

# Survey of symptoms, respiratory function, and immunology and their relation to glutaraldehyde and other occupational exposures among endoscopy nursing staff

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## Abstract

**Objectives**—To find the nature and incidence of symptoms experienced by a large sample of hospital endoscopy nurses. To find whether nurses in endoscopy units develop asthma under current working conditions in endoscopy units. To obtain analytically reliable data on exposure concentrations of glutaraldehyde (GA) vapour in endoscopy units, and to relate them to individual hygiene and work practices. To characterise any exposure-response relations between airborne GA and the occurrence of work related symptoms (WRSs). Due to the growing concern about the perceived increase in WRSs among workers regularly exposed to biocides, all of whom work within a complex multiexposure environment, a cross sectional study was designed.

**Methods**—Current endoscopy nurses (n=348) from 59 endoscopy units within the United Kingdom and ex-employees (who had left their job for health reasons (n=18) were surveyed. Symptom questionnaires, end of session spirometry, peak flow diaries, skin prick tests (SPTs) to latex and common aeroallergens, and measurements of total immunoglobulin E (IgE) and IgE specific to GA and latex were performed. Exposure measurements included personal airborne biocide sampling for peak (during biocide changeover) and background (endoscopy room, excluding biocide changeover) concentrations.

**Results**—All 18 ex-employees and 91.4% of the current nurses were primarily exposed to GA, the rest were exposed to a succinaldehyde-formaldehyde (SF) composite. Work related contact dermatitis was reported by 44% of current workers exposed to GA, 56.7% of those exposed to SF composite, and 44.4% of ex-employees. The prevalence of WRSs of the eyes, nose, and lower respiratory tract in current workers exposed to GA was 13.5%, 19.8%, and 8.5% respectively and 50%, 61.1%, and 66.6% in the ex-employees. The mean percentage predicted forced expired volume in 1 second (ppFEV<sub>1</sub>) for ex-employees (93.82, 95% confidence interval (95% CI) 88.53 to 99.11) was significantly lower (p<0.01) than that of current workers exposed to GA (104.08, 95% CI 102.35 to 105.73). Occupational peak flow diaries

completed by current workers with WRSs of the lower respiratory tract showed no evidence of bronchial asthma (<15% variation). Six per cent of the population had positive latex SPTs. Positive indications of one GA specific IgE and 4.1% latex specific IgE occurred. There was no conformity between the latex specific IgE and positive SPTs. Positive SPTs to latex were associated with WRSs of dermatitis and ocular WRSs, but no other WRSs. Exposures were above the current maximum exposure limit (MEL) of 0.2 mg/m<sup>3</sup> (0.05 ppm) in eight of the units investigated. A significant relation existed between peak GA concentrations and work related chronic bronchitis and nasal symptoms (after adjustment for types of local ventilation) but not to other WRSs. Peak GA concentrations were significantly higher in units that used both negative pressure room and decontaminating unit ventilation.

**Conclusion**—This study documents a significant level of symptoms reported in the absence of objective evidence of the physiological changes associated with asthma. Ex-employees and current workers with WRSs warrant further study to elucidate the cause and mechanisms for their symptoms. Ventilation systems used for the extraction of aldehydes from the work area may be less effective than expected and due to poor design may even contribute to high peak exposures.

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The excellent biocidal activity of glutaraldehyde (GA), a 5-carbon dialdehyde (structural formula OHC.CH<sub>2</sub>.CH<sub>2</sub>.CH<sub>2</sub>.CHO) has long been recognised.<sup>1</sup> Gastrointestinal, endoscopy, and bronchoscopy units within the United Kingdom, have used GA since 1963. The activated alkalisied GA solutions display broad spectrum antimicrobial activity that is effective against viruses,<sup>2-6</sup> gram negative and gram positive bacteria, bacterial spores,<sup>7</sup> mycobacterium species,<sup>8-10</sup> and fungi.<sup>7</sup> Also, its non-corrosive nature, allowing universal acceptance by manufacturers' of biomedical equipment, and its low comparative cost makes GA the main choice of cold sterilants or disinfectants in the United Kingdom health service.<sup>11</sup>

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Glutaraldehyde had been used within the health service for 18 years before the first publication associating exposure to GA with work related symptoms (WRSs).<sup>12</sup> Since then several case reports<sup>13-20</sup> and one epidemiological study<sup>21, 22</sup> have related exposure to GA to one or more WRSs. Hygiene studies have investigated the relation between different biocide dependent activities and airborne concentrations.<sup>23-28</sup> The highest exposures and therefore presumed health risk occurs during a spillage or during biocide changeover. The reported incidence of WRSs due to GA have increased over the past few years.<sup>29-31</sup>

Due to the growing concern about the perceived increase in WRSs among workers regularly exposed to biocides, all of whom work within a complex multiexposure environment, a cross sectional study was designed. The aim of this study was:

- (1) To find the nature and prevalence of symptoms experienced by a large sample of hospital endoscopy nurses.
- (2) To find whether nurses in endoscopy units develop asthma under current working conditions in endoscopy units.
- (3) To obtain analytically reliable data on exposure concentrations of GA vapour in endoscopy units, and to relate them to individual hygiene and work practices.
- (4) To characterise any exposure-response relations between airborne GA and the occurrence of WRSs.

### Methods

In this cross sectional study 19% of all endoscopy units within the United Kingdom were approached by written letter of invitation. Mostly, no additional contact with local management or ethics committees was required, although when requested this was undertaken.

#### CRITERIA FOR SELECTION

All current workers within each unit were approached about participation. Ex-workers were identified through local employment records. Workers who had left employment from the endoscopy unit within the preceding 5 years were contacted by a letter of invitation asking if they had left for any health reason. Those responding positively to this question were invited for further investigation.

#### INDIVIDUAL SYMPTOM SCREENING QUESTIONNAIRE

An adaptation of the Medical Research Council respiratory questionnaire<sup>32</sup> was used to assess the presence of work related upper and lower respiratory tract and skin symptoms by a trained interviewer. The WRSs were defined as symptoms improving on rest days (weekends or study days not on the unit) or symptoms experienced as more severe during a work shift. Additional data including: personal demographic details, current and past occupational data, the use of personal protective equipment, smoking history, previous exposure to spillage, and previous medical diagnosis of asthma, bronchitis, eczema, or hay fever were recorded.

For the purpose of the study, WRSs of contact dermatitis were defined as contact skin rash, which occurred when working on the endoscopy unit and could not be attributed to known non-occupational agents.

#### EX-EMPLOYEE SYMPTOM QUESTIONNAIRE

The ex-employee symptom questionnaire had the same format as the current workers' symptom questionnaire. It differed only in the questions that enquired about present work and whether regular biocide contact occurred, and symptom questions enquired as to whether past WRSs had been present and whether they were continuing.

#### WORK ENVIRONMENT QUESTIONNAIRE AND ENVIRONMENTAL STUDY

A single work environment questionnaire was administered at each unit participating. It was completed by the senior member of the nursing staff. It identified the number of endoscopy nurses currently employed; endoscopy list days; when the highest staffing levels occurred; the type, the duration of use, and mode of use of the mechanical ventilation for the room and decontaminating washers, past and present; the type and duration of decontaminating washers used and the biocide in use. A site inspection was used to confirm the work environment and the personal work practices in use and any discrepancies were clarified.

#### LUNG FUNCTION TESTS

##### *Spirometry*

Spirometry was performed, on each participant, with a daily calibrated Vitalograph dry wedge spirometer at the end of an endoscopy session. The highest of two reproducible (within 5%), recordings of forced vital capacity (FVC) and forced expiratory volume in one second (FEV<sub>1</sub>) were measured (American Thoracic Society's snowbird workshop<sup>33</sup>). The FEV<sub>1</sub> and FVC results were directly read from the body temperature pressure saturated with water vapour (BTPS) scale, as the temperature range between units was 19–25°C. The results are presented as the mean percentage predicted FEV<sub>1</sub> (ppFEV<sub>1</sub>), which takes into account each subject's age, sex, and height. Predicted values of FEV<sub>1</sub> and FVC were derived from the European Community's summary equation.<sup>34</sup> A 15% negative correction factor for predicted FEV<sub>1</sub> and FVC in Asians was applied.<sup>35</sup>

##### *Peak expiratory flow rate*

Peak expiratory flow rate (PEFR) recordings were requested from any nurse who reported one or more WRSs of the lower respiratory tract.

The recording started on waking and was performed 2 hourly throughout the day, until sleep, for 1 month. The recordings were performed during work and rest days. Mini-Wright meters were used for the PEFR recordings. All subjects were instructed on the correct technique and the best of three readings was documented, as long as the highest two readings differed by no more than 20 l/min, otherwise more readings were required. The

diaries were examined by two experienced occupational respiratory physicians and by the occupational asthma system (OASYS-2) computer program for the presence of WRSs of bronchial asthma.<sup>36</sup>

#### SKIN PRICK TESTS

Skin prick tests (SPTs) were performed by the method recommended in the position paper by the Executive Committee of the European Academy of Allergology and Clinical Immunology (EAACI), (1992) guidelines.<sup>37-38</sup> Standardised prick test extract solutions were provided by the Stallergen company (Paris). Fifty per cent glycerin was the preservative used. The use of short acting antihistamines in the past 48 hours, long acting antihistamines in the past 2 months, and high potency topical steroids in the past 3 weeks was recorded and precluded participation in the SPTs. The test solutions were phenolated glycerol saline (negative control), histamine HCl 1 mg/ml (positive control), *Dermatophagoides pteronyssinus*, latex, mixture of 12 grasses, *Alternaria*, cat, and dog fur. The final test results were read off after 20 minutes. A weal diameter 3 mm greater than the control was taken as a positive result.

#### IMMUNOLOGY MEASUREMENTS

Total immunoglobulin E (IgE) and IgE specific to GA analyses were performed by the Biomedical Sciences Group, Health and Safety laboratory (Sheffield) and IgE specific to latex by the Allergy Analysis Centre, a division of EURO/DPC (Gwynedd). Inhibition by the GA IgE radio allergosorbent test (RAST) was recorded as positive when the RAST% binding was greater than or equal to 0.88% as long as the total serum IgE was less than or equal to 120 KU/l. The IgE latex RAST inhibition analysis was positive at or above class II (which converts to a threshold of 0.70 KU/l on the continuous concentration scale).

#### INDUSTRIAL HYGIENE MEASUREMENTS

Industrial hygiene measurements for airborne concentrations of aldehyde biocides were made with personal samplers and the Occupational Safety and Health Administration (OSHA) method 64.<sup>39</sup> One nurse on each unit was asked to wear the precalibrated personal airborne sampler, which was connected through a vinyl tube to an air monitoring cassette, attached at the clavicular level. The monitoring cassette contained a 37 mm glass fibre filter coated with 2,4-dinitrophenylhydrazine (2,4-DNPH) and phosphoric acid. The production and subsequent analysis of the 2,4-DNPH coated filters with high performance liquid chromatography (HPLC) and an ultraviolet (UV) detector, was performed by the RPS group (Manchester). Two categories of airborne sampling were performed at each unit. In the first, termed background concentrations, with sampler flow rates of 200 ml/min, airborne measurements were taken from initial exposure to the end of that endoscopy session, excluding any biocide changeover period. The second samples, termed peak concentrations, were measured

over the shorter period of a biocide changeover, with personal sampler flow rates of 1 l/min. Peak and background concentrations were mutually exclusive. A time weighted average (TWA) biocide concentration could be calculated from the pump sampling rate and the collection period. With the flow rates mentioned no breakthrough of the aldehydes occurred. Field blanks were submitted with each unit's samples to allow for any corrections needed.

#### STATISTICAL METHODS

Background and peak airborne aldehyde concentrations were found to follow positively skewed log normal distributions, so they were transformed to natural logarithms for analysis with parametric statistical methods. Where appropriate, results are presented detransformed back into the original units (as geometric means (95% confidence intervals (95% CIs))).

Symptom prevalences were assumed to follow binomial distributions.

As a cohort study design was used, odds ratios (95% CIs) were computed from hazard ratios estimated from Cox's regression methods (with unit follow up times for each subject). The odds ratios estimate the increased risk of a symptom occurring associated with: (a) each category level relative to the baseline level for categorical influencing variables; (b) a unit increase in the level of normally distributed influencing variables; (c) a doubling in the level of log normally distributed influencing variables.

It was thought inappropriate to assume that the correlations between subjects within the same unit would be the same as the correlations between subjects from different units. Therefore, multilevel modelling methods were used throughout to adjust for effects of the individual units. The 95% CIs reported are based on appropriate robust SEM estimates.

Significance was set at the conventional 5% level throughout. Only a few subjects were found with each symptom of interest, so the statistical analysis was considered primarily exploratory rather than definitive and no adjustments were made to significance levels for multiple comparisons. All computations were done with the STATA statistical computer package.

#### Results

Of 61 endoscopy units approached throughout the United Kingdom, 59 in 58 hospitals (24 central teaching and 34 district general hospitals), were accessed over a period of 1 year. The two units not taking part did not reply to two requests within the time frame of the study in their regions. Three hundred and forty eight (74.4%) endoscopy nurses currently working from a total target population of 466 took part in the study. Four refused to take part, 114 were on annual or study leave, and eight were on sick leave at the time of the initial screening assessment. All eight nurses on sick leave during the initial visit were interviewed by phone,

Table 1 Prevalence of work related symptoms (WRSs) among current workers and ex-employees

Symptom category	Current nurses with WRSs (n=348) n (%)	Current nurses with WRSs exposed to GA (n=318) n (%)	Current nurses with WRSs exposed to SF (n=30) n (%)	Ex-employees with WRSs at time of endoscopy§ (n=18) n (%)
Chronic bronchitis*	4 (1.1)	3 (0.9)	1 (3.3)	3 (16.7)
Persistent cough	12 (3.5)	10 (3.2)	2 (6.6)	10 (55.6)
Wheeze	9 (2.6)	8 (2.5)	1 (3.3)	8 (44.4)
Chest tightness	17 (4.9)	17 (5.3)	0	10 (55.6)
Shortness of breath	8 (2.3)	7 (2.2)	1 (3.3)	7 (38.9)
Lower respiratory tract symptom†	30 (8.6)	27 (8.5)	3 (10.0)	12 (66.6)
Nasal irritation‡	67 (19.3)	63 (19.8)	4 (13.3)	11 (61.1)
Eye irritation‡	47 (13.5)	43 (13.5)	4 (13.3)	9 (50.0)
No WRS	243 (69.8)	223 (70.1)	20 (66.7)	0
Contact dermatitis	157 (45.1)	140 (44.0)	17 (56.7)	8 (44.4)

\*Diagnosis defined as: cough daily for at least 3 months in 1 year for 2 consecutive years.

†Any one of the lower respiratory tract symptoms: chronic bronchitis, persistent cough, wheeze, shortness of breath or chest tightness.

‡Symptom category as defined by questionnaire.

§All ex-employees in the table stopped work for health reasons.

but none reported a work related symptom as the cause of their sick leave.

Sixty eight ex-employees had left within the past 5 years, 26 (38.2%) had done so for health reasons. Eighteen (69.2%) of the 26 were traced and all participated in the study. The remaining eight could not be traced.

Three hundred and nineteen of the 348 current workers (91.6%) and all the ex-employees were women. The geometric mean number of years spent on the endoscopy unit by the current workforce was 2.2 years (range: 1 month to 19 years) with 74.1% being employed for less than 5 years. Of the ex-employees, 85% had started endoscopy work after 1985 (50% since 1990).

In 53 units, 318 current workers were exposed to GA, 30 in six units primarily used the SF composite. All the ex-employees used GA, although two had also used an SF composite as well as GA. Sixteen of the 18 ex-workers have continued in the nursing profession and hence may have coincidental exposure to biocides, other airborne chemicals, and particulates (including latex) but only one has continuing exposure to aldehydes.

#### SYMPTOMS

Table 1 presents the crude prevalence rates of WRSs in all current workers, current workers subcategorised by exposure to GA or SF, and in ex-workers.

Contact dermatitis followed by nasal and then eye irritation were the WRSs most often reported in the three groups of current workers. Reasons given by ex-employees for leaving included one who left work because of WRSs of contact dermatitis and another because of WRSs of headaches and sinusitis.

Table 2 Mean % predicted FEV<sub>1</sub> compared between non-smokers and smokers currently working, asymptomatic and symptomatic current workers, and current and ex-employees

Compared categories (actual number)	Mean % predicted FEV <sub>1</sub>	95% CI
Non-smokers (n=197)	104.73	102.62 to 106.94
Smokers (n=104)	102.86	100.25 to 105.47
Current workers with no WRSs of the lower respiratory tract (n=275)	104.54	102.84 to 106.24
Current workers with WRSs of the lower respiratory tract (n=26)	99.26	92.85 to 105.93
Current workers (n=301)	104.08	102.35 to 105.73
Ex-employees (n=14)	93.82	88.53 to 99.11

Ten of the 12 ex-employees with WRSs of the lower respiratory tract when employed on the endoscopy units, continued to have one or more symptoms of the lower respiratory tract despite no longer being in direct contact with GA (one has continued exposure), two other ex-employees left due to WRSs of the nose, and two due to WRSs of the eyes and nose. Six ex-employees record persistent eye or nasal irritation, five of whom have no continuing exposure to GA. All the people that complained of persistent symptoms still work as nurses.

Ten of the 12 ex-employees had a latency period of greater than 3 months (range 3 months to 7 years) before the start of one or more of their WRSs of the lower respiratory tract. Three had latency periods of 3 years or more. Six of 12 with WRSs of the lower respiratory tract recorded symptoms occurring only on workday evenings or nights.

Of the current workers 22.4% (78) reported one or more lower respiratory tract symptoms not related to work, 22.4% (78) reported nasal and 14.9% (52) ocular symptoms. Forty one (11.8%) had a diagnosis of eczema confirmed by a doctor.

#### LUNG FUNCTION ANALYSIS

Three hundred and one (86.5%) of the 348 current workers and 14 of the 18 ex-employees produced reproducible spirometry. Of the 47 absent results in current workers 15 subjects could not perform reproducible tracings, eight nurses had been interviewed by phone, and 24 nurses declined to perform the procedure. A summary of the ppFEV<sub>1</sub> readings compared between current and ex-workers, smokers and non-smokers, and symptomatic and asymptomatic workers is presented in table 2.

There was no significant difference in ppFEV<sub>1</sub> between non-smokers and smokers nor in symptomatic compared with asymptomatic workers. A significantly lower lung function was present in the ex-employees compared with the current workers, although there were few ex-employees.

#### PEFR RECORDINGS IN SYMPTOMATIC WORKERS

Of the 30 current workers with WRSs of the lower respiratory tract, 17 completed PEFR diaries, which could be satisfactorily analysed.

Table 3 Skin prick test (SPT) results to common aeroallergens and latex in current workers and ex-employees

	House dust mite	Grass	Alternaria	Cat	Dog	Latex
Positive SPT in current workers (n (%)) (n=336)	73 (21.8)	84 (25.0)	15 (4.5)	31 (9.2)	10 (3.0)	20 (6.0)
Positive SPT in ex-employees (n (%)) (n=18)	4 (22.2)	2 (11.1)	0	0	1 (5.6)	1 (5.6)

House dust mite=Dermatophagoides pteronyssinus.

The diaries were analysed by two experienced occupational respiratory physicians with traditional visual appraisal and also with the OASYS-2 analysis program. The two occupational physicians, independently, reported no cases of bronchial asthma because of an absence of greater than 10% diurnal variation in PEFR recordings. An OASYS-2 score of more than 2.51 indicates the likely presence of a significant effect of WRSs in the serial PEFR diaries. Three recordings exceeded this cut off point, with results of 2.60, 3.00, and 3.50, re-examination of these diaries by visual appraisal concluded that there was no evidence of asthma (defined by a PEFR variability of greater than 15%) in any of these diaries.

#### IMMUNOLOGICAL TESTS

Three hundred and thirty six (96.6%) of the current workers and all ex-employees had skin prick tests (SPT) performed. Table 3 shows the results of the SPTs in current and ex-employees to common aeroallergens, and table 4 shows results of SPTs to latex in current workers with lower respiratory tract, nasal, ocular and skin symptoms.

One of the 30 (3.3%) current workers with WRSs of the lower respiratory tract, six of the 42 (14.3%) with ocular irritation ( $p<0.05$ ), four of the 66 (6.9%) with nasal irritation, and

15 of the 157 (9.6%) with dermatitis ( $p<0.01$ ) had a positive SPT to the latex allergen. One ex-employee, who had persistent WRSs of the lower respiratory tract, had a positive SPT to latex.

There was only one current worker with positive IgE specific to GA. She had WRSs of the eyes and nose but not of the lower respiratory tract.

Three hundred and twenty one blood samples were taken for IgE to latex. Thirteen (4.1%) were positive. Two of these (one current worker and one ex-employee) had WRSs of the lower respiratory tract, three were current workers with WRSs of the eyes and nose. Eight (61.5%) of the 13 subjects with a positive test to IgE specific to latex had WRSs of dermatitis (non-significant). There was no conformity between the positive latex SPTs and positive latex serology.

#### SPILLAGE ANALYSIS

Two hundred and nine (65.7%) current workers and 14 (77.8%) ex-employees were exposed to a GA spillage of over 0.5 l; 21 current workers (70%) to a SF composite spill. Spills of this size were seldom encountered (once or twice a year) in 83.0% of current workers and 64.3% of ex-employees. The most prevalent symptoms encountered by current workers were nasal and ocular irritation. Lower respiratory tract symptoms were as prevalent as nasal and ocular symptoms after a spill in the ex-employees. The relation between current symptoms and previous spills were explored in current workers exposed to GA. It showed that people experiencing work related irritation of the nose ( $p<0.01$ ) and eyes ( $p<0.05$ ), but not WRSs of the lower respiratory tract ( $p=0.2$ ), were more likely to have been exposed to a GA spill than workers without these WRSs. Subgroups of workers exposed to SF and ex-worker were too small for separate analysis.

#### MEASUREMENTS OF EXPOSURE TO ALDEHYDE

Table 5 presents the mean geometric peak and background measurements of exposure to aldehyde. Four units (19 nurses) had peak GA or SF concentrations below the lower limit of detection ( $0.001 \text{ mg/m}^3$ ). There were eight units with peak airborne concentrations but none with background concentrations of GA over the current MEL of  $0.2 \text{ mg/m}^3$  (0.05 ppm).

The relation between peak exposure to GA and symptoms is recorded in table 6. Only for WRSs of chronic bronchitis (defined as cough productive of sputum for greater than 3 months of the year for at least 2 years and either worse during the work shift or improving on rest days) was exposure to GA significantly associated with an increased risk of symptoms.

Table 4 Skin prick test (SPT) to latex in symptomatic current workers

	Positive in current workers with WRSs of the lower respiratory tract n (%)	Positive in current workers with WRSs of the eyes n (%)	Positive in current workers with WRSs of the nose n (%)	Positive in current workers with WRSs of dermatitis n (%)
SPT to latex	1 (3.3)	6 (14.3)*	4 (6.9)	15 (9.6)**

\* $p<0.005$ ; \*\* $p<0.01$ , Fisher's exact test.

Table 5 Airborne aldehyde concentrations

Aldehyde airborne concentrations	Geometric mean (range) $\text{mg/m}^3$
Peak glutaraldehyde (n=43 units with 267 nurses)	0.06 (<0.001-1.08)
Background glutaraldehyde (n=52 units with 308 nurses)	0.01 (0.002-0.1)
Peak succinaldehyde (n=6 units with 30 nurses)	0.11 (<0.001-1.20)
Background succinaldehyde (n=6 units with 30 nurses)	0.02 (<0.001-1.93)
Peak formaldehyde (n=6 units with 30 nurses)	0.03 (<0.001-0.18)
Background formaldehyde (n=6 units with 30 nurses)	0.01 (<0.001-0.38)

Table 6 Association between peak GA concentrations and WRSs: adjusted for smoking; months worked on the unit; number of hours spent on the unit; and number of hours spent decontaminating endoscopes

WRSs	Unadjusted		Adjusted	
	RR	(95% CI)	RR	(95% CI)
Chronic bronchitis	2.14	(0.995 to 4.586)	1.6	(1.247 to 2.054)
Persistent cough	0.72	(0.519 to 1.011)	0.76	(0.540 to 1.063)
Wheeze	0.52	(0.338 to 0.793)	0.52	(0.323 to 0.826)
Chest tightness	0.93	(0.687 to 1.256)	0.94	(0.690 to 1.275)
Shortness of breath	1.62	(0.819 to 3.191)	1.51	(0.967 to 2.359)
Lower respiratory tract symptom	0.98	(0.747 to 1.297)	1.03	(0.796 to 1.320)
Nasal irritation	1.16	(0.919 to 1.454)	1.13	(0.927 to 1.374)
Eye irritation	1.16	(0.880 to 1.541)	1.13	(0.907 to 1.407)

RR=relative risk.

Table 7 Distribution of washing and ventilation systems by number of current staff

	n (%)
Main washing system:	
Semiautomatic	116 (33.3)
Automated	232 (66.7)
Secondary washing system:	
Manual or open	48 (13.8)
Semiautomatic or automatic	300 (86.2)
Decontamination ventilation:	
No	69 (19.8)
Yes	279 (80.2)
Room ventilation:	
None	115 (33.0)
Negative pressure	146 (42.0)
Positive pressure	63 (18.1)
Others	24 (6.9)

None of the other WRSs, adjusted or unadjusted, showed any significant relation with either peak (table 6) or background (not presented) airborne concentrations of aldehyde.

Two GA spillages occurred during study visits and exposure samples were taken at the time. The TWA exposures to GAs were 0.27 mg/m<sup>3</sup> for a spill of about 1 l in an unventilated room and 0.439 mg/m<sup>3</sup>, for a spill greater than 5 l in a positive pressure theatre.

#### COMPARISON OF DECONTAMINATING UNITS

Endoscope decontaminating units were of three types: open or manual, semiautomated, and automated. No unit used open baths as primary decontaminating systems although eight units used them as a back up system (table 7). Analysis of ventilation systems and their associations with concentrations of airborne GA and WRSs of the upper and lower respiratory tract is shown in table 8. Units with a decontaminating unit and negative pressure ventilation had higher mean (geometric) peak airborne concentrations than all other types of system. Symptoms (significant for nasal irritation  $p < 0.01$ ) were more commonly experienced in units with negative pressure ventilation whether they had decontaminating system ventilation or not. The analysis of the relation between symptoms and peak GA concentration was repeated after correction for the additional confounding effect of type of ventilation system used. The association between peak GA concentration and nasal irritation then reached

Table 9 Association between peak GA concentrations and WRSs adjusted for type of ventilation

WRSs	RR	(95% CI)
Chronic bronchitis	4.08	(1.236 to 13.47)
Persistent cough	0.71	(0.501 to 0.997)
Wheeze	0.57	(0.363 to 0.888)
Chest tightness	0.93	(0.668 to 1.298)
Shortness of breath	1.99	(0.771 to 5.164)
Lower respiratory tract symptom	0.95	(0.711 to 1.255)
Nasal irritation	1.19	(1.012 to 1.402)
Eye irritation	1.3	(0.963 to 1.750)

RR=relative risk.

significance and that for WRSs of chronic bronchitis were enhanced (table 9). There was no association between exposure to GA and the other WRSs of the lower respiratory tract, which were more prevalent than chronic bronchitis.

#### Discussion

The modern healthcare environment that our workers experience contains various occupational respiratory hazards. As well as aldehydes, exposure to latex can be considerable, drugs used may be aerosolised along with other vapours and cleaning materials, microbial matter may be generated and air conditioning systems may be sources if inadequately maintained. Although this study represents an explorative cross sectional study of symptoms and hygiene variables in a group of healthcare workers exposed to aldehydes without a control group, it provides several interesting and surprising results. It could be argued that the addition of a control group would have given a clearer perspective of the additional risk of exposure to aldehydes. However, we thought that a control group would not have eliminated other confounding exposures—such as latex—as its use is so prevalent in healthcare settings. Furthermore, the lack of a control group did not have any effect on the ability to detect asthma in the exposed population, a key objective of this investigation. Therefore an open explorative approach was taken. However, accepting the absence of a control group means that the findings have to be interpreted with a degree of caution.

The most prevalent symptom encountered among the 318 current workers exposed to GA

Table 8 Airborne concentrations of GA and prevalence of WRSs by endoscopy unit ventilation

Factor	Type of ventilation				
	Decontamination unit ventilation only	Decontamination unit + negative pressure room ventilation	Decontamination unit + positive pressure room ventilation	Negative pressure room ventilation only	No ventilation
Sample size	84	110	58	50	16
Peak GA concentration*	0.068(0.047 to 0.100)	0.118(0.085 to 0.165)	0.062(0.049 to 0.079)	0.014(0.009 to 0.021)	0.021(0.006 to 0.080)
Background GA concentration*	0.019(0.015 to 0.025)	0.012(0.010 to 0.015)	0.015(0.013 to 0.019)	0.009(0.007 to 0.012)	0.025(0.016 to 0.040)
Prevalence of WRSs (n (%)):					
Chronic bronchitis	0	1 (0.9)	2 (3.4)	0	0
Persistent cough	4 (4.8)	3 (2.7)	0	3 (6.0)	0
Wheeze	2 (2.4)	3 (2.7)	0	2 (4.0)	1 (6.3)
Chest tightness	5 (6.0)	7 (6.4)	2 (3.4)	2 (4.0)	1 (6.3)
Shortness of breath	1 (1.2)	4 (3.6)	1 (1.7)	1 (2.0)	0
Lower respiratory tract symptom	8 (9.5)	11 (10.0)	3 (5.2)	4 (8.0)	1 (6.3)
Nasal irritation	12 (14.3)	28 (25.5)	6 (10.3)	14 (28.0)	3 (18.8)
Eye irritation	9 (10.7)	15 (13.6)	8 (13.8)	10 (20.0)	1 (6.3)

No units had positive pressure room ventilation on its own.

\*Geometric mean (95% CI)

and 30 workers exposed to SF composite was WRSs of contact dermatitis at 44.0% and 56.7% respectively. This high prevalence of dermatitis is similar to that found in a previous cross sectional study.<sup>20, 21</sup> Eight of the 18 (44.4%) ex-employees, all of whom worked with GA, also had WRSs of contact dermatitis, one had stopped endoscopy work because of this. Six of the eight who continued in nursing after leaving endoscopy units had persistent dermatitis.

Work related nasal and ocular irritation were common at current exposure concentrations and more prevalent than lower respiratory tract symptoms, which were relatively uncommon. Nasal symptoms related to work were dose dependent on peak GA concentrations, suggesting a direct irritant effect. Conversely there was no dose-response relation between exposure measures and lower respiratory tract symptoms with the exception of chronic bronchitis, which was in fact the least prevalent symptom. The association may be spurious because of the few people involved, but remained after adjustment for smoking. Chest tightness and persistent cough were the most prevalent symptoms. There was no dose-response relation between these symptoms and exposure to GA, SPT to latex, IgE specific to latex or GA, or pulmonary function (although symptomatic workers had a non-significant trend to a lower FEV<sub>1</sub>). It is of particular interest that none of the current workers who completed a 4 week peak flow monitoring assessment because of their symptoms actually had a greater than 10% variability in peak flow readings to imply an asthmatic process of any sort. However, 13 of the symptomatic workers failed to participate in PEFr recordings and the survey included only about 800 person-years of exposure. The presence of the lower respiratory tract symptoms in the absence of lung function (PEFR) changes great enough to imply asthma raises the possibility that the aetiology is primarily irritant.

Three people had a work related pattern to their recordings, in the absence of asthma, according to the OASYS-2 program analysis, which with a cut off of more than 2.51 has been shown to give a specificity of 94% and a sensitivity of 75% for an independent diagnosis of occupational asthma.<sup>36</sup> This degree of specificity and sensitivity approaches that of a visual assessment by a specialist occupational respiratory physician.<sup>40, 41</sup> These three current workers particularly warrant further investigations, although in all three people the maximum peak expiratory flow variation (worst work day : best day off) was only 5%. On the basis of the study protocol these people were deemed not to have asthma irrespective of their OASYS-2 score.

There is clearly a group of workers who leave the endoscopy environment because of health effects including symptoms of the skin and upper and lower respiratory tract. As expected the reporting of past symptoms is high in this group, but again there is no consistency in the immunological markers to suggest a sensitisation process and despite leaving the endoscopy environment and having no direct exposure to

GA most of these ex-employees, who still work as nurses, continue to have persistent symptoms and pulmonary function significantly lower than that of the current endoscopy staff.

In the six ex-employees in whom one or more of the WRSs of the lower respiratory tract occurred on workday evenings or nights the symptom history would be consistent with an allergic aetiology, as would the protracted period of latency (similar to that reported by Gannon *et al*<sup>20</sup>). These authors have shown in controlled unblinded GA challenges late phase asthmatic reactions in most of their subjects, with protracted latency. However, these challenges need to be interpreted with a degree of caution.<sup>19</sup>

The immunology results showed no overall association to the presence of WRSs. A recent publication<sup>42</sup> has also shown the lack of positive IgE specific to GA in people thought to have GA induced WRSs. It was suggested that the low molecular weight of GA would lead to only a small percentage of exposed workers having a raised specific IgE response. In the rest, GA would act through non-immune and other unknown immune mechanisms.

Latex SPTs were positive in 6% and latex specific IgE in 4.1% of subjects, but there was a poor correlation between them. The only significant associations were between SPTs for latex in current workers and WRSs of dermatitis and eye irritation.

Measured exposure to GA in this study varied widely from undetectable to high levels in the two monitored accidental spills.

Over the past 5 years there has undoubtedly been a nurse led impetus to improve their working environment, so that none of the study units now use manual washers as primary systems, most (66.5%) use fully automated units. However, 13.6% still use manual washers as back up units. This study has also shown, as have previous industrial hygiene studies,<sup>22-25</sup> that regular high acute inhalational exposure occurs during biocide changeover. Concentrations of GA above the current MEL of 0.2 mg/m<sup>3</sup> are common. This is a direct result of the fact that most endoscopy units in the United Kingdom are not designed at inception, but have haphazardly developed their working environment and working practises over the past 3 decades. Many of our study units did not follow Health and Safety Executive, control of substances hazardous to health (COSHH),<sup>43-45</sup> or British Society of Gastroenterology<sup>46, 47</sup> recommendations and guidelines on ventilation systems, decontaminating washer units, safe biocide use protocols, unit air conditioning systems, and the use of appropriate personal protection.

One of the most interesting and unexpected findings is that the units in this study that used decontaminating unit extraction ventilation with negative pressure room ventilation resulted in significantly greater peak airborne GA concentrations and an increase in at least the nasal symptoms experienced by their workers. The higher airborne concentration of GA probably occurs because it has a higher vapour density (3.4) than air, and poorly designed unit

extraction systems may just draw GA up and across the workers' breathing zone rather than it remaining low within the room and escaping below the breathing zone.

In summary, airborne peak concentrations of GA above the MEL are common due to poor compliance with health and safety guidelines. There is a high prevalence of WRSs of dermatitis the cause of which needs further investigation. Work related symptoms of the upper airways and eyes are common at current exposure concentrations and are probably irritant in nature. Lower respiratory tract symptoms in the current workers are uncommon and are also probably irritant in nature. The aetiology of these symptoms may be multifactorial. Bearing in mind the number of ex-employees with continuing symptoms, latex and other environmental factors other than GA may be responsible for many of them. The current workers may well represent a survivor population as their WRSs prevalence profile and work environments differed significantly from the ex-employees.

Although occupational asthma to GA has been documented previously, this study has identified no definite cases in current workers in an epidemiological study of over 300 workers. The use of controlled blinded occupational challenge in association with cough studies in current and ex-symptomatic workers may help to establish the mechanism for the symptoms.

Careful attention to ventilation systems is required to ensure that inadvertent exposure is not increased rather than reduced by inappropriate use and design of ventilation systems.

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