Title: Solvent vapours in incubators: a source of exposure among neonates?

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Solvent vapors in incubators: a source of exposure among neonates ?

Hygiene practices in neonatal units require the use of disinfecting solutions containing ethanol or isopropanol. Newly disinfected hands or soaked swabs introduced inside the incubators may emit vapors leading to alcohol exposures to the neonates. Alcohol emissions from hands and other occasional sources (e.g. soaked disinfecting swabs) lead to measurable levels of vapors inside incubators. Average isopropanol and ethanol concentrations ranging from 33.1 to 171.4 mg/m^3 (13.8 to 71.4 ppm) and from 23.5 to more than 146 mg/m^3 (9.8 to >61 ppm) respectively were measured inside occupied incubators (n=11, measurement time about 230 min) in a neonatal unit of the Centre Hospitalier Universitaire Vaudois in Lausanne during regular activity. Exposure concentrations in wide range of possible situations were then investigated through modeling using the one-box dispersion model. Theoretical modeling suggested typical isopropanol peaks and average concentrations ranging between 10^2 and 10^3 mg/m^3 ($4{\cdot}10^1$ - $4{\cdot}10^2$ ppm), and 10^1-10^2 mg/m^3 (4-$4{\cdot}10^1$ ppm), respectively. Based on our results we suggest several preventive measures to reduce the neonate's exposures to solvent vapors.

Lösungsmitteldämpfe in Inkubatoren: Eine Belastungsquelle für Neugeborene ?

Hygienemaßnahmen in Frühgeburtenabteilungen erfordern den Gebrauch von Desinfektionsmitteln, welche Ethanol oder Isopropanol beinhalten. Frisch desinfizierte Hände und andere Quellen (z.B. Tupfer) können in Inkubatoren messbare Dämpfe freisetzen, die zu Alkoholbelastung bei Neugeborenen führen. In besetzten Inkubatoren (n=11) einer Frühgeburtenabteilung des Universitätskrankenhauses in Lausanne, reichen die durchnittlichen Isopropanol- und Ethanolkonzentrationen, während eines normalen Arbeitstag, von 33.1 - 171.4 mg/m^3 (13.8 - 71.4 ppm) beziehungsweise von 25.5 zu mehr als 146 mg/m^3 (9.8 zu >61 ppm). Expositionskonzentrationen vieler möglicher Situationen wurden mit einem „One-box dispersions model" modelliert. Die Resultate legen typische Isopropanol Höchst- und Durchschnittswerte nahe, welche zwischen 10^2 - 10^3 mg/m^3 ($4{\cdot}10^1$ - $4{\cdot}10^2$ ppm), beziehungsweise 10^1 - 10^2 mg/m^3 (4-$4{\cdot}10^1$ ppm) variieren. Aufgrund unserer Ergebnisse schlagen wir einige Präventivmaßnahmen vor, um bei Frühgeborenen die Belastung mit Lösungsmitteldämpfen zu verringern.

AUTHOR INDEX

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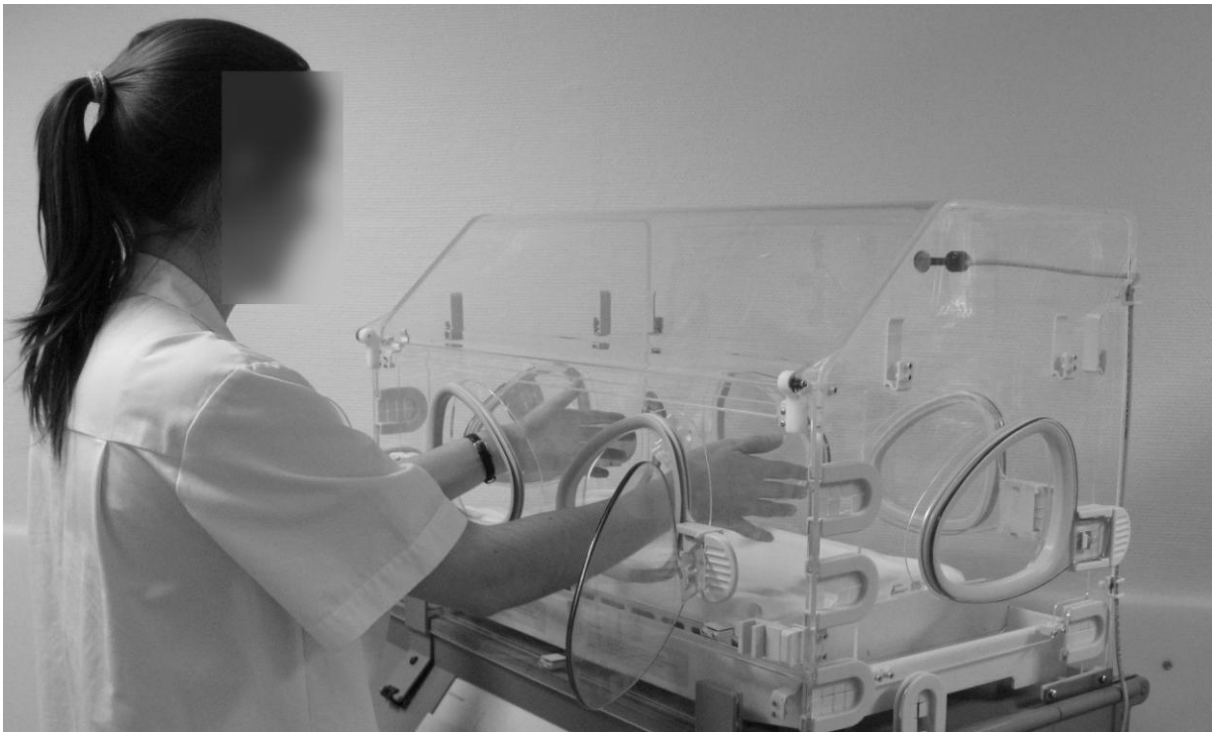
INTRODUCTION

Incubators are widely used in neonatology to maintain suitable environmental conditions for neonates. The incubator is a small volume chamber enclosed by a bottom shell and a transparent top casing. The ventilation system for this chamber regulates the air flow and is equipped with a humidifier. To maintain constant humidity, air flow and temperature, the nurses/doctors introduce only his/her hands and forearms inside the incubator, using small apertures in the top casing (see figure1).

Figure 1. Incubator used in neonatology (front doors open and forearms inside)



Part of the hygiene practice used by the workers in neonatal units require disinfecting the hands by rubbing them with alcoholic solutions either based on ethanol or isopropanol [1,2]. The user is recommended to wait (about 1 minute) for complete alcohol evaporation before introducing his/her hands into the incubators. In practice, the workers happen to insert their hands into the incubators probably before complete evaporation due to a high workload or to the neonates' urgent needs. This practice could lead to an increase in organic solvent vapors inside the incubators.

Available data on neonate's exposure to alcoholic vapors is scarce. Until now no study has investigated the neonate's exposure while in incubators. Cortical hemodynamic modifications in the olfactory region of the brains of preterm infants have been found after exposure to odorous substances routinely used in the neonatal intensive care [3]. An accidental death of a neonate (1500g, 37 week gestation), following an acute exposure, due to isopropanol exposures has also been reported [4].

The aim of our study was to assess neonates' exposures to ethanol and isopropanol concentrations inside the incubators using both field measurements and theoretical modeling. The results were expected to refine current recommendations regarding the use of hand disinfectants by neonatal nurses/doctors/parents.

MATERIAL AND METHODS

Study population

This study was performed at the Neonatal Unit at the Centre Hospitalier Universitaire Vaudois. Hand disinfectants in clinical use at the time of the study were Sterillium® (45% 2-propanol and 30% 1-propanol) and Sterillium Virugard® (95% ethanol) (Bode, Beiersdorf AG, Münchenstein, Switzerland). The manufacturer recommends to: "rub your dry hands with at least 3 ml alcoholic solutions for 30 seconds".

Field measurements

Eleven field measurements were performed in both both neonatal intensive and special care units (NICU resp. NSCU). Convenience sampling was used because of restricted access and possible interferences with intensive or continuous care activities in the neonatal units. Isopropanol and ethanol concentrations were measured inside incubators using a direct-reading instrument; a photoionisation detector (Toxi Rae®, Rae Systems Inc., Sunnyvale, California, USA), and cumulative air concentration (230 ±19 minutes) using charcoal absorption tubes (Anasorb CSC 226-01, SKC inc., Eighty Four, PA, USA) and pocket pumps (100 ml/min, SKC pocket pump, Blanc-Labo, Tolochenaz, Switzerland). The photoionisation detector was calibrated with 2-propanol (for Sterillium®) or ethanol (Sterillium Virugard®) before each measurement. Ambient air concentrations (outside the incubators) were measured using the same method as described for air concentrations inside the incubators.

Staff's hands disinfection as well as the opening and closing of the incubator's apertures are referred to as interventions. Hands disinfections, incubator manipulations (e.g.

opening/closing apertures), and introduction of hands in the incubators were recorded by a pediatric resident concomitantly to the measurements.

The charcoal tubes were analyzed by desorption with CS_2, and quantified using a gas chromatography (Capillary column CPSIL 8B, 60m, Chrompack, Middelburg, Germany) with a FID detector. The detection limit was of 1 µg/tube (NIOSH 1400 alcohols 1).

Exposure modeling

The alcohol air concentrations inside the incubators are influenced by numerous parameters. It is therefore not practical to investigate the range of possible situations in an experimental way. Due to the convenience sampling used (n=11), the number of field measurements available was not representative and an alternative to experimental measurements was necessary. Exposure modeling was therefore used to estimate isopropanol exposures in a wide range of input parameters and to investigate parameters' influence on exposure. Results obtained from simulation can easily be extrapolated to similar exposure situations (e.g. different chemicals).

The one box model, also called Well-Mixed Box (WMB) Model, has been used in this paper [5]. The key hypothesis of the model is that an ideal mixing occurs in the room (or the volume considered). In practice, ideal mixing is seldom achieved, particularly in large or complex volumes because of dead-spaces or short-circuits. In our study, the volume considered is small (157 lt) and hence, this limitation of the model would be low. Moreover, experimental measurements indicated that the isopropanol decrease inside incubator followed an exponential kinetic (linear decrease of the pollutant concentration logarithm over time), as expected from an ideal-mixing. In the WMB model, sinking (adsorption) is neglected, and the relationships between the pollutant concentration Ci [mg/m^3], the ventilation flow Q [m^3/s], the emission rate E [mg/s], and the compartment volume V [m^3] are expressed by a differential mass balance over time:

$$V \cdot \frac{dC_i}{dt} = E(t) - Q \cdot (C_i(t) - C_{i0}) \quad \text{(eq. 1)}$$

Introducing air renewal R[time^{-1}] (R = Q/V), and assuming a clean incoming air (C_{i0} = 0) gives:

$$V \cdot \frac{dC_i}{dt} = E(t) - R \cdot V \cdot C_i(t) \qquad \text{(eq. 2)}$$

Where E(t) is a constant, this equation can be integrated and has an analytical solution.In our case however, emission varies over time as it occurs when newly disinfected hands are introduced inside the incubators. E(t) can be expressed as a function of the following parameters: the time lag (TL) between two intervention (the time duration between two interventions inside the incubator), the disinfection ratio (DR) (the average number of interventions preceded by hand disinfection divided by the total number of intervention) and the amount of alcohol emitted during a specific intervention e (i being the total number of interventions during the simulated period).

$$E(t) = f(DR, TL, e_1 \ldots e_i) \qquad \text{(eq. 3)}$$

The amount of alcohol emitted (e) inside the incubator during a specific intervention depends on the amount of disinfectant solution used (Md) and the time lapse (referred in this paper as “waiting time after use of disinfectant” or WT) between the disinfection of the hands and their introduction into the incubator. Only Md and WT parameters were included in our study. Additional parameters that may affect evaporation such as hand surface, skin temperature, and local ventilation conditions during disinfection were not explicitly considered.

$$e = f(WT, M_d) \qquad \text{(eq. 4)}$$

The one box theoretical model (eq. 2) was implemented using simulation software (Ithink, version 7.0, isee systems inc. Lebanon, NH, USA). Numeric simulations were conducted for a wide range of input parameters in order to generate typical concentration profiles and to assess the influence of some exposure determinants. .

Assessing model parameters

All the incubators included in this study were of the same model (Dräger IC 8000 Draeger Medical AG & Co. KG, Lübeck, Germany). Their inner air volume (V) was of 157 liters. R (air renewal) was obtained experimentally using an empty incubator set at 32.5°C and 50% humidity. Isopropanol (100 µl) was injected inside the incubator through a front aperture

with a syringe. The concentration decrease after injection was measured by photoionisation and used to assess air renewal according to the one-box model analytical solution [5].

Three air renewal situations were considered: (1) all apertures closed, which is expected when no work was required; (2) two front apertures open, which is expected shortly before and after interventions; and (3) forearms and hands inside incubators (through the open apertures), which is expected during intervention. Each experiment was repeated three times. The repeat averages were used in the model. TL (time lag) and DR (disinfection ratio) were obtained by observation while performing the measurements. TL and DR were 21.9 min (n=56, SD=23.1) and 70%, respectively, in the continuous care unit, and 9.9 min (n=63, SD=10.3) and 38%, respectively, in the intensive care unit. The latter reflected higher workloads and time constraints. It should be noted that the disinfection ratios were within the range of hand hygiene compliance levels observed in previous studies [6].

Md was assessed experimentally. Hand disinfections were performed repeatedly by the same pediatric resident who was asked to use "smaller than usual" (n=9; 0.322 g, SD 0.035), "usual" (n=9; 0.668 g, SD 0.063), and "larger than usual" (n=10; 1.368 g SD 0.194) amounts of Sterillium®. The bottle of disinfectant was weighed before and after each use, using a Mettler P163 balance (Mettler Inc AG, Zürich, Switzerland).

Three WT durations were considered: regular hand cleaning practice (1 minute), an unintentional underestimate of the WT (30 seconds), and a situation requiring immediate attention (10 seconds), where the regular hand cleaning practice was not respected.

Three alcohol emission (Ej) scenarios were considered using the Md and WT values previously obtained: a "small" (smaller than usual Md, WT 30 seconds), "fair" (usual Md, WT 30 seconds), and "large" emission scenario (larger than usual Md, WT 10 seconds). All three scenarios were performed by the pediatric resident. Isopropanol concentrations inside the incubator were measured concomitantly by direct-reading. Each experiment was repeated three times. Ej was then calculated using the mass-balance relationship (eq. 2) and the isopropanol concentrations (corresponding to Ci in the model).

RESULTS

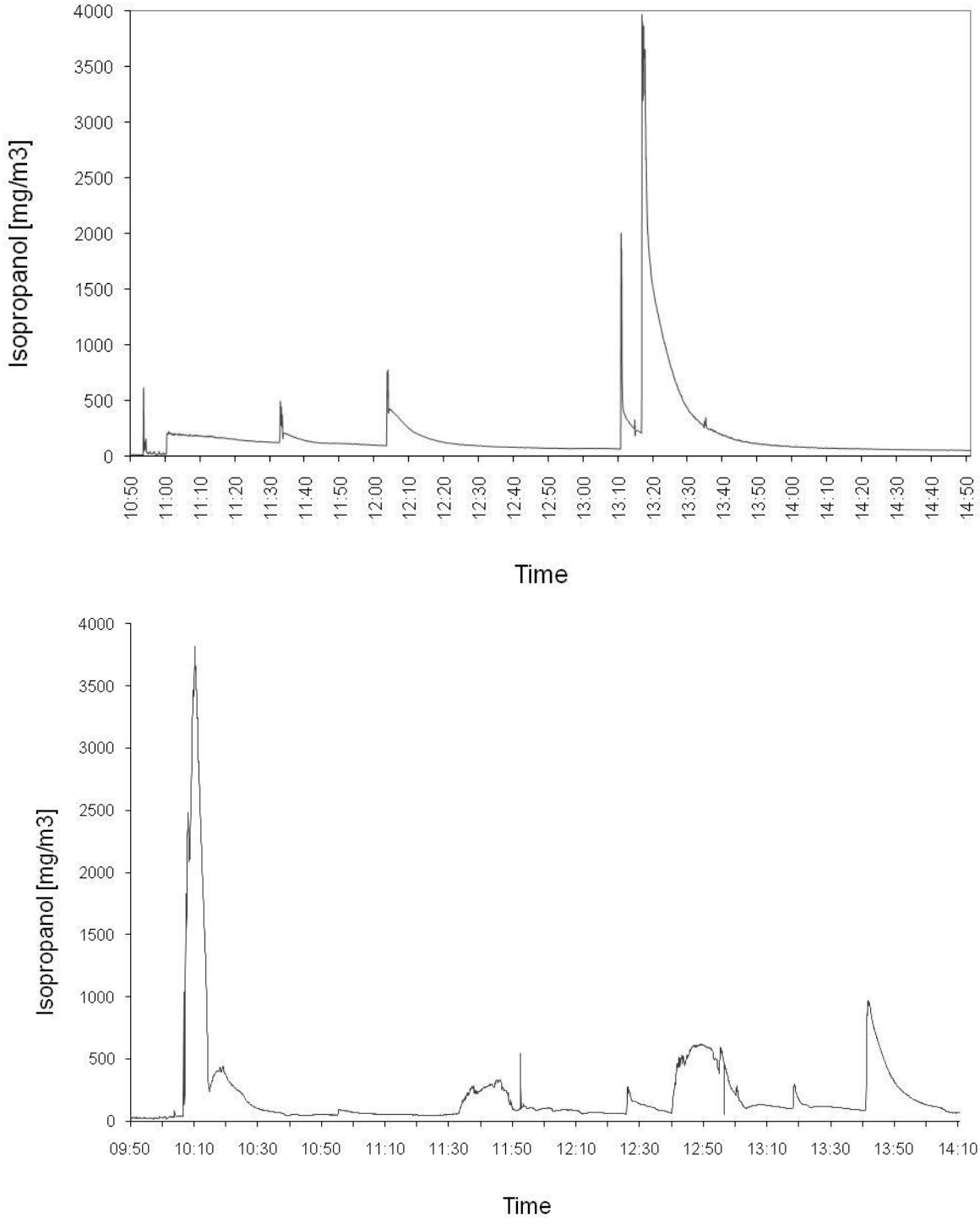
Field measurements

Our field results indicate that neonates in incubators were exposed to measurable ethanol and isopropanol concentrations from disinfectants, especially peak exposures. Average isopropanol and ethanol concentrations found inside the incubators through sampling

were of, respectively 83.6 mg/m^3 SD 103.3 mg/m^3 and 45.7 mg/m^3 SD 27.5 mg/m^3 (air renewal range was 7.1 -19.6 h^{-1}),. Lower levels of isopropanol and ethanol, respectively of 12.6 mg/m^3 and 4.4 mg/m^3 were detected in the ambient air (outside the incubators).

Typical exposure profiles measured inside incubators are shown in Figure 2. High exposure concentrations, up to 3 g/m^3 were observed during short time periods.

Figure 2. Temporal profile of isopropanol concentrations as measured in NICU (a) and NSCU (b) incubators



Although all measurements were performed in the same unit the concentrations profiles were of different shape. The neonatal special care unit (NSCU) profiles obtained through direct reading measurements (figure 2a) showed several well identifiable peaks followed by an exponential decrease while irregular increases and decreases were observed on the NICU profiles (figure 2b). This difference reflected the more complex tasks required in intensive care (longer interventions, successive opening/closing, more handling inside incubator) compared to special care.

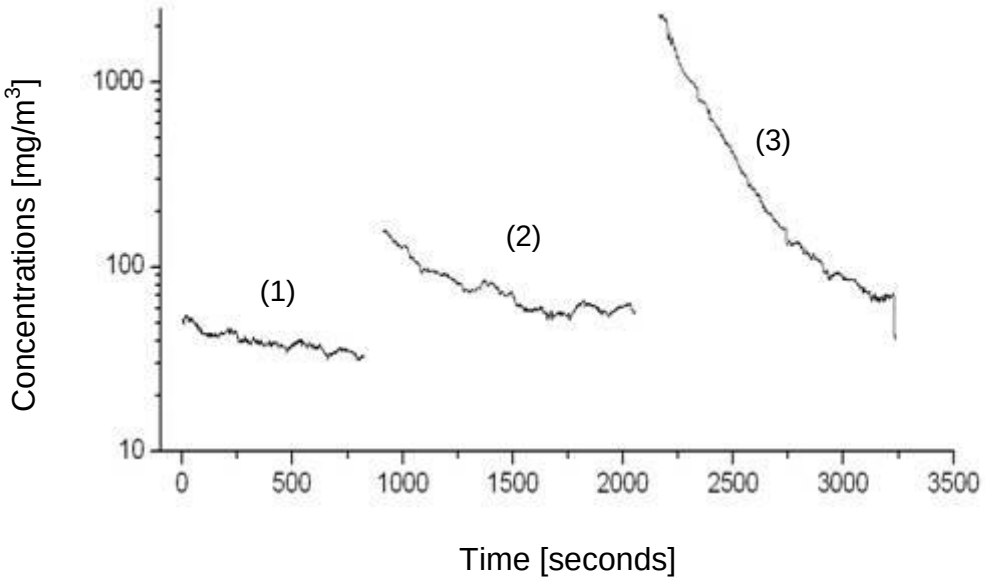
Exposure modeling

Air renewal rates with apertures closed, two front apertures open, and forearms and hands inside incubators were found to be 7.1, 10.8, and 19.6 h^{-1}, respectively. A constant supply of fresh air is maintained, even in closed-aperture conditions, in order to maintain adequate hygrometric and temperature conditions within the incubator. The “clearance” of the solvent vapors in closed-aperture conditions is nevertheless lower than in open-apertures condition due to the lower air renewal.

Isopropanol concentrations inside the incubators following hands introduction for the three considered scenarios are presented in Figure 3. The maximum isopropanol concentration (above 1000 mg/m^3) was obtained for the “large” emission scenario. The corresponding isopropanol amounts emitted inside incubator for “small”, “fair”, and “large” emission scenarios were 8.9, 16.3, and 230 mg, respectively.

Figure 3. Measured isopropanol concentrations following the introduction of hands according to:

(a) the ”small” emisson scenario
(b) the “fair” emission scenario
(c) the “large” emission scenario.



An example of a typical modeled exposure profile, in “fair” emission conditions (usual disinfectant amount, WT 30 seconds), in a NICU obtained through simulation is presented in Figure 4. In order to reflect the variability of the work, lognormal distributions were used for time lag (TL) and amount emitted per intervention (e_i). Peak concentrations reached 600 mg/m^3 and lead to mean concentrations of 64.8 mg/m^3 in this simulation profile. Interestingly, the highest concentrations reached were when the time lag between two “peaks” was short, typically below 10 minutes. If an additional pollutant was introduced into the incubator while the previous “peak” had not cleared, the resulting cumulative concentration was higher than what was reached with a single peak emission.

Table 1. Simulation parameters used to compare scenarios

Scenario	*Air renewal, R [h^{-1}]*	*Amount emitted per intervention, e_i [mg]*	*Waiting time, WT [s]*	*Time Lag, TL [min]*
a (large emission, apertures closed)	7.1	230	10	3-60
b (large emission, apertures open)	19.6	230	10	3-60
c (fair emission, apertures closed)	7.1	16.3	30	3-60
d (small emission, apertures closed)	7.1	8.9	30[1]	3-60
e (fair emission, apertures open)	19.6	16.3	30	3-60
f (small emission apertures open)	19.6	8.9	30[1]	3-60

(1) A WT of 1 min did not produce measurable amounts of alcohol inside the incubators and was thus not considered. A WT of the 30 s rather than 1 min was therefore considered in this scenario

We compared the simulation results obtained from various exposure conditions, assuming constant time lags in each run. The simulation parameters used are summarized in Table 1. Although theoretical, this approach allows assessing the influence of simulation parameters on potential exposure. The mean concentrations obtained for various time lags, emission scenarios, and air renewal scenarios (apertures open or closed) are shown in Figure 5.

Figure 4. Example of a computerized exposure profile

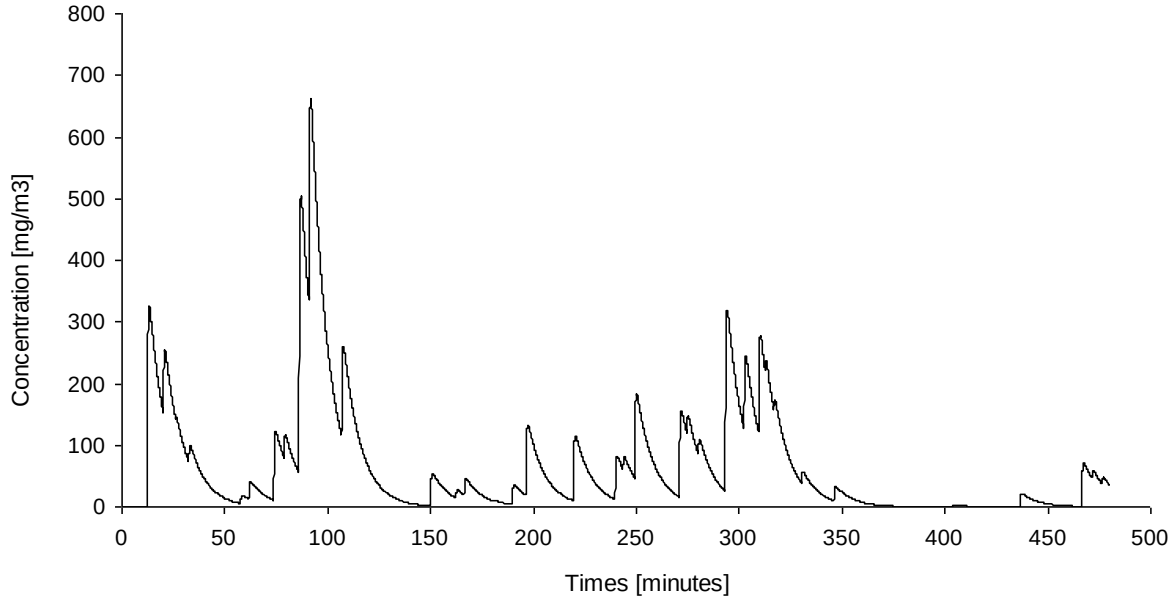
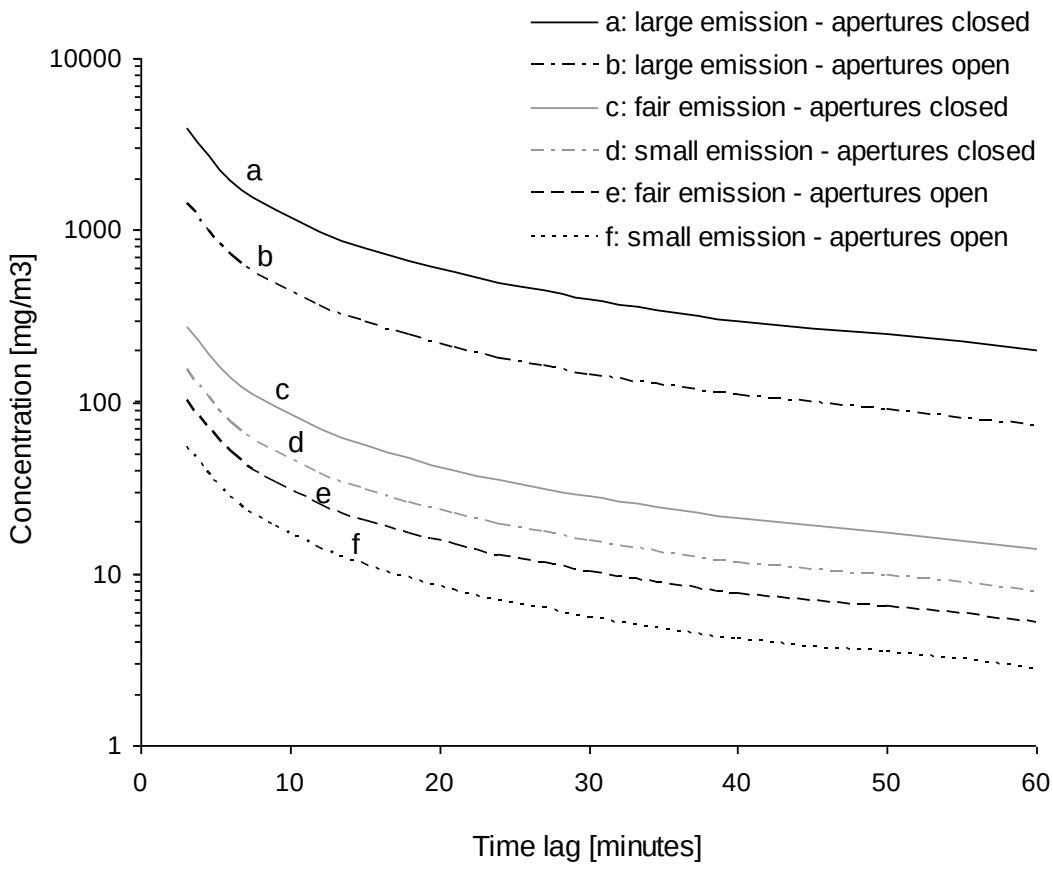


Figure 5. Sensitivity analysis: mean isopropanol concentrations for various emission scenarios, time lag and air renewal conditions



Generally, the mean isopropanol concentration was strongly affected by simulation parameters values and three orders of magnitudes were found between the lowest (3 mg/$m^{3,}$ scenario a, TL = 3 min) and highest (4000 mg/m3, scenario f, TL = 60 min) predicted values. When other simulation parameters remain unchanged, the air renewal conditions affect average isopropanol concentrations similarly and isopropanol concentrations obtained for closed apertures were 2.7 times higher than for open apertures. The "large" emission scenarios (scenario a and b) lead to average concentrations, ranging between 70 and 3900 mg/m^3. These values are 14 times higher than the results obtained for "fair" emissions under similar conditions (scenarios c and e). The situation is similar for the time lag parameter, for which a dramatic increase in average alcohol concentration can be observed below 10 minutes.

Disinfecting solutions based on ethanol or isopropanol will lead to different simulation results in terms of absolute concentration levels; however, the pollutant dynamic behavior (kinetics) and its sensitivity to the simulation parameter (e.g. air renewal rate) were independent of the chemical considered. Similar behavior may therefore be found for other disinfectant used in neonatal care units.

DISCUSSION

Vapors from alcoholic disinfecting solutions (ethanol and isopropanol) were found in measurable concentrations in neonatal incubators. Considering that lower levels of ethanol and isopropanol concentrations were found in ambient air, the alcohol concentrations measured inside the incubators can be attributed to the introduction of vapor-emitting disinfectant within the incubator. Newly disinfected hands were the most common source of peak exposures observed. Disinfecting swabs, soaked with isopropanol, may also be unintentionally forgotten after a procedure, leading to a longer-lasting elevated level of alcoholic vapors. Once for instance, the photoionisation detector reacted strongly to the presence of a mother's perfumed scarf, which was lovingly left next to her baby's head. There is no way to know whether the perfume vapors were detrimental or unpleasant to the baby. Solvent emitting objects should nevertheless be avoided in a general sense due to the limited volume of incubators. In addition, various anatomical, clinical and even near infrared spectroscopy studies have shown that the olfactory system is indeed functional by 28 weeks of gestation [7], and perfume or other vapor emitting materials may affect the baby's well

being or development. Reducing the emission of alcoholic vapors inside incubators may contribute to the well-being of newborns in neonatal units.

Little is known with regard to possible health effects in neonates from exposures to isopropanol or ethanol vapors. For inhalation, only one neonatal case of accidental alcohol inhalation has been reported [4]. The preterm neonate has an immature skin and a high body surface to weight ratio making them prone to skin absorption. In a rabbit model, Martinez et al. have shown that that transdermal isopropanol absorption can be significant [8]. However, no data on neonatal human skin absorptive properties exist. Percutaneous systemic ethanol and isopropanol intoxications in preterm and term neonates have been described but were always due to intense direct contact between skin and liquid ethanol or isopropyl alcohol [9-12]. For neonates supported by assisted ventilation, exposure to alcohol vapors inside incubators could be less than expected. A percutaneous absorption of alcohol vapors seems improbable although both ethanol and isopropanol are known to be absorbed by the neonatal skin when in direct contact with the liquid form.

Exposure prediction through modeling indicated that time-related parameters (waiting time after use of disinfectant and time lag between two interventions) were key factors for exposure concentration levels. Peaks of exposure, either due to emissions from the hands or to the cumulative effects of repetitive interventions, were important sources of increase in the predicted average exposure.

Preventive measures should be implemented to decrease neonate’s exposures to solvent vapors. Acting on air renewal conditions (e.g. favoring bigger incubators, keeping apertures open after interventions) will contribute to reducing the overall exposures but may impair the environmental control function of the incubator. The most effective prevention is to reduce emissions from the hands. We recommend several prevention measures:

- A 1-minute waiting time after use of disinfectant appears sufficient to avoid significant emissions within incubators and should therefore be respected. A shorter waiting time after use of disinfectant, which may be sufficient for most hand-rubbing situations, appears inappropriate when performing duties on neonates in incubators. Measurable levels of alcoholic solvents have been found for waiting times less than or equal to 30 seconds. Organizational measures, such as increasing awareness of alcohol vapor exposures to neonates when using disinfectants, should be implemented.
- In general, a disinfecting solution container limiting the amount of product used (e.g. containers with push buttons) is favored. This measure would prevent the inadvertent

use of excessive amounts of solution (requiring longer evaporation times). It is interesting to note that, in the specific case of Sterillium®, the 3 ml amount recommended by the producer is higher than the "larger than usual" amount of product considered in this study.

- Currently, the best hand disinfection solutions are still based on alcohol [3]. There are thus no good alternatives to be considered for the care of neonates in incubators. A disinfecting alcohol with a very short evaporation time (e.g. ethanol) could decrease potential exposure of neonates to solvents.
- The use of electrical hand-dryers to reduce the evaporation time after hand rubbing should be investigated. Fast hand-drying may be of particular interest when situations requiring immediate attention occur regularly (e.g. intensive care units).

This paper highlights exposure situations resulting from hand disinfection practices in neonatal units. The small inner volume of the incubators facilitates temperature and humidity control, but it may also lead to concentration levels in pollutant higher than in ambient air when emission sources are present. Preventive measures should be implemented to avoid unnecessary exposures in these micro-environments, while maintaining a high-level of hygiene. Care must be taken when implementing preventive measures in order to preserve both incubator air quality requirements and hand hygiene requirement.

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