PRELIMINARY REPORT ON EXPERIMENTAL STUDIES IN HERBICIDE CANCEROGENESIS

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Communication presented by the Ordinary Academician Prof. G. Cavallo at the meeting of 14th March 1980

SUMMARY: Short-term results of an experimental study in herbicide cancerogenesis are reported. Dichlobenil (2,6-bischlorobenzonitrile) produces tumours (hepatocellular carcinoma, mesothelioma, liposarcoma and lymphoma) by both subcutaneous and intraperitoneal inoculations of low doses (2 parts per million) in Swiss whitish mice.

RÉSUMÉ: On vient de presenter les résultats préliminaires d'une expérimentation conduite sur le souris avec dichlobenil (2,6-bischlorobenzonitrile). La substance produit des tumeurs (carcinome de la foie, mésothéliomes, liposarcomes et lymphomas) avec injection souscutanée et intraperitoneal avec une très petite dose (2 parts par million) dans le souris albino Swiss.

Several present epidemiological and experimental studies in Canada, Sweden and U.S.A. (1) investigate cancer hazard due to exposure to herbicide, after some reports pointed out that amitrole (2), phenoxyacids (3) and chlorophenols (4) are carcinogenic.

An increased incidence rate of tumours of the mesoderm (primary tumours of the pleura, pericardium, peritoneum, tunica vaginalis of the testis and surface mesothelium of the ovary) has been found among people living in the countryside of Alessandria and it seemed pertinent, therefore, to examine cause-effect relationships between cancer and exposure to the most largely used herbicides in our district.

Their active principles are the following: dichlobenil (2, 6-bischlorobenzonitrile), atrazine (2-chloro-4-ethylamino-6-isopropyl-amino-s-

triazine), simazine [2-chloro-4,6-bis (ethylamino)-1,3,5-triazine] and triphluralin [N,N-bis (N-propyl)-2,6-bis-nitro-4-trifluoromethyl-aniline].

Dichlobenil that was the first tested chemical substance is used as selective herbicide of vineyards and as common herbicide of playgrounds, edges of roads, railways, avenues, ditches and industrial areas.

Preliminary results of our experimental investigation which is still being carried out are reported.

MATERIAL AND METHODS

2 mg. of dichlobenil were suspended in 1000 ml. of saline.

A group of 50 Swiss whitish mice was treated with subcutaneous inoculations of 0.25 ml. of suspension at 3-day intervals for 13 times.

A group of 50 Swiss whitish mice was treated with intraperitoneal inoculations of 0.25 ml. of suspension at 3-day intervals for 13 times.

An untreated group of 200 animals was used as control.

Animals were kept for 4 months after exposure. 2 animals from each group were deliberately killed at 15-day intervals beginning from the first month after axposure had ended.

19 spontaneous deaths were registered in the group treated with subcutaneous inoculation, the first one at the 45th day after the first injection.

7 spontaneous deaths were registered in the group treated with intraperitoneal inoculations, the first one at the 45th day after the first injection.

3 animals in the control group have died of cannibalism.

RESULTS

Morphological lesions induced by subcutaneous inoculations of dichlobenil are presented in table 1 and figure 1.

Table 1:

Morphological lesions	Number of animals
Hepatocellular carcinoma	3 (6%)
Atypical liver regeneration	4
Diffuse hyperplasia of perihepatic mesothelium	4
Liver vascular ectasias	6
Hyperplasia of the lymphoid tissue in lymph nodes draining the site of inoculation (left thigh)	50

Morphological lesions induced by intraperitoneal inoculations of dichlobenil are presented in table 2 and figures 2, 3 and 4.

Table 2:

Morphological lesions	Number of animals
Mesothelioma *	6 (12%)
Atypical mesothelial hyperplasia	8
Liposarcoma of the mesentery	1 (2%)
Undifferentiated large cells lymphoma in mesenteric lymph nodes	2 (4%)
Liver vascular ectasias	5

* hyperplasia of endothelium lining mesenteric lymphatic vessels was observed in all cases of mesothelioma and one case was suggestive of lymphatic spread of neoplastic mesothelial cells.

All the tumours were found after 50-70 days from the beginning of exposure to dichlobenil.

No tumour was found in the control group.

CONCLUSIONS

Data presented in tables 1 and 2 suggest that dichlobenil might be carcinogenic as it produces tumours in experimental animals in both the site of inoculations (peritoneal cavity) or liver where it probably concentrates after subcutaneous injections in order to be metabolized.

The aim of our future study will be to determine if dichlobenil is carcinogenic when mice are given by drinking water.

REFERENCES

1) MUIR C.S. & WAGNER G. (eds.): Directory of On-going Research in Cancer Epi demiology. IARC Pubblications No. 28, Lyon 1979.
2) AXELSON O. & SUNDEL L.: Work Environ. Health *11*, 21, 1974.
3) AXELSON O.: Scand. J., Work Environ. Health *4*, 85, 1978
4) HARDELL L. Q.: Laekartidnignen *75*, 3535, 1978.