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Research Article

Infections in Injection Drug Users: The Significance of Oral Bacteria and a Comparison with Bacteria Originating from Skin and Environmental Sources

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ABSTRACT

Infections are common in IV drug users (IVDU). Heroin was by far the most common drug abused in our series of 80 patients. The spectrum of infections in our patients with ages ranging from 20-63, varied from mild skin infections to life threatening and fatal conditions such as septic shock, necrotizing fasciitis, spinal cord infarction and endocarditis with cerebral septic emboli. Our studies showed that bacterial infections in IV drug users originate from three different sources: 1. Skin (contaminated hands) 2. Oral microbiota 3. Environmental sources including water, soil and plants. The most common skin bacteria isolated were methicillin susceptible and methicillin resistant *Staphylococcus aureus* (MSSA and MRSA). In our study *Streptococcus anginosus* group was the most common oral bacteria in IVDU with *Streptococcus intermedius* predominating, followed by group A *Streptococcus*, *Prevotella* spp., *Eikenella corrodens*, *Haemophilus parainfluenzae* and group C *Streptococcus*. A variety of environmental bacteria were isolated, but the total number of patients in this group was smaller. Bacteria originating from water, soil or plants present were: *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, *Delftia acidovorans*, *Comamonas* sp., *Chryseobacterium* spp., *Klebsiella* spp., *Serratia marcescens*, *Burkholderia cepacia*, *Pseudomonas fluorescens* and *Acinetobacter*. Twenty four out of 48 (50%) *Staphylococcus aureus* infected patients were bacteremic, followed by 6/10 (60%) group A *Streptococcus* infected cases. Life threatening infections were more common with those infected with *Staphylococcus aureus* or *Pseudomonas aeruginosa*. Few had *Candida* sp., likely of oral origin. Hepatitis C was less common (2/37) 5.4% in the group with oral bacteria and more frequent in MSSA/MRSA patients (13/47) 27.7%. There was 1 coinfection with human immunodeficiency virus each in oral and skin bacteria associated groups. The bacteria isolated provided a clue to the source of infections and habits of the IV drug users.

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Introduction

Injection drug use is associated with multiple physical, medical, social, psychological, occupational and financial problems. Infections reported include Human immunodeficiency virus, hepatitis C, and a variety of bacterial infections such as cellulitis and abscesses in different parts of the body, necrotizing fasciitis, osteomyelitis, septic arthritis, spinal epidural abscess, endocarditis, septic emboli and even *Mycobacterium tuberculosis* vertebral osteomyelitis, anthrax and wound botulism associated with "skin popping" [1-14]. Here we present an analysis of infections associated with IVDU encountered in our health network. The bacterial origin of infections in our study could be traced to 3 main

sources: 1. Skin bacteria 2. Oral bacteria 3. Environmental bacteria associated with water, soil and plants. The bacteria isolated gave a clue as to the habits of the drug users. There have been multiple reports of oral bacteria associated with infections of drug users, mostly associated with "needle licking" [5]. About one third of intravenous drug users have been reported to lick needles [15].

In our study 43 out of 80 (53.8%) intravenous drug users had infections with oral bacteria. The significance of the "*Streptococcus milleri*" group found in the mouth in soft tissue infections of intravenous drug users has been documented in the past [2]. Since then, not much has been reported on the role of these bacteria, now referred to as the "*Streptococcus*

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anginosus” group, comprising of *Streptococcus anginosus*, *Streptococcus intermedius* and *Streptococcus constellatus*. In our study of 1321 Streptococcal isolates, 336 (25.4%) belonged to the *Streptococcus anginosus* group with 21/336 (6.3%) in IVDU. *Streptococcus intermedius* (16/21) was the most common *Streptococcus* in soft tissue infections of intravenous drug users. Group A *Streptococcus* (GAS) was next more frequent (11 patients) with most oral bacteria associated bacteremia (6/8) 75% caused by this organism. We present a complete analysis of all oral isolates from a total of 80 IVDU and a comparison with infections from non-oral sources.

Methods

We evaluated 80 IVDU patients admitted to our network of 10 hospitals, 9 located in Eastern Pennsylvania and one in adjacent Warren County New Jersey, for a period of 3 years ending in October 2019. The ages of patients ranged from 20 to 63. There were 47 males (58.8%) and 33 females (41.2%). MALDI-TOF MS (matrix assisted laser desorption ionization- time of flight mass spectrometry) was used by the laboratory to identify the isolates. The charts were manually studied for the clinical presentation, sites of infections, types of infections, organisms isolated and mortality.

Results

Forty three out of 80 (53.8%) IVDU patients had bacterial isolates of oral origin (Table 1). Forty-seven (58.8%) had skin bacteria from contaminated hands (Table 2) and 10 (12.5%) had bacteria from environmental sources (Table 3). Some were infected with bacteria from more than one source. Heroin was the most common drug abused. In those with oral infections 32 were heroin users, with 7 cocaine users, 4 methamphetamine users and 2 unspecified. In those with skin bacteria isolated, there were 30 heroin users, 10 cocaine users, 14 methamphetamine users and 2 were not recorded. Some abused a combination. In those with infections from water, soil or plant bacteria there were 9 heroin users, and 4 each of cocaine and methamphetamine users.

Twenty-five (31.3%) of those with bacteria of oral origin had upper extremity infections (cellulitis, abscess or thrombophlebitis). Only 3 had lower extremity infections. Few in this group had serious infections. Only serious infections in the oral group were associated with group A *Streptococcus*, 6/11 (54.5%) with bacteremia and one case of pneumonia requiring intubation due to a drug overdose. There were 24 polymicrobial infections, in patients with infections due to oral bacteria (oral bacteria only 12, oral and skin flora 10, oral and environmental flora 2). Twenty-one in the oral group were *Streptococcus anginosus* group isolates, 16 *Streptococcus intermedius*, 3 *Streptococcus anginosus* and 2 *Streptococcus constellatus*. Only 2 were bacteremic, one each of *Streptococcus constellatus* and *Streptococcus constellatus*. There were 11 patients with group A *Streptococcus*. Six out of 11 patients with group A *Streptococcus* were bacteremic. *Prevotella* spp. were the next most prevalent (6): *P. oralis* 2, *P. denticola* 1, *P. buccae* 1, *P. melaninogenica* 1 and *Prevotella* sp. 1). Other isolates were: *Eikenella corrodens* 5, *Haemophilus parainfluenzae* 3, group C *Streptococcus* 2, group F *Streptococcus* 1, *S dysgalactiae* 1. Majority of soft tissue infections of oral origin were in the extremities, mostly upper extremity (34/43). The

most common diagnosis was forearm abscess 22/34. Of the 4/80 deaths, only 2 had oral bacteria. Both patients who died had positive blood cultures for GAS.

Table 1: Mouth organisms isolated in infections of injection drug users.

Group	Organism	Species	Number of isolates
Oral bacteria	<i>Streptococcus anginosus</i> group (21)	<i>Streptococcus intermedius</i>	16
		<i>S.anginosus</i>	3
		<i>S. constellatus</i>	2
	<i>Streptococcus</i> sp.	Group A <i>Streptococcus</i>	11
		Group C <i>Streptococcus</i>	2
		Group F <i>Streptococcus</i>	1
		<i>S dysgalactiae</i>	1
	<i>Prevotella</i>	<i>Prevotella oralis</i>	2
		<i>P. denticola</i>	1
		<i>P. buccae</i>	1
		<i>P. melaninogenica</i>	1
		<i>Prevotella</i> sp.	1
	<i>Eikenella</i>	<i>Eikenella corrodens</i>	5
	<i>Haemophilus</i>	<i>Haemophilus parainfluenzae</i>	3
Oral fungi	<i>Candida</i> (could also be a skin contaminant)	<i>Candida albicans</i>	3
		<i>C. glabrata</i>	1
		<i>C. parapsilosis</i>	1
		<i>C. dublinensis</i>	1

Thirty two out of 80 (40%) IVDU infections were associated with bacteremia. Only 10 (12.5%) were associated with oral bacteria: group A *Streptococcus* 7, *H. parainfluenzae* 1, *S. intermedius* 1, *S. constellatus* 1. Serious infections were uncommon in IVDU with infections due to oral bacteria. One patient had a life-threatening *S. aureus* and *H. parainfluenzae* aortic and tricuspid polymicrobial endocarditis and one group A *Streptococcus* infected patient with pneumonia and a drug overdose required intubation.

Serious infections were common in those infected with skin bacteria. The majority in this group were infected with *Staphylococcus aureus* (MSSA/MRSA), with bacteremia in (24/48) 50%, Spinal epidural abscess or vertebral osteomyelitis (10/48) 21%, 9 (18.8%) with endocarditis (tricuspid valve 4, tricuspid and aortic 1, tricuspid and pulmonary 1, mitral 1, aortic and mitral 1). Septic arthritis 5 (10.4%) with one each of shoulder, sacro-iliac, sternoclavicular, knee and hip joint infections. Polymicrobial infections (15/48) 31.3% in this group

were: skin and oral flora 10, skin and environmental flora 3, skin only 2. There was one isolate each of group B and group G *Streptococcus* associated with mixed infections in this group.

Table 2: Infections with bacteria likely originated from dirty hands of 47 injection drug users.

<i>Staphylococcus aureus</i> (MSSA > MRSA)	47
<i>Staphylococcus hemolyticus</i>	1
Coagulase negative <i>Staphylococcus</i>	1
Group G <i>Streptococcus</i>	1
<i>Escherichia coli</i>	2
<i>Enterococcus faecalis</i>	1
<i>Enterobacter cloacae</i>	1
<i>Clostridium</i> sp.	1
<i>Lactobacillus</i>	1

Environmental bacteria found in our study were *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, *Delftia acidovorans*, *Commamonas* sp., *Chryseobacterium* spp., *Klebsiella* spp., *Serratia marcescens*, *Burkholderia cepacia*, *Pseudomonas fluorescens* and *Acinetobacter*. Ten out of 80 (12.5%) IVDU bacterial isolates were of environmental origin. All were polymicrobial infections with skin flora except one patient with a monomicrobial *Stenotrophomonas maltophilia* positive blood culture. Serious infections in this group were one each of *Pseudomonas aeruginosa* endocarditis requiring replacement of tricuspid and aortic valves and a case of vertebral osteomyelitis.

Table 3: Environmental bacteria isolated from infections of injection drug users.

Organism	Number of isolates
<i>Pseudomonas aeruginosa</i>	3
<i>Pseudomonas fluorescens</i>	1
<i>Stenotrophomonas maltophilia</i>	3
<i>Klebsiella pneumoniae</i>	2
<i>Klebsiella oxytoca</i>	1
<i>Klebsiella variicola</i>	1
<i>Chryseobacterium indologenes</i>	1
<i>Chryseobacterium</i> sp.	1
<i>Delftia acidovorans</i>	1
<i>Commamonas</i> sp.	1
<i>Burkholderia cepacia</i>	1
<i>Citrobacter freundii</i>	1
<i>Acinetobacter</i> sp.	1

Five out of 43 (11.6 %) in the “oral” and 10/37 (27%) in the “non-oral” bacterial infection groups were hepatitis C positive. One in each group was HIV positive. There were 3 deaths 1. MSSA bacteremia, lower extremity cellulitis, saphenous vein thrombophlebitis, methamphetamine overdose and cardiac arrest 2. Hepatitis C with liver cancer and MSSA spontaneous bacterial peritonitis (history of IVDU) 3.

Sepsis with group A *Streptococcus* and MRSA, right arm phlebitis and hydronephrosis (methamphetamine and cocaine user).

Discussion

Drug abuse is a serious problem in the United States. Death rates have been trending upwards with 70,237 Americans dying from overdoses of illicit and prescription drugs in 2017 according to National Institute of drug abuse statistics [16]. In additions to overdose deaths there is considerable morbidity and mortality due to infection. Infections vary from mild skin infections to life threatening and fatal conditions. Injection drug use is associated with human immunodeficiency virus infection, hepatitis C associated with needle sharing and bacterial infections due to unclean injection habits and bacteria found in material injected or liquids used to dissolve the drugs. Recurrent infections are common. Present study highlights the infections caused by oral bacteria and compares them with infections due to skin and environmental flora. Most life-threatening infections were due to *Staphylococcus aureus* from contaminated skin (Table 5). Tap water and lemon juice used to dissolve drugs have been reported to cause disseminated candidiasis and *Pseudomonas* endocarditis respectively [11, 17, 18]. Human immunodeficiency virus and hepatitis C are transmitted by needle sharing. Hepatitis C was detected in 50% of injecting drug users in a clinic in Cyprus [19]. Bacteria of oral origin, group A *Streptococcus*, *Actinomyces odontolyticus*, *Fusobacterium nucleatum*, *Prevotella melaninogenica*, *peptostreptococcus micros*, *Veilonella* sp., “*Streptococcus milleri* group”, *Fusobacterium necrophorum*, *Prevotella denticola*, *Eikenella corrodens*, *Prevotella buccae*, and *Candida* spp. have been reported in IVDU. Infections associated with oral bacteria usually result from needle licking [3, 20-25]. Wound licking was reported in one study [23].

In our study most common oral bacteria were the *Streptococcus anginosus* group with *Streptococcus intermedius* predominating (Tables 1 & 4) followed by Group A *Streptococcus*, *Prevotella* spp., *Eikenella corrodens* and *Haemophilus parainfluenzae*. Oral bacteria other than Group A *Streptococcus* were usually associated with localized infections. Group A *Streptococcus* was often invasive, responsible for most blood stream infections in this group. Overall most life-threatening infections (Table 5) were associated with *Staphylococcus aureus* (from contaminated hands), *Pseudomonas aeruginosa* (plant /water) and group A *Streptococcus* (oral). Soil and plant associated bacteria except *Pseudomonas aeruginosa* did not appear to be invasive in our study. *Stenotrophomonas maltophilia* a bacterium associated with plant rhizomes, soil and water was found in 3 of our patients. However, there were no invasive infections.

Multiple unsafe practices associated with infection in IVDU include needle sharing, needle licking, reuse of needles, infrequent skin cleansing, wound licking and non-sterile liquids used in dissolving drugs. Some of the reasons reported for needle licking include ritualistic practices, cleaning the needle, enjoying the taste of the drug, checking the quality of the drug and checking that the needle was in a usable condition [15]. Ideally all drug users should be detoxified and stop drug use. Persistent drug users must use clean needles, avoid licking or touching the needle, clean the skin before injection and sterile solvents must be used to dissolve drugs.

Table 4: *Streptococcus intermedius* associated infections in IVDU.

Sex	Age	Source of culture	Organism/organisms	Site of infection	Drug use
M	60	Blood	<i>Streptococcus intermedius</i>	Right upper extremity thrombophlebitis	Heroin
F	35	Abscess	<i>Streptococcus intermedius</i>	Left hand	Heroin, barbiturate
F	46	Abscess	<i>Streptococcus intermedius</i> , <i>Serratia</i> , MRSA	Left forearm	Heroin
F	30	Abscess	<i>Streptococcus intermedius</i>	Left forearm	Heroin
M	34	Abscess	<i>Streptococcus intermedius</i>	Left arm	Opiate, methamphetamine, THC
M	51	Abscess	<i>Streptococcus intermedius</i>	Right forearm	? Heroin
F	29	Abscess	<i>Streptococcus intermedius</i> , <i>Haemophilus parainfluenzae</i>	Left forearm	Methamphetamine
M	36	Abscess	<i>Streptococcus intermedius</i>	Left forearm	Heroin
F	40	Abscess	<i>Streptococcus intermedius</i>	Right calf	Heroin, cocaine, benzodiazepine
M	28	Abscess	<i>Streptococcus intermedius</i>	Left forearm	Opiate, THC
M	38	Abscess	<i>Streptococcus intermedius</i>	Right ankle, Hepatitis C+	Heroin
M	20	Abscess	<i>Streptococcus intermedius</i>	Left upper extremity abscess	Opiate, methamphetamine, THC
M	45	Abscess	<i>Streptococcus intermedius</i>	Left biceps abscess	Opiate
M	58	Abscess	<i>Streptococcus intermedius</i> , <i>Prevotella</i> sp., <i>Eikenella corrodens</i>	Left forearm abscess, HIV+	Heroin, THC

MRSA = methicillin resistant *Staphylococcus aureus*, THC = Tetra hydro cannabinol

Table 5: Life threatening infections in 80 injection drug users.

Staphylococcal Bacteremia and sepsis	24
Endocarditis	9
Vertebral osteomyelitis/ spinal epidural abscess	8
Septic arthritis	7
Polymicrobial bacteremia and sepsis	2
<i>Streptococcus intermedius</i> bacteremia and sepsis	1
<i>Streptococcus constellatus</i> bacteremia and sepsis	1
Spinal cord infarction	1
Pneumonia (one on ventilator)	2
Spontaneous bacterial peritonitis	1

Conclusion

Oral bacteria were common in injection drug users. Most of these infections were polymicrobial. *Streptococcus anginosus* group were the most frequent isolates in soft tissue infections, caused by oral bacteria with a predominance of *Streptococcus intermedius*. Group A *Streptococcus* was responsible for most cases of bacteremia in this group. Oral bacteria were associated with far less life-threatening infections than “non-oral bacteria”. Skin bacteria were mostly MSSA OR MRSA. A high percentage of Infections in this group were life threatening. There were more hepatitis C associated with “non-oral”

bacterial IVDU, which could be a coincidence. Whether “needle licking” has a protective effect on transmission of hepatitis C is not known. A larger study will be required to determine the significance of this finding.

Competing Interest

None.

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