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Sleeping with the Enemy: Everything You Need to Know about the Biology, Clinical Significance, and Laboratory Identification of Bed Bugs

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Abstract

The world has experienced a major global resurgence of bed bug infestations over the past 2 decades. While bed bugs do not serve as vectors of disease, their bites and household infestations result in significant psychological distress, clinical manifestations, and economic costs. Most human bed bug infestations are caused by the "common bed bug," *Cimex lectularius*, or the "tropical bed bug," *C. hemipterus*. Zoonotic cimicids also occasionally feed on humans. Bites are the most commonly reported manifestation of infestations, although findings may be subtle and overlooked for some time. The bugs can be submitted to the laboratory for identification, and therefore, clinical microbiologists should be familiar with their key identifying features and how they can be differentiated from similar-appearing arthropods. This review covers the biology and epidemiology of bed bugs; aspects of laboratory collection, identification, and reporting; and the clinical implications of bed bug infestations.

Introduction

"Good night, sleep tight; don't let the bed bugs bite." This version of the well-known rhyme was first published in 1896 in the book *What They Say in New England* by Clifton Johnson, but variations of this verse can be found in the literature in the decades before [1]. While a seemingly innocent bedtime rhyme, it reflects the reality of life in colonial New England, in which residents went to bed hoping not to be bitten by these blood-sucking pests while they were sleeping. We now know that bed bugs have long been associated with human habitats, being found in references throughout history and from archaeological sites dating back 3,500 years [2]. Bed bugs were thought to have spread throughout Asia and Europe in the early centuries of the Common Era, and later traveled to the Americas aboard ships of early European sailors [3]. By the 1900s, bed bugs were estimated to be in 1/3 of the dwellings in European cities and disproportionately affected those living in poor, crowded neighborhoods. While bed bugs do not serve as vectors of disease, their bites and household infestations result in psychological distress, a range of unpleasant clinical manifestations, property loss, and other substantial economic costs [4-6]. It was only with the widespread household use of dichloro-diphenyl-trichloroethane (DDT) and other potent long-lasting pesticides throughout the 1940s to 1960s that the prevalence of bed bug infestations significantly decreased worldwide [3].

Unfortunately, the world is now experiencing a major resurgence in bed bug infestations, with an explosion of reports beginning around the turn of the century [4, 7]. Although the exact cause of this resurgence is unknown, it is thought to be due to multiple factors, including widespread resistance to commonly used pesticides, increased domestic and international travel, and the decline in public health pest control programs that occurred in the latter half of the 1900s [8].

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Bed bugs can be submitted to the clinical laboratory for identification, and thus, clinical microbiologists should be familiar with their key morphologic features and how they can be differentiated from similar-appearing arthropods. Accurate identification is necessary for determining the cause of a patient's clinical manifestations and is also used to guide control efforts. This review addresses the aspects of laboratory collection, identification, and reporting of bed bugs, as well as their biology and epidemiology and the clinical implications associated with infestations.

Species Implicated in Human Infestations

Bed bugs are obligatory hematophagous (blood-feeding) insects in the family Cimicidae of the order Hemiptera (the "true bugs"). Most human infestations with bed bugs are caused by the "common bed bug," *Cimex lectularius*, or the "tropical bed bug," *C. hemipterus*. *C. lectularius* (from the Latin *cimex*, bug, and *lectularius*, couch or bed) has a cosmopolitan distribution and feeds on humans, bats, and birds. Bed bugs probably originated as a bat parasite and adapted to humans very early on, possibly when humans were still cave dwellers [9]. *C. hemipterus* (Latin *hemipterus*, half winged) also feeds on bats and birds, in addition to humans, but have a more tropical and subtropical distribution, primarily limited to within 30° north and south of the equator [10] (see "Epidemiology of *C. lectularius* and *C. hemipterus*" below).

In addition to *C. hemipterus* and *C. lectularius*, a few other members of the Cimicidae (cimicids) have been documented to feed on humans. Most of these zoonotic cimicids are parasites of bats or birds but will feed on humans in the absence of their natural hosts or when humans live in close proximity to, or have frequent contact with, the natural host (such as poultry farmers or when human habitations become colonized by anthropophilic bats and birds). Some examples are the bat bugs *C. pipistrelli* in Europe, *C. pilosellus* and *C. adjunctus* in North America [11,12], and *Leptocimex boueti* in Africa [13] and bird parasites, such as the "Mexican chicken bug," *Haematosiphon inodora*; the "swallow bug," *Oeciacus vicarious*; the "chimney swift bug," *Comexopsis nyctalis*; and the "Colorado bed bug," *Hesperocimex coloradensis*, in North America [12].

Biology and Life Cycle

Like all members of the order Hemiptera, bed bugs are hemimetabolous, meaning that immature stages (nymphs) resemble smaller versions of the adult and there is no dormant stage (pupa) between immature stages and adults. All bed bugs that have been implicated in human infestations have seven developmental stages: egg, five nymphal instars, and adult [4], with the exception of *H. inodora*, which has only four nymphal instars [9] (Fig. 1). All nymphal instars and adults of both sexes require a blood meal [4].

The duration of the life cycle of beg bugs is variable based on temperature and humidity. Under average conditions in a controlled

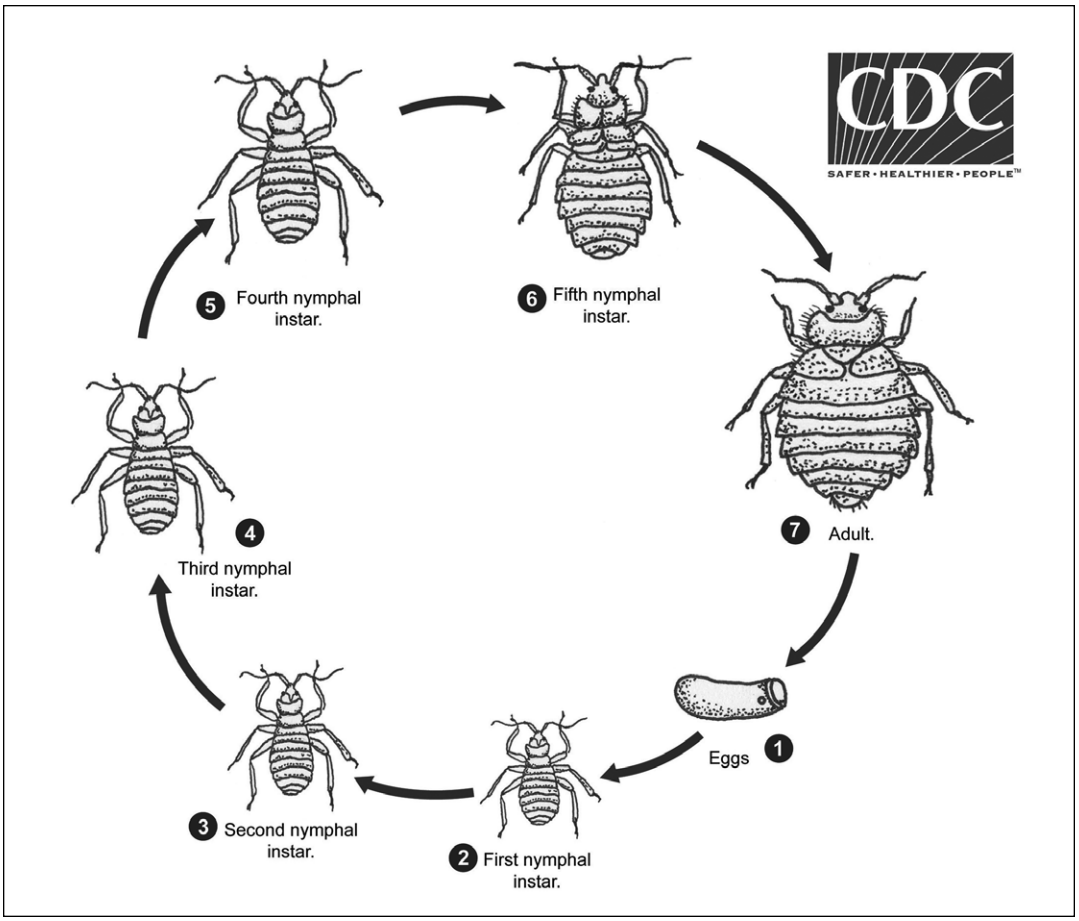

Figure 1. Life cycle of bed bugs. (Image courtesy of the CDC-DPDx.)

environment (such as in a home or hotel), eggs take 1 to 2 weeks to hatch and then about two months for nymphs to become adults [14]. Adults usually live up to about 4.5 months [14], but under cooler conditions, a well-fed adult can live for up to one year or so [15].

Bed bugs are primarily nocturnal feeders, while spending the day hidden away from direct light in secluded areas called harborage areas. The peak feeding time is between 1 and 5 AM [4]. They usually spend about 5 to 15 minutes feeding and feed once every few days based on host availability, returning to their harborage areas, where molting, breeding, and oviposition take place. Bed bugs are positively thigmotactic (seeking contact with objects) and specifically prefer habitats where they can be in contact with rough substrates. In cases of heavy infestations, large quantities of bugs congregate together, forming brood centers where their empty egg shells, nymphal exuviae (shed cuticle), and feces accumulate [9].

It is still not completely understood how bed bugs find a host. Several external factors may play a role, including light, temperature, and host stimuli, such as breath or carbon dioxide production. Under experimental conditions, bed bugs seemed less likely to leave harborage areas in the absence of host stimuli, such as breath [16]. When bed bugs do hone in on a host stimulus, the pathway to the host is not necessarily a direct line, and the insects exhibit stop-and-start searching [16]. In human habitations, where people tend to return to the same place to sleep on a regular basis, harborage areas are likely to occur within close proximity, so host stimuli can be reliably and regularly detected. It has also been proposed that color could influence where bed bugs form harborage areas [17]. Common locations for harborage areas in homes include under mattresses, seat cushions, and rugs.

While bed bugs do not normally attack domestic pets, such as cats and dogs, they can feed on them, and as such, pets may serve as reservoir hosts for bed bugs [18].

Epidemiology of *C. lectularius* and *C. hemipterus*

Bed bugs have been found on every continent in the world, hidden away in homes, schools, libraries, stores, offices, public transport, tropical resorts, and even research stations in Antarctica. As mentioned above, *C. lectularius* has a cosmopolitan distribution, whereas *C. hemipterus* has a more tropical and subtropical distribution. Both species have been involved in the resurgence over the past 2 decades [4], and thus, the geographic impact may be broader than if only one species was involved.

The actual nationwide prevalence of bed bug infestations is difficult to determine, as infestations are not a nationally notifiable disease in the United States, and they are not routinely monitored by other countries at a national level. However, the National Pest Management Association (NPMA) and the University of Kentucky have documented the bed bug resurgence in the United States through a series of surveys since 2010 [19] and have provided important insights into what pest control companies and their clients have encountered during the period. Their 2010 study of 521 U.S. pest control companies found that 95% of survey respondents had encountered a bed bug infestation during the past year—a marked contrast to surveys conducted prior to 2000, in which only 25% of respondents had encountered a bed bug infestation. Their accompanying survey of 429 international pest management companies found similarly high frequencies for encountering a bed bug infestation in Mexico/Central America (80%), Canada (98%), and Europe (92%) [19]. Similar findings have been reported by independent country and regional surveys [4].

Over subsequent NPMA surveys, U.S. pest control companies reported increasing incidences of bed bug infestations and noted that bed bugs were more difficult to control than infestations with ants, termites, and cockroaches [20,21]. Summer was noted to be the season for receiving frequent complaints about bed bugs, and 91% were found in single-family homes, followed by apartments/condominiums (89%), hotels/motels (68%), nursing homes (59%), daycare centers and schools (47%), and offices (46%). Interestingly, hospitals accounted for 36% of bed bug infestations reported by survey participants, and public transportation accounted for 19% [22].

More details regarding bed bug infestation rates can be found in a number of smaller regional studies. For example, a 2014 survey by the New York City Department of Health and Mental Hygiene revealed that 5.1% of all respondents had a bed bug infestation in the past 12 months, with rates as high as 12% in some areas [23]. Similarly, a survey of row homes in South Philadelphia, Pennsylvania, found that 66 of 596 residents (11.1%) reported a recent bed bug infestation [24]. The investigators were able to verify a current infestation in 15 of the 22 households (68.2%) inspected. Finally, a 2014 New Jersey study used a combination of interviews, inspections, and insect monitors to assess infestation rates in 2,372 low-income apartments across 43 buildings in four cities. Their efforts revealed an overall infestation rate of 12.3% (range, 3.5% to 29.5%) [7]. Of note, nearly half of the affected residents in the New Jersey study were unaware of the bed bug infestation in their apartment, thus highlighting the challenges faced in eliminating these pests in domestic settings.

It has long been appreciated that bed bugs do not discriminate by race, gender, or socioeconomic status [19] and readily feed on rich and poor alike. However, those with low incomes may be more likely to suffer from bed bug infestations, as they are more likely to live in overcrowded conditions that favor the spread of bed bug infestations, more likely to use second-hand furniture, and less able to afford a professional exterminator.

Clinical Relevance

Despite their sanguinivorous behavior, there is no evidence that bed bugs transmit blood-borne pathogens in real-world settings [25]. Bed bug bites are the most commonly noted sign of a bed bug infestation [4,22,26]. Bed bugs puncture the skin and draw up blood using a fine, needle-like stylet [4]. While feeding, bed bugs inject saliva containing anticoagulants and other proteins, which trigger a host inflammatory response in some individuals. However, the reaction to bed bug bites varies significantly. A metanalysis of the literature published between 1960 and October 2008 found that the most common cutaneous finding was a subtle

punctum at the bite site, with little to no surrounding erythema [26]. This lack of obvious findings may explain why some infestations initially go unnoticed. The finding that most commonly prompted individuals to seek medical care was the presence of more obvious bites in the form of pruritic, erythematous, maculopapular cutaneous lesions measuring 2 to 5 mm in diameter [26] (Fig. 2). The extent of pruritus and erythema was noted to increase with repeated bites in some individuals, while the reaction time decreased significantly. Occasionally, more severe complex reactions were also noted, such as bullae and secondary impetigo [26]. These clinical findings were reflected in a recent study of 706 adult patients presenting to an emergency department in Cleveland, Ohio, for any medical reason, of which 169 (24%) reported a past or current bed bug infestation and 253 (37%) reported a history of being fed on by a bed bug [27]. Of the patients with a history of bed bug feeding, 68% reported an associated pruritic reaction and 24% reported associated blistering lesions. Bed bug bites are commonly seen in clusters or linear arrangements, and bites are classically described as being in groups of three (referred to as "breakfast, lunch, and dinner" bites). However, this has been recently challenged by several authors who have noted singular to widespread bites without clear groupings of three [4]. The lesions associated with the bites can take days to weeks to resolve, depending on the severity of the cutaneous reaction [4].

In addition to cutaneous reactions, systemic allergic reactions, such as urticaria, angioedema, hypotension, and even anaphylaxis, may rarely be noted. This appears to reflect the host immunological response to bed bug salivary proteins, such as nitrophorin [26] and a 40-kDa apyrase-like nucleotide binding enzyme. Finally, there have been a number of indirect impacts of bed bug infestations, including mental health impacts (e.g., fatigue, anxiety, shame, and distress) and reactions to chemical control agents [4].

Bed bug bites can be challenging to diagnose clinically, given their non-specific and variable nature [4]. Therefore, a definitive diagnosis relies on identification of the insects in the patient's environment and, occasionally, on the patients themselves. Treatment of bites is generally with topical over-the-counter or prescription anesthetics and corticosteroids. Topical or systemic antibiotics may also be indicated in cases of bacterial superinfection. Systemic inflammatory reactions are treated with antihistamines, corticosteroids, and/or epinephrine as indicated [26].

Control

Bed bug infestations can be very challenging to eradicate due to their resistance to multiple commonly used insecticides and their cryptic nature [4]. For these reasons, evaluation, identification, and eradication of infestations are best undertaken by an experienced pest control expert [4]. In brief, the control process begins with positive identification of the infestation, followed by the application of insecticides and nonchemical control options as appropriate. Subsequent evaluation and risk management procedures (i.e., those designed to prevent reintroduction of the bugs) are key components of the success of the eradication efforts.

Figure 2. Characteristic bed bug bites. Although they can be difficult to differentiate from the bites of other arthropods, they are generally pruritic and seen in a linear or clustered arrangement. (Image courtesy of the Mayo Foundation for Medical Education and Research.)

Laboratory Collection, Identification, and Reporting

Specimen collection and handling

Bed bugs and insects suspected to be bed bugs should be submitted to the diagnostic laboratory in a liquid preservative, such as ethanol, isopropanol, or 10% formalin (e.g., that used for ova and parasite examinations) to avoid desiccation and subsequent alteration of important diagnostic morphologic features [28]. In addition, these chemical preservatives kill blood-borne pathogens associated with the gut contents of the bug(s).

Morphologic features of adults and nymphs

Adult bed bugs have most of the inherent characteristics of members of the order Hemiptera. They possess three pairs of legs, one pair of four-segmented antennae, and two compound eyes; the mouthparts are modified into a beak for sucking blood (Table 1 and Fig. 3). Adult bed bugs are ovoid to elongate and dorsoventrally flattened and on average measure 4.0 to 5.0 mm long (up to 10.0 mm long after a blood meal). They are golden brown to dark red-brown in color; younger nymphs may be pale straw colored [28,29].

Grossly, bed bugs are divided into three distinct body regions: the head, the prothorax, and the remainder of the body (which includes the middle and hind thoracic segments and the abdomen). The head possesses the bulbous, multi-faceted eyes. Unlike kissing bugs (the other medically important group of hemipterans), bed bugs do not possess ocelli (simple eyes usually located behind the compound eyes). The front of the facial area (clypeus) is extended into a semielliptical projection. The beak is held under the head and body when not feeding.

The prothorax possesses the first pair of legs. The dorsal surface of the prothorax (pronotum) is a single plate that is laterally expanded (explanate) and contains a lateral row of hairs (setae). The length of the setae along the edge of the pronotum can be diagnostically helpful. The remainder of the body contains the

Table 1. Morphologic comparison of bed bugs with other medically important arthropods submitted to the diagnostic laboratory.

Feature	Value							
	Bed bugs (Cimicidae)	**Kissing bugs (Reduviidae)**	**Hard ticks (Ixodidae)**	**Soft ticks (Argasidae)**	***Sarcoptes scabiei***	***Demodex* spp.**	**Fleas (Siphonaptera)**	**Lice (*Pediculus*, *Pthirus*)**
Size (microscopic or macroscopic)	Macroscopic	Macroscopic	Macroscopic	Macroscopic	Microscopic	Microscopic	Macroscopic	Macroscopic
No. of body regions	3	3	2	1	2	2	3	3
Eyes present	Yes	Yes	Sometimes	No	No	No	Sometimes	Yes
Antennae present	Yes	Yes	No	No	No	No	Yes	Yes
No. of legs	6	6	8 (larvae have 6)	8 (larvae have 6)	8 (larvae have 6)	8 (larvae have 6)	6	6
Functional wings	No	Yes (adults only)	No	No	No	No	No	No
Other features	Hemelytral pads in place of functional wings; mouthparts prolonged into beak	Large insects with functional wings as adults; mouthparts prolonged into beak	Dorsal shield (scutum) present; mouthparts extended anteriorly (prognathous)	Flat, ovoid body; mouthparts hidden from above	Microscopic, round to ovoid body, long filamentous setae at end of legs	Microscopic, slender body; terminal part of body modified into elongate opisthosoma	Laterally compressed; legs modified for long-distance jumping	Mouthparts not extended into a beak; legs with raptorial claws adapted for grasping hairs

middle and terminal thoracic segments (mesothorax and metathorax, respectively), each possessing a pair of legs, and the abdomen. Bed bugs do not possess functional wings and have lost the ability to fly. The forewings have been reduced to small pads (hemelytral pads), and there is no trace of hindwings. The abdomen is exposed and consists of 11 segments [9].

The nymphs of bed bugs are very similar to the adults but are smaller, lack hemelytral pads, and have ecdysial lines running along the back of the head and down the middle of the thorax. The ecdysial lines are the point at which the old cuticle separates during the start of molting [9].

Identification of the species of cimicids reported from humans

Features for identifying cimicids to the genus or species level include the relative lengths of the antennal segments, the length of the beak, and the length of the setae on the edge of the pronotum, as well as less obvious features of the head, pronotum, and genitalia. Figure 4 shows a key to the species of cimicids associated with human infestations. For the most part, identification of cimicids to the genus or species level is not needed for clinical management of the patient, but there may be times when it is beneficial to at least separate *C. lectularius* and *C. hemipterus* from the zoonotic species (see "Reporting" below).

Reporting

Reporting of bed bugs, as with other arthropods submitted to the diagnostic laboratory, should be to the level that is most important for clinical management of a patient or potential control measures [28]. The vast majority of cimicids submitted to the diagnostic laboratory are *C. lectularius* or perhaps *C. hemipterus*; very rarely are bat and bird bugs submitted for identification. In most instances, reporting as "bed bug" or "*Cimex* species" is sufficient. However, it would be beneficial to make some distinction between the human bed bugs and zoonotic species, as it could have implications for whether control measures are initiated in the household of the

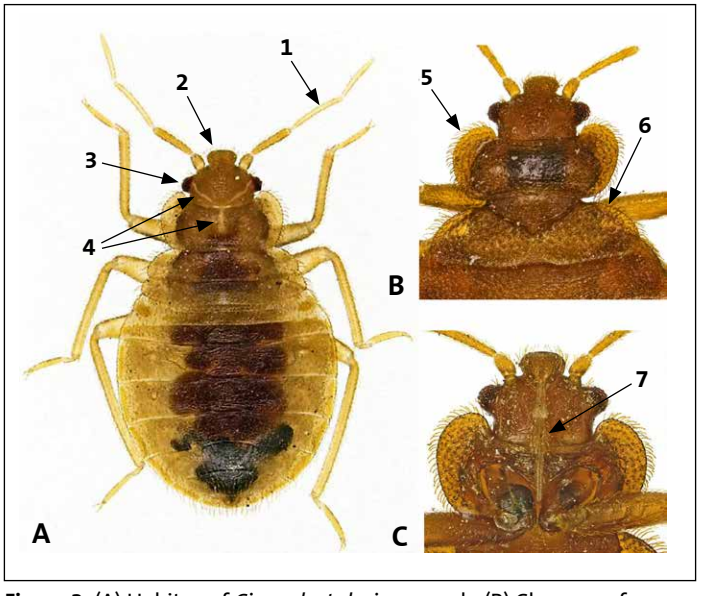

Figure 3. (A) Habitus of *Cimex lectularius* nymph. (B) Close-up of head and thorax of adult *C. lectularius*. (C) Ventral view of head and prothorax of adult *C. lectularius*. (1) Antenna, (2) clypeus, (3) eye, (4) ecdysial lines, (5) pronotum, (6) hemelytral pad, and (7) beak. (Images courtesy of Salvador Vitanza, Ph.D.)

patient or at a care facility, such as a hospital or nursing home. Infestations of the zoonotic species are usually short-lived, so control measures are usually not implemented except perhaps for management or control of the natural host. Ultimately, the responsibility for how far a bed bug or related arthropod is reported is up to the Medical Director [28].

References

[1] Johnson C. What they say in New England; a book of signs, sayings, and superstitions. Boston: Lee and Shepard; 1896.

[2] Panagiotakopulu E, Buckland P. *Cimex lectularius L.*, the common bed bug from Pharaonic Egypt. Antiquity 1999;73:908-11.

[3] Potter MF. The History of bed bug management – with lessons from the past. Am Entomol 2011;57:14-25.

[4] Doggett SL. Bed bugs: clinical relevance and control options. Clin Microbiol Rev 2012;25:164-92.

[5] Scarpino SV, Althouse BM. Uncovering the hidden cost of bed bugs. Proc Natl Acad Sci USA 2019;116:7160-2.

[6] Xie S. Dynamics of bed bug infestations and control under disclosure policies. Proc Natl Acad Sci USA 2019;116:6473-81.

[7] Wang C. Bed bugs: prevalence in low-income communities, resident's reactions, and implementation of a low-cost inspection protocol. J Med Entomol 2016;53:639-46.

[8] Joint statement on bed bug control in the United States from the U.S. Centers for Disease Control and Prevention (CDC) and the U.S. Environmental Protection Agency (EPA). 2010. Available from: https://stacks.cdc.gov/view/cdc/21750 [accessed 12 April 2020].

[9] Usinger RL. Monograph of the Cimicidae (Hemipera - Heteroptera) Thomas Say Publications in Entomology, vol. VII. College Park, Maryland: Entomological Society of America; 1966.

[10] Campbell BE. Recent documentation of the tropical bed bug (Hemiptera: Cimicidae) in Florida since the common bed bug resurgence. Florida Entomol 2016;99:549-53.

[11] Goddard J, Baker GT, Ferrari FG, Ferrari C. Bed bugs (*Cimex lectularius*) and bat bugs (several *Cimex* species): a confusing issue. Outlooks Pest Manag 2012;23:125-7.

[12] Mullen GR, Durden LA. Medical and veterinary entomology. 3rd ed. Cambridge, MA; Elsevier; 2019, p. 792.

[13] Miller D. Bed bugs (Hemiptera: Cimicidae: *Cimex* spp.) In Capinera JL, ed. Encyclopedia of entomology Dordrecht: Springer Netherlands; 2008, p. 405-17.

[14] Busvine JR. Insects and hygiene: the biology and control of insect pests of medical and domestic importance. 3d ed. London; New York: Chapman and Hall; 1980, p. 568.

[15] Omori N. Comparative studies on the ecology and physiology of common and tropical bed bugs, with special references to the reaction to temperature and moisture. J Formosan Med Assoc 1941;60:555-729.

[16] Suchy JT, Lewis VR. Host-seeking behavior in the bed bug, *Cimex lectularius*. Insects 2011;2:22-35.

[17] McNeill CA. Behavioral responses of nymph and adult *Cimex lectularius* (Hemiptera: Cimicidae) to colored harborages. J Med Entomol 2016;53:760-9.

[18] AMVA. Bed bugs and pets FAQ. 2012. Available from: https://www.avma.org/resources/pet-owners/petcare/bed-bugs-and-pets-faq [accessed 31 December 2019].

[19] Potter MF, Rosenberg B, Henricken M. Bugs without borders – executive summary: defining global bed bug resurgence. National Pest Manag Assoc; 2010; p. 5.

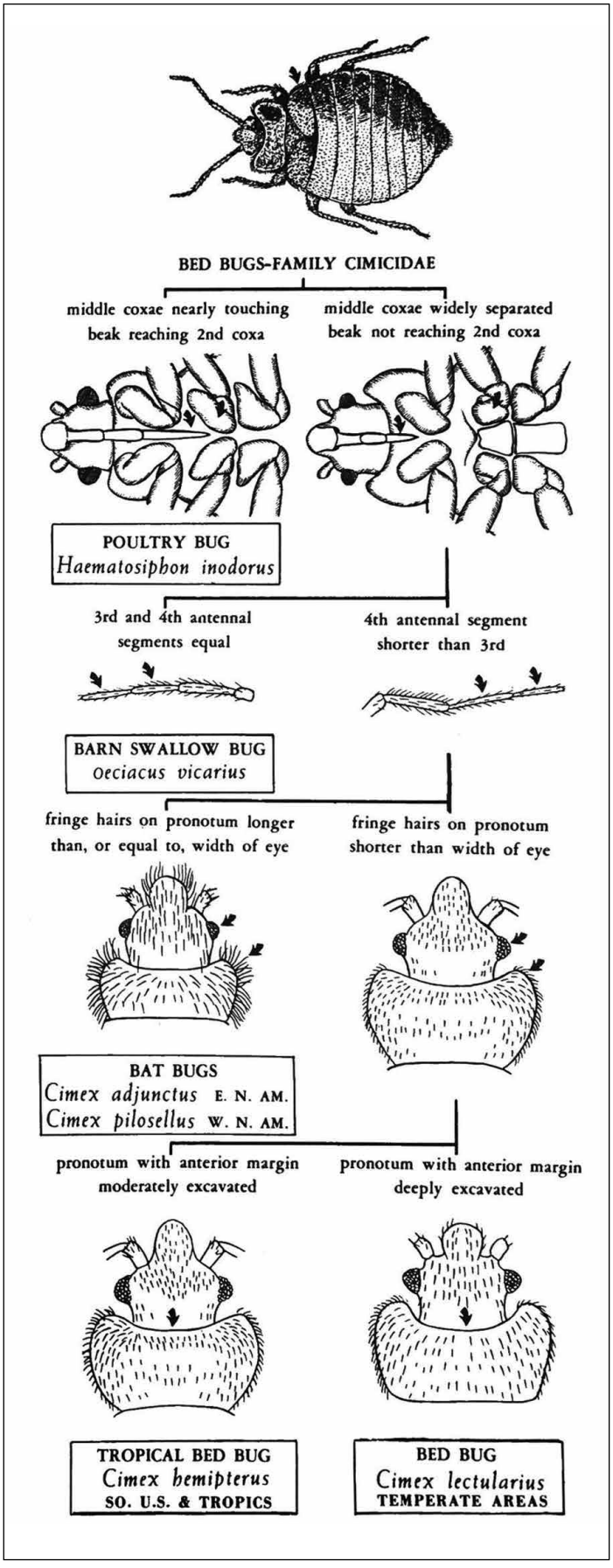

Figure 4. Key to members of the family Cimicidae associated with human infestations. (Image courtesy of the CDC-DPDx.)

[20] Potter MF, Haynes KF, Fredericks J, Henricksen M. Bed bug nation: are we making any progress. In Pestworld; National Pest Management Association, 2013.

[21] Potter MF, Haynes KF, Fredericks J. Bed bugs across America: the 2015 Bugs Without Borders Survey. In Pestworld; National Pest Management Association; 2015, p. 44.

[22] Bed bug facts and statistics. 2018. Available from: https://www.pestworld.org/all-things-bed-bugs/bed-bug-facts-statistics/ [accessed April 13, 2020].

[23] Community Health Survey Public Use Data. 2014. Available from: https://www1.nyc.gov/site/doh/data/data-sets/community-health-survey-public-use-data.page [accessed April 21, 2020].

[24] Wu Y. A door-to-door survey of bed bug (*Cimex lectularius*) infestations in row homes in Philadelphia, Pennsylvania. Am J Trop Med Hyg 2014;91:206-10.

[25] Lai O. Bed bugs and possible transmission of human pathogens: a systematic review. Arch Dermatol Res 2016;308:531-8.

[26] Goddard J, deShazo R. Bed bugs (*Cimex lectularius*) and clinical consequences of their bites. JAMA 2009;301:1358-66.

[27] Sheele JM. Cimicosis in persons previously fed upon by bed bugs. Cureus 2019;11:e5941.

[28] Mathison BA, Pritt BS. Laboratory identification of arthropod ectoparasites. Clin Microbiol Rev 2014;27:48-67.

[29. Mathison BA, Pritt BS. Arthropod benchtop reference guide. Northfield, IL: Coll Am Pathol 2015, p. 82.