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The mystery of dry indoor air – An overview

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ABSTRACT

"Dry air" is a major and abundant indoor air quality complaint in office-like environments. The causality of perceived "dry air" and associated respiratory effects continues to be debated, despite no clear definition of the complaint, yet, has been provided. The perception of "dry air" is semantically confusing without an associated receptor but mimics a proto-state of sensory irritation like a cooling sensation. "Dry air" may also be confused with another common indoor air quality complaint "stuffy air", which mimics the sense of no fresh air and of nasal congestion. Low indoor air humidity (IAH) was dismissed more than four decades ago as cause of "dry air" complaints, rather indoor pollutants was proposed as possible exacerbating causative agents during the cold season. Many studies, however, have shown adverse effects of low IAH and beneficial effects of elevated IAH. In this literature overview, we try to answer, "What is perceived "dry air" in indoor environments and its associated causalities. Many studies have shown that the perception is caused not only by extended exposure to low IAH, but also simultaneously with and possibly exacerbated by indoor air pollutants that aggravate the protective mucous layer in the airways and the eye tear film. Immanent diseases in the nose and airways in the general population may also contribute to the overall complaint rate and including other risk factors like age of the population, use of medication, and external factors like the local ambient humidity. Low IAH may be the single cause of perceived "dry air" in the elderly population, while certain indoor air pollutants may come into play among susceptible people, in addition to baseline contribution of nasal diseases. Thus, perceived "dry air" intercorrelates with dry eyes and throat, certain indoor air pollutants, ambient humidity, low IAH, and nasal diseases.

1. Introduction

"Dry air" continues to be among the most abundant and common complaints about perceived indoor air quality (IAQ) since the first questionnaire investigations of office environments, e.g. Skov et al. (1990) and Bluyssen et al. (1996, 2016). For instance, data collected from 122 office buildings in 1996–99, altogether 11154 employees, showed complaint rates of dry air (35%), stuffy air (34%), dust or dirt in the indoor environment (25%), and draught (22%) (Reijula and Sundman-Digert, 2004). Other examples are shown in Table 1 together with "reported "stuffy air", another common and abundant IAQ complaint, e.g. in schools (Järvi et al., 2018). Further, many intervention studies have shown alleviation of "dry air" and symptoms (dry eye/throat) upon elevated indoor air humidity (IAH) (Wolkoff, 2018). For instance, in one study office workers (n = 39; 25-60 years) were single-blind exposed to clean dry (15% relative humidity (RH)) versus normal (43% RH) air continuously for 4 weeks each and changed back over 12 weeks test period (Jan-Feb) at 21°C. More than half of the workers (54%) reported the air "too dry" at dry condition as opposed to only 10% "slightly dry" in normal condition, while dry mouth/throat amounted to 31% versus 10% in dry and normal conditions, respectively (Gavhed and Klasson, 2005). Further, 28% of the workers reported daily "runny nose" in dry condition in contrast to only 8% in the normal condition. Furthermore, reduction of nose and throat symptoms has been demonstrated among patients undergoing continuous positive airway pressure therapy by the addition of humidification with a heated tube to the mask, e.g. Nilius et al. (2018). The abundance and persistency of the IAQ complaint is indeed surprising in view of modern offices characterized by use of more indoor environmentally friendly building materials and products and more elaborate ventilation and cleaning strategies during the last three decades.

The causality of "dry air" complaints continues to be debated in the literature. For example, Pejtersen et al. (2006) stated "It seems that perceived dry air is something different from humidity and there is a need to validate this question" in agreement with Andersen et al. (1974), who concluded "subjects' assessment of humidity is unreliable". This is further reflected in inconsistent associations between RH measurements and reported IAQ complaints about dry/humid air, e.g. Järvi et al. (2018), while others do find positive associations, e.g. Azuma et al. (2017).

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Table 1
Examples of prevalence (%) of common indoor air quality complaints and symptoms in offices and aircraft cabins.

Study offices/aircraft cabin	Recall period (weeks) ≥1 symptom/week	Dry air[a] Too dry[b]	Stuffy air[c] Too little air[d]	Dry eyes	Dry nose blocked/stuffy/runny	Dry throat
Bluyssen et al. (2016) OFFICAIR	4	47[a]	38[c]	35	14	23
Brightman et al. (2008) BASE Study	4	25[b]	31[d]	19	13	7
Bluyssen et al. (1996) AUDIT	4	–	–	39	33	36
Lukcso et al. (2016)	4	32[a]	37[i]	59[i]	63	31
Marmot et al. (2006) Whitehall	2	–	–	33	~27	18
Pejtersen et al. (2006)	1	19–50[a,e]	21–54[c,e]	–	10-14	-
Reijula and Sundman-Digert (2004)	12	34–37[a,f]	30–36[c,f]	–	20	14
(Lindgren et al. (2007) Aircraft cabin		1.8–2.2[g]	3.1[h]	–	–	–

a) Dry air. b) Too dry. c) Stuffy air. d) Too little air. e) Depending on number of workers in office (open-space) room. f) All age groups; smokers (40%). g) Scale: Very dry (0) – Very humid (6). h) Scale: Fresh (0) – Very stuffy (6). I) Dry, burning, irritated, itching, tearing.

Dry (or wet/humid) air as a standard IAQ parameter cannot be perceived, *per se*, due to lack of a relevant receptor (Nagda and Rector, 2003) nor confirmed under controlled exposure conditions from 10% to 70% RH (Andersen et al., 1973); thus, a physico-chemical and physiological rationale and a semantic understanding of its perceptual meaning is inadequate. For instance, complaints of low RH were dismissed as an explanation for "dry air" (Andersen et al., 1974, 1979) and instead, indoor air pollutants were considered causative, e.g. (Sundell and Lindvall, 1993; Fang et al., 2004; Sun et al., 2009). Recent research, however, indicates that the perception of "dry air" not only has to be assessed receptor-wise, but also that a multi-facetted approach should be applied to understand the complaint and its physiological causes in view of low IAH, working conditions, and indoor air pollutants (Wolkoff, 2018).

Different perceptions and associated causes, e.g. upper airway diseases, could influence the combined complaint rate of e.g. "dry nose". Further, it is unclear whether perceived "humid or wet air" could be confused by the body sensation of feeling humid (sweaty). It is conceivable that "dry air" and "stuffy air" perceptually overlap and exacerbate each other, and possibly also with other perceptions and symptoms; furthermore, that "dry nose" as a disease may trigger or overlap the perception of "dry air". Thus, "dry air" as an explicit IAQ parameter is semantically imprecise and, it is evident "dry air" needs a redefinition and rationale that reflects its physiological causalities. Thus, the purpose of this overview is an attempt to disentangle, "what is dry air" as an IAQ parameter, and further to identify its causes and possible interactions adding to the complaint rate and associated symptoms in office-like environments.

2. Method

This overview analyzes studies about the indoor IAQ parameter "dry air". Searches in PubMed and Google Scholar were carried out for "dry air" in combination with: "airways", "eyes", "indoor air quality", "humidity", "particles", "pungency", "mucociliary clearance", "sensory irritation", "throat irritation", "ocular surface", and combined with own selection of literature compiled during the last decades up to September 2018, cf. (Arundel et al., 1986; Nagda and Hodgson, 2001; Doty et al., 2004; Derby et al., 2016; Wolkoff, 2018), and without focus on extreme high IAH conditions. Association with moisture damage of constructions is excluded in this overview.

3. Results

3.1. History of "dry indoor air"

Historically, indoor pollution was claimed to be the primary cause of the perception "dry air" rather than low IAH (Sundell and Lindvall, 1993; Fang et al., 2004; Sun et al., 2009; Qian et al., 2016). For instance, Andersen et al. (1974) dismissed humidification as beneficial in offices based on 78 hours' exposure of young (n = 8; 21–26 years) male students to (particle-free) dry air (9% RH) versus normal air (50% RH) in a climate chamber, because the students rated the air as dry on different body surfaces (e.g. eyes) during the dry air condition, however, not statistically significant. Thus, "dry air" was considered unreliable as a perception. Furthermore, the authors concluded that complaints about e.g. dry eyes were caused by "other (risk) factors" occurring simultaneously with cold outdoor temperature during the cold season, e.g. dust particles. This agrees with the findings that young males (n = 8) were less affected by exposure to low RH than elderly men (n = 8), who could not sense air dryness despite a longer mucociliary (saccharine) clearance time (Sunwoo et al., 2006b). This indicates that the age of the subjects is a salient risk or facilitating factor for diminished mucociliary clearance at increasing age, e.g. Puchelle et al. (1979) and Ho et al. (2001). Other studies, however, have not observed such dependence; for instance, the classic study with 174 smoking and non-smoking males (n = 85) and females (n = 89) (mean 42.5 years) in which no significant correlation was found between age and mucociliary flow rate (clearance time) (Ewert, 1965). However, the reason for this could be a larger variance in between one age group than between all studied age groups.

Many intervention studies have later demonstrated beneficial effects of elevated IAH and alleviation of complaints and symptoms in office-like environments in agreement with the reanalysis by Nagda and Hodgson (2001) and Gavhed and Klasson (2005); this includes also intervention in hospitals, e.g. Skoog (2006) and aircraft cabins, Lindgren et al. (2007). As pointed out by Gavhed and Klasson (2005), the discrepancy between the studies by Andersen et al. (1974) and Sundell and Lindvall (1993), and the experiences gained in field intervention studies could be a different baseline prevalence of perception (symptoms) during the exposure studies than during the season. For instance, clean room workers at 55% RH complained more about dry symptoms of eye, nose, and throat than other workers working at 65% RH, which could be explained by the workers live in a high humidity region (Su Sb et al., 2009). Thus, the reporting outcome appears sensitive to the external ambient environment (i.e. both climate and air pollutants) and individual risk factors, e.g. age. It is noteworthy to cite the conclusion by Andersen et al. (1974): "It is suggested that these complaints (dry air: added by author) are not caused by the low humidity per se but by one or several of the other factors occurring simultaneously with the dry air in the winter – i.e. low outside temperature, higher dust levels, or higher SO_2 levels". This agrees with the finding by Mizoue et al. (2004) that complaints generally are substantially higher during the cold season. It should be pointed out, however, that this and other human exposure studies, in general, have been carried out with young healthy subjects and not elderly subjects (40–65 years); this might have resulted in different outcomes concurrent, *inter alia* by lower mucociliary activity.

It is important to notice that the positive outcome of intervention studies by elevated IAH should not be ascribed solely to the IAH and its

physiological impact on the eyes and airways, *per se*. The concentration of indoor particles may differ, by altered deposition on surfaces and resuspension from floor surfaces, and simultaneously with an altered profile of VOC emissions from materials, cf. Wolkoff (2018); further, the observation that re-emission of bioaerosols from infested surfaces at low RH are higher in comparison with high RH (Frankel and Madsen, 2014). The lower particle and bioaerosol concentration and differently perceived IAQ (odor) by the VOCs may have a beneficial effect on the eyes and airways by reduced exposure, see Section 3.4.2.

3.2. General considerations about reporting of complaints and symptoms in office-like environments

Generally, women report IAQ problems and work-related symptoms more often than men and allergic persons and smokers report indoor air problems more often, and experience work-related symptoms more often than non-allergic persons and non-smokers (Reijula and Sundman-Digert, 2004; Lukcso et al., 2016). In view of reported complaint rates in offices it is relevant to consider that there may be a lower limit from which rates are unlikely to surpass. For instance, it was concluded based on an on-line health survey of 7637 building occupants that "It is therefore not surprising that in any building complex there would be complaints about temperature and humidity arising from as many as 20% of occupants in buildings fully in compliance with ASHRAE recommendations" (Lukcso et al., 2016). Similarly, reported dry and irritated eyes may stem from both eye disease (diagnosed and non-diagnosed) (Wolkoff, 2017). Further, "It comes as no surprise that subjects with diagnosed allergies and asthma are more likely to report symptoms of respiratory origin. However, they were also more likely to report symptoms of all kinds, including musculoskeletal complaints" (Lukcso et al., 2016); for instance, allergic rhinitis, cf. Graudenz et al. (2006). Two important issues come to mind, first, the cause of reporting may as well be within host factors than by environmental factors, and second, it may be difficult to reach complaint rates below 20% (group-wise), as previously set as a tentative lower limit regarding the sick-building syndrome (SBS) symptoms; from another perspective, we are dealing with a window of complaint rates above 20%. From the viewpoint of occupational medicine and hygiene it is, of course, highly desirable, identifying all causalities to help office workers with severe complaints and symptoms, to be able to improve comfort and reduce their complaints, where possible, both group-wise and on the individual level. One additional issue to consider is the recall period and its influence on the complaint rate, see (Wolkoff, 2013).

Personal factors that include both psychological (e.g. mood, stress) and psychosocial (e.g. hierarchical) issues should also be recognized, because they may influence the report of the IAQ parameters and symptoms, e.g. De Peuter et al. (2004), Runeson et al. (2007), and Azuma et al., 2015) and be bidirectional in reporting (the chicken/egg situation), e.g. Brauer et al. (2006) and Janssens et al. (2011).

3.3. What is perceived "dry air" and what causes it?

The term "dry air" was originally not defined, when the so-called "sick-building syndrome" was established (WHO, 1986); rather it was mentioned that the typical SBS symptoms were accompanied with complaints about stuffiness, poor air, dry air, noise, light, and too cold or too high temperature. Later "dry air" and "stuffy air" became common parameters in questionnaires about assessment of perceived IAQ in offices and in addition to indoor air-related symptoms.

It has been suggested that the perception of dryness in eyes and mucosal membranes "are associated with a loss of energy from the corresponding part of the body" (Reinikainen and Jaakkola, 2003). Thus, one may ask whether it is possible without a relevant receptor to assess "dry air" from dry nose (stuffy nose) and dry throat as separate perceptions or "dry air" is confused or interchangeable with "dry nose", at least to some extent, in part in agreement with the unreliability of assessing "dry air" as concluded by Andersen et al. (1974). "Dry skin", another common complaint in offices (e.g., Reinikainen and Jaakkola, 2003; Sunwoo et al., 2006a), has been associated with air velocity (draft) in offices (Bakke et al., 2007); although not reported, it is possible that this symptom also could trigger report of "dry air". Thus, it appears that dry nose is the driving force in reporting "dry air". For instance, Hildenbrand et al. (2011) characterize "dry nose" from subjective perception of a "somewhat dry nose to visible crusting of the nose", and with many combinations (modified by author):

- Sensation of dryness in the nose
- Itchy and mild burning sensation
- Nasal congestion (stuffy nose)
- Crusting, scabs and "bogies"
- Nosebleed

Nasal congestion has been described as the "perception of reduced nasal flow or a sense of facial fullness" (Naclerio et al., 2010), which may mimic "stuffy air". It is noteworthy that about 50% of allergic rhinitis patients experience nasal congestion as a predominant symptom (Naclerio et al., 2010). This would contribute substantially to the baseline of complaint in line with about 10–30% prevalence of allergic rhinitis worldwide (Riechelmann et al., 2003; Naclerio et al., 2010). Thus, the perceptions of "dry air" and "stuffy air" may not only in part intercorrelate, but also be associated with "dry nose" in a chicken and the egg situation, and possibly affected also by "dry skin", see Fig. 1. Hildenbrand et al. further suggest possible causes of "dry nose" (modified by author):

- Local mechanical irritation
- Climatic or environmental factors, as
  - Low outdoor and indoor air humidity
  - High room temperature or hot environment
  - Long-haul flights with low RH
- Workplace conditions
  - Dry clean-room condition
  - Extreme temperatures (cold, heat)
  - Dusty conditions
- Side effects by use of certain medication (incl. use of drugs)
- Symptoms of other diseases and disorders
- Anatomical changes to the outer and inner nose, with modification of normal airflow
- Allergic rhinitis by exposure to house dust mites and molds (and pollen)
- Permanent sequelae of surgery on the nose and paranasal sinuses and wound healing phase after surgery in the nose
- Obstructive sleep apnea or continuous positive airway pressure treatment thereof.
- Old age (> 60 years).

Both use of certain medication, *inter alia* with diuretic properties, and old age are risk factors for the elderly working force. Furthermore, Hildenbrand et al. (2011) and Naclerio et al. (2010) point out anatomical changes and atrophy of the nasal mucosa resulting in complaints of nasal breathing and "dry nose". This can be manifested *inter alia* by shortening of columella, reduced mucociliary clearance time with further reduction of goblet cells and elastic fibers in the nasal mucosa, reduced sensitivity of nasal mucosa, enlarged nasal cavity (tissue swelling), and finally decrease in body water as pointed out by Slavin (2009); this may lead to reduced mucociliary clearance and eventually result in nasal congestion and dry nose and throat, e.g. during long-haul flights (Hinninghofen and Enck, 2006).

It should be noted that rhinitis patients that are exposed to "cold-dry-air" perceive nasal congestion, sneezing, and rhinorrhea more intensely than healthy subjects, e.g. Naclerio et al. (2007) and Kim and Jang (2012). Trigeminal nerve endings are known to respond to

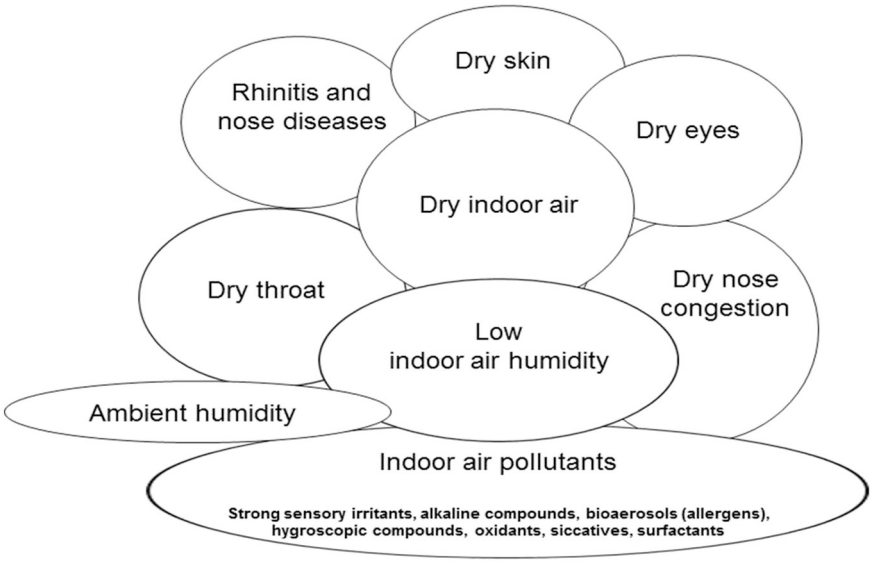

Fig. 1. Schematic presentation of perceptions of dry nose, dry air, dry throat, dry eyes, dry skin, nose diseases interacting with ambient air humidity, low indoor air humidity and indoor air pollutants.

innocuous cooling via activation of TRPM8 receptors (Lumpkin and Caterina, 2007) and believed to contribute to the perception of the nasal airflow (Zhao et al., 2011). For instance, the nasal airflow in nasal sinus disease patients is lower at dry and/or cold air conditions in comparison to room air condition (Zhao et al., 2011); furthermore, the forced expiratory volume within 1 sec was shown to decrease by increase of water loss from extended dry air exposure (McFadden Jr. et al., 1999). The studies, thus, indicate that the perception of the nasal airflow (i.e. congestion/stuffiness) is modulated by ambient room temperature and IAH and possibly mediated through mucosa cooling and trigeminal sensory input (Zhao et al., 2011, 2014). Although, it is assumed that the indoor air concentrations, in general, of strong sensory irritants are orders of magnitude lower than their thresholds for eye and upper airway irritation, the sense of cooling could be considered a proto-state of sensory irritation, see Section 3.4.2.

Water loss in the respiratory epithelium may also play an important role by the continuous need for evaporation of water from its surface (i.e. desiccation). An increase of the airflow (ventilation) in the nose may cause a larger hyperosmolaric surface that moves more distal and this stimulates the epithelial cells to release inflammatory mediators possibly leading to nasal congestion, e.g. by swelling (Naclerio et al., 2010). Cold-dry-air led to significantly higher osmolarity than methacholine or histamine among cold-dry-air responders than non-responders, thus confirming that the osmolarity in nasal secretions has increased after a cold-dry-air challenge (288 to 306 mOsm/kg H_2O) (Naclerio et al., 2007). “Desiccation of the epithelium includes desquamation, leukocyte infiltration, vascular leakage, and mast cell degranulation, all of which may worsen inflammation”, and this may further stimulate the epithelial cells to release inflammatory mediators if the hyperosmolaric surface has not reached moisture neutrality (Naclerio et al., 2007). Further, hyperosmolar challenge may cause histamine and leukotriene (C4) release. It is concluded that the histamine release is probably caused by hyperosmolar stimuli in mast cells and the release is greater among those responding to cold-dry-air (e.g. asthmatics) than healthy non-responders. Thus, nasal congestion may be perceived as “dry air” because of extended desiccation and a hyperosmolaric surface, cf. Naclerio et al. (2010). Furthermore, in the end, desiccation of the epithelium may increase bacterial adherence and allow for greater penetration of foreign species, like particles (e.g. bioaerosols) (Naclerio et al., 2007).

3.4. Potential risk factors of perceived dry indoor air

Although there is no humidity receptor, “dry air” as a perception in the eyes and airways could potentially be caused by low IAH, VOCs (sensory irritants), particles and bioaerosols, or in combination, as discussed below.

3.4.1. Impact of low indoor air humidity

Low IAH by itself has been shown to be associated with elevated reporting of symptoms by desiccation processes in the eyes and upper airways (Wolkoff, 2017, 2018). Vocal loading at low RH may further exacerbate mouth and throat symptoms, especially among women (Vintturi et al., 2003). Elevated IAH may alter the immediately perceived IAQ by change of the emission rate profile of polar VOCs from building products as opposed to non-polar VOCs, but indoor levels, in general, are orders below thresholds to cause sensory irritation (trigeminal stimulation) in the eyes and upper airways (Wolkoff, 2013, 2018). The odor emission profile, however, may alter the perceived IAQ. It should be noted that low IAH has been found to be associated with the increase of reported “stuffy air” specifically for men (Bakke et al., 2007).

Elevated IAH has been shown to lower the particle concentration; for instance, respirable particles were significantly lower in humidified condition in an aircraft cabin (Lindgren et al., 2007), in agreement with slightly less perception of “dry air”. Still, one must be cautious in interpreting the apparent beneficial effect in intervention studies by increase of the IAH. Secondary effects from altered deposition and resuspension from e.g. floor surfaces may change the overall particle and bioaerosol concentration affecting their impact and perception of “dry air”, and possibly simultaneously with restoring of the precorneal eye tear film and mucous membranes in the nose; further, the VOC emission profile from surfaces may alter the immediately perceived IAQ (Wolkoff, 2018).

Ewert (1965) showed a significant correlation between mucociliary flow rate (clearance time) and RH, both among smokers and among non-smokers, and as a total group (n = 174); the mucociliary flow rate approached zero in 60% of studied case at RH below 40%. Furthermore, smokers differed significantly from non-smokers with the lowest average flow rate among the smokers, which leveled out at high RH. Clearly, IAH is an important factor (perhaps the most important) that influences the mucociliary clearance and is age dependent (see 3.1);

thus, the lower mucociliary activity by exposure of elderly people to low IAH may enhance the susceptibility of the mucous membranes towards sensory irritants, oxidants, particles, and bioaerosols.

3.4.2. Impact of sensory irritants (organic volatiles)

Exposure to low IAH may mimic sensory irritation (Doty et al., 2004; Nielsen and Wolkoff, 2017) by the cooling effect (e.g., Zhao et al. (2011); Dalton et al. (2018)) and possibly be exacerbated by exposure to sensory irritants, if contact to nerve endings are facilitated by an altered and less stable eye tear film (dry spots) or desiccated mucous membranes (lower mucociliary clearance time). Perceived rating of sensory irritation was significantly correlated with perceived "tissue dryness" in healthy non-smoking subjects (n = 20, 10 males) exposed to propylene glycol (a common solvent in many consumer products) (Dalton et al., 2018). Using the strong sensory irritant formaldehyde as an example, Cain et al. (2008) speculate if "dryness as a symptom of chemical exposure seems to belong to a category of proto-irritation", whether this is generalizable is an open question. Doty et al. (2004) mention 9 different sensory irritation correlates: stinging, piquancy, burning, tingling, freshness, prickling, irritation, itching, and cooling. Using acetone as an example, Doty et al. point out that the threshold for eliciting the sensation as "cooling" may be perceived at considerably lower concentration than for eliciting tingling or stinging sensations. Possibly, perceived "dry air" could, in part, be a cooling sensation, caused by water evaporation from extended exposure to low IAH (i.e. high airflow), in agreement with (Reinikainen and Jaakkola, 2003) and (Zhao et al., 2011) and by certain sensory irritants. Dalton et al. (2018) suggest that the perception of sensory irritation experienced by the subjects to exposure of propylene glycol could be due to its hygroscopic properties resulting in the feeling of dryness in both eyes and nose, and the subjects, consequently, are confused. The suggestion, however, needs substantiation at indoor relevant concentrations.

Generally, concentrations of indoor VOCs are orders of magnitude below their threshold for eliciting sensory irritation in eyes and upper airways (Wolkoff, 2013) with the exception of formaldehyde and acrolein in certain conditions; especially, when mucous membranes in the nose or the eye tear film have been compromised by extended exposure to low IAH or high temperature that alters the eye tear film stability, i.e. thinning, break-up and the formation of local dry spots (Wolkoff, 2017). Dry eyes' symptom (by low IAH) could result in the perception of dry (throat) air (mucous membrane), because, if the "sense of dryness" is caused by stimulation of trigeminal nerve endings, it is fair to speculate that irritated or dry eyes may cross interact with nerve endings from the nose and *vice versa*, cf. Baroody et al. (2008). Likewise, "a patient with nasal inflammation may have an altered baseline of nasal trigeminal sensitivity that could exacerbate obstructive symptoms" (Zhao et al., 2014; Saliba et al., 2016), i.e. a lower threshold for sensory irritation.

Inflammatory reactions initiated by exposure to VOCs are unlikely, since they are not considered allergenic (Nielsen et al., 2007; Nurmatov et al., 2015; Wolkoff and Nielsen, 2017). This conclusion is in part supported by no increased susceptibility in o-albumin-sensitized (asthmatic) mice exposed to either formaldehyde or chlorine, respectively (Larsen et al., 2013; Johansson et al., 2017). Furthermore, subjects with seasonal allergic rhinitis exposed to ammonia did not alter the response to sensory irritation in comparison to healthy controls (Pacharra et al., 2017).

3.4.3. Impact of particles

Wiik (2011) concluded "real cause of the sensation of "dry air" is "dusty air" and upper respiratory symptoms (e.g. dry/sore throat, nasal congestion) in office workers were found to be associated with "air dryness perception" and dusty floors (Azuma et al., 2015).

Particle dynamics is complex and the influence of IAH is by far from sufficiently explored. Alteration of the inhalable particle chemical composition, the deposition and resuspension that occur from surfaces may depend on different RH and the particle size distribution, and thus influence the perceived IAQ and the effect on the eyes and airways. Resuspension of particles from floor surfaces depends on *inter alia* physico-chemical and surface properties, and the RH (Mølhave et al., 2000; Qian et al., 2014). While there is some indication that the resuspension is lower from certain hard surfaces (e.g. hardwood and vinyl flooring) at high RH for all particle sizes, no such effect is seen for textile carpets (Qian et al., 2014; Tian et al., 2014). Floors are an important reservoir of human-associated bacteria and virus, thus, resuspended floor dust from human activity may be an important contributor of exposure to bioaerosols, cf. Hospodsky et al. (2012). However, detailed knowledge about IAH dependence on deposition and resuspension is clearly lacking and the mechanisms of survival, transmission, and infectivity of virus and bacteria associated with IAH and temperature is far from well understood (Wolkoff, 2018).

So far, controlled human exposure studies with indoor particles have not been convincing about acute effects, cf. Wolkoff (2013). For instance, Andersen et al. (1979) exposed healthy students (n = 16; 21–26 years; 11 smokers) to inert particles coated with carbon black (aerodynamic range = 2–13 μm) for 8 hours at concentrations of 2, 10, and 25 mg/m^3 in a climate chamber (23 °C, 50% RH) during the cold season. Only four subjects (25%) complained about dryness in the nose and throat at 2 mg/m^3, a concentration about two orders of magnitude higher than normally encountered in public buildings, e.g. Mandin et al. (2017). Clearly, the physico-chemical properties of the particles and their solubility in mucus influence the impact on the nose, throat, and least in the eye, in that order, e.g. as shown for hydrated calcium sulfate (Cain et al., 2004). For example, a blinded and randomized nose-only exposure study of healthy subjects (n = 32; 25 years; 18 males) exposed for three hours (21 °C, 36% RH) to 0.5, 1.0 and 5.0 mg/m^3 calcium carbonate or sham air showed a significant dose-response relationship for subjective sensation of nasal obstruction, dryness, and decrease of nasal secretion and patency (Riechelmann et al., 2003); this is contrary to the studies with inert dust and office dust, respectively by Andersen et al. (1979) and Hauschildt et al. (1999). In a follow-up study, a significant increase of sensation of nasal dryness was observed in healthy non-smoking subjects (n = 30; 22–32 years; 11 males) nose-only and blindly exposed to 150 or 500 μg/m^3 standard urban dust in comparison with sham air (Riechelmann et al., 2004); further, an increase of inflammatory biomarkers was observed in nasal secretions after the urban dust exposure. Similarly, significant effects of *inter alia* throat irritation, need of coughing and dry nose were observed in young subjects (n = 10; mean 27.5 years; 4 males) exposed to about 0.4 mg/m^3 total office dust versus sham condition (0.04 mg/m^3) for three hours in a climate chamber (21 °C; 23.5 % RH). These effects worsened over time. The findings should be considered cautiously due to the possibility of random significance and significant overlap of symptoms (Pan et al., 2000); however, it should be assessed in view of a substantially lower RH than in previous studies from this laboratory. The above studies taken together show how the outcome of the study strongly depends on type of particles and possibly also the IAH. It is not possible to assess the risk of health/comfort effects to be expected from the indoor air particle exposures, which usually are at least one order of magnitude lower than the chamber exposure concentrations. However, the studies indicate that certain indoor particles can impact nose and airways, although at higher than usually encountered indoor concentrations, but their impact at lower indoor concentrations could be exacerbated by a low IAH, as suggested by Andersen et al. (1974), i.e. dry nose possibly translated as "dry air", and by aggravated mucous membranes as suggested by Zhao et al. (2014).

It has been suggested that settled man-made vitreous fibers are associated with reported sensory irritation symptoms due to their morphology (Salonen et al., 2009) and this agrees with the finding that levels of airborne particles (> 0.5 μm diameter) were significantly higher in offices with work-related eye and upper airway symptoms than in offices without reported symptoms (Lappalainen et al., 2013). In another study of office workers respiratory symptoms (dry/sore

throat, nasal congestion) were found to be associated with smaller particles (> 0.3 μm) (Azuma et al., 2018). This is supported by two intervention studies. One study showed substantial reduction of eye, nasal and facial complaints after the replacement of partially coated glass wool ceiling boards, emitting vitreous fibers, with fully coated ceiling boards (Palomäki et al., 2008) and in another study the removal of powdering floor polish from linoleum floors in a school reduced eye, nasal, throat and lower airway symptoms (Malmberg et al., 2000). In a third study, release of particles from a ceiling material indicated an association with eye problems (Thriene et al., 1996); however, such studies must be interpreted cautiously without follow-ups and knowledge about the IAH.

In general, the morphology and physico-chemical properties of the particle surfaces and particle sizes are important regarding their impact on the eyes and airways. “Dry eyes”/”dry air” may also be mediated through inhalation of aggravating particles. For instance, studies have shown associations of altered eye tear film with combustion-related particles or proxies of combustion, e.g. traffic, see Wolkoff (2017), and alkaline aerosols during polish removal of a floor (Wieslander and Norbäck, 2010). Further, surface active compounds like benzalkonium chloride and particles like quartz may also cause compositional changes of mucous membranes in the eyes and airways (Zhao and Wollmer, 2001), thus becoming more susceptible to low IAH and aggressive pollutants, and possibly mimic “dry air”. However, high concentrations of e.g. surfactants in dust particles appear to be required to initiate sensory irritation in the airways, cf. Wolkoff et al. (2003).

3.4.4. Combined effects

Combined effects of low IAH and exposure to air pollutants should also be considered as originally suggested by Andersen et al. (1974) and later by Zhao et al. (2014). For instance, in a large cross-sectional study low IAH and ozone were associated with dry eye symptoms and dry eye diseases (Hwang et al., 2016), in agreement that extended exposure to ozone (or photochemical reaction products) may deplete the anti-oxidative system of the eye tear film (Schmut et al., 1994; Lee et al., 2013; Paananen et al., 2015; Seen and Tong, 2017) and low IAH exposure alters the eye tear film (Wolkoff, 2017). Further, rats with experimentally evaporative dry eyes showed to be more susceptible to exposure of titanium dioxide nanoparticle causing inflammatory reactions than normal rats (Han et al., 2017). It is reasonable to hypothesize that low IAH alters the eye tear film stability, thus becoming more vulnerable to aggressive chemicals like ozone or its reactive products or particles with radical formation capacity (i.e. ROS). Furthermore, stratified corneal epithelial cells exposed to formaldehyde (100 μg/m^3) at low RH at the air-liquid-interface showed increased cell death and inflammation (Vitoux et al., 2018); a concentration far below reported objective changes of the eye, e.g. Lang et al. (2008) and Mueller et al. (2013).

Desiccation (incomplete humidification) of eyes and airways by prolonged exposure to low IAH may alter both the eyes and airways becoming more susceptible to air pollutants below known no-observed-effect-levels for single exposures. Desiccation of the eyes for several causes will result in altered eyes with an increase of break-up of the eye tear film, and further lead to an imbalance and elevated osmotic pressure (Wolkoff, 2017). Severe desiccation of mucous in the airway surfaces increases the viscosity leading to less effective mucociliary clearance and longer saccharin clearance time (Sunwoo et al., 2006a; Munkholm and Mortensen, 2014); ultimately, this will lead to formation of plaques and plugs, cf. (Randell and Boucher, 2006). Many studies show associations between hyperosmolarity and morphological (composition and molecular structure) changes of the eye tear film and symptoms (Baudouin et al., 2013; Bron et al., 2014; McMonnies, 2015).

Mice studies indicate that sensory irritation in the upper airways is unaffected by low RH and o-albumin-sensitized mice (asthmatic mice) appear to be less affected than normal mice about bronchoconstriction at very high formaldehyde levels; this may be due to excess mucus production in the asthmatic animals (Larsen et al., 2013). However, it is not possible to generalize this finding to air pollutants with other physico-chemical properties.

It appears obvious that “dry air (dry nose)” not only depends on the exposure period of low IAH, but possibly also seasonal exposure to low ambient AH both at home and during commuting. Whether “stuffy air” is correlated with “dry air/dry nose” or it is an independent perception associated with perceived IAQ (odor) and dust particles, it is fair to say that IAH plays a role, also. Overall, it appears evident that incomplete humidification of the eye tear film and the mucous membranes in the nose and airways by exposure to low IAH is enough to be causative of perceived “dry air”, but may be exacerbated depending on age, gender, and exposure duration, indoor air pollutants mimicking sensory irritation or a proto-state thereof, and season, and geographical location. Thus, an increase of IAH alleviates both the perception of “dry air” and symptoms of dry eyes and upper airways according to Gavhed and Klasson (2005), Bakke et al. (2007), and in Wolkoff (2018) in conflict with conclusions by Sundell and Lindvall (1993), Fang et al. (2004), and Sun et al. (2009), and Qian et al. (2016).

3.5. Diseases

Disease related irritation and inflammation in the nose and throat can be experienced as stuffy (swelling) or runny nose, e.g. rhinitis sicca (Hildenbrand et al., 2011). It is fair to suggest that the perception “stuffy air” may be associated with this disease, *inter alia* provoked by allergens, bacteria and virus. The disease may be non-allergic or allergic in nature, and subjects with chronic rhinosinusitis may have a lower threshold for sensory irritation. Conversely, subjects suffering from seasonal allergic rhinitis and asthma have reduced ability to condition cold dry air (Assanasen et al., 2001) and precondition with hot, humid air alleviated *inter alia* nasal congestion, when challenged with allergens (Baroody et al., 2000). Whether “stuffy air” as feeling lack of fresh air (odor) could be associated with congested (stuffy) nose and “dry air” is not known.

4. Conclusion

“Dry air” is not only unreliable as an IAQ perception, “dry air” is also semantically misleading due to lack of an associated receptor. “Dry air” and “dry nose”, and possibly “stuffy air” as perceptions appear to be interrelated.

Clearly, particles do impact nose, throat, and the eyes to some extent. Their impact may be exacerbated by an altered (desiccated) eye tear film or nose and throat mucous membranes. Furthermore, elevation of the IAH from low to medium level generally may reduce the concentration of some particle types depending on walking activity and floor type, and the deposition and resuspension dynamics. This agrees with findings in many intervention studies in offices, which have shown a relief of “dry air” and sensory-mimicking symptoms by elevation of IAH. This can either neutralize the moisture content in eyes and airways simultaneously with altered room concentration of particles and bioaerosols.

It is relevant to consider that perceived dryness may be confused with sensory irritation as elicited by a cooling sensation. If pollutants should cause the feeling of dryness, it is generally not trigeminal stimulation, *per se*, but could be a proto-state thereof elicited by a cooling sensation; this may be triggered by exposure to hydroscopic VOC/particles that initiate a desiccation process in the nose and throat. Further, the sensory/cooling perception may be exacerbated by a susceptible mucous membrane, which is aggravated by nasal diseases or moisture imbalance by extended exposure to low IAH or due to pollutants with hygroscopic and siccative properties.

Reported dryness as perceived measure is multifaceted spanning from exposure to low IAH, people suffering from nasal diseases, impacted by their age and use of medication. Further, exposure to indoor air pollutants may alter the mucous membrane or initiate sensation

mimicking a proto-state of sensory irritation; impact by the outdoor ambient humidity is also possible.

Overall, elevation of IAH may be beneficial by: 1) retain the humidity balance in mucous membranes and mucociliary activity, and in the eye tear film, 2) less resuspension of particles from certain floor surfaces upon human activities (e.g. walking), 3) increase of the size and weight of hygroscopic particles that may increase the deposition rate on floor surfaces and thus, size-dependent, deposit in the nose rather than reaching the throat, and 4) alter the particle surface morphology depending on the physico-chemical properties of the particles and their surfaces, e.g. hygroscopic and siccative properties or radical formation capacity, 5) decrease the infectivity of influenza and other virus, 6) due to its multifaceted causality and unreliability as an IAQ parameter, it is questionable whether “dry air” as perception can predict airway diseases.

In summary, the causalities of perceived “dry indoor air” are multifaceted with low IAH as a common denominator concerted with many risk factors, both environmental and personal. Clearly, controlled experimental data from indoor realistic exposures is warranted for further substantiation.

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Declaration of interest

The author declares no conflicts of financial interest.

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