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Selective Adherence as a Determinant of the Host Tropisms of Certain Indigenous and Pathogenic Bacteria

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The relationship between the selective abilities of bacteria to adhere and their predilections for colonizing different mammalian hosts was investigated by using bacteria indigenous to the tongue dorsum of humans and rats as models. *Streptococcus salivarius* and *S. sanguis* averaged 22.6 and 2.8%, respectively, of the cultivable bacteria recovered from swab samples of the tongues of five humans, but these organisms were not indigenous on the tongues of rats (Charles River strain). *S. faecalis* and serum-requiring diphtheroids were consistently prominant on the tongues of rats, but they were not detected on the tongues of the humans examined. The ability of these organisms to adhere to the tongue surface of the hosts was compared by introducing mixtures of streptomycin-resistant strains into the mouths of human volunteers and rats. *S. salivarius* adhered in higher proportions to the dorsal tongue surface of humans than did strains of *S. faecalis* and the serum-requiring diphtheroid. *S. sanguis* also adhered to human tongues better than the serum-requiring diphtheroid. However, *S. faecalis* and the serum-requiring diphtheroid sorbed in higher proportions to the tongues of rats. In an in vitro assay, human strains of *S. pyogenes* and *S. salivarius* attached in higher numbers to buccal epithelial cells derived from humans than to those obtained from rats, whereas the reverse was observed with a serum-requiring diphtheroid derived from rats. Collectively, these studies show that bacteria sorb with a high degree of specificity to the tissues of different mammalian hosts, and the relative adherence of the organisms studied correlated with their natural host tropisms. The selective adherence of *S. salvarius* and *S. faecalis* was similar to the tongues of conventional and germ-free rats, suggesting that the presence of an indigenous bacterial flora did not significantly influence their attachment selectivity. Moreover, the ability of these organisms to colonize the tongues of gnotobiotic rats lacking an indigenous flora paralleled their adherence selectivity. Direct scanning microscopic observations indicated that the tongue dorsum of conventional rats is highly papillated but contains relatively sparse bacterial populations. Indigenous organisms colonized the bases of papillae on the anterior tip and lateral edges of the tongue as discrete microcolonies, but bacteria were rarely observed on other papillae. This localized and restricted pattern of colonization and the spatial distribution of the microcolonies of indigenous bacteria present also suggest that antagonistic interactions are unlikely to account for the bacterial tropisms observed for colonization of the tongues of rats.

Differences exist in the composition of the indigenous bacterial flora that colonizes the intestinal canal and the oral cavity of humans and various animals (18, 22, 24, 27-29). Similarly, several pathogenic bacteria display a sharply restricted range of hosts that they infect under natural conditions. This host restriction has hindered studies of the natural ecology of many human pathogens because they generally fail to colonize the mucosal surfaces of common experimental animals when inoculated by oral or nasal routes. Why the colonization of many indigenous and pathogenic bacteria is limited to only some tissues and organs of some host species has never been clear.

Bacteria indigenous to the human mouth also display distinct tropisms for colonizing various oral surfaces, and several recent studies have shown that the predilection of a number of oral species for colonizing a given oral surface is related to their specific ability to attach to the surface (10, 11, 17, 32). This permits colonization by preventing the organisms from being washed away by oral secretions. The mouth, therefore, appears to be a useful and unique model for studying the underlying principles

that account for the natural tropisms of bacteria. It contains desquamating keratinized and nonkeratinized epithelial surfaces and the teeth. These surfaces are readily accessible for sampling over long periods of time, and each harbors a distinct collection of bacteria (11). Moreover, the composition of the oral flora differs between mammalian species (11, 18, 22, 29).

The present investigation was initiated to determined whether the predilection of certain bacteria for selectively colonizing oral tissues of different mammalian hosts was related to their abilities to adhere. Bacteria indigenous to the tongues of humans and rats were chosen for study because of the accessibility of the tongue for experimentation.

MATERIALS AND METHODS

Cultures and cultural conditions. *Streptococcus salivarius* strain CM6 and *S. sanguis* strain H7P were human oral isolates described previously (32, 33). *S. faecalis* strain 1RA was recently isolated from the oral cavity of humans (kindly provided by H. V. Jordan, Forsyth Dental Center), and *S. faecalis* strain E1 was isolated from tongue swabbings of rats in the present study. A serum-requiring (SR) diphtheroid, strain MS3, was freshly isolated from the tongues of rats. *S. pyogenes* strain SB1 (M type 6) was isolated from a human throat infection and provided by S. Bellack, Lincoln State School, Lincoln, Ill. *S. pyogenes* strain C203 (M type 3) was obtained from the American Type Culture Collection.

The streptococci were maintained by weekly transfer in Trypticase soy (T. soy) broth (BBL) and, with the exception of the *S. pyogenes* strains, on plates of Mitis-Salivarius (MS) agar (Difco). The latter organisms were carried on T. soy agar (BBL) plates containing 5% sheep blood. The SR diphtheroid strain MS3 was maintained in T. soy broth supplemented with 10% chicken serum and on blood agar plates. All cultures were incubated at 35 C in Brewer jars containing 80% N_2, 10% H_2, and 10% CO_2. Mutants resistant to 2,000 μg of streptomycin per ml were prepared as previously described (32); such strains were designated by the suffix "R."

Natural distribution of the bacterial species studied. The dorsal surface of the tongues of five humans and five rats (Charles River strain, Charles River Breeding Laboratory, Wilmington, Mass.) was sampled by vigorous swabbing with Calgi swabs. The samples were dispersed in modified Ringer solution as described previously (15, 32), and appropriate dilutions were plated in duplicate on MS agar for the enumeration of *S. salivarius, S. sanguis,* and organisms resembling the SR diphtheroid. Samples were also plated on Pfizer selective enterococcus agar (13) (Pfizer Inc., New York, N.Y.) for enumerating enterococci and on T. soy blood agar plates for determining the total cultivable count. All plates were incubated anaerobically for 2 to 3 days at 35 C.

Adherence of streptomycin-resistant streptococci to the dorsal tongue surface of humans and rats. Overnight T. soy broth cultures of streptomycin-resistant strains were centrifuged, and the organisms were washed twice and suspended in 0.01 M phosphate-buffered saline, pH 7.2. The suspensions were adjusted on the basis of optical density to contain approximately 2×10^8 organisms/ml. Mixtures of appropriate strains were prepared, and 1-ml samples were placed on the dorsal surface of the tongues of five humans and five rats. The humans were instructed to distribute the mixture throughout their mouths and expectorate after 5 min. Swab samples of the human and rodent tongues were obtained approximately 45 to 60 min later. The samples were dispersed in Ringer solution, and dilutions were plated on appropriate media containing 200 μg of streptomycin per ml. Dilutions of the original mixture placed into the mouths of the humans and rats were also plated on streptomycin-containing media. After incubation, the proportion of each streptomycin-resistant strain in the samples was determined; colonial morphology permitted the distinction of strains in the mixtures studied. The ratios of each organism recovered from the tongue samples were multiplied by the reciprocal of their ratios present in the original mixture to reflect equal opportunity to attach (32). These were converted into a percentage, which was designated the percentage of relative adherence

In vitro adherence of streptococci to human and rat buccal epithelial cells. The ability of *S. pyogenes* strains SB1 and C203 to adhere to human and rat buccal epithelial cells was determined by using an in vitro system previously described (10). Strains of *S. salivarius* and the SR diphtheroid were included for comparative purposes. Washed bacterial suspensions containing 2×10^8 cells/ml in phosphate-buffered saline were prepared from overnight T. soy broth cultures. Equal volumes of the washed bacterial suspensions were mixed with washed suspensions containing 10^5 human or conventional rat buccal epithelial cells per ml. The mixtures were incubated for 1 h at 35 C in a shaking water bath, after which the epithelial cells were washed free of unattached bacteria by membrane filtration (10). The mean number of bacteria attached per epithelial cell was determined by direct light microscopic enumeration of 25 epithelial cells. Samples of each epithelial cell suspension were also incubated with buffer and then counted in a comparable manner to determine the number of bacteria that were already attached to their surface at the time of collection; these values (usually 5 to 15 bacteria/cell) were subtracted to obtain the mean net number of test organisms that attached.

Colonization of *S. salivarius* CM6 and *S. faecalis* 1RAR on the tongues of gnotobiotic rats. Two duplicate experiments were performed to compare the ability of *S. salivarius* strain CM6 and *S. faecalis* strain 1RAR to colonize the dorsal tongue surface of gnotobiotic rats. Six germfree rats were maintained in flexible plastic isolators and fed Charles River diet 7RF. The animals were infected with a mixture containing approximately equal numbers of each organism. This was prepared from overnight T. soy broth cultures adjusted to an optical density of

0.8 at 550 nm. Three rats were removed from the isolator 4 and 7 days after infection. The dorsal surface of their tongues was vigorously rubbed with Calgi swabs. These were dispersed in Ringer solution, and dilutions were spread on the surface of MS agar plates. After anaerobic incubation for 2 days, the proportions of *S. salivarius* and *S. faecalis* were determined.

Scanning electron microscopy. Three conventional rats were killed by chloroform inhalation. The animals were decapitated and their mandibles and tongues were removed by dissection. These were fixed in formaldehyde-glutaraldehyde, dehydrated, air-dried from absolute acetone, and coated with palladium gold. The specimens were examined with a JEOL U3 scanning electron microscope.

RESULTS

Natural distribution of the bacteria studied on the dorsal surface of human and rat tongues. The natural distribution of the bacteria studied on the dorsal tongue surface of five humans and five rats is listed in Table 1. *S. salivarius* and *S. sanguis* have been previously shown to constitute a significant percentage of the flora colonizing the dorsal tongue surface of humans (10, 32). These organisms were uniformly present on the tongues of the five humans examined, and they averaged 22.6 and 2.8%, respectively, of the total organisms cultivable on anaerobically incubated blood agar plates. In rats, however, *S. salivarius* was not detected on the tongues of any of the five animals examined. *S. sanguis* was detected in only one animal, where it constituted less than 0.1% of the recoverable organisms. Samples from all rats examined yielded a predominant colony type on MS agar which was that of a gram-positive pleomorphic diphtheroid. Colonies on MS agar were flat, 2 to 3 mm in diameter, and nonmucoid, suggesting that the organisms did not synthesize large quantities of extracellular polysaccharide from sucrose. Though these organisms grew on MS agar on primary isolation, they could not be transferred to fresh MS agar plates. However, they would grow on blood agar plates or in T. soy broth supplemented with serum; therefore, they are referred to as serum-requiring (SR) diphtheroids. Strain MS3 was catalase negative and fermented glucose, sucrose, mannose, fructose, maltose, lactose, inulin, raffinose, trehalose, melibiose, and cellobiose to terminal acidities of pH 5 to 5.5. Sorbitol, mannitol, and arabinose were not fermented. Organisms with identical colonial morphology averaged 31.2% of the total cultivable flora from the tongues of rats, but they were not detected on the human tongues examined. These organisms were not identified further. Enterococci were readily demonstrable on the tongues of all rats studied, but none were detected on the human tongues examined. Several isolates proved to be strains of *S. faecalis* by using selected biochemical tests suggested by Isenberg et al. (13). This observation agrees with the recent report that strains of *S. faecalis* are not regularly found on human tongues and, if present, are low in number (12). The total numbers of bacteria recovered from the human tongues averaged $6.8 \times 10^6 \pm 2.9 \times 10^6$ per swab, whereas similar samples from the tongues of rats contained almost 100-fold fewer organisms; these averaged $9.3 \times 10^4 \pm 3.4 \times 10^4$ organisms per swab. Although two to four times more surface area of the human tongues was probably sampled by the swabbing technique used, this alone would not account for the large differences in the numbers of bacteria recovered between humans and rats. These data suggest that the microbial biomass present on the tongues of rats is considerably less than that on human tongues.

TABLE 1. *Natural distribution of some bacteria on the tongues of humans and rats*

Organism	Mean % of total cultivable flora	
	Humans (5)	Rats (5)
S. salivarius	22.6 ± 6.4[a]	<0.01 (not detected)
S. sanguis	2.8 ± 0.3	<0.1
S. faecalis	<0.0002 (not detected)	1.2 ± 0.6
SR diphtheroid	<0.1 (not detected)	31.2 ± 11.5

[a] Mean and standard error of mean.

Scanning electron microscopic observations of the dorsal surface of the tongues of rats. Direct scanning microscopic observations of the dorsal surface of the tongues of conventional rats confirmed the presence of relatively sparse bacterial populations. The tongue surface was heavily papillated (Fig. 1), and examination at higher magnification indicated that most of the papillae were completely free of bacterial cells; similar observations have been recently reported by others (3). Moreover, organisms were not observed to be entrapped between these papillae or within the folds of glandular structures present (Fig. 2). However, papillae present at the anterior tip of the tongue and those along its lateral edges contained indigenous bacteria. Coccal forms colonized the base of these papillae as discrete microcolonies (Fig. 3 and 4), but few bacterial cells were present on the tips of the papillae. The localized pattern of colonization observed suggests that bacteria colonize the tongues of rats in a highly specific and restricted manner.

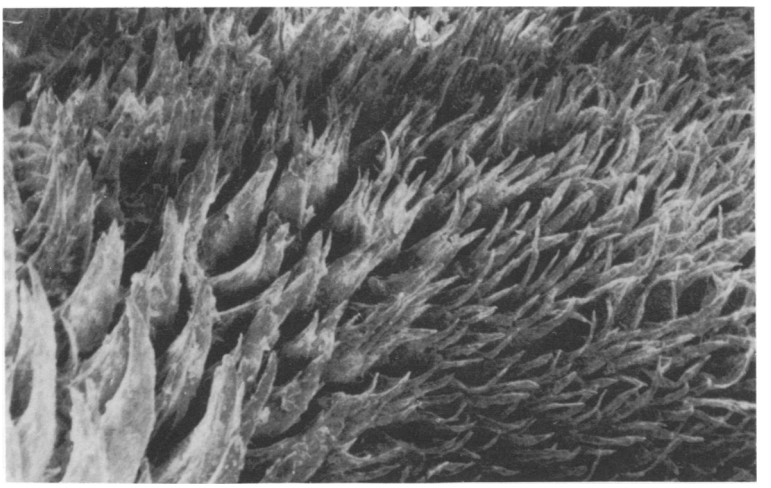

FIG. 1. *Higher magnification of Fig. 3 showing a microcolony of coccal forms present on the base of a papillus (×2,500).*

Adherence of streptomycin-resistant bacteria to the dorsal surface of human and rat tongues in vivo. The ability of bacteria isolated from humans and rats to sorb to the tongue dorsum of their respective hosts was studied by using mixtures of strains labeled by the induction of streptomycin resistance. Much higher proportions of *S. salivarius* strain CM6-R were recovered from the human tongues relative to *S. faecalis* strain E1-R and to the SR diphtheroid strain MS3-R (Table 2). However, when the identical mixtures were applied to the tongues of rats, higher proportions of *S. faecalis* strain E1-R and the SR diphtheroid were recovered. The adherence of strains CM6-R and E1-R to the tongues of conventional and germfree rats was similar. The adherence of *S. faecalis* strain 1RA-R, which had been isolated from humans, was similar to that of rodent strain E1-R. *S. sanguis* strain H7P-R, which was derived from humans, also attached in higher proportions to the human tongue dorsum than did the SR diphtheroid strain MS3-R derived from rats. It is apparent that the bacterial species studied exhibit remarkable specificities in the degree to which they attach to the tongues of humans and rats, and their adherence correlates with their natural tropisms within these respective hosts.

In vitro attachment of bacteria to human and rat buccal epithelial cells. The ability of two human pathogenic strains of *S. pyogenes* to attach to human and rat buccal epithelial cells was studied in an in vitro assay (Table 3). Both strains attached in higher numbers to human epithelial cells than to those obtained from rats; the differences were statistically significant ($P < 0.001$, Student's t test). In agreement with the observations made in vivo, *S. salivarius* strain CM6 also attached in higher numbers to human buccal epithelial cells than to those of rats, whereas the SR diphtheroid strain MS3 isolated from rats sorbed in greater numbers to rat buccal epithelial cells. These observations are consistent with those of a previous study in which we observed that human strains of *S. salivarius* and *S. sanguis* attached in higher numbers to human buccal epithelial cells than to those derived from germfree rats (10). Although the abilities of bacteria to attach to different host tissues were not specifically compared in that study, it was further noted that *Actinomyces naeslundii* strain I, a human oral isolate, attached to human buccal epithelial cells better than *Actinomyces viscosus* strain T6 isolated from rodents and a strain of *S. faecalis* (10).

Colonization of *S. salivarius* strain CM6 and *S. faecalis* strain 1RA-R on the tongues of gnotobiotic rats. In view of the sharp difference between strains of *S. salivarius* and *S. faecalis* to adhere to the tongue dorsum of conventional rats, it was of interest to compare the ability of these organisms to colonize the tongues of gnotobiotic rats lacking an indigenous flora that could affect their colonization. In the first experiment, somewhat higher proportions of *S. faecalis* strain 1RA-R were recovered 4 days after infection with a mixture of these organisms, but by 7 days *S. faecalis* accounted for almost 95% of the bacterial population (Table 4). Essentially similar data were obtained in the second experiment, with the exception that *S. faecalis* strongly dominated

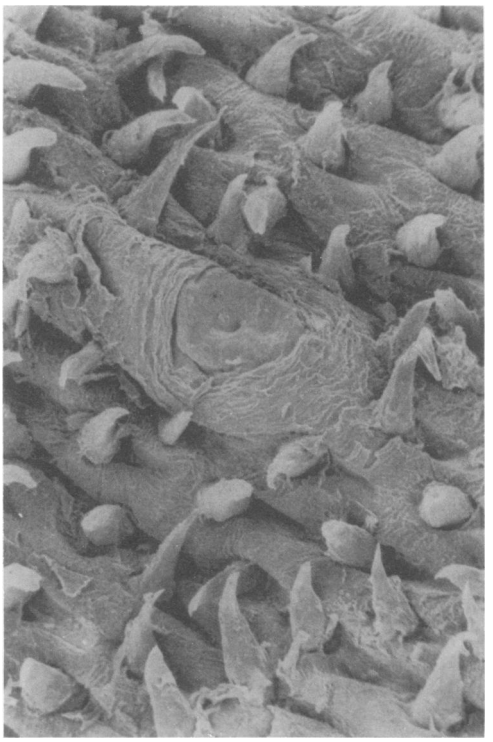

FIG. 2. *Scanning electron photomicrograph of an interior portion of the dorsal tongue surface of a conventional rat showing a glandular structure and isolated filiform papillae (×125). Bacterial cells were not observed on the papillae or within epithelial tissue folds when examined at higher magnification.*

over *S. salivarius* at both 4 and 7 days after initial infection. It is apparent that *S. faecalis* possesses an innately greater capacity for colonizing the tongues of rats than *S. salivarius* even in the absence of other potentially competing bacteria.

DISCUSSION

A variety of recent studies have shown that the tropisms which several bacterial species exhibit for colonizing specific sites within the human mouth are related to the selective abilities of these organisms to attach (7, 10, 11, 17, 32). Bacteria unable to attach to an oral surface evidently are washed away by the bathing secretions and cannot colonize. The present study has shown that strains of *S. faecalis* and a serum-requiring diphtheroid, which naturally colonize the tongue dorsum of rats, adhere far better to the tongues of rats than to those of humans. Conversely, strains of *S. salivarius* and *S. sanguis*, which are prominent on the human tongue, adhere better to this organ in their natural host. It is apparent that bacteria attach with a remarkable degree of specificity to the tissues of different mammalian hosts, and the correlations observed between the adherence and natural distribution of the bacteria studied strongly imply that adherence plays an important role in determining their host tropisms.

There are other data which support this view. Previous studies have shown that virulent strains of *S. pyogenes* attach well to human buccal or pharyngeal epithelial cells (7). In the present study, two such strains sorbed in higher numbers to human buccal epithelial cells than to those of rats. It is interesting to note that *S. pyogenes* may frequently be isolated from oral tissues of humans during the course of a throat infection, whereas rodents are only rarely infected by group A streptococci under natural conditions. Moreover, most strains of lactobacilli isolated from chickens have been reported to attach to chicken crop epithelial cells, whereas lactobacilli of human or rodent origin do not (9, 31). Conversely, a high percentage of *Lactobacillus* strains iso-

FIG. 3. *Scanning electron photomicrograph of the filiform papillae present along the lateral edges of the tongue dorsum of a conventional rat (×980). Bacteria colonized the basal two-thirds of such papillae as discrete microcolonies.*

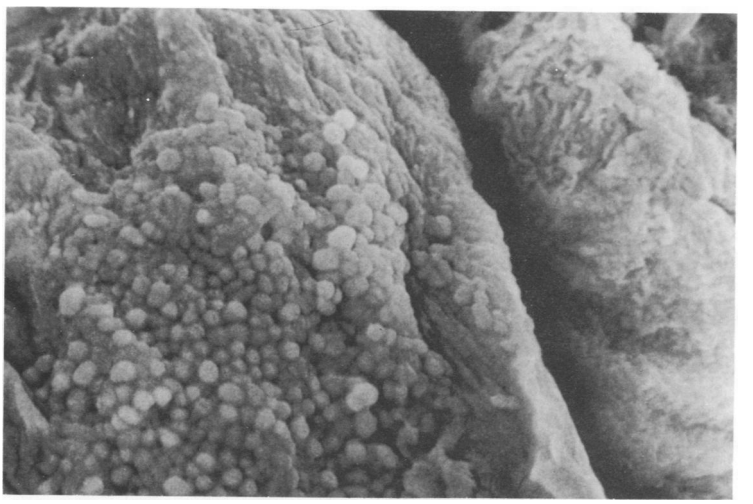

FIG. 4. *Scanning electron photomicrograph of the posterior tongue dorsum of a conventional rat showing its heavily papillated surface* (×75).

TABLE 2. *In vivo adherence of streptomycin-labeled streptococci to human and rat tongues*

Mixture	Source	Mean relative adherence		
		Human (5)	Conventional rats (5)	Germfree rats (5)
S. salivarius CM6-R	Human	94.1 ± 5.3[a]	4.8 ± 1.3	4.5 ± 2.3
S. faecalis E1-R	Rat	5.9 ± 5.3	95.2 ± 1.3	95.5 ± 2.3
S. salivarius CM6-R	Human	98.9 ± 0.6	19.6 ± 5.7	
S. faecalis 1Ra-R	Human	1.1 ± 0.6	80.4 ± 5.7	
S. salivarius CM6-R	Human	98.9 ± 0.7	27.9 ± 6.6	
SR diphtheroid MS3-R	Rat	1.1 ± 0.7	72.1 ± 6.6	
S. sanguis H7P-R	Human	98.0 ± 1.2		
SR diphtheroid MS3-R	Rat	2.0 ± 1.2		

[a] Mean and standard error of mean.

TABLE 3. *Bacterial adherence to human and rat buccal epithelial cells in vitro*

Organism	Mean no. of bacteria/cell	
	Human	Rat
S. pyogenes SB-1	205 ± 21[a]	112 ± 22[b]
S. pyogenes C203	154 ± 18	29 ± 7[b]
S. salivarius CM6	251 ± 13	61 ± 23[b]
SR diphtheroid MS3	12 ± 7.9	146 ± 27[b]

[a] Mean and standard error of mean.
[b] $P < 0.001$.

TABLE 4. *Colonization of S. salivarius CM6 and S. faecalis 1Ra-R on the tongues of gnotobiotic rats*

Expt no.	Days after infection	No. of rats	Mean % *S. salivarius*	Mean % *S. faecalis*
1	4	3	41.3 ± 23[a]	58 ± 23
	7	3	5.4 ± 1.8	94.6 ± 1.8
2	4	3	7.5 ± 3.3	92.5 ± 3.3
	7	3	5.7 ± 3.0	94.3 ± 3.0

[a] Mean and standard error of mean.

lated from rats attached to keratinized stomach epithelium of rats. However, strains of *S. faecalis* studied in the present investigation were found to attach better to the tongues of rats than to human tongues, irrespective of whether they were derived from humans or rodents. Enterococci are only found sporadically on the tongues of humans and, when present, their numbers are low (Table 1; 12); thus they cannot be considered indigenous to this site. Nevertheless, the similar adherence selectively exhibited by the human and rat strains studied

indicates that one cannot generalize and conclude that strains of a bacterial species isolated from a given host necessarily adhere better to all tissues of that host than to those of other mammals or fowl.

Differences in diet composition and the availability of nutrients have frequently been assumed to account for the tissue and host tropisms of some bacteria. However, there are few direct data supporting this possibility. For example, the growth requirements of bacteria indigenous to a tissue of one mammalian species are not recognized to be significantly different from those which colonize other hosts. Compared with environments such as the sea or soil, the mucous surfaces of humans and animals constitute a relatively rich nutrient milieu, and the diverse collections of indigenous bacteria colonizing these surfaces include organisms with simple nutritional demands as well as those which are highly fastidious (11). Thus nutritional parameters seem to exert only weak selective influences.

It has also been suggested that organisms which mimic the tissue components of a particular host may escape antigenic recognition and thus colonize that host (14). Evidence to support this possibility stems from the findings that many bacteria possess heterophile antigens that cross-react with human blood group components (30). Bacteria indigenous to a given mammalian species have also been suggested to be less immunogenic in their natural host than nonindigenous organisms, and this has been hypothesized to enable them to maintain high population levels (1, 2, 8). However, several arguments may be advanced which suggest that escaping antigenic recognition is not the sole factor accounting for the tissue and host tropisms of bacteria. Highly immunogenic pathogens may infect an appropriate host in high numbers, and in some instances their populations persist for long periods of time, i.e., during the carrier state. On the other hand, many pathogenic and benign organisms are unable to even initiate colonization of a particular host; therefore they have little opportunity to evoke an immune response, irrespective of their innate immunogenic properties. Moreover, such a hypothesis implies that most members of a given mammalian host population would have antibodies that prevent the colonization of many nonindigenous bacteria; yet normal animal serum, i.e., that of rabbits, rarely contains significant levels of antibodies to organisms that are not indigenous. On the contrary, in humans, detectable levels of antibodies are generally present in both serum (6, 21) and secretions (4, 15, 26) that are reactive with indigenous species. A developing body of literature suggests that bacterial populations are able to persist in a host by undergoing antigenic drift that enables them to evade the immune responses they evoke (5, 4, 23, 25).

The indigenous flora resident in a given mammalian species could elaborate growth-inhibitory substances that inhibit the colonization of nonindigenous organisms. Such antagonistic interactions specifically affecting growth may be important in some instances (19, 20). However, the bacterial density on the tongue dorsum of conventional rats was found to be low, and most organisms present were confined to the base of discrete papillae present at the tip or lateral edge of the tongue. The spatial separation of the microcolonies of indigenous bacteria present, and the lack of colonizing bacteria on most tongue papillae, would appear to minimize the possibility of growth-inhibiting substances accounting for the tropisms of the species studied in this site.

Preexisting oganisms have been reported to exert antagonistic influences that affect microbial colonization in the mouths of rodents (11, 16). For example, streptomycin-resistant strains of *S. faecalis* were not found to implant for long periods of time in the mouths of ex-germfree rats harboring an indigenous flora that included enterococci, though such strains persistantly colonized germfree animals (12). The basis of this antagonism could be due to competition for nutrients or to interference with the attachment of the introduced organisms. The latter might be accomplished by preexisting bacteria occupying and competing for available receptor sites required for attachment, or by enzymatically modifying exposed receptors. Data are available suggesting that such a mechanism may be involved in the suppression of *Candida albicans* by indigenous bacteria (16). However, the selectivity observed in the attachment of strains of *S. salivarius* and *S. faecalis* to the tongues of rats are not explainable on the basis of specific adherence-inhibiting effects of indigenous bacteria; these streptococci attached with similar selectivity to the tongues of germfree as well as conventional rats. Since the ability of streptococcal species to colonize the tongues of gnotobiotic rats lacking competing bacteria closely paralleled their experimentally observed adherence, it seems unlikely that their divergent abilities for colonizing this site could be due to antagonistic interactions.

Differences must exist between the surface components of tissue cells from various mammalian species, as well as between different bacteria, to account for the high degree of adherence

selectivity observed. It is reasonable to believe that the chances for perpetuation of a bacterial species would have been increased if the organism could have adapted to colonize many hosts over the course of evolution. The fact that this has not occurred with many pathogenic and indigenous bacteria suggests that a complex set of surface properties is required for adherence and colonization rather than a single component that would be readily altered by mutation. These host-parasite adherent interactions are reminiscent of those involved in recognition between various mammalian cells. In fact, blood group-reactive substances have been associated with the epithelial cell receptors involved in the attachment of some infectious agents, including oral streptococci (33). Since cell surface glycoproteins or glycolipids possessing blood group antigenicity differ in their distribution between animal species, they could account for the host and tissue specificities involved in the bacterial adherent interactions observed in the present investigation. It is also possible that components of a bacterium that are similar to those of a host play a role in host-parasite adherent interactions in a manner similar to the way surface components of mammalian cells enable them to recognize and adhere to each other.

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