#3

Ramirez, Angelica Public comment

LATE DIST

From: Marc Chytilo <marc@lomcsb.com>
Sent: Friday, July 10, 2020 12:07 PM
To: sbcob
Subject: corrected submittal - item # 3
Attachments: LOMC to BOS 7-10-20 B package.pdf

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Clerk – I realized the exhibits in my recent submittal for item # 3 were out of order and two lacked exhibit headers - attached is a corrected copy with the exhibits identified and in proper order. The substance is identical and I would prefer that this version be entered into the record and the previous one not submitted, however as this is arriving to you at 12:05, if you would mark this as late, I prefer you use the version that was timely submitted and not be identified as late submitted

Thanks for your courtesy in this regard

Best regards

Marc

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LAW OFFICE OF MARC CHYTILO, APC

ENVIRONMENTAL LAW

July 10, 2020

Chairman Gregg Hart
Santa Barbara County Board of Supervisors
105 E. Anapamu Street, Fourth Floor
Santa Barbara, California 93101

RE: Item # 3, July 14, 2020, Cannabis Permitting Ordinance Amendments

Chair Hart and Members of the Board of Supervisors:

As you are aware, this office has been deeply involved in the implementation of the County's cannabis cultivation permitting program. This office, and the groups and individuals we have represented, are not opposed to cannabis cultivation, but are individually and collectively cognizant, based on personal experience and knowledge of what has and can happen in the field, of the multitude of avoidable significant impacts from this new industry that some members of the Board do not fathom. As you are aware, the PEIR found that the ordinance would cause twelve distinct significant impacts, including continuing nuisances. While the statute of limitations for judicial review of the 2018 PEIR has passed, the Board should not construe that as a license to unnecessarily cause avoidable impacts that disproportionately impact certain communities.

For cannabis cultivation to survive as a sustainable industry in Santa Barbara County, land use entitlements must be carefully crafted to address a suite of site-specific and project-specific issues to ensure these operations fit where they are proposed. While the proposed ordinance amendments are a small step in the right direction, they fall well short of the changes needed to harmonize these activities with long-standing surrounding land uses, and cannabis cultivation operations will continue to threaten the viability of conventional agriculture, deliver intolerable nuisance odors to residential areas, and many will operate in an illegal manner immune from County enforcement.

The report of the Grand Jury confirmed that the ordinance adoption process was deeply flawed on environmental, ethical, and financial basis. Statements dismissing the Grand Jury's Findings only inflate the perception of County indifference to the problems being experienced by County farmers and residents. These are not only current problems from existing grows, but include anticipated future problems based on the awareness that if these issues are not addressed at the outset, the County has placed itself in an extremely weak and vulnerable position when claims of vested rights will be used to curtail future County efforts to contain the problems that are today being ignored.

Members of the Board claim that permit appeals were delaying processing and issuance of cannabis permits, and that issuance of permits was a condition of the County being able to take enforcement actions against the many cannabis operators currently operating without permits, ostensibly under Art. X. In fact, the delays in cannabis permit issuance for many projects, and nearly every Carpinteria area project, are the result of existing unpermitted structures which now must be made legal by being brought into the cannabis permits. Appeals and the Planning Commission are not delaying approvals,

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it is the result of the many illegal and unpermitted improvements undertaken where cannabis has been and is proposed to be grown.

There is no legal basis for the claim that the County may not take enforcement action against the currently-operational unpermitted cannabis grows, particularly in Carpinteria. Under the Land Use and Development Code, any existing grows are legal only to the size, scope and nature of the operations that were in existence on January 19, 2016. Expansion of operations, and conversion from medical to recreational cannabis, is not allowed, and the County may not turn a blind eye to these illegal operations. *Hanson Bros. Enters. V. Bd. Of Supervisors* (1996) 12 Cal.4th 533, 564 ("the county lacks the power to waive or consent to violation of the zoning law.").

Members told the public that they are anxious to seeing cannabis cultivation permits move forward so the Board may "give a thumbs up or thumbs down" on these projects and select which operators should be allowed to proceed, recognizing that some projects and operators should not be approved, even if they meet the weak development standards in the cannabis ordinance. Under the existing and proposed ordinance, however, the Board will <u>not</u> have the ability to review those projects unless they are appealed, and under County counsel's guidance, will have very limited discretion to condition or deny them (unless, of course, a Conditional Use Permit is required). To claim there will be Board review of these permits, unless appealed, is incorrect and materially misstates the Board's role in review of cannabis permits under the regulatory structure currently in place, and contemplated with the nominal changes being considered.

The cannabis ordinance and permitting process remains structurally deficient from its failure to meaningfully address malodors emitted during cultivation activities. Two separate problems are posed by the two general forms of cultivation practiced and proposed in the County.

<u>Outdoor grows</u>, generally on AG-II zoned lands, generate odors while plants are in their flowering phase, increasing in intensity to the point of harvest, where proposed ordinance changes require drying and processing in sealed facilities. That is one positive step. These outdoor grows are generally undertaking multiple harvests annually using short-cycle varieties and methods, and pose conflicts with surrounding agriculture and with downwind residences and communities. The PEIR asserted that odor impacts would be mitigated by Odor Abatement Plans (MM AQ-5) that are supposed to "ensure that odors are . . . generally confined within the cannabis activity site property." [PEIR 3.3-24]

The PEIR relied on a flawed assumption that imposing odor controls on AG-II cannabis cultivation operations would conflict with agricultural policies allowing choice of crops. Changes and clarification in law establish this justification was incorrect, and that Odor Control Plans can and should be required in AG-II areas.

The PEIR relied on the Uniform Rules and APAC review process to ensure compatibility between a proposed cannabis cultivation project and nearby agricultural operations. "Additionally, land use compatibility with adjacent agricultural crops would be ensured by APAC review which ensures compatibility with agricultural uses, and cannabis activities would not conflict with properties that are subject to Williamson Act contracts." [PEIR 3.2-20] The Board's subsequent changes to the Uniform Rules eliminated this essential compatibility analysis, leading to the unresolved conflicts with surrounding agriculture that are the core basis of disputes between proposed cannabis operations and existing agriculture on AG-II lands. These conflicts must be address and resolved in advance of entitlement – once permits are issued, the County's ability to apply additional needed controls will be severely compromised by vested rights.

Recommendation: The Board should direct revision to the Uniform Rules to identify cannabis cultivation operations as compatible, not qualifying uses under the Williamson Act, and direct the Agricultural Preserve Advisory Committee to conduct a compatibility review of all proposed cannabis cultivation operations and impose conditions sufficient to ensure compatibility between proposed cannabis cultivation operations and existing nearby agricultural operations.

The Board should also revise the Ordinance to require Odor Abatement Plans for AG-II cannabis cultivation operation applications.

In addition, the Board should convene a balanced working group of interested parties to develop a Scope of Work for independent research studies and reports to address terpene taint of wine grapes and other identified agricultural conflicts. Such studies and reports should establish: 1) the rates of terpene emissions for common varieties of cannabis grown outdoors in Santa Barbara County; 2) terpene absorption rates for common varieties of wine grapes grown outdoors in Santa Barbara County; and 3) detection thresholds for terpenes in wine. This science is essential to facilitate the resolution of this conflict and provide a basis for buffer sizes and other strategies to avoid this conflict.\[1] The County Agricultural Commissioner reported to the Agricultural Advisory Committee on July 9 that this process has "stalled" and the Ag Commissioner and Planning and Development Department Director are awaiting direction from the Board on this research. Board direction is needed.

Finally, a network of monitors and computer model providing accurate and reliable meteorological conditions in cannabis cultivation regions in the County is desperately needed. Permits processed to date have relied on interpolated wind data from distant sites. Santa Barbara County's primary agricultural areas each experience microclimates and terrain-dominated wind conditions. The behavior of wind directly affects the locations and nature of odor episodes, and the airborne transport of terpenes as well as agricultural chemicals. Your Board authorized Director Plowman to require submittals of meteorological studies or wind data as components of cannabis cultivation applications. July 19, 2019. On site wind data is essential due to microclimates. The Board should direct submittal of this information unless the Planning Director determines it unnecessary.

Mixed Light cannabis cultivation operations (in greenhouse structures) pose a different set of issues and problems. A portion of the plants in greenhouses are continuously in odorous flowering stage. Thus odors are not periodic, but constant. These are generally in AG-I areas, and in Carpinteria, greenhouses are sited adjacent to residential areas and in the midst of schools, day care and youth facilities. Some of these greenhouses were growing medicinal cannabis in 2016 and can claim a right to continue this same level of cannabis cultivation operations, however the Coastal Zoning Ordinance

[1] See Exhibits 1-2, commentaries from leading cannabis industry scientists, including "Good Science makes Good Neighbors" (addressing specifically the Santa Barbara County vintner/cannabis conflicts), Exhibit 1; and "The Current Approach to Cannabis Emissions Regulations Stinks" (discussing odor detection thresholds), Exhibit 2.

and state law prohibit the expansion of those operations in size, or conversion to non-medial varieties or sale in the recreational market. Prop 64 and subsequent laws established that while the use and cultivation of recreational cannabis was not illegal in the state, all such activities are subject to local laws and requirements, including the County's Article X, in addition to state licensing requirements.

Odors from greenhouses remains a significant problem in areas of Carpinteria. Vapor-phase odor control systems demonstrate mixed effectiveness, and downwind residents are exposed not only to the terpene odors but the deodorant as well. It should be evident to the Board that continuous exposure of nearby residents and children to deodorants is undesirable. While the deodorants may not include known Toxic Air Contaminants that are demonstrably hazardous for short-term (acute) exposure, chronic exposure is a different matter.\[2] While the PEIR's MM AQ-5 contemplated that vapor-phase systems would disperse deodorants "within the cannabis site" and be "generally confined within the cannabis activity site property" [PEIR 3.3-24] it is evident that deodorants are wafting beyond property lines and trespassing onto other parcels, some nearby, and some more distant.\[3] The retrofit of old greenhouses is not appropriate, and the Board's best available control technology for greenhouses should include an amortization process to mandate conversion of all greenhouses to purpose built structures capable of containing and filtering all odors. This is the recommendation of Dr. Vizuete, a cannabis industry scientist that has submitted expert reports to the County in other proceedings.\[4]

Board members should not dismiss lightly the findings and recommendations of the Grand Jury. It is incumbent on the Board to find solutions to issues that adversely affect the health and quiet enjoyment of thousands of County residents and threaten other mainstays of the County's economy. The Board should acknowledge the shortfalls in the ordinance, in the environmental review process, and in the implementation of this program. The County should take steps to make its permit review and legislative processes more transparent and fair to the public, and to competing applicants.

It is incumbent on the industry and its representatives to acknowledge that the ordinance is imperfect, and strive to find realistic and sustainable solutions to these issues. Affected neighbors need to work with applicants and find sustainable solutions. This cannot happen if applicants know that the Board will approve any and every project – there is no reason to compromise, and as both the Grand jury and Planning Commission have noted repeatedly, all paths lead to Superior Court. It appears that if the Board will not admit that the PEIR is deeply flawed, will not recognize the potential for fundamental existential conflicts among existing agriculture and cannabis, and continually intentionally eschew the authority needed to properly regulate cultivation operations, the process will remain dysfunctional and unresolved until judicial review is complete. This represents a colossal mistake by the County and disservice to both the cannabis industry and the public.

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[2] See Exhibits 4 & 5, studies addressing the health effects of sustained exposure to malodors, and the adverse reaction of chemically sensitive individuals to exposure to terpenes. The cursory treatment of these issues in the PEIR is no excuse or justification for allowing sustained exposure of the County's residents to these controllable air pollutants.
[3] See Exhibit 3, a Planning and Development Department memo to Carpinteria Growers indicating that the vapor phase systems have been ineffective at controlling odors.
[4] See Exhibit 6, "The Overlooked Elephant in the Greenhouse Design Room", Dr. William Vizuete, arguing that "a robust odor control system can be integrated into greenhouse design and control systems" rather than retrofitting greenhouses.

I urge the Board to adopt the incremental changes discussed on June 11, and would prefer that you strengthened them to prevent odors beyond the property line and expanded the scope of your authority by reducing the threshold for Conditional Use Permits. The Board should direct staff to further advance the recommendations contained herein to transition greenhouse grows to engineered structures that can contain and treat all odors, and address agricultural conflicts by correcting the Uniform Rules to ensure APAC compatibility review and mandating odor abatement plans for AG-II cannabis cultivation operations, based on a standard of no odors beyond the property line.

Respectfully Submitted,

Marc Chytilo

Officer at Pacific Environmental Analytics. In this month's Better
ok at the tension facing rural communities trying to reconcile traditional
:ultivation.

: mix of residents with a range of livelihoods and motivations for where
; for rural communities is a struggle to develop strategies that allow
to coexist with their neighbors living off their land in working farms that
road congestion and other issues. Even among neighboring farmers
promises. For example, "pesticide drift" from vintners applying chemicals
lecimate the value of adjacent cannabis fields if the deposited pesticides
is concern that natural emissions of cannabis plant volatiles, such as
:yards. While pesticide drift has been relatively well studied, and impacts
tory pesticide testing, characterizing the impact of cannabis volatiles on
ubstantially less understood and yet there has been almost no research
:.

ving disputes in an equitable manner and enabling all members of a
potential impacts of cannabis volatiles on vineyards, it is essential to
core controlling processes including cannabis emission rates for
ınd dispersion factors, deposition rates and chemical transformations
ıken up by grapes. In addition, it is necessary to ascertain the ultimate
ıining an objective odor/flavor detection threshold in wine along with the
have a negative (taint), neutral (no impact) or even positive
rofile depending on the amount present.

n between cannabis cultivation and vineyards requires considering not
:annabis operation (e.g., direct quantification of complex emission
g leaf and bud enclosure measurement systems and atmospheric
;) but also input from the neighboring vineyard (e.g., measuring
ɔr molecules (hundreds of compounds including terpenes, thiols,
g headspace analysis of grapes and wine). Together these analyses
ɔf these two agricultural industries and provide critical data and insights
l identify solutions. The ultimate outcome of collaboration is a fair and
ity concerns and moving forward with mutual benefit.

rs that must be considered and evaluated in order to ascertain the
ations on nearby vineyards. In order to have full and complete answers
:arch is necessary and that will clearly require collaboration between
:e both sides have put down their swords and put their heads together
eighbors.

:. In this month's Better Business Column, we are going to look at the
əlds and their relevance to the timely issue of Cannabis emissions

in your fridge, an unpleasant odor is something we've all experienced
; odor, and how do we perceive it? Odor can be defined as the subjective
›ry organs are stimulated by individual volatile organic compounds
arby air. And due to the subjectivity of the olfaction process, the VOCs
ıer may find desirable. There are many types of VOCs that cause us to
es, aldehydes, sulfurs, amines, and most common to Cannabis, terpenes.
using VOCs is being emitted doesn't necessarily mean that we will even
ittle-discussed phenomenon known as Odor Detection Thresholds.

ction thresholds are a scientific name for the concentration at which a
verage human nose. In the Cannabis world, scientists have attempted to
)Cs that are emitted from Cannabis plants. For example, a-pinene was
:s per million), and limonene had an ODT of ~0.038 ppm (Abraham et al.,
nportant to note that while these thresholds are both relatively low, they
DT than limonene. This means that a-pinene will produce noticeable
nene. In other words, a-pinene is more potent than limonene. Therefore,
their Cannabis plants emits 0.019 ppm of a-pinene and 0.037 ppm of
ecause 0.019 > ODT of 0.018) but we would not smell the limonene
ıonene being present in a higher quantity than a-pinene.

; VOCs emitted in the largest amounts must be responsible for the
nple between a-pinene and limonene shows that this is not necessarily
›resent in large quantities may have no odor; whereas, other
nay have a very strong odor. Furthermore, recent PEA client-projects
ıg one potential hypothesis that compounds present in smaller
re responsible for the pervasive odor. Because of this, it is important for
ɪnflate the mere presence of VOCs with the existence of an odor. Rather,
tes of individual VOCs and compare them to published ODTs in order to
ınd is actually causing an odor. Only then can proper regulations of both
e standards that treat odor-causing VOCs individually with regard to

ːd one due to its inherent subjectivity and relatively low thresholds for
sure that Cannabis emissions regulations target those VOCs that are
ns that take away the subjective nature of odor and equip regulators
ul crafting of regulations. The importance of ODTs in objectively

Exhibit 3

Memorandum

Date: May 7, 2020

To: Carpinteria Cannabis Growers

From: Lisa Plowman
Planning & Development

Subject: Odor Control

Over the last three months the Planning & Development Department has received a substantial uptick in odor complaints with some residents saying that the odor is significantly worse than it had been in the previous months. This has also been observed by Department staff. It is our understanding that the increase in odor may have to do with non-functioning odor control, poorly designed or implemented odor control, outdoor processing, improper venting, and/or illegal grows (some within City boundaries).

Please be advised that the Department takes this increase in complaints about odor very seriously and we want to reiterate that odor must be adequately addressed. For example, we are concerned that some of the growers vent their greenhouses through the sides allowing odors to escape without proper treatment. This type of facility will need to adjust their odor control infrastructure to ensure that the odor is actually being addressed before it leaves the site.

As you know, the Land Use Development Code states the following:

Section 35.42.075.C.6. Odor Abatement Plan.

The applicant for cultivation, nursery, manufacturing (volatile and non-volatile), microbusiness, and/or distribution permits, shall (1) prepare and submit to the Department for review and approval, and (2) implement, an Odor Abatement Plan. No odor abatement plan shall be required in AG-II zoning, unless a CUP is required. The Odor Abatement Plan must prevent odors from being experienced within residential zones, as determined by the Director. The Odor Abatement Plan shall be implemented prior to the issuance of final building and/or grading inspection and/or throughout operation of the project, as applicable.

The Odor Abatement Plan must include the following:

a. A floor plan, specifying locations of odor-emitting activity(ies) and emissions.
b. A description of the specific odor-emitting activity(ies) that will occur.

c. A description of the phases (e.g., frequency and length of each phase) of odor-emitting activity(ies).

d. A description of all equipment and methods to be used for reducing odors. A Professional Engineer or a Certified Industrial Hygienist must review and certify that the equipment and methods to be used for reducing odors are consistent with accepted and available industry-specific best control technologies and methods designed to mitigate odor.

e. Approved odor control systems, subject to certification as required in Subsection d above, may include, but are not limited to:

(1) Activated carbon filtration systems.

(2) Vapor-phase systems. Vapor-phase systems must comply with the following:

(a) The resulting odors must be odor-neutralizing, not odor-masking.

(b) The technology must not be utilized in excessive amounts to produce a differing scent (such as pine or citrus).

(c) Use of these systems must have supporting documentation to demonstrate that the systems meet United States Environmental Protection Agency's Acute Exposure Guideline Levels or similar public health threshold.

(3) Other odor controls systems or project siting practices that demonstrate effectiveness in controlling odors.

If it is found that certain odor abatement systems are not effective at "preventing odors from being experienced within residential zones", the Department will require the use of an alternative system that is consistent with the Best Available Control Technology (BACT) which could include a closed air circulation system with carbon filtration.

If you have any questions about the information contained herein, please contact my office at 805-568-2086.

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Exhibit 4

Critical Review: The Health Significance of Environmental Odor Pollution*

DENNIS SHUSTERMAN
Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Air Toxicology and Epidemiology Section
Berkeley, California

ABSTRACT. Environmental odor pollution problems generate a significant fraction of the publicly initiated complaints received by air pollution control districts. Such complaints can trigger a variety of enforcement activities under existing state and local statutes. However, because of the frequently transient timing of exposures, odor sources often elude successful abatement. Furthermore, because of the predominantly subjective nature of associated health complaints, air pollution control authorities may predicate their enforcement activities upon a judgment of the public health impact of the odor source. Noxious environmental odors may trigger symptoms by a variety of physiologic mechanisms, including exacerbation of underlying medical conditions, innate odor aversions, aversive conditioning phenomena, stress-induced illness, and possible pheromonal reactions. Whereas relatively consistent patterns of subjective symptoms have been reported among individuals who live near environmental odor sources, documentation of objective correlates to such symptoms would require as-yet unproven research tools. Therefore, given our current state of knowledge, any differential regulatory response to environmental odor pollution, which is based upon the distinction between community "annoyance reactions" and "health effects," is a matter of legal—not scientific—interpretation.

LOCAL PUBLIC HEALTH and air pollution control officials frequently consult the California Environmental Protection Agency (Cal-EPA) regarding the health significance of odorous air pollutants, particularly when such pollutants are associated with perceived sources of toxicologic hazard. Cal-EPA investigators have found that the apparent health impact of odors on communities that surround hazardous waste, agricultural, and industrial air emission sources frequently defies explanation in classic toxicologic terms.

I. Community responses to odor pollution

A variety of municipal, agricultural, and industrial activities are sources of odorous air emissions. Municipal odor sources include sewage treatment plants, storm drain systems, and sanitary landfills. Agricultural sources include livestock feed lots, poultry farms, composting and other biomass operations, and pesticide

*Whereas this study was not part of the Indoor Air '90 proceedings, the editors approved it for publication in this special issue.

operations. Industrial sources include pulp mills, geothermal steam plants, petroleum refineries, foundries, bakeries, breweries, rendering plants, metal degreasing and painting operations, and hazardous waste sites, among others. Communities that adjoin many such sources in California have been studied with respect to odor annoyance and health status; several of these studies are reviewed below.

A. Municipal odor sources

Bruvold et al.[1] conducted a study of community annoyance reactions downwind from two sewage treatment plants that had identified hydrogen sulfide emission problems. Environmental monitoring documented hydrogen sulfide levels in the 1 to 6 part-per-billion (ppb) range in the affected neighborhoods; these levels, which exceeded those identified in control areas, were below the current California 1-h ambient air quality standard of 30 ppb. A survey questionnaire was used to determine that exposed neighborhoods exceeded comparison neighborhoods with regard to (a) the percentage of people who noticed an odor and (b) the degree of self-reported odor annoyance. In addition, a variety of coping behaviors (including staying indoors, temporarily leaving the neighborhood, complaining to officials, and considering a change of residence) were reported. Approximately one in nine respondents in exposed neighborhoods reported that they or their family members had been made sick by the odors, although illness of sufficient severity to prompt medical attention was rare (i.e., fewer than 1% of respondents).

B. Agricultural odor sources

Odors associated with pesticide applications may derive from the solvents used in pesticide formulation, from odoriferous sulfur groups within the pesticide compound itself, or from odoriferous byproducts of the manufacturing process. Scarborough et al.[2] examined the prevalence of physical symptoms in three small agricultural communities exposed to drift from the cotton defoliants tributyl phosphorotrithioate (DEF®) and tributyl phosphorothioite (FOLEX®). Exposure assessment indicated that, while residents were exposed to subtoxic levels of the parent defoliants, they were exposed to levels of impurities (butyl mercaptan and dibutyl disulfide) with clearly discernible odors. Compared to three non-defoliant-exposed agricultural communities, there was a significant excess in self-reported nausea, diarrhea, rhinitis, fatigue, eye and throat irritation, headache, shortness-of-breath, and wheezing.

Ames and Stratton[3] investigated an episode of community odor pollution by *n*-propyl mercaptan, a breakdown product of MOCAP® or ethoprop (O-ethyl *S,S*-dipropyl phosphorodithioate), a nematocide. Subsequent to the application of MOCAP® to a 145-acre potato field that was adjacent to a small town in Northern California, numerous odor and symptom complaints were registered with local health officials. No toxicologically mediated pesticide effects could be identified, but a community survey of more than 400 households revealed a strong relationship between perceived odors (both frequency and intensity) and a variety of self-reported symptoms, including headache, diarrhea, eye, nose and throat irritation, hay fever and asthma attacks.

C. Industrial odor sources

Pulp mills. Numerous studies in the United States and in Scandinavia have examined the health status of communities near sulfate ("kraft") pulp mills. Health endpoints examined have included acute and chronic respiratory diseases and a variety of annoyance symptoms (including headache, nausea, and eye and throat irritation). The principal odorants emitted by kraft pulp mills are hydrogen sulfide, methyl mercaptan, dimethyl sulfide, and dimethyl disulfide.[4] Although one potent lower-respiratory irritant, sulfur dioxide, accompanies odorant emissions from pulp mills, levels of sulfur dioxide in communities that surround pulp mills generally have not exceeded applicable air quality standards. Likewise, community respiratory disease rates for asthma, bronchitis, and emphysema (controlling for employment in the mills) have not been elevated.[5,6]

In contrast to respiratory disease, sensory annoyance is significantly related to odorant exposures from pulp mills. Jonsson et al.[7] conducted an odor annoyance study in Eureka, California, downwind from two kraft pulp mills. Odor annoyance was found to be positively related to odor exposure zone, a finding validated by olfactometry (see below). Deane and Sanders[8] conducted a community symptom survey, also in Eureka, examining the odor exposure zones designated in the above study. The investigators found that self-reported headache and odor annoyance were associated with residential proximity to pulp mills, but that this geographic relationship did not remain true for other respiratory, gastrointestinal, or neurological symptoms.

Refineries. Goldsmith[9] conducted a symptom prevalence survey among residents in three neighborhoods that were various distances from petroleum refineries in Southern California. The intensity of odor exposure in these three zones was validated using olfactometry. Both frequency of odor perception and degree of odor annoyance was related to exposure zone. Those who were bothered "very much" or "moderately" by odors also had significantly higher rates of self-reported eye or nose irritation, dizziness, and nausea.

Hazardous waste sites. Interview studies were conducted near three hazardous waste sites by the California Department of Health Services. A positive relationship was found between odor exposure zone (i.e. geographic area) and the prevalence rates of a variety of self-reported symptoms, including headache, nausea, eye and throat irritation, and sleep disturbances.[10-12] Reporting of symptoms was more prevalent among those who reported "environmental worry" than among those who did not profess worry, even in unexposed (control) neighborhoods.[13] When subgroups of waste-site neighbors were examined, both by frequency of odor perception and by degree of environmental worry, the two variables were found to exert both individual and synergistic effects on symptom reporting.[14]

The elevated symptom prevalence rates reported in these California studies are consistent with observations near other hazardous waste sites.[15-18] In virtually all studies of hazardous waste-site neighbors in which population exposures have occurred exclusively by the airborne route, the so-called "serious" health effects (e.g., cancer, total mortality, and adverse reproductive outcomes) are no more common in the exposed than in the control neighborhoods.[10-12,15-17] Also, with rare exception,[16] perception of "chemical odors" by community members figured prominently in the identification of the hazardous waste site as an environmental problem.

D. Summary of community studies

A common feature of studies conducted in California is that measured or modeled exposures to airborne toxicants occurred at levels well below those known to cause acute symptoms by recognized toxicological mechanisms. The odorants identified in each of the California studies were reduced sulfur gases—compounds with odor thresholds 3 to 4 orders of magnitude lower than their thresholds for respiratory irritation or systemic toxicity.[19,20] Given this toxicologic margin of safety, it will be argued that the most plausible explanation for the symptoms reported involves nontoxicologic odor-related mechanisms. Prior to considering this argument, however, the stimulus-response characteristics of odor perception and sensory irritation are briefly reviewed.

II. Sensory irritation and olfaction: physiology and measurement

Whereas odor and taste are usually thought of as the two "chemoreceptive" sensory modalities, a third modality—sensory irritation or pungency—also operates in the nasal mucosa, and it affects the perception of odorant compounds. The olfactory (first cranial) nerve, which mediates odor perception per se, perforates the cribriform plate that separates the cranial cavity from the upper reaches of the nasal cavity, and it gives rise to bilateral patches of specialized olfactory epithelium, which have a total area of approximately 5 cm² (Fig. 1).[21] Also innervating the nasal mucosa, nasopharynx, and oropharynx are branches of the trigeminal (fifth cranial) nerve, which is responsible for the perception of irritation or pungency in both taste and smell (the so-called "common chemical sense"). The olfactory and trigeminal systems project to separate portions of the brain but have overlapping functional consequences, as will be clarified later.

A. Sensory irritation

The trigeminal system and its counterpart in the lower respiratory tract, the vagus (tenth cranial) nerve, mediate a variety of protective reflex responses to potentially life-threatening chemical irritants. In experimental animals, upper-respiratory tract irritants produce a reduction of respiratory rate (or even frank breath-holding), along with rhinitis, lacrimation, and cough. Lower-respiratory tract irritant exposures likewise produce cough, but instead of breath-holding produce rapid, shallow respirations and bronchorrhea. In humans, both upper- and lower-respiratory tract irritant exposures may produce bronchoconstriction in susceptible individuals.[22]

Sensory irritation, in most cases, is related to chemical reactivity.[23] For an irritant gas or vapor, one speaks of the substance's warning properties, or its ability to produce immediate upper respiratory irritation. Such irritation triggers protective physiologic reflexes, alerts the exposed individual to danger, and initiates escape behavior. For a given degree of chemical reactivity, the warning properties of a gas or vapor tend to correlate with its water solubility.[22] Examples of irritants that have good warning properties (i.e., high water solubility) are ammonia and sulfur dioxide. A compound that shows an intermediate degree of warning is chlorine, whereas ozone, phosgene, and nitrogen dioxide—all relatively insoluble gases—provide minimal warning of exposure. Alarie[22] uses the term *sensory irritant* or *upper-respiratory tract irritant* to denote irritant gases or vapors that have good warning properties; *pulmonary irritant* is used for chemicals with poor warning properties; and *respiratory irritant* denotes substances in the intermediate group. Prolonged exposure to high levels of irritants (e.g., exposures to agents with poor warning properties or exposures in which escape is impeded) may result in the development of tracheobronchitis, chemical pneumonitis, or noncardiogenic pulmonary edema.

Individuals frequently report the gradual onset of irritative symptoms during exposures to irritants from indoor air pollution (e.g., environmental tobacco smoke, combustion sources, or "offgassing" of furnishings or building materials).[24] The fact that it may take several hours for irritants in indoor air to produce symptoms should be noted by investigators charged with studying

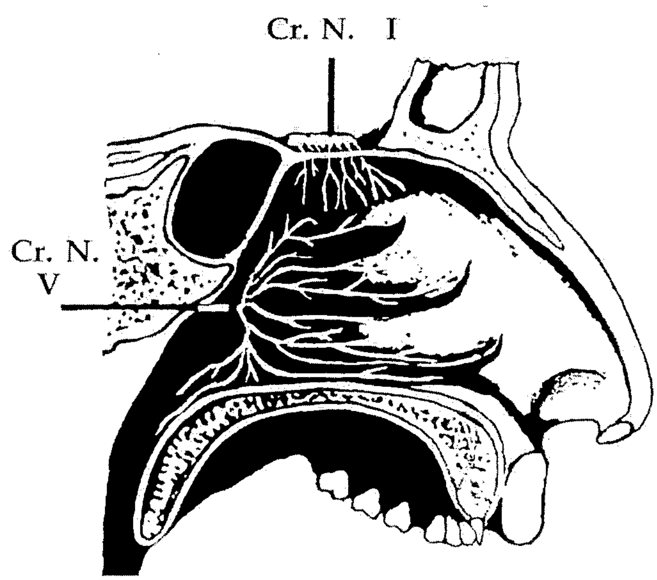

Fig. 1. Simplified anatomy and innervation of the lateral wall of the nasal cavity: Cr.N.I = first cranial (olfactory) nerve; Cr.N.V = fifth cranial (trigeminal) nerve. (Modified, with permission, from Turner.[21])

irritative symptoms, whether from indoor or outdoor exposures. Thus, differential reporting of irritant symptoms among individuals who have nominally equivalent exposures may relate not only to differing susceptibility (e.g., smokers are less sensitive to nasal irritant exposures[25]), but also to differing activity patterns and durations of exposure.

B. Olfaction

Olfaction, in contrast to irritation, has multiple dimensions, including intensity, qualitative odor identification, and an aesthetic dimension (so-called hedonic tone or pleasantness).[23] The process of olfaction begins when odorant molecules are trapped in the nasal mucus overlying the olfactory epithelium. Molecules then diffuse through that largely aqueous environment, and they make contact with the cilia of the olfactory receptor cells. A non-specific odorant binding (carrier) protein, which presumably aids in this diffusion process, has recently been identified in nasal mucus.[26] Cain[27] holds that much of the observed variability in odor potency among different compounds is related to physicochemical properties that influence molecular delivery to the receptor site, e.g., vapor pressure and water and lipid solubility. Others believe that the flexibility of a given molecular structure or the presence of selected functional groups are the major determinants of odor potency.[28-30]

Recent research has illuminated the mechanisms of odor perception at the receptor level. Olfactory transduction, or the generation of nerve impulses in response to odor stimuli, involves the reversible binding of odorant molecules to receptor proteins on the membrane of the olfactory cilia. In turn, these receptors participate in an intracellular signalling cascade that involves (successively): release of alpha subunits from GTP-binding ("G") proteins; activation of adenylate cyclase; an increase in intracellular cyclic AMP concentration; and, finally, the opening of sodium channels with a consequent electrical depolarization of the cell.[31-33] Subsequent processing of olfactory signals has been studied at various levels of neural organization, ranging from lateral connections in the olfactory bulb to high-level cortical activity.[34-37]

Recently, dramatic progress was made in the quest to identify olfactory receptors and to determine the specificity with which they bind odorants. Buck and Axel,[38] using molecular biological techniques, cloned a number of genes coding for olfactory receptor proteins in the rat. The genetic diversity documented among these receptors suggests that diverse odors might be recognized as a result of receptor specificity rather than neural processing of "odor components."[39]

C. Psychophysics

Measurement of the stimulus-response characteristics of sensory stimuli (including odorants and irritants) constitutes a branch of science known as "psychophysics." Psychophysical studies describe either the perceived intensity as a function of exposure level ("psychophysical scaling") or the minimum exposure necessary for conscious perception to occur ("threshold determination"). Specific psychophysical techniques are discussed below.

The most widely used technique of psychophysical scaling is the method of magnitude estimation. With this method, subjects are presented with randomly varying concentrations of an odorant or irritant. The respondent ranks the first stimulus with an arbitrarily chosen number; subsequent stimuli are then assigned numbers on the respondent's own scale that reflect the perceived intensity compared with the first stimulus.[40] Despite obvious interindividual variation inherent to this method, after normalization to a common scale, the data tend to reflect a similar dose-response slope (or "psychophysical function") across subjects. Another method, that of intensity matching, involves trained observers who match the perceived odor intensity of a given concentration of a test compound with known concentrations of an index compound, usually *n*-butanol. Intensity estimates so generated are said to be "normalized to the butanol scale."[40,41] In general, when psychophysical scaling methods are used, the perceived intensity of an odorant or irritant stimulus is proportional to the logarithm of the stimulus concentration, which accords with the so-called "Weber-Fechner Law."[42]

A more familiar concept is odor threshold. A threshold is a level below which an individual (or a group of individuals) cannot reliably perceive a stimulus. Subclasses of odor thresholds include odor detection thresholds (for which the respondent signals awareness that an odor of some sort is present) and odor recognition thresholds (in which the respondent identifies an odor). In reality, such determinations are so exquisitely dependent upon the conditions of measurement that the implication of an absolute limit of odor detection is problematic at best.[23,41] Methods for determining odor thresholds are listed below.

(1) **Single-sample methods.** Subjects are presented with an ascending, descending, or random series of odorant concentrations, and they are asked to respond whether an odor is present or not. There are two major sources of bias or error that complicate results obtained by this method: (a) order of stimulus presentation (ascending series tend to produce anticipatory responses; descending series tend to produce olfactory fatigue and blunt perception at low concentrations); and (b) difference in subjects' "decision criteria," or degree of caution in identifying odors.

(2) **Multiple-sample methods.** Subjects are presented with multiple odor dilution ports (normally, three or four) and are asked which port contains the odorant. Results obtained by this method tend to exhibit less variability related to the subjects' decision criteria.

(3) **Method of extrapolation of intensity response.** This method involves generation of intensity scaling data above the odor threshold and an estimation of the threshold, which is achieved by extrapolation to an arbitrarily low-odor scale value. A variant of this method involves intensity matching (i.e., matching perceived intensities of the odorant being studied to those of a comparison compound, most often *n*-butanol). The

threshold concentration of the study odorant is then estimated by extrapolating down to the equivalent threshold on the butanol scale.

Odor thresholds obtained by the single- and multiple-sample techniques are often expressed as the lowest concentration at which an odorant stimulus is detected (or identified) in a given fraction of trials by one-half of the subjects in a panel.[41] However, considerable information is lost when only average values are conveyed. For example, for most odorants, population sensitivity follows a log-normal distribution; the slope of the cumulative distribution varies from compound-to-compound.[43] Important systematic differences in olfactory sensitivity also occur with respect to age group (the elderly are less sensitive), smoking status (decreased sensitivity), and sex (in most studies, females are more sensitive).[44-49] In addition, there can be quantitative or qualitative alterations in odor perception in (a) atopic (allergic) individuals[50]; (b) individuals occupationally exposed to irritant gases, vapors, and particulates[51-57]; and (c) various other clinical states.[58] These interindividual differences in sensitivity may be important when community responses to odor abatement efforts are predicted. In addition to interindividual variability, there is considerable intraindividual variability in olfactory acuity from trial-to-trial and from day-to-day.[59,60]

In addition to interindividual and random variation in odor sensitivity, other factors may be operative in determining a person's odor acuity at a particular time. Adaptation refers to a diminution of perceived odor intensity over time in response to a constant exposure, and it is typically responsible for about a 60% attenuation of perceived intensity over a matter of minutes.[61] At the extreme, high-level exposures to some agents (e.g., hydrogen sulfide) can produce rapid and reversible olfactory fatigue or "paralysis."[20,53] Conversely, there is evidence that repeated exposure to an odorant results in enhancement of odor recognition and detection via a process of training; this phenomenon may occur in individuals who live in a community affected by an industrial odor source.[62]

Whereas chemical compounds vary in their relative odorant and irritant potencies, very few can be considered "pure irritants" or "pure odorants." Three compounds used experimentally as "pure irritants" are (1) o-chlorobenzylidene malononitrile (CBMN), (2) diphenylaminochloroarsine (DACA), and (3) carbon dioxide.[22,63] However, the odorant and irritant properties of most substances cannot be separated easily. This was illustrated in an experiment in which odorant stimuli were presented to alternate nostrils in patients with unilateral surgical ablation of the trigeminal nerve (hence, unilateral inability to perceive irritant stimuli). Odor sensitivity in these subjects was lower on the side with the trigeminal ablation, despite the fact that the odorants applied (propanol, butanol, and butyl acetate) produce little, if any, perceived irritation at the concentrations employed.[64] These observations evidenced that the common chemical sense (trigeminal nerve) may contribute to perceived odor magnitude, even when sensory irritation is not evident.

An important consideration when assessing environmental odor pollution is the frequent co-presence of multiple odorants and/or irritants. Odors tend to combine on a less-than-additive basis (hypoadditivity) without regard to the nature of the odorants involved or their degree of similarity.[27,65] A practical application of hypoadditivity is the combination of two or more odorants to achieve odor masking or counteraction.[66] The situation is simpler for combinations of irritants. Cometto-Muniz et al.[67] used the method of magnitude estimation to examine the perceived irritancy of various mixed concentrations of formaldehyde and ammonia. They found that an additive model is a reasonable approximation for the combined effects of these irritants, although small deviations occur toward hypoadditivity with low concentrations and toward hyperadditivity with high concentrations.[67]

Most environmental odor pollution problems involve exposure to potent odorants (e.g., reduced sulfur gases) at sub-irritant concentrations. These potent odorants tend to exhibit relatively "flat" psychophysical functions, i.e., large differences in concentration are accompanied by relatively small differences in perceived odor magnitude. Thus, a given relative reduction in perceived odor intensity in the community requires a larger proportionate reduction in odorant concentration when a potent odorant is involved.[68-70] This factor is frequently cited in cost-benefit analyses of abatement strategies for sources emitting potent odorants.

III. Pathophysiology of odor-related symptoms

As was noted previously under "community responses to odor pollution," most symptoms reported by individuals who are near environmental odor sources are acute in onset, self-limited in duration, and subjective (thus, difficult or impossible to substantiate objectively). Important questions exist regarding the long-term health risks associated with community exposures to airborne chemicals from industrial sources; however, if conventional toxicologic paradigms are used, the low levels of exposure that are usually documented would be linked to small increments in probability of developing latent diseases—and not linked with acute symptoms. (Whereas several air pollutants are regulated for their acute toxicity—ozone, sulfur dioxide, nitrogen dioxide, and carbon monoxide—these compounds do not have prominent odors at the levels at which they are regulated.) Thus, explanation of acute odor-related symptoms near industrial, agricultural, or hazardous waste sources focuses on the differentiation of acute toxicity from non-toxicologic, odor-related health effects.

A. Relationship of odor perception to acute toxicity

The industrial hygiene literature contains reference to the "odor safety factor," which is the ratio of the (8-h) occupational "threshold limit value" (or "TLV") to the odor threshold for a given compound.[43] In this scheme, a large odor safety factor indicates a wide margin of safety between a barely perceptible (odorous)

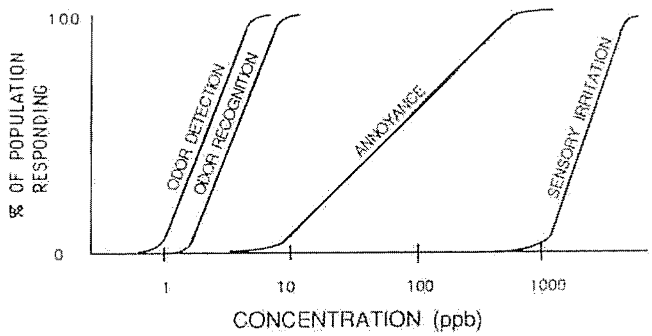

Fig. 2. Relationship of odor perception, annoyance, and sensory irritation for hydrogen sulfide. (Adapted from Flesh and Turk,[71] Amoore and Hautala,[43] and Ruth.[19])

concentration of a gas or vapor and a concentration expected to produce toxicity (often acute irritation) in an occupational setting. Thus, if a gas or vapor produces acute irritation near or even below its odor threshold (i.e., has a low odor safety factor), odor-related symptoms in the community may reflect the intrinsic toxicity of the compound involved. An odorant chemical that has a "moderate" odor safety factor (greater than 10–25) could also produce acute toxicity among community members, but only if present at concentrations that substantially exceed its odor threshold.

Notwithstanding the above possibilities, acute odor-related symptoms can (and do) occur in the absence of toxicologically credible exposures. For example, the common industrial sulfur gases (hydrogen sulfide, various mercaptans, and thiophenes) have odor thresholds orders of magnitude lower than levels known to cause symptoms by classical toxicologic or irritative mechanisms; yet, these gases are often associated with "annoyance" and symptom reporting at levels that barely exceed their odor thresholds (Fig. 2).[71] Such highly odorous compounds are found in a variety of industrial and hazardous waste materials, and they occur as breakdown products of some commercial pesticides. Thus, barring the applicability of other mechanisms of acute toxicity, when community exposures are confined to sub-irritant levels of one or more odorant compounds, explanation of acute odor-triggered symptoms must invoke non-toxicologic, odor-related mechanisms. These mechanisms have been postulated to include innate odor aversions; innate pheromonal phenomena; odor-related exacerbation of underlying conditions; odor-related aversive conditioning; odor-related, stress-induced illness; mass psychogenic illness; and recall bias.

B. Innate odor aversions

Although individual factors are clearly important in explaining odor response, everyday experience indicates that there are many odorants that are perceived by most individuals as either pleasant or unpleasant. The English language contains a variety of descriptive adjectives (e.g., aromatic, putrid, rancid) and nouns (e.g., stink, stench), which attest to the communality of olfactory aesthetics. Whereas it seems plausible that many odor aversions are rooted in childhood hygienic experiences, Steiner[72] reports that newborn babies react with predictable facial expressions to nominally pleasant and unpleasant odors and interpretes this as evidence for the existence of innate odor aversions. Cross-culturally, similar patterns of self-reported odor associations have been obtained among interviewees in Germany and Japan (admittedly not a random sample of cultures); unpleasant odors include "exhaust fumes and smoke . . . burnt and deteriorated food . . . excrement . . . body odor and sweat."[73] Akin to the concept of innate odor aversions, the term *reflex nausea* has been used by Cain and Garcia-Medina to refer to involuntary visceral responses to odors.[74] In experimental subjects, exposure to malodors decreases performance of such complex tasks as proofreading,[75] and even the suggestion of the presence of a malodor (i.e., a sham odor) can produce an increase in the number of physical symptoms reported.[76]

C. Innate pheromonal phenomena

Odorant chemicals that trigger hormonal or reflex behavioral responses in an organism are termed *pheromones*. It was initially believed that pheromonal phenomena were confined to non-human species. More recently, however, researchers have documented an effect of odorous androgenic steroids secreted in sweat in regulating the female estrus cycle.[77-79] The relationship, if any, of such human phenomena to potential adverse health effects from environmental odor pollution is, at this time, purely conjectural.

D. Odor-related exacerbation of underlying conditions

One pre-existing medical condition that may confer hypersusceptibility to odors is bronchial asthma. Whereas perfumes and flowers have traditionally been associated with triggering of asthma attacks, the odor of cleaning products, paints, and petroleum products has also been implicated in some individuals.[80-82] Another example of augmented odor sensitivity is seen in "morning sickness," or nausea that occurs during early pregnancy.[83] Anecdotal case reports of environmental odor effects in pregnancy include heightened nausea in response to the odor of polyvinylchloride plastic in a waterbed factory and in response to odoriferous petroleum sludge uncovered while gardening (author—unpublished data).

It has also been speculated that pre-existing psychological conditions (e.g., hypochondriasis or somatization disorder) might render some individuals more symptomatic in response to odorant stimuli.[84] In fact, in a survey of adults living near two malodorous hazardous waste sites in Louisiana, it was found that symptom reporting was related to hypochondriasis.[17] However, this personality trait was equally prevalent in exposed and control neighborhoods, and a more important variable in explaining differences in symptom prevalence by area were individuals' beliefs that hazardous waste sites degraded the environment (see discussion of "environmental worry," below).

E. Odor-related aversive conditioning

Many investigators have documented what appear to be conditioning phenomena after acute over-exposures to irritant (or other acutely toxic) chemicals. After the initial traumatic exposure, these patients report that they experience a variety of symptoms in response to low-level (i.e., odorant) exposures, including the panic or hyperventilation symptom cluster (i.e., anxiety, sweating, tachycardia, "air hunger," paresthesias, lightheadedness, and nausea).

Tabershaw and Cooper[85] studied individuals after they experienced a documented pesticide intoxication; recurrent headache and nausea, which occurred during and after minimal exposure to solvent-containing products, were reported. Tabershaw and Cooper speculated that a conditioning to the odor of the solvent carrier had occurred, and termed this phenomenon *acquired intolerance to pesticides*. Schottenfeld and Cullen[86] referred to "atypical post-traumatic stress disorder" (PTSD) in the case of a worker who was repeatedly exposed to irritant levels of phosphoric acid vapors; although the worker was transferred out of the department in which he was exposed, he persisted with complaints of respiratory irritation and chest pain in response to an ever-widening array of odorant chemicals in the home and workplace. Shusterman et al.[87] described workers who developed intolerance to odors (of phosphine gas in one case and formaldehyde in another) after traumatic overexposures. They suggested that classical (respondent) conditioning had occurred and that an odorant concentration of the particular gas or vapor served as a conditioned stimulus for a panic response. This phenomenon was termed *behavioral sensitization to irritant/odorants*.

The concept of acquired odor intolerance has also been applied to individuals absent an identified traumatic overexposure. Gyntelberg et al.[88] documented recurrent attacks of dizziness, nausea, and weakness in a subset of solvent-exposed workers. Challenge with solvent vapors at odorant (but sub-narcotic) levels reproduced the symptoms, but did not produce any abnormalities of vestibular function, as evidenced by electronystagmography. The authors referred to this finding as "acquired intolerance to solvents." Dager et al.[89] documented panic-like symptoms among workers exposed to organic solvents. In these patients, the initial onset of symptoms occurred when solvent exposure occurred in the workplace, but subsequent panic attacks occurred both with and without workplace triggers. Bolla-Wilson et al.[90] described "conditioning of physical symptoms after neurotoxic exposures," in which the classical conditioning paradigm was applied to recurrent neurological symptoms triggered by low-level (odorant) chemical exposures. Recently, it has been proposed that the term *odor-triggered panic attacks* be applied to individuals who display odor-induced autonomic arousal symptoms, regardless of the nature of the antecedent exposure (i.e., traumatic versus nontraumatic exposure history).[91]

Despite the apparent utility of learning theory in explaining some odor-related symptoms, exposures of a magnitude sufficient to produce frank aversive conditioning are rare in environmental (as distinct from occupational) settings. Nevertheless, it is possible that more subtle types of associational learning may influence individuals' responses to environmental odors.

F. Odor-related, stress-induced illness

So called "environmental stress" has been studied after both natural and man-made disasters. Davidson et al.[92] documented impaired concentration, insomnia, and elevated urinary catecholamine excretion among residents near the disabled Three Mile Island (TMI) nuclear power plant. Davidson and Baum extended this line of investigation in an unpublished study in which residents near a toxic waste site were compared with those in a control neighborhood. They found increased rates of symptom reporting and somatization, increased feelings of helplessness and depression, and decreased psychomotor performance. Also found were elevated urinary catecholamine excretion (similar to the TMI residents), interpreted by the authors to be a characteristic stress response (Andrew Baum, Personal Communication, 1990). Although blood pressure was not directly examined in the hazardous waste site study, blood pressure elevations were associated with chronic stress and high catecholamine excretion in another TMI study.[93]

The related issue of self-reported "environmental worry" has been examined epidemiologically and shown to be related to symptom reporting, both among hazardous waste site neighbors[17] and in residents distant from such sites.[13] A similar variable, "belief in exposure," was shown to be related to both symptom reporting and psychological distress, independent of proximity to a hazardous waste site.[94] Shusterman et al.,[14] noting that symptom prevalence near three hazardous waste sites was related to both degree of environmental worry and frequency of odor perception, suggested that environmental odors may precipitate ("cue") acute stress among individuals who perceive the odor source as a toxicologic risk.

In this context, it is interesting to consider the range of physical effects that are attributed to psychological stress. Acutely, stress produces reversible elevations in blood pressure, both in normotensives and in patients with hypertension.[95-97] Acute stress also decreases gastric motility in some patients who have functional (non-ulcer) dyspepsia,[98] and it increases scalp muscle tension (as documented by electromyography) in patients with muscle tension headaches.[99,100] Chronic stress has been implicated in the development of coronary artery disease[101,102] and peptic ulcers,[103,104] although given the predominantly retrospective design of these studies, their interpretation is controversial. Also disputable is the role of stress in the development of chronic hypertension.[105-107] Thus, although an intuitively plausible mechanism, attribution to environmental odor pollution of a causal role in the development of chronic stress-related illnesses is, at this time, conjectural.

C. Mass psychogenic illness

Illness clusters that involve epidemic fainting, nausea, hyperventilation, or panic symptoms have been termed *mass psychogenic illness.* Mass psychogenic phenomena are suspected when symptoms spread rapidly in a closed population (e.g., workplace or school), and no credible causal agent can be identified. In such situations, ambient odors frequently play an important role in the propagation of alarm, often against a backdrop of psychosocial stressors.[108-110] Rapidly spreading symptoms, however, are not generally characteristic of the community health complaints documented near environmental odor sources.

H. Recall bias

In epidemiologic studies of odor-related health effects, the uniform elevation of reported symptoms, particularly those that involve multiple organ systems, raises the question of recall bias.[17] Recall bias occurs when an adverse health outcome, the publicity surrounding an environmental issue, or another factor (such as odor perception) affects the accuracy of recall for a particular symptom.[111] One strategy for identifying recall bias is to inquire about symptoms for which no credible link can be postulated with the exposure (i.e., "sham" variables). It has been postulated, for example, that toothache could be related neither to upper respiratory irritation nor to odor-related autonomic arousal, and might be used as an appropriate sham variable in studies of environmental odor pollution.[13]

IV. Characterizing environmental odor pollution

Environmental odorant exposure can be documented by either instrumental methods (qualitative identification or quantitative measurement of airborne odorant chemicals) or by psychophysical methods (description or intensity estimation of odors by naive or trained observers). Both play a role in the day-to-day operation of air pollution control agencies. Special studies, frequently commissioned by industrial facilities facing regulatory action, may characterize odor sources using highly sophisticated techniques.

A. Instrumental techniques

Instrumental techniques can be broken down into two major subtypes: volumetric sampling and real-time instrumentation. Volumetric techniques utilize time-delimited atmospheric samples (typically collected on adsorbant resins, in Tedlar bags, or in evacuated stainless steel canisters), which are subsequently analyzed by gas chromatography. These techniques tend to be more sensitive than real-time instrumentation; however, valid results are predicated upon sampling at the time of a perceived odor peak, expeditious analysis, and stringent quality control measures (i.e., field blanks, instrument blanks, and spiked samples). In addition to sensitivity, volumetric techniques provide the advantage of specificity (i.e., simultaneous identification of a wide range of individual chemical species). This latter feature may be important when an attempt is made to identify an unknown, but potent, environmental odorant.[112]

Real-time instruments, which are often less sensitive than volumetric sampling, provide an opportunity to document short-term variations in odorant chemical concentration. However, selectivity may be a problem with real-time monitors, e.g., the measurement of "total reduced sulfur gases" (TRS) near kraft pulp mills. Here, temporal variations in the relative contributions to TRS of its constituent gases (each having a different odorant potency) may render TRS fluctuations that are difficult to interpret vis-à-vis community odorant exposure.

Hybrid instrumental techniques are also possible in which, for example, peak real-time instrument readings automatically trigger volumetric sampling. (For the pulp mill example described above, such a technique would create the opportunity to document variations in the relative composition of the TRS stream.) Another hybrid technique, citizen-triggered volumetric sampling, utilizes pre-evacuated cannisters or timed air pumps, which are activated by community members at the time of perceived odors (Robert Reynolds, Personal Communication, 1989).

B. Psychophysical methods

Psychophysical methods for the documentation of environmental odors are collectively termed *olfactometry,* although this label encompasses many different specific techniques. At the most elementary level, trained observers simply describe perceived odors in the field. At the next level of complexity, dilutional methods (as discussed in the following section) may be used to quantitate the intensity of an environmental odor. Also at an intermediate level of complexity, trained observer panels can, either in the field or in a laboratory, compare the intensity of a sampled atmospheric odor with a reference compound (typically, *n*-butanol). The most technologically sophisticated level of combined psychophysical and instrumental methodology is via "organoleptic evaluation of gas chromatographic effluents"—better known as "smell chromatography." This technique involves splitting the output of a chromatography column between the instrument's detector and an observer port, during which procedure an observer identifies the odors associated with chemical "peaks" as they are eluted.[113,114] This technique is sometimes applied in efforts to identify unknown odorants.

V. Odor pollution and environmental policy

Air pollution standards, in general, apply to either emissions or ambient air quality; both approaches are employed in the regulation of environmental odor pollution. Emission standards pertain to specific source types. Monitoring of such sources has the advantage of being site-specific, but the disadvantage of requiring dispersion modeling if community exposures are to be estimated. Ambient air quality standards, while addressing more directly the issue of environmental quality in the community, often require mobile monitoring and source apportionment before a violation can be attributed to a specific emitter. Nuisance statutes, when applied to environmental odor pollution situations, enable either public or private parties to seek abatement of an odor source, which is based upon interference with quality of life and the enjoyment of one's property (see, for example, California Health and Safety Code, Section 41700). These various approaches are reviewed in greater detail below.

Emission standards. Emission standards have been used by the Environmental Protection Agency to regulate specific industries, normally in the form of New Source Performance Standards (NSPSs). Most notably, a number of odor-related NSPSs have been devised for the regulation of reduced sulfur gas emissions (TRS) from pulp mills.[115] At a local level, the San Francisco Bay Area Air Quality Management District has established emission standards for five chemical types (dimethylsulfide, ammonia, mercaptans, phenolic compounds, and trimethylamine); emission point concentration limits were set at 100 times the odor threshold for the substances in question.[116,117]

Ambient air quality standards. Ambient air quality standards have been established by some states for the regulation of odorant exposures. California adopted a 30 ppb, 1-h ambient air quality standard for hydrogen sulfide, which is based on the assumptions that the average annoyance threshold for hydrogen sulfide is approximately five times its mean odor detection threshold, and that approximately 40% of residents would express annoyance at the level of exposure described.[70] In comparison, Connecticut has ambient air quality standards for 53 odorant compounds.[41] One municipality—Jacksonville, Florida—has established an ambient TRS standard (in contrast to EPA's TRS emission standard) to deal with the three pulp mills within its borders.[118]

Odor nuisance statutes. Odor nuisance statutes vary considerably in their details; however, their common intent is to prevent or abate environmental insults that interfere with the well-being of community residents and their enjoyment of their property.[119] Thus, odors that cause an individual to stay indoors, to temporarily leave the neighborhood, or that are irritating or annoying without causing specific behavioral adaptations, would qualify as nuisances. Abatement of an odor nuisance is possible through both private and public actions (the latter typically brought by air pollution control agencies). Whereas "annoying" odors are recognized in the law as constituting a nuisance, effective abatement of public nuisances by responsible agencies is highly variable, and private nuisance actions place a considerable financial burden upon plaintiffs.[41,120]

Some air quality districts, faced with the fact that odor problems constitute a majority of complaints from the public, have devised special regulations for the abatement of odor nuisances. The Bay Area Air Quality Management District, under its Rule 7, has established a quasi-ambient standard for odorant exposure. This standard is based on the assumption that, for a given odorant or mixture of odorants, the annoyance threshold is a fixed multiple of the odor threshold. In practice, an inspector who responds to a community odor complaint obtains a specimen of community air, and, using a dilutional olfactometer, presents a fourfold dilution of the specimen to a panel of fellow employees whose odor detection ability has been validated as being within a normal range on the day of testing.[117] If two of three panelists reliably detect the offending odor, a nuisance citation is issued. In the case of one pulp mill located within the jurisdiction of the district, 33 of 36 samples so obtained supported the issuance of nuisance citations (Dario Levaggi, personal communication, 1989).

In California, a legal distinction is made between *annoyance* and *actual injury*; the latter term applies to a health complaint that ". . . in the opinion of a licensed physician or surgeon, requires medical treatment involving more than a physical examination" (Health and Safety Code, Section 42400.2 [c]). The determination of an "actual injury" results in more than a twofold difference in the maximum daily fine for an odor nuisance violation. It has been noted, however, that this distinction is difficult to translate into practice because a single individual's decision to seek medical attention for a symptom (e.g., for a headache) could (if the individual were instructed to take a medication) influence the gravity of the nuisance violation, independent of other circumstances surrounding the episode.[120]

VI. Future research needs

A major difficulty for public health and air pollution personnel who deal with allegations of odor-related health effects is the largely subjective nature of the complaints. Faced with similar problems, researchers in indoor air pollution have searched for sensitive measures of upper-respiratory tract irritation that are capable of objectively documenting irritation at its early stages.

In one study of subjects who were exposed to progressively increasing concentrations of environmental tobacco smoke, blink rate was shown to be an objective correlate of subjective eye irritation.[121] Eye symptoms were also the focus of a study in which self-reported eye irritation in office workers was correlated with slit lamp findings on ophthalmologic examination. Both abnormally rapid precorneal film breakup time (using fluorescein dye) and punctate epithelial staining of the bulbar conjunctiva (using lissamine green stain) were associated with elevated symptom reporting;[122] similar findings with regard to precorneal film breakup time have been reported elsewhere.[123] Photographic techniques have been used to document increases in conjunctival bloodflow ("redness"), which is characteristic of eye irritation from exposure to either allergens or dust.[124-125] Changes in nasal airflow impedance have been documented in human subjects exposed to irritant vapors from carbonless copy forms, with impedance increases occurring at lower exposure levels than either subjective irritation or congestion.[126] Finally, spectrographic acoustic analysis of voice recordings have shown decreased harmonics-to-noise ratio ("hoarseness") in patients with vocal cord nodules and polyps, and could similarly be used to document irritant-related voice changes.[127]

All of the epidemiological reports reviewed earlier in this review involved retrospective ascertainment of symptoms. From a methodologic standpoint, once an environmental odor problem is initially identified, subsequent attempts to correlate symptoms and odors should ideally utilize data gathered prospectively (i.e., using symptom logs and real-time environmental monitoring). Given the self-limited nature of most odor-related symptoms and the rapidly fluctuating character of environmental odorant exposures, such data could be used to conduct a time-series analysis (a more rigorous analytical method of analyzing evanescent symptoms than the use of period prevalence rates).[128] However, such studies would, in some cases, be dependent upon improved real-time instrumental techniques, given the superiority of the human nose to the laboratory in detecting many odors.

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The California Department of Health Services sponsored a working conference entitled "The Health Effects of Environmental Odor Pollution," held in Davis, California on January 19–20, 1989. This article reviews many of the topics discussed at that meeting, augmented by the ongoing literature review being conducted within the Department. The aim of this review is to provide a resource for local health officials who are charged with responding to questions regarding the health impact of environmental odor pollution.

The following individuals provided direction for this review through lecturing, participation in panel discussions, and active planning for the Working Conference on Environmental Odor Pollution: John Amoore, Ph.D.; Theodore Belsky, Ph.D.; William Bruvold, Ph.D.; William S. Cain, Ph.D.; Laurence Chaset, J.D.; James Cone, M.D., M.P.H.; T. Timothy Crocker, M.D.; Laura Davidson, Ph.D.; William Draper, Ph.D.; Mr. Richard Duffee; John Dwyer, J.D.; Mr. Steven Ellis; John Girman, Ph.D.; Lynn Goldman, M.D., M.P.H.; Robert Harrison, M.D., M.P.H.; Mr. Dario Levaggi; Michael Lipsett, M.D., J.D.; Melanie Marty, Ph.D.; Raymond Neutra, M.D., Dr.P.H.; George Preti, Ph.D.; Mr. Robert Reynolds; Mr. Charles Sassenrath; Robert Stephens, Ph.D.; William Vance, Ph.D.; and Charles Wysocki, Ph.D. Additional editorial assistance was provided by: Richard Ames, Ph.D., M.P.H.; Andrew Baum, Ph.D.; Enrique Cometto-Muniz, Ph.D.; Norman Kado, Ph.D.; Richard Jackson, M.D., M.P.H.; Susan Knasko, Ph.D.; Jane Lipscomb, R.N., Ph.D.; Neal Maizlish, Ph.D.; Susan Thollaug, R.N., M.P.H.; and Lauren Zeise, Ph.D.

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ORIGINAL RESEARCH

Exhibit 5

Terpenes and Terpenoids in Chemical Sensitivity

William J. Rea, MD, FACS, FAAEM; Carolina Restrepo, MD; Yaqin Pan, MD

ABSTRACT

Context • Terpenes and terpenoids are a diverse class of organic compounds produced by a variety of plants, particularly conifers. Chemically sensitive patients can be targeted by terpenes and terpenoids, resulting in a triggering of symptoms and pathology. Often patients cannot clear their symptoms from exposure to chemicals unless terpenes and terpenoids are avoided and neutralized along with chemical avoidance and treatment.

Objective • This article evaluates the presence, diagnosis, and treatment of terpenes exposure in chemically sensitive patients.

Design • A double-blind, placebo-controlled, 2-part study was designed to establish the chemically sensitive state of the patients in part 1, followed by a second set of challenges to determine each patient's concurrent sensitivity to terpenes and terpenoids in part 2. In all of the challenges, normal saline was used as a control. A case report illustrates the history of 1 patient and describes the authors' treatment methods.

Setting • The study was developed and conducted at the Environmental Health Center of Dallas (EHC-D) because the environment within the center is 5 times less polluted than the surrounding environments, as determined by quantitative air analysis and particulate counts.

Participants • A total of 45 chemically sensitive patients at EHC-D with odor sensitivity to terpenes. The cohort included 18 males and 27 females, aged 24-62 y.

Intervention • Patients were deadapted (4 d) and evaluated in a 5-times-less-polluted environment, which was evaluated using air analysis and particulate counts. After deadaptation, the patients were challenged by inhalation in a controlled, less-polluted glass steel booth inside an environmentally controlled room with an ambient air dose of the toxics in the order of parts per billion (PPB) and parts per million (PPM). These toxics included formaldehyde, pesticide, cigarette smoke, ethanol, phenol, chlorine, newsprint, perfume, and placebo. They were also challenged intradermally with extracts of volatile organic compounds (VOCs), including formaldehyde, orris root, ethanol, phenol, cigarette smoke, chlorine, newsprint, perfume, terpenes, terpenoids, and placebo.

Outcome Measures • Inhaled challenges recorded pulse, blood pressure, peak bronchial flow, and other signs and symptoms 30 min before and at 15-min intervals for 2 h postchallenge. Intradermal challenges recorded wheal size and the provocation of signs and symptoms.

Results • Different numbers of patients were tested for each terpenes source because of time-related factors or the cumulative effect of testing, which made patients unable to continue. Of 45 chemically sensitive patients in the study, 43 demonstrated sensitivity to terpenes.

Conclusions • This particular patient group was positive for a number of toxic and nontoxic chemicals provoking their symptoms. This study shows there was a connection between VOCs, other chemicals, and terpenes in chemically sensitive patients in a prospective cohort study. It has also shown the potential for terpenes to exacerbate symptoms of chemical sensitivity. Further research on this topic is recommended. (*Altern Ther Health Med.* 2015;21(4):12-17.)

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While diagnosing and treating chemically sensitive patients at the Environmental Health Center of Dallas (EHC-D) under less polluted conditions, the authors observed some patients complain that the odor of plants (terpenes) caused their chemical sensitivity to exacerbate and manifest by spontaneous bruising, petechia, edema, acne, or inability to walk a straight line with eyes open or closed. These patients' chemical sensitivity could not be controlled until the odors were recognized and then eliminated or neutralized by injection.

Terpenes and terpenoids are 2 of the most common natural incitants involved in chemical sensitivity, along with toxic chemicals such as natural gas, pesticides, herbicides, volatile organic chemicals, and metals. Terpenes are a class of natural hydrocarbons having a relationship to isoprenes, which are building blocks of natural substances. Isoprene consists of 5 carbon atoms attached to 8 hydrogen atoms (C_5H_8).[1] The most common isoprene is 2-methyl-1,3-butadiene, which was found in the breath analysis of the patients by Guenther et al.[2] Terpenoids are an oxygenated derivative of hydrocarbons or new compounds structurally related to isoprene. More than 5000 structurally determinate terpenes are known. Terpenes have an odor that appears to be pleasant to normal people but is toxic to chemically sensitive patients.[3] The odors of pine or cedar are examples of natural terpenes that can trigger many reactions in the body, including all the major systems, as seen in the authors' series of patients. Not only are the terpenes released from natural plants such as pine, cedar, hogwort, juniper, eucalyptus, and camphor, or natural plant derivatives, such as turpentine, but they are in the air from oil refineries, natural rubber factories, and isopentenyl pyrophosphate and dimethylallyl pyrophosphate factories.

Isoprenes are emitted in almost equivalent quantities as fumes from plants as methane gas is from the earth, accounting for almost one-third of all natural hydrocarbons released into the atmosphere.[2] Chemically sensitive patients can be targeted by terpenes and terpenoids resulting in triggering of symptoms and pathology, just as toxic chemicals do. Often chemical avoidance and treatment do not clear these patients' symptoms until they have been treated by elimination and intradermal neutralization of terpenes.

Camphor is a terpenoid known as 1,7,7-trimethylbicyclo(2.2.1)heptan-2, with the chemical formula $C_{10}H_{16}O$. It is found in the wood of the camphor laurel *Cinnamomum camphora*, a large evergreen tree very common in California and the southern United States.[1] Camphor contains volatile chemical compounds in all plant parts. Camphor has 6 chemical variants including (1) camphor; (2) linalool; (3) 1,8-cineole; (4) nerolidol; (5) safrole; and (6) borneol. Another common source is synthetic disinfectants.

MATERIALS AND METHODS

Participants

The cohort was composed of 45 patients at EHC-D who demonstrated chemical sensitivity to ambient doses of chemicals such as natural gas, pesticides, formaldehyde, phenol, chlorine, cigarette smoke, newsprint, and/or ethanol. In addition, each of the participants also complained of terpene sensitivity, particularly the odors of pine, mountain cedar, ragweed, hogwort, eucalyptus, and mint, as well as natural rubber. Even though they avoided exposure to and the authors retreated for the chemicals, the participants remained ill because of their sensitivity to the odors of the terpenes, which persisted 365 days per year. The cohort included 18 males and 27 females, aged 24 to 62 years.

Setting

The study was developed and conducted at the Environmental Health Center of Dallas (EHC-D) because of the less polluted environment, as determined by quantitative air analysis and particulate counts. EHC-D was designed to minimize chemical and particulate emissions. Surfaces and structural materials of copper, porcelain, steel, aluminum, and glass were used for this reason. A recirculating ventilation system was used to prevent outside air toxics from entering. High-quality, charcoal, paper, and steel filters were used in the ventilation system to shield patients from fumes of any outgassing, extraneous gasses, and extraneous particulates that entered. Employees and patients were also not allowed to use any chemicals including perfume and scented cosmetics inside the facility. The resulting environment within EHC-D is 5 times less polluted than the environment outside the facility.

The air was evaluated for pollutants at the EHC-D and quantified on a daily basis with standard tests that identify fine particulate matter (10 parts per billion [PPB], 2.5 PPB), sulfur dioxide, nitrogen dioxide, carbon monoxide, ozone, pollen, mold, benzene, arsenic, cadmium, polycyclic aromatic hydrocarbons,[4] and others. Using the same air pollutant tests, the results were compared with other areas of the building that were not designed and ventilated in the same manner. The air within the clinic was free of pesticides, solvents, and terpenes.

Design

The study was divided into 2 parts, both conducted within the less-polluted environment of the EHC-D. Double-blind procedure was employed for both parts, using normal saline as a placebo.

A chemically sensitive cohort of 45 patients exhibiting odor sensitivity to terpenes and terpenoids was evaluated under less-polluted, environmentally controlled conditions for diagnosis and treatment. These patients lived in a specially designed, 5-times-less polluted, environmentally controlled wing of the hospital or outpatient living facility, as determined by air analysis and particulate count. They were deadapted by fasting for 4 days. Their total burden of toxics was reduced as they eliminated some chemicals and particles from their bodies while reducing intake by breathing less-polluted air and ingesting no food. During deadaptation, they also became extremely aware of ambient odors.

The first challenge was an ambient dose of inhaled chemicals in a glass steel booth inside an environmentally controlled room. Ambient doses in the order of PPB were

Table 1. Double-blind Inhalant Challenge of Ambient Chemicals in 45 Terpene-sensitive Patients With Chemical Sensitivity in a Less-polluted Room of the Less-polluted Wing at EHC-D

Chemical	Tested (N)	Positive (n)	% Positive	Dosage (PPM)
Perfume	45	45	100.0	Ambient
Newsprint	40	40	100.0	Ambient
Pesticides	21	18	85.7	<0.0034
Formaldehyde	18	15	83.3	<0.20
Cigarette smoke	42	35	83.3	Ambient
Ethanol	21	16	76.2	<0.50
Phenol	22	15	68.2	<0.20
Chlorine	23	12	52.2	<0.33
Placebo	45	0	0.0	Normal saline

Abbreviations: EHC-D, Environmental Health Center of Dallas; PPM, parts per million.

Table 2. Double-blind, Intradermal Challenge of Ambient Chemicals in 45 Terpene-sensitive Patients With Chemical Sensitivity

Chemical	Tested (N)	Positive (n)	% Positive	Dosage (PPM)
Formaldehyde	18	18	100.0	<0.20
Orris root	42	40	95.2	0.05
Ethanol	41	35	85.4	<0.50
Cigarette smoke	42	35	83.3	0.05
Newsprint	39	28	71.8	0.05
Perfume	39	26	66.7	0.85
Phenol	17	9	52.9	<0.20
Chlorine	11	6	54.5	<0.33
Placebo	45	0	0.0	Normal saline

Abbreviation: PPM, parts per million.

obtained by setting each chemical in an open glass container inside the booth for 10 minutes. Patients were challenged with perfume, newsprint, pesticides, formaldehyde, cigarette smoke, ethanol, phenol, chlorine, and placebo to prove their chemical sensitivity. Patients had pulse, blood pressure, peak bronchial flow, and other signs and symptoms recorded 30 minutes before and at 15-minute intervals for 2 hours postchallenge. The second challenge in part 1 was an intradermal provocation challenge in the environmentally controlled room. Patients were challenged with formaldehyde, orris root, ethanol, cigarette smoke, newsprint, perfume, phenol, chlorine, and placebo. Each intradermal test was measured for wheal size and the provocation of signs and symptoms.

In part 2, the intradermal challenge conditions of part 1 were replicated and the challenges consisted of pine, trees, ragweed, mountain cedar, grass, and placebo. Each intradermal test was, again, measured for wheal size and the provocation of signs and symptoms.

RESULTS

The patients of this series were positive for numerous chemicals, toxic and nontoxic, establishing the chemical sensitivity when challenged in the deadapted state in a less-polluted, specially designed, controlled environment. They were also proven sensitive to the terpenes by intradermal challenge, confirming these patients' responses to the odors of pine, cedar, grass, tree, ragweed, and mountain cedar terpenes.

Different numbers of patients were tested for each toxin or terpenes because of time-related factors, such as patients who had to leave with other obligations or the cumulative effect of testing, which made patients unable to continue. The group of patients tested in the inhalant challenge (Table 1) was significantly sensitive to perfume (100%), newsprint (100%), pesticide (85.7%), formaldehyde (83.3%), cigarette smoke (83.3%), ethanol (76.2%), phenol (68.2%), and chlorine (52.2%), whereas the intradermal challenge was significant for formaldehyde (100%), orris root (95.2%), and ethanol (85.4%). Cigarette smoke (83.3%) showed similar results in both intradermal and inhalant challenges. The intradermal challenge of terpenoids and terpenes (Table 2) showed a significantly high percentage of patients sensitive to pine (60.5%), trees (38.9%), ragweed (27.8%), mountain cedar (18.9%), and grass (8.1%). None of the patients reacted to the placebo (normal saline) in the inhalant or intradermal challenges in part 1 of the study.

In part 2, the terpenes intradermal challenges (Table 3) showed 23 of 38 (60.5%) patients were sensitive to pine terpenes, 14 of 36 (38.9%) were sensitive to tree terpenes, 10 of 36 (27.8%) were sensitive to ragweed terpenes, 7 of 37 (18.9%) were sensitive to mountain cedar terpenes, and 3 of 37 (8.1%) were sensitive to grass terpenes; therefore, it was established that these patients were not only sensitive to toxic chemicals but also the odor of plant terpenes. None of the patients reacted to the placebo (normal saline) in the intradermal challenge in part 2 of the study. The results show that 43 of 45 (95.6%) chemically sensitive patients were sensitive to terpenes.

Patient management included massive avoidance of pollutants, including terpenes in the air; oxygen therapy (4-8 L/min of oxygen for 2 h/d for 18 d); intradermal immunotherapy (consisting of histamine 05/5 dilution [1:3000] 4 times/d using a dose of 0.10 cm^3);

Table 3. Double-blind Intradermal Challenge of Sensitivity to Various Types of Terpenes and Terpenoids

Terpenes and Terpenoids	Tested (N)	Positive (n)	% Positive	Dosage (PPB)
Pine	38	23	60.5	0.05
Trees	36	14	38.9	0.05
Ragweed	36	10	27.8	0.05
Mountain cedar	37	7	18.9	0.05
Grass	37	3	8.1	0.05
Placebo	38	0	0	Normal saline

Abbreviation: PPB, parts per billion.

serotonin (05/4 dilution 4 times/d using a dose 0.10 cm^3); capsaicin (0.05/4 dilution using a dose of 0.10 cm^3 every 4 d); and terpenes antigens (0.05/3-0.05/6 dilution every 4 d). Intradermal treatment for terpenes and terpenoids was done with optimum testing doses including pine, trees, grass, ragweed, and mountain cedar terpenes. The patients did well with treatment and 43 of 45 improved their symptoms as a result.

CASE REPORT

A 71-year-old, white female teacher with a history of chronic anemia came to EHC-D with the complaint of a 25-year history of frontal headache, described as a sharp band of pain that was episodic, presenting 2 to 3 times per week for approximately 20 minutes. Spontaneous exacerbations and remissions had occurred in the prior several years, particularly during the winter. She also reported tinnitus, tingling, numbness, and paresthesias that were related to episodes of dyspnea, epistaxis, nasal discharge, postnasal drip, eye itch, wheezing, and cough.

She had been treated with a variety of medication and had a medical history of chronic sinusitis, anemia, hypothyroidism, hypercholesterolemia, small-calcified intramural leiomyomas, ovarian cysts, and irritable bowel syndrome. No surgery or hospitalization had occurred.

The patient had a history of hypersensitivity to trees, including mountain cedar and pecan trees, and to grasses including Bermuda, Johnson, and Timothy grasses. Her symptoms were triggered by the odor of pine and cedar trees 365 days per year. She smelled a strange odor each time she walked into the house, which had been built in 1968 in a pine/cedar forest, with the interior of the house made primarily of pine and cedar. Table 4 shows test results and evaluation of her house related to an indoor air sample taken on November 11, 2013. The sample was analyzed for the presence of volatile organic compounds (VOCs) and aldehydes, including terpenes and camphor.

This patient was proven to have chemical sensitivity by inhaled challenge and intradermal provocations. When a breath analysis was performed, the patient had levels of camphor, α-pinene, and acetic acid. She also had a positive inhaled provocation to α-pinene and acetic acid. She also had a positive intradermal provocation to α-pinene. Camphor and acetic acid were not tested because of the unavailability of these antigens.

The patient reduced her chemical load and used her available antigens for treatment (Table 5). She removed as much camphor from her house as possible. As a result, she became free of headaches and other symptoms for the first time in 28 years. She has since lived a vigorous life.

Table 4. VOC Air Analysis[a] in House of Participant as Described in Case Report

Chemical	Patients House Interior	Normal House (Control)
Acetic acid	15 PPB	6.1 PPBV
α-Pinene	2 PPB	0.4 PPBV
β-Pinene	1 PPB	0.2 PPBV
Acetic acid, ethyl ester	4 PPB	1.1 PPBV
Acetic acid, butyl ester	2 PPB	0.4 PPBV
Limonene	27 PPB	4.9 PPBV
4-Terpineol	1 PPB	0.2 PPBV
L-Camphor	14 PPB	2.3 PPBV
DDE[b]	2.86 PPB	0 PPB

Abbreviations: VOCs, volatile organic compounds; PPB, parts per billion; PPBV, parts per billion by volume; DDE, dichlorodiphenyldichloroethylene; DDT, dichlorodiphenyltrichloroethane; PPM, parts per million.

[a]Air analysis by Philips method: a detection of VOC in alveolar breath for the presence of chemicals by chromatography and mass spectrometry.[5]

[b]DDE is an organochlorine pesticide metabolite of DDT.[6] DDT is highly persistent in the environment, with a reported half-life of 50 y. Expected DDE levels are 0 PPM. Finding this substance is significant because it exposes suppresses levels of serum immunoglobulin and antibody titers.[7] It inhibits leucocytes and macrophage migration at the cellular level and increases chemical overload leading to hypersensitivity.

Table 5. Intradermal Neutralization Case Report

Intradermal Neutralization	Dosage
Antigen: pine terpene	0.5 cm^3 of the 1/0.25 dilution
Antigen: tree terpene	0.5 cm^3 of the 1/3000 dilution
Antigen: ragweed terpene	0.5 cm^3 of the 1/1.25 dilution
Antigen: mountain cedar terpene	0.5 cm^3 of the 1/3000 dilution
Antigen: grass terpene	0.5 cm^3 of the 1/1.25 dilution
Antigen: placebo	Normal saline

DISCUSSION

This study found a relationship among the sensitivities to the terpenes of pine mountain cedar, tree terpenes, and airborne chemical pollutants. It has shown that a connection exists between VOCs and terpenes in chemically sensitive patients.[8]

The various chemicals and the terpenes acted on all patients based on their individual susceptibilities. Therefore, some had persistent responses to more terpenes than others or identified the chemicals that triggered each patient's symptoms as was illustrated in the case report.

The research team was particularly surprised by how camphor became airborne and apparently was made by the combination of acetic acid and odor from pine terpenes in the house. Camphor can be made in the air by a combination of acetic acid and pinene (α and β) and can be a significant factor in terpene sensitivity, a result that the current study found and that it is significant to chemical sensitivity. Camphor may have been in more houses than were reported in our study, but the patients did not report the distinct odor in their houses. Its significance should be observed in further evaluations.

Both chemicals and terpenes can be part of the chemical sensitivity and if the terpenes are ignored and not treated by elimination and intradermal neutralization, these types of chemical sensitivity patients will not improve.

By decreasing each patient's overload in combination with other substances such as pesticides and formaldehyde, 43 of 45 patients improved their symptoms with treatment. This result is attributed to the total decrease in body pollutant load from the controlled environment, the intradermal neutralization, and avoidance of chemicals and terpenes.

This phenomenon of mixed toxins occurring within a room's ambient air was unidentifiable until the effects of chemicals were eliminated by placing the patients in a less-polluted, controlled environment and allowing them to become deadapted. Then an individual's sensitivity to pollutant and terpenes could be seen as the patient was unmasked from the toxic environment and then was presented with individual challenges.

The current study's participants are among the first to report terpenes and terpenoid sensitivity among their triggering agents for chemical sensitivity. The authors do not know whether the participants' sensitivity to terpenes came first or followed the onset of the chemical sensitivity. Either is possible because the terpenes and terpenoids from plants are as prevalent in ambient air within the outdoor environment as is methane gas, which is emitted from the earth[2] and is the number-one trigger, along with pesticides, of the chemically sensitive. These exposures could have occurred when the patients were living in a home that contains terpenes offgassed by the pine furniture,[9] flooring, or cabinetry; in a home that generated camphor when pine was combined with ambient acetic acid; or in a home in the midst of a terpene polluted forest.[10] It has been shown that VOCs, pesticides, and other toxins can disturb the cell membrane, allowing Ca^{++} and Na^{+} into the cell. When the Ca^{++} combines with protein kinases A and C and is phosphorylated, it can increase sensitivity by a factor of 1000.[11] This may be what happened to those patients who developed terpene sensitivity. Perhaps this mechanism explains both VOC and terpene sensitivity.

Because all of these studies were performed in a controlled, 5-times-less polluted environment and because 43 of 45 patients improved with initial and long-term treatment of not only the reduction of the total environmental toxic load but intradermal neutralization of the terpenes, our observations appear valid. Terpenes sensitivity exits and can be eliminated by avoidance and intradermal neutralization.

The case report emphasizes the complexity of the chemical exposure in the home as shown in Figure 1, where ethanol is made when one mixes acetic acid with other chemicals yielding ethanol or acetyl chloride. In our series ethanol was positive in 76.2% of patients by the inhalant challenge and in 85.4% of patients by intradermal challenge. The sensitivity from exposure could be from petrochemicals or combining acetic acid and terpenes, such as the formation of camphor (Figure 2).

The puzzling phenomenon in the current case study was the presence of camphor in the patient's home air and its significance in relationship to sensitivity. The majority of the camphor usually comes from camphor dermal applications.[12-15] What is unusual about the results of the current study is that the toxic camphor was in the indoor air of the case study patient's indoor air. Her symptoms had a strong ambient air association with camphor exposure; however, she had used no camphor. The ambient air apparently created or contained the camphor, probably by a combination of α-pinene, β-pinene, and acetic acid, which is known for creating camphor, as shown in Table 4 and Figure 2.[16,17] Apparently the camphor in the air was enough to sensitize the patient.

Figure 1. Mixing acetyl chloride with acetic acid forms ethanol.

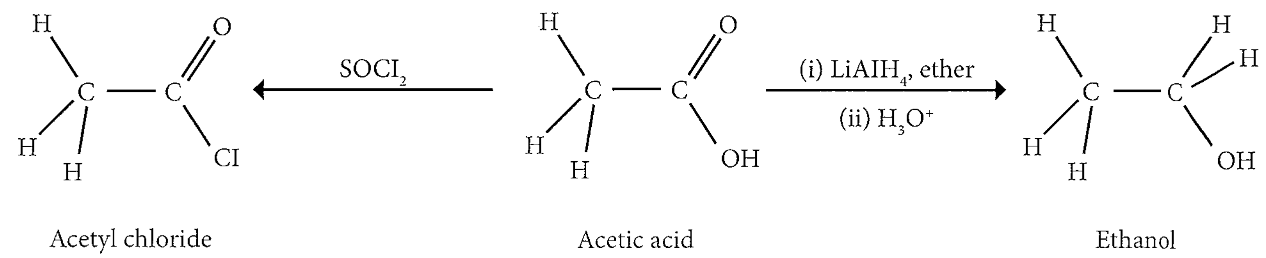
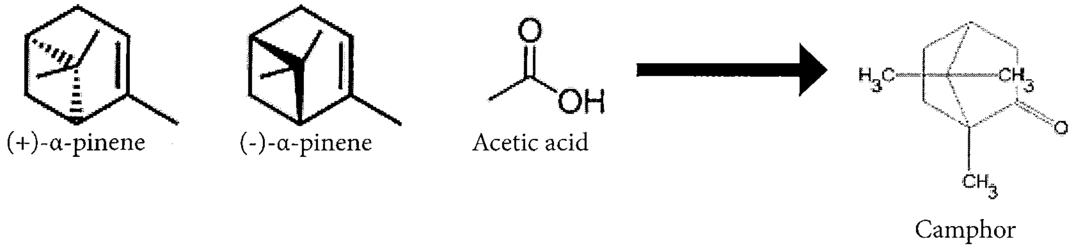


Figure 2. Mixing α-pinene or β-pinene with acetic acid forms camphor.



CONCLUSION

The current study is the first in which chemically sensitive and terpene sensitive patients were studied in a less-polluted, environmentally controlled area of the EHC-D clinic and hospital, revealing case data that contained information about low levels of VOCs and terpene sensitivity. The patients exhibited signs and symptoms from some of their exposures, which illustrated the response in the whole series of patients.

The study found a potential source of sensitivity to terpenes in pine, mountain cedar, and tree terpenes as air pollutants. A particular patient was discussed in the case study who showed a significant frequency of symptoms from chronic inhalant exposure to air in which camphor was made from a combination of α- or β-pinene and acetic acid in her home's environment. The case study showed that camphor was toxic and compromised the patient's daily activities and exacerbated her chemical sensitivity. Further research on this topic is recommended.

The participants in the study showed positive responses to a number of toxic and nontoxic chemicals that provoked symptoms. This study has shown that a connection exits between VOCs, other chemicals, and terpenes in some chemically sensitive patients.

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:, CHIEF SCIENTIFIC OFFICER AT PACIFIC ENVIRONMENTAL ANALYTICS. In last month's explored how cannabis cultivation potentially affects air quality and ways to measure ire focusing on greenhouse design and shining a light on a too often overlooked but

our research, we've visited multiple types of cannabis cultivation facilities. In Denver, rehouse space and ex-business parks. In New Jersey, we've observed modular rooms it of existing defunct greenhouses. In California, we've seen plans for so-called er, the standard growing approach is of course greenhouses. Though they come in enlo style, hoop, side-venting, roof-venting, side-fan venting and so on—the fact e cultivation is, and will likely remain, the most popular form of cultivation due to its energy, weather and climate control, year-round cultivation and light control. We've Cannabis Business Times numerous extremely helpful articles on cannabis tenance.

versation? What two-syllable word (that happens to be one of the most likely reasons not raised? ODOR.

ers and engineers do a fantastic job of drafting creative plans to meet cultivator gation, lighting and other variables. But it has become evident that odor control is not gn requirement. This is a critical mistake that others can learn from. We've observed ter-the-fact when odor and emissions complaints start to roll in and the cultivator is lity to address these issues. Unfortunately, this is often a case of too little too late as st permits due to unaddressed or insufficiently addressed odor issues. Rather than d committing unbudgeted resources, proven and effective odor control measures iginal design plans. When done properly, a robust odor control system can be esign and control systems, making the entire process more streamlined, efficient and r investment by addressing a critical compliance concern.