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American Industrial Hygiene Association Journal

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/aiha20>

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Published online: 04 Jun 2010.

To cite this article: Patricia Heinsohn & Don L. Jewett (1993) EXPOSURE TO BLOOD-CONTAINING AEROSOLS IN THE OPERATING ROOM: A PRELIMINARY STUDY, American Industrial Hygiene Association Journal, 54:8, 446-453, DOI:

[10.1080/15298669391354946](https://doi.org/10.1080/15298669391354946)

To link to this article: <http://dx.doi.org/10.1080/15298669391354946>

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EXPOSURE TO BLOOD-CONTAINING AEROSOLS IN THE OPERATING ROOM: A PRELIMINARY STUDY

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A personal sampling study was conducted to assess exposure to blood aerosols in the operating room. The breathing zones of primary and assistant surgeons were monitored using a personal cascade impactor configured with three stages corresponding to effective cut-off aerodynamic diameters of 14.8 μm , 3.5 μm , and 0.52 μm , respectively. Hemastix was used to assess the hemoglobin content of each particle size fraction. The arithmetic mean exposure concentration for primary surgeons ($n = 14$) was 1.4 $\mu\text{g Hb/m}^3$ (range, none detected to 7.4 $\mu\text{g Hb/m}^3$), while that for assistant surgeons ($n = 12$) was 1.8 $\mu\text{g Hb/m}^3$ (range, 0.3 to 4.8 $\mu\text{g Hb/m}^3$). Hemoglobin was detected in Stage 2 in 26 (90%) of the samples, in Stage 5 in 19 (66%) of the samples, and in Stage 8 in 11 (38%) of the samples. These data show that the mucous membrane lining of the upper respiratory tract and alveolar macrophages in the gas-exchange region are likely to be exposed to aerosolized blood in the operating room. Until further research determines the potential of infected blood aerosols to transmit disease, the authors recommend the proper use of respiratory protection equipment instead of surgical masks because the latter do not offer adequate protection.

Hepatitis B virus (HBV) and human immunodeficiency virus (HIV) are among the bloodborne pathogens that pose the most significant hazard to health care workers. Both HBV and HIV are capable of being transmitted by percutaneous or permucosal exposure

to infective blood, as in accidental needlestick and splash. HBV is further documented to have been transmitted oropharyngeally in individuals wearing surgical masks,⁽¹⁾ suggesting an aerosol route of exposure. HIV has not been demonstrated to be transmitted by aerosol, but there is a theoretical possibility that infection can occur by this means.

Particles measuring less than 5 μm in aerodynamic diameter are capable of depositing in the gas-exchange region of the respiratory tract, where alveolar macrophages are found. Previously, HIV has shown the ability to infect alveolar macrophages in vitro by binding with their CD4 receptor sites.⁽²⁾ There is no reason to believe that the mucous lining of the respiratory tract is less vulnerable to infection than the mucous membranes involved in transmission by known routes. Indeed, the Centers for Disease Control (CDC) have stated that the mucous membranes of the eyes, nose, and mouth should be considered potential portals of entry.⁽³⁾ Conceivably, then, airborne transmission of HIV is possible, provided that personnel are exposed to an inhalable blood aerosol containing this pathogen.

In previous work, we demonstrated that common surgical power tools are capable of generating inhalable blood-containing aerosols.⁽⁴⁾ We defined the size distribution of these aerosols, quantified the amount of hemoglobin (Hb) present, and similarly characterized a series of blood aerosols that had previously shown the ability to infect human T-cell tissue cultures with HIV.⁽⁵⁾ Prompted by the possibility that inhalable blood aerosols may exist in the breathing zones of operating room personnel and that such aerosols may be infective, a personal sampling study was conducted to assess exposure in the operating room.

METHODS

Sampling Strategy

Common procedures in orthopaedics, urology, cardiothoracic surgery, vascular surgery, and obstetrics were selected for study. These operations either involve the use of surgical power tools similar to those previously evaluated^(3,4)

Reported in part in *Essentials of Modern Hospital Safety, Second Edition*, edited by W. Charney and J. Schirmer. Lewis Publishers, Inc., Chelsea, MI, 1992. Used with permission.

This work was supported in part through a National Institute for Occupational Safety and Health and ERC, Inc. cooperative agreement.

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FIGURE 1. The impactor was oriented perpendicularly and secured to the chest during sampling.

or are likely to generate blood splatter from which satellite aerosol might emanate.

“Worst case” exposure assessment was performed by monitoring the breathing zones of operating room personnel who experience the greatest risk of exposure. Because of their close proximity to the operative site and activities during surgery, these individuals are usually the primary and assistant surgeons. Air sampling commenced at the time of gowning just before surgery and concluded at the time of gown removal after surgery. Fifteen surgical and three non-surgical procedures were monitored.

Air Sampling Procedure

Air was sampled with a personal cascade impactor (Model 298; Andersen Samplers, Inc., Atlanta, GA), which is designed to determine the breathing zone concentration of aerosol by particle size fraction.⁽⁶⁾ The sampling results of the first operation indicated that exclusion of several impactor stages would increase the sensitivity of our sampling/analysis method, so the impactor was configured with Stages 2, 5, and 8 for all subsequent monitoring. These three stages correspond to effective cut-off aerodynamic diameters (ECADs) of 14.8 μm , 3.5 μm , and 0.52 μm , respectively, at the design flow rate of 2 L/min, assuming a particle density of 1.0 g/cc. A 5- μm poststage filter made of polyvinyl chloride was used. The cowl and visor were attached to the impactor during sampling to eliminate the possibility of contamination by blood splatter.

The assembled impactor, including the cowl and visor, was placed in the sampling train for calibration of the

sampling pump (Mine Safety Appliance, Pittsburgh, PA), which was performed in a sealed jar. After calibration, the impactor assembly and a narrow strip of cloth used to suspend it from the neck were sterilized with ethylene oxide. Thereafter, the unit and cloth “necklace” were handled using standard sterile technique.

Subjects wore the sampling pump beneath their sterile paper gown. The sterile cloth “necklace” was tied around the neck, and the impactor and pump were connected with sterile tubing. The impactor was oriented perpendicularly and secured to the chest using sterile tape, with care taken not to occlude the sampling inlet (Figure 1).

Sampling was performed at 2 L/min to enable direct application of published impactor sampling effectiveness data.⁽⁶⁾ Ungreased mylar collection media was used as recommended for the collection of liquid aerosols. At the conclusion of sampling, post-calibration of the sampling pump was performed with the impactor in line.

Analysis of Hemoglobin

Hemastix strips (Miles Inc., Elkhart, IN), which are used routinely in clinical laboratory medicine to determine the presence of Hb in urine, were used to detect blood in the collected samples. According to the manufacturer, the lowest concentration of Hb in urine that can be reliably detected by this product is 0.15 ng/ μL . Because it could not be assumed that the limit of detection in a matrix of urine is identical to that in the study’s assay matrix of distilled water, successive dilutions of bovine blood in distilled water were performed to determine the following lower limits of detection for three color end-points: *trace*, 0.13 ng Hb/ μL ; *1+*, 0.17 ng Hb/ μL ; *2+*, 0.48 ng Hb/ μL . (To evaluate the reliability with which end-points were interpreted, six known concentrations of Hb were measured eight times each using six different lot numbers of Hemastix. Only 2% of the results [1 of 48 replications] were beyond the expected variation, indicating a high degree of reliability.) The specificity of Hemastix is discussed in Appendix I.

After each run, 400 μL of 0.01% Tween in distilled water were added to each of three disposable beakers (one for each piece of mylar collection medium) and verified to be free of hemoglobin by testing with Hemastix. Using tweezers, the pieces of mylar were removed from the impactor stages,

placed in the beakers, and mixed for 1 minute to dissolve the collected sample. The solutions were tested with Hemastix and the results recorded. When a result was equal to or greater than 2+, the solution was diluted and retested. Any result that fell between two values was read as the lower concentration.

An experiment was done to determine whether sonication or additional mixing time would enhance aerosol dissolution from the mylar, but these measures did not increase recovery. Either the above-described method of dissolution recovers much of the Hb fraction of the aerosol, or the peroxidase activity of the deposited Hb degrades with time, or both. Because the amounts of Hb detected establish minimum levels of exposure, no further attempt was made to enhance recovery. For the same reason, there was also no attempt to measure any Hb that might have deposited on the poststage filter.

Calculation of the subject's breathing zone concentration of Hb was based on (1) the total amount of Hb deposited in the impactor, (2) the sampling efficiency of the impactor,⁽⁶⁾ and (3) internal loss,⁽⁶⁾ as expressed by:

$$\sum [\text{Hb}_{\text{stage}}] \times 400 \mu\text{L}/\text{stage effectiveness correction}$$

where the effectiveness correction factors are 0.61 for Stage 2, 0.95 for Stage 5, and 0.99 for Stage 8^{(7)*} (see Appendix II, Calculations 1 and 2).

RESULTS

The results, including the calculated breathing zone concentration of Hb to which each subject was exposed, are given in Table I. The arithmetic mean exposure concentration for primary surgeons ($n = 14$) was $1.4 \mu\text{g Hb}/\text{m}^3$ (range, none detected to $7.4 \mu\text{g Hb}/\text{m}^3$), while that for assistant surgeons ($n = 12$) was $1.8 \mu\text{g Hb}/\text{m}^3$ (range, 0.3 to $4.8 \mu\text{g Hb}/\text{m}^3$). Exposure among obstetricians ($n = 3$) ranged from none detected to $0.9 \mu\text{g Hb}/\text{m}^3$. Hb was detected in Stage 2 (ECAD = $14.8 \mu\text{m}$) in 26 (90%) of the samples, in Stage 5 (ECAD = $3.5 \mu\text{m}$) in 19 (66%) of the samples, and in Stage 8 (ECAD = $0.52 \mu\text{m}$) in 11 (38%) of the samples.

Because these data describe a potentially hazardous breathing environment, the results were used to estimate the amount of Hb each subject might have inhaled and deposited

in their respiratory tract (see Appendix II, Calculation 3). These estimations are also presented in Table I.

DISCUSSION

The present study was prompted by the possibility that exposure to a bloodborne pathogen can occur if an infected blood aerosol of an inhalable size distribution is present in the breathing zone. Even though it is not yet known whether bloodborne pathogens transmit disease by the airborne route of exposure, we decided to determine if such an exposure actually does occur in the hospital operating room. The most logical way to determine exposure to a bloodborne pathogen is to directly sample for, identify, and quantify that pathogen. However, this approach challenges the underlying premise of the CDC's universal precautions and requires knowing the patient's septicemic status. Use of a surrogate analyte to assess exposure, as was done in the present study, circumvents these issues and obviates the problems of non-specific sampling methods, inadequate collection efficiency for the number of organisms present, and the relative insensitivity of culturing. For evaluating HIV exposure, though, the use of Hb as a surrogate analyte does have its own unique complexities (see Appendix III).

An epidemiologic approach to establishing an association between exposure to aerosolized bloodborne pathogen and disease is not feasible, because the appropriate study must control for all known risk factors, identify a group of control subjects (surgeons who are not exposed to blood aerosols), and establish the septicemic status of patients. Most likely, the definitive research effort will be an infectivity study in an animal model. The consequences of incorrectly presuming that pathogens such as HIV cannot be transmitted by blood aerosol warrant a conservative position on the issue of exposure until there is conclusive evidence to support or refute this mechanism of disease transmission. Unfortunately, such evidence may not be available for quite some time.

Data collected in this study indicate that primary and assistant surgeons are exposed to inhalable blood-containing aerosols in the operating room. As discussed earlier, the mucous membranes of the upper respiratory tract may be vulnerable to bloodborne pathogens, and the present data have shown that these mucous membranes are likely to be exposed to blood aerosol in the operating room. At Stage 5, which includes a particle size capable of depositing in the tracheobronchial and gas-exchange regions (ECAD = $3.5 \mu\text{m}$), 66% of the samples were positive for Hb, and 38% of the samples were positive for Hb at Stage 8 (ECAD = $0.52 \mu\text{m}$), which also includes a particle size capable of depositing in the gas-exchange region, where CD4 receptor sites can be found on alveolar macrophages. If only regional respiratory tract deposition is hazardous, comparing total exposure values is not a valid way of assessing relative risk in all cases. For example, in Procedure No. 3, the risk posed by the primary surgeon's exposure is not necessarily three times that of the first assistant if only alveolar exposure is

* The effectiveness of the personal cascade impactor is higher than that of any other commercial cascade impactor available. However, as is the case with all particulate samplers, its effectiveness for particles larger than $10 \mu\text{m}$ is lower than that for particles of smaller size. Each of the correction factors is an average value for the particle sizes collected on that stage. The correction factor for Stage 2 was assigned by the impactor's designers without knowing the largest particle size that can be collected by that stage, and the largest particle size challenge in the validation study was $23 \mu\text{m}$. Thus, the correction factor of 0.61 is a minimum average value. Because it is not feasible to determine experimentally a more accurate correction factor, this minimum average value provided by the designers was used.

TABLE I. Exposure to Inhalable Blood-Containing Aerosols During Surgery

No.	Type of procedure	Subject monitored	Sampling time (min)	Impactor stage	Hemastix reading (dilution)	Hb concentration		Estimated amount of Hb inhaled and deposited, per size fraction (ng) ^A
						per size fraction (ng)	overall ($\mu\text{g}/\text{m}^3$)	
1	arthroplasty	primary surgeon	171	1	1+	131	0.8	84
				2	trace	85		60
				3	neg	0		0
				4	trace	58		49
				5-8	neg	0		0
		first assistant surgeon	132	1	2+	369	2.1	236
				2	1+	111		79
				3	trace	67		52
				4	neg	0		0
				5-8	neg	0		0
2	arthroplasty	primary surgeon	159	2	trace	85	0.5	60
				5	neg	0		0
				8	1+	69		9
		first assistant surgeon	136	2	3+, 2+ (1:3.5)	1102	4.5	782
				5	1+	72		63
				8	trace	53		7
3	arthroplasty	primary surgeon	137	2	3+, 2+ (1:5)	1574	7.4	1118
				5	3+, 1+ (1:5)	358		313
				8	trace	53		7
		first assistant surgeon	160	2	3+, 1+ (1:5)	557	2.6	395
				5	2+	202		176
				8	trace	53		7
4	arthroplasty	primary surgeon	198	2	3+, 1+ (1:5)	557	1.6	395
				5	1+	72		63
				8	trace	53		7
		first assistant surgeon	168	2	1+	111	0.7	78
				5	1+	72		63
				8	trace	53		7
5	aneurysmal resection	primary surgeon	390	2	3+, 1+ (1:5)	557	0.9	395
				5	1+	72		63
				8	neg	0		0
		first assistant surgeon	293	2	3+, 1+ (1:5)	557	1.1	395
				5	1+	72		63
				8	trace	0		0
6	prostatectomy	primary surgeon	167	2	1+	111	0.5	79
				5	trace	55		48
				8	neg	0		0
		first assistant surgeon	163	2	trace	85	0.3	60
				5	neg	0		0
				8	neg	0		0
7	prostatectomy	primary surgeon	161	2	trace	85	0.3	60
				5	neg	0		0
				8	neg	0		0
		first assistant surgeon	169	2	1+	111	0.3	79
				5	neg	0		0
				8	neg	0		0

TABLE I. Continued

No.	Type of procedure	Subject monitored	Sampling time (min)	Impactor stage	Hemastix reading (dilution)	Hb concentration		Estimated amount of Hb inhaled and deposited, per size fraction (ng) ^A
						per size fraction (ng)	overall ($\mu\text{g}/\text{m}^3$)	
8	arthroplasty	primary surgeon	180	2	1+	111	0.5	79
				5	trace	55		48
				8	neg	0		0
		first assistant surgeon	167	2	1+	111	0.5	79
				5	trace	55		48
				8	neg	0		0
9	ventricular malformation repair	primary surgeon	180	2	1+	111	0.5	79
				5	trace	55		48
				8	neg	0		0
		first assistant surgeon	202	2	2+, trace (1:5)	426	1.2	302
				5	trace	55		48
				8	neg	0		0
10	arthroplasty	primary surgeon	138	2	2+, 1+ (1:5)	557	2.6	395
				5	1+	72		63
				8	trace	53		7
		first assistant surgeon	105	2	1+	111	0.8	79
				5	trace	55		48
				8	neg	0		0
11	nephrectomy	primary surgeon	188	2	trace	85	0.4	60
				5	trace	55		48
				8	neg	0		0
		first assistant surgeon	155	2	3+, 1+ (1:10)	1115	4.8	792
				5	2+, 1+ (1:5)	357		312
				8	trace	53		7
second assistant surgeon	176	2	2+, 1+ (1:5)	557	2.5	395		
		5	1+	72		63		
		8	trace	53		7		
13	childbirth, caesarian section	primary surgeon	61	2	trace	85	1.7	60
				5	trace	55		48
				8	trace	53		7
14	childbirth, vaginal ^B	obstetrician	24	2	neg	0	undetectable	0
				5	neg	0		0
				8	neg	0		0
15	childbirth, caesarian section	primary surgeon	37	2	neg	0	undetectable	0
				5	neg	0		0
				8	neg	0		0
16	childbirth, vaginal ^B	obstetrician	53	2	neg	0	undetectable	0
				5	neg	0		0
				8	neg	0		0
17	childbirth, caesarian section	primary surgeon	65	2	1+	111	1.3	79
				5	trace	55		48
				8	neg	0		0
18	childbirth, vaginal ^B	obstetrician	44	2	trace	85	0.9	60
				5	neg	0		0
				8	neg	0		0

^A Assuming no personal protection.^B Nonsurgical procedure performed in the labor & delivery room.

hazardous. The development of effective controls such as National Institute for Occupational Safety and Health (NIOSH)/Mining Safety and Health Administration (MSHA)-approved respiratory protection equipment must rely on size-selective measurements of Hb concentration.

The true risk of exposure may be greater than our results indicate. These calculations assume 100% recovery of the aerosol sample, but the solvent did not remove all of the aerosol deposited on the surface of the mylar collection medium. In separate laboratory experiments, mylar media was spiked with known quantities of Hb and analyzed with Hemastix after drying. Recovery efficiency varied inversely with concentration; lower spike concentrations were recovered with greater efficiency than were higher ones. In light of this finding, it seemed inappropriate to assign one or more recovery efficiencies without further experimentation.

Another factor in underestimation, which is inherent in the use of indicator strips such as Hemastix, was the recording of equivocal readings on the color chart as the lower of two concentrations. It is important to recognize that, for two reasons, it is not possible to accurately interpolate Hb concentrations between color end-points. Every color block on the Hemastix indicator strip represents a range of Hb concentrations, and the relationship between the end points and their corresponding Hb concentrations is not linear. The level of accuracy obtained with this semiquantitative means of assessment was part of the study design.

If particles smaller than 0.52 μm were present in the breathing zone and were collected, they may have been captured on the 5.0- μm poststage filter. The possibility that this small fraction might have been present in the samples—especially the 11 that were positive at Stage 8—cannot be dismissed. Previous area sampling with a low-pressure cascade impactor has demonstrated that samples containing the ECAD of Stage 8 (0.52 μm) also contain smaller-sized particles.^(4,5)

Even though the results indicate that the collected aerosols contained particle sizes small enough to be inhaled and deposited anywhere in the respiratory tract, there was a general trend of decreasing Hb content with decreasing particle size. Bearing in mind that 62% of the samples contained no Hb in Stage 8, the contribution of the filter would have been negligible if the particle size distribution had been unimodal. If, on the other hand, the particle size distribution had been bimodal with a peak below 0.82 μm , the contribution of the filter would be unknown.

The results were not falsely elevated as a result of sample contamination from blood splatter. Splatter is approximately 50 μm in size,⁽⁸⁾ ballistic in nature, and, unlike inhalable aerosols that are capable of being collected by the impactor, does not travel with the gas (air) streamline. Rather, it is unidirectional from its point of generation. As Figure 1 illustrates, splatter could have entered the sampler only in the unlikely event that (1) the trajectory of the splatter had been directly aligned with the narrow space between the cowl and visor, which would have required the wearer to be turned 90 degrees from the source, and (2) the splatter had impacted with some part of the sampler. If such contamina-

tion had occurred, it would have been suspected by the author at the time of monitoring, evident when the sampler was disassembled in the laboratory for analysis, and reflected by a gross elevation in the results of the Hb analysis.

A complicating factor in exposure assessment of primary and assistant surgeons is that these individuals may exchange tasks unpredictably, especially in teaching hospitals, and thus do not represent homogeneous exposure groups. Other issues to be addressed are the risk of exposure to other operating room personnel, possible differences in exposure risk among personnel in specialties not considered here, and whether exposure is due solely to the use of surgical power tools, or if it is partly due to satellite aerosol from splatter. The positive test for Hb in one of the three nonsurgical procedures (vaginal childbirth) suggests that aerosol exposure might be possible in the presence of splatter alone.

Further work may determine whether modifications in the design and/or use of surgical equipment can minimize exposure to blood-containing aerosols. Until such work has been done, we recommend the use of NIOSH/MSHA-approved respiratory protection equipment instead of surgical masks, because the latter do not seal against the face and generally do not effectively filter particles less than 5 μm in size.⁽⁹⁾ Respirators must be selected and fit-tested by a qualified person to ensure a tight seal, and wearers must be trained in the correct use of this equipment.

ACKNOWLEDGEMENTS

The authors thank Alan Rosen, M.D., and Siobhan Murphy for their assistance in sample collection, and Judith Simon for preparing the manuscript.

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APPENDIX I

The Specificity of Hemastix

Hemastix is based on the peroxidase-like activity of Hb that catalyzes the oxidation-reduction reaction between cumene hydroperoxide and 3,3',5,5'-tetramethylbenzidine. This reaction forms a complex whose color is directly proportional to the concentration of Hb. False-positive reactions can be caused by myoglobin and oxidizing contaminants such as hypochlorite and microbial peroxidase. For this reason, ethanol rather than bleach was used for surface disinfection of the impactors after each run.

Although hypochlorite and microbial peroxidase are not likely to be present in blood, a normal level of myoglobin can be as high as 6.6×10^{-11} g/ μL serum.⁽¹⁰⁾ In a spectrophotometric assay version of the Hemastix method (which was not used to analyze the breathing zone samples because it has not yet been optimized or validated), the specific activity of myoglobin was determined to be 21 times *less* than that of Hb (0.051 versus 1.073 absorbance units/ μg). Assuming a normal blood Hb of 15 g/dL, Hb is 4.1×10^6 times more plentiful than myoglobin in normal blood. Considering this substantial concentration gradient and the appreciable difference in specific activity, myoglobin is unlikely to be an interfering substance in this study. Even if surgical injury of tissue could cause a different Hb-to-myoglobin ratio than is found in normal blood, an earlier experiment in which an aerosol of tendon and bone created in the absence of blood

proved Hemastix-negative⁽⁴⁾ is even stronger evidence that myoglobin is unlikely to be an interfering substance.

Urine tests with Hemastix may be falsely negative in the presence of ascorbic acid (Vitamin C) concentrations of 5 mg/dL or greater. The concentration of ascorbic acid in normal plasma is no more than 2 mg/dL,⁽¹⁰⁾ so this substance is unlikely to inhibit the Hemastix reaction.

APPENDIX II

Sample Calculations

Sample Description:

Type of procedure:	arthroplasty
Subject monitored:	primary surgeon
Sampling time:	137 minutes
Air volume sampled:	270 L

Experimental Parameters:

Hemastix end points:	trace, 0.13 ng/ μL ; 1+, 0.17 ng/ μL ; 2+, 0.48 ng/ μL
Volume of distilled water:	400 μL
ACGIH algorithm of inspirable fraction:	SI(d) = $0.5(1 + e^{-0.06d})$ ⁽¹¹⁾
ACGIH reference man parameters:	$V_t = 1450$ mL; $f = 15$ bpm

Calculation 1—Mass of Hb in the breathing zone, per size fraction

$$\text{For Stage 2: } 2.4 \text{ ng}/\mu\text{L} \times 400 \mu\text{L} = 960 \text{ ng} \\ 960 \text{ ng}/0.61 = 1574 \text{ ng}$$

Calculation 2—Concentration of Hb in the breathing zone, over all stages

$$\frac{\sum \text{Mass of Hb in the Breathing Zone per size fraction}}{\text{volume of air collected}} = \frac{1574 \text{ ng} + 358 \text{ ng} + 53 \text{ ng}}{270 \text{ L}} \\ \times \frac{1 \times 10^3 \text{ L}}{1 \text{ m}^3} \times \frac{1 \mu\text{g}}{1 \times 10^3 \text{ ng}} \\ = 7.4 \mu\text{g}/\text{m}^3$$

APPENDIX II TABLE I

Impactor Stage (ECAD)	Hemastix Reading (dil.)	Effectiveness			Mass of Hb in the Breathing Zone		Total Deposition in the Respiratory Tract for Nasal Breathing [†]		Mass of Hb Inhaled and Deposited
		[Hb]/ μL	[Hb]/400 μL	Correction Factor	Inspirable Fraction	Tract for Nasal Breathing [†]	Mass of Hb Inhaled and Deposited		
2 (14.8 μm)	3+, 2+ (1:5)	$0.48 \times 5 = 2.4$ ng	960 ng	0.61	1574 ng	0.71	1.0	1118 ng	
5 (3.5 μm)	3+, 1+ (1:5)	$0.17 \times 5 = 0.85$ ng	340 ng	0.95	358 ng	0.91	0.96	313 ng	
8 (0.52 μm)	trace	0.13 ng	52 ng	0.99	53 ng	0.98	0.14	7 ng	

[†]Expressed as a fraction;⁽¹²⁾ assuming a mean flow rate of 750 mL³/sec, a breathing cycle of 4 sec, and a tidal volume of 1500 mL.

Calculation 3—Estimated amount of Hb inhaled and deposited, per size fraction

The deposited mass of Hb ($\text{Mass}_{\text{dep Hb}}$) is the predicted mass of Hb inhaled and deposited in the respiratory tract. It is the product of the mass of Hb in the breathing zone per size fraction, the head airways collection efficiency, and the lung deposition efficiency for particles that penetrate the head airways.

$$\begin{aligned}\text{Mass}_{\text{dep Hb}} (\text{for Stage 2}) &= (1574 \text{ ng}) \times (0.71) \times (1.0) \\ &= 1118 \text{ ng} \\ &= 1.12 \text{ }\mu\text{g}\end{aligned}$$

APPENDIX III

***Exposure to HIV in Blood Aerosol:
Estimation of Respiratory Tract Deposition***

Assuming that exposure to an HIV-infected blood aerosol is hazardous, it is possible to calculate the TCID_{50} (median tissue culture infective doses) corresponding to the

surrogate Hb concentrations reported in Table I, provided that one also knows the equivalent number of HIV TCID per unit measure of Hb.

For two reasons, defining the TCID Hb equivalent with accuracy is a complex matter. First, the amount of HIV in blood varies greatly with disease stage; the titer has a potential range that spans four orders of magnitude, depending on the degree of viremia. Second, this equivalency value must account not only for that fraction of bloodborne virus associated with the blood cells but also that fraction not associated with cells, or the cell-free fraction. The cell-free fraction can range from 5 to 100 TCID/mL plasma in HIV-seropositive individuals and from 5 to 50 000 TCID/mL plasma in AIDS patients.⁽¹³⁾ Assuming a normal blood Hb of 15g/dL, the low-end titer of 5 TCID/mL plasma corresponds to 1.83×10^{-5} TCID/ μg Hb.

With current technology, it is not yet possible to determine the TCID Hb equivalent for the cell-associated fraction. Hence, any calculation of respiratory tract deposition of HIV would be based solely on the cell-free fraction and therefore underestimate actual exposure.