

THE SPECTRUM OF CLINICAL CONDITIONS ASSOCIATED WITH 40 CASES OF HAEMOPHILUS BACTEREMIA

S D Puthucheary
M L Thong

SYNOPSIS

Forty cases of bacteremia due to *H. influenzae* were seen from September 1971 to June 1979. In 22 patients bacteremia was associated with meningitis and in 14 patients with pneumonia. Meningitis and/or pneumonia was present in 32 (80%) out of the 40 patients. Six patients had associated findings in the gastrointestinal tract. In the remaining two patients, the bacteremia was associated with osteomyelitis in one infant and septic abortion in a 22 year old female. The importance of blood cultures in establishing an etiological diagnosis in patients presenting with infections of various types is stressed.

INTRODUCTION

H. influenzae is one of the important bacterial species causing serious infections, especially in children. This organism is involved in a wide range of clinical conditions ranging from asymptomatic colonisation of the upper respiratory tract to severe systemic diseases such as meningitis. Turk and May (1) divided the various types of infections into two general groups:

- (a) acute, usually severe, pyogenic conditions undoubtedly caused by the hemophilii,
- (b) conditions which do not appear to be caused by the hemophilii but in which they play an important secondary role.

The infections in the first group affect mainly infants and young children between two months and three years of age and commonly caused by type b strains as first reported by Pittman (2, 3). Meningitis is the most serious and common clinical entity in this group. Acute epiglottitis, pneumonia, otitis media, septic arthritis, osteomyelitis, abscesses and cellulitis are also encountered but less frequently. The various clinical entities are believed to be local manifestations of *H. influenzae* bacteremia and two or more local manifestations may be present in a patient at the same time (4, 1, 5, 6). *H. influenzae* bacteremia can result in the recovery of the organism from unusual sites or lesions (7, 8, 6).

The following is a report on 40 cases of *H. influenzae* bacteremia seen over a period of eight years. The different clinical conditions associated with the bacteremia are presented and discussed in varying detail.

Department of Medical Microbiology
Faculty of Medicine
University of Malaya
Kuala Lumpur
Malaysia

S D Puthucheary
Assoc Professor

M L Thong
Lecturer

MATERIALS AND METHODS

Liquid broth 10 ml (nutrient broth containing 0.05% sodium polyanethol sulphonate) and Robertson's cooked meat medium were used for blood cultures. Five to 10 ml of blood, collected aseptically was split between the two bottles which were then incubated at 36°C. Subcultures were made from the blood culture bottles after one, three and seven days' incubation, onto blood agar and chocolate agar plates.

Other clinical specimens such as cerebrospinal fluid, pleural fluid, purulent exudates and skin and wound swabs were collected in the usual manner and cultured on media including blood agar and chocolate agar plates.

Strains of *H. influenzae* were identified on the basis of: a) microscopic appearance in the Gram stain, b) colonial morphology on chocolate agar and lack of hemolysis on blood agar, and c) requirements for both X and V factors using nutrient agar (Oxoid) and commercial discs containing the factors.

All freshly isolated strains of *H. influenzae* were grown on Levinthal agar plates for 18 hours at 36°C. A known capsulated strain was included on each plate as a positive test control. Capsulated strains showing bright iridescence when viewed with obliquely transmitted light, were typed by the slide agglutination procedure using type specific antisera a to f obtained from Hyland laboratories, Costa Mesa, California as recommended by Turk and May (1). Biotyping of the strains was carried out by the method of Killian (9) who reported that indole production, urease activity and ornithine decarboxylation could be used to differentiate strains of *H. influenzae* into five biotypes (I to IV).

RESULTS

Forty cases of *H. influenzae* bacteremia were seen during the seven years and ten month period of this study. Table I shows the recovery of *H. influenzae* in association with the various sites of infection or clinical diagnosis. Of these forty cases, 37 were children and only three were adults. Among these patients were 16 with meningitis, four

with meningitis and pneumonia, two with meningitis and septic arthritis and 10 with pneumonia only.

Associated infections among the eight remaining patients with *H. influenzae* bacteremia were: two cases of diarrhoea in young children due to cow's milk intolerance following acute infective enteritis; one 13 month old boy with a day's history of diarrhoea, a temperature of 38°C and 7% dehydration who was successfully treated with a six day course of parenteral penicillin and kanamycin; one case of peritonitis in a seven year old boy with nephrotic syndrome; one case of osteomyelitis and cellulitis in an eight month old infant, one case of cholangitis in a 66 year old man; one 22 year old female with septic abortion; and one patient with acute abdomen who had refused surgery. This patient had a past history of cholecystectomy and an episode of acute pancreatitis. He developed abdominal rigidity with general tenderness and a swinging temperature. He recovered after treatment with chloramphenicol. These findings are summarised in Table II.

Bacteremic Meningitis:

The laboratory findings of the 22 children with meningitis are summarised in Table III. The ages in this group ranged from two days to 24 months. All except one were males, with one Chinese, six Indians and seven Malays.

The diagnosis of pneumonia was established only when the organism was isolated from blood, lung tissue or pleural fluid in a patient with physical or radiological evidence of pneumonia.

Two patients in this group died of massive pneumonia due to non-capsulated strains of *H. influenzae* belonging to biotype II and III. One of them had malnutrition and was hospitalized for pneumonia on two previous occasions. This child, a 23 month old Indian boy, was admitted in a severely dyspnoeic and toxic condition. He improved initially on antibiotic therapy but collapsed and died on the eighth hospital day. The other, a four month old Indian male, was admitted in respiratory distress and died the same day. Autopsy revealed severe bilateral bronchopneumonia. The only neonate, in this group, developed apnoeic spells and a temperature of 38°C on the second day of life. Chest X-ray

TABLE I
SITES OF INFECTIONS/CLINICAL DIAGNOSIS ASSOCIATED WITH
H. INFLUENZAE BACTEREMIA

	Number of Patients		Number Died
	Children	Adults	
Meningitis	16		1
Meningitis and pneumonia	4		
Meningitis and septic arthritis	2		
Pneumonia	10		2
Osteomyelitis and cellulitis	1		
Peritonitis	1		
Septic abortion		1	
Cholangitis		1	
Acute abdomen		1	
Gastro-intestinal tract	3		
Total	37	3	3

TABLE II
HEMOPHILUS BACTEREMIA:
EIGHT CASES UNASSOCIATED WITH MENINGITIS OR PNEUMONIA

Case No.	Age in years	Sex	Clinical diagnosis	Sero-type	Bio-type
1	7	M	Nephrotic Syndrome Primary Peritonitis	f#	I
2	66	M	Cholangitis	-	II
3	63	M	Septicemia Acute abdomen	-	II
4	1 1/12	M	Gastroenteritis	b	I
5	8/12	M	Diarrhoea due to milk intolerance	-	II
6	3/12	F	Diarrhoea due to milk intolerance	-	II
7	8/12	F	Osteomyelitis	a	II
8	22	F	Septic abortion	-	II

Also isolated from scrótal fluid

TABLE III
CASES OF BACTEREMIC MENINGITIS DUE TO H. INFLUENZAE

Case No.	Age in months	Sex	CSF Examination		H. influenzae from blood	
			GNB seen	Culture	Sero-type	Bio-type
1	13	M	+	+	b	I
2	8	M	-	+	b	II
3	18	M	+	+	b	I
4	NB	F	-	+	ND	ND
5	3	M	+	+	b	I
6	8	F	+	+	a	II
7	10	F	+	+	b	II
8	9	M	+	+	b	I
9	6	F	-	+	b	I
10	8	F	+	-#	ND	ND
11	17	F	+	+	b	I
12	8	F	+	+	b	I
13	8	F	+	+	b	I
14	24	F	+	+	b	I
15	7	M	+	+	b	I
16	5	F	-	-*	-	ND
17	4	F	+	+	b	II
18	1	M	-	-#	b	I
19	16	M	+	+	b	II
20	9	F	+	+	b	II
21	15	F	+	+	ND	ND
22	9	F	+	+	b	II

#CSF was only collected three days after initiation of antibiotic therapy

*CSF heavily blood stained because of a traumatic tap

NB = new born ND = not done

GNB = Gram negative bacillus

TABLE IV
CASES OF BACTEREMIC PNEUMONIA DUE TO *H. INFLUENZAE*

Case No.	Age in months	Sex	Other sources of <i>H. influenzae</i>	Chest X-Ray	Sero-type	Bio-type
1	Newborn	M		Hyaline, membrane, mediastinal emphysema	-	ND
2	19	M	Pleural fluid	R effusion, LLL collapse consolidation	b	II
3	8	M	CSF	R effusion, R base consolidation	b	II
4*	24	M		Bilateral bronchopneumonia	-	III
5	11	M	Pleural fluid	L effusion LLL pneumonia	b	I
6	5	M		R effusion, RUL RMZ pneumonia	b	I
7	8	M	CSF, pleural fluid	R effusion, RLL pneumonia	b	I
8	9	M	CSF	RLL bronchopneumonia	b	I
9	19	M		L effusion, LLL bronchopneumonia	b	II
10	24	F	CSF	Bilateral bronchopneumonia	b	I
11	15	M		Bilateral bronchopneumonia	-	ND
12	6	M		Bilateral bronchopneumonia	-	ND
13*	4	M		Bilateral bronchopneumonia	-	II
14	13	M		RLL bronchopneumonia	-	I

LLL = left lower lobe RMZ = right mid zone RUL = right upper lobe
RLL = right lower lobe * = fatal cases

revealed hyaline membrane and mediastinal emphysema. The child was treated with parenteral ampicillin and kanamycin and became afebrile after 24 hours.

Except for six non-capsulated strains among the blood isolates, all strains isolated were capsulated and belonged to serotype b. Eleven of the blood isolates were biotyped. Six were found to belong to biotype I, four to biotype II and one to biotype III. The isolates from the fatal cases belonged to biotypes II and III.

DISCUSSION

There were forty cases of *H. influenzae* bacteremia seen between September 1971 and June 1979. It has been stated often that the frequency of recovery of *H. influenzae* from clinical specimens is directly related to the interest and experience of the investigator. It is essential that special attention be given to the culture media, particularly in the

content of V factor used for the routine examination of clinical material. *H. influenzae* may be missed entirely if the proper medium is not used, thus accounting for the failure to isolate this organism from purulent material from certain cases of *H. influenzae* disease.

The diagnosis of *H. influenzae* disease can be established with certainty when the organism is recovered from blood, body fluids or tissue aspirates. The recovery of the organism from respiratory secretions or other mucosal surface in only presumptive evidence of an etiological relationship.

Bacteremia due to *H. influenzae* was often associated with meningitis (10, 5, 6) and our findings substantiates this. *H. influenzae* is the single most common cause of meningitis in children admitted to this hospital (11). It is also the commonest cause of bacterial meningitis in the United States (12), Australia (13), Jamaica (14), Canada (15), and Finland (16) but second only to meningococcal meningitis

in Britain (17, 18) and second to pneumococcal meningitis in Nigeria (19). Details of *H. influenzae* meningitis have been published elsewhere by the authors (20).

Excluding meningitis, pneumonia is the most common manifestation of *H. influenzae* type b bacteremia (10, 5). In young children, *H. influenzae* pneumonia is frequently associated with empyema and meningitis (5, 21). This association emphasises the importance of examining the spinal fluid of young infants with *H. influenzae* pneumonia and empyema (4). It is also important that chest X-rays are done in children with *H. influenzae* meningitis or other infections (21).

Pneumonia due to *H. influenzae* cannot be differentiated by clinical, radiological or laboratory features from other bacterial or non-bacterial pneumonias (4, 21). There is, therefore, a need for the use of routine blood cultures and cultures of pleural fluid (when available) in patients with pneumonia to establish the etiological diagnosis before starting antibiotic therapy (21). Lung aspirates may be necessary for culture in those patients who have negative blood cultures and respond poorly to conventional therapy (22). It has been found that bacteremia may not always be detected with a single blood culture and two blood cultures are recommended, preferably at different times (5).

It is probable that *H. influenzae* bacteremia would be recognised more frequently if blood cultures were done more often from patients presenting with infections of various types, particularly serious respiratory tract infections (23, 10). In this present study there were two cases of diarrhoea due to milk intolerance and one case each of gastroenteritis, osteomyelitis, peritonitis, septic abortion, acute abdomen and cholangitis associated with *H. influenzae* bacteremia. In such cases, cultures of the blood may provide a specific and reliable bacteriologic diagnosis, when cultures from other sites fail to identify the etiologic agent, thereby assisting in providing optimal antibiotic therapy.

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