
CME Review article

Supported by a grant from AstraZeneca LP

Allergic reactions to *Triatoma* bites

John E. Moffitt, MD*; Daniel Venarske, MD*; Jerome Goddard, PhD†; Anne B. Yates, MD*; and Richard D. deShazo, MD*

Background: *Triatoma* bugs are best known in the medical community as vectors of trypanosomiasis (Chagas disease). However, bites of *Triatoma* bugs are a cause of local cutaneous reactions and anaphylaxis, mainly in the western and southwestern United States. The reactions typically occur at night during sleep, and the bite may not be recognized. There is continuing public interest in medical complications of bites of these bugs, although the scope of the problem remains undefined.

Objective: To review the relevant medical literature, identify present knowledge, and determine future research goals for allergy to *Triatoma*.

Data Sources: Computerized databases were used to search the medical literature for articles in the English language on *Triatoma* bites, allergy and entomology, and Chagas disease.

Study Selection: Almost all identified articles on *Triatoma* allergy were used. Only selected articles on *Triatoma* bites and entomology were pertinent to the objectives. Articles on Chagas disease were limited to cases in the United States.

Results: Bites of *Triatoma* bugs have been known to cause anaphylaxis for more than a century. These insects inhabit a large area of the United States, but to date most reports of allergic reactions to their bites have originated in the West and Southwest. The reactions typically occur at night during sleep following a bite on uncovered skin and may be unrecognized. Procalin has been identified as the major salivary allergen of *Triatoma protracta* and was recently cloned and expressed through recombinant technique. Allergenic reactivity has been demonstrated to salivary gland extracts of 2 species. The extracts of these 2 species have not shown immunologic cross-reactivity. Immunotherapy using a salivary gland extract appeared to be beneficial in a small number of patients; however, no commercial testing or treatment allergen is available.

Conclusions: *Triatoma* bites appear to be an important cause of anaphylaxis, especially in the western and southwestern United States. Because exposure to these insects often occurs during sleep, the incidence of allergic reactions to them is unclear. An epidemiologic study should be performed to determine the incidence, prevalence, and range of allergic responses to the bites of these insects. The lack of commercial antigen limits diagnostic and treatment capabilities. The development of an allergen under the Orphan Drug Act should be encouraged.

Ann Allergy Asthma Immunol. 2003;91:122–128.

INTRODUCTION

Triatoma, a genus of kissing or conenose bugs, have their greatest impact on human disease by serving as vectors of Chagas disease. In addition, *Triatoma* bites have been known to cause allergic reactions since 1894¹ (Fig 1). Although much less is known about insect bite allergy than Hymenoptera sting allergy, insect bites are also an important cause of anaphylaxis. Allergic reactions have been reported following many different types of arthropod bites, primarily *Triatoma*, flies, or mosquitoes.^{2,3} Several different *Triatoma* species are present in the United States, and collectively they occupy a large domain that stretches from the West Coast eastward into the southeastern United States^{4,5} (Fig 2). Allergic reactions are reported most commonly in the western portion of this

domain. Because the *Triatoma* bite is usually painless and inflicted during sleep, the person may not be aware of the bite, and resulting allergic reactions may not be diagnosed or mistakenly attributed to other causes.^{3,5}

This study was undertaken to review the relevant medical literature, identify present knowledge, and determine future research goals for allergy to *Triatoma*. Computerized databases were used to search the medical literature for articles in the English language on *Triatoma* bites, allergy and entomology, and Chagas disease. Almost all identified articles on *Triatoma* allergy were used. Only selected articles on *Triatoma* bites and entomology were pertinent to the objectives. Articles on Chagas disease were limited to cases in the United States.

CLASSIFICATION AND BIOLOGY OF TRIATOMA

Kissing bugs belong to the insect family Reduviidae, sometimes called *reduvid bugs*, and specifically to the subfamily Triatominae (Fig 3). Within this subfamily, some but not all species fall under the genus *Triatoma*. Triatomines may also be in other genera.

* Departments of Pediatrics and Medicine, University of Mississippi Medical Center, Jackson, Mississippi.

† Mississippi Department of Health, Jackson, Mississippi.

Received for publication June 10, 2002.

Accepted for publication in revised form November 22, 2002.



Figure 1. *Triatoma sanguisuga*. Photograph courtesy of the Centers for Disease Control and Prevention, Atlanta, Georgia.

There are at least 10 *Triatoma* species found in the United States, but only approximately 6 of these are commonly encountered (Table 1).^{4,6} Allergic reactions have been reported after bites by 5 species (*Triatoma protracta*, *Triatoma gerstaeckeri*, *Triatoma sanguisuga*, *Triatoma rubida*, and *Triatoma rubrofasciata*).⁷ *T. protracta* and *T. rubida* are the species most often reported to cause allergic reactions in California and Arizona, respectively.^{3,8,9}

Triatoma bugs feed on blood meals of vertebrate hosts, such as bats, other small and medium-sized mammals, birds, and humans.¹⁰ Kissing bugs proceed from the egg stage, through 5 nymphal stages, and eventually to adulthood. All stages of nymphs and both sexes of adults must take a blood meal to survive. Most species require approximately 5 to 12 months to complete their development, depending on temperature and availability of blood meals.⁶

The pests are often found in association with their host nests or caves, rodent burrows, or human houses. For example, *T. protracta* are often found in wood rat nests. Bugs periodically fly away from the nests of their hosts in nocturnal cyclical flights and may be attracted to lights at dwellings, subsequently gain entrance, and try to feed. Species that are able to colonize homes usually do so in substandard structures with cracks and crevices, mud walls, thatch roofs, and the like.^{3,6,7,10}

Domestic and peridomestic kissing bug species found in Mexico, Central America, and South America colonize cracks and crevices inside homes and feed on human inhabitants at will. Since kissing bugs are nocturnal insects, they are seldom observed during daylight hours. Feeding occurs



Figure 2. Approximate US distribution of 5 *Triatoma* species reported to cause allergic reaction.

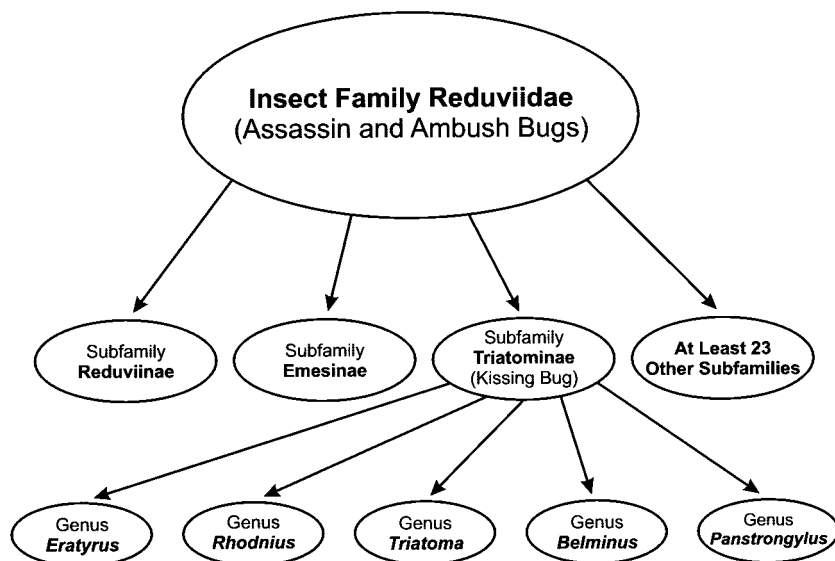


Figure 3. Classification of insects in the family Reduviidae.

almost exclusively at night and may take more than a half hour to complete. Adults are capable of ingesting 2 to 4 times their body weight in blood. During or soon after feeding, the bugs begin to defecate, voiding excess water, uric acid, and hemoglobin from the undigested portion of the previous blood meal on the skin and into the wound of the host.^{6,7,10}

EPIDEMIOLOGY

The prevalence and incidence of kissing bug sensitization and clinical allergy are unknown. It probably varies greatly, depending on the area of the country. Although kissing bugs are found throughout a large area of the United States, allergy to *Triatoma* bites is more commonly reported in the West and Southwest. Whether this is due to species differences in allergenicity, heavier infestation, increased numbers of human bites, reporting bias, or other factors is unknown. The authors are aware of some patients with suspected allergic reactions to *Triatoma* in the southeastern United States as well. Although all reports of allergic reactions to date have been to *Triatoma* species, other members of the kissing bug family have the potential to produce allergic bite reactions. In one highly endemic area of Santa Barbara County, California, the prevalence of *Triatoma* allergy as defined by a history of allergic bite reaction and elevated serum IgE levels to *T. protracta* salivary extract by radioimmunoassay (RIA) among 120 local inhabitants was found to be 6.7%.⁹ As the human population expands into the *Triatoma* habitat, allergic reactions to *Triatoma* bites may become a more common problem.

REACTIONS TO TRIATOMA BITES

The nocturnal bite occurs on uncovered skin and is usually painless. Most people who are bitten experience no reaction. Although the bite is not usually noticed, it leaves a small punctum without surrounding erythema.^{3,5,8,11} Several types

of local reactions have been reported to include puncti, papules, vesicles or bullae, cellulitis, and urticaria.

Patients may develop delayed local reactions at the site of bites, which have been described as urticarial or cellullitic in appearance. Lesions may be papular or similar to that of other insect bites or may consist of groups of small vesicles several centimeters in diameter surrounding an erythematous and edematous wound.¹² Lymphangitis and lymphadenitis may be associated with large urticarial lesions that range in size from 10 to 15 cm in diameter or with hemorrhagic, bullous lesions most common on the hands or feet.¹² These various lesions remain visible from 3 days up to 1 week.^{4,5,8}

Anaphylactic reactions after bites typically awaken the patient from sleep with itching, burning, or respiratory symptoms associated with the typical symptoms of anaphylaxis.^{3,4,5,11} Only a few reports provide information about the clinical features exhibited by patients who have experienced anaphylactic reactions (Table 2). In the largest and most detailed study, Pinnas et al⁸ described generalized cutaneous symptoms, such as urticaria, angioedema, flushing, or pruritus, in 32 patients. Gastrointestinal symptoms, such as nausea, vomiting, diarrhea, or abdominal cramps, occurred in 13 patients; respiratory symptoms, such as wheezing, dyspnea, and laryngeal edema, in 11 patients; and syncope or hypotension in 11 patients. Vaginal bleeding and abdominal pain have been reported to occur with several episodes of anaphylaxis due to *Triatoma* bites and may be unique features of anaphylaxis to bites of these insects.^{3,5,8,13}

TRIATOMA ALLERGENS

Salivary fluid and structures of *Triatoma* possess several proteins that could be potential allergens. Six different esterases have been found in the hemolymph of *Triatoma infestans*.¹⁴ Marshall and Street³ and Rohr et al⁴ described methods

Table 1. Ten *Triatoma* Species Found in the United States

<i>Triatoma</i> species	Probable range
<i>Triatoma gerstaeckeri</i> *	New Mexico, Texas
<i>Triatoma incassata</i>	Arizona
<i>Triatoma indictiva</i>	Arizona, New Mexico, Texas
<i>Triatoma lecticularia</i> *	Arizona, California, Florida, Georgia, Illinois, Kansas, Louisiana, Maryland, Missouri, New Mexico, North Carolina, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas
<i>Triatoma neotomae</i>	Arizona, California, New Mexico, Texas
<i>Triatoma protracta</i> *	Arizona, California, Colorado, Nevada, New Mexico, Texas, Utah
<i>Triatoma recurva</i> *	Arizona
<i>Triatoma rubida</i> *	Arizona, California, New Mexico, Texas
<i>Triatoma rubrofasciata</i>	Florida
<i>Triatoma sanguisuga</i> *	Alabama, Arizona, Arkansas, Florida, Georgia, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Ohio, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas, Virginia

* Most common species.

to obtain an extract of dissected salivary glands from *T. protracta* in 1982 and 1984. In 1982, IgE-mediated hypersensitivity was supported as the cause of anaphylaxis in a single patient who demonstrated a positive skin test result and binding of serum by RIA to salivary gland extract. The patient's serum also supported a positive Prausnitz-Kustner reaction to this material. Then, Rohr et al⁴ used salivary gland extract to perform IgE RIAs on serum samples from 5 patients with histories of anaphylactic reactions to *Triatoma*. These patients' sera bound to this material at 200% to 400% greater than control serum. All 5 patients demonstrated positive intradermal skin test results to salivary gland extract. In contrast, only 2 of 71 controls had positive skin test results.

In another study, Marshall et al⁹ reported that 17 of 20 individuals known to be allergic to *Triatoma* had elevated IgE RIA results to salivary gland extract from *T. protracta*. They also found the prevalence of *Triatoma* allergy as defined by elevated IgE levels to *Triatoma* salivary gland extract by RIA and history of a *Triatoma* bite reaction to be 6.7% (8 of 120) in inhabitants of a heavily infested area of southern California; only one subject had a positive RIA result but no history of a reaction to a *Triatoma* bite. The clinical significance of asymptomatic sensitization is unknown. Hymenoptera venom asymptomatic sensitivity carries a modest risk of subsequent anaphylactic reactions.¹⁵ In a Brazilian study, Nascimento et al¹⁶ found that many Chagas disease patients and controls living in areas infested by *T. infestans* had detectable IgG antibodies against salivary gland proteins from that species; only low levels of IgE could be detected. This may explain why there are not frequent reports of allergic reactions from these areas.

Pinnas et al⁸ analyzed serum samples from 38 patients with histories of allergic reactions to *T. rubida* or *T. protracta* for

the presence of IgE by radioallergosorbent test (RAST) to various extracts made from these 2 species (Table 3). In addition, they performed RAST inhibition studies to determine if immunologic cross-reactivity exists between salivary proteins of the 2 organisms. They found that sera from patients had IgE directed against saliva-containing extracts from one or the other of the 2 species but found no immunologic cross-reactivity. In 1986, Chapman et al¹⁷ reported the identification and partial purification of an 18- to 20-kDa protein from the saliva of *T. protracta* that represented 89% of the allergenic activity of the salivary fluid. Paddock et al¹⁸ recently reported the identification of procalin, the 20-kd major salivary allergen of *T. protracta* and its successful cloning and recombinant expression. Collectively, these studies support classic type I hypersensitivity as the cause of anaphylaxis to *Triatoma* bites.

MANAGEMENT OF TRIATOMA ALLERGY

Management of *Triatoma* allergy is similar to that of anaphylaxis due to bites and stings of other insects for which no immunotherapy is available.⁵ Personal protection measures from kissing bugs involve avoidance where possible and the use of pesticides approved for indoor use. For instance, sleeping in adobe or thatched-roof huts in endemic areas should be avoided and bed nets should be used when this is not possible.¹⁰ Domestic or peridomestic kissing bug species (Mexico, Central America, and South America) may be controlled by proper construction of houses, sensible selection of building materials, sealing of cracks and crevices, and precision targeting of insecticides within the home. In the United States, prevention of bug entry into homes may involve outdoor light management (ie, lights placed away from the house, shining back toward it, instead of lights attached to the house) and sealing entry points around the home. Examination of blankets and sheets to make sure that no *Triatoma* are present and removal of piles of paper, clothing, and other clutter from the bedrooms may reduce hiding places. Since *Triatoma* bugs rarely bite covered skin, wearing of pajamas with long legs and sleeves is recommended. Some also recommend the use of insect repellants on exposed skin before sleep. Nests of natural hosts (primarily rodents) around the home should be eliminated.^{3,6,7,10} Patients should have epinephrine kits available to use in case of subsequent reactions and should be advised to adopt measures to reduce the likelihood of getting additional bites. Premedication with antihistamines during the height of the bug season has also been proposed but not proven to be effective.

IMMUNOTHERAPY

The first report of the use of immunotherapy to prevent anaphylaxis was by Marshall and Street in 1982.³ A single patient allergic to *T. protracta* bites was treated with salivary gland extract. After treatment, the patient had a mild cutaneous reaction to a challenge bite. Although the challenge result was positive, immunotherapy was considered to be beneficial, since the reaction to the challenge was much less severe

Table 2. Clinical Data from Reports of Allergic Reactions to *Triatoma*

Source, y	No. of patients	Age range, y	M:F	No. of reports					
				Local cutaneous (only) reaction	Generalized cutaneous reaction*	Respiratory†	Hypotension‡	Gastrointestinal§	Other¶
Pinnas et al, ⁸ 1986	38	12–78	18:20	2	32	11	11	13	4¶
Rohr et al, ⁴ 1984	5	Unknown	Unknown		..				
Marshall and Street, ³ 1982	1	Unknown	0:1		1	0	1	1	1#
Edwards and Lynch, ⁵ 1984	1	65	0:1		1	0	1	0	0

* Urticaria, angioedema, generalized pruritus, or flushing.

† Dyspnea, bronchospasm, or laryngeal edema.

‡ Syncope or hypotension.

§ Nausea, vomiting, diarrhea, or abdominal cramps.

¶ Uterine bleeding, headache, convulsions, or dizziness.

|| Detailed clinical information is given for only 2 patients. All 5 are described as having life-threatening reactions.

Uterine bleeding or dizziness.

Table 3. Immunologic Data from Selected Reports of Patients with *Triatoma* Allergy

Source, y	Patient no.	Assays for <i>Triatoma</i> -specific IgE	Skin test results	Immunotherapy
Pinnas et al, ⁸ 1986	38	36 had positive RAST* results	Not done	Not done
Rohr et al, ⁴ 1984	5	5 had positive RIA results to <i>Triatoma protracta</i> salivary gland extract	5 had positive skin test results to <i>T. protracta</i> salivary gland extract	5/5 had negative bite challenge results after immunotherapy†
Marshall and Street, ³ 1982	1	Positive RIA results to <i>T. protracta</i> salivary gland extract	Positive skin test result and Prausnitz-Kustner reaction	Patient received immunotherapy, bite challenge resulted in mild cutaneous reaction

Abbreviations: RAST, radioallergosorbent assay; RIA, radioimmunoassay.

* A result of 1+ or greater to salivary gland extracts; 22 were positive to *Triatoma rubida* and 15 positive to *T. protracta*; 1 was positive to both.

† One of 5 patients initially had a positive bite challenge result after 14 weeks of immunotherapy but subsequently had a negative challenge result after 33 weeks of immunotherapy.

than the previous reactions the patient had experienced. Subsequently, Rohr et al⁴ used *T. protracta* salivary gland extract for immunotherapy on 5 additional patients (Table 3). Each patient had a history of a systemic allergic reaction to a *Triatoma* bite and positive skin test and RIA results to the *T. protracta* extract. The first patient underwent a *T. protracta* bite challenge at week 14 of immunotherapy and developed mild urticaria from the challenge. This patient continued to receive immunotherapy and subsequently was rechallenged at week 33 of immunotherapy. The patient had no reaction except for a local wheal and mild erythema at the bite site. The other 4 patients all underwent bite challenges between weeks 28 and 32. None had reactions more than local wheal and erythema. IgG and IgE anti-*Triatoma* levels were monitored during immunotherapy. IgG anti-*Triatoma* levels consistently rose after the fourth week and plateaued by about the 12 week of immunotherapy in all patients. The IgE responses initially increased for all patients before reaching a plateau at 12 to 14 weeks. Thus, immunotherapy with this material appeared to be protective for patients with *T. protracta* allergy.

Although results of this study are promising, no further trials of immunotherapy have been reported, and there re-

mains no commercial material for skin testing or immunotherapy to *T. protracta* or any other *Triatoma* species. No commercial product for skin testing or treatment has been available for general use in the United States for approximately 20 years.

CHAGAS DISEASE

Although extremely rare in the United States, Chagas disease is the most serious worldwide human health problem posed by kissing bugs.^{10,19–24} The parasite *Trypanosoma cruzi* of Chagas disease lives in the intestinal tract of the bugs. Several species of *Triatoma* defecate during or shortly after feeding and deposit the parasite on the host's skin. The parasite invades the host's skin when the skin is damaged due to scratching. Chagas disease begins as an acute illness with fever, lymphadenopathy, hepatosplenomegaly, cardiac dysfunction, and meningoencephalitis. Survivors of the acute phase, which carries a mortality of 2% to 10%, then enter an indolent phase in which they are asymptomatic. This phase may last for 10 to 20 years before myocardial dysfunction and enteromegaly develop.

Table 4. Clinical Characteristics of Patients Diagnosed as Having Chagas Disease in the United States^{19–24}

Clinical case*	Age at presentation	Sex	Location	Presenting symptoms	Diagnostic method	Treatment
1	10 mo	Female	Corpus Christi, TX	Fever, listlessness	Peripheral smear	Tetracycline
2	2–3 wk	Male	Bryan, TX	Not reported	Not reported	Not reported
3	56 y	Female	Lake Don Pedro, CA	Fever	Peripheral smear	Nifurtimox
4	7 mo	Male	South Texas	Fever, anorexia	PCR (post mortem)	None
5	18 mo	Male	Rutherford County, TN	Fever, irritability	PCR	Benznidazole

Abbreviation: PCR, polymerase chain reaction.

* The second case was never fully reported in the literature. The diagnosis in the fourth case was made post mortem due to a review of pathology slides for a case conference.

Although North American species of *Triatoma* have tested positive for *T. cruzi*, Chagas disease is rare in the United States. The low incidence of the disease in the United States may be due to less virulent *Trypanosoma* species, a lower density of *Triatoma* species in this country, or the 20- to 30-minute delay in defecation after eating noted in the North American *Triatoma* species.^{10,12,14}

There are at least 5 reports of Chagas disease in the United States (Table 4). Four of these 5 cases occurred in patients younger than 2 years. Patients came from both the Southwest and Southeast, areas where *Triatoma* are endemic. The diagnosis was made by a variety of methods, and the treatment method was different in each case reported.

CONCLUSION

We know little about kissing bug entomology and in particular information on behavior inside homes. Is this behavior the same as that of the bugs in Mexico and Central and South America? Knowledge of this behavior is crucial to control strategies. Are these insects killed by the usual pesticides approved for indoor use? The effectiveness of commonly used pesticides labeled for “nuisance” pests is unknown. We need more information about best pesticide practices and other control measures. We know of no currently available pesticides that have labeling for use on kissing bugs.

Triatoma allergy should be considered in unexplained causes of anaphylaxis in *Triatoma* endemic areas, particularly if reactions occur during sleep. As population growth continues to intrude on their natural habitat, the incidence of *Triatoma* allergy may increase. An epidemiologic study to determine the incidence, prevalence, and range of allergic responses to the bites of these insects should be performed. Although immunotherapy appears to have been successful in a small number of patients to reduce the risk of anaphylaxis due to bites of *T. protracta*, the lack of commercial testing materials in the United States limits diagnostic and treatment capabilities. There is a clear need for such materials. The successful identification, cloning, and recombinant expression of the major salivary allergen from *T. protracta* is a significant advance. Further development and study of *Triatoma* allergens under the Orphan Drug Act should be encouraged. Since no antigenic cross-reactivity appears to exist between *T. protracta* and *T. rubida*, separate antigens for testing

and treatment may be required. Until effective antigens are available, physicians can only provide the limited information available on insect habitat, available information on avoidance, and initiation of self-treatment if reactions occur.

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- Requests for reprints should be addressed to:
John E. Moffitt, MD
Departments of Pediatrics and Medicine
University of Mississippi Medical Center
Jackson, MS 39216
E-mail: jemoffitt@ped.umsmed.edu
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CME Examination

Moffitt JE, Venarske D, Goddard J, Yates AB, deShazo RD. 2003;91:122–128.

Self-Assessment Exam Questions

- Chagas disease results from the fact that *Trypanosoma cruzi* are resident in the *Triatoma* _____.
 - saliva
 - gastrointestinal tract
 - exoskeleton
 - reproductive tract
- Available data suggest that the *Triatoma* allergen responsible for anaphylaxis is in the insect _____.
 - feces
 - exoskeleton
 - saliva
 - reproductive tract
- Avoidance of *Triatoma* exposure includes all *except*:
 - proper sealing of cracks in homes
 - removal of clutter in bedrooms to reduce hiding places
 - attaching bright lights to the home's exterior to frighten away the bugs
 - wearing pajamas with long sleeves and long legs
- Anaphylaxis from a *Triatoma* bite typically occurs during what activity?
 - outdoor recreation
 - while eating
 - while working
 - while sleeping
- Most reports of *Triatoma* allergy in the United States originate in which area(s) of the country?
 - Midwest and Northeast
 - Northwest
 - Southeast
 - West and Southwest

Answers found on page 194.