Assessment of exposure to ethanol vapors released during use of Alcohol-Based Hand Rubs by healthcare workers

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Air exposure;  
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Summary  
Background: Despite the increasing use of Alcohol-Based Hand Rub solutions, few studies have quantified the concentrations of inhaled ethanol.  
Objective: The aim of this study was to assess ethanol exposure during hygienic and surgical hand disinfection practices.  
Method: Ethanol concentrations were measured at the nose level of a wooden dummy and human volunteers. Two systems were used in parallel to determine short-term ethanol vapor exposures: activated charcoal tubes followed by gas chromatography analysis and direct reading on a photoionization detector (PID).  
Exposure was assessed for 4 different sequences (\(N=10\)) reproducing hand rubs for simple surgery, nursing care, intensive care and surgical scrub.  
Results: The ethanol concentrations measured were of a similar order between the dummy and volunteers. The concentrations obtained by PID were higher than the gas chromatography values for the simple care (45%) and nursing care (27%) sequences and reflected specific exposure peaks of ethanol, whereas ethanol concentrations were continuously high for intensive care (440 mg m\(^{-3}\)) or surgical scrub (650 mg m\(^{-3}\)).

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Introduction

Nosocomial infections are a major public health problem. The importance of hand hygiene in preventing these infections and in limiting the spread of bacteria have been demonstrated repeatedly, and healthcare workers have been encouraged to use Alcohol-Based Hand Rubs (ABHRs) [1–3]. ABHRs have become the preferred procedure over antimicrobial soaps [4,5] for both saving time and achieving greater effectiveness [6,7]. Their use also leads to improvement in healthcare workers’ compliance [8–11].

The World Health Organization supported ABHR implementation. Many studies have reported ABHR compliance in hospital workplaces, with variations between 3 and 144 times per hour [4,12]. In adult intensive care units, authors observed 0.13–6.25 rubs per patient, per nurse and per hour, 40–70 opportunities per day in neonatal intensive care units and 13 per hour in medical wards [12–15].

No study has reported secondary effects of toxicity from the ethanol contained in ABHR solutions for target organs such as liver or in the neurological, cardiac and pulmonary systems. Ethanol could be absorbed into the body via several mechanisms: transcutaneous passage, inhalation (vapor exposure) and exceptional ingestion.

Several studies have previously investigated the dermal absorption of ethanol from ABHR and reported either a small absorption [16,17] or a lack of passage [18–20]. The half-life of ethanol evaporation on the skin is 12 s [21]. Some studies quantified ethanol concentrations in blood and exhaled air after hand rubs with ethanol products, but the detected concentrations remained below threshold toxicity values [22,23]. All of these studies concluded that skin absorption during ABHR does not present a short-term risk for human health.

However, few authors gave much consideration to the pulmonary absorption of alcohol vapors. One study considering occupational alcohol vapor exposure reported a blood alcohol level of approximately 1.3 mg/100 mL after 19 min without significant further increase after lengthy exposure [24]. Therefore, respiratory tract absorption of ethanol should also be taken into account.

Conclusion: Ethanol concentrations were similar for these two exposure assessment methods and demonstrated a relationship between handled doses and inhaled doses. However, the ethanol vapors released during hand disinfection were safe for the healthcare workers.

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A study on dermal and pulmonary absorption of n-propanol and isopropanol indicated that the amounts absorbed were very low and unlikely to induce adverse health effects [25]. However, another study found that intensive use of an ethanol-based sanitizer induced an increase in concentrations of urinary ethanol biomarkers [26].

Due to the anticipated and needed growth of ABHR use in healthcare facilities, there is a need to consider the impact of their use in workplaces and to estimate caregivers’ exposure over the short- and long-term.

In this study, the amount of ethanol inhaled during ABHR use for nosocomial infection control in different care activities was estimated.

Materials and methods

The assessment of ethanol vapor exposure after ABHR was performed under controlled experimental conditions (several hand disinfection sequences were reproduced in a room with humidity and temperature measured), initially on a wooden dummy and a second time on volunteer hospital workers. To determine short-term ethanol exposures, in parallel, we performed direct reading from a photoionization detector (PID) and used a standard technique of sampling on charcoal tubes and subsequent analysis by gas chromatography.

Exposure conditions

Exposure to ethanol vapor was measured by reproducing the actual practice of hand disinfection as recommended to ward staff. Each procedure was repeated 10 times and was undertaken on a wooden dummy and on healthcare volunteers. The distances from nose to hot plate for the dummy and nose to hands for the volunteers were similar, measuring 45 cm in length (Fig. 1).

The hand disinfection sequences were applied in a 54 m³ room with two closed windows and a closed door. No controlled air exchange occurred during applications.
Figure 1  Experiment with wooden model and voluntary healthy adult.

Figure 2  Sequences of hand rubbing for hygienic disinfection (sequences I–III) and surgical disinfection (sequence IV).
Four different sequences of hand rubbing were tested as described in Fig. 2. For hygienic hand disinfection, three sequences were applied with 3 mL of ABHR solution for 30 s of friction on each of the humans and 2 min on the wooden dummy: sequence I for general surgery (two hand disinfections with a waiting time of 10 min), sequence II for care (three hand disinfections with 5- and 3-min breaks corresponding, respectively, to material preparation for care and to realization of care) and sequence III for many care events in the intensive care unit (nine hand disinfections with 5.5-min breaks). The number of hand-cleaning opportunities in the intensive care unit ranged from 10 to 60 per hour [13,14]; we choose the low end of the range for this study (10 rubs per hour). Sequence IV represented surgical hand disinfection before any surgical intervention or high infection risk gesture (friction with 2 × 6 mL of ABHR solution until completely dry).

At Nancy University Hospital, Aniosgel 85 NPC® (Anios Laboratories, France) was exclusively used. The study was performed using this ABHR solution with 70% ethanol (700 mg/g ethanol, glycerin, glycerides and fatty acid and polyethylene glycol esters, acrylic polymer, d-α-bisabolol, water).

**Tests on the wooden dummy**

In the experiments with the wooden dummy, the ABHR solution was placed on a hotplate at 36 °C and spread over the plate with a plastic tool until completely dry. The evaporation in its entirety required 1 min for sequences I—III and 2 min for sequence IV.

**Tests on healthcare workers**

In the experiments with the healthcare volunteers, we used a modified protocol of Kramer et al. [22]. All hand rubs were tested on the same 12 volunteers (6 males, 6 females). Inclusion criteria were a minimum age of 18 years and the ability to perform a standardized application according to Norm EN 1500:1997 [27]. Three milliliters of ABHR solution was placed on the palm of the hand, and the hands were rubbed together for 30–60 s until completely dry. For sequence IV, the overall quantity was 12 mL, with two successive rubs with 6 mL of ABHR. The first involved the hands, wrists and forearms, including elbows, while the second stopped halfway up the forearm. The duration of each rub was at least 1 min.

**Determination of ethanol concentration in air**

Two sampling systems were used simultaneously for each exposure model (dummy’s head and volunteers).

**Sampling and analysis on charcoal tubes**

This first technique quantified the overall exposure to ethanol vapors (exposure concentrations) during hand disinfection sequences.

For the collection of air samples, two sections of 100 mg + 50 mg coconut charcoal tubes (SKC 22601, L = 70 mm, φ int = 4 mm) were used at a sampling rate of 0.2 L/min (portable Gilian LFS 113 sampling pump). After taking in air, the charcoal tubes were stored before analysis at +4 °C for up to 10 days. All samples were treated under the same conditions. The first and second sections of the charcoal tubes were transferred separately into two glass vials and were desorbed in 1 mL of dichloromethane (CH2Cl2, Merck 1.06049). The vials were sealed and placed in ultrasonic waves for 30 min to obtain a desorption coefficient of 96%.

The analysis of ethanol concentrations in the supernatant was performed by gas chromatography in a modification of the method described by INRS [28]. This technique uses Split/Splitless injection (injector 1177 EFC 21 Split/Splitless) with flame ionization detection (Gas Chromatograph GC 3900, Varian® with DEFC 11 detector). A mega-bore capillary column CP-SIL 19CB (25 m × 0.53 mm × 2 μm, Varian® CP7657) was used for separation. The conditions of the chromatography were 220 °C injector temperature, 200 °C detector temperature and 55 °C column temperature. The flow rates of hydrogen and air were fixed at 25 mL min⁻¹ and 300 mL min⁻¹, respectively. Calibration was performed according to the method of an internal standard, with 0.5 μL of methanol (CH3OH, VWR 1.06008) added to the vial. The detection limit for ethanol with this technique was 0.1 mg L⁻¹. The results of the analysis were obtained using Galaxie™ Software (Varian®, Les Ulis, France).

**Photoionization detector (PID)**

The second technique allows the evaluation of exposure to organic compounds in real time, taking into account possible short-duration peak concentrations. It allows for an analysis of exposure profile, displaying a peak at pollutant detection and returning to zero when the pollutant exposure has ended.

A direct reading multi-detector PID2 (portable photo-ionization Drager®, Stasbourg, France) was used with an energy of 10.6 eV for the UV lamp, a Teflon/polypropylene input filter (1 μm) and a pump with an inflow rate higher than 300 mL min⁻¹ to continuously carry air through the PID. It measures values between 0 and 2000 ppm. The equipment was calibrated with a 100 ppm reference gas (isobutylene). The ethanol concentration was expressed in equivalent units of ppm isobutylene;
Data calculation: exposure of healthcare workers during work activity

The occupational exposure of healthcare workers by inhalation was estimated from data obtained during the hand disinfection sequences. In this study, the data were expressed as means ± SD. The assessment of exposure to ethanol vapors released during ABHR for one day’s work was given by the following formula: \( Q_{\text{daily}} = Q_{\text{sequence}} \times \alpha \times \gamma \times \nu \times \phi \), with \( Q_{\text{sequence}} \) being the quantity of ethanol vapor during the sequence (mg), \( \alpha \) being the percentage absorbed by inhalation from the emission value (according to the literature [29]: values were set at 62%, 70% and 80%), \( \gamma \) being the tidal volume (500 mL for a healthy adult), \( \nu \) being the respiratory rate (16 cycles min\(^{-1}\)) and \( \phi \) being the number of occurrences per day.

The number of occurrences of exposure equals the number of achieved frictions. The frequency of sequence I was estimated at 24 uses per working day (a nurse has 12 care patients in a nursing unit and performs 2 acts of this type per patient per day). The frequency of sequence II was estimated at 12 (a nurse performs one daily technical gesture per patient and supports 12 patients). For sequence III, a nurse working in an intensive care unit supports 3 patients in a specialized intensive care unit or 5 patients in a classical intensive care unit; for this paper, we used a mean number of 4 supported patients. The nurse performs a range of specialized care tasks per day per patient. This sequence corresponds to the number of opportunities per hour for which compliance is maximal, which we estimated to be 8. The mean number of surgical operations was estimated at 5 for sequence IV.

In a second step, we estimated the amount of ethanol absorbed during work life \( (Q_{\text{life}}) \) as given by the formula: \( Q_{\text{life}} = Q_{\text{daily}} \times \beta \), with \( Q_{\text{daily}} \) being the quantity of ethanol inhaled during a working day and \( \beta \) the number of working days according to the current French regulations (set at 31 years with 217 working days per year, i.e., 6727 days).

Results

Evaluation of overall exposure to ethanol vapors

Comparison of test dummy versus human

Exposure values of ethanol obtained from the dummy were always higher than values from volunteers (Table 1), and the differences were more significant when measured by PID: 14% for sequence I, 19% for sequence II, 27% for sequence III and 6% for sequence IV. When measuring by chromatography, the dummy values were still correspondingly higher, 7%, 6%, 30% and 2%, respectively. During friction with ABHR solution, the duration of ethanol exposure was higher in the dummy experiments (2 min for hygienic disinfection and 5 min for surgical rub) than in the human volunteer experiments (1 min for hygienic disinfection, 3 min for surgical rub).

Comparison of different gestures

Our results show that the mean values of ethanol exposure during the various hand disinfection sequences, obtained by chromatography and PID, were higher during surgical scrub (sequence IV). Here, the ethanol concentrations varied between 617 and 696 mg m\(^{-3}\). For routine hygienic disinfection of hands, we obtained, in decreasing order, sequence III (between 346 and 450 mg m\(^{-3}\)),

<table>
<thead>
<tr>
<th>Table 1 Ethanol exposure values for the dummy and human volunteer.</th>
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<tbody>
<tr>
<td>Hand disinfection sequences</td>
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<tr>
<td>Hygienic hand disinfection</td>
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<tr>
<td>Surgical hand disinfection</td>
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</table>

SD, standard deviation.
sequence II (between 263 and 404 mg m\(^{-3}\)) and finally sequence I (between 137 and 275 mg m\(^{-3}\)) (Table 1).

**Evaluation of exposure profiles to ethanol**

Exposure profiles during the different hand disinfection sequences were analyzed by the Multi-PID2 detector.

**Comparison of dummy versus human**

This study demonstrates that there was no difference in overall kinetic exposure profiles between the dummy and the human volunteers (Fig. 3). From the beginning of hand friction with ABHR solution, we can observe a peak of ethanol followed by a return to the normal value when exposure to ABHR solution ends. However, the number of peaks is higher with the dummy. Similarly, for sequences
I–III, the exposure time is longer by approximately 78 s with the dummy (149 ± 42 s) compared to the volunteers (71 ± 13 s). The exposure duration for the surgical rub (sequence IV) was 136 s for healthcare volunteers versus 283 s for the dummy. We observed a non-immediate return to zero, as in the other profiles. The return to zero appeared at the end of friction after mean periods of 456 s for the volunteers and 849 s for the dummy.

Comparison of different gestures
This study shows that exposure begins instantaneously during the hygienic hand rub (sequences I–III) and also ends instantaneously when the rub stops. However, during the surgical rub (sequence IV), the exposure to ethanol vapors is much higher, and the subjects continue to be exposed for several minutes after the rub stops, though in lower amounts.

Exposure assessment during professional life
Using the dummy, the assessment of ethanol quantities absorbed during a full professional life ranged from 2.1 to 3.4 kg or 1.4 to 2.5 kg of pure alcohol according to the PID or the chromatography methods, respectively. For volunteers during the same period, the estimated exposure ranges from 1.8 to 3.0 kg or 1.3 to 1.9 kg of pure alcohol according to the PID or the chromatography methods, respectively (Table 2). These quantities are fourfold lower for the surgical hand rub (dummy data: 0.6–0.8 kg with PID, 0.6–0.7 kg with chromatography; human data: 0.6–0.8 kg with PID, 0.7–0.6 kg with chromatography).

Discussion
This study assessed exposure to ethanol vapors during the use of ABHR solution for hand disinfection by healthcare workers. The daily quantities of alcohol handled are important and vary according to hospital ward and type of hand rub. Most studies assessing exposure to alcohol during ABHR have measured blood alcohol concentrations. The respiratory tract is the principal means of ethanol absorption, while dermal absorption is considered low (approximately 1%) [14,24,30].

Experimental conditions
Our study has focused on ethanol concentrations in air during four different sequences of hand rubbing and using two analytical methods. The ethanol concentration in the air is on the order of a few hundred milligrams per cubic meter: 137–544 mg m⁻³ after hygienic hand disinfection and 617–696 mg m⁻³ after surgical hand disinfection.

A study by Kramer et al. [22] reported low blood concentrations of ethanol after ABHR; consistent with data retrieved by exposure through the lungs (inhalable fraction) they reported absorption of 31.5 mg of ethanol after hygienic hand disinfection and 154.2 mg after surgical hand disinfection. By determining the concentration of ethanol in the air breathed and modeling the physiological and elimination mechanisms of ethanol according to the different compartments in the human body, it should be possible to explain the results measured in the blood during this study. The inhaled ethanol is rapidly distributed almost uniformly throughout the body due to its high solubility in water. Distribution is very rapid in highly vascularized organs, such as the brain, lungs and liver, with maximum concentrations in the cerebrospinal fluid and urine and a plasma concentration that is slightly higher (1.1 times) than the average concentration in the organs. Various factors, such as the inhalation rate and the tidal volume, could affect ethanol inhalation, leading to an absorption efficiency ranging from 30% to 80% [31,32].

In our study, we wished to eliminate these inter-individual variations encountered with volunteers. For this reason, we succeeded in creating an experimental model using a wooden dummy under controlled conditions to study ethanol exposure by inhalation during various care sequences. All exposure values of ethanol obtained from the dummy were slightly higher than those from the volunteers, both in quantity and in rub time for identical kinetics. All of the parameters were controlled with the dummy, while only the quantity of ABHR solution delivered was controlled on volunteers. This difference could be explained by the possible loss of a small quantity of ABHR solution in the volunteers’ experiments. Depending on hand size and the amount of product (ABHR solution) falling to the ground, this limits the amount actually used for hygienic friction. The friction time and the amount present at nose level were directly proportional to the quantity of product on the hands. Similarly, in our study, the time of ethanol evaporation on the human skin was faster than on the hot plate of the dummy; thus, the duration of ethanol exposure was higher in the dummy experiments than in the human volunteer experiments for both hygienic disinfection and surgical rub. In agreement with the hand rub protocol, the ABHR should stop only when the skin is dry. The first explanation is that evaporation
<table>
<thead>
<tr>
<th>Hand disinfection sequences</th>
<th>Method of measurement</th>
<th>Exposure time (min)</th>
<th>Opportunity number (per working day)</th>
<th>Rate of ethanol retention</th>
<th>Assessment of ethanol absorbed (mg)</th>
</tr>
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<tbody>
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<td></td>
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<td></td>
<td></td>
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<td>Dummy during sequence Human during life working</td>
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<td>15.0 2646706  13.1  2319477</td>
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<td>0.7</td>
<td>16.9 2988216  14.8  2618764</td>
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<td>0.7</td>
<td>10.3 1813110  9.6  1701343</td>
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<td>0.7</td>
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<td>0.7</td>
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<td>0.7</td>
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<td>0.7</td>
<td>17.7 649299  18.3  673995</td>
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<td>0.7</td>
<td>19.5 716184  19.7  725592</td>
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<tr>
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<td>818496</td>
<td>0.7</td>
<td>20.2 742056  21.0  770280</td>
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</table>
time is directly related to the amount of ethanol on the skin and on the plate, as the volunteer may lose a portion of the product. The second explanation is that the duration of the rubs was conditioned by the total evaporation of the ABHR solution. The evaporation is shorter with the volunteers because the friction of the hands can cause a local increase in temperature and can thus accelerate the evaporation of alcohol. This phenomenon cannot occur with the dummy in the context of the constant temperature of the hot plate. Alcohol is very volatile, so even a slight increase in temperature accelerates evaporation.

Exposure to ethanol vapors

In our experiments, during the various hand disinfection sequences, the PID detector indicated that the instantaneous values of ethanol concentration in the air after ABHR were high. The peak values often exceeded the display capability of the device; therefore, the true values are above the data displayed. However, these values cannot be compared to the short-term exposure level for ethanol adopted in France (STEL = 9500 mg m⁻³) for an exposure of 15 min in the air of the working premises. The peak values displayed by the PID were obtained during a very short period, on the order of seconds with a maximum of 1 min, and only observed during the friction period and not for 15 min. If we calculate the average values of ethanol exposure over the duration of 15 min, the values obtained, regardless of the method of measurement, range from 140 to 700 mg m⁻³. These values are well below the STEL value of 9500 mg m⁻³. However, symptoms related to acute exposure could still be observed in people with sensitivity (e.g., headaches or numbness); these symptoms generally appear after 30 min of exposure to a concentration of 2620 mg m⁻³ for a healthy subject. A report on the exposure of workers to ethanol indicated that a sudden change in ethanol concentrations from 0 to 3600 mg m⁻³ may cause temporary irritation [31]. For shorter periods (5–10 min) with higher concentrations (9500 mg m⁻³), immediate irritation of the eyes and the upper respiratory tract (cough) could be observed. Even in people exposed to the STEL, very few will report any adverse effect. However, some health professionals may be more sensitive and may therefore have some minor symptoms. The presence of more sensitive individuals may explain the results of an epidemiological study conducted on 50 caregivers at the University Hospital of Nancy. This study revealed that 8% of nurses, when interviewed about using the ABRH solution, described irritation of the upper respiratory tract during hygienic hand rubbing [33]. In the case of vapor inhalation of ethanol, the risk of severe acute poisoning is low because the anesthetic effects of ethanol are only observed at high concentration levels that would induce unacceptable irritation [13,30,34–37]. Furthermore, all effects are transient and disappear very quickly after exposure. In cases of repeated exposure (e.g., in subjects regularly ingesting ethanol), a certain tolerance appears. In cases of repeated inhalation of ethanol vapors, eye and upper airway irritation, headaches, fatigue and decreased vigilance have been reported [13,34–37]. However, despite a few old unconfirmed observations, there is no evidence that chronic inhalation may have effects on liver and heart disease similar to those produced by repeated excessive intake. However, a 15 year cohort study covering 1282 workers in the rubber and tire industry did identify a significant association between ethanol exposure and mortality from ischemic heart disease in subjects over 50 years old [37].

In our study, the amount of ethanol breathed by a nurse or doctor was estimated for hygienic and surgical disinfection of hands with ABHR solution. The daily work of a health professional combines different situations. We must therefore modify the estimations according to professional activity. However, even if the inhaled amount is negligible for a short period of time, the estimation throughout a professional career represents the absorption of several kilograms of pure alcohol and thus could cause long-term side effects. These results agree with a recent study of assessment of exposure to alcohol vapor during hand disinfection using two types of commercial ABHR solutions (ethanol and combined alcohols) [38]. This research showed that the use of ABHR solution leads to the absorption of very low doses of alcohols, but repeated inhalation of high alcohol concentrations raises the question of possible adverse health effects.

Conclusion

In this study, we succeeded in creating an experimental model, which allows us to study several parameters, such as the distance between hand and nose or the effect of wearing a surgical mask during exposure. It is difficult to test the impact of wearing a staff mask because the instruments used for measuring are too large to place behind the surgical mask. This study demonstrates that we have created an experimental model with controlled conditions that could be used to replace humans or to perform tests in the laboratory.
Exposure to ethanol vapors during hand rubbing

This study also shows the link between ethanol vapor exposure and the use of ABHR solution, but the exposure values are well below the limitations on exposure to ethanol that have been enacted in different countries. Although the concentrations of ethanol in the air remain tolerable, an acute exposure of short duration at high concentration was observed in our study by measuring it in real time with PID. Few data are available on the health effects of sudden and repeated exposure to high concentrations of ethanol. It appears essential to protect sensitive populations and particularly pregnant women, for whom exposure to alcohol, even at low doses, may induce possible harmful effects on the fetus. Ethanol crosses the placenta freely, and similar concentrations are found in the maternal and fetal blood, leading to questions regarding its use in pregnant women. This question has serious implications for nursing staff because they consist mostly of young women of childbearing age. Healthcare workers are unintentionally exposed to ethanol vapors during ABHR, and hand hygiene programs will encourage increasing use of these products in future years. While waiting for complementary studies on sudden and repeated exposures to high concentrations of ethanol, protection appears necessary for sensitive healthcare workers.

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Competing interests

Alexis Hautemanière, MD PhD, was supported by Anios laboratories. Djihane Ahmed-Lecheheb, PhD student, was supported by ANRT (National Association of Research Technology) and Anios Laboratories. The others authors declare no conflicts of interest.

Ethical approval

Not required.

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