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Qualitative identification and characterisation of self-reported symptoms arising in humans during experimental exposure to cold air

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ABSTRACT

Background: Exposure to cold air is associated with increased morbidity and mortality in the general population. It is difficult to study the effects of whole-body exposure to cold air under controlled conditions in real life. **Objectives**: The aim of this study was to (1) explore and describe the experience of symptoms in humans during experimental and controlled exposures to cold air, by using controlled environmental chamber exposures and qualitative methodology, and to (2) categorise the symptoms. **Method**: The study used a randomised, double blind design, in which 34 subjects undertook rest and moderate-intensity exercise in an environmental chamber set to two or three different temperatures (0, −10, and −17°C) on separate occasions. During the chamber exposures, subjects were interviewed. Qualitative content analysis was selected as the method of analysis. **Findings**: Subjects reported 50 distinct symptoms during the exposures. The symptoms were grouped into ten sub-categories and two major categories; airway versus whole-body symptoms. **Conclusion**: We have identified a broad range of symptoms in humans undertaking rest and moderate-intensity exercise at sub-zero temperatures. The symptoms and their categories may well be used to more extensively and quantitatively map cold-induced morbidity.

Introduction

For the 4 million people who live in the Arctic region [1], engaging in outdoor activities leads inevitably to regular cold air inhalation during the winter months. Amongst the general population, cold air exposure is associated with increased morbidity and mortality [2], especially sensitive are the elderly and those with cardiopulmonary diseases [3–6]. In a Finnish survey, 26% of men and 31% of women reported that they experience cold-related airway symptoms [7]. In otherwise healthy respondents, respiratory mucus production typically occured at −7 °C whereas onset of cough, wheezing and dyspnea was reported at −18°C or colder [7]. A higher prevalence of cold-induced symtptoms in patients with allergic rhino-conjunctivitis and asthma [7] may lead to avoidance of outdoor activities during cold spells [8,9]. In patients with COPD, cold outdoor temperatures may aggravate respiratory symptoms, increase rescue inhaler use and impair lung function [10].

Winter endurance athletes, such as cross-country skiers, are repeatedly exposed to cold air during prolonged training sessions and competitions, and show an increased prevalence of airway symptoms, bronchial hyperreactivity and asthma [11]. Respiratory symptoms are also very common among children participating in physical activity in cold environments [12].

Environmental chambers aim to imitate real climatic conditions. Experimentally controlling environmental exposures, accounting for the effects of facial cooling, whole-body exposure and direct cold air inhalation is a prerequisite to further explore pathophysiological mechanisms responsible for environmentally induced morbidity. Whole-body exposure to sub-zero temperatures in a climatic chamber has been shown to induce proximal airway obstruction in healthy participants as well as patients with obstructive lung disease [13–21].

Symptoms may function as early warnings for subsequent morbidity. In epidemiological surveys, symptoms have been defined a priori, and only a few studies have investigated the emergence of airway symptoms during experimental exposure to cold air. Lower airway symptoms have usually been limited to shortness of breath,

wheezing, prolonged cough, phlegm production, and chest pain [9] whereas upper airway responses have been defined as rhinorrhea, congestion, and sneezing [22–25]. To the best of our knowledge, no qualitative studies have identified symptoms that arise during cold air exposure.

The purpose of this study was to (1) explore and describe the experience of symptoms in humans during experimental exposure to cold air, by using controlled environmental chamber exposures and qualitative methodology, and to (2) categorise the symptoms. We expected to detect a large number of distinct symptoms.

Methods

Environmental chamber

A cold air environment was simulated using the 21 m^2 (75 m^3) environmental chamber located at the Swedish Winter Sport Research Centre, Mid Sweden University, Östersund. The chamber is equipped with a treadmill (RL 2700E, Rodby Innovation, Vänge, Sweden), 1 m wide and 2.7 m long, outfitted with a safety harness system (Figure 1). Frost-resistant windows permit visual contact and communication between personnel in- and outside of the chamber. The chamber utilises two systems to control ambient conditions; a temperature controller (TC; Inuwell AB, Östersund, Sweden) and a hypoxic compressor supplying 1500 L/min dehumidified air to the chamber (HC; K2 1500, Hypoxico, New York, USA). Room air composition was set to 20.9% O_2 for all trials. For each trial, the desired set point temperature was inputted into the TC system. Chamber temperature was displayed by the TC system as a mean value from four sensors located at opposite ends of the side walls; front left (1.6 m), front right (1.6 m), back left (1.6 m) and back right (1.3 m). Relative humidity (rh) inside the chamber was detected by a humidity sensor located adjacent to the front right temperature sensor.

Absolute humidity (g/m^3) in the chamber was calculated based on the relative humidity (rh) and temperature (T) in °C, according to

$$\text{AbsH} = \frac{6.112 \cdot rh \cdot 2.1674 \cdot e^{\frac{(17.67 \cdot T)}{(T+273.15)}}}{T + 273.15}$$

Chamber performance together with surrounding laboratory and outdoor temperature is presented in Table 1.

Design

The study used a randomised, double blind design, in which 20 subjects were exposed to three different air temperatures during three separate testing sessions, and 14 subjects were exposed to two different air temperatures on separate occasions. The exposures were performed in a randomised order and took place in the environmental chamber.

Ethical approval was obtained from the Regional Ethical Review Board, Umeå (DNR 2015–245-31M).

Subjects

In order to obtain extensive descriptions as well as capture similarities and differences [26], 34 adult volunteers were recruited using local advertising into four participant groups.

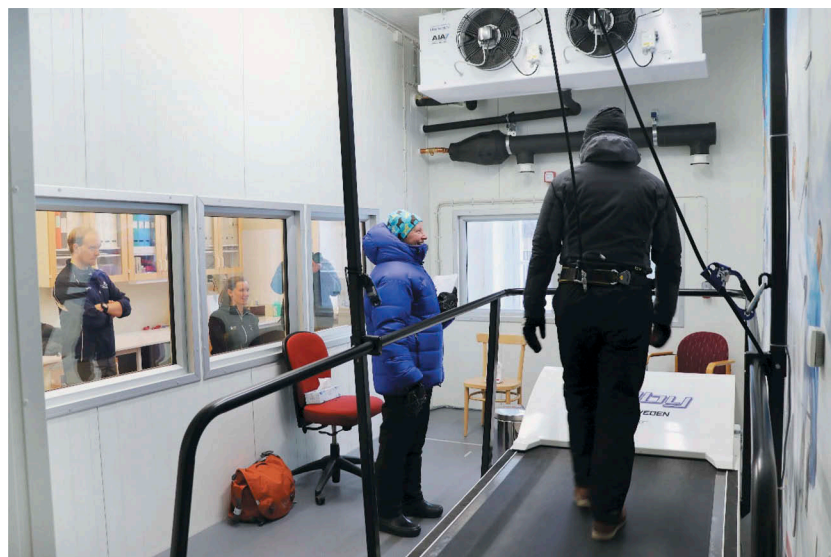Group 1 included 13 healthy subjects (8 men and 5 women), without allergy and lung disease, who did

Figure 1. The environmental exposure chamber. Photo by Sara Rönnberg/Region Jämtland Härjedalen.

Table 1. The target and observed milieu in the environmental chamber, surrounding laboratory, and outdoors at Swedish Winter Sport Research Centre, Mid Sweden University, Östersund, Sweden. Data presented as mean (SD).

Target temperature	0°C	−10°C	−20°C
Chamber temperature, °C	0.19 (0.19)	−10.40 (0.83)	−16.80 (0.65)
Relative humidity, %	31.11 (6.51)	58.93 (8.61)	71.88 (4.41)
Absolute humidity, g/m^3	1.53 (0.32)	1.35 (0.21)	1.01 (0.10)
O_2, %	20.64 (0.15)	20.54 (0.17)	20.56 (0.09)
CO_2, ppm	822 (164)	824 (169)	845 (160)
Outer laboratory temperature, °C	18.41 (1.45)	17.89 (1.26)	17.23 (0.33)
Outdoor temperature, °C	−2.45 (5.01)	1.20 (2.72)	0.70 (1.45)

not take regular medication and had never been regular smokers. Group 2 included seven subjects (6 men and 1 women) with allergic rhinoconjunctivitis (typical allergic eyes/nose symptoms as well as positive skin prick test for at least one airborne allergen). The subjects had never smoked regularly and had not neither symptoms of nor physician-diagnosed lung disease. Group 3 included 11 subjects (4 men and 7 women) with physician-diagnosed asthma. All except one subject had used daily inhaled corticosteroids for the preceding 3 months. One subject used only a beta-2-agonist approx. two times per week during exercise. The subjects with asthma had a mean (SD) forced expiratory volume in one second (FEV1) of 3.63 (0.85) L, 91 (11) % of predicted values and mean (SD) FEV1/ forced vital capacity (FVC) of 0.78 (0.06) post-bronchodilatation. Group 4 included three subjects (1 man, 2 women) with chronic obstructive pulmonary disease (COPD), with > 10 packyears ((number of cigarettes smoked per day/20) x number of years smoked) of smoking and daily inhaled pharmacotherapy. Two subjects had COPD stage-2 category B and one had stage-3 category A [27].

Procedure

After inclusion, all subjects underwent exercise testing and therafter 2 or 3 cold air exposures, all on different test occasions. At visit 1, the subjects were informed about the baseline exercise test, the exposures in the chamber, and that the exposures would be ca 0° C, −10°C, or −20°C (groups 1 and 2 only), and that they should bring appropriate clothing for the exposures.

Baseline exercise test

Prior to first exposure, subjects performed a ramped maximal exercise test to volitional exhaustion on a motorised treadmill (Rodby Innovation, Vänge, Sweden). The test for groups 1–3 followed the Bruce treadmill protocol [28], with the total test duration used to estimate subjects´ maximal oxygen consumption (VO2max) according to previously described methods [28,29]. For group 4, the test was conducted in line with the ramped protocol developed for COPD patients described by Cooper et al. (2010). VO_{2max} was then estimated by entering the final speed and gradient in to ACSM walking equation [30]. Heart rate was monitored continuously throughout the test (Polar S610, Polar Electro, Kempele, Finland). All except two subjects (both in the COPD group) achieved >90% of age-predicted maximum heart rate (HR_{max}) during the test; a common predetermined endpoint for incremental exercise testing (estimated using the formula: age-predicted $HR_{max} =$ 208–0.7*age; Tanaka et al. [31]). Subject characteristics and test results are reported for all groups in Table 2.

Exposures and interviews

Groups 1 and 2 were exposed to target temperatures 0 °C, −10 °C, and −20°C in the environmental chamber for 60 min on three separate occasions. The lowest target temperature of −20°C was below the lower operating limit for the chamber with two occupants, which emerged at approx. −17°C. An intermediate analysis revealed no unique symptoms at the lowest setting (−17°C), and this exposure was dropped for group 3 and 4. Each exposure consisted of alternating 15-minute periods of standing resting and walking on a treadmill at a speed to elict 50% VO_{2max}. The treadmill gradient was

Table 2. Subject characteristics and exercise test results. Data are presented as mean (SD), except otherwise stated.

	Healthy		Allergic rhinoconjuncitivitis		Asthma		COPD	
	Men	Women	Men	Women	Men	Women	Men	Women
Subjects, n	8	5	6	1	4	7	1	2
Age, y mean (range)	39 (24–65)	39 (24–50)	38 (30–47)	25	31 (22–55)	31 (21–43)	70	73 (72–73)
Height, m	1.82 (.04)	1.66 (.05)	1.79 (.06)	1.66	1.81 (.04)	1.67 (.08)	1.72	1.57 (.04)
Weight, kg	77.0 (6.9)	60.9 (7.1)	75.4 (10.7)	69.1	76.6 (5.0)	66.6 (6.1)	76.6	69.1 (.03)
Incremental test duration, s	15.4 (1.8)	13.6 (1.9)	15.7 (1.1)	15.0	12.1 (1.7)	11.0 (1.3)	14.0	13.7 (2.6)
Estimated $\dot{V}O_2$max, ml·kg^{-1}·min^{-1}	55.1 (6.0)	49.0 (6.8)	56.1 (3.7)	56.2	43.7 (5.7)	40.0 (4.5)	24.5	23.9 (2.9)
% age-predicted maximal HR	101 (5)	100 (4)	104 (6)	102	103 (3)	101 (5)	77	91 (8)

set to 6% for groups 1–3 and 1% for group 4. Treadmill speed was adjusted to achieve 50% VO$_{2max}$ solving the ACSM walking equation for desired VO$_2$ at a fixed gradient: VO$_2$ (mL·kg^{-1}·min^{-1}) = 0.1·S + 1.8·S·G + 3.5 where speed (S) is in m·min^{-1} and gradient (G) in percent [31].

During exposure periods, subjects were interviewed by the authors RS or CK throughout the rest and exercise period of each exposure. All subjects were given the opportunity to talk as long as they wished. After each interview, subjects were asked if she/he had anything more to add. We used focused open interviews in line with recommendations of Tjora [32,33] to use short interviews: (1) if the theme is highly limited, (2) if one believes that trust is created relatively quickly, and (3) when the topics addressed are not very sensitive or difficult for the participants.

According to recommendations for focused interviews [32,33], we used an interview guide to maintain structure and allow subjects to reflect on their experience of symptoms during the exposure. The interview guide included questions concerning experience of symptoms, how symptoms were perceived, and symptom intensity using the Borg CR10 scale [34]. The Borg CR10 scale is a category-ratio (CR) scale anchored at the number 10, which represents extreme intensities. It is a general intensity scale for most subjective magnitudes that with special anchors can be used to measure exertion and pain [34]. Follow-up questions were used: "Earlier you experienced (symptom), how does it feel now?". Interviews were conducted individually, and the researcher was inside the chamber with the subject for the duration of the exposure.

Qualitative analysis

Qualitative content analysis was selected to systematically and methodically identify and categorise [33] the manner in which various cold-related symptoms were expressed.

Subject interviews were transcribed verbatim including information about symptoms, time of symptom onset, and the timing of symptom reports during the exposure period. Each interview was anonymised prior to analysis. The first step of the analysis was to read through each interview as a whole in order to get a sense of the material. In the next step, a time axis was established for each exposure based on the elements of the exposure (rest 1–15 min, work 1–15 min, rest 2–15 min and work 2–15 min), where each mention of cold-related symptoms was mapped chronologically. The same subject may have stated the same symptoms several times. The analysis is based on the number of times the symptoms were stated [33,35] as well as the proportion of subjects who experienced each symptom.

To improve credibility of the analysis [36–38], RS and CK discussed and analysed the material through parallel processes, together and individually until consensus was reached [39]. The symptoms that were judged to be related were placed into sub-categories with a description of the symptom. These sub-categories were then aggregated into major categories.

Results

The 34 study subjects reported 50 distinct *symptoms* during the exposures. These symptoms were grouped into ten sub-categories and *two major categories*.

Frequency of distinct symptoms in each study group

Symptoms occurred during the first rest period and were reported throughout the whole exposure period. A total of 40 distinct symptoms was reported by the healthy (group 1) as well as the asthmatic subjects (group 3). Subjects with allergic rhinoconjunctivitis (group 2) reported 43 distinct symptoms and the three subjects with COPD reported 15 distinct symptoms. A description of the symptoms, and their frequency of occurrence is depicted in Table 3.

The five most common symptoms reported by the highest proportion of subjects in each group are presented in Table 4.

Sub-categories and major categories

The symptoms that emerged in the analysis were judged to belong to 10 different sub-categories: (1) "mucus in the nose", (2) "irritation in the nose", (3) "irritation of the mouth and throat", (4) "irritation in the chest", (5) "cold in the airways", (6) "breathlessness", (7) "cold in the face", (8) "cold in the extremities", (9) "shivering" and (10) "increased body temperature". Their relative occurrence is reported in bold numbers in Table 3.

The ten sub-categories were grouped into two major categories. Sub-categories 1–6 were judged to belong to the major category of *symptoms of upper and lower airways*, and sub-categories 7–10 were judged to belong to the major category of *general whole-body sensations*.

Discussion

We have identified 50 distinct symptoms in humans at rest and during moderate exercise that arise during controlled experimental exposures to temperatures between 0° and −17°C. These symptoms were grouped

Table 3. Symptoms reported during exposure to 0, −10 and −17°C in an environmental chamber stratified by subject group. Data are presented as the frequency (n) that each symptom was reported during the exposures and the proportion (%) of symptoms arising in a given sub-category from each group.

Sub-category	Symptom	Healthy, n (%)	Allergic rhinoconjunctivitis, n (%)	Asthma, n (%)	COPD, n (%)
Mucus in the nose		**(30)**	**(20)**	**(16)**	**(20)**
	Runny nose	141	65	51	11
	Congealed mucus	50	13	5	0
	Moisture in the nose	5	1	0	0
Irritation in the nose		**(2)**	**(7)**	**(3)**	**(0)**
	Blocked nose	0	1	0	0
	Nasal Congestion	4	5	4	0
	Rough in the nose	0	2	0	0
	Burning in the nose	9	14	2	0
	Pain inside the nose	0	2	0	0
	Stinging in the nose	1	2	5	0
Irritation in the mouth and throat		**(8)**	**(7)**	**(10)**	**(20)**
	Tickling in the pharynx	3	1	4	0
	Wheezing	1	1	1	0
	Burning in the throat	2	2	1	0
	Dryness in the mouth	16	7	3	1
	Dry throat/pharynx	12	14	5	0
	Increased mucus production in the throat/pharynx	10	2	18	10
	Roughness in the throat/pharynx	4	1	2	0
	Stinging sensation in the throat/pharynx	1	1	0	0
Irritation in the chest		**(0)**	**(0)**	**(22)**	**(23)**
	Phlegm production	0	0	13	0
	Chest pain	0	0	12	0
	Cough	0	0	14	7
	Difficulty in breathing	0	0	25	5
	Constriction of the airways	0	0	12	1
Cold in the bronhcii		**(3)**	**(8)**	**(4)**	**(0)**
	In the airways	4	3	10	0
	In the mouth	3	5	0	0
	On the tounge	1	2	0	0
	Cold in the chest	2	3	2	0
	Cold in the throat	7	11	1	0
	Cold in the nose	4	6	2	0
Breathlessness		**(3)**	**(4)**	**(4)**	**(0)**
	Increased breathing	2	7	0	0
	Fatigue	0	1	0	0
	Shortness of breath	20	9	15	0
Cold in the face		**(21)**	**(17)**	**(11)**	**(12)**
	Tightness around the eyes	9	8	1	0
	Watery eyes	19	10	6	5
	Cold at the tip of the nose/nose	50	22	14	1
	Cold around the mouth	43	18	11	1
	Tightness around the mouth	3	0	4	0
	Dry lips	0	0	1	0
	Cold ears	14	10	1	0
Cold in the extremities		**(17)**	**(17)**	**(19)**	**(12)**
	Fingertips	21	9	4	0
	Fingers	21	17	12	1
	Hands	21	2	3	0
	Toes	15	14	9	1
	Feet	8	6	3	2
	Arms	6	2	4	0
	Legs	17	18	32	3
Shivering		**(7)**	**(9)**	**(5)**	**(7)**
	Cold in the body	39	27	16	4
	Rigid body	4	3	0	0
	Chills	2	4	1	0
Increased body temperature		**(8)**	**(12)**	**(5)**	**(5)**
	Sweaty	27	17	2	0
	Warm	27	29	14	3

into 10 sub-categories and two major categories; airway versus whole-body symptoms.

Our qualitative interviews revealed numerous symptoms of cold air exposure, many more than those commonly used in epidemiological surveys on cold air associated morbidity. Overall, symptoms arising from the upper airways were frequent in healthy subjects as well as in subjects with allergic rhinoconjunctivitis or obstructive

Table 4. Five most common symptoms by proportion of subjects in an experimental exposure chamber for 1 h at intermittent rest and moderate exercise. Data presented as number of subjects (n).

Healthy * (n = 13)	Allergic rhinoconjunctivitis * (n = 7)	Asthma ** (n = 11)	COPD ** (n = 3)
Runny nose, 12	Runny nose, 7	Runny nose, 11	Runny nose, 3
Cold at the tip of the nose, 10	Cold at the tip of the nose, 5	Cold in lower extremities, 8	Cough, 2
Cold in the body, 10	Cold in the body, 5	Increased mucus production in the throat/ pharynx, 7	Increased mucus production in the throat/ pharynx, 2
Cold around the mouth, 9	Cold in lower extremities, 5	Difficulty in breathing, 6	Difficulty in breathing, 2
Congealed mucus in the nose (thick snot), 8	Cold around the mouth, 4	Cold in the body, 5	Watery eyes, 2

*Exposed to 0, −10, and −17℃.
**Exposed to 0 and −10℃.

lung disease. The most common symptom, runny nose, has regularly been associated with exposure to cold air [23,24,40].

Other common airway symptoms detected in the present study were symptoms belonging to the sub-category "irritation in the nose", such as burning and stinging sensation, and in the sub-category of "irritation in the mouth and throat", the symptoms most commonly reported such as dryness of the mouth, pharynx and throat, and increased mucus production had generally not been reported in other epidemiological surveys.

The most common whole-body symptoms arose within the sub-category of "cold in the face", where cold at the tip of the nose and cold around the mouth were the most commonly described symptoms.

Cold air exposures may induce cold extremities, also detected in our experimental setup. Cold in the fingers, legs and a general cold sensation in the body were the most frequent symptoms in the sub-categories "cold in the extremities" and "shivering", respectively. Pienimäki et al. [41] reported that as ambient temperature decreases more physical symptoms are reported, with 90% of participants reporting feeling cold in the extremities at -23℃. Piedrahita et al. [42] and Dovrat and Katz Leurer [43] showed similar results in participants who worked in a cold indoor environment, where physical symptoms were most prominent, mostly in the fingers but also in the musculoskeletal system.

Symptoms from the lower airways were limited to subjects with asthma or COPD. This is in line with epidemiological studies showing that cold-related symptoms from lower airways are more often reported by subjects with obstructive lung disease [7,9,11,44].

In this study, there were few subjects with COPD which has to be taken into consideration. Among the subjects with COPD, cough was the most commonly reported symptom followed by difficulty breathing and constriction in the airways. These symptoms have also been detected in previous epidemiological surveys of patients with chronic bronchitis and COPD [7,10].

Although we did not perform any formal statistical comparisons, our impression is that some differences in symptoms arose between groups. In the healthy group, the sub-categories "mucus in the nose" and "cold in the face" appear to be more common compared to other groups. Among subjects with allergic rhinoconjunctivits, the sub-category "irritation in the nose" occurred frequently. Emergence of lower airway symptoms was limited to subjects with asthma or COPD, even though these subjects were only exposed to 0 and −10℃. We did not observe any obvious gender differences.

In these qualitative interviews, we used systematic and quantitative description of the manifest content of communication [33]. The symptoms described by the study subjects were presented in 10 sub-categories and two major categories based on the symptoms and their anatomical origin. Some of the symptoms may predominantly arise as a consequence of cold air inhalation, such as" irritation in the chest" and difficulty breathing whereas other symptoms may have an association with the physical activity, such as "breathlessness", shortness of breath, and increased breathing.

Limitations and strengths of the study

The experimental set-up may have some limitations to internal and external validity. As clothing was not standardised between or within subjects, poor or inappropriate clothing may have influenced the perception of cold air. The cooling fans in the roof of the environmental chamber contributed to a high noise level and several subjects felt that the wind swirled in the chamber, which was perceived as artificial since the wind does not usually spin in the same way when one is outdoors. Despite this, subjects perceived the environmental chamber exposures as realistic in comparison to outdoor conditions, which

can be seen as a strength of the study. Another strength of the study was that the environmental chamber had a "sterile" appearance, removing visual cues, such as frost or ice, that could be used to evaluate ambient temperature.

The symptoms detected in the present study are a consequence of low to moderate intensity exercise in cold air. We believe that the moderate exercise intensity of 50% $VO_{2\ max}$ used in the present study may have been too low to trigger lower airway symptoms in subjects without respiratory disease at these temperatures. The results therefore highlight the need for further studies in sub-zero temperatures with higher workloads.

The study was neither designed to nor had the sample size/distribution to evaluate the effect of age on symptoms arising during cold air exposure.

Conclusion

We have identified a broad range of symptoms that arise during rest and moderate exercise in sub-zero temperatures, in both healthy participants and patients with respiratory disease. These symptoms were grouped into 10 sub-categories and two major categories; airway versus whole-body symptoms. These symptoms and their sub-categories may be used to more extensively and quantitatively map cold-induced morbidity.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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