1986

Predictive factors for bacteremia in outpatient adults

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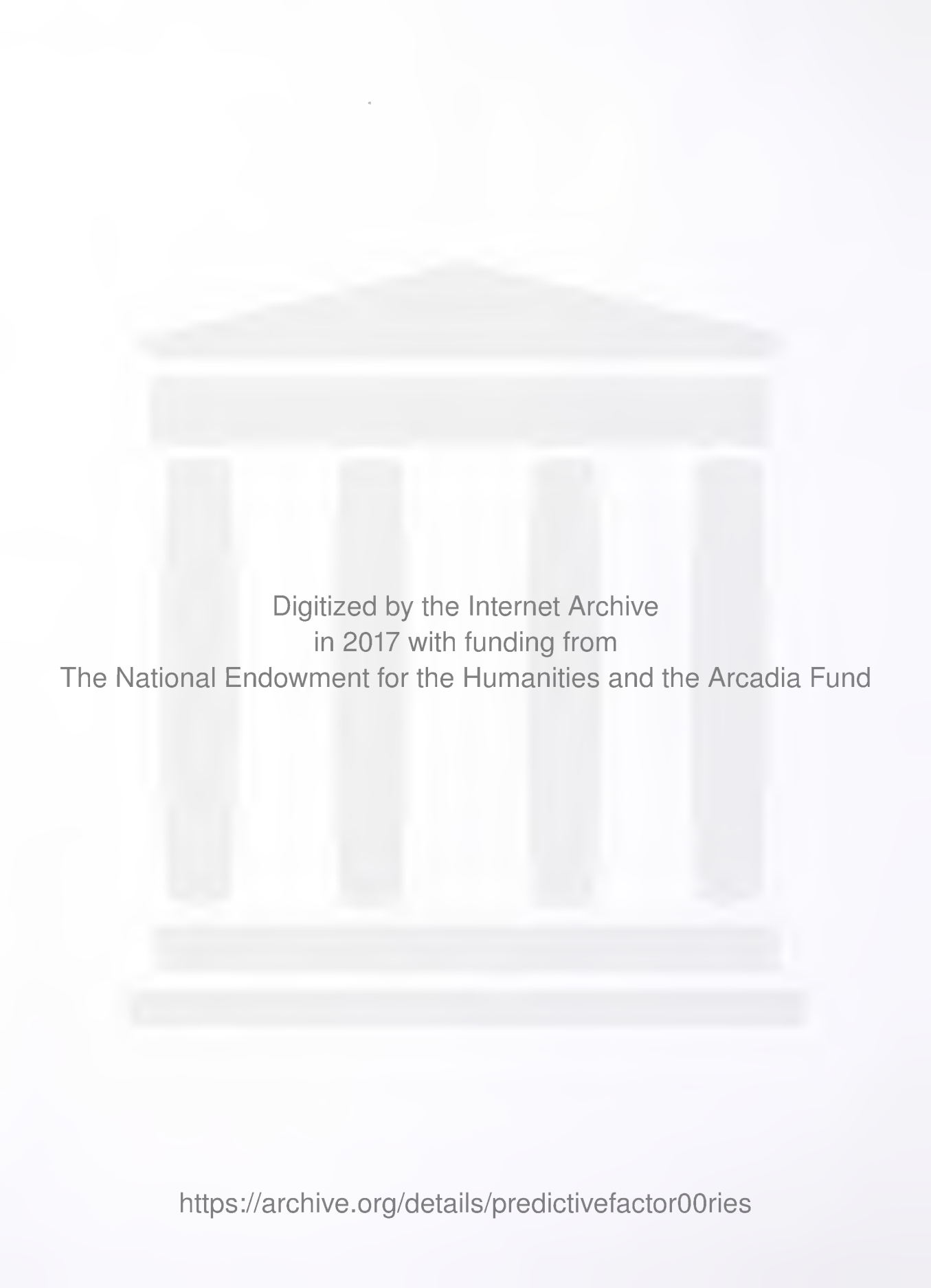

PREDICTIVE FACTORS FOR BACTEREMIA IN OUTPATIENT ADULTS

BY

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A Thesis Submitted to
Yale University School of Medicine
in Partial Fulfillment
of the Requirements for the Degrees of
Doctor of Medicine
and
Master of Public Health
1986

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ACKNOWLEDGEMENTS

I thank Dr. Robert Baltimore for his continuous guidance, enthusiasm and support throughout this project, and for the time he spent reading innumerable drafts and discussing many aspects of the thesis. I thank Dr. John Mellors for his many insights into the design of this project and for his eye for detail and precision.

I also thank the following people who had a direct and significant input into this project:

Helen Schweidler and Aleksander Kuperberg cheerfully provided the many lists of data upon whith this thesis was built.

Dr. S. C. Edberg and his staff in the microbiology lab, especially Sandy Waycott, enlightened me to the details of culturing blood.

Dr. Penny Canny and Dr. James Jekel generously shared their statistical knowledge throughout this project.

My parents helped me from afar through this thesis and through the many years of medical school.

Mark De Souza introduced me to high-dose coffee and urged me on when the going was difficult.

I also thank the night shift of the LEPH computer room who made the long nights there entertaining, to say the least.

Many thanks to all of you.

ABSTRACT

A three year retrospective case-control study examined clinical and laboratory data of outpatients who had had bacterial blood cultures taken in the Yale-New Haven Hospital Emergency Room. Seventy-seven of the 79 patients (97.4%) with growth in at least one blood culture were studied. The 21 patients classified as true positives served as the case group for the study. Ninety-eight patients with no growth acted as unmatched controls. They represented a 10% random sample of all the patients without growth. Fifty-two patients were classified as contaminants.

Rates were estimated at 357 outpatients cultured per year with 7 true positives per year (1.9% of all outpatient blood cultures) and 17 (4.9%) contaminants per year (4.9% of all outpatient blood cultures).

Useful predictors for bacteremia include: 1) absolute band count greater than 2,000, 2) non-caucasian race, and 3) presence of pneumonia, urinary tract infection, or skin/soft tissue infection. All cases had one or more predictive factors, while only 54 (55.0%) of the controls did. Five (23.8%) of the cases had all three predictive factors, while only 2 (2.0%) of the controls did. The odds ratio for bacteremia increased to 23.7 with one predisposing factor, 42.9 with two, and 195.8 with all three predisposing factors.

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Chapter 1

INTRODUCTION

1.1 BACTEREMIA

BACTEREMIA. The word conjures the vision of an extremely sick patient with hypotension, and prostration... virtually at death's door (46).

Fortunately, not all bacteremia is that severe: It actually occurs as a spectrum with one extreme resembling the "septic" picture above and the other resembling the transient bacteremia that occurs daily secondary to brushing of teeth or a vigorous bowel movement. This study examines patients in the middle of the bacteremic spectrum: The ill but ambulatory patient with bacteremia.

1.1.1 BACTEREMIA IN GENERAL

Bacteremia is associated with a number of infections, including gonorrhea, pneumonia, cellulitis, and urinary tract infections. It is also associated with surgical procedures and instrumentation. Bacteria spreading from the primary site of infection to the blood can lead to sepsis, which carries a mortality rate as high as 25% (20).

Although bacteremia may be suspected in a given clinical setting, the only way to prove it is to isolate a pathogen in a blood culture. No constellation of signs or symptoms is diagnostic of bacteremia. No definitive rules dictate how many blood cultures to take, or which patients to culture. The culture procedure may also vary from person to person. Typically, a fever work up includes two sets of blood cultures (four bottles, two aerobic and two anaerobic), but often only one set is taken. One study did examine the number of cultures needed to diagnose bacterial endocarditis (3). It concluded that most cases were detected with six bottles. Unfortunately, few such rules exist for the use of blood cultures in other infections.

1.1.2 OUTPATIENT BACTEREMIA

The outpatient bacteremic is ill, but not sick enough for admission to the hospital. This situation is not

uncommon in pediatrics, but some workers claim that in adults, this situation is impossible: Any adult who is bacteremic is sick enough to be admitted, at least for observation. However, the phenomenon of outpatient bacteremia in adults is documented at least twice in the literature (16, 44).

1.1.2.1 ADULT OUTPATIENT BACTEREMIA

The first group to look at outpatient bacteremia in adults was Eisenberg, et al., in 1976 (16). Blood cultures were collected from 210 of 565 febrile patients in the emergency room. Some of these patients were admitted and some discharged from the emergency room. Among those discharged, only one out of 124 (0.8%) was considered to have a true positive culture, and 4 (3.2%) were considered to have contaminated cultures. (Of the cultures with growth, 80% were contaminants). The positive culture rate was much higher in those admitted: 9 out of 86 (10.4%) compared with the 0.8% positive rate in outpatients.

This information may lead one to speculate that bacteremia occurs rarely in outpatients. However, Eisenberg's study lacked precision on several counts: First, the source population was comprised of all adults who came

into the emergency room with fever. No mention was made as to whether the patients were selected because of suspected bacteremia. The only criterion seemed to be that the temperature was greater than 37.6° C. Since fevers in adults can result from causes other than bacteremia, one would expect an artificially low rate of positivity from this unfocused culturing. Secondly, only 30.9% of those eligible for the study were actually cultured. It is not stated whether this was a random sample or a convenience sample, or if some other criteria were used to select this 30.9%. Thirdly, the criteria used to determine contaminants were not clearly defined.

A more recent two-part study by Stair, et al., focused on patients who had had blood cultures taken in the emergency room (44). One hundred consecutive outpatients who had had blood cultures taken were examined prospectively. Ten had positive blood cultures, but only 4 were considered true positives, giving a 4% positivity rate and a 6% contamination rate. In the second part of the study, records from 400 patients were studied retrospectively. Seventeen patients had growth in their blood cultures. Only two, however, were considered true positives, giving a positive rate of 0.5%.

1.1.2.2 PEDIATRIC OUTPATIENT BACTEREMIA

Outpatient bacteremia has had more intensive study in pediatrics. In the early 1970s, the "new disease" of outpatient bacteremia was "discovered," probably because pediatricians began drawing more blood cultures to look for bacteremia secondary to pneumonia or meningococcus, and then sending the children home. Numerous studies have examined clinical correlates, including temperature, leukocyte count, and band count, and created indices based on these clinical findings to guide the clinician to the patients most likely to be bacteremic (4,5,13,19,25-31,36,40,45,50).

1.2 PURPOSE

The purpose of this study includes the following three goals:

1. To approximate the rates at which blood cultures are taken in adult outpatients, along with the rates of positivity and contamination.
2. To determine which factors may be correlated with the presence of bacteremia in outpatient adults.
3. To create an index which may be useful in guiding the clinician in the decision of whether or not to take blood cultures in a particular outpatient adult.

Chapter 2

MATERIALS AND METHODS

2.1 STUDY POPULATION

The study population came from the emergency room of Yale-New Haven Hospital in New Haven, CT. This emergency room serves approximately 70,000 people per year, primarily from New Haven and surrounding towns. Of these, approximately 10,000 are admitted, and the remaining 60,000 treated as outpatients. When a patient arrives, he or she is triaged into the appropriate area of the emergency room. The patients with medical complaints (as opposed to pediatric, gynecologic, or surgical complaints) are triaged to the medical area. This study draws only from the medical area which serves approximately 20,000 inpatients and outpatients per year.

Outpatients who had had blood cultures taken in the

emergency room medical services were identified by means of a source list made by the hospital computer information service. It listed all patients who had had blood cultures drawn in the emergency room between 1 February 1983 and 31 January 1986. The listing provided patient name, unit number, culture number, and presence or absence of growth for the blood culture. If the patient had been discharged from the emergency room (the so called outpatient) his or her name would definitely appear on the list. However, since some people have blood cultures taken in the emergency room and then are admitted, some inpatients may appear on the list as well. Thus, the list of outpatients with blood cultures includes some inpatients.

2.2 BLOOD CULTURE PROCEDURE

If the house officer or attending physician suspects that the patient may be bacteremic, s/he may obtain blood for culture. This is done by first locating an adequate vein for venipuncture, preferably the antecubital vein. Ideally, the area is cleaned three times with a betadine solution. Ten milliliters (ml) of blood are taken; five ml are put into an aerobic culture bottle and five ml are put

into an anaerobic bottle. The needle is usually changed before each bottle is inoculated to avoid contamination. One aerobic bottle together with one anaerobic bottle is called a set of cultures. The culture procedure is not standardized; medical students, nurses, or other staff members may draw the cultures. The adequacy of cleaning the culture site, and the maintenance of sterile procedure varies from person to person and time to time. As discussed in the introduction, the indications for taking blood cultures are not uniform.

The cultures are sent to the bacteriology laboratory where they are processed as follows: Aerobic bottles are filled to 13 times the head space with a mixture of 5% carbon dioxide and 95% air, and placed in a shaker apparatus in an incubator at 37.0° in order to hasten the growth of any organisms present. Anaerobic bottles are filled with 5% hydrogen, 10% carbon dioxide and 85% nitrogen and placed motionless in the incubator.

Growth is detected using a Bac-Tek machine which samples the gas inside the bottles. Since the carbon substrates in the nutrient broth are radioactively labeled with C_{14} any bacterial growth will result in radioactively labeled carbon dioxide (6,11). Thus, if growth has occurred, the Bac Tek machine will detect the radioactive CO_2 and sound an alarm if the level is sufficiently above

background. When this occurs, a small amount of liquid growth media is taken from the culture bottle, fixed on a slide and gram stained. At this time subcultures are placed on selective and non-selective media. The house officer is notified of the gram stain results as soon as they are available. Final identification is usually available within 72 hours and often as early as 24 hours. The bottles are tested for growth three times per day for the first two days, since the majority of growth appears during that time. After two days the cultures are tested only once per day. The blood culture lab processes between 45 and 60 sets of cultures a day and reports an overall positivity rate of five to nine percent.

2.3 TYPE OF STUDY

As stated in the introduction, the purpose of this study is two fold:

1. To determine how many blood cultures are taken in the emergency room along with the rates of positivity and contamination.
2. To determine what clinical or laboratory data may be helpful in predicting which patients are bacteremic.

These two approaches may necessitate different study designs: for rates, a cohort or cross-sectional study is needed in order to determine the denominator for the rates (23). This cohort could also be used to determine predictive factors, however, it may not be the most efficient study design to answer this question. For example, if the overall percent positivity were 5%, and the percent negative were 95%, for every case, 19 non-cases would be available for comparison. While this may add to the overall power of the statistical analysis, it requires studying an impractical number of patients. Therefore, a case-control design may be more efficient for determining possible predictive factors.

2.4 CASE-CONTROL STUDY

The case-control design is used to study rare events (23). Since the overall rate of bacteremia in outpatients may be as low as 0.5%, it can be considered a rare event. Therefore the case-control approach is appropriate for detecting and quantifying differences in laboratory and clinical factors between bacteremic and non-bacteremic patients.

2.4.1 SELECTION OF CONTROLS

One of the most critical parts of the case-control design is the selection of appropriate controls (23). Inappropriate controls may lead to erroneous conclusions. In this study, controls are selected from the group of people who fulfill all of the following criteria:

1. Blood culture taken in the emergency room between 1 February 83 and 31 January 86,
2. Not admitted from emergency room,
3. No growth reported from blood culture.

They differ from cases only in that their blood cultures grew no organisms (ie bacteremia was suspected but not detected).

This control group does not represent the entire adult emergency room population, but only those who had blood cultures taken, that is those patients in which bacteremia is suspected. This limitation must be kept in mind later on when the results are applied to the study population.

The source list contained all outpatients who had had cultures taken in the emergency room along with a few inpatients. To produce a control group, a 10% random sample was taken from the patient's marked NG (no growth), using a random number table (33). This subset, too, contained both

outpatients and inpatients. Inpatients were identified and eliminated at this point by checking the admissions lists in medical records or by checking the patients medical record. Information from these patients was extracted as described in section 2.6.

2.4.2 CASES AND CONTAMINANTS

The source list marked all positive cultures as GROWTH. This subset included both true positives and false positives (contaminants). Contaminants may be from the skin (1), or from some other source of contact while obtaining the specimen, from the bottle itself (21), from the blood drawing equipment (15), or from the agar plates used for subculture.

2.4.3 CASE DEFINITION

The case definition used in this study includes the following four characteristics:

1. Blood culture taken in the emergency room between 1 February, 1983 and 31 January, 1986.
2. Patient not admitted from emergency room.
3. Growth reported from blood culture.

4. Growth determined not to be a contaminant.

The first three characteristics are fairly straightforward. However, the fourth needs a better definition, namely what is a contaminant. This will be discussed in the following section.

2.5 CRITERIA FOR DIFFERENTIATING CASES AND CONTAMINANTS

Many researchers consider all coagulase negative Staphylococcus, Bacillis species and diphtheroids as contaminants. However, doing so may inadvertently eliminate occasional true positives. All of these so called contaminants may cause bacteremia. In fact, one study found that 33 out of 437 patients who grew coagulase negative staphylococcus had actually had an episode of true bacteremia (22). Therefore criteria are needed to assure that true positives are not eliminated along with the contaminants.

Few studies have examined how to determine whether a culture is contaminated or truly positive. McGregor and Beatty (24) proposed a system that goes beyond looking only at the organism. They also consider clinical evidence for

bacteremia including:

> ...patient's history and findings of physical examination, temperature course, white blood cell counts, results of other types of cultures, clinical course, presence of blood dyscrasias or intravenous polyethylene catheters, evidence of recent intravenous drug abuse...

They also found that true positives were more likely to have multiple bottles positive (69%) than were contaminants (11%).

For this study, the determination of case or contaminant status will be based on the following guidelines:

1. Organism: certain organisms are found on the skin and therefore are more likely to appear as contaminants. For this reason, coagulase negative Staphylococcus will be considered a contaminant unless the patient is an intravenous drug abuser or has an indwelling catheter. Other organisms, such as E. coli, H. influenzae, Strep. pneumoniae, and N. gonorrhoeae rarely appear as contaminants and, therefore, will be considered true positives.

2. Number of bottles positive: As per MacGregor (24) the contaminants are more likely to have multiple cultures positive when multiple cultures are taken, while contaminants are more likely to have fewer positive cultures.

3. Patient's predisposing factors: Includes intravenous drug abuse, indwelling prosthesis, valvular heart disease, diabetes.

4. Other positive cultures: Finding the organism in the blood and at another infected culture site greatly supports the status of true positive.

Based on the above criteria, a judgement was made by two separate people as to whether the culture was indeed a true positive. It is important to remember that no criteria can classify true positives or false positives with 100% assurance. Therefore, two additional categories were created: Possible true positive and Possible contaminant. Thus, the positive cultures will be classified as:

1. True Positive if there was little question that the organism was a true positive by the above criteria.
2. Possible True Positive if most of the evidence pointed to the organism being a true positive but some doubt remained, or the two people evaluating the culture disagreed as to whether it was a true positive.
3. Contaminant if there was little question that the organism was a contaminant by the above criteria.
4. Possible Contaminant if most of the evidence pointed to the organism being a contaminant but some doubt remained.

For this study, only true positives will be used as cases in the case-control analysis. It is important to remember that the above attempts to categorize what is actually a spectrum of certainty or uncertainty.

2.6 EXTRACTION

Clinical information from the emergency room visit was obtained from the emergency room record sheet and recorded on the extraction form (see appendix A.1). If the patient's permanent medical record could not be found, or if the sheet could not be located in the permanent record, the carbon copy, kept in the emergency room, was used.

In order to reduce bias, cases and controls were extracted for all information (except for the variable, follow up) before the blood culture result was known. After recording the blood culture result the charts of patients with positive cultures were reexamined to determine if any follow-up occurred and to find any data that might be helpful in determining if the culture were a true positive (for instance, other culture results were sought).

2.7 EXTRACTION FORM

The extraction form was used to collect data thought to be related to the presence of bacteremia. Name and unit number were needed to locate the medical record. All data was pooled--no patient is individually identifiable. A copy of the extraction form can be found in Appendix A.1.

2.8 DEFINITIONS

The following subsections contain the definitions used to code the clinical and laboratory information from the emergency room sheet onto the extraction form.

2.8.1 DEMOGRAPHIC DATA

Age, sex and race recorded as reported on the top of the emergency room sheet.

2.8.2 VITAL SIGNS

Temperature, blood pressure, and pulse recorded as reported on emergency room sheet. In the case of multiple entries the first entry was recorded.

2.8.3 PREDISPOSING FACTORS FOR BACTEREMIA

A number of predisposing factors are recorded in the literature (43), primarily from inpatient studies. Those

included on the extraction form are described below.

2.8.3.1 INSULIN DEPENDENT DIABETES MELLITUS

Reported as such on the emergency room sheet. Also acceptable is diabetes mellitus with insulin listed under meds, or as type I or juvenile onset diabetes mellitus.

2.8.3.2 NON-INSULIN DEPENDENT DIABETES MELLITUS

This predisposing factor recorded as positive in NIDDM is recorded on the emergency room sheet or if DM is recorded and oral hypoglycemics are listed under medications.

2.8.3.3 INTRAVENOUS DRUG ABUSE

This predisposing factor is considered positive if current use of intravenous drugs or a history of intravenous drug use is reported.

2.8.3.4 IMMUNOSUPPRESSIVE DRUG USE

This predisposing factor considered positive if patient is currently using or has recently used immunosuppressive drugs.

2.8.3.5 SPLENECTOMY

This predisposing factor considered positive if the patient has a history of surgical removal of the spleen or has functional splenectomy.

2.8.3.6 ORGAN TRANSPLANT

This predisposing factor recorded as positive if the patient has a history of organ transplantation.

2.8.3.7 CANCER

History of cancer recorded on emergency room sheet.

2.8.3.8 OTHER IMMUNODEFICIENCY

Immunodeficiency not covered in the categories above (e.g. AIDS, agammaglobulinemia).

2.8.3.9 VALVULAR HEART DISEASE

Sufficient criteria include a history of valvular heart disease or rheumatic heart disease. The presence of a heart murmur is <u>not</u> sufficient.

2.8.3.10 SICKLE CELL DISEASE

History of sickle cell disease.

2.8.3.11 IMPLANTED PROSTHESIS

Includes heart valve, pacemaker, implanted pump, indwelling urinary catheter, artificial joint, or other permanent indwelling foreign body.

2.8.3.12 GRANULOCYTOPENIA

Absolute granulocyte count less than 1000 per cubic millimeter.

2.8.4 BLOOD CULTURE RESULTS

The organisms present in the blood culture bottles were recorded from records kept by the blood culture laboratory. "1st bottle" indicates the aerobic bottled while the "2nd bottle" indicates anaerobic. Note that an aerobic/anaerobic set represents one blood culture. Also, both of the media will generally support the growth of most aerobes or anaerobes.

2.8.5 HEMATOLOGY

The values for leukocyte count with differential and erythrocyte sedimentation rate were recorded as reported on the emergency room sheet, or on the listing of these values provided by the laboratory computer. If more than one value is reported, the first is recorded.

2.8.6 PYURIA

Pyuria is considered to be present if more than five white blood cells are present per high powered field (400x) in spun urine sediment (7).

2.8.7 POSITIVE CHEST X-RAY

A chest x-ray is considered positive if it contains a new infiltrate or new area of consolidation.

2.8.8 LOCATION OF INFECTION

The location of infection was determined by evaluating all the data found on the emergency room sheet, then the author decided, on clinical grounds, as to the anatomical location of the infection. The specific definitions are found below.

2.8.8.1 PNEUMONIA [PULMONARY]

(NOTE: This location of infection was misprinted on the extraction form. It should have read "pulmonary infection" rather than "pneumonia" on the extraction form). It is defined by presence of cough, or productive cough with the abundance of a single organisms in the sputum, as evidenced by a sputum culture or gram stain, along with a positive chest x-ray (as defined above).

2.8.8.2 OTHER RESPIRATORY

Defined as presence of cough or productive cough in absence of a positive chest x-ray. It also includes inflammation or infection of the oropharynx or tonsils.

2.8.8.3 URINARY TRACT INFECTION [UTI]

Defined by the presence of urinary tract symptoms, including frequency, urgency, dysuria or costovertebral angle tenderness in conjunction with pyuria (>5 WBC/HPF).

2.8.8.4 CSF/MENINGES

Presence of meningeal signs with nucleated cells present on lumbar puncture, if performed.

2.8.8.5 SEPTICEMIA

If the infection cannot be considered present primarily in another organ system, and the patient manifests the signs of septicemia, including fever, increased leukocyte count, and low blood pressure.

2.8.8.6 GASTROINTESTINAL TRACT

Nausea, vomiting or diarrhea in conjunction with abdominal pain or tenderness, with no evidence of non-gastrointestinal source (for instance, genito-urinary infection with abdominal pain.)

2.8.8.7 SKIN INFECTION

Presence of an abscess, cellulitis, impetigo, or recognizable exanthem.

2.8.8.8 ENDOCARDITIS

Characterized by new murmur or change in old murmur, with fever and characteristic signs for endovascular infection, including a new murmur or a change in an existing murmur splinter hemmorhages, Roth's spots, Janeway lesions.

2.8.8.9 UNDETERMINED

If the clinical data do not point to a specific organ

system as listed above, then the patient is placed in this category.

2.8.9 DISCHARGED ON ANTIBIOTICS

Yes if antibiotic is noted on emergency room sheet, no if otherwise.

2.8.10 FOLLOW UP

This variable is applicable only for patient's with positive blood cultures. The patients chart was searched for evidence of either a follow-up visit to the emergency room or a follow-up telephone call from the emergency room. Due to limitations in data sources, follow-up to clinics or to private physicians is unknown. The specific definition of each type of follow-up can be found below.

1. NO FOLLOW-UP is recorded if no evidence of follow-up can be found.
2. RETURN TO EMERGENCY ROOM, NOT ADMITTED is recorded if evidence in the chart indicates that the patient returned to the emergency room for re-evaluation and was not admitted. This evidence could include an emergency room sheet from the follow-up visit or a note on the sheet from the initial visit.
3. RETURNED TO EMERGENCY ROOM, ADMITTED: as in 2. above except the patient is admitted.
4. OTHER includes telephone calls, or other communication with the patient.

5. NOT APPLICABLE: All controls were placed in this category since they would not be expected to be followed up.

2.9 STATISTICS

The data were entered into an IBM PC XT computer and analyzed using Perfect Calc software. The two tailed t-tests performed on the continuous variables were for independent groups. Yate's correction was used in Chi-square calculations in two by two tables. When a table contained a cell with an expected value less than five, then Fischer's exact test was used to determine the Chi-square. Epistat software was used to calculate chi-square and perform Fischer's exact test. In the calculation of odds ratios, for 2x2 tables that contained zero in one or more cells, a correction factor of 0.5 was added to each cell, as described in Fleiss (17).

Appendix A

TABLES FROM CHAPTER 2, MATERIALS AND METHODS

OUTPATIENT BLOOD CULTURES IN ADULTS:

1. Name: _____ 2. Hospital Unit #: _____ | V1 ID# __ __ __ __

3. Study #:_____ 4. ER Date ___/___/___ 5. BC Date ___/___/___ | V2 EDA __ __
| V3 EMO __ __

6. Age:_____ 7. Sex __M =1 __F =2 8. Race___ caucasian [=1] ___ hispanic [=4] | V4 EYR __ __
___ black [=2] ___ other (specify:)
___ asian [=3] | V5 BMO __ __
___ not spec. [=9] _____ | V6 BDA __ __
| V7 BYR __ __

9. Temp.: ___ ___ ___ . ___ 10. BP: ___ ___ ___ / ___ ___ ___ 11. Pulse: ___ ___ ___ | V8 AGE __ __
| V9 RAC __

12. List up to four predisposing factors: ___ ___ ___ ___ | V10 TEM __ __ __ __

(none) [=00] Other immunodeficiency [=08] | V11 BPS __ __ __
Insulin-dependant diabetes mellitus [=01] Valvular heart disease [=09] | V12 BPD __ __ __
Non-insulin-dependant diabetes mellitus [=02] Sickle-cell disease [=11] | V13 PLS __ __ __
Intravenous drug use [=03] Implanted prosthesis [=12]
Immunosuppressive drug use [=04] Alcohol abuse [=13] | V14 PF1 __ __
Spleenectomy [=05] Granulocytopenia [=14] | V15 PF2 __ __
Organ transplant [=06] other disease (specify): | V16 PF3 __ __
Cancer [=07]; type: _____ | V17 PF4 __ __
_____
| V18 B11 __ __
| V19 B12 __ __

13. Blood culture #1: 1st bottle: ___ ___ 2nd bottle: ___ ___ contam.: ___no [=0] ___yes [=1] | V20 CT1 __

14. Blood culture #2: 1st bottle: ___ ___ 2nd bottle: ___ ___ contam.: ___no [=0] ___yes [=1] | V21 B21 __ __
| V22 B22 __ __

15. Blood culture #3: 1st bottle: ___ ___ 2nd bottle: ___ ___ contam.: ___no [=0] ___yes [=1] | V23 CT2 __
[yes= organism code; no=00; not done=99]
| V24 B31 __ __
| V25 B32 __ __

16. White blood count: ___ ___ . ___ 17: ESR ___ ___ | V26 CT3 __

18. % Segs ___ ___ 19. % Bands ___ ___ 20. %lymphs ___ ___ 21. %ALs ___ ___ | V27 WBC __ __ __
| V28 SEG __ __

22. Pyuria (>5/HPF): ___ no [=0] ___ yes [=1] ___ not done [=9] | V29 BND __ __
| V30 LYM __ __

23. Positive chest x-ray: ___ no [=0] ___ yes [=1] ___ not done [=9] | V31 ALM __ __
| V32 ESR __ __

24. Presumed location of infection:
___ pneumonia [=01] ___ septicemia [=05] ___ undetermined [09] | V33 PYU __
___ other resp. [=02] ___ GI tract [=06] ___ other (specify): | V34 CXR __
___ urinary tract [=03] ___ skin infection [=07]
___ CSF/Meninges [=04] ___ Endocarditis [=08] _____ | V35 LOC __ __

80 [

26. Discharge diagnosis: _____ ___ [=code] | V36 DXX __ __

81 [

27. Discharged on antibiotics? ___ no [=0] ___ yes [=1] Type_____ | V37 RXX __

82 [

28. Follow up. | V38 FUX __
___ no follow up [=1] ___ other [=8]_____
___ returned to ER, not admit. [=2] ___ not applicable [=9]
___ returned to ER, admit. [=3]

83 [

84 [

Chapter 3

RESULTS

3.1 GENERAL DESCRIPTIVE STATISTICS

The patients studied were taken from a computer list generated by the hospital computer information service. The list consisted of patients who had had blood cultures drawn in the emergency room between 1 February 1983 and 31 January 1986. All those with growth reported were taken, along with a 10% random sample of those patients with no growth. A total of 262 patients with blood cultures were selected. After eliminating the patients who were admitted, 179 remained: 100 without growth in their blood cultures, and 79 with growth. The emergency room sheets for two patients in each group could not be found. Thus, 98 of the 100 cases without growth and 77 of the 79 cases with growth were extracted.

3.1.1 CONTROLS

The 98 patients from the no growth group comprise the control group, representing a 10% sample of all those listed as "no growth". From now on they will be referred to as controls.

3.1.2 CASES AND CONTAMINANTS

The 76 patients represent 97.4% of all the outpatients with growth in their blood cultures. This group was further divided by the investigator and one advisor into four groups as follows:

True Positives	21
Probable True Postives	4
Probable Contaminants	4
Contaminants	48
Total	77

(The definitions for these categories can be found in the Materials and Methods chapter, section 2.5). Appendix B.1 and B.2 list the organisms found in cases and contaminants, respectively. Appendix B.3 lists the true positives, along with age, sex, number of bottles positive, and other

important clinical and laboratory data. Similarly, Appendix B.4 lists this information for the contaminants and probable contaminants.

3.1.3 COMPARISON OF CONTROLS AND CONTAMINANTS

Since much of the analysis of this essay rests on the comparison of cases and controls, it is important that the determination of true positivity be as accurate as possible. One assurance of this accuracy comes from careful application of the definitions put forth in the Materials and Methods section.

One way to assess the accuracy of case determination is to compare the contaminants to the controls. There should be no statistically significant difference between the control data and the contaminant data. Similarly contaminants should differ from cases in the same ways that controls differ from cases.

A complete listing of the comparison between contaminants and controls is found in Appendix B.5. Briefly, this comparison revealed no statistically significant differences between contaminants and controls in all areas examined. The comparison between contaminants and cases is found in Appendix B.6. This second comparison revealed that

contaminants differed from cases statistically in the same way that controls differed from cases.

3.2 PRELIMINARY STATISTICS

The case group was compared with the control group. Statistical tests performed include the chi-square test, the t-test and Fischer's exact test where appropriate. The results appear in the subsections below. When numeric results are presented in the text, case data will be given first, followed by control data, unless otherwise noted. T-test results on continuous variables will be given as mean $\pm$ standard deviation.

Many results are expressed as odds ratios [OR]. An odds ratio greater than one indicates that the factor in question is positively associated with bacteremia, while an odds ratio less than one means that a factor is negatively associated with bacteremia. Also listed is a 95% confidence interval [CI]. The odds ratio for any particular calculation has a 95% chance of lying somewhere in that interval. However, the reported odds ratio is the best estimate. If the confidence interval does not include unity [1], then the result is statisticly significant; if the confidence

interval includes unity, then the result is not significant.

3.2.1 DEMOGRAPHICS

In comparing age, the cases and controls did not differ significantly [38.15 + 19.59 vs. 38.4 ± 18.8]. There was no statistical difference in gender: Females represented 47.6% of the cases and 45.9% of the controls (p=0.95). As for race, cases showed an increased proportion of non-caucasians (blacks and hispanics) when compared with controls [65.0% vs. 36.8% p=0.04]. A complete listing of the demographic data appears in Appendix B.7.

3.2.2 VITAL SIGNS

No statistically significant difference appeared in mean temperature (101.28 ± 1.34 vs. 101.45 ± 1.92, p=0.53), systolic blood pressure (129.8 ± 20.7 vs. 127.2 ± 22.5 p=0.64) or diastolic blood pressure (74.0 ± 12.6 vs. 74.5 ± 18.2 p=0.92) or pulse (101 + 7 vs. 99 ± 20. p=0.55). (See also Appendix B.8.)

3.2.3 PREDISPOSING FACTORS

Only seven of the possible 13 predisposing factors appeared in either the case or control group. These seven are insulin dependent diabetes mellitus [IDDM], non-insulin dependent diabetes mellitus [NIDDM], intravenous drug abuse [IVDA], cancer , valvular heart disease, implanted prosthesis, and alcohol abuse. Over 38% of the cases had one or more predisposing factors, while only 28.6% of the controls had one or more predisposing factors, giving an odds ratio of 1.53. This difference was not statistically significant.

Analysis of specific predisposing factors revealed no statistically significant differences between cases and controls in any of these seven groups. A detailed listing appears in Appendix B.9.

3.2.4 LABORATORY DATA

Comparison of leukocyte count [WBC] in cases and controls revealed a statistically significant increase in WBC in the case group (12.73 ± 5.60 vs. 9.87 ± 4.67 $p=0.02$). A similar increase was found in the band count [% bands] (20.5 ± 17.06 vs. 10.8 ± 10.57 $p=0.002$). A statistically significant difference also appeared in the

segmented neutrophil count [% segs]. However, the mean percentage was lower in cases than in controls (59 ± 15.02 vs. 69 ± 14.8 p=0.007). No difference appeared in lymphocyte count, atypical lymphocyte count or total neutrophil count [% segs + % bands]. Erythrocyte sedimentation rate [ESR] showed no statistically significant difference. However, this test was performed on only 40 of the 121 cases and controls. (A complete listing of this information can be found in Appendix B.10).

3.2.5 PYURIA

Pyuria was found in 4 (19%) cases and 16 (16.2%) controls. This proved to be an insignificant difference. Pyuria was not tested in 33.3% of the cases and 53.1% of the controls. A full listing of the results appears in Appendix B.11.

3.2.6 CHEST X-RAY

Statistically, a positive chest x-ray was no more likely to appear in cases than in controls, although there was a tendency in that direction as evidenced by an odds ratio [OR] of 2.7. This procedure was performed on only

60.7% of cases and 40.9% of controls. The results appear in Appendix B.11.

3.2.7 LOCATION OF INFECTION

The analysis of location of infection, as defined in the previous chapter, produced several interesting results. Pulmonary infections accounted for 33.3% of the infections in cases and only 11.2% in controls ($p=0.03$) for an odds ratio of 3.95. Similarly, urinary tract infections [UTI] accounted for 23.8% of infections in cases and only 7.1% in controls ($p=0.057$) for an odds ratio of 4.10. Skin infections were found in 9.5% of the cases and 3.1% of controls ($p=0.21$) with an OR of 3.33.

Two categories, other respiratory infections and undetermined infections, proved to be negative predictors with odds ratios less than 0.30. This means that there was a higher association between these two locations of infection and non-case status. However, neither of these associations proved statistically significant. Infections of the central nervous system, gastrointestinal tract, or other locations showed no significance. A complete table of locations of infection can be found in Appendix B.12.

3.2.8 DISCHARGE DIAGNOSIS

Analysis of discharge diagnosis revealed that 33.3% of cases were discharged with pneumonia, while only 10% of controls were (p=0.016; OR=4.4). Urinary tract infections accounted for 23.8% of cases and only 7.1% of controls (OR=4.06, P=0.06), and cellulitis 9.5% cases and 3.1% controls (P=0.21 OR=3.33). However 24.4% of <u>controls</u> were discharged with viral syndrome, while <u>no</u> cases were. Similarly, unidentified fever was found only in controls (6.1%) and never in cases. Neurological/ETOH consisted of people who came in with neurological diseases such as seizures, syncopy, or ethanol withdrawl. The category 'other' included cancer, pain, possible meningitis, metabolic disturbances, asthma, and congestive heart failure. Complete results are found in Appendix B.13.

Appendix B

TABLES FROM CHAPTER 3, RESULTS

B.1 FREQUENCY OF ORGANISMS FOUND IN CASES

ORGANISM	FREQUENCY
ESCHERICHIA COLI	5
STREPTOCOCCUS PNEUMONIAE	5
HAEMOPHILUS INFLUENZAE	2
NEISSERIA GONORRHOEAE	2
SALMONELLA, GROUP B	2
STAPHYLOCOCCUS AUREUS	1
CAMPYLOBACTER JEJUNI	1
PEPTOCOCCUS ASACCAROLYTICUS	1
PROVIDENTIA STUARTI	1
STREPTOCOCCUS, GROUP A	1
TOTAL	21

B.2 FREQUENCY OF ORGANISMS FOUND IN CONTAMINANTS

ORGANISM	FREQUENCY
STAPHYLOCOCCUS COAG. NEG.	30
PROPRIONIBACTERIUM SP.	5
BACILLIS SP.	3
AEROBIC DIPHTHEROIDS	2
BACILLIS CEREUS	2
BACILLIS POPILLIAE	1
BACTEROIDES SP.	1
MICROCOCCUS	1
NEISSERIA SUBFLAVA	1
STAPHYLOCOCCUS AUREUS	1
STREPTOCOCCUS SALIVARIUS	1
STREPTOCOCCUS SANGUIS	1
STREPTOCOCCUS VIRIDANS	1
Mixed: STAPH COAG. NEG. S. SALIVARIUS	1
Mixed: STAPH. COAG. NEG. S. VIRIDANS	1
TOTAL	52

B.3 CASES: BLOOD CULTURE RESULT, OTHER CULTURE RESULTS, AND OTHER CLINICAL INFORMATION

AGE/ SEX	ORGANISM	BOTTLES POS /TOTAL BOT.	OTHER POS CULTURES	OTHER *
53/M	S. AUREUS	1/4	-	IDDM CELLULITIS
25/M	SALMONELLA	1/4	-	-
21/M	STREP. PNEU.	2/2	-	POS CXR
17/M	STREP GP A	1/2	THROAT	-
28/F	N. GONORRHOEAE	1/2	-	IVDA
15/F	STREP. PNEU.	1/4	-	POS CXR
91/F	PROV. STUART	3/4	URINE	PYURIA
30/M	PEPTOCOCCUS	1/2	-	IVDA CELLULITIS
40/F	H. FLU	1/4	-	POS CXR
28/F	STREP. PNEU.	2/2	SPUTUM	POS CXR
58/M	E. COLI	1/4	-	PYURIA
48/M	STREP. PNEU.	1/4	-	POS CXR
73/F	CAMPYLO. JEJ.	1/2	-	-
32/F	E. COLI	1/4	URINE	PYURIA
35/M	SALMONELLA	1/4	-	IVDA
24/F	E. COLI	4/4	URINE	-
28/F	E. COLI	3/4	URINE	-
24/M	H. FLU	4/4	-	POS CXR
??/?	E. COLI	1/2	-	PYURIA
21/M	STREP. PNEU.	1/2	-	POS CXR
59/M	N. GONORRHOEAE	1/2	-	-

* IDDM = INSULIN DEPENDANT DIABETES MELLITUS
IVDA = INTRA-VENOUS DRUG ABUSE
NIDDM = NON INSULIN DEPENDANT DIABETES MELLITUS
OSTEO = OSTEOMYELITIS
POS CXR = POSITIVE CHEST X-RAY
PYURIA = GREATER THAN 5 WBC PER HPF

B.4 CONTAMINANTS: BLOOD CULTURE RESULT, AND OTHER CLINICAL INFORMATION

AGE/SEX	ORGANISM	BOTTLES POS /TOTAL BOT.	OTHER *
68/F	STREP. VIRIDANS	1/2	NIDDM
??/F	STAPH. COAG. NEG.	2/2	NO PF
29/M	STAPH. COAG. NEG.	1/4	NO PF
40/F	STAPH. COAG. NEG.	1/2	IDDM
30/M	STAPH. COAG. NEG.	1/2	IVDA, ETOH
21/F	STAPH. COAG. NEG.	1/4	NO PF
55/F	STAPH. COAG. NEG.	1/4	CA
31/F	AER. DIPHTHEROIDS	1/2	NO PF
70/F	STAPH. COAG. NEG.	2/4	CELLULITIS
34/F	BACILLIS CEREUS	1/4	NO PF
63/M **	PROPRIONIBACTERIA	1/6	CA
27/M **	PROPRIONIBACTERIA	1/2	IVDA/RHD
32/M	STREP. SALIVARIUS	1/4	NO PF
47/F	STAPH. COAG. NEG.	1/4	NO PF
64/F	STAPH. COAG. NEG.	2/2	CA
23/M	STAPH. COAG. NEG.	1/6	IVDA
27/F	STAPH. COAG. NEG.	2/6	NO PF
60/F	STAPH. COAG. NEG.	1/2	NO PF
74/M	BACILLIS CEREUS	1/4	NO PF
99/F **	MIXED: S. C. NEG. STREP. SAL.	2/2	CA
24/M	STAPH. COAG. NEG.	1/6	NO PF
28/M	STAPH. COAG. NEG.	1/2	NO PF

* CA = CANCER
ETOH = ALCOHOL ABUSE
IDDM = INSULIN DEPENDANT DIABETES MELLITUS
IVDA = INTRAVENOUS DRUG ABUSE
NIDDM = NON INSULIN DEPENDANT DIABETES MELLITUS
NO PF = NO PREDISPOSING FACTORS
RHD = RHEUMATIC HEART DISEASE

** PROBABLE CONTAMINANT

CONTINUED ON NEXT PAGE

CONTINUATION OF APPENDIX B.4

B.4 CONTAMINANTS: BLOOD CULTURE RESULT, AND OTHER CLINICAL INFORMATION

AGE/SEX	ORGANISM	BOTTLES POS /TOTAL BOT.	OTHER *
46/M	STAPH. COAG. NEG.	1/2	NO PF
51/F	BACILLIS SP.	1/4	IMP PROS
25/M	STAPH. COAG. NEG.	1/4	IVDA
21/F	STAPH. COAG. NEG.	1/2	NO PF
21/M	STREP. SANGUIS	1/4	NO PF
22/M	AER. DIPHTHEROIDS	1/2	SICKLE CELL
56/M	STAPH. COAG. NEG.	1/4	NO PF
23/F	STAPH. COAG. NEG.	1/4	IVDA
59/F	MIXED: S. C. NEG. STREP. VIR.	2/2	NO PF
77/F	NEISSERIA SUBFLAVA	1/4	NO PF
24/M	PROPRIONIBACTERIA	1/4	NO PF
18/F	STAPH. COAG. NEG.	1/2	NO PF
52/F	PROPRIONIBACTERIUM	1/2	IDDM
43/F	STAPH. AUREUS	2/2	NO PF GASTRITIS
31/M	PROPRIONIBACTERIA	1/2	NO PF
23/F	BACILLIS SP.	1/4	NO PF
27/M	BACTEROIDES	1/2	NO PF
72/M	STAPH. COAG. NEG.	2/4	NIDDM
23/F	STAPH. COAG. NEG.	1/2	NO PF
52/M	STAPH. COAG. NEG.	1/4	NO PF
22/F	STAPH. COAG. NEG.	2/6	IVDA
25/M **	MICROCOCCUS	1/4	IVDA
19/M	STAPH. COAG. NEG.	1/2	NO PF
36/M	BACILLIS	1/2	NO PF
59/F	STAPH. COAG. NEG.	1/2	NO PF
27/F	STAPH. COAG. NEG.	1/2	NO PF
35/M	STAPH. COAG. NEG.	1/2	IVDA, ETOH
64/F	BACILLIS POPILLIAE	1/4	NO PF
36/M	STAPH. COAG. NEG.	1/4	IVDA

* IDDM = INSULIN DEPENDANT DIABETES MELLITUS
IMP PROS = IMPLANTED PROSTHESIS
IVDA = INTRAVENOUS DRUG ABUSE
NIDDM = NON INSULIN DEPENDANT DIABETES MELLITUS
NO PF = NO PREDISPOSING FACTORS
** PROBABLE CONTAMINANT

B.5 COMPARISON OF CONTAMINANTS AND CONTROLS

FEATURE	CONTAMINANTS N=52		CONTROLS N=98		P *
AGE	41.4 ± 19.5**		38.4 ± 18.8		0.63
TEMPERATURE	101.2 ± 1.7		101.5 ± 1.92		0.53
SYSTOLIC BP	127.7 ± 20.7		127.2 ± 22.5		0.91
DIASTOLIC BP	74.2 ± 16.2		74.5 ± 18.2		0.92
PULSE	97.0 ± 19.0		99.0 ± 20.0		0.65
LEUKOCYTE COUNT	10.1 ± 5.0		9.9 ± 4.7		0.79
% SEGS	70.0 ± 16.0		69.2 ± 14.9		0.77
%BANDS	7.9 ± 10.0		10.8 ± 10.5		0.11
SEX					
MALE	24	(46.2)***	53	(54.1)	
FEMALE	28	(53.8)	45	(45.9)	0.45
RACE					
WHITE	26	(50.0)	61	(62.2)	
NON-W	26	(50.0)	36	(37.8)	0.18
# P. F.					
0	31	(59.6)	70	(71.4)	
1	17	(32.7)	23	(23.5)	
1 or 2	21	(40.4)	28	(28.6)	0.20

* VALUE CALCULATED BY CHI-SQUARE, T-TEST, OR FISCHERS EXACT TEST WHERE APPROPRIATE.

** MEAN ± S.D.

*** COUNT (PERCENT)

B.6 COMPARISON OF CONTAMINANTS AND CASES

FEATURE	CONTAMINANTS N=52		CASES N=21		P *
AGE	41.4 ± 19.5**		43.9 ± 23.8		0.64
TEMPERATURE	101.2 ± 1.7		101.2 ± 1.3		0.99
SYSTOLIC BP	127.7 ± 20.7		128.3 ± 20.1		0.89
DIASTOLIC BP	74.2 ± 16.24		72.8 ± 11.9		0.72
PULSE	97.1 ± 18.8		100.5 ± 7.7		0.61
LEUKOCYTE COUNT	10.1 ± 5.0		12.3 ± 5.4		0.09
% SEGS	70.0 ± 16.0		60.8 ± 14.6		0.02
%BANDS	7.9 ± 10.0		19.3 ± 16.0		<0.01
SEX					
MALE	24	(46.2)***	11	(52.4)	
FEMALE	28	(53.8)	10	(48.6)	0.93
RACE					
WHITE	26	(50.0)	7	(35.0)	
NON-W	26	(50.0)	13	(65.0)	0.67
# P. F.					
0	31	(59.6)	13	(61.9)	
1	17	(32.7)	10	(38.1)	
2	4	(7.7)	0	(0.0)	0.83

* P-VALUE CALCULATED BY CHI-SQUARE, T-TEST, OR FISCHERS EXACT TEST WHERE APPROPRIATE.

** MEAN ± S.D.

*** COUNT (PERCENT)

B.7 DEMOGRAPHIC DATA: CASES VS. CONTROLS

FEATURE		CASES N=21	CONTROLS N=98	OR	95% CI	P *
SEX	M	11 (52.4)	53 (54.1)***			
	F	10 (47.6)	45 (45.9)	0.93	(0.33-2.64)	0.92
RACE						
	W	7 (35.0)	61 (62.2)			
	B	13 (65.0)	32 (32.7)			
	H	0 (0.0)	4 (4.1)			
	B+H	13 (0.0)	36 (1.0)	0.32	(0.01-0.96)	0.04

FEATURE	CASES	CONTROLS	P *
AGE	38.2 ± 19.6**	38.4 ± 18.9	0.97

B.8 VITAL SIGNS: CASES VS. CONTROLS

FEATURE	CASES	CONTROLS	P *
TEMP.	38.15 ± 19.59	38.35 ± 18.78	0.97
SYS. BP	129.8 ± 20.7	127.2 ± 22.5	0.64
DIAS. BP	74.1 ± 12.6	74.5 ± 18.2	0.92
PULSE	101 ± 12	99 ± 20	0.55

* P-VALUE CALCULATED BY CHI-SQUARE, T-TEST, OR FISCHERS EXACT TEST WHERE APPROPRIATE.
** MEAN ± S.D.
*** COUNT (PERCENT)

B.9 PREDISPOSING FACTORS: CASES VS. CONTROLS

FEATURE*		CASES N=21	CONTROLS N=98	OR	P **
IDDM					
	Y	1 (4.8)	1 (0.8)***		
	N	20 (95.2)	97 (97.0)	4.85	0.32
NIDDM					
	Y	0 (0.0)	3 (3.1)		
	N	21 (100.0)	95 (96.9)	0.75	0.56
IVDA					
	Y	3 (14.3)	13 (13.3)		
	N	18 (85.7)	85 (86.7)	1.09	0.56
CANCER					
	Y	1 (4.8)	3 (3.1)		
	N	20 (95.5)	95 (96.9)	1.58	0.55
VHD					
	Y	0 (0.0)	5 (5.1)		
	N	21 (100.0)	93 (94.9)	0.40	0.37
IMP PROS					
	Y	1 (4.8)	1 (1.0)		
	N	20 (95.2)	97 (99.0)	4.85	0.32
ETOH					
	Y	2 (9.5)	7 (7.1)		
	N	19 (90.5)	91 (92.9)	1.37	0.50

* IDDM = INSULIN DEPENDANT DIABETES MELLITUS
NIDDM = NON INSULIN DEPENDANT DIABETES MELLITUS
IVDA = INTRAVENOUS DRUG ABUSE
VHD = VALVULAR HEART DISEASE
IMP PROS = IMPLANTED PROSTHESIS
ETOH = ALCOHOL ABUSE

** P-VALUE CALCULATED BY CHI-SQUARE, T-TEST, OR FISCHERS EXACT TEST WHERE APPROPRIATE.

*** COUNT (PERCENT)

B.10 LABORATORY DATA: CASES VS. CONTROLS

FEATURE *	CASES N=21	CONTROLS N=98	P **	MISSING
WBC	12.73 ± 5.6***	9.9 ± 4.7	0.02	1
% SEGS	59.0 ± 15.0	69.2 ± 14.9	<0.01	3
% BANDS	20.6 ± 17.1	10.8 ± 10.6	<0.01	2
% LYMPHS	13.3 ± 10.8	12.0 ± 10.1	0.84	2
% ATYP. LYMPHS	0.8 ± 1.3	0.8 ± 2.7	0.98	2
% SEG + BANDS	79.6 ± 14.2	79.9 ± 12.1	0.92	3
ESR	20.0 ± 11.8	30.8 ± 17.5	0.20	81
ABS SEGS	7.6 ± 3.9	7.0 ± 3.5	0.51	3
ABS BANDS	3.1 ± 3.0	1.2 ± 1.5	<0.01	3
ABS SEG+ BAND	10.6 ± 5.7	8.1 ± 4.2	0.03	3

* WBC = LEUKOCYTE COUNT
ESR = ERYTHROCYTE SEDIMENTATION RATE
ABS = ABSOLUTE COUNT: (% CELL TYPE) X WBC

** P-VALUE CALCULATED BY CHI-SQUARE, T-TEST, OR FISCHERS EXACT TEST WHERE APPROPRIATE.

*** COUNT (PERCENT)

B.11 PYURIA AND POSITIVE CHEST X-RAY: CASES VS. CONTROLS

FEATURE	CASES N=21	CONTROLS N=98	OR	95% CI	P *
PYURIA					
YES	4 (19.0)**	16 (16.2)			
NO	10 (47.6)	35 (35.4)	0.88	(0.19-3.73)	0.49
NOT DONE	7 (33.3)	52 (53.1)			
POS CXR					
YES	6 (28.6)	10 (10.2)			
NO	8 (38.1)	36 (36.7)	2.7	(0.63-11.53)	0.22
NOT DONE	7 (33.3)	52 (53.1)			

* P-VALUE CALCULATED BY CHI-SQUARE, T-TEST, OR FISCHERS EXACT TEST WHERE APPROPRIATE.

** COUNT (PERCENT)

B.12 LOCATION OF INFECTION: CASES VS. CONTROLS

FEATURE	CASES	CONTROLS	OR	95% CI	P *
PULM	7 (33.3)	11 (11.2)	3.95	(1.14-13.5)	0.03
OTHER RESP	1 (4.8)	15 (15.3)	0.28	(0.02-2.21)	0.18
UTI	5 (23.8)	7 (7.1)	4.1	(0.97-16.8)	0.06
CNS	0 (0.0)	3 (3.1)	0.63	-	0.56
GI	2 (9.5)	12 (12.2)	0.75	(0.01-4.04)	0.21
SKIN	2 (9.5)	3 (3.1)	3.33	(0.14-27.1)	0.21
UNDET.	3 (14.3)	38 (38.8)	0.26	(0.06-1.03)	0.44
OTHER	1 (4.8)	9 (9.2)	0.49	(0.01-4.23)	0.44
TOTAL	21	98			

* P-VALUE CALCULATED BY CHI-SQUARE, T-TEST, OR FISCHERS EXACT TEST WHERE APPROPRIATE.

** COUNT (PERCENT)

B.13 DISCHARGE DIAGNOSIS: CASES VS. CONTROLS

FEATURE	CASES	CONTROLS	OR	95% CI	P *
VIRAL SYND	0 (0.0)	24 (24.5)	0.07	-	<0.01
PNEUMONIA	7 (33.3)	10 (10.2)	4.4	(1.25-15.4)	0.02
UTI	5 (23.8)	7 (7.1)	4.06	(0.97-16.8)	0.06
CELLULIT.	2 (9.5)	3 (3.1)	3.33	(0.13-27.1)	0.21
GI	3 (14.3)	10 (10.2)	1.46	(0.12-6.67)	0.41
OTHER RESP.	1 (4.8)	10 (10.2)	0.44	-	0.39
UNIDENT FEVER	0 (0.0)	6 (6.1)	0.33	-	0.30
OTHER INF	1 (4.8)	8 (8.2)	0.56	-	0.50
NEURO/ ETOH	1 (4.8)	5 (5.1)	0.93	-	0.71
OTHER	1 (4.8)	15 (15.3)	0.28	-	0.18
TOTAL	21	98			

* P-VALUE CALCULATED BY CHI-SQUARE, T-TEST, OR FISCHERS EXACT TEST WHERE APPROPRIATE.

** COUNT (PERCENT)

Chapter 4

DISCUSSION

4.1 COHORT CALCULATIONS

Even though the above calculations have been performed in a case-control format, it is possible to calculate rates from the data collected, because the controls were drawn as a random 10% sample of the total population without growth. Therefore it represents an unbiased sample of all patients with negative cultures.

The best estimate of the total number of outpatients in the three year period without growth is 10x100=1000, since the 100 controls represent 10% of the total. A confidence interval for this estimate can be calculated (17), but since the best statistical estimate is 1000, this is the number that will be used in subsequent computations.

Combining the 1000 no-growth cultures with the 77 cases

and contaminants yields 1077 patients over the three year period. This number will be used as the overall denominator for subsequent calculations. It represents the best estimate of all the patients seen in the ER who had at least one set of blood cultures taken and were not admitted.

4.1.1 RATES

Cultures were taken from a total of 1077 outpatients over three years, or from approximately 357 patients per year. Since the medicine branch of the emergency department evaluates approximately 20,000 patients per year, this means that approximately 1.8% of patients have blood cultures taken in the emergency room. However this number underestimates the actual percentage of cultures taken in outpatients, since the denominator, 20,000, includes both outpatients and patients who were admitted.

The overall positivity rate (both contaminants and true positives) is 77/1077 = 7.1%. The true positivity rate is 21/1077 = 1.9%. The contamination rate is 52/1077 = 4.8%. These figures are comparable to those in Stair's (44) and Eisenberg's (16) studies, reviewed in Chapter 1.

4.1.2 HYPOTHESES

After the data were collected, but prior to analysis, a number of hypotheses were formulated as to what factors would be positive or negative predictors for bacteremia. The results are shown in Appendices C.1 and C.2.

4.2 PREDICTORS OF BACTEREMIA

These data can also be used to help the clinician in the emergency room setting, decide whether or not to take a blood culture. The results of the following analyses are not applicable to all emergency room patients: Since the patients in this study were those who had BCs taken, presumably the house officer in the emergency room thought s/he was bacteremic. Thus the source population is a subset of the general emergency room population--the subset of outpatients who may be bacteremic. Therefore in order to apply the following results, the patient

1. must be seen in the emergency room
2. is going to be discharged
3. is suspected to be bacteremic

If all three of the above criteria are fulfilled, then the following rules will apply.

4.2.1 POSITIVE PREDICTORS

As mentioned in the results section, there are several positive predictors for an increased risk of bacteremia. These include non-white race, and a pulmonary or urinary tract location of infection. In addition, the mean leukocyte count [WBC], and mean % band count were both significantly higher in cases than in controls.

4.2.1.1 LEUKOCYTE COUNT [WBC]

Further examination of the leukocyte count revealed that it is a useful predictor of bacteremia. Patients with a leukocyte count greater than 15,000 were more likely to be bacteremic (OR = 2.8) but this result was not statistically significant. However, a leukocyte count greater than 20,000 proved to be a better predictor with an odds ratio of 7.9 ($p=0.02$). Therefore, WBC greater than 20,000 is a significant positive predictor for bacteremia. However, only 4 (20%) cases and 3 (3.1%) controls had a leukocyte count greater than 20,000. Although this may produce a

statistically significant result, it is of questionable value since so few patients had leukocyte counts greater than 20,000.

4.2.1.2 BAND COUNT

The band count also proved to be a useful predictor of bacteremia. Eight cases (40%) had a band count greater than 30%, while only 5 controls (3.1%) had a band count greater than 30% ($OR=12.26$, $p<.001$). Thus % band count has a statistically significant positive association with bacteremia.

Not surprisingly, the absolute band count (calculated by multiplying % bands by leukocyte count) showed a similar association. Eleven cases (55%) had an absolute band count greater than 2000, while only 14 (14.6%) of controls did (OR = 7.6 95% CI = 2.24 - 23.38). This cut-off point of 2,000 is clinically reasonable--Wintrobe (49) reports the mean number of bands found in normal controls as 630 $\pm$ 410, with a range of 0-1450. Therefore a count greater than 2000 would be well above the normal range, and be a more specific test for an elevated band count.

The list of statistically significant positive predictors now includes the following:

1. Leukocyte count greater than 20,000
2. Band count greater than 30%
3. Absolute band count greater than 2,000
4. Race, non-caucasian
5. Location of infection: pulmonary or urinary tract

4.2.1.3 NEGATIVE PREDICTORS

Only one statistically significant negative predictor appeared in the results: the discharge diagnosis of viral syndrome. However a discharge diagnosis is difficult to apply in the clinical setting. More applicable and useful information may be gleaned from the location of infection category. Even though the results are not statistically significant, the locations of infection of "other respiratory" and "undetermined" gave odds ratios of 0.12 and 0.26 respectively (see Appendix B.12). Thus, both were strongly negative predictors. Other possibly helpful negative predictors include a leukocyte count less than 5,000 (or possibly < 10,000), absolute band count less than 2000, or % bands less than 5% (Appendix C.2).

4.3 APPLICATION ON POSITIVE AND NEGATIVE PREDICTORS

It may be possible to apply the predictors found above to the clinical setting. The scenario would be something like this: A house officer has seen a patient in the emergency room and thinks s/he may be may be bacteremic. However s/he does not appear to be sick enough to be admitted to the hospital. The house officer needs some data base to assist him or her in deciding whether or not to take a blood culture before discharging the patient.

Individual predictors may be of some help. For instance, if the patient has an absolute band count greater than 2,000, since the OR is 7.1, s/he will have a greater chance of being bacteremic than a similar patient with an absolute band count less than 2,000. Other predictors can similarly be applied in this situation.

Taking more than one predictive factor at a time will provide greater predictive ability than individual factors. For example, one study found that while a patient with one of a possible five predisposing factors may have a four fold greater chance of having a bacterial infection, having three of the five factors produces an 11.5 fold increase (32).

The above is an example of a clinical prediction rule which "reduce(s) the uncertainty inherent in medical practice by defining how to use clinical findings to make

predictions" (48). In order to be useful, a good clinical prediction rule must define both the outcome event and the predictive findings well. In addition, the predictors should be readily available to the clinician.

Three predictors were chosen since they are all statistically significant in this analysis, are easily obtained, and readily applied by the clinician.

1. RACE; non-caucasian
2. ABSOLUTE BAND COUNT; $\geq$2000
3. LOCATION OF INFECTION; Pneumonia, urinary tract infection, or skin/soft tissue infection.

The results are as follows:

# OF FACTORS	CASES		CONTROLS		OR *	95% CI
0	0	(0.0)	44	(44.9)	1.0	-
1	10	(47.6)	39	(39.8)	23.7	(1.3- 417.0)
2	6	(28.6)	13	(13.3)	42.9	(2.3- 810.8)
3	5	(23.8)	2	(2.0)	195.8	(8.3-4629.0)
TOTAL	21		98			

*Odds ratio using patients with no predictive factors as the referrant group.

Since one of the cells contains zero value [0], the odds ratio estimate is arrived at by adding 0.5 to each cell, then calculating the odds ratio (as described in Fleiss (17). Since the 95% confidence interval does not contain unity [1] for one, two, or three factors, all of

these results are statistically significant. The above table demonstrates that the more predictive factors present, the more likely the patient is to be bacteremic, with an impressive gradient in the odds ratio. Also remarkable is the fact that all cases have at least one of the predictive factors, and only 2% of the controls have all three factors, while 23.6% of the cases have all three.

The information in the above table could be applied in the clinical setting to help the physician in the emergency room in deciding whether or not to take a blood culture, since bacteremia is associated with an absolute band count greater than 2000, non-white race, and pneumonia, urinary tract infection or skin/soft tissue infection.

4.4 COST

A total of 1072 cultures were taken and an average of 1.6 bottles per person yields approximately 1715 sets of cultures over three years. The culture bottles and equipment to draw the blood costs about $4.00. Currently the laboratory charges $14.00 to process one set of BC regardless of whether or not they are positive. Thus, the total cost of outpatient blood cultures over three years is

1715 X $18.00 = $30,820, or about $10,000 per year. The blood culture lab processes about 18,000 blood cultures per year, hence the blood cultures from adult medical outpatients represent only about 3.1% of the cultures processed.

4.5 FOLLOWUP

A retrospective study such as this presents many difficulties in determining exactly what type of benefits are derived from taking these blood cultures (23). The data show that five out of 21 patients with positive cultures were followed up in the Yale-New Haven Emergency Room. None of these follow up visits appeared to result in a change of therapy. However, this does not mean that the remaining 16 patients received no follow up. They could have visited another ER, or a clinic or their private physician. This lack of information makes any cost-benefit analysis (14) difficult, if not impossible.

4.6 CONCLUSIONS

This study shows that blood cultures are rarely true positives, with a 1.9% positivity rate. In the case of Yale-New Haven Hospital, this means only 7 outpatient cultures are positive per year, out of approximately 350. The contamination rate is over twice the true positive rate (4.9%). Thus, if a culture is positive, it is more likely to be a contaminant than a true positive.

This investigation demonstrates that some factors, namely non-caucasian race, an absolute band count greater than 2,000 and a site of infection of pneumonia, urinary tract infection, or skin/soft tissue infection are all positive predictors for bacteremia. All cases had at least one of these factors, and as more factors were present, the likelihood of bacteremia increased. Over three fourths (84.7%) of the controls had one or fewer predictive factors and almost half (44.9%) had none of these three factors.

Considering the low positivity rate and high contamination rate in outpatient blood cultures, one may question why blood cultures are taken at all. The primary reason is that the consequences of bacteremia can be so serious that no one wants to take the chance of not detecting it. The relatively benign procedure of taking a blood culture may provide an early lead on a potentially dangerous blood-borne organism, and may also prevent costly

admissions to "rule out" sepsis. Alternatively, taking blood cultures is costly and increases the hospitals responsibility for tracking down and treating patients with positive cultures (42).

The results of this study can be applied in the clinical setting to focus blood culturing on patients in whom bacteremia is most likely; that is those with two or more predisposing factors. In addition, since almost half of the controls had no predisposing factors, and all cases had at least one predisposing factor, patients with a low likelihood of bacteremia (i.e. no predisposing factors) can now be avoided, saving the time, cost, effort and pain of taking unnecessary blood cultures.

4.7 RECOMMENDATIONS

Further research on this topic should include a prospective cohort study, which would improve on this case control study in several ways. It would provide more accurate clinical and laboratory data. Other cultures from the patient could be followed up more readily, and the patient could be contacted more easily, if needed, for follow-up information. In addition, the house officers

could be asked why they decide to take a blood culture from a particular patient, and how they determine whether a positive result is a true positive or a contaminant.

Appendix C

TABLES FROM CHAPTER 4, DISCUSSION

C.1 FACTORS HYPOTHESIZED TO INCREASE RISK OF BACTEREMIA

FACTOR	ODDS RATIO	P	HELPFUL PREDICTOR
AGE>55	0.96	0.81	NO
AGE>70	1.13	0.82	NO
TEMP>101.0	2.0	0.29	POSSIBLE
TEMP>102.5	0.67	0.66	NO
WBC>15K	2.8	0.13	YES BUT NOT SIG.
WBC>20K	7.9	0.02	YES
ESR>25	-	-	DONE IN <50%
ESR>35	-	-	
POS CXR	-	-	DONE IN <50%
%SEGS>70	0.5	<0.01	NEG. PREDICTOR
%BANDS>5	1.9	0.37	SUGGESTIVE BUT NOT SIG.
PREDISPOSING FACTORS			
IDDM	4.85	0.32	NO, NOT SIG.
IVDA	1.10	0.57	NO
VHD	0.0	0.37	NO

C.2 FACTORS HYPOTHESIZED TO DECREASE RISK OF BACTEREMIA

FACTOR	ODDS RATIO	P	HELPFUL PREDICTOR
AGE<50	0.86	0.96	NO
TEMP<100	0.88	0.55	NO
NO PF	0.65	0.54	NO
WBC<10K	0.57	0.37	NO
%SEGS<60	3.90	0.01	NO-POS.PRED
%BANDS<5	0.52	0.35	SUGGESTIVE BUT NOT SIG.
NO PYURIA	-	-	DONE IN <50%
NEG CXR	-	-	DONE IN <50%

Appendix D

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