Spirometric changes following the use of pesticides

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التغيُّرات في قياسات التنفس بعد استخدام مبيدات الهوامّ

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الخلاصة: أُجريت دراسة في لبنان للمقارنة بين الوظيفة التنفسية لعمال مصنع لمبيدات الهوامّ pesticides، بلغ عددهم 19 عاملاً، وبين فئة شاهدة control، مؤلفة من عمال مصنع آخر بلغ عددهم 43 عاملاً. و لم يكن هناك فرق بين الفئتين من حيث التدخين. وقد برهنت قياسات القِيَم القاعدية للوظيفة التنفسية على تدنِّي الحجم الزفيري القسري، وبطء معدل سَرَيَانِهِ (الحجم الزفيري القسري في الثانية الأولى، وسَرَيَان الزفير القسري عند النقطة من 25٪ إلى 75٪ من بداية السعة الحيوية القسرية، ونسبة الحجم الزفيري القسري في الثانية الأولى إلى السعة الحيوية القسرية) في الأشخاص العاملين في مصنع المبيدات، ممَّا يعني أن الانسداد ربما يرتبط بالتعرُّض المزمن للمبيدات. وبعد مرور 4 ساعات من العمل وُجد أن كل المتغيرات التنفسية لازالت متدنِّية بدرجة يُعْتَدُّ بها إحصائياً في الأشخاص المعرَّضين للمبيدات، ولو أنهم لم تلاحظ تغيرات حادة في الوظيفة التنفسية لديهم. وبرهنت نسب الأرجحية، على أن العمال المتعرضين للمبيدات، تزيد مخاطر تعرضهم لاضطراب نسبة الحجم الزفيري القسري في الثانية الأولى إلى السعة الحيوية القسرية بمقدار 5.6 أضعاف، كما تزيد مخاطر تعرُّضهم لاضطراب سَرَيَان الزفير القسري عند النقطة من 25٪ إلى 75٪ من بداية السعة الحيوية القسرية بمقدار 16.5 ضعفاً. وكانت مدة المكوث في مصنع المبيدات ذات ترابط يُعْتَدُّ به إحصائياً باضطراب القياسات التنفسية.

ABSTRACT We compared the respiratory function of 19 pesticide factory workers and a control group of 43 other factory workers in Lebanon. The groups had no difference in smoking status. Baseline measurements of respiratory function showed significantly lower forced expiratory volume and flow rates (FEV_1, $FEF_{25–75\%}$, and FEV_1/FVC ratio) among subjects working with pesticides, i.e. obstruction may be linked to chronic exposure to pesticides. After 4 hours of work, all respiratory variables were still significantly lower in pesticide-exposed subjects, but no acute changes in respiratory function were seen. Pesticide-exposed workers had 5.6 times higher risk of abnormal FEV_1/FVC ratio and 16.5 higher risk for abnormal $FEF_{25–75\%}$. Duration of occupation in the pesticide factory was significantly correlated with abnormal respiratory measures.

Modifications spirométriques suite à l'utilisation de pesticides

RÉSUMÉ Une étude réalisée au Liban a comparé la fonction respiratoire de 19 travailleurs des usines de pesticides et d'un groupe de 43 travailleurs d'autres usines. Il n'y avait pas de différences entre les groupes concernant le statut tabagique. Les mesures initiales de la fonction respiratoire ont montré des taux significativement inférieurs pour le volume expiratoire maximum seconde et le débit expiratoire maximal (VEMS, DEM25-75 %, rapport VEMS/CVF) chez les sujets travaillant avec des pesticides, c'est-à-dire que l'obstruction peut être liée à l'exposition chronique aux pesticides. Après quatre heures de travail, toutes les variables respiratoires étaient significativement inférieures chez les sujets exposés aux pesticides, mais aucune modification de la fonction respiratoire n'a été observée. L'odds ratio a montré que les ouvriers exposés aux pesticides avaient un risque 5,6 fois plus élevé d'avoir un rapport VEMS/CVF anormal et 16,5 fois plus élevé d'avoir un DEM25-75 % anormal. Il y avait une corrélation significative entre la durée de l'emploi dans l'usine de pesticides et les mesures respiratoires anormales.

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Introduction

Occupational exposure to pesticide produces the greatest hazard for individual exposure to these toxic substances [*1*], by inhalation, dermal or oral exposure [*2,3*]. Exposure levels depend on the nature and formulation of the pesticide, utilization techniques, hygiene and environmental conditions [*4*]. The physical, chemical and aerodynamic properties of the product, anatomy of the respiratory tract and individual physiology are the main determinants of particle deposition [*3*].

In developed countries, legislation provides some protection against the dangers of occupational use of pesticides [*2*], whereas in developing countries, the safety problems are neglected and workers may not be legally protected against the toxic effects of pesticides at work [*5*]. Inhalation of pesticide dust, vapours, mists and gases may therefore represent a significant occupational hazard [*6*] with workers vulnerable to acute toxic episodes and chronic intoxication [*1*]. Among occupationally exposed workers, the prevalence of symptoms and the risk of acute intoxication increase with increasing number of working years [*7*].

Few epidemiological studies have been conducted throughout the world to evaluate the short and long-term effects on the respiratory system of occupational exposure to pesticides. Mortality and morbidity studies are commonly performed, whereas respiratory effects have been less studied, due to the difficulty of evaluating respiratory exposure [*8–11*] in addition to the confounding effect of workers' lifestyle (smoking, physical conditions, climate). Moreover, pesticide residues can have physicochemical transformations into products that are more or less active, and can be found in the dust to which workers are exposed [*8*].

Acute toxic effects are well known from basic toxicological and clinical studies. Immunological and neurological effects on the respiratory system linked to the local and systemic toxic actions of pesticides have been reported. Beside allergic phenomena, the development of respiratory problems is mainly due to the overwhelming toxic effect on cell reparation [*12*]. Oxidative stress, present whenever some pesticides are inhaled, may initiate diseases such as chronic bronchitis, emphysema, fibrosis and cancer [*13*]. Occupational asthma, reactive–airways dysfunction syndrome, or even a transient hypersensitivity elicited by irritation may occur [*14*].

This study in Lebanon aimed to evaluate the respiratory function variables of workers employed in a pesticides processing factory in a developing country and compare the effect of acute exposure to pesticides of these workers with a group of workers not occupationally exposed to pesticides.

Methods

The study compared the respiratory function of a group of factory workers occupationally exposed to pesticides and a control group not occupationally exposed. Workers were interviewed and respiratory function measurements were taken before and after a work shift. The study was conducted in March 2000, when the external temperature in the region reached an average daily maximum of 25 °C.

Sample

The pesticide-exposed sample was taken from a pesticides conditioning factory in Hosrael at Byblos (Mount Lebanon). All the factory workers, except the administrative

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workers, were included in the study sample.

The control sample was taken from workers at 4 nutritional products factories, chosen to ensure the absence of occupational exposure to respiratory pesticides: Choueifat (fruit juice dilution and conditioning), Harissa (cheese production from fresh milk), Bekaata (ice cream production) and Kfarkatra (sweets baking). All non-administrative workers were included in the control sample.

The interviewees were informed that the study was to evaluate "their general health status" and all of them gave their consent to participation.

Questionnaire

A pretested questionnaire was used: the standardized and validated American Thoracic Society Chronic Respiratory Diseases Questionnaire [*15*], adapted to the local language. It was orally administrated to both groups of workers by previously trained interviewers who were aware of the exposure status of the subjects and of the objectives of the study. For each subject, the questionnaire was administered for 10 minutes at 07.30 hours in the morning.

The questionnaire included detailed information about workers' social and demographic characteristics, health status, employment history and exposure to pesticides. Several potential confounding variables were assessed: previous occupation, sex, age, body mass index (BMI), active and passive smoking, general health status and family medical history. The types of pesticide products used at work, duration of exposure, tasks performed and protective measures taken were recorded. Information was collected about previous occupational and non-occupational exposure to pesticides (agricultural, house, garden). Respiratory symptoms regularly suffered (chronic cough, expectoration, wheezing and dyspnoea) were noted.

Respiratory function measurements

Respiratory measurements were performed before the morning shift (08.00 hours) and 4 hours later (12.00 hours). Respiratory function measurements were made using a portable spirometer, the Spirovit SP-1 (Schiller, Switzerland) with disposable filters (SP-150), designed for ambulatory pulmonary function measurement. Calibration was carried out in the morning of each use. The device measures actual respiratory flow, at a precision of 2%, in addition to predicted values according to age, sex, height, weight, and race. The regression equation used was that of the European Coal and Steel Community Standards for individuals over 18 years of age, generally used for Mediterranean countries [*16*], and Quanjer and Tammeling comparisons for those under 18 years [*17*].

Dependent variables were based on respiratory function measures before and after pesticides use:

- forced vital capacity (FVC), i.e. volume in litres from peak inspiration to the end of the forced exhalation;
- forced expiratory volume at 1 second (FEV_1), i.e. the volume expired during 1 second while performing the FVC;
- FEV_1/FVC ratio;
- forced expiratory flow at 25–75% ($FEF_{25-75\%}$) or maximal mid-expiratory flow rate (MMFR), which is the average expiration flow rate during the middle 50% of the FVC [*19,20*].

Each spirometric test was repeated 3 times to allow the choice of the best values, according to the American Thoracic Society criteria (2 values of FEV_1 and FVC

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should not differ by more than 5% or 100 mL) [*18*].

Spirometric measurements conducted before work accounted for baseline respiratory values, affected by past chronic exposure to pesticides. Absolute and relative values (ratio of actual to predicted values) were noted. Binary classification of respiratory measures was made for baseline variables, considering values < 80% of those predicted as abnormal; for FEV_1/FVC ratio, any value below 80% was considered abnormal [*21*]. Spirometric measurements conducted after 4 hours of work evaluated a possible effect of acute occupational exposure to pesticides on respiratory volumes and flows. Relative changes from baseline were also calculated as: (2nd value – 1st value)/1st value.

Analysis

Data were analysed using *Stata* software, release 5 (Drive East University, USA). An alpha risk of 5% and beta risk of 20% were accepted. Bilateral statistical tests were performed: chi-squared test for categorical variables, Mann–Whitney test for comparing means of continuous variables in cases of non-homogeneous variance or non-normal distribution, and Student *t*-test in cases of homogeneous variance and normal distribution. Spearman rank correlation was applied for correlation of continuous variables. A Mantel–Haenszel test was used for bivariate analysis, and a multiple regression for multivariate analysis.

Results

Demographic characteristics

The characteristics of both groups of workers are presented in Table 1; 43 non-exposed subjects and 21 pesticide-exposed subjects were assessed. Two subjects were eliminated from the pesticide-exposed group due to inadequate data; the remaining number was 19.

There were statistically significant differences in age, sex and weight between the 2 groups. All the pesticide workers (100%) were males compared with 77.7% of non-exposed workers ($P < 0.02$). Pesticide workers were older (mean age 39.8 years versus 28.0 years, $P < 0.001$) and heavier in weight (84.6 kg versus 70.7 kg, $P < 0.001$). They had also spent a longer time in the industry (mean 10.6 years versus 5.3 years, $P < 0.001$).

Smoking and medical history

No significant differences were seen in the percentage of past or current smokers, in the mean number of cigarettes smoked or in the cumulative smoking exposure expressed as mean number of pack-years (no. of years respondent has smoked on average 1 pack per day) (Table 1).

There were no significant differences between pesticide-exposed and non-exposed workers in terms of self-reported respiratory symptoms and other diseases. None of the interviewed subjects reported having any chronic respiratory problems (asthma or chronic bronchitis) diagnosed by a doctor.

Occupational and extra-occupational exposure to pesticides

The current occupational use of liquid pesticides was assessed in the chemical plant where subjects were working: 12 subjects were employed in conditioning a pyrethroid pesticide (cypermethrin 25% in xylene solution) and 9 subjects were exposed to a carbamate pesticide (isopropoxyphenyl methylcarbamate 20% in a mixture of cyclohexane 10% and xylene 60%). The

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Table 1 **Demographic and social characteristics of workers occupationally exposed and not exposed to pesticides**

Demographic/social characteristic	Non-exposed workers (*n* = 43)	Pesticide-exposed workers (*n* = 19)	*P*-value
	Mean (SD)	**Mean (SD)**	
Age (years)	28.0 (9.7)	39.8 (10.1)	< 0.001
Weight (kg)	70.7 (12.4)	84.6 (10.6)	< 0.001
Height (m)	172.0 (8.4)	171.6 (4.0)	0.80
BMI (kg/m^2)	23.8 (3.1)	28.6 (3.0)	< 0.001
Time in industry (years)	5.3 (5.0)	10.6 (12.0)	< 0.001
Smoking frequency			
Cigarettes/day (No.)	17.8 (10.9)	15.5 (8.3)	0.60
Pack-years (No.)	5.2 (7.4)	7.2 (11.6)	0.86
	No. %	**No. %**	
Smoking status			
Ex-smoker	1 2.3	2 10.5	0.38
Current smoker	20 46.5	8 42.1	
Non-smoker	22 51.2	9 47.4	

n = ***number of participants.***
SD = standard deviation.
BMI = body mass index.
[a]***Pack-years = no. of years respondent has smoked on average 1 pack per day.***

tasks performed consisted of filling small receptacles from large reservoirs of liquid pesticides, on a 6 metre long production line. The production rate was 5000 litres of finished product per 8 hours of work. The tasks were performed manually and workers did not use any special protection (i.e. no specialized masks, gloves or clothes), except for cotton masks worn by 8 of the pesticide workers.

No significant difference existed between exposed and non-exposed workers in self-reported previous occupational and non-occupational exposure to pesticides (domestic use, residential and indirect exposure), except that a higher percentage of exposed workers (66.8%) had suffered previous occupational exposure during agricultural work than non-exposed workers (0%) ($P = 0.001$).

Respiratory function variables

Baseline measurements of respiratory function made in the morning before the working shift (Table 2) show significantly lower FEV_1, $FEF_{25–75\%}$, and FEV_1/FVC ratios among subjects working with pesticides. After 4 hours of work, all respiratory variables were still significantly lower in pesticide-exposed subjects. Multiple regression analysis indicated poorer spirometric measures among pesticide-exposed workers ($P < 0.05$) except for the FVC ($P > 0.05$), for both the first measures (morning, pre-shift) and second measures (midday, post-shift). No statistically significant differences were noted between workers who wore cotton masks and those who did not ($P > 0.05$).

Table 3 shows the mean percentage difference in respiratory function measures

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Table 2 **Mean baseline (morning, pre-shift) and follow-up (midday, post-shift) respiratory function measures of workers occupationally exposed and not exposed to pesticides**

Respiratory measures[a]	Mean (SD) value		*P*-value
	Non-exposed workers (*n* = 43)	Pesticide-exposed workers (*n* = 19)	
1st measure			
Relative FVC (%)	93.6 (11.3)	90.5 (13.7)	0.39
Relative FEV_1 (%)	98.7 (10.8)	87.7 (14.0)	< 0.001
FEV_1/FVC (%)	89.7 (7.6)	80.5 (9.9)	< 0.001
Relative $FEF_{25–75\%}$ (%)	103.5 (21.2)	74.5 (26.0)	< 0.001
2nd measure			
Relative FVC (%)	95.2 (9.3)	87.4 (12.7)	0.01
Relative FEV_1 (%)	102.0 (11.1)	92.4 (16.4)	0.03
FEV_1/FVC (%)	91.2 (6.4)	86.7 (6.1)	0.01
Relative $FEF_{25–75\%}$ (%)	107.5 (26.1)	85.3 (21.9)	< 0.001

n ***= number of participants.***
[a]Relative values = measured/predicted values.
SD = standard deviation.
FVC = forced vital capacity; FEV_1 = forced expiratory volume at 1 second; $FEF_{25–75\%}$ = forced expiratory flow at 25–75%.

(based on the difference between the second and first measures for individual workers). Both groups showed a trend towards improved values for all respiratory function measures on the second measures (midday, post-shift) compared with the first measures (morning, pre-shift), except for the FVC which showed a decrease between the 2 measures in pesticide-exposed workers.

Table 4 shows the proportion of workers in both groups with abnormal respiratory function measures, i.e. baseline values < 80% of predicted values. A significantly higher proportion of pesticide workers had abnormal respiratory variables than non-exposed workers, 26.3% versus 4.7% for relative FEV_1, 47.4% versus 14.0% for FEV_1/FVC ratio and 57.9% versus 4.7% for $FEF_{25–75\%}$. Significant correlations were found between industrial pesticide use and abnormal relative respiratory measures. Mantel–Haenszel adjustment for smoking, past exposure to pesticides outside the factory, age, sex, weight and BMI were made for abnormal respiratory values. Adjusted odds ratios (ORs) obtained were significantly higher than 1, with no interaction between the adjustment variables and occupation exposure to pesticides. A high percentage of workers with abnormal respiratory function measures were found in both groups, especially those exposed to pesticides at work. The ORs showed that pesticide-exposed workers had 5.6 times the risk of abnormal FEV_1/FVC ratio and 16.5 times the risk for abnormal relative $FEF_{25–75\%}$ (Table 4).

Correlations between the duration of work in the pesticides plant and baseline

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Table 3 **Percentage change between baseline (morning, pre-shift) and follow-up (midday, post-shift) respiratory function measures of workers occupationally exposed and not exposed to pesticides**

Respiratory measures[a]	% change in value		*P*-value
	Non-exposed workers (*n* = 43)	Pesticide-exposed workers (*n* = 19)	
Relative FVC	+2.5	–2.5	0.05
Relative FEV_1	+3.6	+5.3	0.18
FEV_1/FVC	+2.1	+8.9	< 0.01
Relative $FEF_{25–75\%}$	+4.5	+20.9	< 0.01

n = ***number of participants.***
[a]***Relative change from baseline = (2nd measure–1st measure)/1st measure.***
FVC = forced vital capacity; FEV_1 = forced expiratory volume at 1 second; $FEF_{25–75\%}$ = forced expiratory flow at 25–75%.

respiratory variables are shown in Table 5. There was a significant contribution of duration of occupation in the pesticide factory to respiratory measure variances (i.e. 44% of the FEV_1/FVC ratio and 12% of the $FEF_{25–75\%}$ could be explained by duration of occupational exposure) ($P < 0.001$).

Discussion

The study participants were all healthy workers who did not report any pre-existing respiratory disease. Despite that, statistically significant differences were found for forced respiratory volumes and flows

Table 4 **Frequency of abnormal baseline respiratory function measures of workers (< 80% of predicted values) occupationally exposed and not exposed to pesticides**

Respiratory measures[a]	Non-exposed workers (*n* = 43)		Pesticide-exposed workers (*n* = 19)		Adjusted OR[b] (95% CI)	*P*-value
	No.	% with abnormal value	No.	% with abnormal value		
Relative FVC	5	11.6	4	21.5	2.0 (0.4–10.6)	0.44
Relative FEV_1	2	4.7	5	26.3	7.3 (1.1–63.4)	0.02
FEV_1/FVC	6	14.0	9	47.4	5.6 (1.4–23.8)	< 0.001
Relative $FEF_{25–75\%}$	2	4.7	11	57.9	16.5 (2.5–140.3)	< 0.001

n = ***number of participants.***
[a]***Relative values = measured/predicted values.***
[b]***Adjusted for smoking status, past exposure to pesticides, age, sex, weight and body mass index.***
FVC = forced vital capacity; FEV_1 = forced expiratory volume at 1 second; $FEF_{25–75\%}$ = forced expiratory flow at 25–75%.

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Table 5 **Association of work duration in pesticides industry with abnormal baseline respiratory function measures for 19 occupationally exposed workers**

Respiratory measures[a]	Spearman rank correlation coefficient (r_s)	Variance (r^2)	*P*-value
Relative FVC	–0.47	0.22	0.02
Relative FEV_1	–0.46	0.22	0.01
FEV_1/FVC	–0.66	0.44	< 0.001
Relative $FEF_{25–75\%}$	–0.35	0.12	< 0.001

[a]Relative value = measured/predicted value.
FVC = forced vital capacity; FEV_1 = forced expiratory volume at 1 second; $FEF_{25–75\%}$ = forced expiratory flow at 25–75%.

before and after work shifts, with consistently lower values for pesticide-exposed workers for FEV_1, $FEF_{25–75\%}$ and FEV_1/FVC ratio. This could be the effect of chronic professional exposure to pesticides, which gave lower baseline and post-shift values. The measured variables are particularly robust tests and their low values provide clear signs of pulmonary obstruction among workers in the pesticides industry. This is especially true for the $FEF_{25–75\%}$, which gives an indication of peripheral airway obstruction. It is believed to be a more sensitive index of airway obstruction than the FEV_1, especially in the small airways that are dependent on the elastic and resistant properties of the distal airways than on the subject's spirometer performance [*14*].

It was not possible to demonstrate an effect of acute exposure to pesticides on the respiratory system because respiratory function improved after 4 hours of work in both groups of workers. This could be explained by a natural circadian increase of respiratory volumes and flows [*14*], or by a learning effect of the spirometer breathing method. The increase was seen for all measures, except for FVC, which decreased. The decrease in relative FVC could be an indication of pesticides workers' fatigue, an inadequate realization technique or the occurrence of a mixed obstructive and restrictive pattern of lung disease [*22*]. The explanation of these observations remains to be explored in further studies. Acute effects of pesticide exposure have been reported in the literature; in a double-blind randomized study on asthmatics, acute exposure to insecticide aerosols induced respiratory symptoms and decreased respiratory function measures [*30*].

A temporal relationship existed between chronic exposure to pesticides and baseline respiratory measures among the study subjects. Abnormal baseline respiratory function measures correlated with length of exposure to pesticides, with duration of work in the industry accounting for 12% to 44% of the contribution to variances in respiratory measures.

A number of factors may have affected the findings non-differentially. Workers did not report any respiratory disease confirmed by a doctor and the respiratory function measures only indicated infraclinical pulmonary impairment. Respiratory symptoms and previous occupational and domestic exposure to pesticides were self-

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reported and the standardized questionnaire may have not elicited all relevant information. The sensitivity of the portable spirometer may have been low.

Nevertheless, our results are comparable to those found by other authors. The proportion of pesticide workers with abnormal respiratory variables (ranging from 26.3% for relative FEV_1 to 57.9% for $FEF_{25–75\%}$) was even higher than those seen by Kossmann et al., who evaluated respiratory functions of pesticides factory workers and found obstructive pulmonary impairment among 20% of workers in addition to chronic bronchitis [*23*]. A study conducted by the same author demonstrated abnormal respiratory flows among 25% of pesticide plant workers [*24*]. Moreover, a case of occupationally related asthma was reported in 1993 for a pesticide plant worker; he had a FEV_1/FVC ratio of 0.76 and a FEV_1 that significantly decreased after exposure to pesticides, in addition to asthma symptoms. Cessation of exposure improved his condition [*25*].

In rural environments where pesticides are heavily used, occupational asthma is frequent [*26*]. Several studies have been conducted on the respiratory health of professional agricultural workers [*22,27–29*]. Most of them demonstrated a chronic specific effect of pesticides on respiratory function, in addition to chronic bronchitis and asthma problems. This demonstrates the consistency of our results with those of other researchers.

The results we obtained for chronic effects are also biologically plausible. Carbamates, during acute intoxication, can cause respiratory disturbances, such as bronchial hypersecretion, cough, dyspnoea and asphyxia [*2,20*]. This may be due to the systemic effects of carbamates after inhalation, at doses very much lower than those causing similar responses after dermal or oral exposure [*12*]. Pyrethroid derivatives are allergens, causing asthma-like attacks and anaphylactic reactions [*20,26*]. In addition, organic solvents used in pesticide fabrication and dilution can themselves be toxic agents leading to the observed respiratory abnormalities [*20*].

In conclusion, chronic exposure of workers to industrial pesticides seems to be associated with a decrease in respiratory function, while acute exposure showed no clear effect. Causality between chronic exposure to pesticides and reduced pulmonary function variables cannot be demonstrated, but further studies could provide firmer evidence for this relationship. Protective measures for exposed workers should be implemented in pesticide factories, especially in developing countries such as Lebanon. The introduction and enforcement of laws regarding pesticides manufacture and use is necessary in order to control pesticide risks on the health of factory workers.

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Network of WHO Collaborating Centres in occupational health

The Network of Collaborating Centres makes a substantial contribution to the goal of "occupational health for all"; they are the "on-the-ground" actors and play a key role in capacity building. WHO estimates that only about 10% to 15% of workers worldwide have some kind of access to occupational health services, and extending coverage is a key challenge. The existing multilateral and bilateral collaboration is being further developed to transmit information and sharing of experience between countries and institutions. In 2001 a Workplan 2001–2005 was prepared and progress was reviewed at the Sixth Network Meeting held in Iguassu Falls, Brazil, in February 2003 which is set out in the *Compendium of projects of the WHO Collaborating Centres in occupational health*. Further information on WHO's work in occupational health is available at: http://www.who.int/occupational_health/en/

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