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REFERENCES

- 1. Gambichler T, Breuckmann F, Boms S, Altmeyer P, Kreuter A. Narrowband UVB phototherapy in skin conditions beyond psoriasis. *J Am Acad Dermatol.* 2005;52(4):660-670.
- Meduri NB, Vandergriff T, Rasmussen H, Jacobe H. Phototherapy in the management of atopic dermatitis: a systematic review. *Photodermatol Photoimmunol Photomed*. 2007;23(4): 106-112.
- **3.** Kalia S, Toosi B, Bansback N, et al. Assessing adherence with phototherapy protocols. *J Am Acad Dermatol.* 2014;71(6): 1259-1261.
- 4. Yentzer BA, Gustafson CJ, Feldman SR. Explicit and implicit copayments for phototherapy: examining the cost of commuting. *Dermatol Online J.* 2013;19(6):18563.
- Koek MBG, Sigurdsson V, van Weelden H, Steegmans PHA, Bruijnzeel-Koomen CAFM, Buskens E. Cost effectiveness of home ultraviolet B phototherapy for psoriasis: economic evaluation of a randomised controlled trial (PLUTO study). BMJ. 2010;340:c1490.

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Supplemental Table I. Distribution of nonadherent patients by number of phototherapy treatments attended

| # Treatments | N (%) of early non-adherent | | | |
|--------------|-----------------------------|--|--|--|
| 0 | 103 (67.3) | | | |
| 1 | 15 (9.8) | | | |
| 2 | 7 (4.6) | | | |
| 3 | 7 (4.6) | | | |
| 4 | 9 (5.9) | | | |
| 5 | 5 (3.3) | | | |
| 6 | 7 (4.6) | | | |

Clinicopathological and dermoscopic features of angio-eccrine hyperplasia in clear cell acanthoma

To the Editor: While the histological epidermal criteria (psoriasiform acanthosis, pale-appearing keratinocytes, parakeratosis, and neutrophilic exocytosis) of clear cell acanthoma (CCA) are usually well known,¹ the dermal ones have been less investigated. We attempted to evaluate the frequency of vascular and eccrine findings in CCA and to correlate them with dermoscopy (Fig 1 and Supplemental Fig 1 [available at http://www.jaad.org]).

Histological specimens of CCA removed in the last 8 years have been reviewed. For each sample, we evaluated gender, age, anatomical site (lower limbs or other anatomical sites), presence of angio-eccrine hyperplasia (AEH), and vascular hyperplasia of the papillary dermis (VHPD).We defined as VHPD the usual presence of a vascular hyperplasia in the papillary dermis; while as AEH, the presence of a hyperplastic vascular component associated with an increase of the eccrine glands and hyperplasia of the sweat glands, in the medium and deeper dermis. In order to evaluate a possible exogenous role on the pathogenesis of VHPD and AEH, we tested Human Herpes virus 8 (HHV8) expression, through an immunohistochemical essay. For a statistical reprocessing of data, we used the Fisher exact test between AEH and the single variables.

A total of 20 specimens of CCA from 12 men (60%) and 8 women (40%) were collected (Table I). Median age of the cohort was 67.5 years (range, 37-77 years). Fifteen specimens (75%) were referred to lesions removed on the lower limbs, 4 (20%) on the trunk, and 1 (5%) on the upper limbs. In 16 (80%) specimens, we found AEH in the dermis. Among those, 11 (55%) cases showed also a VHPD. Notably, in 4 (20%) cases, both AEH and VHPD were absent. Dermoscopic images were available for 15 cases, including the 4 cases without AEH and VHPD (Table I). For these latter 4 cases, dermoscopy revealed unusual features including irregular arranged hairpin, dotted, and glomerular (coiled) vessels (Fig 2). In contrast, the remaining cases revealed the typical "string of pearls" vascular pattern (Fig 1). None of the analysed specimens showed positivity to HHV8. We found a significant association between AEH and VHPD (P = .02) and between AEH and dermoscopy (P = .001), while for the other variables the statistical significance was not reached. Furthermore, no significant correlation was found for histologic and dermoscopic findings, according to the anatomical site.

AEH is a frequent and repetitive dermal clue in CCA (Supplemental Fig 2; available at http://www.jaad.org).



Fig 1. Clinical and dermoscopy (inset) of a clear cell acanthoma located on the lower limb. Dermoscopy reveals a typical "string of pearls" vascular pattern.

Table I. Clinic-pathological and dermoscopicalbaselines of clear cell acanthoma (CCA)

| Patient N° | Age | Gender | Site | VHPD | AEH | Dermoscopy |
|------------|-----|--------|-------|------|-----|------------|
| 1 | 77 | F | LL | _ | _ | AP |
| 2 | 69 | М | LL | _ | Yes | NP |
| 3 | 76 | М | LL | — | Yes | PLD |
| 4 | 75 | М | LL | Yes | Yes | PLD |
| 5 | 48 | F | LL | Yes | Yes | PLD |
| 6 | 45 | F | Trunk | _ | _ | AP |
| 7 | 70 | М | LL | Yes | Yes | PLD |
| 8 | 48 | F | LL | _ | Yes | PLD |
| 9 | 37 | М | UL | — | Yes | NP |
| 10 | 37 | М | LL | _ | Yes | PLD |
| 11 | 60 | F | LL | Yes | Yes | PLD |
| 12 | 57 | М | LL | _ | - | AP |
| 13 | 60 | F | LL | Yes | Yes | PLD |
| 14 | 62 | М | LL | Yes | Yes | PLD |
| 15 | 68 | М | LL | _ | - | AP |
| 16 | 73 | F | LL | Yes | Yes | PLD |
| 17 | 67 | F | LL | Yes | Yes | NP |
| 18 | 70 | М | Trunk | Yes | Yes | NP |
| 19 | 70 | М | Trunk | Yes | Yes | NP |
| 20 | 70 | М | Trunk | Yes | Yes | PLD |

AEH, Angio-eccrine hyperplasia; *AP*, atypical pattern; *LL*, lower limbs; *N*, patient's number; *PLD*, typical pinpoint-like/dotted vessels with a pearl—necklace-like distribution; *NP*, not provided; *UL*, upper limbs; *VHPD*, vascular hyperplasia of the papillary dermis.

The absence of AEH/VHPD is associated with an unspecific dermoscopy, without creating the typical dotted and coiled vessels arranged in a linear and reticular distribution (Supplemental Fig 3; available at http://www.jaad.org).² In fact, these latter are directly related to AEH, which explains the linear and organized distribution of vessels, as well as with VHPD, which corresponds to the capillaries oriented perpendicular within the elongated dermal papillae.

The presence of AEH/VHPD increases the dermoscopic sensitivity and specificity of CCA, reducing



Fig 2. Clinical of a clear cell acanthoma (CCA) of the trunk. Dermoscopy (inset) shows linear and irregular hairpin vessels (flower-like) and globular/dotted vessels. The lesion was in the differential diagnosis with amelanotic melanoma. Histologically, there was an absence of angio-eccrine hyperplasia (AEH) and vascular hyperplasia of the papillary dermis (VHPD).

pitfalls with thick hypomelanotic/amelanotic melanomas, other pink tumors, and inflammatory lesions, as psoriasis where the vessels occupy the whole lesion.²⁻⁴

The pathogenesis of CCA remains unknown, and the absence of HHV8 excludes its probable role in the angiogenesis of AEH/VHPD. Maybe the higher incidence of CCA in lower limbs of elderly patients favors a reactive nature, probably induced by a stasis dermatitis.

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REFERENCES

- 1. Shalin SC, Rinaldi C, Horn TD. Clear cell acanthoma with changes of eccrine syringofibroadenoma: reactive change or clue to etiology? *J Cutan Pathol.* 2013;40:1021-1026.
- Tiodorovic-Zivkovic D, Lallas A, Longo C, et al. Dermoscopy of clear cell acanthoma. J Am Acad Dermatol. 2015;72(1 Suppl): S47-S49.

- **3.** Zalaudek I, Hofmann-Wellenhof R, Argenziano G. Dermoscopy of clear-cell acanthoma differs from dermoscopy of psoriasis. *Dermatology*. 2003;207:428. author reply: 429.
- Zalaudek I, Argenziano G, Giacomel J. Dermatoscopy of non-pigmented skin tumors: pink-think-blink. Boca Raton, FL: CRC Press, Taylor & Francis Group; 2016.

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Lack of evidence that bedbugs transmit pathogens to humans

To the Editor: The global population of bedbugs that feed on humans (*Cimex lectularius, Cimex hemi-pterus,* and *Leptocimex boueti*) has undergone a significant resurgence since the late 1990s. Due to increased international travel and pesticide resistance, bedbugs once thought to be native to certain geographic locations have been found in other parts of the world. Bedbugs present a socioeconomic burden because they are costly to eradicate and infestations often recur. According to the US Environmental Protection Agency, bedbugs are "a pest of significant health importance," and upwards of 45 disease pathogens have been reported in bedbugs.^{1,2} It stands to reason to ask if bedbugs might transmit human pathogens.

We performed a literature review on August 6, 2015, and searched the computerized medical bibliographic databases PubMed, EMBASE, CINAHL, and Web of Science with the search terms: "bedbug" OR "cimex lectularius." A total of 1790 articles were returned, and 12 articles were suitable for inclusion (clinical and laboratory published studies [1990 to 2015] investigating bedbugs as potential vectors of infectious disease) after screening of titles, abstracts, and/or full-text articles. These articles demonstrated that although bedbugs may carry pathogens such as methicillin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus faecium, and hepatitis B virus, and may be competent vectors of Bartonella quintana and Trypanosoma cruzi, there were no confirmed cases of human disease transmission.

Previous reports suggest that, although a number of different disease pathogen species have been detected in or on bedbugs, there is a lack of definitive evidence that bedbugs transmit human pathogens.^{1,3} An important challenge for scientists is to determine the reason for this interesting finding. One hypothesis relates to the fact that bedbugs are the only hematophagous arthropod that both feeds on humans and mates by traumatic insemination. Traumatic insemination results in the repeated introduction of pathogens and repeated immune stimulation in the female bedbug, and may thereby select for higher levels of immunity in bedbugs. As a result, the survival and viability of pathogens maintained within bedbugs may be affected.¹ Another hypothesis is that bedbug saliva has been reported to contain lysozymes and other peptides that may have antimicrobial activities.^{4,5}

Future research related to these or other hypotheses might lead to greater scientific understanding of how to limit pathogen transmission in humans, and be of significant benefit for patients and global health by preventing human transmission of a variety of infectious diseases.

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REFERENCES

- 1. Delaunay P, Blanc V, Del Giudice P, et al. Bedbugs and infectious diseases. *Clin Infect Dis.* 2011;52(2):200-210.
- United States Environmental Protection Agency. List of Pests of Significant Public Health Importance. 2015. Available at: http://www2.epa.gov/insect-repellents/list-pests-significantpublic-health-importance. Accessed August 16, 2015.
- Goddard J, deShazo R. Bed bugs (Cimex lectularius) and clinical consequences of their bites. JAMA. 2009;301(13): 1358-1366.
- Doggett SL, Dwyer DE, Penas PF, Russell RC. Bed bugs: clinical relevance and control options. *Clin Microbiol Rev.* 2012;25(1): 164-192.
- Francischetti IM, Calvo E, Andersen JF, et al. Insight into the sialome of the bed bug, cimex lectularius. J Proteome Res. 2010;9(8):3820-3831.

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Supplemental Fig 1. Histological features of a clear cell acanthoma, with a vascular hyperplasia of the papillary dermis (VHPD). (Hematoxylin and eosin stain; original magnification: $\times 10$)



Supplemental Fig 2. A-B, Angio-eccrine hyperplasia (AEH) at level of the dermis; (Hematoxylin and eosin, $10 \times$ and $20 \times$); **C**, A particular of the AEH. (Hematoxylin and eosin, $40 \times$); **D**, A particular of a usual vascular hyperplasia of the papillary dermis (VHPD). (Hematoxylin and eosin; original magnification: $\times 40$)



Supplemental Fig 3. A, Clinical image of another CCA with atypical dermoscopic features; **B**, Dermoscopy shows hairpin vessels with a central area of hyperkeratosis. The lesion was in the differential diagnosis with keratoacanthoma and seborrheic keratosis. Histologically. there was an absence of angio-eccrine hyperplasica (AEH) and vascular hyperplasia of the papillary dermis (VHPD).