spp.	–	–	2	–	2	0.54
Haemophilus para-influenzae	1	1	–	–	2	0.54
Total	150	71	78	67	366	100.00

the neonatal period and up to the age of one year, the commonest organisms were *Haemophilus influenzae* (27 per cent), *Strept. pneumoniae* (25.3 per cent), the Enterobacteriaceae (22.8 per cent) and *Staph. pyogenes* (11.4 per cent). The predominant organisms isolated from patients in the second year of life were *Strept. pneumoniae* (27.7 per cent), *Staph. pyogenes* (19.2 per cent), and the Enterobacteriaceae (19.2 per cent). After two years of age and up till adult life, majority of cases of bacterial meningitis were caused by *Strept. pneumoniae* and *Neisseria meningitidis*. On the whole, meningitis caused by the Gram-negative bacilli (*Haemophilus* influenzae, the *Enterobacteriaceae* and *Pseudomonas aeruginosa*) affected the lower age groups (neonates and infants) more than the adults.

Staphylococcal meningitis was highest in the age group one month to one year and over 50 per cent of these infants had meningomyelocele. Meningococcal meningitis occurred more commonly in patients over ten years of age.

The *in-vitro* antibiotic sensitivity pattern of the bacteria isolated are is shown in Table IV. All the 99 strains of *Strept. pneumoniae* and 40 strains of *Neisseria meningitidis* isolated were sensitive to penicillin. All the 55 strains of *Haemophilus influenzae* tested were sensitive to ampicillin and

TABLE III

Age Distribution of 366 Patients with Positive C.S.F. Cultures

Organism	*1 Day to 1 Month*	*1 Month to 1 Year*	*1 Year to 2 Years*	*2 Years to 5 Years*	*5 Years to 10 Years*	*Over 10 Years*	*Total*
Streptococcus pneumoniae	4	40	13	7	8	27	99
Haemophilus influenzae	–	43	6	3	2	1	55
Neisseria meningitidis	–	2	3	3	5	27	40
Staph. pyogenes	–	18	9	–	2	7	36
Pseudomonas aeruginosa	7	12	5	–	2	3	29
Escherichia coli	5	9	5	3	–	3	25
Klebsiella spp.	4	11	1	1	2	1	20
'Coliforms'	7	7	3	–	–	2	19
Salmonella spp.	5	8	–	2	–	–	15
Proteus spp.	4	1	–	–	–	2	7
Strept. viridans	–	–	–	2	–	4	6
Non-haemolytic strept.	1	1	1	–	–	1	4
Staph. epidermidis	2	2	–	–	–	–	4
Strept. faecalis	1	1	–	–	–	–	2
Haemophilus parainfluenzae	–	2	–	–	–	–	2
Alicaligenes spp.	–	1	1	–	–	–	2
Strept. pyogenes	1	–	–	–	–	–	1
Total	41	158	47	21	21	78	366

septrin; only one strain was resistant *in-vitro* to chloramphenicol. Seventy-seven per cent of the *Staph. pyogenes* isolated were resistant to penicillin. Only 3.4 per cent of *Pseudomonas aeruginosa* and 48 per cent of *Esch. coli* isolated were sensitive to chloramphenicol and ampicillin. However, ampicillin was more effective against Gram-negative bacilli than chloramphenicol. All the 29 strains of *Pseudomonas aeruginosa* isolated were sensitive to carbenicillin.

Discussion

The present study has revealed a bacteriological diagnostic rate of only 6.3 per cent. This low s olation rate may be explained by the fact that most of the patients, particularly children, with clinical diagnosis of meningitis were indeed cases of some other febrile illness associated with convulsions, and perhaps signs of meningism. Also some of the patients might have taken ineffective underdose of certain antimicrobial agents before coming to the hospital. As has been shown, the highest bacteriological diagnostic rate was in 1970, and 70 per cent of the strains of *Neisseria meningitidis* isolated occurred during that period. This apparent higher incidence of meningococcal meningitis during 1970 was most probably due to the massive population movements and consequent overcrowding during and immediately after the end of the Nigerian Civil War rather than any alteration in the pattern of

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Salmonella spp.	5	8	–	2	–	–	15
Proteus spp.	4	1	–	–	–	2	7
Strept. viridans	–	–	–	2	–	4	6
Non-haemolytic strept.	1	1	1	–	–	1	4
Staph. epidermidis	2	2	–	–	–	–	4
Strept. faecalis	1	1	–	–	–	–	2
Haemophilus parainfluenzae	–	2	–	–	–	–	2
Alicaligenes spp.	–	1	1	–	–	–	2
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TABLE IV

Sensitivity Pattern of 319 C.S.F. Isolates to Antibiotics

Organism	*Number of Strains Tested*	*Per cent of Sensitive Strains*												
		P	*S*	*T*	*C*	*CO*	*AMP*	*G*	*SEPT*	*CB*	*MY*	*NV*	*GENT*	*PY*
Strept. pneumoniae	99	100	8	98	100	–	–	–	–	–	–	–	–	–
Haemophilus influenzae	55	–	100	100	98.2	–	100	–	100	–	–	–	–	–
Neisseria meningitidis	40	100	85	95	95	–	–	100	–	–	–	–	–	–
Staph. pyogenes	36	22.2	44.4	61.1	69.4	–	–	–	–	100	100	100	–	–
Pseudomonas aeruginosa	29	–	3.4	6.7	3.4	93.3	–	–	–	–	–	–	96.6	100
Escherichia coli	25	–	24	32	48	92	56	–	–	–	–	–	–	–
Klebsiella spp.	20	–	37.5	25	87.5	–	62.5	–	–	–	–	–	–	–
Salmonella spp.	15		13.3	46.7	60	100	100	–	–	–	–	–	–	–
Total	319													

P = Penicillin G 1.5 units
T = Tetracycline 10 /ug
Co = Colistin (Sulphamethate sodium)200 /ug
G. = Sulphafurazole 500 /ug
CB = Methicillin 10 /ug
NV = Novobiocin 5 /ug
PY = Carbenicillin 25 /ug

S = Streptomycin 10 /ug
C = Chloramphenicol 10 /ug
AMP = Ampicillin 25 /ug
SEPT = Trimethoprim/Sulphamethoxazole 25/ug
MY = Lincomycin 10 /ug
GENT = Genticin 10/ug
– = Not tested

disease in Ibadan. Meningococcal meningitis is usually associated with overcrowding (W.H.O. Chronicle, 1973), and is commoner in the northern parts of Nigeria where epidemics occur frequently especially during the dry season than in the south (Waddy, 1952). It is noteworthy that no seasonal variation in the incidence of *Neisseria meningitidis* infection was found throughout the 45-month period of review.

Pneumococcal meningitis occurs frequently as a complication of lobar or bronchopneumonia, and is commoner in children than in adults (Wilson and Miles, 1964). In the present review, pneumococcal meningitis occurred in 53.5 per cent of children aged one month—two years. This high incidence in this age group is perhaps to be expected since according to Hendrickse (1966), post-measles bronchopneumonia is one of the commonest causes of death in Nigerian children. There were two pregnant women with pneumococcal meningitis in this review. The susceptibility of pregnant and puerperal women to pneumococcal meningitis in Ibadan has been reported by Lucas (1964).

The high incidence (78.8 per cent) of *Haemophilus* meningitis in infants is in accord with reports by other workers (Audu, 1966; Seriki, 1970; Barclay, 1971). It is noteworthy that the blood cultures of 88.8 per cent of the infants with *H.* influenzal meningitis yielded the same organism.

The predominance of enterobacterial meningitis in the neonatal period in the present study has also been noted by Barclay (1971) who reviewed 508 cases of acute pyogenic meningitis admitted to the paediatric wards, University College Hospital, Ibadan, between January 1964 and May 1969.

It is observed in this study that there is a high incidence of staphylococcal meningitis (9.8 per cent). Previous reports from different parts of

tropical Africa have been silent on this condition. *Staph.* pyogenes accounted for only 5 (1.25 per cent) of a total 397 pyogenic bacteria recovered from C.S.F. between 1960 and 1964 at UCH Ibadan (Montefiore, D., personal communication). The association of staphylococcal meningitis with cases of meningomyelocele requires further study in order to throw more light on the effective hospital management of these cases since most of the strains isolated were resistant to the commonly used antibiotics in this hospital.

Successful treatment of infections in any locality depends largely on the use of antimicrobial agents to which the causative organisims are sensitive. In many parts of tropical Africa, most laboratories do not undertake full bacteriological identification and sensitivity testing of organisms; therefore a majority of clinicians have resorted to empirical antibiotic combinations to treat potentially fatal pyogenic infections (Montefiore, 1972).

Some years ago, the 'triple therapy' regime, consisting of sodium penicillin G, suphadiazine and chloramphenicol, was instituted as the initial treatment of all cases of clinically diagnosed pyogenic meningitis in the department of Paediatrics UCH, Ibadan (Seriki, 1970). The regimen has since been adopted by most hospitals in Nigeria. But the results of the present study have shown that the antibacterial spectrum of this regimen can no longer cover all the bacteria causing pyogenic meningitis in children in this environment. For instance, in the neonatal period where the predominant organisms are the *Enterobacteriaceae* and *Pseudomonas aeruginosa*, the antibiotic of choice should be carbenicillin, a drug which attains adequate concentration in the C.S.F. when given intravenously. Ampicillin is as effective or slightly more effective than chloramphenicol for the treatment of *Haemophilus* meningitis in children. Barrett *et al.*, (1966) have shown clinically and by laboratory studies that satisfactory ampicillin level is achieved in the C.S.F. of patients with acute suppurative meningitis. Ampicillin is free from the possible haematological toxicity occasionally encountered after chloramphenicol therapy. The effective treatment of penicillin-resistant staphylococcal meningitis requires intrathecal methicillin since other routes of administration do not give satisfactory C.S.F. level with this drug (Blacow, 1972).

The emergence of chloramphenicol-resistant Gram-negative bacilli as revealed in the present study may be related to the widespread and accepted use of chloramphenicol in the treatment of typhoid and other infections. Koch (1960) found that there was a direct correlation between the use of chloramphenicol and the emergence of resistant strains of many bacteria. There is also evidence that the simultaneous administration of penicillin and chloramphenicol as is the current practise may be antagonistic (Wallace *et al.*, 1965). From both the findings of the present study and recent knowledge of mechanism of actions of antibiotics, there is a need to re-appraise the efficacy of the triple therapy. However, before effecting any radical change in the 'blind' treatment of pyogenic meningitis in children, properly controlled trials of the current regimen with some other available anti-microbial agents such as ampicillin, gentamicin or trimethoprim/sulphamethoxazole combination should be undertaken, with careful bacteriological backing. For example, in the neonatal period a combination of ampicillin and gentamicin or kanamycin is reported by Yow *et al.*, (1973) to be very effective. In older infants and children the same authors have suggested ampicillin as the appropriate initial therapy, pending bacteriological reports on sensitivity pattern of the causative organisms.

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