
Anaphylaxis in emergency department patients 50 or 65 years or older

Ronna L. Campbell, MD, PhD*; John B. Hagan, MD†; James T. C. Li, MD, PhD†; Samuel C. Vukov*; Abhijit R. Kanthala, MBBS*; Vernon D. Smith, MD*; Veena Manivannan, MBBS*; M. Fernanda Bellolio, MD*; and Wyatt W. Decker, MD*

Background: Anaphylaxis is a potentially life-threatening allergic reaction commonly managed in the emergency department (ED). Data describing patients 50 or 65 years or older with anaphylaxis are limited.

Objective: To describe the presentation and management of patients with anaphylaxis who were 50 or 65 years or older and to compare these findings with those of younger patients.

Methods: A consecutive cohort study of patients presenting to an ED with approximately 80,000 visits per year was conducted. Patients who met diagnostic criteria for anaphylaxis from April 2008 to June 2010 were included. Data were collected on suspected causes, signs and symptoms, management, ED disposition, and follow-up.

Results: The study included 220 patients. Food was the most common suspected cause of anaphylaxis for patients younger than 50 (42.2%) or 65 years (38.5%) but was much less common in patients 50 (14.8%, $P < .001$) or 65 years or older (14.3%, $P = .01$). Cardiovascular symptoms were more likely to occur in older patients (≥ 50 years old, 55.6% vs 30.1%, $P < .001$; ≥ 65 years old, 64.3% vs 32.3%, $P = .002$). Patients 50 or 65 years or older were less likely to be dismissed home directly from the ED (≥ 50 years old, 35.2% vs 56.6%, $P = .006$; ≥ 65 years old, 32.1% vs 54.2%, $P = .03$) and were less likely to be prescribed self-injectable epinephrine (≥ 50 years old, 40.7% vs 63.3%, $P = .004$; ≥ 65 years old, 32.1% vs 61.5%, $P = .003$).

Conclusions: In ED patients presenting with anaphylaxis, age of 50 or 65 years or older is associated with a decreased likelihood of food-induced anaphylaxis, increased likelihood of experiencing cardiovascular symptoms, decreased dismissal to home directly from the ED, and decreased prescriptions for self-injectable epinephrine.

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INTRODUCTION

Anaphylaxis is a severe, systemic allergic reaction that is sudden in onset and potentially fatal.¹ Anaphylaxis is most commonly immediately managed in the emergency department (ED).^{2,3} Although there is no universally accepted definition of anaphylaxis, diagnostic criteria were proposed by the Second Symposium on the Definition and Management of Anaphylaxis.¹

Few data are available on characteristics and management of older patients presenting to the ED with anaphylaxis in contrast to studies of pediatric patients in which these aspects have been well described.^{3–6} The objective of this study was to determine the suspected causes, clinical features, short-term medical management, emergency department diagnosis and disposition, and subsequent outpatient management and

follow-up of patients 50 or 65 years or older who present to the ED with anaphylaxis and to identify differences when compared with patients who are younger than 50 or 65 years. Although many studies of older patients compare those younger than 65 years with those 65 years or older, we also compared patients younger than 50 years with all patients 50 years or older to determine whether the same characteristics would be found when using a younger age cutoff.

METHODS

Design and Setting

A retrospective cohort study of patients presenting to the ED of Saint Mary's Hospital was conducted. Saint Mary's Hospital is a 1,265-bed tertiary referral hospital. The ED is a 51-bed facility that provides care for more than 75,000 patients each year, most of whom come from Olmsted County and the 6 adjacent counties in southeastern Minnesota. The study was approved by the Mayo Clinic institutional review board.

Study Participants

Electronic medical records of ED patients diagnosed as having anaphylaxis, allergic reactions, insect stings, and related diagnoses from April 2008 through June 2010 were identified. Patients who met National Institutes of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network

Affiliations: * Department of Emergency Medicine, Mayo Clinic, Rochester, Minnesota; † Division of Allergic Diseases, Mayo Clinic, Rochester, Minnesota.

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(NIAID/FAAN) criteria for the diagnosis of anaphylaxis and provided research authorization were included.¹ A biphasic reaction was defined as any reaction meeting NIAID/FAAN criteria occurring after complete resolution of initial symptoms. Only the first visit for each patient during the study period was included.

Variables

Electronic medical records were reviewed by a research fellow, and 20% of cases were verified by an ED physician. Data were collected on suspected causes, timing of symptom onset, presenting signs and symptoms, self-administered medications, emergency medical services management, ED management, ED disposition, ED follow-up, and incidence of biphasic reactions using a standardized data abstraction form. Data were then entered into a SAS-DMS database.

Statistical Analyses

Statistical analysis was performed using JMP 8 software (SAS Institute Inc, Cary, North Carolina). Data analysis included descriptive statistics. Odds ratios (ORs) with 95% confidence intervals (CIs) and *P* values were determined. *P* values represent χ^2 values unless otherwise noted.

RESULTS

During the study period, a total of 224 ED patients fulfilled the NIAID/FAAN criteria for the diagnosis of anaphylaxis. Two hundred twenty patients provided research authorization and were included in the study. Table 1 lists the demographics of the sample. Overall, 58.2% of the study sample was female. Patients younger than 18 years were less likely to be female (34%, *P* = .02). Patients aged 18 to 64 years were more likely to be female (67%, *P* < .001). Patients 65 years and older tended to be more likely to be female, but the difference was not statistically significant (61%, *P* = .26). The median age of the study population was 33.6 years (interquartile range, 18.8-49.6 years). Fifty-four patients (24.5%) were older than 50 years, and 28 (12.7%) were older than 65 years. The percentage of minority patients was small, reflecting the high prevalence of whites in the community.

Table 1. Study Sample Demographics

Demographics	No. (%) of patients (N = 220)
Age, median (IQR), y	33.6 (18.8-49.6)
Age ≥50 y	54 (24.5)
Age ≥65 y	28 (12.7)
Female	128 (58.2)
Race	
White	199 (90.5)
Other	11 (0.5)
Black	5 (0.02)
Asian	3 (0.15)
Unknown	2 (0.01)

Abbreviation: IQR, interquartile range.

Suspected causes and history of asthma are listed in Table 2. The most common identifiable cause of the anaphylactic episode was medications for patients with 50 years or older (24.1%) and for patients 65 years or older (25.0%). Food was the most common cause of anaphylaxis for patients younger than 50 years (42.2%) and in patients younger than 65 years (38.5%) but was much less frequently the cause in patients 50 years or older (14.8%; OR, 0.24; 95% CI, 0.11-0.54; *P* < .001) and in patients 65 years or older (14.3%; OR, 0.27; 95% CI, 0.09-0.80; *P* = .01). Contrast had a greater likelihood of being the suspected cause in patients 50 years or older (14.8%) compared with patients younger than 50 years (3.0%; OR, 5.6; 95% CI, 1.8-17.9; *P* = .001) and in patients 65 years or older (21.4%) compared with patients younger than 65 years (3.7%; OR, 7.2; 95% CI, 2.2-23.4; *P* = .002). Patients 50 years or older were less likely to have a history of asthma (27.7% vs 11.1%; OR, 0.33; 95% CI, 0.13-0.81; *P* = .02), and patients 65 years or older had similar results (26.0% vs 7.1%; OR, 0.22; 95% CI, 0.05-0.95; *P* = .03).

The signs and symptoms of anaphylaxis are listed in Table 3. Mucocutaneous symptoms were the most common manifestations in all age groups. No significant difference was found in the overall incidence of mucocutaneous symptoms between children (patients <18 years old) and adults. Cardiovascular symptoms were more likely to occur in older patients (≥50 years old; 55.6% vs 30.1%; OR, 2.9; 95% CI, 1.5-5.5; *P* < .001; ≥65 years old; 64.3% vs 32.3%; OR, 3.8; 95% CI, 1.7-8.7; *P* = .002). Patients 65 years or older were more likely to have hypotension (21.4% vs 6.8%; OR, 3.7; 95% CI, 1.3-10.8; *P* = .02).

As indicated in Table 4, no significant differences were found in anaphylaxis management with regard to medications administered before ED arrival or during the ED visit. Overall, 54.1% of patients were diagnosed as having anaphylaxis at the time of disposition from the ED. No significant difference was found with regard to the ED diagnosis of anaphylaxis in patients 50 or 65 years or older.

Patient disposition is given in Table 4. With regard to overall ED disposition, 113 patients (51.3%) were dismissed directly home from the ED, and 67 (30.5%) were admitted to the emergency department observation unit (EDOU). After admission to the ED, 3 patients were admitted to the hospital (2 patients to the general medical department and 1 to the intensive care unit [ICU]). Eighteen patients (8.2%) were admitted to the general medical department, and 22 (10.0%) were admitted to the ICU. Patients 50 or 65 years or older were less likely to be dismissed home directly from the ED (≥50 years old; 35.2% vs 56.6%; OR, 0.42; 95% CI, 0.22-0.79; *P* = .006; ≥65 years old; 32.1% vs 54.2%; OR, 0.40; 95% CI, 0.17-0.93; *P* = .03). Patients 65 years or older were more likely to be admitted to the hospital (21.4% vs 6.3%; OR, 4.1; 95% CI, 1.4-12.0; *P* = .02) and the ICU (21.4% vs 8.3%; OR, 3.0; 95% CI, 1.1-8.5; *P* = .04).

At the time of dismissal from the ED, ED, ED, or inpatient unit (general medical department or ICU), a total of 127 patients (57.7%) were given a prescription for self-injectable

Table 2. Comparison of Suspected Causes and History of Asthma

	No. (%) of patients by age, y				P value by age, y	
	<50	≥50	<65	≥65	≥50	≥65
History of asthma	46 (27.7)	6 (11.1)	50 (26.0)	2 (7.1)	.02	.03
Suspected cause						
Food	70 (42.2)	8 (14.8)	74 (38.5)	4 (14.3)	<.001 ^a	.01 ^a
Medication	35 (21.1)	13 (24.1)	41 (21.4)	7 (25.0)		
Venom	19 (11.4)	8 (14.8)	22 (11.5)	5 (17.9)		
Latex	1 (0.6)	0	1 (0.5)	0		
Contrast	5 (3.0)	8 (14.8)	7 (3.6)	6 (21.4)	.001 ^a	.002 ^a
Other	6 (3.6)	4 (7.4)	10 (5.2)	0		
Unknown	30 (18.1)	13 (24.1)	37 (19.3)	6 (21.4)		

^a Two-tailed Fisher *P* value.

Table 3. Comparison of Presenting Signs and Symptoms

	No. (%) of patients by age, y					P values by age, y	
	<50	≥50	<65	≥65	Overall	≥50	≥65
Mucocutaneous	153 (92.2)	48 (88.9)	177 (92.2)	24 (85.7)	201 (91.4)		
Flushing	50 (30.1)	23 (42.6)	61 (31.8)	11 (39.3)	73 (33.2)		
Pruritus	81 (48.8)	26 (48.1)	97 (50.5)	10 (35.7)	108 (49.1)		
Diffuse urticaria	99 (59.6)	25 (46.3)	109 (56.8)	15 (53.6)	124 (56.4)		
Angioedema	80 (48.2)	27 (50.0)	92 (47.9)	15 (53.6)	107 (48.6)		
Gastrointestinal	63 (38.0)	19 (35.2)	72 (37.5)	10 (35.7)	82 (37.3)		
Emesis	34 (20.5)	6 (11.1)	37 (19.3)	3 (10.7)	40 (18.2)		
Abdominal pain	19 (11.4)	1 (1.9)	19 (9.9)	1 (3.6)	20 (9.1)		
Nausea	37 (22.3)	14 (25.9)	44 (22.9)	7 (25.0)	51 (23.2)		
Diarrhea	10 (6.0)	1 (1.9)	11 (5.7)	0	11 (5.0)		
Respiratory	139 (83.7)	39 (72.2)	157 (81.8)	21 (75.0)	178 (80.9)		
Cough	20 (12.0)	5 (9.3)	22 (11.5)	3 (10.7)	25 (11.4)		
Voice change	32 (19.3)	9 (16.7)	36 (18.8)	5 (17.9)	41 (18.6)		
Dyspnea	115 (69.3)	31 (57.4)	129 (67.2)	17 (60.7)	146 (66.4)		
Wheezing	43 (25.9)	11 (20.40)	48 (25.0)	6 (21.4)	54 (24.5)		
Cyanosis	4 (2.4)	1 (1.9)	5 (2.6)	0	5 (2.3)		
Stridor	7 (4.2)	1 (1.9)	8 (4.2)	0	8 (3.6)		
Hypoxemia	9 (5.4)	4 (7.4)	12 (6.3)	1 (3.6)	13 (5.9)		
Cardiovascular	50 (30.1)	30 (55.6)	62 (32.3)	18 (64.3)	64 (29.1)	<.001	.001
Hypotension	11 (6.6)	8 (14.8)	13 (6.8)	6 (21.4)	20 (9.1)	.09	.02 ^a
Chest pain	15 (9.0)	8 (14.8)	19 (9.9)	4 (14.3)	28 (12.7)		
Presyncope	23 (13.9)	13 (24.1)	28 (14.6)	8 (28.6)	37 (16.8)		
Syncope	6 (3.6)	3 (5.6)	7 (3.6)	2 (7.1)	9 (4.1)		

^a Two-tailed Fisher *P* value.

epinephrine. Among patients dismissed from the ED or EDOU, 113 (63.8%) received a prescription for self-injectable epinephrine. Among patients dismissed from an inpatient unit, 14 patients (32.6%) received a prescription for self-injectable epinephrine. Patients 50 or 65 years or older were less likely to be prescribed self-injectable epinephrine (≥50 years old; 40.7% vs 63.3%; OR, 0.40; 95% CI, 0.21-0.75; *P* = .004; ≥65 years old, 32.1% vs 61.5%; OR, 0.30; 95% CI, 0.13-0.69; *P* = .003). In addition, patients 50 or 65 years or older were less likely to have a documented previous prescription for self-injectable epinephrine (≥50 years old; 9.3% vs 30.7%; OR, 0.23; 95% CI, 0.09-0.61; *P* = .002; ≥65

years old; 3.6% vs 28.7%; OR, 0.09; 95% CI, 0.01-0.70; *P* = .004). A total of 8 patients (3.6%) had a biphasic reaction. Although all patients with a biphasic reaction were younger than 50 years, this difference did not reach statistical significance. Overall, 80 patients (36.4%) were evaluated by an allergist after their ED evaluation for anaphylaxis. No significant differences were found with regard to allergist evaluation in patients 50 or 65 years or older.

DISCUSSION

Few data are available on characteristics and management of older patients presenting to the ED with anaphylaxis. To our

Table 4. Patient Management, Diagnosis, and Follow-up

	No. (%) of respondents by age, y				P value by age, y	
	<50	≥50	<65	≥65	≥50	≥65
Treatment (self, EMS, or ED)						
Antihistamines (H ₁ and/or H ₂)	154 (92.8)	49 (90.7)	179 (93.2)	24 (85.7)		
Bronchodilators	57 (34.3)	16 (29.6)	67 (34.9)	6 (21.4)		
Steroids	136 (81.9)	47 (87.0)	161 (83.9)	21 (75.0)		
Epinephrine	79 (47.6)	24 (44.4)	94 (49.0)	9 (32.1)		.10
Diagnosis						
Anaphylaxis	85 (51.2)	34 (63.0)	104 (54.2)	15 (53.6)		
Allergic reaction	80 (48.2)	17 (31.5)	86 (44.8)	11 (39.3)	.03	
ED disposition						
ICU	13 (7.8)	9 (16.7)	16 (8.3)	6 (21.4)		.04
General medical department	11 (6.6)	7 (13.0)	12 (6.3)	6 (21.4)		.02 ^a
EDOU	48 (28.9)	19 (35.2)	60 (31.3)	7 (25.0)		
Home	94 (56.6)	19 (35.2)	104 (54.2)	9 (32.1)	.006	.023
Self-injectable epinephrine prescribed	105 (63.3)	22 (40.7)	118 (61.5)	9 (32.1)	.004	.003
Previous self-injectable epinephrine prescription	51 (30.7)	5 (9.3)	55 (28.7)	1 (3.6)	.002	.004
Biphasic reaction	8 (4.8)	0	8 (4.2)	0		
Allergist follow-up	62 (37.4)	18 (33.3)	73 (38.0)	7 (25.0)		

Abbreviations: ED, emergency department; EDOU, emergency department observation unit; EMS, emergency medical services; ICU, intensive care unit.

^a Two-tailed Fisher *P* value.

knowledge, there have been no previous studies analyzing the potential impact of older age on the suspected causes, presentations, and management of anaphylaxis in ED patients. The relative paucity of information on older patients may in part be due to the decreased incidence of anaphylaxis in this population.^{7,8} In this study, describing 220 patients presenting to a single ED, significant differences in presentation and management of anaphylaxis were found in patients 50 or 65 years or older.

Consistent with previous studies, we found that children with anaphylaxis were more likely to be male, whereas patients aged 18 to 64 years were more likely to be female.⁸ The most common identifiable cause of anaphylaxis in patients 50 or 65 years or older was medications. This is likely because older patients are more likely to be taking multiple medications and therefore are at higher risk of developing anaphylaxis secondary to medication use. Patients 50 or 65 years or older were also more likely to experience anaphylaxis secondary to intravenous contrast dye. This finding is likely secondary to the increased exposure of older patients who more frequently undergo diagnostic procedures using contrast dye in our population of ED patients because previous studies have not shown an increased susceptibility to contrast reactions in older patients.^{9,10} Patients 50 or 65 years or older were significantly less likely to have food as the suspected cause. Overall, the results presented here are consistent with the findings of Alves et al,¹¹ who found that food-related anaphylaxis became relatively less frequent with increasing age and the proportion of drug-induced anaphylaxis increased with age. Furthermore, an epidemiologic study of anaphylaxis hospitalizations in Florida demonstrated an association

between young age and increased risk of hospitalization for food-induced anaphylaxis.¹² ED patients older than 50 or 65 years were less likely to have a history of asthma. These results are consistent with the results of Webb and Lieberman,¹³ who found that atopy was associated with younger age in anaphylaxis patients presenting to an allergy-immunology practice.

In our study, cardiovascular signs and symptoms were more likely to occur in patients 50 and 65 years or older. When cardiovascular signs and symptoms were analyzed individually, patients 65 years or older were also significantly more likely to experience hypotension, and patients 50 years or older tended to have more hypotension, although the results did not reach statistical significance. The increased cardiovascular instability in older patients may be due to a decreased ability to activate compensatory mechanisms secondary to medications such as β -blockers or increased comorbidities such as peripheral vascular or coronary artery disease. In addition, the increased cardiovascular involvement may be related to the increased proportion of iatrogenic causes (medications and intravenous contrast dye) in older patients, which have been associated with increased severity of anaphylaxis.¹⁴ Despite the fact that older patients were more likely to experience hypotension, they were not more likely to receive epinephrine for management of the event. In fact, although results were not statistically significant, patients 65 years or older tended to be less likely to receive epinephrine.

Although overall only slightly more than half of the patients in this study were diagnosed as having anaphylaxis, these findings are consistent with previous ED-based studies

of anaphylaxis. The underdiagnosis of anaphylaxis in ED patients presenting with allergic reactions despite multisystem organ involvement has been recognized for more than 10 years.¹⁵ More recent studies on the ED management of acute allergic reactions have confirmed this. Clark et al^{16,17} demonstrated that 51% of patients diagnosed as having allergic reactions due to food and 31% of patients diagnosed as having insect sting allergy were, in fact, found to have had anaphylaxis. The underdiagnosis of anaphylaxis in the ED may be related to the lack of universally accepted diagnostic criteria.¹ Furthermore, some of the symptoms of anaphylaxis are vague (eg, shortness of breath, lightheadedness), and given that in many cases anaphylaxis is self-limited, signs may have resolved before presentation in the ED. These factors, combined with the lack of sensitive and specific biomarkers that are available in a timely manner, often make the ED diagnosis of anaphylaxis problematic. Measures such as testing of peak expiratory flow rates in the evaluation of shortness of breath or performing nasopharyngoscopy in the evaluation of suspected laryngeal edema may aid in more accurate diagnosis. In addition, prospective validation of the NIAID/FAAN criteria is needed for these criteria to become more widely adapted into clinical practice. Finally, further research is needed to develop sensitive and specific biomarkers that will aid in the timely and accurate diagnosis of anaphylaxis.

Patients 50 or 65 years or older were less likely to be dismissed directly from the ED, and patients 65 years or older were more likely to be admitted to the general medical department or ICU. Increased hospitalizations found here are consistent with a population-based study of patients hospitalized for anaphylaxis, which showed that the likelihood of hospitalization for anaphylaxis increased with age.¹²

Guidelines recommend that all patients with anaphylaxis secondary to an allergen that might be encountered in a nonmedical setting should carry self-injectable epinephrine and be referred to an allergist.¹ Overall, 57.7% of patients received a prescription for self-injectable epinephrine. This proportion is higher than that found in a previous population-based study² of anaphylaxis at our institution from 1990 to 2000 in which 42.6% of patients who were dismissed from the ED, EDOU, or an inpatient unit after an anaphylactic episode received a prescription for self-injectable epinephrine. Our finding that 63.8% of patients dismissed from the ED or EDOU received a prescription for self-injectable epinephrine is significantly higher than the rates of self-injectable epinephrine prescriptions found by Clark et al^{16,18} in multicenter studies of ED management of food and insect sting-induced anaphylaxis (22% and 27%, respectively). The cause of the increased rate of prescriptions for self-injectable epinephrine in this population is unknown but may reflect a trend toward increased guideline compliance secondary to the introduction of the NIAID/FAAN criteria for the diagnosis of anaphylaxis and the academic setting in which this study was conducted.¹ However, the increased rate is not due to the inclusion of patients dismissed from the inpatient setting

because we found that patients dismissed from the ED or EDOU were more likely to receive a prescription for self-injectable epinephrine than patients dismissed from an inpatient setting. As noted above, current guidelines recommend that patients with anaphylaxis secondary to an allergen that might be encountered in a nonmedical setting should carry self-injectable epinephrine. It is not clear whether those patients who are evaluated in the emergency setting after experiencing anaphylaxis secondary to an iatrogenic cause should be dismissed with a prescription for self-injectable epinephrine based on the risk of a biphasic reaction. This may be particularly true if the patient was observed in an observation setting or as an inpatient. Further studies are needed to identify those patients who have the greatest risk of experiencing a biphasic reaction, and guidelines specifically addressing this issue may be helpful.

Overall, patients 50 or 65 years or older were less likely to be prescribed self-injectable epinephrine at the time of dismissal from the ED, EDOU, or inpatient setting. This decrease in self-injectable epinephrine prescriptions in patients 50 or 65 years or older may be at least in part accounted for by the fact that these patients were more likely to have iatrogenic causes of anaphylaxis and are therefore less likely to reencounter the allergen after dismissal to home. In addition, older patients were more likely to be admitted to the hospital. Also, as noted above, admitted patients were less likely to receive a prescription for self-injectable epinephrine. Therefore, this may also partially account for the decreased in self-injectable epinephrine prescriptions in these patients. The decrease in self-injectable epinephrine prescriptions cannot be accounted for by documented previous self-injectable epinephrine prescriptions because these patients were less likely to have a documented prior prescription for self-injectable epinephrine. The fact that only slightly more than one-third of patients were evaluated by an allergist suggests underuse of this service and agrees with the findings reported in other studies.^{2,16,18}

The relatively low rate of biphasic reactions observed in this study is consistent with prior retrospective studies of anaphylaxis.¹⁹⁻²¹ No statistically significant difference was found in the incidence of biphasic reactions when patients were analyzed based on age. This finding is consistent with prior studies because the occurrence of biphasic reactions in patients older than 50 and 65 years has been documented in several studies.^{20,22,23}

The primary limitations of this study are those inherent in retrospective medical record reviews. The true number of cases of anaphylaxis from a medical record review may be underestimated or overestimated secondary to the varying quality of information in the electronic medical record. However, data on ED medical management, self-injectable epinephrine prescriptions, and disposition are all electronically captured and not dependent on physician documentation. In addition, only patients evaluated in a single tertiary care academic emergency department were included and the sample size is relatively small. Finally, based on the exploratory

nature of this study, *P* values were not corrected to account for multiple hypothesis testing; therefore, it is possible that more than 5% of the significant findings may be spurious. These limitations should be addressed in a future large, multicenter, prospective study.

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Requests for reprints should be addressed to:

Ronna L. Campbell, MD, PhD
Department of Emergency Medicine
Mayo Clinic
200 First St SW
Rochester, MN 55905
E-mail: campbell.ronna@mayo.edu