ENVIRONMENTAL RESEARCH **73,** 193–199 (1997)
ARTICLE NO. ER973744

Psychiatric Disorders among Egyptian Pesticide Applicators and Formulators[1]

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Received March 5, 1996

Two hundred eight pesticide formulators, 172 pesticide applicators, and 223 control subjects (72 from an urban region matching the pesticide formulators and 151 from a rural area matching the pesticide applicators) underwent psychiatric assessment. The study aimed to screen for psychiatric morbidity using a standardized screening tool, the General Health Questionnaire, and a widely recognized system of diagnosis and classification, the revised third edition of the *Diagnostic and Statistical Manual of Psychiatric Disorders* (DSM-III-R). Significantly higher frequencies of psychiatric disorders were found in the exposed groups. The predominant diagnosis was depressive neurosis; the most frequent symptoms were irritability and erectile dysfunction. Theoretical and practical implications of these findings are discussed.

INTRODUCTION

In Egypt, more than 120,000 subjects participate in the annual application of pesticides (carbamates, pyrethroids, and organophosphates, singly or in combination) in cotton fields. Application takes places three times each year (May, July, and September). Applicators are seasonally or permanently employed by local agriculture associations affiliated with the Ministry of Agriculture.

The health effects of pesticide usage remain a priority, particularly in developing countries. In Egypt, 10,000 to 60,000 tons of pesticides are annually used in agriculture or for public health reasons. Most are formulated locally in urban and rural areas. Safety measures are generally poorly applied, and workers lack proper knowledge or training in safe handling of these chemicals (Amr *et al.,* 1993).

Among the hazards of pesticide exposure, neurological changes have been repeatedly described (Johnson *et al.,* 1987, 1990; Devinsky *et al.,* 1992). Most of these studies, however, were mainly concerned with the effects of acute poisoning; those concerned with the effects of long-term exposure are still relatively limited. The assessment of psychiatric morbidity relative to chronic pesticide exposure is often limited to one of several neurobehavioral dimensions studied, e.g., Profile of Mood States (McNair *et al.,* l971), a subtest of the Neurobehavioral Core Test Battery, or the mere application of self-reported questionnaires, e.g., Beck Depression Inventory or Taylor Manifest Anxiety Scale (Rodnitizky *et al.,* 1978).

The aforementioned observations are quite surprising in view of the fact that evidence for postulating a cholinergic hypothesis of depression was originally derived from early studies in the 1960s on the psychological effects of a variety of cholinesterase inhibitors in man (Janowsky and Risch, 1987).

The General Health Questionnaire (GHQ) introduced by Goldberg (1972) is among the most widely used screening instruments designed to detect "hidden psychiatric illness" in community and primary care settings. Individuals are assessed for psychiatric "caseness"; some are assigned the label "cases" and others the label "noncases."

The scaled version of the GHQ (GHQ28) (Goldberg and Hillier, 1979) provides information on four dimensions of psychiatric morbidity: somatic symptoms, anxiety/insomnia, social dysfunction, and severe depression. The instrument has been extensively tested in various cultures and linguistic groups, generally yielding positive results (Koeter *et al.,* 1989). It has been used by other researchers in Egypt and has proven to be both suitable and fea-

[1] This work was supported by a fund from the International Development Research Center (IDRC), Canada, as a part of the Project of Pesticide Intoxication (Phases I and II) (1987–1997), supervised by M. M. Amr, Professor of Environmental Medicine and Occupational Diseases, Department of Occupational Medicine, Cairo University, Egypt.

0013-9351/97 $25.00

sible to use in the Egyptian culture (Okasha *et al.,* 1988). Furthermore, an attempt to validate it in Egyptian subjects has demonstrated adequate sensitivity and specificity (Amr *et al.,* 1994a).

Finally, the classification of psychiatric disorders has witnessed in the past decade a continuous and overwhelming movement toward the application of operational diagnostic criteria for diagnosis and classification to ensure adequate reliability of psychiatric diagnosis, as well as communication and comparison of research efforts. In this regard, the third edition of the *Diagnostic and Statistical Manual of Psychiatric Disorders* (DSM-III) (American Psychiatric Association, 1987) and its revised edition (DSM-III-R) (American Psychiatric Association, 1989) have become among the most widely used systems of classification.

This study aimed to screen for psychiatric morbidity among subjects involved in the seasonal application of pesticides using a standardized screening tool, the GHQ, and a widely recognized system of diagnosis and classification, the *DSM-III-R.*

SUBJECTS AND METHODS

The participants were a group of 208 pesticide formulators working in 2 different plants, 172 pesticide applicators, and 223 control subjects (72 from an urban textile factory who were matched with the pesticide formulators and 151 from a rural area who were matched with the pesticide applicators). The control subjects were chosen from the same communities as the exposed population and were matched for age and socioeconomic and educational levels. None of the control subjects had a prior history of direct exposure to pesticides, either at work or in the community.

The pesticide plants were formulating organochlorine, organophosphate, carbamate, synthetic pyrethroid, and other multipurpose chemical compounds. The randomly selected formulators were directly exposed to these chemicals for at least 40 hr per week for at least 9 months of the year for at least 2 consecutive years.

Pesticide applicators were randomly selected from workers involved in the annual application of pesticides (carbamates, pyrethroids, organophosphates, and organochlorines, singly or in combination) for at least 2 consecutive years at two large-scale "model farms" belonging to the Ministry of Agriculture.

All subjects were assessed in the field by two psychiatrists. One administered the GHQ and the other assigned the *DSM-III-R* diagnosis (if one was assigned).

Exposed and control subjects were compared for the following variables: (1) frequency of psychiatric disorders, (2) frequency of GHQ caseness, and (3) different GHQ dimensions.

Diagnoses were made in accordance with the *Diagnostic Manual of Psychiatric Disorders* (DMP-1), first edition (Egyptian Psychiatric Association, 1979). The comparisons were made using the χ^2 statistic in the case of the categorical data, and using the Student t test (two-tailed) in the case of the continuous data.

RESULTS

Frequencies of psychiatric disorders and symptoms in pesticide formulators and their matched control groups are shown in Table 1. Psychiatric disorders were significantly higher among pesticide formulators (50%) than in the control group (32%). Depressive neurosis was also significantly higher in the formulators (19.2%) than among the control group (6.9%).

Irritability and erectile dysfunction were significantly more frequent in the exposed group ($P < 0.01$ and $P < 0.001$, respectively). No significant differences were found for the other symptoms.

Pesticide formulators were classified to identify two groups with different durations of exposure: Group 1 was made up of those exposed for ⩽10 years

TABLE 1

Frequencies of Psychiatric Disorders and Symptoms among Pesticide Formulators and Matched Control Subjects

	Pesticide formulators (n = 208)		Control subjects (n = 72)	
	n	%	n	%
Psychiatric disorders				
Total psychiatric disorders	104	50**	23	32
Depressive neurosis	40	19.2*	5	6.9
Situational/reactive depression	40	19.2*	12	16.7
Erectile dysfunction	11	5.3	2	2.8
Other disorders	13	6.2	4	5.5
Symptoms				
Irritability	70	33.6**	10	13.2
Depressed mood	69	33.2	18	25
Insomnia	54	25.7	12	16.7
Erectile dysfunction	56	26.9***	3	4.2
Loss of interest	34	16.3	13	18
Headache	22	10.7	6	8.3

* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.

TABLE 2
Frequencies of Psychiatric Disorders and Symptoms in Pesticide Formulators with Different Durations of Exposure

	Group 1, ⩽ 10 years		Group 2, ⩾15 years		Group 3, ⩽5 years		Group 4, ⩾20 years	
	n	%	*n*	%	*n*	%	*n*	%
Psychiatric disorders								
No psychiatric disorders	53	58.9	41	42.3*	36	73.5	25	47.2**
Total psychiatric disorders	37	41.1	56	57.7*	13	26.5	28	52.8**
Depressive neurosis	12	13.3	30	30.9**	5	10.2	17	32.1**
Situational and reactive depression	15	16.7	16	16.5	6	12.2	8	15.1
Erectile dysfunction	4	4.4	4	4.12	1	2	1	1.9
Other disorders	6	6.7	6	6.2	1	2	2	3.8
Symptoms								
Irritability	20	22.2	44	45.4**	4	8.2	24	45.3***
Depressed mood	24	26.7	40	41.2*	9	18.4	21	39.6*
Insomnia	18	20	30	30.9	6	12.2	17	32.1*
Erectile dysfunction	16	17.8	34	35**	6	12.2	19	35.8**
Loss of interest	11	12.2	20	20.6	3	6.1	10	18.9
Headache	5	5.5	15	15.5*	1	2	7	13.2*

* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.

($n = 90$); group 2 consisted of those exposed for ⩾15 years ($n = 97$). Another classification was made to identify those exposed for ⩾20 years (group 3; $n = 53$) and those exposed for ⩽5 years (group 4; $n = 53$) (Table 2). Comparisons of groups 3 and 4, representing the extremes of exposure durations, showed that the frequency of psychiatric disorders was significantly greater in group 4 than in group 3.

Table 3 shows the frequency of psychiatric disorders, in general, and the frequency of dysthymic disorder, in particular, among the pesticide applicators and their matched control subjects. (Dysthymic disorder is a chronic depressive state lasting 2 or more years that is associated with at least two of the following symptoms: poor appetite, insomnia, low energy or fatigue, low self-esteem, poor concentration, and feelings of hopelessness [American Psychological Association, 1987].) Psychiatric disorders were significantly higher in applicators (30.7 and 23.8%, respectively) than in control subjects (17.2 and 14.6%, respectively).

TABLE 3
Frequency of Psychiatric Disorders in Pesticide Applicators and Control Subjects

	Pesticide applicators ($n = 172$)		Control subjects ($n = 151$)	
Psychiatric disorders	*n*	%	*n*	%
Total psychiatric disorders	53	30.7**	26	17.2
Dysthymic disorder	41	23.8*	22	14.6
Adjustment disorder	12	6.9	4	2.6

* $P < 0.05$.
** $P < 0.005$.

Table 4 shows that the frequency of GHQ cases was significantly higher ($P < 0.001$) in the exposed subjects (64.9%) than in control subjects (35.1%).

The scores of pesticide applicators and their matched control subjects on different GHQ dimensions are shown in Table 5. The applicators scored significantly higher than control subjects on all dimensions. Similar results were found for the GHQ total score.

DISCUSSION

The results showed a significant increase in the frequency of psychiatric disorders in pesticide-exposed applicators and formulators compared with

TABLE 4
Frequency of GHQ Cases in Pesticide Applicators and Matched Control Subjects

	Pesticide applicators ($n = 172$)		Control subjects ($n = 151$)	
GHQ cases	*n*	%	*n*	%
Noncase	78	45.3	98	64.9
Case	94	54.7	53	35.1

Note. $\chi^2 = 12.7$; $G = 12.9$; $P < 0.001$.

TABLE 5
GHQ Dimensions in Pesticide Applicators and Matched Control Subjects

GHQ dimension	Pesticide applicators (n = 172), mean ± SD	Control subjects (n = 151), mean ± SD	Statistical significance	
			t	P
Somatic symptoms	2.54 ± 1.72	2.29 ± 1.98	3.47	<0.001
Anxiety and insomnia	2.24 ± 1.47	1.47 ± 2.0	3.11	<0.01
Social dysfunction	1.19 ± 1.67	0.68 ± 1.52	2.87	<0.01
Severe depression	0.93 ± 1.53	0.46 ± 0.13	33.13	<0.0001
GHQ total score	6.99 ± 6.34	4.19 ± 5.43	4.11	<0.0001

controls. This parallels the results of other studies indicating that neurobehavioral impairments were only detectable in workers with long-term or high-dose exposure (Spurgeon *et al.,* 1992; Rasmussen *et al.,* 1993).

However, certain methodologic issues must be considered. First, this series consisted only of applicators and formulators, who are heavily and continuously exposed. Thus, the generalizability of the findings must be recognized as being limited to a special group of subjects. In other words, the findings do not necessarily apply to other high-risk populations or under different exposure conditions. Second, the study investigators were actively looking for psychiatric morbidity and therefore might have overdiagnosed the condition of interest. Third, subjects were assessed using an open clinical interview and diagnoses were made according to a local system of classification. This made communication of results quite difficult and the screening procedure less standardized.

Nevertheless, this study has important implications. Regarding individual clinical disorders, the high frequency of depressive neurosis in exposed subjects—with frequency differences being more pronounced when long-term exposure subjects were isolated—contrasts with the frequency of situational and reactive depression, which was nearly equal in all groups studied. Although both disorders are depressive, they are clinically distinct subtypes.

Situational and reactive depression develops as a direct result of a causative stress that determines its onset and course (acute or chronic). It is always related to the persistence of the causative stressor(s) or situation (s) (Egyptian Psychiatric Association, 1979). In this study, subjects developing depressive reactions in response to a variety of stressors (financial, marital, physical illness, work, etc.) were included in this category. On the other hand, depressive neurosis is usually chronic, of mild or moderate severity, with no apparent precipitating or causative factor. It is characterized by a mood of unhappiness, inability to cope with day-to-day affairs, lack of energy, excessive fatigue, insomnia, and lack of concentration (Egyptian Psychiatric Association, 1979).

Thus, it seems that chronic exposure to pesticides might be associated with a specific qualitatively distinct subtype of depression (depressive neurosis), as well as increased frequency of insomnia and depression, particularly with long exposure. This suggestion is reinforced by early studies in the 1950s and 1960s (Rowntree *et al.,* 1950; Bowers *et al.,* 1964) showing that exposure to cholinesterase inhibitors (di-isopropyl fluorophosphate, organophosphorus insecticides, and others) was associated with symptoms reminiscent of depressive neurosis (depressed mood, lethargy, insomnia, and lack of concentration).

The potential relationship between pesticides exposure and depressive neurosis is quite interesting in view of the literature implicating cholinergic hyperactivity in the etiology of depression (Janowsky *et al.,* 1972), in which depression was postulated to represent a disease of relative cholinergic predominance (Janowsky and Risch, 1987). From this perspective, the high frequency of depressive neurosis, as well as depressed mood and insomnia in the sample as a whole, specifically in subjects exposed for 20 years or more, could be attributed to the cholinomimetic properties of pesticides. Such conjecture is supported by studies of the psychological and electroencephalographic effects of organophosphate exposure that demonstrated depression, increased arousal, and enhanced rapid eye movement during sleep (Metcalf and Holmes, 1969; Duffy *et al.,* 1979; Duffy and Burchfield, 1980), effects similar to those induced by the cholinomimetic agent physostigmine (Reynolds *et al.,* 1987).

It would be worthwhile for future studies to explore the association between depressive neurosis, depressive mood, and insomnia and cholinesterase levels, as well as the response to anticholinergic agents. Such approaches require consideration of the role of possible confounding variables, such as the stress of being subjected to potential hazards of pesticides, which may precipitate fear of poisoning or depressive reactions.

Irritability was one of the most frequent symptoms observed in exposed subjects; its frequency was higher with longer exposure. This finding is supported by other studies in which irritability was a frequently reported symptom, especially in persons having long-term solvent exposure (Hogstedt *et al.,* 1984; Fidler *et al.,* 1987). The high frequency of ir-

ritability is also quite important in view of the recent suggestion that enhanced activation of hypothalamic cholinergic receptors may underlie aggressive behavior in humans exposed to cholinesterase inhibitors (Devinsky *et al.,* l992). This hypothesis was based on case reports of unprovoked aggressive behavior following exposure to pesticides in the community (Devinsky *et al.,* l992) and well-controlled experimentation in animals (Smith *et al.,* 1970).

Erectile dysfunction, whose frequency was significantly higher in the exposed group, may have both organic and psychological causes. An organic etiology is suggested by the possible association between pesticides exposure and neuropathy (Johnson, 1982; Lotti, 1986). Alternatively, erectile dysfunction might be associated with decreased sexual desire that is part of a depressive state.

CONCLUSION

In this study, increased psychiatric morbidity was found in pesticide applicators and formulators compared with control subjects. This was illustrated by the high frequency of clinical psychiatric disorders and GHQ cases, as well as by the higher scores on all GHQ dimensions. This replicates our previous findings in a study of pesticide manufacturers (Amr *et al.,* 1994b); however, in this study, more standardized methodologic tools were applied.

The frequency of dysthymic disorder was significantly higher in the exposed group than in control subjects. Furthermore, the prevalence of dysthymic disorder in the exposed group is strikingly higher than in the Egyptian urban community (4.1%) (Okasha *et al.,* 1988). Such a finding supports the hypothesis that pesticide exposure might be associated with a distinct depressive state that is qualitatively different from other forms of depression (Amr *et al.,* 1994b).

Early studies of the neuropsychiatric effects of cholinomimetic drugs demonstrated that exposure to such agents was associated with depressive symptomatology (depressive mood, lethargy, insomnia, and lack of concentration (Rowntree *et al.,* 1950). These observations led to the hypothesis that cholinergic hyperactivity might underlie depressive states (Janowsky and Risch, 1987). Our findings concerning dysthymic disorder make it worthwhile to pursue additional efforts to test such a hypothesis in pesticide-exposed subjects using objective biological monitors of cholinergic activity. The potential fruitfulness of such an approach is further supported by the finding that exposed subjects scored higher than control subjects on the "severe depression" subscale of the GHQ.

The increased frequency of GHQ "cases" detected in the exposed group parallels the increased frequency of psychiatric disorders diagnosed using *DSM-III-R*. These findings have important methodologic implications, especially in research involving neuropsychological batteries because performance on these batteries may be confounded by the subject's psychological state (Walsh, 1978). Additional studies are needed to explore this potential effect. Furthermore, because a worker's psychological health influences work duration and production, our findings with the GHQ suggest that screening for psychiatric morbidity is worthwhile and should be implemented in workplace settings. This suggestion is also supported by the high scores of exposed subjects on the social dysfunction subscale, which comprises items concerned with "satisfaction with task," "not doing things well," and others.

Our study showed significant differences between exposed subjects and controls on the somatization subscale of the GHQ. In fact, the highest t values were obtained on this subscale. This finding is in agreement with the high frequency of dysthymic disorder found in this study's sample. In fact, transcultural studies comparing Egyptian and Western depressives (Okasha *et al.,* 1988; Gawad and Arafa, 1980) showed a higher frequency of somatic symptoms in Egyptian depressives and implicated the cultural concept of disease, that is, Egyptian patients do not verbalize their mood or translate their feelings into body language. They mask depressed mood with multiple somatic symptoms that occupy the foreground, while the emotional component recedes into the background. From their perspective, it is more socially acceptable and culturally appropriate to have physical rather than "psychological" symptoms. Similar observations have been made in other transcultural studies (Binitie, 1975; Kleinman, 1977; Katon *et al.,* 1982), that is, that the predominant communication of affective distress such as depression in many cultures is via somatic terminology, particularly in non-Western societies. This has led to the recent introduction of the term "somatothymia" to describe the phenomenon of utilizing somatic language to communicate psychological distress (Stoudemire, l991).

This issue is worthy of emphasis for several reasons. For example, regarding neurobehavioral assessment methods and their application in developing countries, especially in the case of self-report questionnaires or other psychometric tools, Okasha *et al.* (1988) found that the Beck Depression Inventory was less sensitive than the GHQ in detecting depressive states in the general community. He ar-

gued that this might be explained by false-negative answers to items relying on the subject's ability to verbalize his or her emotional state. In addition, a tendency toward somatization may make the results of studies focusing on subjective physical complaints difficult to interpret. That was the case in this study of pesticide formulators and applicators, in which headache and erectile dysfunction were among the most frequent symptoms (Amr *et al.,* 1994b).

Furthermore, in Egypt, where community psychiatric services are limited, most subjects who somatize psychological distress present to general practitioners or primary health care physicians. As a result, they run the risk of undergoing unnecessary investigations and of receiving inappropriate medication. In fact, almost all of the psychiatric cases in our sample were neither recognized nor detected except within the context of the study.

It is important to emphasize that the subscales of the GHQ represent dimensions of symptomatology and do not necessarily correspond to categorical psychiatric diagnoses. Such a dimensional approach in psychiatric assessment would be more informative in neurobehavioral assessment because it is presumably more sensitive in detecting early or mild subclinical psychiatric morbidity. The dimensional model, therefore, would be more appropriate in future studies, especially because it was recently hypothesized that subjective symptoms might be the earliest indicators of adverse exposure effects (Iregren and Gamberale, 1990). If this is the case, early detection of subtle psychological deficit would prevent further complications.

However, the use of the GHQ subscales (factors) does not necessarily mean that the factor structure in this series was the same as that in the population from which the questionnaire was developed. Therefore, additional studies attempting to identify the factor structure of pesticide-exposed populations are needed.

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