Occupational exposure to lindane: clinical and laboratory findings

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The use of organochlorine pesticides is being restricted owing to their relative persistence in the animal ecology. In Hungary only γ-hexachlorocyclohexane, lindane, is used in any quantity. The accumulation and the effects of such accumulation in man have not been investigated much. This is because of the analytical methods employed for the isolation and estimation of lindane in human blood and tissues. Methods used to measure other organochlorine insecticides are not always suitable for lindane.

It has been known for some time that lindane is eliminated more rapidly from animals than are other organochlorine pesticides (Woodard, Davidow, and Lehman, 1948; Asperen and Oppenoor, 1954; Koransky and Portig, 1963), but information about its pharmacokinetics in man is lacking. Small concentrations have been measured in adipose tissue and in blood in the general human population (Hayes, Dale, and LaBreton, 1963; Cieleszky and Czeglédi-Jankó, 1967; Dale, Curley, and Hayes, 1967; Laws, Curley, and Biros, 1967; Engst, Knoll, and Nickel, 1967). In Hungary, the concentrations found in the whole blood of 170 members of the general population ranged from 0·004 to 0·035 ppm (Czeglédi-Jankó, 1969).

In occupational medicine and in animal experiments, overexposures have been followed by neurological disturbances (Dallemagne and Philippot, 1948; Schützmann, 1964; Boyd and Chen, 1968; Major, Dési, Kertai, and Makara, 1968), but no attempts have been made to associate clinical symptoms and electroencephalographic examination (EEG) with the lindane concentrations found in blood. We present here an account of such an investigation.

Subjects and methods

Thirty-seven men working in a fertilizer plant were examined. In the plant sufficient lindane was added to the fertilizer so that the final product contained 1·5% lindane. Industrial hygiene measures were good, but occasionally some workers neglected them.

The examination of each man included a neurological history and examination, EEG, and a whole blood sample. In the assessment of the clinical symptoms, the degrees of abnormality were marked as 0, no changes; +, minor symptoms and signs; ++, more serious symptoms, such as muscular jerking and myoclonia with emotional changes. Similarly, the EEG was graded as 0, no changes; +, increased variation in the frequency and amplitude of wave pattern; and ++, more serious changes without specific EEG signs. The EEGs were recorded with an 8-channel BOM-machine.

The concentration of lindane in 5 ml of whole blood was determined by gas-liquid chromatography using an electron capture detector as described by Czeglédi-Jankó and Cieleszky (1968). The concentrations of lindane in the whole blood of 20 non-occupationally exposed persons were measured as controls.

At the time of examination lindane was the only toxic agent in the plant. Twenty-two of the men had been exposed to aldrin two years previously, and three of
these had had acute poisoning followed by epileptic fits and another three had signs of serious EEG disturbance. There had been no sequelae on ceasing exposure to aldrin.

The concentrations of lindane in whole blood of the 20 members of the general population are shown in Table 1. The highest concentration found was 0.017 ppm. None of these people had any clinical symptoms.

Table 2 shows the findings in the 37 exposed workers. The subjects are listed in order of decreasing concentrations of lindane in whole blood. The data on aldrin exposure two years previously are also shown in Table 2. The concentrations of DDT-derived material in the blood of these men were measured and found to be within the range of members of the general population of Hungary (pp'-DDT 0.008 to 0.072 ppm and pp'-DDE 0.009 to 0.060 ppm).

**TABLE 1**

**LEVEL OF LINDANE IN BLOOD OF GENERAL POPULATION OF BUDAPEST, FEBRUARY 1969**

<table>
<thead>
<tr>
<th>No. of samples</th>
<th>Lindane (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Mean value</td>
<td>0.008</td>
</tr>
<tr>
<td>Range</td>
<td>0.003-0.017</td>
</tr>
<tr>
<td>SE</td>
<td>0.00084</td>
</tr>
</tbody>
</table>

**TABLE 2**

**DURATION OF EXPOSURE, SYMPTOMS AND CONCENTRATIONS OF LINDANE IN WHOLE BLOOD: 37 MEN EXPOSED TO LINDANE IN A MANUFACTURING PLANT IN 1969, AND HISTORY OF PREVIOUS ALDRIN EXPOSURE**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (yr)</th>
<th>Total exposure (yr)</th>
<th>1969 Lindane exposure</th>
<th>1969 Aldrin exposure</th>
<th>EEG before exposure to pesticides</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Conc. lindane in whole blood (ppm)</td>
<td>Conc. lindane in whole blood (ppm)</td>
<td>Clinical symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.000-0.008</td>
<td>0.000-0.008</td>
<td>0.000-0.008</td>
</tr>
</tbody>
</table>

1History of grand mal attack.
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Discussion

It can be seen, in Table 2, that in half of the workers exposed to lindane the concentrations of lindane in whole blood were within the range found for the control group. These men respected the rules of occupational hygiene. On the other hand, those with most symptoms may be those with the largest amounts of lindane in their blood, because they are poor workmen, hygienically, and this is borne out to some extent by the fact that the most careless workman had the highest concentration of lindane (0.340 ppm) in the blood.

It is apparent that the number of men with
clinical symptoms and EEG changes increases when the concentrations of lindane in whole blood are above 0-02 ppm. A threshold value for the occurrence of symptoms on exposure to lindane would account for these findings in subjects with constant exposure to lindane.

The EEG changes observed fall within the range of non-specific abnormalities. Published data indicate that abnormalities of the same type and degree occur in 10 to 20% of the general population with no clinical symptoms. What is of interest from the present study is that, at concentrations of lindane in whole blood greater than 0-02 ppm, such abnormalities were observed in 15 out of 17 cases. The responsibility of lindane for these EEG abnormalities receives further support from the fact that the EEG records of seven men taken before exposure were normal.

Over-exposure to aldrin more than two years earlier had led to clinical evidence of acute poisoning. The past history of these workers was compared with the present but, as can be seen in Table 2, no evidence that the two occupational exposures and their sequelae were related was forthcoming.

Differences in the clinical symptoms and EEG abnormalities caused by aldrin (dieldrin) and lindane are noteworthy. In some men exposed to aldrin and with a concentration of HEOD in whole blood of 0.1 to 0.2 ppm the clinical symptoms are grave and the subjects will often develop epileptic convulsions (Kazantzis, McLaughlin, and Prior, 1964; Avar and Czegledi-Jankó, 1970). For exposure to lindane, the clinical symptoms and EEG abnormalities were less marked but could be observed even when the concentration of lindane in whole blood was only 0-02 ppm.

A concentration of 0-02 ppm lindane in whole blood is close to the upper values in the 20 members of the control group. In fact, among the 170 members of the general population examined in 1967/68 in Hungary, there were some persons with concentrations of lindane in whole blood higher than 0-02 ppm. It is still not clear how to relate the concentrations of lindane in whole blood in the general population with an environmental exposure to those of workmen with permanent occupational exposure. Since the pharmacokinetics of lindane in man are unknown, little further can be deduced from the findings other than to repeat that in the detection and measurement of lindane in whole blood we have a most useful opportunity to survey populations.

When the concentration exceeds 0-02 ppm, symptoms may be evident and the pharmacodynamic effects of the lindane present in the human organism may be very real, at least in so far as persons living in constant over-exposure to lindane are concerned.

Our investigations demonstrate that the concentration of lindane in whole blood of exposed workers should be checked constantly, but this is also an important public health problem in countries where the concentrations of lindane found in the blood of the general population are raised.

References