
Melaleuca tree and respiratory disease

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Background: The role of *Melaleuca quinquenervia* tree as a source of allergen(s) and respiratory irritant(s) is controversial.

Objective: Determine whether Melaleuca tree pollen or odor is medically important.

Methods: A 2-year aeroallergen survey and skin test (ST) results of 1,017 subjects were reviewed. Sixteen subjects were selected based on positive Melaleuca pollen extract (MPE) STs. Double-blind nasal challenges with MPE were performed on six subjects. Single-blind bronchial challenges with MPE were performed on four. To evaluate the irritant effect, 11 subjects received 34 different Melaleuca odor challenges (blossoms, bark, and leaves) through a closed system for up to 30 minutes. Four inhaled an odor from cajuput oil (derived from Melaleuca leaves) for 1 hour. Spirometry was performed before and after odor challenges. Radioallergosorbent test using MPE was compared with MPE STs in 15 subjects.

Results: The aeroallergens survey revealed insignificant numbers of Melaleuca pollen. Ninety-seven of 1,017 subjects were a 2+ or greater intradermal MPE ST. One of 6 double-blind nasal challenges and 1 of 4 single-blind bronchial challenges using MPE were positive in subjects with positive MPE STs. All 38 odor challenges with blossoms, bark, leaves, and cajuput oil were nonreactive. The MPE radioallergosorbent test correlated with MPE ST results.

Conclusions: The Melaleuca tree is not a significant source of aeroallergen. The Melaleuca odor is not a respiratory irritant. MPE antigen(s) has been shown to cross-react with pollen extracts from a proven aeroallergen (Bahia grass pollen) possibly explaining the few cases of positive MPE STs with positive nasal/bronchial challenges.

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INTRODUCTION

Melaleuca quinquenervia (cav.) Blake is native to Australia and has been successfully introduced into numerous countries, including the continental United States. It was brought into south Florida in the early 1900s as an ornamental tree and a potential new commercial source of wood. Because of its high density, incidence of seeding, adaptability to a variety of growth conditions, and resistance to damage by disease, insects, and fire, it spread rapidly throughout south Florida and is considered a firmly established naturalized species.¹

The Melaleuca tree was first reported as a cause of human disease in 1962.² Morton^{2,3} reported subjects who experienced respiratory symptoms after exposure to the tree, and skin irritation after contact with the bark. Other cases^{4,5} have subsequently been reported. Symptoms have been attributed to an irritant or toxic effect of the tree. However, none of these cases have been scientifically studied or properly documented, nor have the case reports been published in the medical literature.

Another name for the tree is the “punk tree” because of its obnoxious odor, and the public often blames the tree for respiratory and allergic reactions. The trees bloom several times per year, becoming covered with large white blossoms (Fig 1). It is easy for the public to believe that these blossoms are a huge source of allergenic pollens.

The present study is designed to determine whether the Melaleuca tree causes or exacerbates respiratory disease. Is Melaleuca an important aeroallergen source? Are subjects with allergic rhinitis and extrinsic asthma who are sensitive to other aeroallergens, also skin and radioallergosorbent test (RAST) sensitive to Melaleuca pollen extract (MPE)? Do Melaleuca skin test (ST)-positive subjects with allergic rhinitis and extrinsic asthma have positive bronchial and nasal challenges to MPE? Does the odor produced by Melaleuca blossoms, bark, and leaves or cajuput oil (derived from Melaleuca leaves) act as a respiratory irritant to persons with allergic rhinitis, asthma, or chronic obstructive lung disease?

MATERIALS AND METHODS

Subjects

A total of 1,017 subjects were selected from the allergy and immunology clinics associated with the University of South Florida College of Medicine, and the James A. Haley Veterans Administration Hospital, Tampa, Florida. Pregnant women, subjects with cardiac disease, and those who had previously received immunotherapy with MPE were excluded. The project was approved by the University of South Florida College of Medicine Committee on Human Subjects and the Tampa Veterans Administration Subcommittee on Human Studies. Informed consent was obtained from all subjects.

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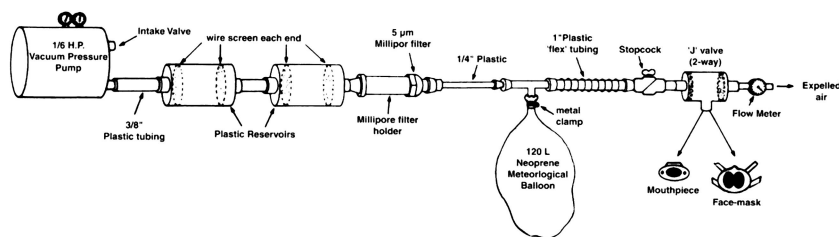


Figure 1. Schematic of odor challenge apparatus.

STs

All subjects underwent allergic evaluation that included STs (percutaneous, 1:10 weight to volume [wt/vol] and intradermal, 1:500 wt/vol) to Tampa Bay area aeroallergens (Greer Laboratories, Lenoir, NC). Before all testing, allergy medications were withheld: bronchodilators, anticholinergics, and α -adrenergic blockers for 24 hours, antihistamines (including terfenadine, the only nonsedating antihistamine available at the time of this study) for 48 hours, hydroxyzine for 96 hours, and cromolyn sodium for 2 weeks. Subjects receiving glucocorticosteroids were challenged at least 24 hours after their last dose of steroid.

New pollen extracts used for testing were made monthly. The extracts used for skin testing and challenge studies were prepared by diluting 1:10 wt/vol stock extract immediately before testing. Histamine and saline solutions were used as controls.

Percutaneous reactions were graded as follows: 1+: erythema smaller than 21 mm; 2+: erythema larger than 21 mm; 3+: wheal 3 mm greater than normal saline control and surrounding erythema; and 4+: wheal with pseudopods and surrounding erythema.

Intradermal test reactions were graded by wheal size with surrounding erythema compared with that of normal saline control: 0: 2 mm or less than control; 1+: 3 to 4 mm greater than control; 2+: 4 to 8 mm greater than control; 3+: >8 mm greater than control; and 4+: wheal with pseudopods and surrounding erythema.

Nasal Challenge (MPE)

Subjects were re-tested intradermally with a 1:500 wt/vol MPE before double-blind MPE nasal challenge. Challenge was conducted only when nasal mucous membranes in each subject were normal. Fifty microliters (two drops of 25 μ L each) of 1:1,000 wt/vol aqueous MPE was placed in one nostril, and two drops of diluent solution in the other. After 20 minutes, the presence or absence of pruritus was recorded, and each nasal cavity was examined for mucosal edema, clear rhinorrhea, mucous stranding, and pallor. Nasal tests were positive when at least three of the following changes were noted: mucosal edema, rhinorrhea, sneezing, change in the color of the mucosa, or pruritus. Higher concentrations of MPE (1:500 and 1:100 wt/vol) were tested if the initial challenge was negative.

Bronchial Challenge (MPE)

Immediately before MPE bronchial challenge, subjects were tested intradermally with 0.02 mL of incremental 10-fold dilutions of MPE (1:10³ to 1:10⁶ wt/vol) until a wheal of at least 8 mm was obtained, and this dilution was used for initial bronchial challenge. Intradermal diluent and histamine controls were done by injecting 0.02 mL of saline and histamine (histamine phosphate, USP, Eli Lilly & Company, Indianapolis, IN; 0.275 mg, equivalent to 0.1 mg histamine/mL), respectively.

Bronchial challenge with MPE was performed as recommended by the National Institute of Allergic and Infectious Diseases of the National Institutes of Health.⁶ The Johns Hopkins dosimeter model D-2A (The Johns Hopkins University College of Medicine at the Good Samaritan Hospital, Baltimore, MD) was used for antigen delivery.⁷ Connected to a tank of compressed air (20 psi), the dosimeter delivered a constant amount of solution from a DeVilbiss #646 nebulizer (DeVilbiss, Somerset, PA) triggered by inhalation. The interval of dosing was set at 0.6 seconds for the MPE challenge. All diluents and antigens were delivered from functional residual capacity to inspiratory capacity.

Asymptomatic subjects were studied when the forced expiratory volume in one second (FEV₁) was at least 80% of the highest previously observed value. FEV₁ was again determined 10 minutes after inhalation of five breaths of diluent. If the FEV₁ was at least 90% of baseline, the subject was challenged with MPE, beginning with five breaths of the antigen concentration which elicited an 8-mm intradermal ST. If <15% reduction from the control FEV₁ occurred 10 minutes after challenge, five breaths of a 10-fold higher concentration of MPE were administered. If the reduction of the FEV₁ was 15 to 19%, the FEV₁ was repeated after an additional 10 minutes. If the repeat FEV₁ was >20% below baseline, this was considered the endpoint. Fewer than five breaths of antigen were given when nearing the endpoint. Subjects were instructed to call the investigator should they experience any delayed symptoms after the challenge.

Bronchial challenge results were recorded in antigen inhalation units (one inhalation of 1:5,000 wt/vol dilution of antigen). The inhalation for each antigen concentration was calculated by multiplying the number of breaths given by 5,000 divided by the reciprocal of the antigen concentration required. The antigen concentration times the number of breaths (usually five) equals the cumulated units for each

exposure unless fewer breaths were used. The dose was recorded as $PD_{20}FEV_1$, ie, the provocative dose required for a sustained reduction of 20% of the FEV_1 .⁶

Odor Challenge Equipment

Odor challenge equipment was assembled as schematically illustrated in Figure 1 and described in the Appendix. Odor source canisters were positioned between the reservoir filling pump and 120-L odor reservoir/inhalation chamber. Pollen and other extraneous particulates were filtered from the inspired air by a 5- μ m Millipore filter (Millipore, Bedford, MA). A mouthpiece and noseclamp were used for the bronchial challenges, and a face mask for the nasal-bronchial challenges.

Odor Challenge With Melaleuca Blossoms, Melaleuca Leaves/Bark, and Melaleuca Leaves/Bark/Blossoms

Baseline room air FEV_1 values were determined before testing. The subject took five inhalations of room air from the inflated balloon followed by a spirogram. If after 10 minutes, a repeat FEV_1 was <10% from baseline, the subject breathed room air from the balloon for 5 minutes followed by a repeat spirogram. If no change in the FEV_1 occurred, after an additional 10-minute wait, spirometry was repeated. The subject then breathed balloon air for 10 minutes. If no significant drop in the FEV_1 occurred, a spirogram was performed 10 minutes later. A baseline spirogram determined if the subject's FEV_1 was within 80% or more of the highest previous observed value.

After having established a baseline, subjects were initially challenged with room air, although they were not informed if they were breathing room air or odor. The canisters were covered so the subjects could not see what they were breathing, although the odors were obvious to the investigators and the subjects participating in the study.

The subject ate lunch after room air challenge. The canisters were filled with the test odor material and a new balloon attached to the system, and inflated with the odor air before the subject returned to the laboratory. The odor challenge followed the same protocol as the room air challenge.

Odor Challenge With Cajeput Oil

Selected subjects were challenged with cajeput oil.⁸ A baseline FEV_1 was obtained on each subject before the challenge. One hundred grams of cajeput oil were placed in an open 12" pie pan which was placed in a 10' $\times$ 30' closed room. Subjects breathed this room air for 1 hour. At the end of the time a spirogram was obtained on each person. Cajeput oil odor was very noticeable, and 2.6 g of oil volatilized during the test.

Methacholine Challenge

A methacholine (methacholine chloride, J. T. Baker Chemical Co, Phillipsburg, NJ) challenge served as a positive control for the dosimeter and the odor challenge system.⁹ The methacholine solution was nebulized through the odor challenge system using a DeVilbiss nebulizer #646 in line be-

tween the pressure pump and the canisters. The methacholine challenge was performed twice on the same subject, once with the balloon in the usual place in the system and once bypassing the balloon.

Progressive methacholine dilutions of 0.075, 0.15, 0.31, 0.62, 1.25, 2.5, 5.0, 10.0, and 25 mg/mL were used. Spirometry was performed 1.5 and 3 minutes after five inhalations of the methacholine dilution. A 20% decrease in FEV_1 was considered a positive test.

The methacholine challenge with the dosimeter was performed as established by the National Institute of Allergic and Infectious Diseases.⁶

Radioallergosorbent Test (RAST)

RAST¹⁰ was performed on serum samples of a subset of subjects in the study. MPE was covalently coupled to cyanogen bromide activated paper discs (Pharmacia Diagnostics, Piscataway, NJ). The specific Melaleuca pollen allergen activity of the human sera tested was expressed as follows: the counts bound on the discs incubated with the subject sera were compared with average counts of discs incubated with Pharmacia reference samples A, B, C, and D containing standardized concentration of specific immunoglobulin (Ig)E/mL for a known pollen antigen, ie, birch. Because background activity was subtracted, the recorded counts represented the quantity of MPE-specific IgE in the subject's serum or birch-specific IgE in the reference samples. If the subject count was higher than the count for reference A, the subject was 4+; if the count was between that obtained with reference A and B, it was recorded as 3+; if between B and C, 2+; between C and D, 1+, and less than D, negative.

Pollen Collection

An aeroallergen survey was made using two aerial samplers: a rotorod with the retracting head (Ted Brown Associates, Los Altos Hills, CA) and a roto-slide sampler (Aquebogue Machine and Repair Shop, Aquebogue, Long Island, NY). The samplers were mounted side by side, five feet apart, on the roof of a three-story building in Tampa, Florida, in an area typical of the central west coast of Florida. There were no close sources of air pollution or buildings that obstructed prevailing winds from any direction. Numerous Melaleuca trees were in the vicinity.

The samplers were operated at preset intervals: 1 minute in every 10 for the rotorod, 1 minute in every 12 for the roto-slide. General Electric G-697 silicone grease (General Electric, Stamford, CT) was used as the coating agent on both rods and slides. Samples were collected every 24 hours. Rods and slides were changed daily, usually at 7:30 AM. When the rods and slides were not changed every 24 hours (weekends and holidays), the count was adjusted accordingly.

The rotorods and roto-slides were stained with modified Calberla's solution and counts made using standard procedures.¹¹⁻¹³ Twenty-four-hour counts were reported as particles per unit volume (pollen grains/cubic meter of air sampled). Climatologic data for Tampa were obtained from the

National Oceanic and Atmospheric Administration (U.S. Weather Service, Silver Spring, MD).

Field Studies

Studies with the fixed head rotorod sampler (Ted Brown Associates, Los Altos Hills, CA) were conducted in the field beneath blooming Melaleuca and oak trees adjacent to stands of Melaleuca. The fixed head rotorod sampler was mounted on a tree branch, fence post, or other convenient object. Sampling periods were for 1 hour at various times of the day under varying weather conditions. The sample pairs (beneath the Melaleuca and oak trees) were obtained the same day, with the first sample collected for 1 hour under one tree and the second sample the next hour under the other type of tree.

RESULTS

STs

Ninety-seven of the 1,017 subjects had positive MPE skin reactions (3 subjects with 2 to 3+ percutaneous, 2 subjects with 4+ intradermal, 13 subjects with 3+ intradermal, and 79 subjects with 2+ intradermal). Of these, 16 study subjects (Table 1) were selected and divided into groups. All asthmatic patients studied had at least 15% reversibility to an inhaled bronchodilator.

Nasal Challenge

Six subjects (8, 10, 12, 13, 14, 15) with allergic rhinitis and positive STs to aeroallergens of the Tampa Bay area, including at least a 2+ intradermal to MPE, were subjected to nasal

challenge with MPE. One (14) had a positive challenge. He developed a moderate degree of mucosal edema, clear rhinorrhea, pruritus, and sneezing when challenged with a 1:100 wt/vol concentration of MPE.

Bronchial Challenge

Four subjects (8, 10, 12, 14) with positive STs to aeroallergens of the Tampa Bay area were subjected to bronchial challenge. These included at least a 2+ intradermal to MPE, who had extrinsic asthma and wheezed at times when Melaleuca trees bloomed. One (10) had a positive bronchial challenge to MPE. The FEV₁ was 55% of the baseline 5 minutes after five breaths of 1:1,000 dilution of MPE. Ten minutes postchallenge, the FEV₁ was 46% of baseline. A subcutaneous injection of adrenalin was given. Ten minutes later (20 minutes after challenge) the FEV₁ returned to 83% of baseline. Ten minutes later and after two puffs of isoproterenol (30 minutes after challenge), the FEV₁ was 111% of baseline. Calculated PD₂₀FEV₁ equaled 0.96 antigen inhalation units.

Odor Challenge

Thirteen subjects (1 to 12, 14) underwent 38 different bronchial or nasal-bronchial challenges to Melaleuca odor or cajuput oil odor (Table 2). Five subjects (1, 8, 10, 12, 14) had allergic rhinitis and extrinsic asthma with positive STs to Tampa Bay aeroallergens and 2+ or greater intradermal to MPE. One subject (3) with allergic rhinitis and extrinsic asthma had a negative ST to MPE. Three subjects (2, 9, 11) with vasomotor rhinitis and intrinsic asthma had a negative ST

Table 1. Melaleuca Study Subjects

Subject	Diagnosis		Melaleuca ST	Melaleuca pollen challenge		Melaleuca odor challenge	
	Nasal	Pulmonary		Nasal	Bronchial	Leaves/bark/blossoms (n)*	Oil†
1	Allergic rhinitis	Extrinsic asthma	2+ Percutaneous			‡ (4)	
2	Vasomotor rhinitis	Intrinsic asthma	Negative			‡ (2)	
3	Allergic rhinitis	Extrinsic asthma	Negative			‡ (3)	
4	None	Intrinsic asthma	Negative			‡ (4)	
5	None	Chronic obstructive lung disease	Not done			‡ (3)	
6	None	Chronic obstructive lung disease	Not done			‡ (4)	
7	None	Intrinsic asthma	Negative			‡ (4)	‡
8	Allergic rhinitis	Extrinsic asthma	4+ Intradermal	‡	‡	‡ (3)	
9	Vasomotor rhinitis	Intrinsic asthma	Negative			‡ (3)	‡
10	Allergic rhinitis	Extrinsic asthma	4+ Percutaneous	‡	§	‡ (2)	
11	Vasomotor rhinitis	Intrinsic asthma	Negative			‡ (2)	
12	Allergic rhinitis	Extrinsic asthma	4+ Intradermal	‡	‡		
13	Allergic rhinitis	None	4+ Intradermal	‡			
14	Allergic rhinitis	Extrinsic asthma	2+ Percutaneous	§	‡		‡
15	Allergic rhinitis	None	4+ Intradermal	‡			
16	None	Extrinsic asthma	Negative				‡

* Refers to number of odor challenges performed. These differed according to substance used for odor source and method of challenge (See Table 2).

† Two controls not included.

‡ Negative challenge.

§ Positive challenge.

to MPE. Two subjects (4, 7) with no nasal disease and intrinsic asthma had a negative ST to MPE. Two subjects (5, 6) with no nasal disease had nonreversible chronic obstructive lung disease (no reversibility with isoproterenol or steroids).

Of the 38 Melaleuca odor challenges (16 bronchial and 22 nasal-bronchial), there were no changes in FEV₁'s to odors or cajeput oil fumes (Table 2). No late symptoms occurred in any subject.

Subject 9 was challenged with methacholine to test the odor challenge equipment system. Both challenges (one with the balloon and one without the balloon) were positive. Subject 7 had a positive dosimeter challenge to methacholine.

RAST Testing

RAST¹⁰ was done on serum samples of 15 subjects in the study and two positive controls (one 4+ intradermal and one 4+ percutaneous). RAST scores and ST results correlated (Fig 2). Two subjects on whom RAST was obtained had a 4+ prick test (wheal >8 mm with pseudopods) and were placed in the 4+ intradermal ST group.

Pollen Collection

Few Melaleuca pollen grains were found on the rotoslide samples (Table 3). Oaks are prolific producers of airborne pollen, and the monthly totals of daily pollen grain counts for oaks during March and April (pollinating months for these trees) were 8,834 and 7,838, respectively. In contrast, monthly totals of daily pollen counts for Melaleuca were 8 and 12, respectively, for April and August (two pollinating months for Melaleuca).

Field Studies

Table 4 compares field sampling results by rotorod beneath a flowering Melaleuca tree and beneath an oak tree 10 to 15 feet from the Melaleuca. The counts for Melaleuca and other pollen grains and for mold spores are comparable, with zero or one to two Melaleuca pollen grains collected beneath the Melaleuca and oak.

DISCUSSION

Although there are various clinical opinions regarding the importance of the Melaleuca tree as a prolific source of aeroallergens or noxious odor, no documented medical literature exists to support this impression. In 1975, two Melaleuca workshops⁵ held in Florida were attended by cit-

Table 2. Distribution of 48 Melaleuca Odor and Pollen Extract Challenges

Odor	Method	
	Bronchial	Nasal/Bronchial
Leaves/bark	7	3
Blossoms	10	9
Leaves/bark/blossoms	Not done	5
Cajeput oil	Not done	4
	Bronchial	Nasal
Pollen extract	4	6

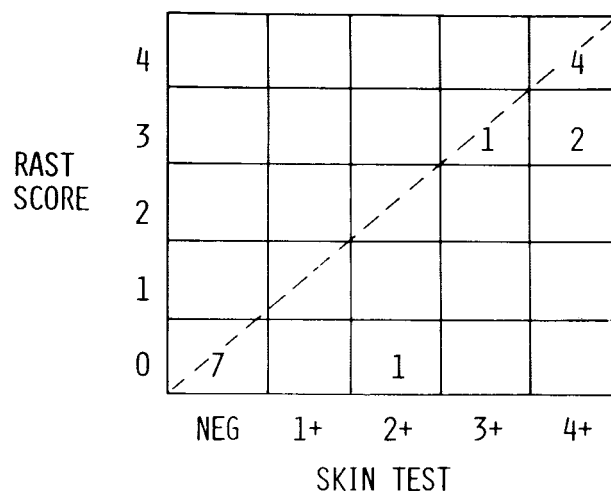


Figure 2. RAST vs intradermal ST for MPE.

izens and representatives of various agencies interested in controlling the spread of Melaleuca trees in south Florida. At those conferences many clinical cases were cited which incriminated the Melaleuca as a source of respiratory disease. None of these case reports had been studied nor had any been published in the medical literature.

The aeroallergen survey performed in this study indicates that Melaleuca does not produce significant quantities of windborne pollen. The Melaleuca tree is a prolific source of nectar for honey bees and accounts for a multimillion dollar honey bee industry in Florida. When in bloom, the flowering tree attracts multitudes of honey bees. The pollen surveys performed beneath flowering Melaleuca trees under varied weather conditions at different times of the year confirm that the tree is primarily insect- and not wind-pollinated. Very small amounts of Melaleuca pollen are airborne even when samples are obtained in close proximity to the tree in bloom. Further, pollens from other plants can be collected in significant amounts from samples obtained beneath the tree.

Table 3. Comparison of Monthly Totals of Daily Pollen Grain Counts by Rotoslide Sampler of Melaleuca and Oak for 1979*

Month	Melaleuca	Oak
January	ND	55
February	ND	99
March	0	8,834
April	8	7,838
May	2	272
June	3	24
July	0	ND
August	12	ND
September	3	ND
October	0	ND

* Counts are in pollen grains per cubic meter of air sampled per day per month.
ND = not done.

Table 4. Representative Pollen Counts From Field Sampling by Rotorod (Collection Time: 1 Hour)

Date	Aeroallergen	Under blooming Melaleuca tree	Under oak tree 10–15 ft from Melaleuca
6/23/79	Melaleuca	1	0
	Ragweed	2	4
	Pigweed	1	1
	Grasses	47	44
	Total molds	51	55
8/23/79	Melaleuca	1	1
	Ragweed	92	99
	Pigweed	7	5
	Dog fennel	2	4
	Marsh elder	3	2
	Nettle	5	3
	Grasses	29	41
	Total molds	55	58
8/31/79	Melaleuca	2	1
	Ragweed	64	70
	Pigweed	4	5
	Mexican tea	1	2
	Dog fennel	3	3
	Marsh elder	2	4
	Nettle	3	2
	Grasses	33	38
	Total molds	42	38
	Melaleuca	3	0
9/10/79	Ragweed	211	224
	Pigweed	3	7
	Marsh elder	26	18
	Nettle	3	2
	Grasses	51	59
	Total molds	315	298
	Melaleuca	1	1
	Australian Pine	25	20
10/11/79	Ragweed	39	45
	Dog fennel	51	10
	Grasses	10	52
	Total molds	683	740
	Melaleuca	0	1
10/18/79	Australian Pine	7	8
	Dog fennel	9	4
	Grasses	32	25
	Total molds	177	146

Contrary to experience with other aeroallergens, few allergic subjects yield positive STs with MPE. Only 3 percutaneous and 94 intradermal ST-positive subjects to MPE were found among the 1,017 subjects who underwent allergic evaluation. RAST results correlated well with MPE ST reactivity indicating that Melaleuca-specific IgE antibodies are detectable by both procedures in sensitized subjects.¹⁰

Twenty-seven percent of subjects with 2+ positive intradermal ST (6-mm wheal) have been shown to have a positive bronchial challenge.¹⁴ Of the subjects who underwent challenge studies, 1 of 6 with proven allergic rhinitis and 1 of 4 with proven extrinsic asthma with 2+ or greater positive

intradermal ST to MPE had positive challenge studies. Cross-reactive antigens have been demonstrated to exist between MPE and Bahia pollen extracts.¹⁵ Bahia grass is a proven aeroallergen, abundant in Florida,¹⁶; thus, the in vivo and in vitro evidence of MPE-specific IgE in some subjects is most likely attributable to primary sensitization of these subjects with Bahia pollen and not Melaleuca pollen.

Limited investigative work has been done on odors as a cause of respiratory disease. Technology to measure odors is generally unavailable, costly, time-consuming, or incompletely validated.¹⁷ Although various odors have been incriminated as a cause of respiratory disease, confirmatory data are lacking. Toluene diisocyanate (TDI) is a low molecular-weight chemical used in the manufacture of polyurethane paints and plastics. Its fumes will sensitize and provoke asthma in 5% of all persons involved in its manufacture.¹⁸ Inhalation challenge is the only test available to confirm such TDI asthma, and confirmation is possible because TDI concentrations in air are measurable. Trimellitic anhydride is another vapor documented to cause asthma.¹⁹

Sensitized persons develop symptoms at very low concentrations, occasionally below limits of odor perception. Several mechanisms have been proposed in explanation of asthma caused by such vapors: 1) a direct irritant or toxic effect, 2) an IgE-mediated reaction, and 3) a release of mediators through a pharmacologic, rather than immunologic, mechanism.²⁰

Methacholine challenge confirmed the adequacy of the system devised to challenge persons to odors emanating from the blossoms of plants and specifically from the blossoms, bark, and leaves of the Melaleuca tree. Although the odors could not be quantitated, they were conspicuous to the investigators and subjects using the equipment described. The ability to provoke bronchoconstriction with methacholine challenge suggests that the system devised for odor challenge is capable of collecting and transmitting volatile vapors. Asthmatic subjects have long been recognized to be exquisitely sensitive to methacholine. Former or asymptomatic asthmatic patients will develop bronchoconstriction upon inhalation of this chemical, with severe asthmatic patients having the greatest sensitivity. All subjects reacted negatively to odor challenge, either by bronchial or nasal-bronchial route, for as long as 30 accumulated minutes, indicating that under controlled laboratory conditions, continuous exposure to this odor does not cause respiratory difficulty, even though 40% of the subjects previously thought it did. It is unlikely that subjects would be exposed to higher concentrations under normal conditions.

Similarly, 2 normals and 4 subjects with asthma did not react to a 1-hour exposure to cajuput oil fumes, an odor that was obvious to all subjects in the room in which it was used. Although other volatile substances may emanate from the Melaleuca tree, cajuput oil is of paramount importance.

This study indicates that persons are rarely allergic to Melaleuca tree pollen and that insignificant quantities of the

pollen are airborne. A rare IgE-sensitive subject may, under unusual circumstances, note an exacerbation of disease after exposure to *Melaleuca* pollen, but this tree is not the source of widespread exacerbations of the disease. The data also indicate that the odor that emanates from the blossoms, leaves, and bark and from cajeput oil of the *Melaleuca* tree does not exacerbate or cause respiratory disease, by either an irritant or toxic effect or by pharmacologic mechanisms not understood.

The *Melaleuca* tree is abundant in south Florida. Its blossom has an unpleasant odor, and it blooms repeatedly throughout the year. Therefore, it is blamed for exacerbation of respiratory disease when, in fact, it does not. Many plants in Florida have been proven to cause hay fever and asthma. These include oaks, grasses, and ragweed. Airborne wind-pollinated plants bloom inconspicuously. More obvious flowering plants are often incorrectly blamed for respiratory problems when, in fact, exacerbations result from such other factors as windborne pollens, climatic changes, air pollution, and mold sensitivity.

APPENDIX

Assembly of Odor Challenge Apparatus

A $\frac{1}{6}$ HP Millipore GE vacuum pressure pump is attached by $\frac{3}{8}$ " plastic tubing to a Bourns 5000–01004 rubber adapter which fits snugly into one end of the first canister or reservoir. The canister/reservoir is a large round container of clear plastic, $1\frac{3}{4}$ " optical density, $1\frac{1}{8}$ " intradermal, 4" diameter, 13" length, with interior wire screens at each end (Warren E. Collins, Inc, Braintree, ME). The first canister is connected directly to the second by means of a Bourns 5000–01004 rubber adapter. Another Bourns adapter connects the second reservoir to the metal hose adapter on the top cap of a 47-mm Millipore filter holder of 100 mL capacity. A one-hole rubber stopper is used on the metal adapter of the filter holder so the Bourns adapter will fit snugly. A 47-mm diameter, 5- μ m pore size Millipore filter is placed in the filter holder to filter pollen particles or other material 5 μ m in diameter or larger. Plastic tubing ($\frac{1}{4}$ ") fits the delivery stem of the Millipore filter holder and connects to one end of a plastic T-shaped connector ($\frac{3}{4}$ " diameter). A small plastic adapter allows for a snug fit of the tubing and the T-connector.

The bottom arm of the plastic T has a 120-L balloon attached by means of a metal aerosol tubing clamp (worm gear with slotted track). The balloon is a 120-L neoprene meteorologic day flight balloon (Kaysam Corp of America, Paterson, NJ). The entire balloon assembly is supported by a ring stand with a three-pronged buret clamp holding the plastic T-connector. The buret clamp holds the T-connector and the balloon over the end of the laboratory counter so that the balloon has space for inflation. When it is completely inflated, the balloon hangs free from the bottom of the T-connector.

The second top arm of the plastic T is connected by plastic flex tubing to a metal stopcock with a $\frac{3}{4}$ " bore and a pin-stop which permits only a one-quarter turn of the plug. With the stopcock closed, the air pumped into the balloon is stopped at the stopcock. With the stopcock open, the air from the balloon has free passage through the system to the mouthpiece or mask.

On the opposite side of the stopcock is a two-way J valve (Warren E. Collins) attached to the stopcock by a rubber adapter. The second opening in the J valve has the mouthpiece or face mask attached. The rubber mouthpiece fits directly over the J valve opening. However, the face mask (Bird Fitrite 4343) requires a Bourns adapter to hold the mask in a steady position. The third opening in the J valve has a Wright's respirometer (flow meter) attached by means of a metal adapter. A buret clamp attached to a metal ring stand supports the entire stopcock and the two-way J valve with face mask or mouthpiece assembly at a level which is comfortable for the subject during the challenge. The buret clamp and clamp holder allows for easy adjustment of the entire J valve and stopcock assembly.

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Obituary—John J. Stablein, III, MD

(1952–2002)

John was a relentless reader, a gifted scholar, an excellent educator, and a compassionate clinician. He authored numerous papers and contributed to several textbooks. He had a lasting impact on the University of South Florida College of Medicine, Division of Allergy where he was a member for 6 years. He is deeply missed by his wife Diane, son David, daughter Kara, his patients, and colleagues.

