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Systematic Search for Present and Potential Portals of Entry for Infective Endocarditis

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ABSTRACT

BACKGROUND Looking for and treating the portal of entry (POE) of infective endocarditis (IE) is important, but published research on this topic is nonexistent.

OBJECTIVES The goal of this study was to systematically search for the POEs of present and potentially new episodes of IEs.

METHODS Patients were systematically seen by a stomatologist, an ear, nose, and throat specialist, and a urologist; women were systematically seen by a gynecologist; patients were seen by a dermatologist when there were cutaneous and/or mucous lesions. Colonoscopy and gastroscopy were performed if the microorganism came from the gastrointestinal tract in patients ≥50 years of age and in those with familial histories of colonic polyposis. Treatment of the POE was systematically considered.

RESULTS The POEs of the present IE episodes were identified in 74% of the 318 included patients. The most frequent POE was cutaneous (40% of identified POEs). It was mainly (62% of cutaneous POEs) associated with health care and with intravenous drug use. The second most frequent POE was oral or dental (29%). A dental infectious focus was more often involved (59% of oral or dental POEs) than a dental procedure (12%). POEs were gastrointestinal in 23% of patients. Colonic polyps were found in one-half of the patients and colorectal adenocarcinomas in 14%. Performance was good regarding the search for an oral or dental or a colonic potential POE, which were found in 53% and 40% of patients, respectively.

CONCLUSIONS Our search for the POEs of present IEs was often successful, as was searching for an oral or dental or a gastrointestinal POE of a new IE episode. We advise the systematic performance of stomatologic examinations in patients with IE and performance of colonoscopy in patients ≥50 years of age or at high risk for colorectal cancer. (J Am Coll Cardiol 2016;67:151–8) © 2016 by the American College of Cardiology Foundation. Published by Elsevier. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Infective endocarditis (IE) is a severe disease, with an in-hospital mortality rate of about 20% (1). Five percent to 10% of patients will have additional episodes of IE (2). Thus, looking for and treating the portal of entry (POE) of IE is particularly important. The POE of the present episode must be identified in order to treat it. The potential POE of a new episode must be searched for in order to eradicate it and thus lower the risk for a new IE episode. Yet published research on this topic is nonexistent. The search for and treatment of the POE are not even mentioned in the most recent guidelines on IE (3,4). We thus undertook a study of the performance of a systematic search for the POE of the present episode of IE and of a potential new episode of IE.

METHODS

Since January 2005, we have been prospectively enrolling all patients hospitalized at our tertiary

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ABBREVIATIONS AND ACRONYMS

ENT = ear, nose, and throat

IE = infective endocarditis

POE = portal of entry

hospital for definite IE according to the Duke-Li criteria (5). Since then, we have been systematically looking for the POE of the present IE episode and for the potential POE of a new IE episode (e.g., a patient's

SEE PAGE 159

present IE is due to *Streptococcus gallolyticus*, the POE of the present IE episode is a colorectal adenocarcinoma, systematic stomatologic examination identifies several dental infectious foci, which are considered potential POEs for a new IE episode). Patients were informed of the study but did not have to provide individual consent, in accordance with French ethics laws.

Patients were systematically seen by a stomatologist (who performed an orthopantomogram), an ear, nose, and throat (ENT) specialist, and a urologist; women were systematically seen by a gynecologist. When there were cutaneous or periorificial mucous lesions on the initial examination, patients were seen by a dermatologist. Cerebral and thoracoabdominopelvic scans were systematically performed. Colonoscopy and gastroscopy were performed if the microorganism came from the gastrointestinal tract, in patients ≥50 years of age, and in those with familial histories of colonic polyposis. Because our center is a tertiary center with cardiac surgery facilities, most patients who are hospitalized for IE at our hospital are transferred from other hospitals. Either the whole antibiotic course and all investigations for the search for the POE were performed during the patient's stay in our hospital, or the patient was transferred to the hospital of origin before the end of the antibiotic course, and we requested that these investigations be performed there.

TABLE 1 Habitat and Potential Portals of Entry of the Causative Microorganisms of Infective Endocarditis*

Microorganisms	Habitat	Portals of Entry
Streptococci		
Oral streptococci		
Group *mitis/salivarius* (e.g., *S. sanguis*, *sanguinis*, *parasanguinis*, *gordonii*, *mitis*, *oralis*, *mutans*, *salivarius*)	Dental plaque, tongue, oral mucosa, oropharynx (Online Refs. 1–6)	Dental and periodontal diseases (Online Refs. 7–9)
Group *milleri* (*S. intermedius*, *constellatus*, *anginosus*)	Oropharynx, subgingival plaque, GI tract, vagina (*S. anginosus*) (Online Refs. 1,10–12)	Dental, periodontal or GI diseases, vaginal infection (uncommon) (Online Refs. 7,8,10,13,14)
Group D streptococci		
S. bovis group (including *S. gallolyticus* subsp. *gallolyticus*)	GI tract (Online Refs. 7,15,16)	Colorectal adenoma and adenocarcinoma (*S. gallolyticus* subsp. *gallolyticus* ++) (Online Refs. 8,16–20), biliary tract, GI tract
Enterococcus faecalis, *Enterococcus faecium*	GI tract, GU tract (Online Refs. 7,15)	Invasive procedures of the GU tract, including cystoscopy, lithotripsy, prostatectomy, cesarean section, curettage (Online Refs. 15,21)
Group B streptococci (*S. agalactiae*)	Oral mucosa, GI tract, vagina, anterior urethra (Online Refs. 1,22)	Colic tumors (benign or malignant) (Online Ref. 7), bacterial translocation from the GI tract (Online Ref. 22), soft-tissue infection, GU tract infection, drug injection (Online Ref. 23)
Group C and G streptococci		
Group C (*S. dysgalactiae*, *S. equi*, *S. equisimilis*, *S. zooepidemicus*)	Nasopharynx, skin, GU tract (Online Ref. 2)	Skin and respiratory tract infections, drug injection (Online Refs. 7,24)
Group C	Nasopharynx, skin, GU tract (Online Ref. 2)	Peripartum GU infections (Online Ref. 25)
Group A streptococci (*S. pyogenes*)	Oropharynx, skin (Online Ref. 26)	Skin and soft tissue infections, pharyngitis, endometritis (Online Ref. 27)
Streptococcus pneumoniae	Nasopharynx (Online Ref. 28)	Pneumonia, otitis media (Online Ref. 29)
Deficient streptococci (*Granulicatella* [*Abiotrophia*] *defectiva*)	Oral microbiota, dental plaque (Online Refs. 2,30)	Drug injection, periodontitis (Online Refs. 31,32)
Streptobacillus moniliformis	Oral cavity of rats, gerbils, mice, guinea pigs (Online Refs. 33,34)	Rat bite or abrasions (Online Refs. 34–36)
Staphylococci		
Staphylococcus aureus	Major sites: anterior nares, pharynx, perineal area Minor sites: skin, intestine (Online Refs. 1,37)	Health care–associated procedures, drug injection, skin and soft-tissue infections (Online Refs. 7,38–41)
Coagulase-negative staphylococci		
S. saprophyticus	Perineal area (Online Ref. 41)	GU tract infections (Online Ref. 42)
S. epidermidis, *capitis*, *haemolyticus*, *hominis*, *saprophyticus*, *schleiferi*, *lugdunensis*, among others	Skin (Online Refs. 1,43)	Skin infections, health care–associated procedures (Online Refs. 7,43)

Continued on the next page

For each microorganism, the most probable POE was inferred from its natural habitat or site of colonization in humans on the basis of a search of published research (**Table 1**). Treatment, if any, of the POE was systematically considered. It was either performed during the patient's stay in our hospital or prescribed.

Health care–associated IE was defined as either IE developing in a patient hospitalized for more than 48 h before the onset of signs or symptoms consistent with IE or IE diagnosed within 48 h of admission in an outpatient with extensive health care contact (received intravenous therapy, wound care, or specialized nursing care at home within 30 days; underwent hemodialysis; received intravenous chemotherapy; resided in a nursing home or long-term care facility). Community-acquired IE was defined as IE diagnosed at the time of admission (or within 48 h of admission) in a patient not fulfilling the criteria for health care–associated infection (6).

RESULTS

Among 444 patients hospitalized at our institution between 2005 and 2011, 318 (320 episodes) were

TABLE 1 Continued

Microorganisms	Habitat	Portals of Entry
HACCEK		
Haemophilus spp., *Aggregatibacter* (*Actinobacillus*) *actinomycetemcomitans*, *Capnocytophaga* spp., *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*	Oropharynx (Online Refs. 7,44,50)	Periodontitis, buccal and dental infections, dental procedures, drug injection (Online Refs. 7,44–49)
Intracellular bacteria		
Coxiella burnetii	Mammals (farm animals, especially parturient females), birds, and arthropods (ticks) (Online Ref. 51)	Inhalation or transcutaneous contact with contaminated fluids, ingestion of raw milk, tick bites (Online Refs. 7,51,52)
Bartonella		
B. henselae	Cats (Online Ref. 53)	Cat scratch or bite, arthropod bite (Online Refs. 7,53,54)
B. quintana	Unknown reservoir beside humans (Online Ref. 53)	Pediculus humanus corporis (Online Refs. 7,55)
Tropheryma whipplei	Human GI tract (Online Refs. 57,58)	Unknown (Online Refs.57,59)
Legionella	Water, especially warm water (natural or artificial) (Online Ref. 60)	Inhalation (Online Ref. 60)
Brucella (*B. melitensis*, *B. abortus*, *B. suis*)	Mammals (e.g., cattle, sheep, goat, camel, buffalo) (Online Ref. 61)	Ingestion of raw milk, cutaneous contact, or inhalation of contaminated fluids (Online Ref. 61)
Enterobacteria		
E. coli, *Salmonella* spp., *Enterobacter* spp., among others	GI tract, perineal area (Online Ref. 1)	Health care–associated procedures, bacterial translocation from the GI tract, drug injection (Online Ref. 7), GU tract infections (*E. coli*) (Online Ref. 62)
Miscellaneous bacteria		
Corynebacterium diphteriae, *C. jeikeium*, *C. striatum*	Environmental, mucosa and skin commensal (Online Ref. 63)	Health care–associated procedures (catheter-related infection, surgery, etc.), drug injection (Online Refs.7,63)
Pseudomonas spp.	Environmental (water) (Online Ref. 64)	Drug injection, health care–associated invasive procedures (Online Refs.7,64,65)
Peptostreptococcus spp.	Oropharynx, chronic skin lesions, GI tract, GU tract	Periodontitis, gingivitis, diabetic foot (Online Ref. 66)
Listeria spp.	Environment (soil, water) (Online Ref. 7)	Ingestion of contaminated food (Online Refs.7,67)
Propionibacterium spp.	Oropharynx, skin (Online Refs.1,68)	Health care–associated invasive procedures (cardiothoracic surgery, catheter related infections) (Online Refs.68,69)
Atypical mycobacteria (e.g., *M. chelonae*, *M. fortuitum*, *M. chimaera*)	Environment (water, soil, plants, animals, inert surfaces) (Online Ref. 71)	Health care–associated invasive procedures (cardiothoracic surgery), contaminated bioprosthetic material (Online Refs.72–74)
Fungi and yeast		
Aspergillus	Environment	Inhalation, cardiothoracic surgery (Online Ref. 70)
Candida	Skin, GI tract	Health care–associated invasive procedures (catheter related infections, surgery), drug injection, cutaneous mycosis, urinary tract infection (Online Refs. 7,75)

*See the Online Appendix for the list of references cited in this table.
GI = gastrointestinal; GU = genitourinary.

TABLE 2 Identified Portals of Entry in 238 Patients With Infective Endocarditis

Portal of Entry	
Cutaneous	96 (40)
Intravenous drug use	21
Nonintravenous drug use	75
Oral/dental	68 (29)
Gastrointestinal	56 (23)
Genitourinary	10 (4)
Ear, nose, and throat	5 (2)
Respiratory	3 (1)
Total	238 (100)

Values are n (%) or n.

included in the present study (we excluded 82 patients who died during hospitalization; 44 medical charts were unavailable for technical reasons).

The median age of the patients was 61 ± 2 years; 75% were men; 29% had native valve disease, 22% had ≥1 valvular prosthesis, and 49% did not have previously known heart disease; 11% had cardiac implantable electronic devices (pacemakers or defibrillators). Microorganisms were streptococci in 41%, staphylococci in 31%, and enterococci in 8%.

POE FOR THE PRESENT IE EPISODE. The POEs for the present IE episodes were identified in 238 patients (74%). Among identified POEs, 40% were cutaneous, 29% were oral or dental, and 23% were gastrointestinal (Table 2).

TABLE 3 Cutaneous Portals of Entry of Infective Endocarditis

Portal of Entry	
Health care–associated infective endocarditis	39 (41)
Vascular access (central venous line, n = 8; peripheral venous line, n = 5; subcutaneous implantable port, n = 4)	17
Infection of a cardiac implantable electronic device	11
Infection of the operative site (cardiac valve replacement, n = 6; vascular surgery, n = 3; orthopedic surgery, n = 2)	11
Community-acquired infective endocarditis	33 (34)
Domestic wound by a sharp object	6
Nonsuppurative skin and soft-tissue infections	5
Diabetic foot ulcer	5
Occupational hand wound	4
Cutaneous abscess and furuncle	4
Venous leg ulcer	3
Pressure ulcer	2
Puncture wound (sea urchin, splinter)	2
Insect bite	1
Prurigo	1
Intravenous drug use	21 (22)
Inoculation disease	3 (3)

Values are n or n (%).

Cutaneous POE. POEs were cutaneous in 96 patients. Cutaneous POEs were health care associated in 41% of these patients, community acquired in 34%, related to intravenous drug use in 22%, and related to inoculation diseases in 3% (louse bite, *Bartonella quintana*, n = 1; tick bite, *Coxiella burnetii*, n = 1; cat scratch disease, *Bartonella henselae*, n = 1).

Vascular access was the main health care–associated cutaneous POE (44%), followed by infection of a cardiac implantable electronic device (28%) and infection of the operative site (28%) (Table 3). Wounds, nonsuppurative skin and soft-tissue infections, and diabetic foot ulcers were the most frequent community-acquired cutaneous POEs.

Staphylococci were responsible for 87% of the 39 cases of IE with health care–associated cutaneous POEs (*Staphylococcus aureus*, 38%; coagulase-negative staphylococci, 49%) (Table 4). *S. aureus* was responsible for 82% of 33 cases of IE with community-acquired cutaneous POEs and for 52% of cases of IE in intravenous drug users.

Oral or dental POE. Overall, a stomatologist saw 62% of patients during their stays in our hospital. Oral or dental POEs were identified in 68 patients. The distribution of lesions is detailed in Table 5, and the distribution of microorganisms is presented in Table 6. Oral streptococci were responsible for 69% of the cases of IE with oral or dental POEs.

Sixty-five of the 68 patients with oral or dental POEs (96%) saw a stomatologist during their stay in our hospital. For organizational reasons, the other 3 patients with oral or dental POEs did not see a stomatologist during their hospital stays but had seen their dentists within the previous 3 months.

Dental procedures to treat POEs were undertaken during 24 patients' stays in our hospital. All other patients were given instructions on dental procedures to be performed.

Gastrointestinal POE. Gastrointestinal POEs were identified in 56 patients. Colonic polyps were present in 46% of these patients (Table 7). Colorectal adenocarcinoma was diagnosed in 14% of the patients. *Streptococcus bovis* group and *Enterococcus faecalis* were responsible for 50% and 29% of cases of IE with gastrointestinal POEs, respectively (Table 8).

Other POE. Urinary POEs were acute pyelonephritis (n = 4), benign prostatic hypertrophy with acute urine retention (n = 1), transurethral resection of the prostate (n = 1), prostate needle biopsy (n = 1), transurethral resection of bladder cancer (n = 1), and urinary self-probing because of chronic urethral stenosis (*S. bovis* group, n = 2; *Enterococcus*, n = 1; *Streptococcus agalactiae*, n = 1; *Escherichia coli*, n = 1).

One female patient had an infection (*S. agalactiae*) of an aseptic necrobiosis of a uterine fibroma. The POE was ENT in 5 patients: pansinusitis with cerebral abscesses (*Streptococcus pneumoniae*, n = 1; *Haemophilus parainfluenzae*, n = 1), tonsil phlegmon (*S. pneumoniae*), recurrence of a laryngeal epidermoid carcinoma (*S. agalactiae*), and repetitive epistaxis with iterative plugging and cauterization of a nasal polyp (*S. aureus*). Three patients had pneumonia, and their blood cultures grew *S. pneumoniae*.

Nonidentified POE. Among 82 episodes with nonidentified POEs, the microorganism habitat was cutaneous in 49%, oral or dental in 22%, and gastrointestinal in 22% (Table 9).

POTENTIAL POE OF A NEW IE. Potential POEs for future IE episodes were as follows:

- continuation of intravenous drug use in 21 patients;
- cutaneous disease in 2 patients: Klippel-Trenaunay syndrome with varicose ulcer and psoriasis with scratching lesions;
- oral or dental infective foci in 66 of 125 patients (53%) who underwent stomatologic examinations: dental infectious focus in 41, radiological dental infectious focus (cyst, granuloma) without clinical lesion in 9, endodontal and periodontal disease in 11, and periodontal disease in 5;
- colonic lesions (polyps, diverticulosis, adenocarcinoma) in 32 of 80 patients (40%) who underwent colonoscopy because they were ≥50 years of age or had familial histories of colonic polyposis: polyps in 13 patients, sigmoid diverticulosis in 15 patients, sigmoid diverticulosis with polyps in 2 patients, diffuse angiodysplasia in 1 patient, and colorectal adenocarcinoma in 1 patient;
- urinary lesions in 11 of 52 patients (21%) who underwent urinary examinations: prostate cancer in 3 patients, benign prostatic hypertrophy with urine retention in 2 patients, urethral stenosis in 2 patients, pyelonephritis in 1 patient, cystinuria with repetitive renal lithiasis in 1 patient, post-radiotherapy bladder in 1 patient, and extrinsic urethral compression by colon cancer in 1 patients (no gynecologic lesions were found in the 16 women >79 years of age who underwent gynecologic examinations); and
- ENT lesions (sinusitis, otomastoiditis, and so on) in 6 of 180 examinations.

DISCUSSION

It seems obvious that the POE in a patient with IE should be searched for and eradicated, ideally during the initial stay, while the patient is receiving antibiotics. Many physicians probably look for and treat the POEs in their patients with IE. Yet there is no recommendation about the POE in recent guidelines on IE (3,4), and there is almost never information on the POE in reports of large series of IE.

At our institution, where the POE of IE is systematically searched for, the POEs of the current IE episodes were found in as many as three-quarters of patients. We consider this very good performance and an a posteriori justification of the systematic search for IE POE.

However, one might argue that the proportion of patients (up to a quarter) for whom POEs were not found is too high. The microorganisms were known in almost all (81 of 82) episodes of IE for which the POEs were not found (Table 9), and this may help uncover a possible POE, even if it is not indubitably identified.

TABLE 4 Microorganisms in Infective Endocarditis With a Cutaneous Portals of Entry

Microorganism	Health Care Associated	Community Acquired	Intravenous Drug Use
Staphylococcus aureus	15 (MR, n = 3)	27 (MR, n = 1)	11 (MR, n = 1)
Coagulase-negative staphylococci	19 (MR, n = 8)	3	
Enterococcus faecalis			3
Group G streptococci	1		
Streptococcus agalactiae		1	
Streptococcus dysgalactiae			1
Streptococcus pyogenes		1	
Klebsiella spp.	1 (*K. pneumoniae*)		2 (*K. oxytoca*)
Propionibacterium spp.	1 (*P.* spp.)	1 (*P. acnes*)	
Fungi			3
Serratia marcescens			1
No identified microorganism	2		

MR = methicillin resistant.

TABLE 5 Oral and Dental Portals of Entry of Infective Endocarditis

Portal of Entry	
Dental procedures in the previous 3 mo	8 (12)
Extraction	4 (6)
Scaling	1 (1)
Endodontic procedure	1 (1)
No details	2 (3)
Dental infectious focus (decay, fracture, traumatism)	9 (13)
Dental infectious focus with no more details	22 (32)
Periodontal disease	7 (10)
Endodontal and periodontal disease	12 (68)
Radiological dental infectious focus (cyst, granuloma) without clinical lesion	9 (13)
Vigorous tooth brushing with frequent bleeding	1 (1)

Values are n (%).

TABLE 6 Microorganisms in Infective Endocarditis With an Oral or Dental Portal of Entry

Microorganisms	
Oral (viridans) streptococci	47 (69)
HACCEK bacteria	7 (10)
Streptococcus pyogenes (group A streptococci)	1 (1)
Streptococcus pneumoniae	1 (1)
Streptococcus dysgalactiae	1 (1)
Gemella morbillorum	2 (3)
Granulicatella (*Abiotrophia*) *defectiva*	1 (1)
Bulleidia extructa	1 (1)
Peptostretococcus anerobius	1 (1)
Neisseria sicca	1 (1)
Acinetobacter spp.	1 (1)
Propionibacterium acnes	1 (1)
No identified microorganism	3 (4)

Values are n (%).
HACCEK = *Haemophilus* spp., *Aggregatibacter* (*Actinobacillus*) *actinomycetemcomitans*, *Capnocytophaga* spp., *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*.

The most frequent POE was cutaneous (40% of identified POEs). It was mainly (62%) associated with health care and with intravenous drug use. The most frequent microorganisms were staphylococci, which were identified in 78% of episodes of IE with cutaneous POEs, as expected from their ecology (Table 1), *S. aureus* in 55%, and coagulase-negative staphylococci in 23%.

The second most frequent POE was oral or dental (29%). Among oral or dental POEs, a dental infectious focus was much more often involved (59% of oral or dental POEs) than dental procedures (12%). Periodontal disease was involved in 28%. The most frequent microorganisms were oral (viridans) streptococci (69%), then HACCEK bacteria (*Haemophilus* spp., *Aggregatibacter* [*Actinobacillus*] *actinomycetemcomitans*, *Capnocytophaga* spp., *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*) (10%). The habitat of viridans streptococci is dental plaque, oral mucosa, and the oropharynx. Their POEs are dental and periodontal disease (Table 1) (7). The oropharynx is the habitat of HACCEK organisms. Their POEs are buccal and dental infections and dental procedures (Table 1) (8).

TABLE 7 Gastrointestinal Portals of Entry of Infective Endocarditis

Portal of Entry	
Upper gastrointestinal tract	5 (9)
Esophageal ulcer	2 (4)
Antrum and fundus atrophy	1 (2)
Esophageal varices + bulb ulcer	1 (2)
Gastrostomy	1 (2)
Lower gastrointestinal tract	51 (91)
Polyps	22 (39)
Unique, ≥1 cm	7 (12)
Multiple, ≥1 cm	5 (9)
Multiple, <1 cm	4 (7)
Multiple, size unknown	6 (11)
Colorectal adenocarcinoma	8 (14)
Sigmoid diverticulosis	11 (20)
Sigmoid diverticulosis + multiple polyps, ≥1 cm	4 (7)
Diffuse angiodysplasia	2 (4)
Active ileitis	1 (2)
Definitive colostomy because of rectal cancer	2 (4)
Colonoscopy with resection of several polyps	1 (2)

Values are n (%).

TABLE 8 Microorganisms in Infective Endocarditis With Gastrointestinal Portals of Entry

Microorganisms	
Streptococcus bovis group (*S. bovis*, *S. equinus*, *S. gallolyticus*, *S. infantarius*, *S. pasteurianus*, *S. lutetiensis*)	28 (50)
Streptococcus agalactiae (group B streptococci)	3 (6)
Streptococcus dysgalactiae	1 (2)
Streptococcus salivarius	1 (2)
Enterococcus faecalis	16 (29)
Enterococcus faecium	3 (5)
Staphylococcus aureus	1 (2)
No identified microorganism	3 (5)

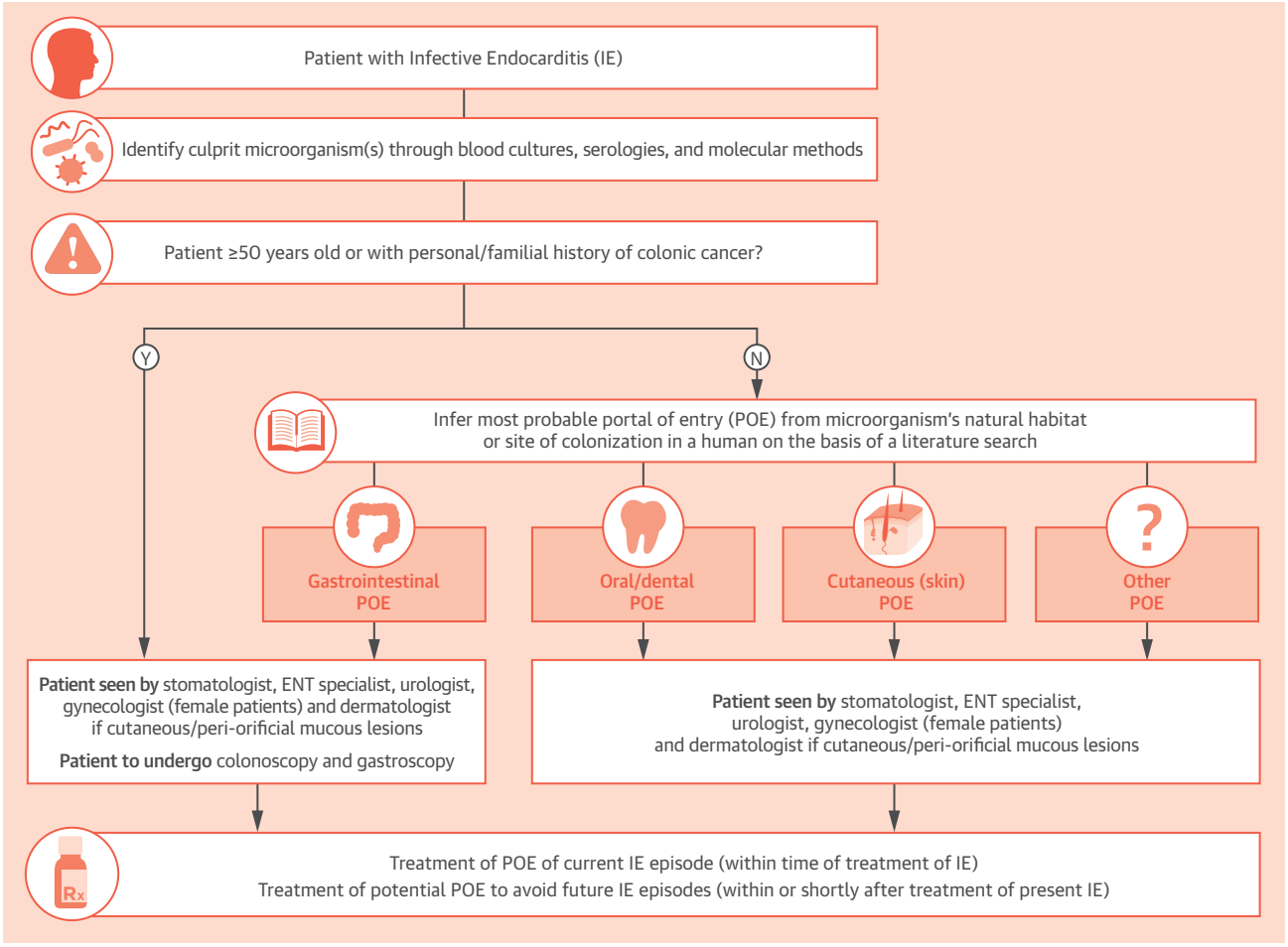
Values are n (%).

TABLE 9 Microorganisms in 82 Episodes of Infective Endocarditis With Nonidentified Portals of Entry

Microorganisms	
Microorganisms with cutaneous habitat	40 (49)
Staphylococcus aureus	23 (28) (MR, n = 3)
Coagulase-negative staphylococci	10 (12)
Propionibacterium (*P. acnes*, *P. granulosum*)	4 (5)
Corynebacterium spp.	3 (4)
Microorganisms with oral/dental habitat	18 (22)
Oral streptococci	12 (15)
HACCEK	2 (2)
Gemella spp.	2 (2)
Streptococcus pyogenes (group A streptococci)	1 (1)
Granulicatella (*Abiotrophia*) *adiacens*	1 (1)
Microorganisms with gastrointestinal habitat	18 (22)
Gastrointestinal streptococci	7 (8)
Streptococcus agalactiae (group B streptococci)	5 (6)
Tropheryma whipplei	3 (4)
Enterococci	2 (2)
Various microorganisms*	5 (6)
No identified microorganism	1 (1)

Values are n (%). **Streptococcus pneumoniae*, n = 3; *Capnocytophaga canimorsus*, n = 1; polymicrobial (group G *Streptococcus* + *Staphylococcus epidermidis*), n = 1.
Abbreviations as in Tables 4 and 6.

CENTRAL ILLUSTRATION **Infective Endocarditis: Flowchart for Identification and Treatment of Portal of Entry**



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The strategy of investigations and treatment of the portal of entry (POE) for the current episode of infective endocarditis (IE) and those for future episodes of IE is shown according to the etiologic diagnosis of IE. ENT = ear, nose, and throat; N = no; Y = yes.

The third most frequent POE was gastrointestinal (23%). Colonic polyps were found in almost one-half of the patients and colorectal adenocarcinoma in 14%. As may be expected, the most frequent responsible microorganisms were *S. bovis* group (*S. gallolyticus*) (50%) and *E. faecalis* (29%). The habitat of the *S. bovis* group is the gastrointestinal tract, and its POEs are colorectal adenoma and adenocarcinoma. The habitat of enterococci is the gastrointestinal and genitourinary tracts, and its POEs are the biliary tree and gastrointestinal or urinary tract infections (9) (**Table 1**).

Concordance between POE and microorganisms (i.e., intravenous drug use and *S. aureus*, dental infection and viridans streptococci, colonic polyps and *S. bovis* group) was excellent. But the POE should not be only presumed because of the microorganism. It should be looked for and treated, if needed.

Potential POEs for additional IE episodes were obvious in drug users continuing drug use and in some patients with chronic cutaneous lesions. The performance of a systematic search for potential POE was low for the ENT region and the genitourinary tract. Performance was good regarding the search for oral or dental or colonic potential POEs, which were found in 53% and 40% of patients, respectively. We limited systematic colonoscopy to patients who had familial histories of colonic polyposis or were

≥50 years of age, because the incidence of colorectal cancer increases in patients aged ≥50 years (10).

Our study showed that with a systematic approach to source identification, the POE can often be identified, and in a substantial proportion of these patients, risk modification can be attempted. This topic is of clinical importance, as it relates to our understanding of the sources of infection in patients with IE and also influences management of patients (e.g., ordering colonoscopy in a patient with *S. bovis* group IE, recommending better maintenance of oral hygiene).

STUDY LIMITATIONS. The present study was performed at a single center; thus, the results may not be applicable to other areas of the world. A POE can be established with certainty only when the microorganism responsible for IE is also identified at the site of the POE and is genetically the same. Thus, the POEs in our study were presumed, not definite.

CONCLUSIONS

A systematic search for the POEs of IE was successful in as many as 74% of patients. Systematically searching for potential oral or dental, gastrointestinal, or genitourinary POEs of new IE episodes was also successful in many patients.

We would advise the systematic performance of a stomatologic examination in patients with IE and performance of colonoscopy in patients ≥50 years of age or at high risk for colorectal cancer. A flowchart for the identification and treatment of POEs is shown in the **Central Illustration**.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: A systematic search can identify the source of bacteremia in three-quarters of patients with IE, and in more than one-third of cases, additional potential POEs can be found that pose a risk for future infections.

TRANSLATIONAL OUTLOOK: Additional studies could be conducted to confirm these findings and assess the efficacy of eradicating potential portals of bacterial entry for the prevention of recurrent endocarditis.

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KEY WORDS colonic abnormalities, cutaneous infections, dental infections

APPENDIX For a reference list of the studies cited in Table 1, please see the online version of this article.