Library

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Date 11 - 5 - 84
19.3.84

Principal Investigator M. Steuelens
Trainee Investigator (if any)
Application No. 84-010 (P)
Supporting Agency (if Non-ICDDR,B)
Title of Study BACTEREMIA IN A DIARRHEAL DISEASE HOSPITAL: ETIOLOGY, EPIDEMIOLOGY & CLINICAL FEATURES
Project status: Limited Study.
(✓) New Study
( ) Continuation with change
( ) No change (do not fill out rest of form)

Circle the appropriate answer to each of the following (If Not Applicable write NA).

Source of Population:
(a) Ill subjects — (Yes) No
(b) Non-ill subjects — Yes (No)
(c) Minors or persons under guardianship — (Yes) No

Does the study involve:
(a) Physical risks to the subjects — Yes (No)
(b) Social Risks — Yes (No)
(c) Psychological risks to subjects — Yes (No)
(d) Discomfort to subjects — Yes (No)
(e) Invasion of privacy — Yes (No)
(f) Disclosure of information damaging to subject or others — Yes (No)

Does the study involve:
(a) Use of records, (hospital, medical, death, birth or other) — (Yes) No
(b) Use of fetal tissue or abortus — Yes No NA
(c) Use of organs or body fluids — Yes No NA

Are subjects clearly informed about:
(a) Nature and purposes of study — Yes No NA
(b) Procedures to be followed including alternatives used — Yes No NA
(c) Physical risks — Yes No NA
(d) Sensitive questions — Yes No NA
(e) Benefits to be derived — Yes No NA
(f) Right to refuse to participate or to withdraw from study — Yes No NA
(g) Confidential handling of data — Yes No NA
(h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure — Yes No NA

5. Will signed consent form be required:
(a) From subjects — Yes No NA
(b) From parent or guardian (if subjects are minors) — Yes No NA
6. Will precautions be taken to protect anonymity of subjects — (Yes) No
7. Check documents being submitted herewith to Committee:
___ Umbrella proposal - Initially submit a overview (all other requirements will be submitted with individual studies).
✓ Protocol (Required)
✓ Abstract Summary (Required)
___ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
___ Informed consent form for subjects
___ Informed consent form for parent or guardian
___ Procedure for maintaining confidentiality
___ Questionnaire or interview schedule *

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary
1. A description of the areas to be covered in the questionnaire or interview which could be considered, either sensitive or which would constitute an invasion of privacy.
2. Examples of the type of specific questions to be asked in the sensitive areas.
3. An indication as to when the questionnaire will be presented to the Cttee. for review.

ee to obtain approval of the Ethical Review Committee for any changes ing the rights and welfare of subjects before making such change.

M Steuelens

Principal Investigator

SECTION 1 - RESEARCH PLAN

(Pilot protocol)

1. TITLE: BACTEREMIA IN A DIARRHEAL DISEASE HOSPITAL: ETIOLOGY, EPIDEMIOLOGY AND CLINICAL FEATURES.

2. PRINCIPAL INVESTIGATOR: Dr. M. Struelens

   CO-INVESTIGATORS: Dr. D. Patte, Dr. M. Bennish

3. STARTING DATE: 1 February 1984

4. COMPLETION DATE: 30 June 1984

5. TOTAL INCREMENTAL COST: US $ 2870.00

6. SCIENTIFIC PROGRAMME HEAD: Dr. Thomas C. Butler

This protocol has been approved by the PATHOGENESIS AND THERAPY WORKING GROUP.

Signature of Programme Head: _____

Date: 2.3.84

7. ABSTRACT SUMMARY:

Accurate bacteriological data on non-typhoidal bacteremia have been prospectively collected. Medical charts of all patients with positive blood culture (S. typhi excluded) from September 1982 through August 1983 will be reviewed as well as charts of every fifth patients with negative blood culture during this period. Pertinent epidemiological characteristics (age, sex, month, nutritional status, enteropathogen, duration of hospitalization prior to onset of bacteremia, outcome) clinical features on the day of bacteremia (mental status, blood pressure, temperature, evidence of pneumonia or meningitis) and selected laboratory findings (leukocytes, platelets, glucose, serum protein) will be abstracted and coded for tabulation by computer. Frequency and case-fatality rates of different type of bacteremia will be calculated. Risk factors (such as age, nutritional status, intravenous infusion, invasive diarrhea) will be evaluated by case-control analysis and salient clinical features (such as fever, hypothermia, shock, associated pneumonia or meningitis) will be described and analysed for influence on survival.

8. REVIEWS:

(a) Research involving human subjects: _____

(b) Research Review Committee: _____

(c) Director: _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION:

1. Objectives:

(a) To describe the etiology and antimicrobial susceptibility of non-typhoidal bacteremic pathogens in ICDDR,B over a 12 months period (data prospectively collected).

(b) To describe the epidemiological and clinical characteristics of patients with bacteremia of different etiology.

(c) To look for risk factors of bacteremia such as nutritional status, invasive diarrhea, prior intravenous infusion.

(d) To utilize the above findings in proposing guidelines for prevention, diagnosis and treatment of bacteremia in ICDDR,B.

2. Background:

Bacteremia is increasingly recognised as a major cause of morbidity and mortality in developed countries (1-2) and accounts for a large part of nosocomial infections. Incidence and case fatality rates are highest at extreme ages (the newborn and the elderly). At high risk are patients with compromised host defences. Neoplasia, mulnutrition, immuno-supressive therapy, cirrhosis of the liver, major burns and trauma, surgery, instrumentation are among the more common such conditions known to predispose to bacteremia.

Etiology varies with age, place, & predisposing condition. Hemophilus influenzae and Streptococcus pneumoniae predominate in the pediatric population, except for the neonatal period when enteric gram-negative rods and group B steptococci are more common. Gram-negative rods (mostly Enterobacteriaceae, Pseudomonaceae and Bacterioideaceae) predominate in the adult population, together with Candida sp and Staphylococcus sp. Multiple antibiotic resistance of these pathogens (particularly in Staphylococcus sp and Enterobacteriaceae, in the hospital setting) is increasing and is a continuous threat to successful therapy of these life-threataning infections, requiring continuous surveillance of antimicrobial susceptibility and introduction of newer drugs at increased costs.

In contrast, little information is available on bacteremia complicating diarrhoeal disease in tropical countries. Bacteremia is known to complicate 5-6% of cases of Salmonella enteritidis gastroenteritis. Predisposing factors are extreme ages, hemoglobinopathies, malignant disorders, liver disease, chronic granulomatous disease. In the healthy individual, Salmonella enteritidis bacteremia appears generally self-limiting but shock and death may result in the debilitated patient. Shigella septicemia is rare in adults with dysentery but is more common (5%) in infants, particularly those who are malnourished, with a significant increase in mortality (5-7).

Campylobacter jejuni/coli bacteremia is similarly reported most common in malnourished infants with enteritis (8) and rarely occurs in older patients; it appears to have an excellent prognosis.

No systematic study of the general pattern of bacteremia in tropical diarrhea is available. A recent review of 11541 blood cultures done at ICDDR,B documents a 1.7% prevalence of non-typhoidal bacteremia over 30,000 admissions (unpublished data). However, only recent improvement of blood culture techniques for the Shigella sepsis study has allowed collection of accurate bacteriological data over a 1-year period.

B. SPECIFIC AIMS:

1. To define the frequency and case-fatality rates of bacteremia of various etiologies by age, sex, month, nutritional status, enteropathogen, prior hospital stay and I.V. therapy.
2. To estimate the proportion of nosocomial and community acquired bacteremia.
3. To describe the occurence of signs of complications, such as mental abnormalities, shock, fever or hypothermia, leukocytosis, thrombocytopenia, hypoglycemia, pneumonia, meningitis.
4. To examine factors influencing survival such as: shock, temperature, nutritional status, appropriate antimicrobial therapy.

C. METHODS OF PROCEDURE:

1. Data collection:

Blood cultures reports will allow selection of all (250) positive cases and every next patient with a sterile culture as controls. Medical charts will be abstracted: epidemiological and clinical information linked to bacteriological data as per coding sheet (see Bacteremia record).

2. Data processing and analysis:

Records will be entered on computer disks and cross-tabulations made according to specific aims, X^2, t-test and non parametric statistics will be used for testing significance of association in the case-control comparison. Relative risks of death will be calculated for the analysis of factors influencing the outcome.

D. RATIONALE AND SIGNIFICANCE:

Non-typhoid bacteremia is increasingly recognised as an important cause of mortality world-wide. Recent research in ICDDR,B (3-5) documents a strong association between bacteremia and fatal outcomes. A previous review of 11541 blood cultures done in ICDDR,B over the past 7 years revealed a 1.7% prevalence of bacteremia in 33301 hospital admission. However, it was not until a prospective study of bacteremia was set up that accurate bacteriological data could be collected. This material provides a unique opportunity to review epidemiological and clinical features of sepsis complicating diarrhoea; no such systematic study was found in the litterature. Guidelines for prevention, diagnosis and treatment can be expected to be generated from this study.

REFERENCES:

1. MacGowan JE, Barnes MW, Finland M: Bacteremia of Boston City Hospital: C urence and mortlity during 12 selected years (1935- 972) with special reference to hospital-acquired cases. J Infect. Dis. 132 : 316, 1975.

2. Weinstein MP et al. The clinical significance of positive blood cultures: A comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. Reviews of Inf. Dis. 1983, 1 : 35.

3. Case control studies of fatal cases of diarrhea, personal communication. Dr. Sahfiqul Islam.

4. Post-mortem studies of fatal diarrheal illness, personal communication, Dr. T. Butler.

5. Struelens M, Kabir I, Bardhan PK, Greenberg B, Butler T. Shigella speticemia: a retrospective study of 66 cases in Balgladesh. Proceedings and Abstracts of the 23rd ICAAC, 1983. Abstract No. 1008.

6. Cherubin CE, Neu HC, Imperato PJ. Septicemia with non-typhoid salmonella. Medicine 53 : 365, 1974.

7. Scragg JN et al. Shigella infection in African and Indian children with special reference to Shigella septicemia. J. Pediatr. 93:796,1978.

8. Eastorica AJ, Penner JL. Serotypes of Campylobacter jejuni and c. coli in bacteremic hospitalized children. J. Infect. Dis 147:592,1983.

Abstract Summary for ERC

1. Subject population: only clinical charts will be used for this study i.e., charts of patients admitted in ICDDR,B, Dacca Hospital with blood culture taken for suspected sepsis.

2. Potential risk : NA

3. NA

4. Methods for safeguarding anonymity: only hospital number will be used instead of patient's name.

5. Consent Form: NA

6. Interview: NA

7. Potential benefit: if NA for the studied subjects, obvious potential benefit would be gained for further assessment of similar patients, earlier suspicion of sepsis in the ward and optimal empirical antibiotic therapy before culture and sensitivity results are obtained.

8. Only medical and bacteriological records will be used.

SECTION III - BUDGET

1.	Personnel	% effort X 5 months	Taka	Dollar
	Dr. M. Struelens	30%	-	1900
	Dr. D. Patte	10%	-	-
	Dr. M. Bennish	10%		650
2.	Supplies and Materials		1000	-
3.	Equipment		-	-
4.	Hospitalization cost		-	-
5.	Animal Resources		-	-
6.	Logistic support		-	-
7.	Printing and reproduction		2000	-
8.	Data processing cost		5000	-
			Tk. 8000	US $ 2550

Conversion rate Tk. 25 = US $ 1

Grand Total = US $ 2870

episodes bacteremia /__/

pital No. /__/__/__/__/__/__/

od cultures

th, day, rank of (+) /__/__/__/ /__/__/__/ /__/__/

/__/__/__/ /__/__/__/ /__/__/

/__/__/__/ /__/__/__/ /__/__/

/__/__/__/ /__/__/__/ /__/__/

/__/__/__/ /__/__/__/ /__/__/

(y,m) /__/__/ /__/__/

(1=m, 2=f) /__/

come (0=OK, 1=death, 2=DORB/absconded) /__/

ATMENT CENTRE

(0=no stay, 1=I.V., 2=no I.V.) /__/

(month,day,time) admission /__/__/__/ /__/__/__/ /__/__/__/

(month,day,time) discharge or death /__/__/__/ /__/__/__/ /__/__/__/

)

(month, day) admission /__/__/__/ /__/__/__/

(month, day) discharge or death /__/__/__/ /__/__/__/

I.V. used prior BC (0=no, 1=yes) /__/

. SOLUTION CULTURE

(99 = not done, if done code of BC) /__/__/

(9 = NA, log CFU/ml) /__/

HISTORY:

Type of diarrhoea	(1=bloody, 2=other)	/___/
Illness duration prior admission	(days)	/___/___/
Diet	(1=breast milk, 2=other)	/___/
Outside therapy	(0=no, 1=AB, 2=other, 9=?)	/___/
Measles past 2 weeks	(0=no, 1=yes)	/___/

ADMISSION PHYSICAL FINDINGS:

Ear pus	(0=no, 1=yes, 9=NA)	/___/
Skin pus	(0=no, 1=yes, 9=NA)	/___/
Edema	(0=no, 1=yes, 9=NA)	/___/
Xerophtalmia	(0=no, 1=X_1, 2=X_2, 3=X_3, 9=NA)	/___/
Weight day 1 (kg)		/___/___/, /___/
Height (cm)		/___/___/___/, /___/

STOOL MICROSCOPY:

Puscells	(max/hpf)	/___/___/___/
E. histolytica	(0=no, 1=cyst, 2=troph)	/___/
G. lamblia	(0=no, 1=yes)	/___/
T. trichuria	(0=no, 1=yes)	/___/
S. stercoralis	(0=no, 1=yes)	/___/

STOOL CULTURE:

S. dys 1	(0=no, 1=yes)	/___/
S. dys 2		/___/
S. flexneri		/___/
S. boydii		/___/

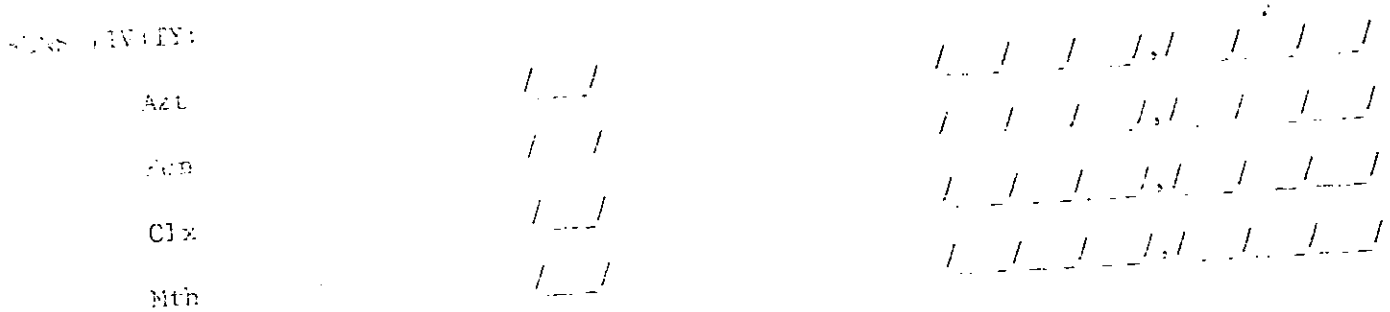
Soll (Biochemie:

S. sonnei	(Cano, Meyes)	/___/
S. typhi		/___/
S. paratyphi A		/___/
S. B		/___/
S. C		/___/
S. D		/___/
S. E		/___/
V. cholerae 01		/___/
NAG		/___/

o. episodes		/__/
atient No.		/__/__/__/__/__/__/
pisode rank		/__/
athogen code		/__/__/
o. pathogens in this BC		/__/
edium	(1=Castaneda, 2=Roche)	/__/
ime before final report	(days, 99=NA)	/__/__/
dentification	(1=tube, 2=API 20E, 3=API 20E+20NE)	/__/

ENSITIVITY:

rug	Disk (1=S, 2=R, 9=NA)	MIC (µg/ml)
G	/__/	/__/__/__/,/__/__/__/
Tob	/__/	/__/__/__/,/__/__/__/
Amk	/__/	/__/__/__/,/__/__/__/
Nal	/__/	/__/__/__/,/__/__/__/
Net	/__/	/__/__/__/,/__/__/__/
Tmp	/__/	/__/__/__/,/__/__/__/
Sxt	/__/	/__/__/__/,/__/__/__/
A	/__/	/__/__/__/,/__/__/__/
C	/__/	/__/__/__/,/__/__/__/
T	/__/	/__/__/__/,/__/__/__/
E	/__/	/__/__/__/,/__/__/__/
Czol	/__/	/__/__/__/,/__/__/__/
Ctax	/__/	/__/__/__/,/__/__/__/
Czid	/__/	/__/__/__/,/__/__/__/


Azt
Clx
Mth

BACTEREMIA: RECORD C= CLINICAL EPISODE

/__/

No. episodes /__/__/__/__/__/

Patient No. /__/__/

Episode rank

DAY BC:

Pulse quality

0=N
1=low volume/weak
2=uncountable/absent 9=NA /__/

Hydration

0=N/mild
1=moderate
2=severe 9=NA /__/

Mental Status

0=N
1=irritable/restless/delirium
2=lethargic/toxic/obtunded
3=coma
4=seizing
9=NA /__/

Temperature ^{o}F

/__/__/__/,/__/

minimum /__/__/__/,/__/

maximum /__/__/__/

Blood pressure, minimum systolic mm Hg

DAY BC ± 1:

Abdominal palpation

0=N/soft
1=tender
2=guarding/rebound
3=rigid
9=NA /__/

Bowel sounds

0=N/active,
1=sluggish
2=absent
9=NA

/__/

Skin rash

0=NO/unknown
1=erythematous
2=purpuric
3=necrotic
4=1+2
5=2+3

/___/

"Septicemia" clinically suspected

(0=no, 1=yes)

/___/

EEK POST BC:

Shock; weak or absent pulse (o=no, 1=yes) /___/

Hours prior death (99=NA) /___/___/

Purpura: 0=no, 1=skin, 2=upper GI guaiac + 3=1+2 /___/

ERAPY:

Before BC/S results (0=inactive, 1=active) /___/

Before BC/S results (0=inactive, 1=active) /___/

BORATORY:

Total leukocytes ($X10^3$) /___/___/___/,/___/

Poly (%) /___/___/

Bands (%) /___/___/

Platelets ($X10^3$/ 1) /___/___/___/

Glucose (m.mol/1) /___/___/,/___/

Na (m.mol/1) /___/___/___/

K (m.mol/1) /___/,/___/

TCO_2 (m.mol/1) /___/___/,/___/

/__/__/__/

maximum [illegible] (/mm^3) /__/__/,/__/__/

maximum fragmentation (% RBC) /__/__/__/

maximum creatinine (umol/l) /__/__/__/

WORK BACK UP:

minimum serum protein (g/l) /__/__/__/

maximum urine puscell (/HPF) /__/__/__/

maximum CSF puscells (/mm^3) /__/__/__/

IF ANY PUS GRAMSTAIN OR CULTURE:

Some organism as blood?

9=NA, 1=compatible by gramstain
0=different
2=identical by culture
3=identical by C/S /__/

Pus source

1=tracheal (2+)
2=skin (2+)
3=ear (2+)
4=urine (20/hpf)
5=CSF (20/mm^3)
9=NA /__/

X-RAYS:

CHEST:

0=not done
1=normal
2=consolidation
3=id + lavitation
4=effusion
5=2+4
6=3+4
7=other /__/

ABDOMEN:

0=not done
1=normal
2=fluid level
3=pneumoperitoneum
4=2+3
5=other
9=NA /__/