

Hemophilus vaginalis bacteremia

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During 1975–77 *Hemophilus vaginalis* bacteremia occurred post partum in eight previously healthy women. Seven had been admitted for delivery at term and one because of threatened abortion. Six underwent cesarean section. Post-partum pyrexia and neutrophilia were the main features. All the patients recovered uneventfully while receiving antibiotics. *H. vaginalis* is an infrequent agent of bacteremia; it affects predominantly women after obstetric trauma.

De 1975 à 1977 des bactériémies à *Hemophilus vaginalis* sont survenues en post-partum chez huit femmes préalablement en bonne santé. Sept patientes avaient été hospitalisées pour accouchement à terme et une a été hospitalisée pour menace d'avortement. Six subirent une césarienne. Les principaux aspects de la maladie furent une pyrexie et une neutrophilie en post-partum. Toutes les patientes se rétablirent sans incidents alors qu'elles recevaient des antibiotiques. *H. vaginalis* est rarement la cause d'une bactériémie; c'est à la suite d'un traumatisme obstétrique que les femmes en sont surtout affectées.

Hemophilus vaginalis (*Corynebacterium vaginale*) is frequently isolated from the female genital tract and is implicated as a cause of vaginitis.^{1,2} Rarely it has been isolated from the blood of patients with post-partum infections. We report here the findings in eight cases of *H. vaginalis* bacteremia in Hamilton during 1975–77, seven of which were studied at St. Joseph's Hospital and one of which was studied at McMaster University Medical Centre.

Methods

Blood was cultured in Vacutainer 50-ml culture tubes (aerobic and anaerobic) with supplemented peptone broth (Becton–Dickinson); 5 ml of blood was inoculated per tube and the tubes were incubated at 35°C. Microorganisms were detected by Gram-staining and subculture to blood agar plates incubated aerobically and anaerobically at 35°C. When bacteremia was detected the patient was followed up by one of us (C.A.-J. or J.R.).

Cervical or high vaginal swabs were inoculated onto a modified Thayer–Martin medium incubated in car-

bon dioxide, MacConkey medium and Columbia base blood agar plates, which were incubated aerobically and anaerobically at 35°C. The organisms were identified according to the criteria of Dunkelberg, Skaggs and Kellogg,³ by α -hemolysis and colonial morphology on blood agar, a negative catalase reaction, failure to reduce nitrate to nitrite and inhibition of growth by hydrogen peroxide. Biochemical sugar reactions were tested in purple broth fermentation medium.⁴

Antibiotic susceptibility was tested on 5% sheep blood in Columbia base agar plates by the disc diffusion method. Two strains failed to grow sufficiently well at 24 hours to be tested by this method.

Results

Patient studies

The pertinent clinical and laboratory data are presented in Table I. In all eight patients, previously healthy young women, *H. vaginalis* bacteremia had developed post partum. Seven had been admitted for delivery at term and because of threatened abortion. Six patients had undergone cesarean section; for two it had been an elective procedure.

Seven patients were febrile, with temperatures not exceeding 40°C, and with leukocytosis and neutrophilia. In three of these patients the temperature returned to normal within 48 hours after the start of antibiotic therapy. In the other three the fever gradually abated over 6 days. Two of the latter three had mixed infections with anaerobic microorganisms. One, who had endometritis, was the only patient with foul lochia; *Bacteroides fragilis* was cultured from the cervical swabs. In the other, three types of organisms were cultured from the blood, and both *H. vaginalis* and *Peptococcus* sp. were isolated from the pus of a wound abscess; the role of *H. vaginalis* could not be determined in this case as the temperature subsided following drainage of the abscess. One patient was febrile at the time of admission, and low-grade pyrexia persisted for 10 days; the effect of therapy was questionable in this case. Fever was not recorded in one patient, but a blood culture was performed because of a rise in her leukocyte count from $6.0 \times 10^9/l$ to $10.2 \times 10^9/l$.

There was no clinical or laboratory evidence of infection elsewhere in these patients.

Bacteriologic studies

The growth of *H. vaginalis* in the blood cultures was detected after 1 to 4 days in seven cases, but not until the 10th day in one case. Changes in the blood culture medium were minimal and always fol-

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lowed detection of bacteria by smear and subculture. Direct Gram-staining of smears showed pleomorphic, gram-variable coccoid and bacillary forms. On subculture the organisms were less pleomorphic and were gram-negative. After 24 hours the growth on blood agar plates consisted of pinpoint colonies with faint α -hemolytic zones, which became more pronounced at 48 hours. The colonies were larger on the anaerobic plates. All the isolates produced acid from starch, glucose and maltose, and did not ferment lactose, salicin or sucrose. Although the agar diffusion method of antibiotic susceptibility testing has not been standardized for slow-growing strains of *H. vaginalis*, those that grew sufficiently were shown to be sensitive to penicillin, ampicillin, erythromycin, clindamycin, chloramphenicol and cephalothin, which generally agrees with the findings of others.^{5,6}

The results of culture of the specimens obtained from the presumed sites of entry of the organism into the bloodstream are shown in Table I. *H. vaginalis* and anaerobic organisms cultured from cervical and vaginal swabs were reported only if present as a heavy growth.

Discussion

H. vaginalis was first described in patients with vaginitis by Gardner and Dukes.¹ Its taxonomic position is still in dispute owing to controversy over whether it should be included in the genus *Corynebacterium*.⁵ When Gram-stained the organisms are gram-variable coccobacilli arranged singly, in pairs or in palisades

suggestive of *Corynebacterium* sp. They require an enriched medium for growth but do not need X factor (hemin) or V factor (niacin adenine dinucleotide), one or both of which are essential for the growth of *Hemophilus* sp.⁵

When cultured from the blood *H. vaginalis* may be confused with the commensal skin *Corynebacterium* sp. that may contaminate blood cultures. Strains of both species grow slowly and may be cultured after 4 days of incubation; they have common biochemical features, such as fermentation of glucose and maltose and failure to reduce nitrate to nitrite. *H. vaginalis* does not produce catalase or ferment lactose, salicin or sucrose; it utilizes starch, producing acid, and its growth is inhibited by hydrogen peroxide.³ Most corynebacteria produce catalase and have varied sugar fermentation reactions; few are inhibited by hydrogen peroxide.

H. vaginalis is associated with a clinically distinct form of vaginitis characterized by a greyish malodorous exudate and the stippling of squamous epithelial cells with gram-variable pleomorphic coccobacilli (vaginal clue cells). The organism has also been isolated from women without vaginitis, which indicates that it may be part of the normal flora of some women.⁷ Its role in the female genital tract probably resembles that of *Candida*: both can be present in small numbers as part of the normal flora, and are of low virulence but can become local pathogens.

In addition to causing vaginitis *H. vaginalis* is a recognized, although uncommon, cause of bacteremia in febrile obstetric patients⁸⁻¹⁰ (the identification of

Table I—Clinical and laboratory data in eight cases of *Hemophilus vaginalis* bacteremia

Case no.	Procedure and indication	Time of onset of fever	Leukocyte count ($\times 10^9/l$)	Culture results		Antibiotic therapy
				Cervical or high vaginal swab	No. of blood sets positive/total no. of sets	
1	Cesarean section Elective	48 hours postop.	23.0	<i>H. vaginalis</i> , normal flora	1/3	Gentamicin, ampicillin
2	Toxemia and cephalo-pelvic disproportion	24 hours postop.	15.4	<i>H. vaginalis</i> , <i>Bacteroides fragilis</i>	2/3	Penicillin, gentamicin, ampicillin
3	Fetal distress	On admission	19.1	Not done	1/3	Ampicillin
4	Elective repeat procedure	Afebrile	10.2	<i>H. vaginalis</i> , normal flora	2/2	Ampicillin
5	Premature rupture of membranes, cephalo-pelvic disproportion	During labour	21.7	<i>B. fragilis</i> , <i>Peptococcus</i> sp. (cultured from amniotic fluid)* <i>H. vaginalis</i> , <i>Peptococcus</i> sp. (cultured from pus of wound abscess)*	3/3 (<i>Peptococcus asaccharolyticus</i> , <i>H. vaginalis</i> , <i>B. disiens</i>)	Penicillin, gentamicin, clindamycin
6	Fetal distress	24 hours postop.	28.3	No growth from culture of placenta*	1/3	Penicillin, gentamicin, clindamycin
7	Other Normal labour, episiotomy	48 hours postop.	14.1	Normal flora	2/2	Ampicillin
8	Dilation and curettage, abortion	48 hours after admission	11.3	<i>H. vaginalis</i> , normal flora	2/2	Ampicillin

*No cervical swab cultures were done.

H. vaginalis in one of these studies⁹ was disputed by Dunkelberg¹¹). Most of the patients that have been described have been healthy women with fever following delivery, usually of healthy infants at term. In some patients there was evidence of chorioamnionitis or endometritis, but most often fever and leukocytosis were the only abnormal findings. Foul-smelling lochia was not a feature in those cases, and its presence, as in one of our cases, could indicate the co-existence of infection with anaerobic organisms. Ten of 19 obstetric patients seen over a 14-year period in the largest fully documented series⁷ had undergone cesarean section; the others had undergone forceps delivery or episiotomy. Our study also indicates that *H. vaginalis* bacteremia with fever occurs mainly in patients undergoing cesarean section, usually because of complications arising during labour, and does not appear to develop following normal vaginal delivery uncomplicated by trauma.

H. vaginalis bacteremia has followed septic abortion, hysterectomy and cervicitis associated with a hydatidiform mole.^{6,9,12} It has also been reported in neonates;¹³ the babies were usually premature, and chorioamnionitis was sometimes present, though the mothers were usually asymptomatic. *H. vaginalis* is part of the male urethral flora,¹⁴ but only one case of bacteremia following transurethral resection of the prostate has been reported.¹⁵

In all the reported cases of *H. vaginalis* bacteremia the genital tract appears to have been the source of infection. *H. vaginalis* was isolated in nearly all the cases in which cervical or vaginal secretions were cultured, but this does not indicate whether there was associated vaginitis or merely colonization.

H. vaginalis bacteremia runs a fairly benign course. With most patients receiving antibiotics the fever subsides in a few days. Ascending antepartum infection is rare, and metastatic suppuration has not been reported. In a few cases stillbirth or perinatal death occurred, but all had obstetric complications, so that the role of the bacteremia is uncertain. Neonatal sepsis is rarely associated with maternal bacteremia. These findings suggest the entry of organisms into the maternal bloodstream at the time of the trauma of delivery.

In vitro antibiotic susceptibility testing indicates that the organism is usually sensitive to penicillin, ampicillin, clindamycin, chloramphenicol, erythromycin and the cephalosporins.¹⁶ A recent report described a very good response to metronidazole of nonspecific vaginitis

associated with *H. vaginalis*, and the failure of ampicillin and sulfonamides to effect a cure. Antibiotics effective in vitro have been used to treat *H. vaginalis* bacteremia, but in view of the benign nature of the illness their effect on the clinical course is uncertain.

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References

- GARDNER HL, DUKES CD: *Haemophilus vaginalis* vaginitis: a newly defined specific infection previously classified "nonspecific vaginitis". *Am J Obstet Gynecol* 69: 962, 1955
- PHEIFFER TA, FORSYTH MS, DURFEE MA, et al: Nonspecific vaginitis. Role of *Haemophilus vaginalis* and treatment with metronidazole. *N Engl J Med* 298: 1429, 1978
- DUNKELBERG WE, SKAGGS R, KELLOGG DS JR: A study and new description of *Corynebacterium vaginale* (*Haemophilus vaginalis*). *Am J Clin Pathol* 53: 370, 1970
- SMITH RF: New medium for isolation of *Corynebacterium vaginale* from genital specimens. *Health Lab Sci* 12: 219, 1975
- LAPAGE SP: *Haemophilus vaginalis*, in *Bergey's Manual of Determinative Bacteriology*, 8th ed, BUCHANAN RE, GIBBONS NE (eds), Williams & Wilkins, Baltimore, 1974, p 368
- VENKATARAMANI TK, RATHBUN HK: *Corynebacterium vaginale* (*Haemophilus vaginalis*) bacteremia — clinical study of 29 cases. *Johns Hopkins Med J* 139: 93, 1976
- MCCORMACK WM, HAYES CH, ROSNER B, et al: Vaginal colonisation with *Corynebacterium vaginale* (*Haemophilus vaginalis*). *J Infect Dis* 136: 740, 1977
- MONIF GRC, BAER H: *Haemophilus* (*Corynebacterium*) *vaginalis* septicemia. *Am J Obstet Gynecol* 120: 1041, 1974
- REGAMEY C, SCHOENKNECHT FD: Puerperal fever with *Haemophilus vaginalis* septicemia. *JAMA* 225: 1621, 1973
- CARNEY FE: *Haemophilus vaginalis* septicemia. *Obstet Gynecol* 41: 78, 1973
- DUNKELBERG WE: *Corynebacterium vaginale*. *Sex Transm Dis* 4: 69, 1977
- ROTHERAM EB JR, SCHICK SF: Nonclostridial anaerobic bacteria in septic abortion. *Am J Med* 46: 80, 1969
- PLATT MS: Neonatal *Haemophilus vaginalis* (*Corynebacterium vaginalis*) infection. *Clin Pediatr (Phila)* 10: 513, 1971
- BOWIE RW, POLLOCK HM, FORSYTH PS, et al: Bacteriology of the urethra in normal men and men with nongonococcal urethritis. *J Clin Microbiol* 6: 482, 1977
- PATRICK S, GARNETT PA: *Corynebacterium vaginale* bacteremia in a man (C). *Lancet* 1: 987, 1978
- MCCARTHY LR, MICKELSEN PA, SMITH EG: Antibiotic susceptibility of *Haemophilus vaginalis* (*Corynebacterium vaginale*) to 21 antibiotics. *Antimicrob Agents Chemother* 16: 186, 1979

Einstein on curiosity

Do not stop to think about the reasons for what you are doing, about why you are questioning. Curiosity has its own reason for existence. One cannot help but be in awe when he contemplates the mysteries of eternity, of life, of the marvelous structure of reality. It is enough if one tries merely to comprehend a little

of this mystery each day. Never lose a holy curiosity.

— Albert Einstein, quoted in "Familiar Medical Quotations", Maurice B. Strauss (ed), Little, Brown & Co.,