Epidemiol. Infect. (2010), **138**, 313–317. © Cambridge University Press 2009
doi:10.1017/S0950268809990483 Printed in the United Kingdom

SHORT REPORT
Staphylococcus aureus is the most common identified cause of cellulitis: a systematic review

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(*Accepted 1 July 2009; first published online 3 August 2009*)

SUMMARY

We utilized Medline to perform a systematic review of the literature to quantify the aetiology of cellulitis with intact skin. Of 808 patients with cellulitis, 127–129 (15·7–16·0%) patients had positive needle aspiration and/or punch biopsy cultures from intact skin. Of the patients with positive cultures, 65 (50·4–51·2%) had cultures positive for *Staphylococcus aureus*, 35 (27·1–27·6%) for group A streptococcus, and 35–37 (27·1–29·1%) for other pathogens. The most common aetiology of cellulitis with intact skin, when it can be determined, is *S. aureus*, outnumbering group A streptococcus by a ratio of nearly 2:1. Given the increasing incidence of community-associated methicillin-resistant *S. aureus* infections, our findings may have critical therapeutic implications.

Key words: Cellulitis aetiology, systematic review.

Cellulitis is a common infection of the skin and its underlying tissues. Unless accompanied by bacteraemia or abscess, the aetiology of cellulitis is usually not pursued clinically because this requires an invasive procedure such as needle aspiration or punch biopsy. *Staphylococcus aureus* and group A streptococcus (GAS) are the most common causes of cellulitis, with the latter typically cited as the most common cause [1–8]. Given the rise of methicillin-resistant *S. aureus* (MRSA) as the predominant cause of suppurative skin infections, a precise understanding of the aetiologies of cellulitis is critical [9]. To this end, we performed a systematic review of the literature to quantify the prevalence of *S. aureus and* GAS in cases of cellulitis.

We performed a literature search to identify the bacteriological diagnosis of cellulitis in humans in PubMed by the key word 'cellulitis'. Our search was limited to English-language clinical trials, letters, meta-analyses, or randomized control trials published between 1966 and 2007. We also examined the bibliography for original research papers that may have contained publications that were missed by our initial search criteria. Investigations of cellulitis were considered eligible for inclusion if they utilized needle aspiration and/or punch biopsy; studies pertaining to ocular, odontogenic, pelvic, or surgical site-associated cellulitis were excluded. Two independent investigators reviewed each abstract and potentially relevant articles were retrieved; any discrepancies in articles selected were resolved by discussion.

Data on patients with a clinical diagnosis of cellulitis were considered only if confirmed by needle aspiration and/or punch biopsy of intact skin. We excluded patients with a documented skin break (including surgical site infection), deep skin or soft tissue infection (e.g. necrotizing cellulitis), concomitant infection in another organ (e.g. osteomyelitis),

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Table 1. *Aetiology of cellulitis*

Source	Dates ranges	Location	Adults (A) or paediatrics (P)	Needle aspiration (N) or punch biopsy (P)	Location of needle aspiration: leading edge (L) or centre (C)	No. of patients cultured (*n*)	Positive cultures[a] (*n*)	Culture positive for *S. aureus* (*n*)	Culture positive for group A streptococcus (*n*)	Culture positive for other pathogen(s)[b] (*n*)
Uman & Kunin, 1975 [10]	NR	Madison, WI	A	N	NR	3	3	0	2	1
Fleisher *et al.* 1980 [11]	1 July 79–31 Dec. 79	Philadelphia, PA	P	N	L	46	21	15	8	2
Ginsberg, 1981 [2]	1 Jan. 76–30 June 76	Boston, MA	A, P	N	NR	16	2	1	1	0
Goldgeier, 1983 [12]	1979–1981	Rochester, NY	A, P	N	L	18	0	0	0	0
Lee *et al.* 1985 [13]	NR	Australia	A	N	NR	21	11–12[c]	9	2	3
Liles & Hall, 1985 [14]	NR	Kansas City, MO	NR	N	L	24	6–7[d]	3	1	2–4[e]
Hook *et al.* 1986 [15]	NR	Seattle, WA	A	N, P	L	17	3	1	1	1
Epperly, 1986 [16]	1 Nov. 84–4 Sept. 85	Fort Benning, GA	A, P	N	L (103), C (70)[f]	103	11	8	1	2
Howe *et al.* 1987 [17]	1 July 86–15 Feb. 87	Portsmouth, VA	P	N	C[g]	20	8	6	3	0
Lutomski *et al.* 1988 [18]	NR	Cincinnati, OH	A	N	L	21	3	1	1	1
Newell & Norden, 1988 [19]	NR	Pittsburgh, PA	A	N	L, C	5	0	0	0	0
Kielhofner *et al.* 1988 [20]	NR	Kansas City, MO	A	N	L	81	27	9	8	10
Duvanel *et al.* 1989 [21]	July 84–Oct. 85	Switzerland	A	N, P	C (6)[h]	23	6	4	1	2
Sachs, 1990 [22]	NR	Philadelphia, PA	A	N	L	24	5	1	1	2
Brook & Frazier, 1995 [23]	June 77–June 87	Bethesda, MD	A, P	N	L[i]	63	12	3	2	7
Lebre *et al.* 1996 [24]	NR	France	NR	N	C[j]	56	9	4	3	2
Total						541	127–129[k]	65	35	35–37[l]

NR, Not reported.

[a] The total number of patients with positive cultures does not equal the total number of patients culture positive for *S. aureus*, group A streptococcus, and other pathogens because some patients had polymicrobial infections.

Table 1 notes (*Cont.*)

[b] Other pathogens cultured but not noted in the table included α-hemolytic streptococcus ($n=4$), group B streptococcus ($n=4$), *P. aeruginosa* ($n=4$), *C. perfringens* ($n=3$), *E. coli* ($n=3$), *P. multocida* ($n=3$), *P. mirabilis* ($n=3$), group D streptococcus ($n=2$), *E. agglomerans* ($n=2$), *K. oxytoca* ($n=2$), *Acinetobacter* sp. ($n=1$), *B. fragilis* ($n=1$), *C. albicans* ($n=1$), *E. cloacae* ($n=1$), group G streptococcus ($n=1$), *H. influenzae* ($n=1$), non-group A streptococcus ($n=1$), *S. milleri* ($n=1$), and *S. sanguis* ($n=1$).

[c] We did not consider three isolates (*S. epidermidis*, *Peptostreptococcus* sp., and *P. acnes*) as causative pathogens; however, given the reporting method in the paper, it was unclear if these organisms occurred in three separate individuals or as part of a polymicrobial infection in one or two individuals. Hence, we cannot calculate with certainty the total number of patients with positive cultures.

[d] We did not consider one isolate (*P. acnes*) as a causative pathogen; however, given the reporting method in the paper, it was unclear if this organism occurred in an individual as a monomicrobial or polymicrobial infection. Hence, we cannot calculate with certainty the total number of patients with positive cultures.

[e] Given the reporting method in the paper, it was unclear if these organisms occurred in four separate individuals or as part of a polymicrobial infection in two or three individuals.

[f] The authors describe aspiration being performed at the midpoint, which was defined as midway between the leading edge and the centre of the cellulitis.

[g] The authors describe aspiration being performed at the point of maximal inflammation (PMI), which was usually the centre of the cellulitis.

[h] The authors performed needle aspirations on only six of the 23 patients.

[i] There was inconsistent technique between patients, but the investigators generally performed the needle aspirations at the leading edge of the cellulitis.

[j] There was inconsistent technique between patients, but the investigators generally performed the needle aspiration at the centre of the cellulitis.

[k] We did not consider three isolates (*S. epidermidis*, *Peptostreptococcus* sp., and *P. acnes*) as causative pathogens; however, given the reporting method in the papers, it was unclear if these organisms occurred in four separate individuals or as part of a polymicrobial infection in one, two, or three individuals. Hence, we cannot calculate with certainty the total number of patients with positive cultures.

[l] Given the reporting method in the paper, it was unclear if these organisms occurred in four separate individuals or as part of a polymicrobial infection in two or three individuals.

Fig. 1. Study flow diagram. This figure shows a schematic of the literature search for the aetiology of cellulitis including *in vitro* investigations, animal investigations, and human investigations. The schematic indicates how many 'hits' were found on the search, number of articles excluded from this systematic review, and reasons for exclusion from our systematic review. [a] Review was determined to be unlikely to have yielded references relating to aetiology of cellulitis based on the abstract (e.g. review of treatment of patients with neutropenia). [b] Inappropriate comparisons for the systematic review included studies relating to: ocular cellulitis, odontogenic cellulitis, pelvic cellulitis, or surgical site-associated cellulitis, treatment of cellulitis, imaging of cellulitis, risk factors for cellulitis, and populations comprised solely of patients with severe underlying disease (e.g. cancer, HIV, or diabetes).

bacteraemia, and/or abscess. Patients were also excluded if microorganisms recovered on cultures were probably skin contaminants (*S. epidermidis*, *Peptostreptococcus* spp., *Propionibacterium acnes*, diphtheroids, *Bacillus* sp., *Corynebacterium* sp., and viridans streptococci).

In total 600 abstracts were reviewed and of these 172 articles were selected for further review (Fig. 1). Sixteen studies met the inclusion and exclusion criteria (Table 1) [2, 10–24] and all but one of the articles were identified via review of bibliographies. Two studies examined exclusively paediatric patients, four both paediatric and adult patients, and ten examined only adults. For most investigations, there was insufficient information to allow us to quantify cellulitis aetiology in patients stratified by the presence or absence of comorbidities. There was also insufficient information to stratify aetiology by body site. These 16 investigations examined 808 patients with cellulitis.

Of these patients, 127–129 (15·7–16·0%) had positive needle aspiration and/or punch biopsy cultures from intact skin. Two articles reported bacteria that are common contaminants as part of a summary of pathogens, making it impossible to tell if the organism was part of a polymicrobial infection or represented the sole pathogen recovered [13, 14]. If it was the latter, the number of positive aspirations would be less.

Positive needle aspiration yield varied from zero to >40% (Table 1) and of the two investigations that included punch biopsies, positive culture yield varied from 18% to 26% [15, 21]. Sixty-five patients grew *S. aureus*, 35 were positive for GAS and 35–37 had other pathogens.

In conclusion, the most common aetiology of cellulitis in cases not associated with skin breaks, deep skin or soft tissue infection, concomitant non-skin infection, bacteraemia, or abscess, when it can be determined, is *S. aureus* which contradicts much conventional teaching [1–8]. However, most cases of cellulitis did not yield positive cultures despite invasive procedures, so it may be that other bacterial species are more common but are more difficult to recover using standard microbiological techniques. Alternatively, other methods may enhance recovery of different organisms. For example, one group of investigators recovered GAS (but not *S. aureus*) from rubbing a moistened swab over the surface of a scab [1] (D. Musher, personal communication), suggesting that non-aspiration methods may increase the yield of this organism (this investigation was not included in the analysis). Nevertheless, over half of all patients with positive cultures yielded *S. aureus* and these patients outnumbered those with GAS by a ratio of approximately 2:1. Given the relatively high prevalence of *S. aureus* in patients with cellulitis with intact skin and the rapid the rise of community-associated MRSA (CA-MRSA) infections, it is imperative to understand the aetiology of cellulitis in areas in which CA-MRSA is endemic; this may have crucial implications for choice of empiric antibiotic therapy. It is therefore probably prudent to treat empirically for MRSA when managing patients who have cellulitis with intact skin.

ACKNOWLEDGEMENTS

We thank Daniel Musher, M.D., Baylor College of Medicine, Gary Fleisher, M.D., Harvard Medical School, and Darla Liles, M.D., Brody School of Medicine at East Carolina University, for their comments. We also thank Jennifer Tan, M.H.S., Harbor–UCLA Medical Center, for her assistance with data collection. This research was supported by a grant M01-RR00425 from the National Institutes of Health through the Harbor–UCLA General Clinical Research Center to Ms. Chira. Dr Miller was funded in part by grants R01-CCR923419 and U01-CI000384-01 from the Center for Disease Control and Prevention.

DECLARATION OF INTEREST

None.

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