Increased susceptibility to gingival colonization by specific HACEK microbes in children with congenital heart disease

Robert Steelman* / Stanley Einzig** / Arpy Balian*** / John Thomas**** / David Rosen***** / Robert Gustafson****** / Lori Gochenour*******

It is well established that infective endocarditis (IE) involving the HACEK (Hemophilus, Actinobacillus, Cardiobacter, Eikenella, Kingella) group of microbes occurs in patients with congenital heart defects (CHD) and in those with prosthetic grafts. Dental caries and gingival disease have been presumed to be the focus of microbial shedding. The purpose of this study was to determine if children with CHD had a more severe gingival inflammatory condition and harbored the HACEK group of microbes to a greater extent than normal children. Two groups of 12 age and sex matched children were selected for this study. The experimental group consisted of twelve children with CHD, 1-1/2 to 8 years of age. The control group consisted of 12 healthy children 2 to 8 years of age. Each child had a gingival index score recorded as described by Massler. Subgingival cultures were obtained. Gingival samples were cultured for HACEK microbes and total Streptococcus (spp) using standard techniques. Fisher's exact test was performed with significance defined at P<0.05. Children with CHD had more severe gingival inflammatory index than the control group (P<0.05). 8/12 CHD patient had Actinobacillus actinomycetemcomitans (A.a.) as compared with 2/12 controls (P<0.05). Furthermore, all cyanotic CHD patients (4/4) had A.a. whereas, only 2/12 controls did (P<0.05). 4/12 CHD patients harbored Eikenella corrodens (E.c.) compared to 1/12 controls (N.S.). There was no significant difference in colonization with E.c. or A.a. between cyanotic and acyanotic patients. No significant difference in total Streptococcus (spp) was found between the two groups. This study suggests that children with CHD have a more severe gingival inflammatory index and are colonized with specific HACEK microbes more so than normal children.

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* Robert Steelman, MD, DMD, Department of Pediatrics, Division of Pediatric Cardiology, WVU School of Medicine Morgantown, WV 26506.
** Stanley Einzig, MD, PhD, Department of Pediatrics, Division of Pediatric Cardiology, WVU School of Medicine Morgantown, WV 26506.
*** Arpy Balian, MD, Department of Pediatrics, Division of Pediatric Cardiology, WVU School of Medicine Morgantown, WV 26506.
**** John Thomas, PhD, Departments of Pathology and Periodontics, WVU School of Medicine, Morgantown, WV 26506.
***** David Rosen, MD, Departments of Anesthesiology and Pediatrics, Division of Cardiothoracic Anesthesia, WVU School of Medicine, Morgantown, WV 26506.
****** Robert Gustafson, MD, Department of Surgery and Pediatrics, Division of Cardiothoracic Surgery, WVU School of Medicine, Morgantown, WV 26506.
******* Gochenour, RDH, MS, Department of Dental Hygiene, WVU School of Dentistry, Morgantown, WV 26506.

FAX: 304-293-1409
Phone: 304-293-7036
EMAIL: Rsteehnan@wvu.edu

Send all correspondence to Robert Steelman, MD, DMD, Department of Pediatrics, Division of Cardiology, West Virginia University, Box 9214 HSCN, Morgantown, WV 26506.

INTRODUCTION

Children with congenital heart defects (CHD) have been noted to have a more severe gingivitis and increased plaque accumulation than children without cardiac defects.[13] Reasons for this observation are not entirely clear, but include a low priority for dental care by care givers of chronically ill children.[3,4] The consequences include not only gingival and dental disease, but also a risk for infective endocarditis (IE).[1,3]

The American Heart Association periodically publishes guidelines for the prevention of IE.[5] These guidelines, especially concerning oral procedures, are directed towards viridans streptococci and Staphylococci (spp), which account for the majority of all cases of IE.[6-8] Although very rare, the HACEK group of microbes (*Haemophilus parainfluenza, Haemophilus aphrophilus, Actinobacillus actinomycecomitans, Cardiobacterium nominus, Eikenella corrodens,* and *Kingella kingae*) have been noted to be associated with bacterial endocarditis in patients with congenital heart defects.[9-18] No study to date has specifically studied the

gingival sulcus of children with congenital heart disease to determine if the HACEK group of microbes is more abundant than in a normal group of children.

The purpose of this study is to determine if children with CHD have a more severe gingival inflammatory condition and harbor specific HACEK microbes to a greater extent than healthy children.

MATERIALS AND METHODS

Twelve children (7 males, 5 females) with CHD (4 cyanotic, 8 acyanotic) ages 1-1/2 to 8 years of age (ave=3.4 years) were age and sex matched with 12 healthy children 2 to 8 years of age (ave=3.6 years). All children selected for this study were enrolled in the general pediatric and cardiology specialty clinics. No child had taken antibiotics within two months prior to participating in the study. No child with CHD was immunocompromised or had congestive heart failure. Peripheral oxygen saturation in the cyanotic children ranged from 75-85%. A gingival inflammatory index was determined for each child as described by Massler.[20]

A #45 sterile paper point was inserted into the gingival sulcus in two separate areas with the greatest degree of gingival inflammation. Microbial cultures were examined for total Streptococcus (spp) and the HACEK group using standard published criteria[21]. All children with CHD had the gingival index recorded and subgingival cultures taken in the operating room prior to corrective surgery (acyanotic patients) or the Fontan procedure (cyanotic patients) under antibiotic coverage just prior to gingival sampling. Normal children were referred to the outpatient dental clinic for recording the gingival index and subgingival culturing. Both the gingival index and subgingival cultures were performed by the same Registered Dental Hygienist for all patients. IRB approval of the protocol was obtained as well as informed consent/assent prior to initiating the study. Fisher's exact test was used to determine significance with respect to microbial colonization and gingival index between and within groups. Significance was defined at $P<0.05$.

RESULTS

Children with CHD had a significantly higher gingival inflammatory index (ave=4.0) than healthy children (ave 1.5) P0.05. Figure 1 shows that children with CHD had either a moderate or severe gingival inflammatory index as compared to the healthy control group, who had a predominantly normal periodontium.

Table 1 shows the quantitative and qualitative microbial flora, expressed as colony forming units, found in both groups of children. Cardiac lesions and gingival index are also included for each subject. Eight of twelve children with CHD had *Actinobacillus actinomycetecomitans* (A.a.) as opposed to 2/12 controls (P0.05). All children with cyanotic CHD (4/4) harbored A.a., whereas, 2/12 healthy controls did (P0.05). There was no significant difference in A.a. colonization between cyanotic and acyanotic children. With respect to Eikenella (E.c.), 4/12 children with CHD harbored the organism compared with 1/12 healthy controls (P=0.06). There was no significant difference in colonization with E.c. between cyanotic and acyanotic patients. No significant difference in total Streptococci spp was found between the cardiac and control groups.

Figures 2 and 3 show gingival index versus A.a. an E.c. colony forming units for cardiac and control groups respectively. The number of patients harboring A.a. and E.c. increased as the gingival index rose (more severe inflammation). A gingival index 3 in the cardiac group was associated with 58% (7/12) of patients colonized with either A.a, E.c. or both, whereas, only 17% (2/12) were colonzied with A.a. or E.c. at a gingival index <3. Healthy control patients harbored A.a. or E.c. only with a gingival index <2. Even at a lower gingival index, the absolute colony forming unit number was greater in children with CHD.

DISCUSSION

It is well established that children with CHD are at increased risk for IE, especially if prosthetic materials are placed during surgical procedures.[6,13,14,17-19] Although rarely encountered, children with congenital heart

Table 1. Qualitative & Quantitative Analysis of Target Bacteria and Gingival Inflammation.

Subjects*	Cardiac Lesion ‡	E.c. (CFU)	Aa (CFU)	Total Step.spp (CFU)	Gingival Index
C1-A	ASD	$13x10^3$	0	$72x10^3$	3
C-2A	VSD	0	$5.2x10^3$	$240x10^3$	6
C3-Cy	TA	$2.4x10^3$	$2.1x10^3$	$1000x10^3$	6
C4-A	VSD	0	0	0	2
C5-A	PDA	$2.6x10^3$	$13x10^3$	$2000x10^3$	6
C6-A	ASD	0	0	$72x10^3$	3
C7-A	ASD	0	0	$680x10^3$	2
C8-A	PDA	0	$10x10^3$	$58x10^3$	2
C9-A	PDA	0	$5.3x10^3$	$1320x10^3$	2
C10-Cy	HLHS	$3.2x10^3$	$2.5x10^3$	$68x10^3$	6
C11-Cy	TA	0	$11x10^3$	$160x10^3$	4
C12-Cy	TA	0	$3.2x10^3$	$2.8x10^3$	6
H1		0	0	$110x10^3$	1
H2		0	0	$510x10^3$	1
H3		0	0	$120x10^3$	1
H4		$3.9x10^3$	0	$12x10^3$	1
H5		0	$4.8x10^3$	$5.3x10^3$	1
H6		0	$1.6x10^3$	$56x10^3$	1
H7		0	0	0	2
H8		0	0	$48x10^3$	4
H9		0	0	$640x10^3$	1
H10		0	0	$410x10^3$	1
H11		0	0	0	2
H12		0	0	$9.6x10^3$	2

* C=Cardiac
Cy=Cyanotic
A=Acyanotic
H=Healthy

‡ ASD=Atrial Septal Defect
VSD=Ventricular Septal Defect
PDA=Patent Ductus Arteriosus
TA=Tricuspid Atresia
HLHS=Hypoplastic Left Heart Syndrome

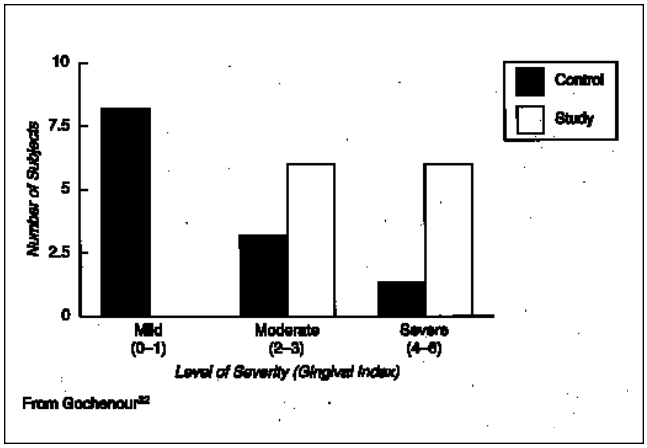

Figure 1. Gingival index.

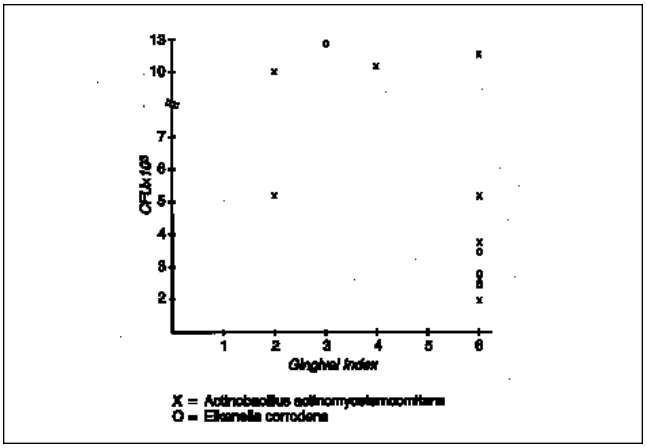

Figure 2. Gingival index vs. CFU in cardiac group.

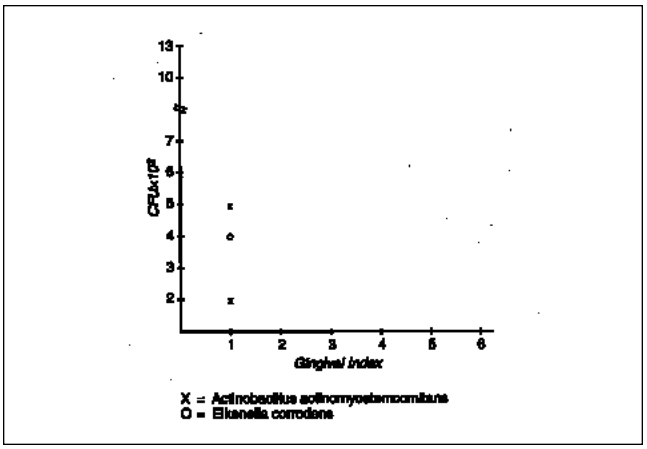

Figure 3. Gingival index vs. CFU in control group.

defects have been known to have acquired infective endocarditis secondary to the HACEK group of microbes.[9,12,16,18,19] It has been postulated that the causative organism resides within the confines of the oral cavity.[7,13,17,18,19] *Actinobacillus actinomycetecomitans* has specifically been identified as the causative organism for IE in children with prosthetic heart valves and shunts where the dentition and periodontal disease were specifically implicated.[18,19]

There is evidence which supports the increased severity of gingival disease in children with CHD. Gould and Picton[2] noted a greater degree of gingival inflammation in cyanotic children with CHD as compared to a control group, which included some acyanotic children with CHD. It was believed that a low oxygen tension and higher hemoglobin level in the cyanotic group contributed to the gingival condition.

Hallet *et al*.[1] and Franco *et al*.[3] found that children with CHD had a higher mean plaque index as compared with healthy controls, and that gingival inflammation was more severe. The high bacteria load associated with dental plaque and gingival disease could place these children at risk for IE. The need for optimal dental care was stressed.

This study has shown that children with CHD harbor a gingival microflora, which differs from that of children without cardiac defects. Seventy-five percent of children with CHD were colonzied with A.a. and 33% with E.c. Interestingly, all of the cyanotic patients harbored A.a. In conjunction with these observations, children with CHD had a moderate to severe gingival index. The reverse was true of the healthy controls. Several studies have suggested that the lack of regular preventive dental care may play a role in increased gingival disease.[1-4,13]

This study appears to corroborate previous observations concerning gingival disease in children with CHD. Although our experimental/control population is small, we have essentially verified the observations of previous studies, which have shown that children with CHD have a more severe gingival condition than healthy controls.[13] We have taken these observations one step further and have shown that a different microflora exists in these children and appears to be independent of cyanosis (oxygen saturation) or type of cardiac defect. Even though children with CHD were not matched with normal children with comparable gingival inflammatory indices, we feel that just the presence of these specific HACEK microbes in children with CHD may jeopardize their health.

Further studies, which involve a greater number of children with CHD, are needed to verify our findings. However, we feel that in light of our finding of a significant increase of specific HACEK microbes in children with CHD along with moderate to severe gingival inflammation, these children should have their oral health care optimized.

CONCLUSION

We have shown that children with CHD harbor a different microflora than a normal group of children. The significance of finding certain HACEK microbes in children with CHD is unknown, however cases of IE

have been known to occur in children with CHD secondary to dental or periodontal disease. Clearly more studies are needed to verify the observations presented in the present study.

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