

Review Paper

Lactobacillus acidophilus and Yogurt in the Prevention and Therapy of Bacterial Vaginosis

Robert Sieber^{a,*} and Uwe-Thomas Dietz^b

^aFederal Dairy Research Station, Liebefeld, CH-3003 Berne, Switzerland

^bDepartment of Gynecology & Obstetrics, Hospital, CH-3303 Jegenstorf, Switzerland

(Received 18 February 1998; accepted 30 June 1998)

ABSTRACT

In the vaginas of women different microorganisms can be found, among others also lactic acid bacteria. These bacteria form an acid milieu that can protect the woman from a vaginal infection. After genital infection the proportion of microorganisms is changed; the numbers of pathogenic organisms such as *Candida*, *Gardnerella* and/or *Trichomonas* increase, the number of lactobacilli decrease. Several studies show that direct application of *Lactobacillus acidophilus* or yogurt in the vagina can be therapeutically useful. There are now some indications that the ingestion of dairy products fermented by *Lactobacillus acidophilus* might also have a therapeutic benefit. © 1998 Elsevier Science Ltd. All rights reserved

Keywords: lactic acid bacteria; yogurt; fermented dairy product; *Lactobacillus acidophilus*; vaginitis; woman

INTRODUCTION

Numerous studies have shown that the vagina of a healthy woman is populated by a variety of microorganisms. The physiological condition of the vagina changes and so do the different microorganisms during a woman's life. The relationship between these organisms is delicately balanced and offers protection against infections of the vagina. When this balance is impaired a woman is at risk of contracting a genital infection. It seems that infection is not only a question of the increasing number of pathological germs but also of the decreasing number of lactobacilli. There is substantiated evidence that a vaginal infection is more likely to be triggered by the decreasing number of lactobacilli leading to relative predominance of pathological organisms.

This article reviews the literature with the emphasis on possibilities of treating vaginal infections with *Lactobacillus (L.) acidophilus* or with dairy products that are produced with this organism. In an investigation concerning the use of over-the-counter preparations and alternative medicine in women with chronic vaginal symptoms, Nyirjesy *et al.* (1997) showed that 44 of 105 patients had used alternative medications, most frequently acidophilus pills (50% orally, 11.4% vaginally) or yogurt (20.5% orally, 18.2% vaginally).

DEFINITION AND EPIDEMIOLOGY OF BACTERIAL VAGINOSIS

Almost 40 years ago Gardner and Dukes (1955) first described a non specific infection of the vagina, with

a fishy smell and discharge. They named this infection after the organism that caused 'Haemophilus vaginalis vaginitis'. Because this organism was not only found in women with the typical signs of this infection but also in women who had neither any symptoms nor were sexually active, controversial discussions about the pathological consequences of this disease took place over years. Due to its unstable gram staining the germ was titled '*Corynebacterium vaginale*' (Zinneman and Turner, 1963) but in 1980 it was renamed in the honor of Gardner '*Gardnerella vaginalis*', because its genus belonged neither to *Haemophilus* nor to *Corynebacterium* (Greenwood and Pickett, 1980). To date, the controversy continues, because numerous (especially anaerobic) microorganisms are involved in the bacterial vaginosis. Names like unspecific colpitis, aminocolpitis, Gardnerella vaginitis, Gardner's vaginitis, anaerobic vaginosis show the attempt to define this disease in a better way. In this article we will use the name Bacterial vaginosis (BV) (Hoyne and Eschenbach, 1985) which is defined as follows. A thin, homogeneous, greyish-white discharge, an elevated vaginal pH (more than 4.5), the occurrence of 'clue cells' (Gardner and Dukes, 1955) on microscopic examination of vaginal smears and intensified fishy smell after adding 10% KOH (liberating amines) to vaginal fluid specimens.

BV is a very common disease that occurs in about 10–30% of all patients, visiting a sexually transmitted disease clinic (Hallen *et al.*, 1987; Pahlson and Larsson, 1991). In a longitudinal study, BV was found in 87 of 780 pregnant women. After 36 gestational weeks only three of 176 women, that had atypical vaginal flora, developed BV and 32 women with BV recovered from the disease, showing a normal flora at the end of pregnancy (Hay *et al.*, 1994).

*Corresponding author.

Epidemiologic literature about BV is devoid of a good representative study about the prevalence of BV. All we seem to know so far is that 30–70% of all women suffering from BV show no symptoms. Whether the elevated prevalence in black people is of genetic origin, depends on smoking behavior, sexual behavior or circumcision, is not clear yet. Using an IUD seems to favor the development of BV (Mead, 1993).

THE PHYSIOLOGICAL AND PATHOLOGICAL VAGINAL ECOSYSTEM

The vaginal microbial flora of a healthy woman

The human vagina is lined by stratified, squamous, nonkeratinized epithelium. The surface is multilayered and the middle and the superficial layers contain glycogen. There are no glands that produce mucus, but the vaginal secretion arises predominantly from transudation of the vaginal epithelium and from the cervical mucus (Paavonen, 1983). The glycogen that is set free by the breakdown of the superficial cells is fermented by enzymes that are secreted by epithelial cells as well as by lactobacilli (Tindall, 1987). This fermentation liberates glucose which is then metabolized to lactic acid. In the last century Döderlein (1894) found the lactobacilli which he described as gram-positive, catalase negative, non-sporeing rods. They were named Döderlein-Bacilli and then identified by Thomas (1928) as *L. acidophilus*. Many authors have isolated *L. acidophilus* from the vagina (Butler and Beakley, 1960; Eschenbach *et al.*, 1989; Kohlmeyer *et al.*, 1994; Lachlak *et al.*, 1996; Lock *et al.*, 1948; McGroarty *et al.*, 1992; Reid *et al.*, 1996; Rogosa and Sharpe, 1980; Sautter and Brown, 1980). Besides *L. acidophilus* other strains could be found in the vaginas of healthy women as shown in Table 1.

Eschenbach *et al.* (1989) identified, in 27 of 28 healthy women, populations of lactobacilli that were able to produce hydrogen peroxide (H_2O_2). The ability to produce this substance may contribute to disease prevention by interference with pathogens. Lactobacilli producing H_2O_2 were found in almost 75% of the strains tested (McGroarty *et al.*, 1992) while Reid *et al.* (1996) found 84% positive strains. It seems that women colonized by H_2O_2 -producing lactobacilli are protected against acquisition of BV (Hawes *et al.*, 1996; Puapermpoonsiri *et al.*, 1996).

Beside lactobacilli there are a variety of other microorganisms in the vagina. In 107 samples Thomas (1928) found *Staphylococcus*, *Diphtheroides*, *B. coli*, *Streptococcus* and *Sarcina*. Sautter and Brown (1980) identified 37 different organisms in sequential vaginal cultures.

The vaginal microbial form of women with bacterial vaginosis

In women suffering from BV many different organisms are found (Hill, 1993; Hillier, 1993) i.e. *Gardnerella vaginalis* (Eschenbach *et al.*, 1989; Fredricsson *et al.*, 1984; Pfeifer *et al.*, 1978; Spiegel *et al.*, 1980), *Acteroides* sp. and *Mycoplasma hominis* (Eschenbach *et al.*, 1989; Spiegel *et al.*, 1980), *Gardnerella vaginalis*, *Bacteroides*, *Ureaplasma urealyticum* (Roy *et al.*, 1994) and *Candida* (Hurley *et al.*, 1974; Sobel, 1993; Geiger *et al.*, 1995). Döderlein-bacilli could be shown in 14 of 44 women with

Table 1. Lactobacillus Species Identified from the Vaginas of Healthy Women

Species	No. of women with indicated species					
	N:	100	100	63	100	53
	Reference:	A ^a	A ^b	B	C	D
<i>L. acidophilus</i>		42	55	13	24	20
<i>L. jensenii</i>		8	12	22	35	7
<i>L. fermentum</i>		16	17	0	0	7
<i>L. casei</i>		6	13	15	18	0
<i>L. gasseri</i>		0	0	3	13	0
<i>L. brevis</i>		26	0	1	0	2
<i>L. plantarum</i>		1	0	2	1	23
<i>L. rhamnosus</i>		0	0	0	0	2
<i>L. cellobiosus</i>		0	0	0	1	0
<i>L. crispatus</i>		0	0	0	3	0
<i>L. delbrueckii</i>		1	3	0	0	0
None		0	0	2	4	6

^a Black women.

^b White women.

References:

A: Kohlmeyer *et al.* (1994).

B: McGroarty *et al.* (1992).

C: Reid *et al.* (1996).

D: Fontaine *et al.* (1996).

a moniliavaginitis, in nine of 47 women with an unspecific vaginitis, but not in 11 women with *Trichomonas* and in seven women with *Monilia* and *Trichomonas* infection (Butler and Beakley, 1960) and in women with *Gonococcus* infection (Thomas, 1928). Furthermore, *Gardnerella vaginalis* infection did not include lactobacilli (Wood *et al.*, 1985). Only four of 67 patients with *Gardnerella vaginalis* showed H_2O_2 producing lactobacilli, but in 24 of them anaerobic lactobacilli were found (Eschenbach *et al.*, 1989). *Candida albicans* is able to produce an immuno-suppressive mycotoxin called gliotoxin (Shah *et al.*, 1995a).

In pregnant women with vaginal infection Westney *et al.* (1994) found *Gardnerella vaginalis* (50%), *Streptococcus* B (43.7%), *Candida albicans* (37.4%), *Trichomonas vaginalis* (13.4%), *E. coli* (6.2%); Hay *et al.* (1994) identified *Mycoplasma hominis* (43.6%) and *Gardnerella vaginalis* (44.9%) and Thorsen *et al.* (1998) described *Gardnerella vaginalis* and anaerobic bacteria and/or *Mycoplasma hominis* (59.6%). Hillier *et al.* (1992) isolated H_2O_2 producing lactobacilli in 10 out of 67 pregnant women with a BV and in 177 of 199 without a BV.

It seems that a BV is almost always an infection with *Gardnerella vaginalis* and a variety of different anaerobic bacteria. Most probably there is an unknown synergism between different microorganisms that is responsible for the increasing number of these specific bacteria. Chen *et al.* (1982) found that the succinate produced by *Gardnerella vaginalis* might increase the number of these other bacteria.

THERAPY OF BV WITH LACTOBACILLUS ACIDOPHILUS

Metchnikoff (1907) was the first to propose the use of lactobacilli for the restoration of a physiological

microbial flora in the gastrointestinal tract. There are studies showing that urinary infections and diarrhea can be treated with lactobacilli (Reid *et al.*, 1990). *L. casei* var. *rhamnosus* was able to prevent urinary infections in rats that had uropathogenic bacteria applied into the bladder (Reid *et al.*, 1985). Also, in women with recurrent urinary infections, *L. casei* GR-1 proved effective after vaginal and perineal implantation (Bruce and Reid, 1988). The effect of *L. casei* GR-1 and *L. acidophilus* 76 on *E. coli* is not due to lactic acid or H₂O₂ but to an unknown substance with a molecular weight between 12,000 and 14,000 (McGroarty and Reid, 1988; Reid *et al.*, 1988).

There are two different methods in the treatment with lactobacilli: The vaginal application and the oral intake of dairy products containing *L. acidophilus*.

STUDIES WITH VAGINAL APPLICATION OF LACTOBACILLI OR FERMENTED DAIRY PRODUCTS

Löser (1920) tried to restore a normal vaginal flora by the application of lactobacilli. Oliveira (1956) reported that in 49 infections with BV the symptoms disappeared and the pH changed from 5 to 6 to less than 4, after *L. acidophilus* application. Similar results were published by Rindi (1955). Twenty patients with chronic moniliasis showed an improvement of their symptoms after treatment with *L. acidophilus* (Will, 1979). Sandler (1979) also noticed improvement in women suffering from moniliasis after they were treated with lyophilized *L. acidophilus* products together with yogurt.

Mohler and Brown (1933) published a study where six of 21 women improved and nine women fully recovered after application of *L. acidophilus*. Exogenous application of Döderlein-bacilli was successful in 18 of 19 cases with unspecific vaginitis, in 22 of 25 cases with *Monilia* vaginitis, in seven of eight *Trichomonas* infections and in six with a combined *Trichomonas* and *Moniliasis* infection (Butler and Beakley, 1960). Comparable results were achieved by Ostrzenski (1974). More than 80% of 239 patients studied by Kanne *et al.* (1986) recovered from a *Moniliasis* vaginitis and stayed free of the disease when using vaginal tablets containing 50 mg lyophilisate of *L. acidophilus* (10^7 – 7×10^8), 0.03 mg estriol and 600 mg lactose. In two double blind, placebo-controlled clinical trials 28 women (Hallen *et al.*, 1992) and 32 nonmenopausal women with BV (Parent *et al.*, 1996) were treated with lyophilized H₂O₂-producing *L. acidophilus*. Immediately after completion of the treatment, 16 had normal vaginal wet smear results, compared to none of the 29 women treated with placebo (Hallen *et al.*, 1992). Four weeks after the start of therapy with vaginal tablets (Gynoflor), the cure rate was 88% in the verum group and 22% in the placebo group (Parent *et al.*, 1996). In a further double-blind, randomized, placebo-controlled trial with 167 patients, the vaccination with Gynatren, a *L. acidophilus* vaccine, was significantly better than the placebo (Siboulet, 1991) confirming the results of former studies (Karkut, 1984; Müller and Salzer, 1983). In a female with multiple vaginal infections a pessary containing freeze-dried *L. casei* var. *rhamnosus* GR-1 was inserted in the vagina. The patient came vaginitis symptom-free (Reid *et al.*, 1994).

Beside the application of lactobacilli, fermented dairy products were also used. Orlowa and Tomaszewitch (1933) used skim milk with *Bacillus bulgaricus*. Treating 25 women who suffered from vaginal discharge with 3 mL yogurt, Gunston and Fairbrother (1975) achieved good results in women with unspecific vaginitis, but had no success when treating *Trichomonas* vaginitis. No effect was observed in women suffering from *Trichomonas* and *Candida*, but in 29 of 38 women with BV the vaginal flora was restored (Friedlander *et al.*, 1986). Collins and Hardt (1980) studied 30 patients with *Candida* infection, comparing vaginal implantation of yogurt, low-fat milk and non-fermented acidophilus milk. They obtained conflicting results: there were three reinfections within three months with no milk product, one with yogurt, one with non-fermented acidophilus milk and 0 with low-fat milk. In a study of 84 women, in their first trimester of pregnancy and suffering from BV, 32 were treated with *L. acidophilus*, 32 with 5% acetic acid and 20 served as a control group. 28 women of the *L. acidophilus* group and 12 of the acetic acid group returned to normal flora, whereas only one of the control group showed no evidence of disease after two months of treatment (Neri *et al.*, 1993). In another study three days after administration of yogurt in 11 women with BV all strains of Gram-negative bacteria disappeared (Chimura *et al.*, 1995). However, Fredricsson *et al.* (1987, 1989) had found only one out of 14 women showing a normal vaginal flora after treatment with a *L. acidophilus* fermented dairy product.

STUDIES WITH ORAL APPLICATION OF YOGURT CONTAINING *L. ACIDOPHILUS*

Hilton *et al.* (1992) studied the efficacy of yogurt containing *L. acidophilus* for the treatment of *Candida* infection. They chose 33 women suffering from *Candida* vaginitis and divided them into two groups. The first group received 240 grams of yogurt daily for six months followed by six months of no treatment. The second group started with no treatment and continued with the yogurt for the other half of the year; thus each woman served as her own control. Eight of the 13 patients finishing the study suffered from a chronic vaginitis, three women had five *Candida* infections and two women had between six and eight infections per year. The colonization of the vagina with lactobacilli and *Candida* was measured and the *Candida* infection was evaluated clinically. As can be seen in Table 2, the control group had significantly more infections and it had less *L. acidophilus* in the faeces and in the vagina than the control group. Unfortunately, the study was not double-blinded. Drutz (1992) pointed out that in future studies an appropriate control would be the pasteurized version of the same yogurt. He tried to explain the results of Hilton's study as follows. *L. acidophilus* may have displaced *Candida* ssp. normally residing in the gastrointestinal tract and may have colonized the vagina from there, subsequently inhibiting colonization of *Candida* ssp. by its competing presence in the vagina.

In a crossover trial Shalev *et al.* (1996) compared daily ingestion of 150 mL of yogurt containing live *Lactobacillus acidophilus* with 150 mL of pasteurized yogurt in 46 women with recurrent BV and candidal vaginitis. At least 28 patients participated during the first four months of

Table 2. Effect of Yogurt Containing *Lactobacillus acidophilus* on *Candida* Infections and Colonizations in Women with Vaginitis (Hilton *et al.*, 1992)

	Yogurt (N = 6)	Control (N = 11)	P value ^a
Mean number of infections per six months ^b	0.38 ± 0.51	2.54 ± 1.66	<0.001
Mean number of positive <i>Candida</i> colonizations per six months ^c	0.84 ± 0.90	3.23 ± 2.17	0.001

^a Paired *t*-test.

^b Defined by the presence of clinical vaginitis: Gram stain positive for yeast, pseudohyphae, an acidic vaginal pH, a positive culture for *Candida* species.

^c Defined by vaginal culture positive for *Candida* species with no clinical evidence of vaginitis.

the study and seven patients completed the entire study protocol. An increased prevalence of colonization of the rectum and vagina by the bacteria and reduced episodes of BV were found after the ingestion of yogurt enriched with live *L. acidophilus*. Lidbeck *et al.* (1987) suggested that *L. acidophilus* in fermented dairy product should be taken continuously in order to maintain high levels of lactobacilli in the intestine.

THE ORIGIN OF VAGINAL LACTOBACILLI

In a study to determine the origin of vaginal lactobacilli, Thomas (1928) fed *L. acidophilus* to two children in whom the organism was not present in the vagina or in the faeces before the study. After ingestion he could identify *L. acidophilus* in both places. The survival of lactobacilli in the gastrointestinal tract is dependent on the strain. *L. acidophilus* is most probably part of the physiological gastrointestinal flora (Bertazzoni Minelli *et al.*, 1993) and seems to survive better in the gastrointestinal tract than does *L. delbrueckii* ssp. *bulgaricus* (Bouhnik, 1993; Conway *et al.*, 1987; Gilliland *et al.*, 1978; Marteau *et al.*, 1992; Patel *et al.*, 1992). There is also a different behavior of *L. acidophilus* strains in the presence of acids and bile acids (Lankaputhra and Shah, 1995).

Lactobacilli must have a certain affinity to the intestinal mucosa to successfully colonize the gastrointestinal tract as it was shown for bifidobacteria (Bernet *et al.*, 1993), *L. acidophilus* (Bernet *et al.*, 1994; Chauvière *et al.*, 1992; Coconnier *et al.*, 1992; Conway *et al.*, 1987), *L. casei* GG (Elo *et al.*, 1991) and possibly *L. delbrueckii* ssp. *bulgaricus* (Conway *et al.*, 1987). The same ability to attach to vaginal epithelial cells was shown by Wood *et al.* (1985). The ability of *Candida* spp. to attach to vaginal cells is better at pH 6 than at pH 3–4. When vaginal cells were first incubated with lactobacilli and later with *Candida* spp. far less *Candida* spp. were able to attach to the cells (Sobel *et al.*, 1981). The mechanisms for this attachment are not yet clearly understood, but proteins, lipoteichoic acid or carbohydrates might be responsible (Andreu *et al.*, 1995).

THE ROLE OF MAINTENANCE OF A PHYSIOLOGICAL VAGINAL FLORA BY LACTOBACILLI

The vagina is protected by lactobacilli because they maintain an acidic environment or because they produce substances that inhibit the activity of other microorganisms. This inhibition is ascribed to lactic acid (Tramer, 1966), hydrogen peroxide (Wheather *et al.*, 1952) and bacteriocins (Pheifer *et al.*, 1978; Piard *et al.*, 1992; Tramer, 1966). After a treatment of the vagina with a low-pH lactate gel a *Lactobacillus*-dominated flora reappeared in 10 pregnant women with BV (Holst and Brandberg, 1990).

It seems that not only the pH but also the lactobacilli are responsible for a protective milieu in the vagina. Neri *et al.* (1993) described a higher success rate in pregnant women treated with yogurt than with acetic acid. A low pH is due to lactobacilli producing lactic acid by metabolizing glycogen (Wylie *et al.*, 1969). The glycogen is converted by enzymes as well as by lactobacilli liberating glucose which is then metabolized to lactic acid (Spiegel *et al.*, 1980). The treatment of bacterial vaginosis by local application of lactobacilli reduced the symptoms in only 12 of 32 cases, compared with metronidazol[®] and placebo, which led to an improvement in 29 of 37 and in 11 of 32 cases respectively (Boeke *et al.*, 1993).

Besides a low pH, the hydrogen peroxide production of lactobacilli seems to be an additional mechanism that regulates the growth and composition of the vaginal flora (Eschenbach *et al.*, 1989). Together with flavoproteins, the oxygen is converted to hydrogen peroxide that is able to inhibit the growth of other microorganisms (Dahiya and Speck, 1968). It is of great importance to note that not all *L. acidophilus* strains are able to produce hydrogen peroxide. In a study by Fitzsimmons and Berry (1994), only nine of 12 strains were able to do so. This is congruent with observations made by Eschenbach *et al.* (1989), who found strains that produced hydrogen peroxide in 6% of affected women and in 96% of healthy women. In a study performed with 275 pregnant women the incidence of H₂O₂-producing lactobacilli was 60% (Hillier *et al.*, 1992). These strains are able to inhibit the growth of *Gardnerella* ssp. and *Bacteroides bivius*. That the hydrogen peroxide is responsible for this inhibition was shown by *in vitro* studies that also investigated the influence of inhibitors (Table 3).

Other *in vitro* studies showed that *L. acidophilus* or *L. casei* ssp. *casei* inhibited the growth of *E. coli* (Kotz *et al.*, 1990; Tramer, 1966), *Mobiluncus mulieris* and *Gardnerella* ssp. (Mardh and Soltesz, 1983; Skarin and Sylwan, 1986) or the growth of *Mobiluncus mulieris* and *Gardnerella* ssp. (Skarin and Sylwan, 1986). *Candida albicans* was not inhibited by coagulase-negative staphylococcus (Nezdarilova, 1992) or by a substance in the filtrates of *L. acidophilus* (Guillot, 1958; Collins and Hardt, 1980) or by *L. acidophilus*. Further, when additional thiocyanate was given, *L. acidophilus* was able to inhibit *Candida albicans* (Fitzsimmons and Berry, 1994). *L. acidophilus* shows an antibacterial activity (Vincent *et al.*, 1959), can produce superoxide dismutase (Gonzalez *et al.*, 1991), hydrogen peroxide (Collins and Aramaki, 1980) as well as different bacteriocins as acidocin (Brink *et al.*, 1994; Shahani *et al.*, 1977; Tahara *et al.*, 1992, 1996), acidophilin (Shahani *et al.*, 1977), acidophilucin A (Toba *et al.*, 1991),

Table 3. Growth Inhibition of *Gardnerella vaginalis* and *Bacteroides bivius* by H₂O₂-producing *L. acidophilus*: Influence of Inhibitors (Klebanoff *et al.*, 1991)

Supplement	<i>Gardnerella vaginalis</i> viable cell count cfu × 10 ⁶ mL ⁻¹	P ^a	<i>Bacteroides bivius</i> viable cell count cfu × 10 ⁶ mL ⁻¹	P ^a
Control	2.31		8.3	
LB ⁺ (4 × 10 ⁶ resp. 7 × 10 ⁵)	0.015	<0.01	0.0002	<0.001
+ Catalase	1.82	ns	3.7	ns
+ Heated catalase	0.013	<0.05	0.0	<0.001
+ SOD	0.006	<0.02	0.0	<0.001
LB ⁻ (4 × 10 ⁶)	1.52	ns	2.8	ns
LB ⁺ (2 × 10 ⁵) + MPO + Cl ⁻	0.0006	<0.001		
- LB ⁺	2.58	ns		
- MPO	1.36	ns		
- Cl ⁻	1.74	ns		
+ Catalase	1.02	ns		
+ Heated catalase	0.005	<0.002		
+ SOD	0.005	<0.002		
- LB ⁺ , + LB ⁻	1.33	ns		
- LB ⁺ , + H ₂ O ₂	0.0	<0.001		

LB⁺ = H₂O₂-generating *L. acidophilus*.LB⁻ = non-H₂O₂-generating *L. acidophilus*.

+ = added; - = omitted.

SOD = superoxide dismutase.

MPO = myeloperoxidase.

ns = not significant.

^a Difference from control.**Table 4.** Microbiology of Different Lactobacillus Products Found on the American Market (Hughes and Hillier, 1990)

Product	Advertised content	Lactobacilli isolated			Other bacteria isolated	
		Species	H ₂ O ₂ prod.	Quantity (cfu g ⁻¹)	Species	Quantity (cfu g ⁻¹)
Yogurt	Not applicable	<i>L. delbrueckii</i> ssp. <i>bulgaricus</i>	+	ND	None	ND
	Not applicable	<i>L. delbrueckii</i> ssp. <i>bulgaricus</i>	+	ND	None	ND
	Not applicable	<i>L. delbrueckii</i> ssp. <i>bulgaricus</i>	+	ND	None	ND
Acidophilus milk	<i>L. acidophilus</i>	<i>L. acidophilus</i>	-	ND	None	ND
	<i>L. acidophilus</i>	<i>L. acidophilus</i>	+	ND	<i>Str. mitis</i> , <i>Pseudomonas</i>	ND
Acidophilus powder	<i>L. acidophilus</i>	<i>L. casei</i> ssp. <i>rhamnosus</i>	+	10 ⁶	<i>Clostridium sporogenes</i> , <i>E. faecium</i>	10 ² , 10 ⁵
	<i>L. acidophilus</i> , <i>L. bulgaricus</i> , <i>L. bifidum</i> , <i>L. thermophilus</i> , <i>L. salivarius</i>	<i>L. casei</i> ssp. <i>rhamnosus</i>	+	10 ⁴	<i>E. faecium</i>	10 ⁵
	<i>L. acidophilus</i> , <i>L. bifidum</i> , <i>Str. faecium</i>	<i>L. casei</i> ssp. <i>rhamnosus</i>	-	10 ⁶	<i>E. faecium</i>	10 ⁶
	<i>L. acidophilus</i>	<i>L. casei</i> ssp. <i>rhamnosus</i>	-	10 ⁶	<i>E. faecium</i>	10 ⁵
	<i>L. acidophilus</i> , <i>L. bulgaricus</i> , <i>Str. thermophilus</i>	<i>L. acidophilus</i>	-	10 ²	None	10 ¹
Acidophilus capsules	<i>L. acidophilus</i>	<i>L. casei</i> ssp. <i>rhamnosus</i>	+	10 ⁴	<i>E. faecium</i>	10 ³
	<i>L. acidophilus</i> , <i>L. bulgaricus</i> , <i>Str. thermophilus</i>	<i>L. casei</i> ssp. <i>rhamnosus</i>	+	10 ⁶	<i>E. faecium</i>	10 ¹
	<i>L. acidophilus</i>	<i>L. casei</i> ssp. <i>rhamnosus</i>	+	10 ³	<i>E. faecium</i>	10 ²
	<i>L. acidophilus</i>	<i>L. casei</i> ssp. <i>rhamnosus</i>	-	10 ⁷	<i>E. faecium</i>	10 ²
	<i>L. acidophilus</i>	<i>L. casei</i> ssp. <i>rhamnosus</i>	-	10 ⁷	<i>E. faecium</i>	10 ¹
Acidophilus- tablets	<i>L. acidophilus</i> , <i>L. bulgaricus</i>	<i>L. acidophilus</i>	+	10 ⁴	<i>E. faecium</i>	10 ²

ND = Not done.

lactacin B and F (Barefoot and Klaenhammer, 1984; Muriana and Klaenhammer, 1991).

ABOUT THE MICROBIOLOGICAL COMPOSITION OF FERMENTED DAIRY PRODUCTS AND OTHER LACTOBACILLI PREPARATIONS

Sour dairy products introduced in world markets recently, may contain not only *L. delbrueckii* ssp. *bulgaricus* and *Str. thermophilus* but also *L. acidophilus* and/or bifidobacteria. Whether these products contain sufficient concentration of *L. acidophilus* at the time of consumption is not clear. A significant decrease of *L. acidophilus* in products stored for seven days at 5°C was shown (Gilliland and Speck, 1977b). In yogurt, only 50% of *L. acidophilus* survived a storage of 14 days at 5°C (Hull *et al.*, 1984). When the concentration was between 10^7 and 10^8 cfu mL⁻¹, there was no decrease within 30 days at 4°C. However, when the concentration was less than 10^5 cfu mL⁻¹ there was a significant reduction in *L. acidophilus* in the same time (Shah *et al.*, 1995b).

Besides fermented dairy products many other *L. acidophilus* preparations are being marketed. In the US these are referred to as Megadophilus, Richidophilus, Mega Potency Acidophilus, Sensidophilus, etc. (Hughes and Hillier, 1990). Similar preparations can be found also in Europe, e.g. Gynophilus in Finland and Gynoflor E in Germany, Austria and Switzerland. These formulae contain not only *L. acidophilus*, but also estriol (0.03 mg) and lactose (600 mg).

Astounding results were published by Hughes and Hillier (1990) who were able to detect *L. acidophilus* in only two of 16 preparations. Only 10 preparations contained lactobacilli that were able to produce hydrogen peroxidase (Table 4). Similar observations were made by Gilliland and Speck (1977a) as well as by Hamilton-Miller *et al.* (1996). These results can be explained by the fact that 90% of the *L. acidophilus* lose their activity when the production is not carefully controlled (Klaenhammer, 1982).

CONCLUSION

The difficulties in the diagnosis and treatment of the bacterial vaginosis arise because the definition of the disease is still not clear and there are multitudes of different tests that are not validated. Therefore more effort should be made to define the disease and to standardize the tests.

Different case reports showed evidence that the therapy of bacterial vaginosis with lactobacilli and specially *L. acidophilus* might be effective. This therapy is already widely used (Drutz, 1992). Besides the topical application the ingestion of fermented dairy products with *L. acidophilus* also seems to be effective (Hilton *et al.*, 1992; Shalev *et al.*, 1996). The results of these investigations indicate that the dairy industry should produce fermented dairy products with *L. acidophilus* in sufficient concentrations (i.e. between 10^7 – 10^8 cfu mL⁻¹) and that these products should not be pasteurized after produc-

tion. Studies have to be carried out to answer the question if every strain of *L. acidophilus* or other probiotic bacteria are advantageous and if H₂O₂-producing *L. acidophilus* are essential for the treatment of BV.

REFERENCES

- Andreu, A., Stapleton, A. E., Fennell, C. L., Hillier, S. L. and Stamm, W. E. (1995) Hemagglutination, adherence, and surface properties of vaginal *Lactobacillus* species. *Journal of Infectious Diseases* **171**, 1237–1243.
- Barefoot, S. F. and Klaenhammer, T. R. (1984) Purification and characterization of the *Lactobacillus acidophilus* bacteriocin lactacin B. *Antimicrobial Agents and Chemotherapy* **26**, 328–334.
- Bernet, M. F., Brassart, D., Neeser, J. R. and Servin, A. L. (1993) Adhesion of human bifidobacterial strains to cultured human intestinal epithelial cells and inhibition of enteropathogen-cell interactions. *Applied and Environmental Microbiology* **59**, 4121–4128.
- Bernet, M. F., Brassart, D., Neeser, J. R. and Servin, A. L. (1994) *Lactobacillus acidophilus* LA1 binds to cultured human intestinal cell lines and inhibits cell attachment and cell invasion by enterovirulent bacteria. *Gut* **35**, 483–489.
- Bertazzoni Minelli, E., Benini, A., Beghini, A. M., Cerutti, R. and Nardo, G. (1993) Bacterial faecal flora in healthy women of different ages. *Microbial Ecology in Health and Disease* **6**, 43–51.
- Bouhnik, Y. (1993) Survie et effets chez l'homme des bactéries ingérées dans les laits fermentés. *Lait* **73**, 241–247.
- Boeke, A. J. P., Dekker, J. H., Eijk, J. T. M., van Kostense, P. J. and Bezemer, P. D. (1993) Effect of lactic acid suppositories compared with oral metronidazole and placebo in bacterial vaginosis—a randomised clinical trial. *Genitourinary Medicine* **69**, 388–392.
- Brink, B. ten, Minekus, M., Vossen, J. M. B. M. van der, Leer, R. J. and Huis in't Veld, J. H. J. (1994) Antimicrobial activity of lactobacilli: preliminary characterization and optimization of production of acidocin B, a novel bacteriocin produced by *Lactobacillus acidophilus* M46. *Journal of Applied Bacteriology* **77**, 140–148.
- Bruce, A. W. and Reid, G. (1988) Intravaginal instillation of lactobacilli for prevention of recurrent urinary tract infections. *Canadian Journal of Microbiology* **34**, 339–343.
- Butler, B. C. and Beakley, J. W. (1960) Bacterial flora in vaginitis. A study before and after treatment with pure culture of Döderlein bacillus. *American Journal of Obstetrics and Gynecology* **79**, 432–440.
- Chauvière, G., Coconnier, M. H., Kernéis, S., Fourniat, J. and Servin, A. L. (1992) Adhesion of human *Lactobacillus acidophilus* strain LB to human enterocyte-like caco-2 cells. *Journal of General Microbiology* **138**, 1689–1696.
- Chen, K. C., Amsel, R., Eschenbach, D. A. and Holmes, K. K. (1982) Biochemical diagnosis of vaginitis: determination of diamines in vaginal fluid. *Journal of Infectious Diseases* **145**, 337–345.
- Chimura, T., Funayama, T., Murayama, K. and Numazaki, M. (1995) Ecological treatment of bacterial vaginosis. *Japanese Journal of Antibiotics* **48**, 432–436.
- Collins, E. B. and Aramaki, K. (1980) Production of hydrogen peroxide by *Lactobacillus acidophilus*. *Journal of Dairy Science* **63**, 353–357.
- Collins, E. B. and Hardt, P. (1980) Inhibition of *Candida albicans* by *Lactobacillus acidophilus*. *Journal of Dairy Science* **63**, 830–832.
- Coconnier, M.-H., Klaenhammer, T. R., Kernéis, S., Bernet, M.-F. and Servin, A. L. (1992) Protein-mediated adhesion of *Lactobacillus acidophilus* BG2F04 on human enterocyte and mucus-secreting cell lines in culture. *Applied and Environmental Microbiology* **58**, 2034–2039.

- Conway, P. L., Gorbach, S. L. and Goldin, B. R. (1987) Survival of lactic acid bacteria in the human stomach and adhesion to intestinal cells. *Journal of Dairy Science* **70**, 1–12.
- Dahiya, R. S. and Speck, M. L. (1968) Hydrogen peroxide formation by lactobacilli and its effect on *Staphylococcus aureus*. *Journal of Dairy Science* **51**, 1568–1572.
- Döderlein, A. (1894) Die Scheidensekretuntersuchungen. *Centralblatt für Gynäkologie* **18**, 10–14.
- Drutz, D. J. (1992) Lactobacillus prophylaxis for *Candida* vaginitis. *Annals of Internal Medicine* **116**, 419–420.
- Elo, S., Saxelin, M. and Salminen, S. (1991) Attachment of *Lactobacillus casei* strain GG to human colon carcinoma cell line Caco-2: comparison with other dairy strains. *Letters in Applied Microbiology* **13**, 154–156.
- Eschenbach, D. A., Davick, P. R., Williams, B. L., Klebanoff, S. J., Young-Smith, K., Critchlow, C. M. and Holmes, K. K. (1989) Prevalence of hydrogen peroxide-producing *Lactobacillus* species in normal women and women with bacterial vaginosis. *Journal of Clinical Microbiology* **27**, 251–256.
- Fitzsimmons, N. and Berry, D. R. (1994) Inhibition of *Candida albicans* by *Lactobacillus acidophilus*: evidence for the involvement of a peroxidase system. *Microbios* **80**, 125–133.
- Fontaine, E. A., Claydon, E. and Taylor-Robinson, D. (1996) Lactobacilli from women with or without bacterial vaginosis and observations on the significance of hydrogen peroxide. *Microbial Ecology in Health and Disease* **9**, 135–141.
- Fredricsson, B., Englund, K., Weintraub, L., Ölund, A. and Nord, C. E. (1987) Ecological treatment of bacterial vaginosis. *Lancet* **i**, 276.
- Fredricsson, B., Englund, K., Weintraub, L., Ölund, A. and Nord, C. E. (1989) Bacterial vaginosis is not a simple ecological disorder. *Gynecologic and Obstetric Investigation* **28**, 156–160.
- Fredricsson, B., Hagstrom, B., Evaldson G. and Nord, C. E. (1984) Gardnerella-associated vaginitis and anaerobic bacteria. *Gynecologic and Obstetric Investigation* **17**, 236–241.
- Friedlander, A., Druker, M. M. and Schachter, A. (1986) *Lactobacillus acidophilus* and vitamin B complex in the treatment of vaginal infection. *Pamminerva Medica* **28**, 51–53.
- Gardner, H. L. and Dukes, C. D. (1955) *Hämophilus vaginalis* vaginitis. A newly defined specific infection previously classified 'nonspecific vaginitis'. *American Journal of Obstetrics and Gynecology* **69**, 962–976.
- Geiger, A. M., Foxman, B. and Gillespie, B. W. (1995) The epidemiology of vulvovaginal candidiasis among university students. *American Journal of Public Health* **85**, 1146–1148.
- Gilliland, S. K. and Speck, M. L. (1977a) Enumeration and identity of lactobacilli in dietary products. *Journal of Food Protection* **40**, 760–762.
- Gilliland, S. E. and Speck, M. L. (1977b) Instability of *Lactobacillus acidophilus* in yogurt. *Journal of Dairy Science* **60**, 1394–1398.
- Gilliland, S. E., Speck, M. L., Nauyok, G. F. and Giesbrecht, F. G. (1978) Influence of consuming nonfermented milk containing *Lactobacillus acidophilus* on fecal flora of healthy males. *Journal of Dairy Science* **61**, 1–10.
- Gonzalez, S. N., Nadra Chaud, C. A., Apella, M. C., Strasser de Saad, A. M. and Oliver, G. (1991) Evidence of superoxide dismutase in *Lactobacillus acidophilus*. *Chemical and Pharmaceutical Bulletin* **39**, 1065–1067.
- Greenwood J. R. and Pickett M. J. (1980) Transfer of *Hämophilus vaginalis* Gardner and Dukes to a new genus, *Gardnerella*: *G. vaginalis* (Gardner and Dukes). comb. nov. *International Journal of Systematic Bacteriology* **30**, 170–178.
- Guillot, N. (1958) Production by *Lactobacillus acidophilus* of a substance active against *Candida albicans*. *Annales de l'Institut Pasteur* **95**, 194–207.
- Gunston, K. D. and Fairbrother, P. F. (1975) Treatment of vaginal discharge with yoghurt. *South African Medical Journal* **49**, 675–676.
- Hallen, A., Jarstrand, C. and Pahlson, C. (1992) Treatment of bacterial vaginosis with lactobacilli. *Sexually Transmitted Diseases* **19**, 146–148.
- Hallen, A., Pahlson, C. and Forsum, U. (1987) Bacterial vaginosis in women attending a STD clinic: diagnostic criteria and prevalence of *Mobiluncus* spp. *Genitourinary Medicine* **63**, 386–388.
- Hamilton-Miller, J. M. T., Shah, S. and Smith, C. T. (1996) 'Probiotic' remedies are not what they seem. *British Medical Journal* **312**, 55–56.
- Hawes, S. E., Hillier, S. L., Benedetti, J., Stevens, C. E., Koutsky, L. A., Wolner-Hanssen, P. and Holmes, K. K. (1996) Hydrogen peroxide-producing lactobacilli and acquisition of vaginal infections. *Journal of Infectious Diseases* **174**, 1058–1063.
- Hay, P. E., Morgan, D. J., Ison, C. A., Bhide, S. A., Romney, M., McKenzie, P., Pearson, J., Lamont, R. F. and Taylor-Robinson, D. (1994) A longitudinal study of bacterial vaginosis during pregnancy. *British Journal of Obstetrics and Gynaecology* **101**, 1048–1053.
- Hill, G. B. (1993) The microbiology of bacterial vaginosis. *American Journal of Obstetrics and Gynecology* **169**, 450–454.
- Hillier, S. L. (1993) Diagnostic microbiology of bacterial vaginosis. *American Journal of Obstetrics and Gynecology* **169**, 455–459.
- Hillier, S. L., Krohn, M. A., Klebanoff, S. J. and Eschenbach, D. A. (1992) The relationship of hydrogen peroxide-producing lactobacilli to bacterial vaginosis and genital microflora in pregnant women. *Obstetrics and Gynecology* **79**, 369–373.
- Hilton, E., Isenberg, H. D., Alperstein, P., France, K. and Borenstein M. T. (1992) Ingestion of yogurt containing *Lactobacillus acidophilus* as prophylaxis for candidal vaginitis. *Annals of Internal Medicine* **116**, 353–357.
- Holst, E. and Brandberg, A. (1990) Treatment of bacterial vaginosis in pregnancy with a lactate gel. *Scandinavian Journal of Infectious Diseases* **22**, 625–626.
- Hoyme, U. B. and Eschenbach, D. A. (1985) Bakterielle Vaginose, Mikrobiologie, Diagnostik, Therapie und Komplikationen. *Deutsche medizinische Wochenschrift* **110**, 349.
- Hughes, V. L. and Hillier, S. K. (1990) Microbiologic characteristics of *Lactobacillus* products used for colonization of the vagina. *Obstetrics and Gynecology* **75**, 244–248.
- Hull, R. R., Roberts, A. V. and Mayes, J. J. (1984) Survival of *Lactobacillus acidophilus* in yoghurt. *Australian Journal of Dairy Technology* **39**, 164–166.
- Hurley, R., Stanley, V. C., Leask, B. G. S. and Louvois, J. de (1974) Microflora of the vagina during pregnancy. In *The normal microbial flora of man*, eds F. A. Skinner, Y. G. Carr. Academic Press, London, pp. 155–185.
- Kanne, B., Patz, B. and Wackerle, L. (1986) Lokale Behandlung vaginaler Infektionen mit Döderlein-Keimen und Estriol im Klimakterium und Senium. *Der Frauenarzt* **3**, 35–40.
- Karkut, G. (1984) Effect of lactobacillus immunotherapy on genital infections in women. *Geburtshilfe und Frauenheilkunde* **44**, 311–314.
- Klaenhammer, T. R. (1982) Microbiological considerations in selection and preparation of *Lactobacillus* strains for use as dietary adjuncts. *Journal of Dairy Science* **65**, 1339–1349.
- Klebanoff, S. J., Hillier, S. L., Eschenbach, D. A. and Waltersdorff, A. M. (1991) Control of the microbial flora of the vagina by H₂O₂-generating lactobacilli. *Journal of Infectious Diseases* **164**, 94–100.
- Kohlmeyer, H. E., Groeneveld, H. T., Plessis, D. du and Steyn, P.-L. (1994) A comparative study of the vaginal *Lactobacillus* population in black and white women. *South African Journal of Science* **90**, 79–81.
- Kotz, C. M., Peterson, L. R., Moody, J. A., Savaiano, D. A. and Levitt, M. D. (1990) In vitro antibacterial effect of yogurt on *Escherichia coli*. *Digestive Diseases and Sciences* **35**, 630–637.

- Lachlak N., Ageron E., Zampatti O., Michel G. and Grimont, P. A. D. (1996) Composition of the *Lactobacillus acidophilus* complex isolated from vaginal flora. *Microbiologica* **19**, 123–132.
- Lankaputhra, W. E. V. and Shah, N. P. (1995) Survival of *Lactobacillus acidophilus* and *Bifidobacterium* spp. in the presence of acid and bile salts. *Cultured Dairy Products Journal* **30**, 2–7 (3).
- Lidbeck, A., Gustafsson, J.-A. and Nord, C. E. (1987) Impact of *Lactobacillus acidophilus* supplements on the human-opharyngeal and intestinal microflora. *Scandinavian Journal of Infectious Diseases* **19**, 531–537.
- Lock, F. R., Yow, M. D., Griffith, M. I. and Stout, I. (1948) Bacteriology of the vagina in 75 normal young adults. *Surgery, Gynecology and Obstetrics* **87**, 410–416.
- Löser, A. (1920) *Zentralblatt für Gynäkologie* **44**, 417, cited after Butler and Beakley (1960).
- Mardh, P.-A. and Soltesz, L. V. (1983) In vitro interactions between lactobacilli and other microorganisms occurring in the vaginal flora. *Scandinavian Journal of Infectious Diseases* **40** (Suppl.), 47–51.
- Marteau, P., Pochart, P., Bouhnik, Y., Zidi, S., Goderel, I. and Rambaud, J. C. (1992) Survie, dans l'intestin grêle, de *Lactobacillus acidophilus* et *Bifidobacterium* sp. ingérés dans un lait fermenté. Une base rationnelle à l'utilisation de probiotiques chez l'homme. *Gastroentérologie Clinique et Biologique* **16**, 25–28.
- McGroarty, J. A. and Reid, G. (1988) Detection of a lactobacillus substance that inhibits *Escherichia coli*. *Canadian Journal of Microbiology* **34**, 974–978.
- McGroarty, J. A., Tomeczek, L., Pond, D. G., Reid, G. and Bruce, A. W. (1992) Hydrogen peroxide production by *Lactobacillus* species: correlation with susceptibility to the spermicidal compound nonoxonyl-9. *Journal of Infectious Diseases* **165**, 1142–1144.
- Mead, P. B. (1993) Epidemiology of bacterial vaginosis. *American Journal of Obstetrics and Gynecology* **169**, 446–449.
- Metchnikoff, E. (1907) *The prolongation of life*. G. P. Putman and Sons, New York.
- Mohler, R. W. and Brown, C. P. (1933) Döderlein's bacillus in the treatment of vaginitis. *American Journal of Obstetrics and Gynecology* **25**, 718–723.
- Müller G. and Salzer H. (1983) Long-term experience in the therapy and prevention of unspecific vaginal discharge with a *Lactobacillus* vaccine. *Wiener Klinische Wochenschrift* **95**, 371–374.
- Muriana, P. M. and Klaenhammer, T. R. (1991) Purification and partial characterization of lactacin-F, a bacteriocin produced by *Lactobacillus acidophilus*. *Applied and Environmental Microbiology* **57**, 114–121.
- Neri, A., Sabah, G. and Samra, Z. (1993) Bacterial vaginosis in pregnancy treated with yoghurt. *Acta Obstetrica et Gynecologica Scandinavica* **72**, 17–19.
- Nezdarilova, J. (1992) Interactions between vaginal lactobacilli and other microorganisms in the vaginal flora. *Scripta medica* **65**, 135–141.
- Nyirjesy P., Weitz M. V., Grody M. H. T. and Lorber B. (1997) Over-the-counter and alternative medicines in the treatment of chronic vaginal symptoms. *Obstetrics and Gynecology* **90**, 50–53.
- Oliveira, J. G. de (1956) *Journal of Clinica Chirurgica Lisbona* **7**, 205, cited after Butler and Beakley (1960).
- Orlowa, R. and Tomaszewitch, M. (1933) *Archiv für Gynäkologie* **154**, 628, cited after Butler und Beakley (1960).
- Ostrzenski, A. (1974) Lyophilized suspension of *Lactobacillus acidophilus* in supportive treatment of mycotic forms of vaginitis in women. *Polski Tygodnik Lekarski* **30**, 197, cited after Collins und Hardt (1980).
- Paavonen, J. (1983) Physiology and ecology of the vagina. *Scandinavian Journal of Infectious Diseases* **40** (Suppl.), 31–35.
- Pahlson, C. and Larsson, P. G. (1991) The ecologically wrong vaginal lactobacilli. *Medical Hypotheses* **36**, 126–130.
- Parent, D., Bossens, M., Bayot, D., Kirkpatrick, C., Graf, F., Wilkinson, F. E. and Kaiser, R. R. (1996) Therapy of bacterial vaginosis using exogenously-applied *Lactobacilli acidophili* and a low dose of estriol: a placebo-controlled multicentric clinical trial. *Arzneimittelforschung* **46**, 68–73.
- Patel, J. R., Dave, J. M., Dave, R. I. and Sannabhadhi, S. S. (1992) Effect of feeding milk fermented with mixed culture of human strains of lactobacilli on faecal lactobacilli and coliform counts in human test subjects. *Indian Journal of Dairy Science* **45**, 379–382.
- Pheifer, T. A., Forsyth, P. S., Durfee, M. A., Pollock, H. M. and Holmes, K. K. (1978) Nonspecific vaginitis: role of *Haemophilus vaginalis* and treatment with metronidazole. *New England Journal of Medicine* **298**, 1429–1434.
- Piard, J. C. and Desmazeaud, M. (1992) Inhibiting factors produced by lactic acid bacteria. 2. Bacteriocins and other antibacterial substances. *Lait* **72**, 113–142.
- Puapernpoonsiri, S., Kato, N., Watanabe, K., Ueno, K., Chongsomchai, C. and Lumbiganon, P. (1996) Vaginal microflora associated with bacterial vaginosis in Japanese and Thai pregnant women. *Clinical Infectious Diseases* **23**, 748–752.
- Reid, G., Bruce, A. W., McGroarty, J. A., Heng, K. J. and Costerton, J. W. (1990) Is there a role for lactobacilli in prevention of urogenital and intestinal infections? *Clinical Microbiology Reviews* **3**, 335–344.
- Reid, G., Chan, R. C. Y., Bruce, A. W. and Costerton, J. W. (1985) Prevention of urinary tract infection in rats with an indigenous *Lactobacillus casei* strain. *Infection and Immunity* **49**, 320–324.
- Reid, G., McGroarty, J. A., Angotti, R. and Cook, R. L. (1988) Lactobacillus inhibitor production against *Escherichia coli* and coaggregation ability with uropathogens. *Canadian Journal of Microbiology* **34**, 344–351.
- Reid, G., McGroarty, J. A., Tomeczek, L. and Bruce, A. W. (1996) Identification and plasmid profiles of *Lactobacillus* species from the vagina of 100 healthy women. *FEMS Immunology and Medical Microbiology* **15**, 23–26.
- Reid, G., Millsap, K. and Bruce, A. W. (1994) Implantation of *Lactobacillus casei* var *rhamnosus* into vagina. *Lancet* **344**, 1229.
- Rindi, V. (1955) *Minerva ginecologica* **7**, 621, cited after Butler and Beakley (1960).
- Roy, S., Sharma, M., Ayyagari, A. and Malhotra, S. (1994) A quantitative microbiological study of bacterial vaginosis. *Indian Journal of Medical Research* **100**, 172–176.
- Rogosa, M. and Sharpe, M. E. (1980) Species differentiation of human vaginal lactobacilli. *Journal of General Microbiology* **23**, 197–201.
- Sandler, B. (1979) *Lactobacillus* for vulvovaginitis. *Lancet* **2**, 791–792.
- Sautter, R. L. and Brown, W. J. (1980) Sequential vaginal cultures from normal young women. *Journal of Clinical Microbiology* **11**, 479–484.
- Shah, D. T., Glover, D. D. and Larsen, B. (1995a) In situ mycotoxin production by *Candida albicans* in women with vaginitis. *Gynecologic and Obstetric Investigation* **39**, 67–69.
- Shah, N. P., Lankaputhra, W. E. V., Britz, M. L. and Kyle, W. S. A. (1995b) Survival of *Lactobacillus acidophilus* and *Bifidobacterium bifidum* in commercial yoghurt during refrigerated storage. *International Dairy Journal* **5**, 515–521.
- Shahani, K. M., Vakil, J. R. and Kilara, A. (1977) Natural antibiotic activity of *Lactobacillus acidophilus* and *bulgaricus*. II. Isolation of acidophilin from *L. acidophilus*. *Cultured Dairy Products Journal* **12**, 8–11 (2).
- Shalev E., Battino S., Weiner E., Colodner R. and Keness Y. (1996) Ingestion of yogurt containing *Lactobacillus acidophilus* compared with pasteurized yogurt as prophylaxis for recurrent candidal vaginitis and bacterial vaginosis. *Archives of Family Medicine* **5**, 593–596.

- Siboulet A. (1991) Vaccination against nonspecific bacterial vaginosis. Double-blind study of Gynatren. *Gynäkologische Rundschau* **31**, 153–160.
- Skarin, A. and Sylwan, J. (1986) Vaginal lactobacilli inhibiting growth of *Gardnerella vaginalis*, *Mobiluncus* and other bacterial species cultured from vaginal content of women with bacterial vaginosis. *Acta Pathologica Microbiologica et Immunologica Scandinavica Section B* **94**, 399–403.
- Sobel, J. D., Myers, P., Kaye, D. and Levison, M. E. (1981) Adherence of *Candida albicans* to human vaginal and buccal epithelial cells. *Journal of Infectious Diseases* **143**, 76–83.
- Sobel, J. D. (1993) Genital candidiasis. In *Candidiasis: Pathogenesis, Diagnosis, and Treatment*, 2 edn, Vol. 225, ed. G. P. Bodey. Raven Press, New York.
- Spiegel, C. A., Amsel, R., Eschenbach, D. E., Schoenkecht, F. and Holmes, K. K. (1980) Anaerobic bacteria in nonspecific vaginitis. *New England Journal of Medicine* **303**, 601–607.
- Tahara, T., Kanatani, K., Yoshida, K., Miura, H., Sakamoto, M. and Oshimura, M. (1992) Purification and some properties of acidocin 8912, a novel bacteriocin produced by *Lactobacillus acidophilus* TK8912. *Bioscience Biotechnology Biochemistry* **56**, 1212–1215.
- Tahara T., Oshimura M., Umezawa C. and Kanatani, K. (1996) Isolation, partial characterization, and mode of action of acidocin J1132, a two-component bacteriocin produced by *Lactobacillus acidophilus* JCM 1132. *Applied and Environmental Microbiology* **62**, 892–897.
- Thomas, S. (1928) Döderlein's bacillus: *Lactobacillus acidophilus*. *Journal of Infectious Diseases* **43**, 218–227.
- Thorsen, P., Jensen, I. P., Jeune, B., Ebbesen, N., Arpi, M., Bremmelgaard, A. and Møller, B. R. (1998) Few microorganisms associated with bacterial vaginosis may constitute the pathologic core: a population-based microbiologic study among 3596 pregnant women. *American Journal of Obstetrics and Gynecology* **178**, 580–587.
- Tindall, V. R. (1987) Vaginal discharge. In *Jeffcoate's Principles of Gynaecology*, 5th edn. Butterworths, London.
- Toba, T., Yoshioka, E. and Itoh, T. (1991) Acidophilucin A, a new heat-labile bacteriocin produced by *Lactobacillus acidophilus* LAPT 1060. *Letters in Applied Microbiology* **12**, 106–108.
- Tramer, J. (1966) Inhibitory effect of *Lactobacillus acidophilus*. *Nature* **211**, 204–205.
- Vincent, J. G., Veomett, R. C. and Riley, R. F. (1959) Antibacterial activity associated with *Lactobacillus acidophilus*. *Journal of Bacteriology* **78**, 477–484.
- Westney, O. E., Westney, L. S., Johnson, A. A., Knight, E. M., Oyemade, U. J., Cole, O. J., Laryea, H., Spurlock, B., Manning, M., Hiza, H. B., Jones, S. and Edwards, C. H. (1994) Nutrition, genital tract infection, hematologic values, and premature rupture of membranes among African American women. *Journal of Nutrition* **124**, 987S–993S.
- Weather, D. M., Hirsch, A. and Mattick, A. T. R. (1952) Possible identity of 'Lactobacillin' with hydrogen peroxide produced by lactobacilli. *Nature* **170**, 623–624.
- Will, T. E. (1979) Lactobacillus overgrowth for treatment of monilary vulvovaginitis. *Lancet* **2**, 482.
- Wood, J. R., Sweet, R. L., Catena, A., Hadley, W. K. and Robbie, M. (1985) *In vitro* adherence of *Lactobacillus* species to vaginal epithelial cells. *American Journal of Obstetrics and Gynecology* **153**, 740–743.
- Wylie, J. G. and Henderson, A. (1969) Identity and glycogen-fermenting activity of lactobacilli isolated from the vagina of pregnant women. *Journal of Medical Microbiology* **2**, 363–366.
- Zinneman, K. and Turner, G. C. (1963) The taxonomic position of *Hämophilus vaginalis* (*Corynebacterium vaginale*). *Pathology and Bacteriology* **85**, 213.