

Assessment of occupational exposures in a general population: comparison of different methods

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Abstract

Objectives—To evaluate the relative merits of job specific questionnaires and various alternative assessment methods of occupational exposures often used in general population studies.

Methods—Subjects were participants in a hospital based case-control study of risk factors for male infertility. Estimates of exposure to organic solvents and chromium, based on job specific questionnaires, generic questionnaires, self reports of exposure, an external job exposure matrix (JEM), and a population specific JEM were compared with passive diffuse dosimeter results and measurements in urine. Urine samples from the end of the shift were analysed for metabolites of toluene, xylene, several glycol ethers, trichloroethylene, and chromium. Passive dosimeter data, metabolites of specific solvents, and urinary chromium concentrations were available for 89, 267, and 156 subjects, respectively. The alternative methods and measurements in urine were compared by means of the Cohen's κ statistic and by computing the positive predictive value, sensitivity, and specificity of the alternative methods against measurements in urine.

Results—Passive dosimeter results indicated that exposure classifications with job specific questionnaire information could discriminate between high and low exposures. The κ coefficients were <0.4 , so agreement between the various methods and measurements in urine was poor. Sensitivity of the methods ranged from 0.21 to 0.85, whereas specificity ranged from 0.34 to 0.94. Positive predictive values ranged from 0.19 to 0.58, with the highest values for job specific questionnaires.

Conclusions—The results indicate that the implementation of job specific questionnaires in a general population study might be worth the extra expense it entails, bearing in mind the paramount importance of avoiding false positive exposure estimates when exposure prevalence is low.

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Keywords: exposure assessment; questionnaires; general population studies

The importance of reliable and valid methods to measure occupational exposures in general

population studies has been described repeatedly, and improvement of methods of assessing exposure has become a central focus of research efforts over the past decade.¹⁻⁴ Researchers have used various ways of grouping subjects with common occupational exposures. Traditionally, studies have been based on the collection of information on job title as a surrogate for occupational exposures. In the early 1980s, the job exposure matrix method was proposed to translate information on job title into specific exposures.⁵ This approach is, however, limited by the fact that exposures may vary widely from worker to worker within the same job title.^{6,7} Moreover, self administered questionnaires have been developed to register exposure at the workplace, usually by means of a checklist.^{8,9} This is probably the most simple and inexpensive method of assessing exposure. Alternatively, some researchers have proposed costly and labour intensive methods—such as the use of job specific questionnaires or interviews, combined with an evaluation by trained experts, for the purpose of inferring occupational exposures.¹⁰⁻¹³

Only limited information exists on the relative merits of these different methods.¹⁴ Quantitative data are rarely available and only a few validation studies with industrial hygiene data have been published.¹⁵⁻¹⁸ It is generally thought not to be feasible to get access to all workplaces or to obtain specimens from each study subject and it is argued that it is costly and complex to set up an exposure survey within a general population. Hence, most of these studies are conducted in specific industrial settings and do not necessarily reflect the exposure assessment as it would be in a general population study.

This paper describes a study of exposure assessment which was conducted as part of a large hospital based case-control study of risk factors for male infertility. Exposure to organic solvents and chromium was assessed by personal dosimetry and through measurements in urine. These measurements can be regarded as an independent type of exposure assessment and provide an opportunity to compare the relative merit of a labour intensive method based on job specific questionnaires on tasks performed and less elaborate methods of collection of exposure data—such as generic questionnaires, checklists of products used, an external job exposure matrix, and a population specific job exposure matrix.

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Materials and methods

SELECTION OF SUBJECTS AND DATA COLLECTION

All subjects were participants in two studies on associations between male infertility and, among others, occupational exposure to organic solvents and heavy metals. Population A comprised men seeking medical advice or treatment from two fertility clinics in The Netherlands. Population B comprised couples who sought in vitro fertilisation (IVF) at one of the two fertility clinics. Firstly, all subjects were asked to fill in a generic questionnaire including open ended questions about details of their current occupation. Also, subjects had to indicate on a checklist any of the following exposures which they may come into contact with during their current occupation: industrial cleaning products or degreasers; paint, glue, or printing inks; paint removers; welding fumes; and other exposures not listed in the checklist. This generic information about job characteristics was used to classify subjects initially as non-exposed or potentially exposed. Potentially exposed subjects were asked to fill in a job specific questionnaire on tasks performed, specifically designed for the particular job. The job specific questionnaires have partly been adapted from questionnaires developed by Blatter *et al.*¹⁹ Each job specific questionnaire elicits details on every occupational task—for example, painting, welding—what products were handled—for example, alkyd paint, stainless steel—how they were handled—for example, spray painting, MMA welding—and the frequency of the activities. The overall participation rate was 76% for the generic questionnaires and 91% of the potentially exposed subjects agreed to fill in a job specific questionnaire.

A total of 249 subjects who filled in a job specific questionnaire were invited to deliver a urine sample at the end of a working day; 218 (88%) subjects participated in this biomonitoring study. A subset of 100 out of these 218 men were also asked to be monitored by a passive diffusion dosimeter (3M, 3500); 89 subjects (89%) agreed. These subjects were randomly selected among the different exposure groups and the number of subjects monitored was aimed to be about equal in each group. Also, a random sample of 63 subjects initially classified as non-exposed according to the generic questionnaires were asked to deliver a urine sample; 49 (78%) agreed to do so. In total, 267 subjects delivered a urine sample after the shift which was analysed for metabolites of organic solvents. Urinary chromium was measured in 156 of these samples and selection was done in such way that a maximum number of presumably exposed subjects was included.

To avoid contamination, subjects had to collect urine in acid washed polyethylene bottles, after a shower and changing into street clothes. Samples were taken, if possible, on a Wednesday, Thursday, or Friday. Subjects were instructed to store the urine samples and dosimeters in their freezer at home until these were collected by a member of the research team. A research assistant visited each subject and collected the samples within 1 week after

the measurement day. Subjects also completed a day specific questionnaire on tasks performed during the measurement day.

LABORATORY ANALYSIS

All urine samples were analysed for hippuric acid (a metabolite of toluene) and methyl hippuric acid (a metabolite of xylene) by reversed phase (C18) high performance liquid chromatography (HPLC) of filtered urine with an isocratic solvent mixture of water:methanol:acetic acid (64.7:35:0.3% vol:vol:vol). Analyses of methoxyacetic acid (metabolite of ethylene glycol monomethyl ether), ethoxyacetic acid (metabolite of ethylene glycol monoethyl ether), and butoxyacetic acid (metabolite of ethylene glycol monobutyl ether) in urine were carried out by gas chromatography.²⁰ Trichloroacetic acid and trichloroethanol (metabolites of trichloroethylene) were analysed colorimetrically according to Tanaka *et al.*²¹ The creatinine content of all urine samples was determined by the Jaffé method. For hippuric acid, which is also present in non-exposed subjects, a cut off point of 1.5 g/g creatinine was chosen to discriminate between occupationally exposed and non-exposed subjects.²² Urinary chromium concentrations were measured by graphite furnace atomic absorption spectrophotometry (AAS) with Zeeman compensation, by the method of standard addition.²³ Urinary chromium concentrations were related to their respective creatinine concentrations.

The passive diffusion dosimeters containing charcoal were screened systematically for the presence of 150 widely used solvents. Analyses of charcoal were conducted with a Hewlett-Packard 5880A gas chromatograph.²⁴ Measurement results were combined in the form

$$X = \sum C_i \quad (i=1, 2, \dots, k)$$

where X is the total volatile organic compound score, i represents the i-th component, C the measured concentration of this component, and k the number of solvent components measured. Also, the aromatic solvent concentration was measured.

METHODS OF ASSESSMENT OF EXPOSURE

Firstly, the detailed job specific questionnaires (JSQs) on tasks performed were compared with data from passive diffuse dosimeters and measurements in urine. Three mutually exclusive groups exposed to organic solvents and chromium were defined with the guidelines shown in table 1. These guidelines were not regarded as an absolute reference for assigning exposure levels but facilitated the standardisation of the exposure assessment process. Besides organic solvents in general, exposure to aromatic solvents was assessed based on job specific questionnaire information. The level of exposure to aromatic solvents was assigned according to the same principles as outlined in table 1—for example, subjects in the high solvent exposure group assessed to be exposed to aromatic solvents were in most instances also classified in the high aromatic solvent exposure group.

Table 1 Main substances and tasks of subjects exposed and not exposed to organic solvents and chromium in an exposure assessment study in a general population in The Netherlands

Exposure group	Main substances/tasks	Frequency
Exposure to organic solvents:		
High	Solvent based paint; contact adhesives; inks; miscellaneous*	≥ 1.0 h/day
Moderate	Solvent based paint; contact adhesives; inks; miscellaneous	>0 and <1.0 h/day
Low or none	Water based paint; glue; degreasers; laboratory solvents	≥ 0.5 h/day
	Water based paint; glue; degreasers; laboratory solvents	<0.5 h/day
Exposure to chromium:		
High	SS welding (excluding TIG); foundry work	≥ 1.0 h/day
Moderate	SS welding (excluding TIG)	>0 and <1.0 h/day
	SS welding (TIG); cutting, polishing, grinding of SS	≥ 0.5 h/day
Low or none	SS welding (TIG); cutting, polishing, grinding of SS	<0.5 h/day

*Specific tasks in chemical industry with high potential for exposure to solvents—for example, vapour degreasing, working in the paint industry.

SS=stainless steel; TIG=gas tungsten arc welding.

The following alternative less elaborate methods were validated by means of measurements in urine: (1) generic questionnaires (GQ) on job characteristics. The exposure scoring procedure relied on knowledge and experience of the researchers. Although less detailed information was available, the same principles as used for the job specific questionnaires were used as guidelines for the assessment of exposures. Hence, based on generic information and self reported exposure it was estimated whether study subjects worked with specific products and the frequency of use of these products was assessed. Subsequently, subjects were assigned to one of the three mutually exclusive exposure groups. (2) Self reported exposure of participants according to the checklist. Subjects who indicated that they came into contact with the following products were classified as exposed to organic solvents and aromatic solvents: industrial cleaning products or degreasers; paint, glue, or printing inks; paint removers; or other solvent products filled in by the participants. Subjects who filled in welding fumes were classified as exposed to chromium. (3) Exposure assessment by the job exposure matrix (JEM) of Hoar *et al.*⁵ Only subjects classified as highly exposed to aromatic solvents according to the JEM were used to provide evidence for exposure. (4) A population specific JEM was created based on the exposure estimates according to the job specific questionnaires. Jobs with ≥50% of the subjects highly or moderately exposed to aromatic solvents were considered to be exposed. The population specific JEM was only constructed for exposure to aromatic solvents, as the prevalence of chromium exposure was low, resulting in few job titles with ≥50% exposed subjects.

STATISTICAL ANALYSIS

For the passive dosimeter data, median and range of volatile organic compound and aromatic solvents were calculated for different exposure groups as assessed by job specific questionnaires. Wilcoxon rank sum test was applied to compare median exposures between exposed and non-exposed subjects. We computed the numbers and percentages of subjects with specific metabolites of solvents in the urine at the end of the shift. Urinary chromium results were presented as geometric mean (GSD) and the statistical tests were performed with ln transformed variables. Comparisons of

geometric means between exposure groups were made with one way analysis of variance (ANOVA) and Student's *t* test. The various exposure assessment methods and measurements in urine were compared with the Cohen's κ statistic. Also, we computed sensitivity, specificity, and positive predictive value assuming that the measurements in urine were closer to the truth. For solvents, information from job specific and generic questionnaires was classified according to a lenient and strict scheme. This resulted in a dichotomy of highly exposed versus all other subjects (strict) and highly and moderately exposed versus other subjects (lenient). The 75th percentile of the urinary chromium distribution was chosen as an arbitrary cut off point to distinguish exposed from unexposed subjects.

Results

The median (range) of volatile organic compounds for different exposure groups according to job specific questionnaires is shown in table 2. The results indicated median volatile organic compound concentrations of 60, 3, and 1 mg.m⁻³ for those designated high, moderate, and low or no exposure, respectively, on the basis of information from the job specific questionnaire. Volatile organic compound concentrations of subjects in the high and moderate exposure group were significantly different from those in the low exposure group. In total, 48 different organic solvents could be detected and of these, toluene was the most widely used (45%), followed by acetone (21%), and xylene (17%).

Table 2 Concentrations of volatile organic compounds (mg/m³) for various organic solvent exposure groups as assessed by job specific questionnaires

Exposure group	N	Median	Range
High	26	60***	1–2673
Solvent based paint	10	46	3–154
Solvent based glue	6	448	2–2673
Printing ink	8	33	1–179
Miscellaneous*	2	20	8–33
Moderate	36	3**	0–160
Paint or glue	7	2	1–10
Degreasers or cleaning products	3	5	2–8
Laboratory solvents	9	2	0–5
Miscellaneous†	17	5	0–160
Low or none	27	1	0–26

p=0.011; *p=0.0001, v low exposure group, by Wilcoxon rank sum test.

*Processing in paint industry and vapour degreasing.

†Simultaneous use of two or more products shown in the table.

Table 3 Concentrations of aromatic solvents (mg/m³) and number of hippuric acid and methylhippuric acid positive subjects for various groups exposed to aromatic solvents as assessed by job specific questionnaires and a group of subjects initially classified as not exposed according to the generic questionnaires

Exposure group	Dosimeter			Metabolites	
	n	Median	Range	n	HA/MHA‡
High†	18	6***	0–569	31	16 (52)
Moderate†	22	1	0–16	53	12 (23)
Low or none†	49	0	0–90	134	9 (7)
Initially classified as not exposed	—	—	—	49	3 (6)

***p=0.0001 v low exposure group by Wilcoxon rank sum test.

†As assessed by job-specific questionnaire.

‡Number (%) of subjects positive for methylhippuric acid or hippuric acid >1.5 g/g creatinine.

Table 4 Concentrations of urinary chromium for various groups exposed to amounts of chromium as assessed by job specific questionnaires, and a group of subjects initially classified as not exposed according to the generic questionnaires

Exposure group	U-Cr concentrations (µg/g creatinine)			
	n	GM	GSD	U-Cr≥5
High†	19	2.3***	2.1	3
Moderate†	15	1.3	1.8	1
Low or none†	102	1.4	1.9	0
Initially classified as not exposed	20	1.2	1.8	0

***p=0.0013 v group initially classified as not exposed, by t test.

†Assessed by job specific questionnaire.

Table 3 shows median aromatic solvent concentrations of 6, 1, and 0 mg.m⁻³ for subjects presumed to have high, moderate, and low or no exposure to aromatic solvents, respectively. Concentrations of aromatic solvents of subjects in the high exposure group were significantly different from those in the low exposure group. The percentage of subjects positive to methylhippuric acid and hippuric acid increased with increasing exposure to aromatic solvents as assessed by job specific questionnaires (52%, 23%, and 7% for subjects with high, moderate, and low or no exposure, respectively). In the group of subjects initially classified as non-exposed 6% of the urine samples were positive for methylhippuric acid or hippuric acid. Metabolites of ethylene glycol monomethyl ether, ethylene glycol monobutyl ether, and trichloroethylene could all be detected in only one urine sample. Metabolites of ethylene glycol monoethyl ether could not be detected at all in the 267 urine samples analysed (not shown).

Table 4 shows the urinary chromium concentrations for the different exposure groups based on job specific questionnaires. The classification scheme yielded geometric mean chromium concentrations of 2.3, 1.3, 1.4, and 1.2 µg/g creatinine for the presumed high, moderate, low or no exposure, and subjects initially classified as not exposed, respectively. The geometric mean urinary chromium concentration of the subjects with high exposure was significantly increased compared with subjects in occupations initially classified as not exposed. These results were confirmed when crude urinary chromium concentrations were used instead of the creatinine adjusted values. Only four out of 156 urine samples contained >5 µg/g creatinine (subjects not occupationally exposed to chromium usually have urine concentrations <5 µg/g creatinine),²² and these subjects were indeed exposed according to information from the job specific questionnaire.

Table 5 summarises the results of comparisons made between methods of assessing exposure to aromatic solvents and measurements of methylhippuric acid and hippuric acid in urine. It can be seen from this table that the κ coefficients were <0.4, so agreement is poor. When measurements in urine were assumed to represent the gold standard, the sensitivity ranged between 0.30 (generic questionnaire (strict)) and 0.85 (checklist). The specificity ranged between 0.34 (checklist) and 0.93 (job specific questionnaire (strict)). The highest positive predictive value was found for the job specific questionnaire information (job specific questionnaire (strict): positive predictive value=0.52, job specific questionnaire (lenient): positive predictive value=0.33), followed by an expert evaluation on the basis of generic questionnaires (generic questionnaire (strict): positive predictive value=0.39, generic questionnaire (lenient): positive predictive value=0.29) and exposure estimates generated by the population specific JEM (positive predictive value=0.27). The positive predictive value for the external JEM was 0.22 and for the self assessment of participants according to a checklist was 0.19 (very low). Combining exposure estimates of the JEMs and self assessments enhanced the positive predictive value to

Table 5 Comparison of alternative exposure assessment methods for aromatic solvents with metabolites of hippuric acid or methylhippuric acid

Method	2x2 Table				Indices of agreement			
	Urine+ Method+	Urine+ Method-	Urine- Method+	Urine- Method-	κ	PPV	Sensitivity	Specificity
JSQ _{strict}	16	24	15	212	0.37	0.52	0.40	0.93
JSQ _{lenient}	28	12	56	171	0.31	0.33	0.70	0.75
GQ _{strict}	12	28	19	208	0.24	0.39	0.30	0.92
GQ _{lenient}	22	18	53	174	0.23	0.29	0.55	0.77
JEM _{external}	24	16	85	142	0.13	0.22	0.60	0.63
JEM _{population}	23	17	62	165	0.21	0.27	0.58	0.73
Checklist	34	6	149	78	0.08	0.19	0.85	0.34
JEM _{external} /checklist	23	17	58	169	0.22	0.28	0.58	0.74
JEM _{population} /checklist	21	19	50	177	0.23	0.30	0.53	0.78

PPV=positive predictive value; JSQ_{strict}=highly exposed subjects according to job specific questionnaire classified as exposed; JSQ_{lenient}=highly or moderately exposed subjects according to job specific questionnaire classified as exposed; GQ_{strict}=highly exposed subjects according to generic questionnaire classified as exposed; GQ_{lenient}=highly or moderately exposed subjects according to generic questionnaire classified as exposed; JEM_{external}=exposure classification according to external job exposure matrix; JEM_{population}=exposure classification according to population specific job exposure matrix.

Table 6 Comparison of alternative methods of assessment of exposures to chromium with urinary concentrations of chromium

Method	2x2 Table				Indices of agreement			
	Urine+ Method+	Urine+ Method-	Urine- Method+	Urine- Method-	κ	PPV	Sensitivity	Specificity
JSQ _{strict}	11	28	8	109	0.26	0.58	0.28	0.93
GQ _{strict}	8	31	7	110	0.18	0.53	0.21	0.94
JEM _{external}	10	29	25	92	0.04	0.29	0.26	0.79
Checklist	16	23	37	80	0.08	0.30	0.41	0.68
JEM _{external} /checklist	9	30	13	104	0.14	0.41	0.23	0.89

PPV=positive predictive value; JSQ_{strict}=highly exposed subjects according to job specific questionnaire classified as exposed; GQ_{strict}=highly exposed subjects according to generic questionnaire classified as exposed; JEM_{external}=exposure classification according to external job exposure matrix

some extent (JEM (external)/checklist: positive predictive value=0.28, JEM (population)/checklist: positive predictive value=0.30).

Table 6 shows the agreement between various exposure methods and urinary chromium concentrations. Only a strict classification scheme was evaluated for the job specific and general questionnaires, as table 4 shows that urinary chromium concentrations were not increased for the subjects with presumed moderate exposure. Again, κ coefficients were low. The sensitivity ranged between 0.21 (generic questionnaire (strict)) and 0.41 (checklist), whereas the specificity ranged between 0.68 (checklist) and 0.94 (generic questionnaire (strict)). Exposure estimates based on job specific questionnaires resulted in the highest positive predictive value (0.58), followed by an exposure evaluation based on generic questionnaires (0.53), self assessment of participants (0.30), and the external JEM (0.29). Again, with a dual assessment method combining estimates of the external JEM with self reports of exposure enhanced the positive predictive value (0.41).

Discussion

Exposure concentrations of organic solvents and urinary chromium were clearly increased in subjects classified as highly exposed according to the job specific questionnaires. Among subjects presumed to be moderately exposed, however, exposure concentrations were much lower and differed only marginally from those of non-exposed subjects. These results suggest that only defining presumably highly exposed subjects as exposed might in some cases be preferable, especially in studies with low prevalence of exposure where the critical concern is to avoid classifying unexposed subjects as exposed.^{25 26} However, the potential gain in positive predictive value of the job specific questionnaires from applying such a strict classification scheme can be offset by a substantially decreasing number of exposed subjects.

If a labour intensive and time consuming exposure assessment procedure—such as the use of job specific questionnaires—is applied, it is necessary to consider whether less elaborate methods would have yielded the same results. Our comparisons suggest that the job specific questionnaires did yield the largest positive predictive value. Hence, the implementation of job specific questionnaires in a study might be worth the extra expense it entails, bearing in

mind the paramount importance of avoiding false positive exposure estimates in most general population studies.^{25 26} Interestingly, the population specific JEM performed somewhat better than the external JEM, illustrating the difficulty of applying JEMs to populations different from those in which the JEM was initially developed.²⁷ In accordance with the theory,^{28 29} combining estimates of a JEM with self reports of exposure enhanced the agreement with urine measurements to some extent. The use of such a dual assessment procedure may be potentially useful in situations where extensive data collection is prohibitive or not feasible, or if experts with appropriate training are not available. Self reports resulted in a low positive predictive value, and overestimation of exposure is probably large. This can severely affect estimates of disease risks and the method should not be used as the sole source of exposure information. However, the checklist resulted in the largest sensitivity and might therefore be useful as an initial screening tool in the framework of a broader exposure assessment strategy.

When interpreting the results it must be stressed that exposure measurements are also prone to error due to spatial and temporal variation in exposure concentrations.^{6 7 30 31} For measurements in urine, day to day variation is particularly critical for metabolites with a short elimination half life³²—such as hippuric acid and methylhippuric acid, and to a lesser extent also urinary chromium.²² Moreover, hippuric acid is also a normal constituent of urine which reduces its usefulness as a qualitative indicator of occupational exposure to toluene. The urinary concentrations of hippuric acid after a low exposure to toluene are difficult to differentiate from background values. Hence, subjects with hippuric acid concentrations <1.5 g/g creatinine might still experience exposure to toluene.

Urinary chromium concentrations are influenced by the solubility of chromium compounds, and solubility may vary between workplaces and tasks. In the context of comparing different exposure classifications, however, the crucial advantage of actually conducting exposure measurements is that sources of errors associated with them are largely independent of errors associated with alternative methods—such as questionnaires or a JEM. Hence, although the exposure measurements do not reflect true exposure, and are themselves “alloyed gold standards”,³³ they provide an

excellent opportunity to evaluate the relative merits of various methods, an issue which is seldom dealt with in an appropriate manner.¹⁴

It should be noted that we could only evaluate the performance of a few different exposure assessment methods. It was not feasible, for instance, to evaluate the performance of detailed interviews which is generally regarded to be one of the most valid assessment procedures. Interviews have the advantage that any misunderstandings or ambiguities can be immediately resolved¹ and it can be hypothesised that such an approach provides a more complete understanding of occupational exposures than self administered job specific questionnaires. The evaluation of the self assessments of participants was limited by the fact that subjects could only fill in exposure to general solvent products and welding fumes, whereas these estimates were compared with metabolites of aromatic solvents and chromium in urine. Furthermore, findings of this study might not apply to the situation of retrospective assessment of exposure because subject's recall for job titles might exceed their ability to recall detailed information on work environments decades ago. Some authors³⁴ have found that subjects give accurate reports of their past employers but little is known about the validity of detailed information on specific tasks or other determinants of exposure which occurred in the past. Differences in validity between job specific questionnaires and alternative methods found in this study might therefore not be applicable to retrospective studies.

Finally, the application of biomarkers or industrial hygiene sampling can be used as an independent basis of comparison of assessment procedures between studies, and over time. This is of key importance when comparing results between studies or if data have to be pooled. For example, in our study population metabolites of ethylene glycol ethers could be detected in only a few urine samples whereas these solvents were widely encountered in another study of the general population conducted several years ago.³⁵ Metabolites of trichloroethylene could only be detected in one sample, which shows that the use of this chlorinated solvent has been restricted in The Netherlands. Alternatively, the group with high exposure to chromium in this population cannot be readily related to chromium concentrations in a population with chrome platers, generally exposed to much higher concentrations of chromium.³⁶ Hence, to increase the comparability across studies an attempt should be made to document quantitative exposures, even if only basic and limited information is available.

In conclusion, as exposure prevalence in the general population is usually low and most pollutants in the workplace are associated with moderate or low risks of disease, improvement in assessing exposure is crucial to design informative epidemiological studies. Results of epidemiological studies should be interpreted in the light of the quality of the exposure assessment methods used, and if available,

information on the validity of the assessment procedure should be included in the scientific report. In some studies, application of a JEM or expert evaluations of job histories will suffice. In most instances, however, it will be necessary to ask detailed questions about tasks and work process, and if possible, to validate these questions through industrial hygiene sampling or measurements in biological media.

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Examples of common forms of references are:

- 1 International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. *JAMA* 1993;269:2282-6.
- 2 Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *N Engl J Med* 1976;294:687-90.
- 3 Weinstein L, Swartz MN. Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology, mechanisms of disease*. Philadelphia: W B Saunders, 1974:457-72.



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