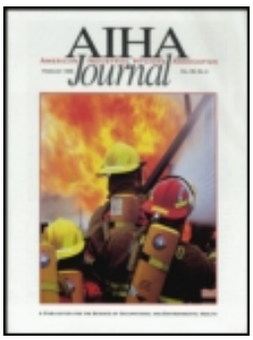

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An Experimental Design Approach to Retrospective Exposure Assessment

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There are several methods currently in use for retrospective estimation of quantitative exposure levels in occupational and environmental epidemiologic studies. The most popular is a job-exposure matrix approach using a combination of existing data and professional judgment. Another method is the use of statistical models based on available exposure data. The authors present an alternative approach using an experimental design in which several factors thought to affect exposure levels are identified and set at specific levels in a cross-classified design. This approach was used to estimate historical exposures to formaldehyde in a mortality study of embalmers. Exposures were estimated as a function of solution concentration, air exchange rate, and autopsied versus intact body. There were 12 combinations involving these 3 factors and a total of 25 embalming procedures (approximately 2 replicates of each combination) performed at a college of mortuary science. In addition to these design factors several covariates such as temperature, humidity, and the occurrence of spills were considered in an analysis of covariance statistical model. The results of the model prediction were validated against published measurements, and field samples were taken in several funeral homes. The overall accuracy of the model predictions was comparable to the variation found in replicate measurements of identical embalming procedures.

Keywords: embalmers, epidemiologic studies, formaldehyde exposure, quantitative exposure levels

To investigate the risk of leukemia and brain cancer among embalmers, a case-control study of these diseases was initiated by the National Cancer Institute and the National Institute for Occupational Safety and Health. In an effort to make this study as comprehensive and powerful as possible, quantitative measures of exposures to chemicals used in embalmings were desired for the entire period of the study. The agents known to be generated during an embalming include formaldehyde, methanol, phenol, particulates, and biological agents. Primary interest in this study centered around the levels of formaldehyde exposure, although all significant chemical and biological exposures were considered.[1]

Several earlier studies of embalmers, funeral directors, and pathologists have suggested a link between working in these professions and leukemia and/or brain cancer.[2–8] None of these studies provided a detailed assessment of formaldehyde exposure levels. Indeed, very little historical data exist to properly characterize formaldehyde levels during the period when this subject group was exposed, which extends as far back as the early 1900s. One approach that has been used successfully in similar situations is the development of a mathematical or statistical model to predict historical exposure levels.[9–13] In the case of mathematical models, algorithms for estimation of exposure levels are developed based primarily on physical principles.[9] Statistical models, on the other hand, are generally based on fitting models to whatever appropriate observational data are available.[10–13] Since very little data existed for use in a statistical model, it was decided that an experimental design would be employed with the cooperation of the Cincinnati College of Mortuary Science (CCMS). The purpose of the experimental design study was to estimate levels of formaldehyde (and other chemical and biological agents) across combinations of environmental factors thought to have an impact on exposure levels. These factors could then be

related to measured exposure levels through regression modeling techniques such as analysis of covariance. The primary objective was to identify exposure factors that could be used to predict levels of formaldehyde exposure. These exposure factors could then be used to predict historical formaldehyde levels for the epidemiologic study, if information could be obtained on these exposure factors by questionnaires used in the case-control study.

Since such an experimental design approach in retrospective exposure assessment has seldom been used, it was also important to evaluate the accuracy of the predicted exposure levels. For this reason the experimental design model was tested against measurements taken in funeral homes where values of the exposure factors were also recorded and against formaldehyde levels reported in the recent literature when several of the exposure factors were reported. The sections that follow provide a description of the protocol for the experimental design, the model development techniques, and the evaluation of the final model predictions.

METHODS

Study Design

To identify factors that might influence exposure levels to chemical and biological agents, a review of the literature was conducted, and walk-through surveys were carried out at 14 funeral homes in the Washington, D.C., area and at CCMS. After consideration of all of these sources, three factors emerged as potential determinants of exposure levels. These were the degree of ventilation in the embalming room, the strength of the embalming solution (concentration of formaldehyde), and the type of embalming case, i.e., intact or autopsied body.

Since the degree of ventilation as measured by the air exchange rate was the factor that seemed most likely to affect the exposure levels, it was set at three levels: low, moderate, and high. The other two factors were set at two levels: high versus low solution strength, and autopsy versus intact embalming case. This design resulted in a $3 \times 2 \times 2$ factorial experiment with 12 cells corresponding to all possible combinations of the 3 factors.

The next step was to determine how many replicates of each combination should be run to provide adequate power for determining real differences among the effects of the selected factors and to provide adequate precision in estimating these effects. Power calculations indicated that four replicates per combination would provide an 80% probability to detect differences of 35% or greater for any two-way interactions at a significance level of $\alpha=0.05$. Therefore, 48 individual embalmings were needed.

The cooperation of CCMS was obtained for use of their embalming room and personnel. They further agreed to control the levels of each exposure factor. Based on the usual frequency of embalmings at CCMS, it was estimated that 48 cases could be obtained in the allotted time of 2 months. Levels for ventilation were selected after an evaluation of the ventilation system in the CCMS embalming room. Solution strengths were selected based on interviews with CCMS staff on historical changes in the formaldehyde concentration in embalming fluid.

A detailed description of the embalming room and procedures for sampling chemical and biological agents has been previously reported.[1] Briefly, the embalming room measured 3 m × 3.7 m with a 2.4-m wall height. Ventilation was provided by the HVAC system through a diffuser located on the ceiling near the center of the room. Room air was exhausted through a wall vent near floor level at the foot of the table. A flow hood was used to measure air exchange rates on three separate days over the course of the study. Air exchange rates were set by allowing the HVAC system to operate unrestricted for the highest setting (13.3 air changes per hour), partially blocking the supply vent for the intermediate setting (5.5 ac/hr), and completely blocking the supply and exhaust vents for the lowest setting (1.1 ac/hr).

The solution concentrations were set to be 1.25 and 2.5% formaldehyde, which are representative of the range of solution strengths used historically. The type of case was either autopsied or intact body. Autopsied cases were defined as having internal organs (and frequently brains) removed so that the body cavity was opened. Due to the experimental nature of this study, air-supplied personal protective equipment was provided to all personnel during each embalming procedure.

Concentrations of formaldehyde were measured in the breathing zone of the embalmer and at three area locations in the room. Breathing zone concentrations and two area samples for formaldehyde were collected on a solid sorbent and analyzed by the OSHA-52 method.[14] A third real-time sample for formaldehyde was collected using a TGM-555 Toxic Gas Monitor (CEA Instruments, Inc., Emerson, N.J.). Samples were collected throughout the complete embalming process. Three sequential breathing zone samples were collected during the embalming of intact bodies. An additional breathing zone sample was collected during the embalming of autopsied bodies. The time-weighted means of these breathing zone samples were used as the dependent variable in the statistical model. All formaldehyde monitoring results were strongly correlated.

A randomized order for the 48 embalmings was provided to the CCMS embalmer and the two industrial hygienists conducting the air sampling. Because of unforeseen delays in obtaining the designated balance in autopsied versus intact bodies, there was not enough time nor funds available to collect all 48 sets of data. Instead, two replicates per combination of exposure factors were collected. Because one combination had already been measured three times when this decision was made, the total number of embalmings was 25. The reduced sample size resulted in a decrease in power such that there was an 80% chance of detecting 35% differences among levels of the main design factors at a significance level of 0.05.

Only formaldehyde concentrations as they relate to the design parameters were included in this model. Data analyses were also conducted using concentrations of other measured agents but are not reported, since they add nothing to the understanding of the exposure assessment technique discussed in this paper and were generally consistent with the results from the formaldehyde modeling.

In addition to the three factors controlled in the experimental design, several covariates beyond control were identified as having possible effects on exposures. Table I indicates the three design factors and a list of all covariates measured in each embalming session. These covariates were then available for potential inclusion in the final prediction model.

Statistical Protocol

The type of regression model used in linking measured concentrations of formaldehyde to the design factors and other measured covariates is commonly described as analysis of covariance (ANCOVA). The purpose of an ANCOVA is to test differences among the mean levels of the design factors and estimate these means adjusted for the effects of uncontrolled covariates. The result, if the model is properly specified, is an unbiased estimate of

TABLE I. Design Factors and Covariates

Design Factors	Levels
Ventilation rate	1.1, 5.5, 13.3 ac/hr
Type of embalming case	autopsy and intact body
Solution strength	1.25% and 2.5% formaldehyde
Covariates	
Occurrence of solution spill	yes or no (12 = yes, 13 = no)
Relative humidity	27–81%
Temperature	67–79°F
Duration of procedure	51–121 min
Injection points	1–6
Volume of solution	18–144 ounces
Use of osmotic gel	yes or no
Use of dryene	yes or no
Use of lysol	yes or no
Use of never leak	yes or no
Use of integ seal	yes or no
Use of inner seal	yes or no

the effect of each design factor on formaldehyde levels. With the small sample size available for this design, the precision of these estimates (standard error) depends on the number of interaction terms (both two-way and three-way) that must be included in the final model. If interactions among the three design factors are not statistically significant, they may be eliminated. This increases the precision with which the effect of each factor can be estimated, since the means for each design factor can be averaged over the levels of the other two design factors. However, the precision of the estimates will be reduced if a number of covariates must also be included in the final model.

Since the power and level of precision were reduced by the decrease in the original design from 48 to 25 embalmings, terms for inclusion in the model with a significance level of 0.10 (instead of the traditional 0.05) were considered. The magnitude of estimated mean differences among levels of each design factor were also considered before the model was finalized. For example, if the impact of a given interaction term was judged to make a substantial difference in estimated formaldehyde concentrations, the significance level criterion was relaxed to include that term in the model.

The residuals in the model were tested against assumptions of both a normal and lognormal distribution. However, as discussed in a recent article describing a statistical modeling approach for prediction of historical ethylene oxide levels in the sterilization industry,[13] the use of a log transformation is inherently desirable, since it induces a multiplicative prediction model. This means that using a log transformation of the measured formaldehyde concentration will cause each design factor to produce a percentage increase or decrease in the estimated concentration. When no transformation is used, the effect of each design factor is to add or subtract a fixed amount of concentration units, which may result in negative estimates. Therefore, a log transformation was used primarily to produce a multiplicative model, since the test of residuals did not reject either a normal or lognormal distribution.

After the final model was selected, the validity of the model for estimating retrospective formaldehyde levels was evaluated. Since the sample size used in the model was small, this was an especially important step before the model could confidently be used in predicting exposures for the epidemiologic study. Model validity was assessed in two ways.

First, members of the study team visited three funeral homes, two in California and one in South Carolina, on five separate occasions. The questionnaire designed for the case-control study that elicits information on work practices over time was administered to the embalmer in each funeral home. The industrial hygienists also made their own assessment of the design factors. Formaldehyde measurements during an embalming were made in a manner similar to those measurements taken at CCMS. These data could then be used in a field test of the model's predictive ability.

Second, the authors identified an additional set of data reported by Wasvick and Anderson[15] that presented formaldehyde concentrations, air exchange rates, and type of embalming (autopsied versus intact) for 10 embalmings in funeral homes in the Minneapolis area.

Considering these two sources together, the resulting evaluation data set consisted of 15 measurements, each taken during a different embalming session. These data were then used to assess the overall accuracy of the prediction model. Overall accuracy consisted of two components: precision and bias. Bias was estimated by subtracting the predicted formaldehyde level from the measured value and then averaging these differences, i.e.,

$$\text{Bias} = \sum_{i=1}^{15} (O_i - P_i)/15 = \sum_{i=1}^{15} d_i/15$$

where O_i = the observed measurement during embalming i;
P_i = the predicted formaldehyde level during embalming i; and
$d_i = O_i - P_i$.

Precision is a measure of variation between the model predictions and the measured values. This is estimated by the standard deviation of the observed differences between predicted and measured values, i.e.,

$$\text{Precision} = \sqrt{\Sigma (d_i - \bar{d})^2/n - 1}$$

The overall estimate of accuracy is the mean square combination of precision and bias, [16] i.e.,

$$\text{Accuracy} = \sqrt{(\text{Bias})^2 + (\text{Precision})^2}$$

RESULTS

Table II shows the arithmetic and geometric mean formaldehyde concentration for each of the 12 combinations of ventilation rate, solution strength, and type of case. The individual embalming concentrations ranged from 0.29 to 8.72 ppm. These data were used in a full analysis of variance (ANOVA) model, initially ignoring the covariates. The full model was used, which included the three main effects, three two-way interactions, and one three-way interaction. Results are shown in Table III for the untransformed data. It was clear from this initial step that ventilation rate was the most important exposure factor, and that some of the interaction terms could be eliminated from the model. When the full model was run with a log transformation of the formaldehyde concentrations, the results were similar, though all interaction terms were even less significant. All subsequent analyses were performed using the log transformation of formaldehyde concentrations.

After removing the three-way interaction, the covariates listed in Table I were added either one at a time or in pairs due to the small sample size. It quickly became apparent that the use of osmotic gel and type of case were essentially describing the same

TABLE II. Summary of Experimental Design Data

Ventilation (ac/hr)	Type of Case	Solution Strength	Sample Size	Geometric Mean (ppm)
1.1	intact	1.25%	2	3.36
1.1	intact	2.50%	2	1.99
1.1	autopsy	1.25%	2	2.93
1.1	autopsy	2.50%	2	7.14
5.5	intact	1.25%	2	3.44
5.5	intact	2.50%	2	2.36
5.5	autopsy	1.25%	2	2.48
5.5	autopsy	2.50%	2	1.28
13.3	intact	1.25%	2	0.59
13.3	intact	2.50%	2	0.65
13.3	autopsy	1.25%	3	1.10
13.3	autopsy	2.50%	2	1.94

Main Effect Means

Ventilation Rate	*Sample Size*	*Geometric Mean (ppm)*
1.1	8	3.44
5.5	8	2.25
13.3	9	0.97
Type of Case		
Intact	12	1.65
Autopsy	13	2.16
Solution Strength		
1.25%	13	1.86
2.50%	12	1.95

variable, since osmotic gel was always used when an autopsied body was embalmed. Therefore, the osmotic gel variable was not considered in subsequent analyses.

After a number of iterations the covariate of primary importance was determined to be the occurrence of spills of embalming fluid, coded as a binary response (yes or no). This variable was included in all subsequent models. No other covariate had a significant effect on formaldehyde concentration. In addition, use of the log transformation of formaldehyde concentration made the inclusion of all interaction terms unnecessary.

TABLE III. Analysis of Variance for Full Experimental Design Dependent Variable: Untansformed Formaldehyde Concentration

Source	d.f.	Mean Square	F-Test	P-Value
Ventilation	2	17.96	8.81	0.004
Type of case (C)	1	3.34	1.68	0.218
Solution strength (S)	1	0.42	0.21	0.657
V × C	2	4.44	2.18	0.153
V × S	2	4.88	2.39	0.130
C × S	1	5.70	2.80	0.118
V × C × S	2	4.08	2.00	0.175
Error	13	2.04		
		$R^2 = 0.73$		

To investigate trends in formaldehyde exposure with quantitative changes in air exchange rate, the rate was entered in the model as a continuous variable using the values 1.1, 5.5, and 13.3 ac/hr. Use of the continuous measure of ventilation rate resulted in a highly significant trend ($p<0.001$). An additional advantage was the ability to estimate changes in formaldehyde concentrations at any quantitative level of ventilation encountered in the case-control study. The final model involves only three terms: air exchange rate, type of case (autopsy versus intact) and occurrence of a spill (see Table IV). Although this is a relatively simple model, it explains 75% of the variation in formaldehyde levels.

EVALUATION OF THE MODEL

As described in the Methods section, the authors compared the predictions of the model with the 5 field-test measurements and the 10 measurements taken by Wasvick and Anderson. Inspection of Table V shows that the second largest deviation between observed and predicted values in the field test data occurred in Observation 5. This observation was made in a funeral home where the air exchange rate could not be accurately measured because an exhaust fan was operating in the room adjacent to the embalming room, with the door between rooms opened. A rate of 3.0 ac/hr was the estimate of ventilation with no active ventilation system. Since a fan was operating in the adjacent room, the authors also made an estimate of 15.7 ac/hr as an upper bound, assuming the fan in the adjacent room was fully effective in ventilating the embalming room. Overall precision and accuracy was calculated using both the upper and lower bound for Field Test 5. As shown in Table V, when all 15 validation measurements were considered as a group, the model agreed very well with the measured concentrations. On average the model predicted formaldehyde concentrations that were 0.18 ppm above the average measured values, i.e., +0.18 ppm bias when using the upper bound for Field Test 5. On a proportional basis, this represents a 35% overestimation of the mean observed concentration.

The overall precision (variation in predicted values around the average bias) was 0.53 ppm. The values for bias and precision when using the lower bound for Field Test 5 were 0.24 and 0.53 ppm, respectively. The overall accuracy was 0.56 ppm in both cases. Therefore, the overall accuracy is of approximately the same magnitude as the average measured formaldehyde exposure level (0.52 ppm). On a multiplicative scale using the equations for bias,

TABLE IV. Final Model Used for Exposure Prediction Dependent Variable: Log Transformation of Formaldehyde Concentration

Exposure Factor	d.f.	Mean Square	F-Test	P-Value
Air exchange rate	1	5.58	27.7	<0.001
Type of case	1	1.87	9.25	0.006
Spill	1	4.86	24.1	<0.001
		$R^2 = 0.75$		

$$\text{Ln (formaldehyde)} = 2.086 - 0.094X_1 - 0.569X_2 - 0.934X_3$$

where = X_1 = air exchange rate (ac/hr)

X_2 = 1 if intact body

= 0 if autopsied

X_3 = 1 if no spill

= 0 if spill occurred

TABLE V. Comparison of Model Predictions to 15 Independent Embalming Results

Embalming		Formaldehyde (ppm)	Air Exchange Rate	Type of Case	Model Prediction (ppm)	Difference
W & V	1	0.33	8.7	I	0.79	+0.46
	2	0.30	3.7	I	1.27	+0.97
	3	0.28	7.8	I	0.86	+0.58
	4	1.10	9.8	I	0.72	−0.38
	5	0.12	21.4	I	0.24	+0.12
	6	0.30	24.6	I	0.18	−0.12
	7	0.33	10.3	I	0.68	+0.35
	8	0.34	8.3	A	1.45	+1.12
	9	0.81	8.4	A	1.44	+0.63
	10	0.50	16.5	A	0.68	+0.18
Field Test	1	0.19	25.0	I	0.17	−0.02
	2	0.42	14.7	A	0.80	+0.38
	3	0.86	15.3	I	0.43	−0.43
	4	1.01	18.6	I	0.31	−0.70
	5	0.85	15.7[A]	I	0.41	−0.44
			3.0[A]		1.35	+0.50

Average bias: +0.18 ppm
Precision: 0.53 ppm
Overall accuracy: (additive scale) $\sqrt{(.18)^2 + (0.53)^2} = 0.56$ ppm
Overall accuracy: (multiplicative scale): multiply and divide by 2.4

[A] These values represent upper and lower bounds for ventilation on Field Test 5. See text for explanation. Overall accuracy and precision are calculated using upper bound of 15.7.

precision, and overall accuracy with the log-transformed data, the resulting overall accuracy is a factor of 2.4. This implies that the model typically will estimate formaldehyde exposures within a range obtained by multiplying and dividing the true exposure by 2.4. This comparison was calculated by assuming that no spills of embalming fluid occurred during the 15 embalmings used in the validation data set. Since there was no information on the occurrence of spills in the published data, the authors also made comparisons assuming spills always occurred. The resulting bias was +1.33 ppm, and precision was 1.18 ppm, resulting in an overall accuracy of 1.78 ppm. Clearly, the model performed better when assuming that no spills occurred.

DISCUSSION

When little or no measurement data exist for estimating historical exposures to be used in a retrospective occupational epidemiologic study, there are only a few options available to the researcher.[17] The research team, particularly the industrial hygienist(s), can make crude estimates of exposure based on expert judgment and knowledge of exposure levels in similar workplace settings where data are available. The research team could also enlist the help of a panel of outside experts familiar with exposure conditions in the industry being studied. Either of these options, however, results in subjective estimates that are necessarily based on many assumptions and generalizations of complex exposure conditions. A more objective estimation procedure has more appeal but requires well-documented historical exposure measurements taken under a variety of conditions that may have been experienced by the study group. In the proposed study of embalmers exposed to formaldehyde, no such retrospective exposure database could be identified. When confronted with this situation, an experimental design approach attempting to identify and recreate historical exposure factors may represent an appealing alternative to subjective estimation or crude categorical exposure characterization.

After a prediction model has been developed from the experimental design data, the most important issue is its reliability in retrospective exposure assessment.[16] The authors attempted to evaluate the model by comparing it with both data reported in the recent literature and field test data gathered specifically for this purpose. Although an overall accuracy of 0.56 ppm appears to be very good, the question of "how good is good enough" still remains. A paired t-test comparing each of the 15 measured formaldehyde levels in the comparison data showed no significant difference between the measured values and the model predictions ($t=1.29$, $p=0.216$). Although this test seems to indicate reasonably good predictions, another way of answering the adequacy of the model is to compare the overall accuracy with the range of exposure levels predicted by the model. This range is from approximately 0.2 to 2.7 ppm time-weighted average formaldehyde during an embalming procedure. Therefore, the overall accuracy of 0.56 ppm is near the lower end of exposures predicted by the model.

Although it is useful to describe the accuracy of the model in terms of the range of predicted values, this still does not answer the question of whether this is sufficient accuracy for use of these predictions in the case-control study. Perhaps a better way to assess the overall accuracy of the model is to compare it to the variation expected in replicate formaldehyde measurements under the same embalming conditions. The replicate error in the 25 experimental embalmings was 1.04 ppm, i.e., standard deviation of residuals in the full experimental design model (with all interaction terms) including the SPILL covariate. On the log scale this resulted in a geometric standard deviation (GSD) of 1.59. This GSD can be used to calculate a 95% confidence interval for predicted concentrations equal to 0.4–2.5 times the predicted value. The multiplicative measure of accuracy estimated from the validation data was a factor of 2.4. The estimated accuracy of the model, therefore, is comparable to the typical variation that could be expected in measuring identical embalming procedures.

Another point to consider in using this model for assigning exposures in the case-control study is that the estimated concentrations represent geometric means, since analysis was done on the log scale. When such estimates of exposure are used in an epidemiologic study, where they will be summed to arrive at cumulative exposure, the arithmetic mean (AM) is the correct measure.[18] Estimates for AMs can be obtained by using the estimated geometric mean (GM) and geometric standard deviation (GSD) in the following equation:

$$AM = \exp(\ln(GM) + 0.5(\ln(GSD))^2)$$

The experimental design approach is often limited by difficulty in controlling all factors that may influence exposure. In this study, for example, the geometry of the embalming room was held constant, since only one location could be used within the budget constraints of the study. It is important to attempt to identify factors at the study initiation that are known or suspected to cause the greatest change in exposure levels. Room geometry was not considered to be a primary determinant of exposure, since the initial walk-through surveys did not reveal a wide variation in room size.

An additional problem that is not addressed is how well the investigators in the case-control study can determine the number or proportion of autopsy embalmings, the ventilation rates experienced historically by embalmers in the study group, and whether or not spills typically occurred. A questionnaire has been designed to elicit answers to these questions, but problems in recall and lack of knowledge about ventilation practices will probably contribute to uncertainty in the exposure estimates, especially since the earliest embalmings in the study occurred in the early 1900s. However, problems of this nature exist with any method used to estimate historical exposures. It seems unlikely that problems with recollection of past conditions would result in bias of exposure estimates.

CONCLUSIONS

In summary, the results of an experimental design approach to retrospective exposure assessment indicated sufficient accuracy to make the use of this model acceptable for the case-control epidemiologic study. Although additional research is needed in model evaluation techniques and assessment of the accuracy of exposure factors determined from questionnaires, the use of the experimental design approach should prove to be a valuable addition to the methods currently employed in retrospective exposure assessment. This approach may also be useful to industries attempting to predict reduction in exposure concentrations after engineering controls or similar exposure reduction measures have been introduced.

REFERENCES

1. **Stewart, P.A., R.F. Herrick, C.E. Feigley, et al.:** Study design for assessing exposures of embalmers for a case-control study: Part I. Monitoring results. *Appl. Occup. Environ. Hyg. 7*:532–540 (1992).
2. **Walrath, J. and J.F. Fraumeni, Jr.:** Mortality patterns among embalmers. *Int. J. Cancer 31*:407–411 (1983).
3. **Walrath, J. and J.F. Fraumeni, Jr.:** Cancer and other causes of death among embalmers. *Cancer Res. 44*:4638–4641 (1984).
4. **Levine, R.J., D.A. Andjelkovich, and L.K. Shaw:** The mortality of Ontario undertakers and a review of formaldehyde-related mortality studies. *J. Med. 26(10)*:740–746 (1984).
5. **Harrington, J.M. and D. Oaks:** Mortality study of British pathologists. *Br. J. Ind. Med. 41*:188–191 (1984).
6. **Stroup, N.E., A. Blair, and G.E. Erickson:** Brain cancer and other causes of death in anatomists. *J. Natl. Cancer Inst. 77*:1217–1224 (1986).
7. **Linos, A., A. Blair, K.P. Cantor, et al.:** Leukemia and non-Hodgkin's lymphoma among embalmers and funeral directors. *J. Natl. Cancer Inst. 82*:66 (1990).
8. **Hayes, R.B., A. Blair, P.A. Stewart, R.F. Herrick, et al.:** Mortality of U.S. embalmers and funeral directors. *Am. Ind. Hyg. Assoc. J. 18*:641–652 (1990).
9. **Yu, R.C., W.Y. Tan, R.M. Mathew, D.A. Andjelkovich, et al.:** A deterministic mathematical model for quantitative estimation of historical exposure. *Am. Ind. Hyg. Assoc. J. 51*:194–201 (1990).
10. **Eisen, E.A., T.J. Smith, D.H. Wegman, et al.:** Estimation of long-term dust exposure in Vermont granite sheds. *Am. Ind. Hyg. Assoc. J. 45*:89–94 (1984).
11. **Dement, J.M., R.L. Harris, M.J. Symons, and C.M. Shy:** Exposures and mortality among chrysotile asbestos workers: Part I. Exposure estimates. *Am. J. Ind. Med. 4*:339–419 (1983).
12. **Woskie, S.R., T.J. Smith, S.K. Hammond, et al.:** Estimation of diesel exhaust exposures of rail workers: I. Current exposures. *Am. J. Ind. Med. 13*:381–394 (1988).
13. **Hornung, R.W., A.L. Greife, L.T. Stayner, et al.:** A statistical model for prediction of retrospective exposure to ethylene oxide in an occupational mortality study. *Am. J. Ind. Med. 25*:825–836 (1994).
14. **Organic Methods Evaluation Branch:** "Organic Methods Evaluation Branch Method No. 52." Salt Lake City, UT: U.S. Dept. of Labor, Occupational Safety and Health Administration, OSHA Analytical Laboratory, 1985.
15. **Wasvick, J.L. and D.E. Anderson:** "Evaluation of Mortician Exposure to Formaldehyde and Infectious Agents with Recommended Controls Relative to New OSHA Standards." Paper presented at the American Industrial Hygiene Conference, St. Louis, MO, 1989.
16. **Hornung, R.W.:** Evaluation of exposure assessment strategies. *Appl. Occup. Environ. Hyg. 6*:516–520 (1991).
17. **Stewart, P.A. and R.F. Herrick:** Issues in performing retrospective exposure assessment. *Appl. Occ. Environ. Hyg. 6*:421–427 (1991).
18. **Seixas, N.S., T.G. Robins, and L.H. Moulton:** The use of geometric and arithmetic mean exposures in occupational epidemiology. *Am. J. Ind. Med. 14*:465–477 (1988).