

Revisiones**Occupational exposure to chlorinated hydrocarbons and pancreatic cancer: review of recent literature****Exposición laboral a hidrocarburos clorados y cáncer de páncreas: revisión de la bibliografía reciente****Shirley Luna-Sánchez^{1,4,5}, María Ruth Lobeto Martínez^{2,4,5}****Collaborator: Jeny Soledad Garay Muñoz^{3,4,5}**

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Abstract

The proportion of pancreatic cancer that can be attributed to occupational exposures is about 12 %, although that is a small percentage, these factors can be prevented and it is important to identify them. Some occupations have been associated with an increased risk of pancreatic cancer, and these apparently have a statistically significant association for exposure to organochlorine or chlorinated hydrocarbons. Objective: To review the recent scientific literature looking for evidence on the relationship between occupational exposure to organochlorines and pancreatic cancer. Methods: A search was conducted in major databases using related descriptors and applying relevance, inclusion and exclusion criteria; finally we selected 10 articles. Results: Three meta- analysis, three cohort studies and four case-control studies were analyzed, finding more bibliographic production between the 2000-2003 and 2007-2011 periods. Conclusions: Some exposures have been associated with increased risk for pancreatic cancer, but in most studies the effect is weak or moderate, often associated with the limited number of participants. Studies that investigate the association by type of occupation do not usually determine specific agents to which the worker is exposed, making it difficult to establish specific associations. It is important to continue studying gene-environment interactions related to the association with K-ras gene in search of more conclusive results that advance the field of prevention of occupational hazards.

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Resumen

La proporción de cáncer de páncreas que puede atribuirse a exposiciones laborales es aproximadamente 12%, aunque representan un pequeño porcentaje, estos factores pueden ser prevenibles, siendo importante identificarlos. Algunas ocupaciones se han relacionado con el aumento de riesgo de cáncer de páncreas, y al

parecer habría una asociación estadísticamente significativa para la exposición a hidrocarburos clorados u organoclorados. Objetivo: Revisar la literatura científica reciente, buscando evidencias sobre la relación entre la exposición laboral a organoclorados y cáncer de páncreas. Metodología: Se realizó una búsqueda en las principales bases de datos utilizando descriptores relacionados y aplicando criterios de pertinencia, inclusión y exclusión seleccionándose 10 artículos. Resultados: Se analizaron tres meta-análisis, tres estudios de cohortes y cuatro estudios de casos y controles, encontrando una mayor producción bibliográfica entre los períodos 2000-2003 y 2007-2011. Conclusiones: Algunas exposiciones se han relacionado con el exceso de riesgo para el cáncer pancreático, sin embargo en la mayoría de estudios se encuentra un efecto débil o moderado a menudo relacionado con la limitada cantidad de participantes. Los estudios que investigan esta asociación por tipo de ocupación no suelen precisar los agentes específicos a los que se encuentra expuesto el trabajador, dificultando establecer asociaciones concretas. Es importante seguir estudiando las interacciones genético-ambientales relacionadas como la asociación con el gen K-ras en busca de resultados más concluyentes que permitan avanzar en el campo de la prevención de riesgos laborales.

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Palabras clave: *Exposición Profesional, Hidrocarburos Clorados, Neoplasias Pancreáticas.*

INTRODUCTION

More than a quarter of a million people are estimated to die of pancreatic cancer worldwide each year, and the incidence is predicted to increase in the future. This appears to be associated with tobacco consumption and obesity, which may be modifiable risk factors, although there may be other factors concerning which there is no proven evidence that should be studied in order to also act on them. The high lethality of exocrine pancreatic cancer further underscores the need to identify risk factors suitable for primary prevention¹⁻³.

The highest incidence and mortality rates of pancreatic cancer are found in developed countries,³ the disease is rare in people under the age of 45, but the incidence increases rapidly thereafter.

Cigarette smoking is the most established risk factor for pancreatic cancer^{2,3,4,6} but only about 25% of the newly diagnosed cases can be attributed to smoking⁴. Factors that probably cause moderate increase in risk include age, diabetes, chronic pancreatitis and obesity^{2,3,7}. Mutation in the K-ras gene is the most common genetic alteration in pancreatic cancer^{8,9} and this is the human tumor with the highest prevalence of K-ras mutations⁹. Other factors are the p53 tumor suppressor genes, p16, FHIT, polymorphisms in genes encoding enzymes that metabolize some of the potentially carcinogenic agents for pancreas as CYP families NAT and GST polymorphisms and genes involved in the repair of DNA¹⁰.

The proportion of pancreatic cancer that may be attributable to occupational exposures has been estimated to be 12%, although represent a small percentage, occupational risk factors are largely preventable, and thus is important to identify and eliminate them⁴.

According to the literature, there is a statistically significant association between exposure to chlorinated hydrocarbons (organochlorines) and pancreatic cancer.^{3,4} traditionally occupations that have been associated with increased risk of pancreatic cancer include: printing and paper manufacturing, chemical, petroleum and rubber industries, transport, dry cleaning, leather tanning, transformer manufacturing plants, the production of pesticides, mechanic and metallurgical occupations, as well as miners, shotfires, stone cutters and carvers, machinery mechanics and fitters, building trades workers and motor vehicle drivers in men, office clerks in women and waiters in both sexes^{1,3,7,10,11}. Other specific agents that might increase exocrine pancreatic cancer risk include asbestos and ionizing radiations^{3,10,12}. Recently, some studies have tried to relate risk occupations, the type and amount of toxic, associated with the development of pancreatic cancer.

Chlorinated hydrocarbons solvents are probably the exposure that has been most consistently associated with pancreatic cancer³. These are a diverse group of organic molecules used in a variety of applications and products, such as solvents, pesticides, and plastics.⁴ Chlorinated hydrocarbons were used widely in agriculture and pest control between the 1940s and 1960s throughout. Due to reported health concerns and persistence in the environment, its use has been restricted. The organochlorine compound DDT was banned in the USA in 1972 and worldwide for agricultural use in 2004, although it is still used limitedly in vector control and agriculture in some countries such as India and North Korea⁴. Until the beginning of the last decade, in Egypt there was reported detection in environmental DDT and other organochlorine pesticides¹¹.

During the 1960s, it became clear that the persistent use of pesticides had a negative impact on the environment. This led to develop epidemiological studies exploring the possible impact of these exposures on human health.

Occupational exposure to chlorinated hydrocarbons may occur in different industries for a variety of agents, as in the rubber and plastic production, chemical manufacturing, pharmaceutical industry, metal industry, dry cleaning, paint removal and laboratories¹⁵.

Chlorinated hydrocarbons and related compounds cover a variety of chemicals with industrial and research applications¹³:

- Trichloromethane (chloroform) and tetrachloromethane (carbon tetrachloride):
 - Applied mainly as laboratory solvents.
 - Are Group 2B⁺ carcinogens (possibly carcinogenic to humans).
- Trichloroethylene, tetrachloroethylene (perchloroethylene) and 1,1,1-trichloroethane:
 - Used mainly in dry cleaning and metal degreasing.
 - Are Group 2A⁺ carcinogens (probably carcinogenic to humans).
- Dichloromethane (methylene chloride):
 - Applied in metal degreasing and paint removal.
- Chloroethylene, better known as vinyl chloride:
 - Vinyl monomer used in the manufacture of plastics,
 - Is a Group 1⁺ carcinogen (carcinogenic to humans).
- Polychlorinated biphenyls (PCBs).
 - Have been used in the manufacturing of electric capacitors and transformers.
 - Are Group 2A⁺ carcinogens (probably carcinogenic to humans).

+ In the Classification of the International Agency for Research on Cancer (IARC).

Our objective is to review the recent scientific literature looking for evidence on the relationship between occupational exposure to organochlorines and pancreatic cancer, as well as to identify whether there are differences in the frequency of age and sex, frequency variations in relation to geographical distribution and describe what occupations have the highest risk of developing pancreatic cancer.

METHODOLOGY

We search on the main bibliographic databases in the health field, especially of occupational medicine, including selected MEDLINE (by PubMed), LILACS, SCiELO, CISDOC, Spanish Bibliographic Index of Health Sciences (IBECS), OSH UPDATE and SCOPUS.

To set the search strategy the following DECS-MeSH descriptors were used: *Pancreatic Neoplasms* (Spanish: *Neoplasias Pancreáticas*), *Hydrocarbons, Chlorinated* (Spanish: *Hidrocarburos Clorados*), *Occupational Exposure* (Spanish: *Exposición Profesional*), *Pesticides* (Spanish: *Plaguicidas*).

A total of 80 articles were obtained, that after removing duplicates had resulted in a collection of 48 articles, which was narrowed down using the criteria of relevance, inclusion and exclusion previously established. After the first screening, 11 articles that met the criteria for the study were obtained, most were obtained through PubMed, SCOPUS and LILACS; of these 11 articles, 2 corresponded to review articles, so they were not included in the assessment study results, although they have taken into account in the preparation of the sections of introduction, discussion and conclusions. An article from the literature of one of the review articles was then added. Finally 10 items for review were selected (Table 1).

Table I. Search Results

Database	Number of found articles	Number of selected articles*
MEDLINE (PubMed)	48	9
IBECs (BVS)	0	0
LILACS (BVS)	15	3
SCIELO	0	0
OSH UPDATE	0	0
CISDOC	0	0
COCHRANE LIBRARY	0	0
SCOPUS	17	4

* After removing duplicates, relevant analysis and applying inclusion and exclusion criteria.

Selection of items:

The first selection of articles was obtained based on the review of their summaries, according to criteria of relevance performed. We applied the following inclusion and exclusion criteria:

Inclusion criteria:

- Studies performed on the human population.
- Essays, experimental studies, meta-analysis, systematic reviews, cohort studies, case-control studies, cross-sectional observational studies.
- Period from January 1, 2000 and January 20, 2014.
- Publications aimed at studying the relationship between pancreatic cancer and occupational exposure.
- Exposure to organochlorines.
- Studies published in English and Spanish.
- National and international studies.

Exclusion criteria:

- Items related to pancreatic cancer with occupational exposure to other chemicals.
 - Studies that do not specified agent occupational exposure.
 - Redundant items.
 - Studies in the general population.
 - Ecological studies.
- Exposure to chlorinated hydrocarbons in relation to other types of cancer.

RESULTS

The articles included in our review are three meta-analyses, three cohort studies and 4 case-control studies; there has been an increase in literature published from 2000 to 2003 and from 2007 to 2011 periods.

Main Findings

Bosch de Basea et al. (2011)¹ state the need to relate occupational exposures with toxic serum levels, which had not been done so far in relation to the risk of this cancer. It is based on data from occupational exposure to chlorinated hydrocarbons and lifestyle of 135 patients with pancreatic cancer. Participants were asked if they had ever worked in any of 10 activities previously defined to be potentially related to pancreatic cancer.

These included pesticide use, handling of petroleum derivatives, the chemical industry, graphic arts, jewelry, manufacture or repair of automobiles, leather tanning and the textile industry. Median serum concentrations of all three PCB congeners (PCBs 138, 153 and 180) were significantly higher in patients whose last occupation was included in ISCO group 7 (Spanish version of International Standard of Occupations 1988): craftsman and related trade workers in manufacturing, construction and mining. Having worked in agriculture did not influence serum concentrations of organochlorines, which was a novelty, since previous studies had linked with the development of pancreatic cancer. The authors suggest the possibility and highlight the usefulness of conducting a case-control study, in which the control group did not develop pancreatic cancer, though they have been exposed to organochlorines, to show the evidence of exposure to these and the risk to development of pancreatic cancer.

Santibañez et al. (2010)³ found that cases with ductal adenocarcinomas were more likely to have been exposed to chlorinated hydrocarbon solvents. The results support the hypothesis of an association between occupational exposure to chlorinated hydrocarbon solvents and pancreatic cancer risk. The study shows that an increased risk of pancreatic cancer was associated with having worked as miners, shotfirers, stone cutters, carvers, machinery mechanics, fitters, building trades workers and motor vehicle drivers in men, office clerks in women and waiters in both sexes.

Andreotti et al. (2009)¹⁴ evaluated the weighted intensity of exposure to thirteen pesticides, and found statistically significant association in exposure-response in relation to pancreatic cancer with two herbicides (EPTC and pendimethalin). Use of DDT was inversely associated with pancreatic cancer risk.

Ojajärvi et al. (2007)² found from 261 studies that the highest MRR (meta-relative risk) is associated with exposure to chlorinated hydrocarbon compounds, concluding that this occupational exposure may increase the risk of pancreatic cancer. In relation to the types of work, increased risk was found on laundry, dry cleaning, metal plating, painting and printing workers, exposed to these agents.

Cocco et al. (2005)¹⁵ conducted a study of mortality from 4,552 workers exposed to DDT during antimalarial operations in Sardinia, Italy from 1946 to 1950. No differences in risk between the exposed group and unexposed were found.

Beard et al. (2003)¹⁶ found a higher mortality rate for pancreatic cancer in subjects exposed to DDT. This study finds a causal association between exposure to DDT and pancreatic cancer, and these results are consistent with the most of previous studies.

Alguacil et al. (2002)⁹ analysed the relationship between past occupational exposure to hydrocarbon solvents and mutations in codon 12 of the K-ras gene in incident cases of pancreatic cancer using a case-control study. Statistical analysis results suggest that subjects exposed to organochlorines had a mutation of k-ras gene, which could have been a trigger in the onset of their pancreatic cancer, this was the main conclusion and it opened a new field of research in this regard because it is the first and only study on occupational exposures and K-ras activation in pancreatic cancer.

Ojajärvi et al. (2001)¹³ conducted a meta-analysis of occupational exposures to chlorinated hydrocarbons and pancreatic cancer. Weak excess risk were found for trichloroethylene, polychlorinated biphenyls, methylene chloride and vinyl chloride, but not for carbon tetrachloride. Studies on occupations for metal degreasing and dry cleaning reveal a significant MRR (especially associated with trichlorethylene, tetrachlorethylene and 1,1,1 - trichloroethane).

Alguacil et al. (2000)⁷ assess occupational exposure to 22 possible carcinogens associated with pancreatic cancer, and found an increased risk for various groups of pesticides highlighting the arsenical type. They found increased risk for organochlorine pesticides and solvents too.

Ojajarvi et al. (2000)¹⁷ studied 92 publications from 1969 to 1998 period, about 161 populations with pancreatic cancer and exposure to 23 physical or chemical agents used in occupational exposures. It concluded that people exposed to chlorinated hydrocarbon compounds have a higher risk of developing pancreatic cancer. Another finding of the study is that the MRR in women is higher than men. They point out that most studies reviewed came from populations in North America and Eastern Europe. Another important point is the scarcity of female population; less than 5% of the total population was women, included in only 7 studies.

We present a description of the main characteristics of these items in the following table (Table II).

Table II. Description of the publications found about organochlorine compounds and pancreatic cancer

Author and year of publication	Title	Country	Population	Sample size (n)	Type of study	Results/ Measure of association
Bosch de Basea M. 2011	Relationships between occupational history and serum concentrations of organochlorine compounds in exocrine cancer	Spain (Barcelona and Huelva)	Incident cases of pancreatic cancer	135	Cohort	Serum concentrations of PCBs: 138: <i>B</i> Coef: 0,64 (95% CI 0,04-1,25), 153: <i>B</i> Coef: 0,66 (95% CI 0,29-1,03) and 180, <i>B</i> Coef: 0,99 (95% CI 0,62-1,36), significantly higher among patients whose last occupation was included in IISCO 7.
Santibañez M. 2010	Occupational exposures and risk of pancreatic cancer	Spain (Alicante and Valencia)	Incident cases of pancreatic cancer and patients with other pathology.	616	Case-control	Cases with ductal adenocarcinomas were more likely to have been exposed to chlorinated hydrocarbons solvents. OR: 4,1 (95% CI 1,11- 15,23, p: 0,04).
Andreotti G. 2009	Agricultural pesticide use and pancreatic cancer risk in the Agricultural health study cohort	USA (Iowa and North Carolina)	Pesticide applicators and their spouses	89 658	Case-control	Organochlorines may be associated with pancreatic cancer, but only among certain populations or conditions. They found statistically significant exposure-response associations for 2 herbicides: Pendimethalin and EPTC. Use of DDT was significantly inversely associated with pancreatic cancer risk: OR 0,4 (95% CI 0,2-0,9).

Author and year of publication	Title	Country	Population	Sample size (n)	Type of study	Results/ Measure of association
Ojajarvi A. 2007	Estimating the relative risk of pancreatic cancer associated with exposure agents in job title data in a hierarchical Bayesian meta-analysis	Sweden, Norway, Finland and Costa Rica	Incident cases of pancreatic cancer	3799	Meta-analysis	Chlorinated hydrocarbons may increase the risk of pancreatic cancer. MRR*:2,21 (95% CI 1,31-3,68).
Cocco P. 2005	Cancer mortality among men occupationally exposed to dichlorodiphenyltrichloroethane	Sardinia, Italy	DDT exposed workers	4552	Cohort	Mortality from pancreatic cancer did not differ between exposed and unexposed subgroups. RR: 0,8 (95% CI 0,4-1,8).
Beard J. 2003	Health impacts of pesticide exposure in a cohort of outdoor workers	Australia	Workers exposed and not exposed to pesticides and general population	3983	Cohort	Mortality from pancreatic cancer was more frequent in subjects exposed to DDT. SMR:** 5,27 (95% CI 1,09-15,40).
Alguacil J. 2002	Occupational exposure to organic solvents and K-ras mutations in exocrine pancreatic cancer	Spain, Finland and Costa Rica	Occupational exposures of EPC cases with and without K-ras mutated tumors.	107	Case-control	The results raise the possibility that hydrocarbon solvents might be involved in the pathogenesis of EPC, possibly through indirect modulation of K-ras activation. OR: 14,81 (95% CI 3,20- UH).

Author and year of publication	Title	Country	Population	Sample size (n)	Type of study	Results/ Measure of association
Ojajärvi A. 2001	Risk of Pancreatic cancer in workers exposed to chlorinated hydrocarbon solvents and related compounds: A meta-analysis	USA, Canada and UK.	Incident cases of pancreatic cancer	41 studies, 59 populations	Meta-analysis	Exposure to chlorinated hydrocarbons was associated with an excess risk of pancreatic cancer. MRR 1,4 (95% CI 1-1,8; 20 populations). The studies on metal degreasing revealed an MRR 2 (95% CI 1,2-3,6 for 6 populations). Those for dry cleaning had an MMR 1,4 (95% CI 1,1-2,4 for 8 populations).
Alguacil J. 2000	Risk of pancreatic cancer and occupational exposures in Spain	Spain	Pancreatic cancer patients and cases with an initial diagnostic of EPC	449	Case-control	Increased risk for different pesticides, for organochlorines: OR 1,2 (95% CI 0,53-2,74) and for chlorinated hydrocarbon solvents OR 2,23 (95% CI 0,21-23,9).
Ojajärvi A. 2000	Occupational exposures and pancreatic cancer: a meta-analysis	Spain, Finland, Sweden, France and Costa Rica.	Exposed to organochlorines incident cases of pancreatic cancer	92 studies, 161 populations	Meta-analysis	Significant excesses they found for organochlorines. MRR: 1,4 (95% CI 1-1,8). MMR for women (MRR 1,8 95% CI 0,7-4,6) was higher than for men (MRR: 1,3; 95% CI 0,9-1,9).

* MRR: meta-relative risk.
 ** SMR: standardized mortality ratio.
 *** UH: unquantifiably high.

DISCUSSION

Although there is evidence of a possible association between pancreatic cancer and organochlorine exposure before 2000, there are few studies that attempt to clarify this association in the workplace, and we have only found 10 studies in the corresponding period of the last 13 years. Most of these studies describe a possible association between occupational exposure to organochlorines and pancreatic cancer^{2,3,7,16,17}, but most of these do not specifically indicate the substances to which the worker was exposed, but rather they are related to the types of work in which these compounds were used.

Of the three meta-analysis and three cohort studies, all of them seem to find a statistically significant positive association, the rest of the studies that correspond to case-control studies mostly show similar data.

The three meta-analysis were performed by Ojajarvi et al. and found a significant association between occupational exposure to chlorinated hydrocarbons and the risk of pancreatic cancer, one of them describe a slightly higher risk in women.¹⁷ Agent exposure studies, refer weak increase risk for trichlorethylene, tetrachlorethylene, methylene chloride, vinyl chloride, chlorohydrin, and polichlorinated biphenyls associated with an increased risk with statistically significant values related to work degreasing metals and dry cleaning (mainly associated with trichlorethylene, tetrachlorethylene and 1,1,1-trichloroethane)¹⁵ the authors emphasize the presence of confounding factors related to other risk factors not controlled in all studies (such as smoking). In addition a potentially confounding factor is the fact that several agents are used concomitantly. Most of studies analyzed populations from North America and Eastern Europe. Another important point to note is the scarcity of female population, less than 5 % of the total population was female, present in only 7 of the 20 studies included in the meta-analysis¹⁷.

With regard to cohort studies, Bosch de Basea's study is the first that link occupational exposures with serum levels and the risk of pancreatic cancer. No high serum levels of organochlorines were found in agriculture workers, which was a novelty, since other studies have linked with the occurrence of cancer pancreas¹. Cocco et al. reported no differences in risk between the group exposed and not exposed to DDT¹⁵. This result contrasts with the findings of Beard et al that coincide with most of the previous studies that found an association between pancreatic cancer risk and exposure to DDT¹⁶.

Related to the case-control studies, Santibañez's findings support the hypothesis that occupational exposure to chlorinated hydrocarbon solvents is associated with the risk of exocrine pancreatic cancer. The occupations with associated risk do not discriminate against the different related agents and some of them are related to the added risk of other interactions such as sedentary jobs³.

In contrast to previous findings, Andreotti et al. found no association between organochlorines and pancreatic cancer. This finding suggests that organochlorines may be associated with pancreatic cancer, but only among certain populations or conditions, the findings also revealed an inverse association for DDT. It is possible that this inverse association may in part be due to a healthy survivor effect among those who had used DDT before it was banned in the 1970s. The female population was included, although in a small proportion, represented by the wives of workers¹⁴.

Alguacil et al. made the first and only study on occupational exposure and activation of the K-ras gene in pancreatic cancer. They concluded that subjects exposed to organochlorines had a mutation of k-ras gene, which could have been a trigger in the onset of pancreatic cancer in this subjects⁹.

While we have described various occupations possibly related to a higher frequency of onset of pancreatic cancer, not all studies have identified the specific type of chemical agent involved, the only study found in this direction is the meta-analysis by Ojajarvi et al. in 2001, which describe a possible link associated with the presence of chlorinated hydrocarbon solvents used in certain occupations such as metal degreasing and dry

cleaning. However, the risk is difficult to establish, since the studies are heterogeneous and the agents that increase risk of pancreatic cancer are difficult to identify.

Furthermore, studies linking certain occupations or occupational exposures with pancreatic cancer do not specify or identify the specific chemical agents to which each group of workers are actually exposed through their main work activity.

Despite these findings, have been observed increases in risk among workers in the rubber, printing, petroleum and chemical industry. There have also been increases in mortality from this neoplasm in tanners, farmers, mechanics and metalworkers. There is a possibility that several chemical interactions and their association are related to the occurrence of the risk, but no studies have developed ability to detect these associations.

Often the type of agent that a worker is exposed cannot be discriminated. Alguacil et al. found that the type of occupation seemed to have some role in the etiology of pancreatic cancer in the Swedish population¹², in Spain the same author discovered evidence supporting previous studies and highlighted the increased risk related to agriculture and textiles jobs in women and the manufacture of dyes and pigments in men¹⁸.

The Andreotti and Silverman's review published in 2012 is consistent with our findings and evidence small quantity of recent publications⁴.

Any difference between the age groups, the gender of workers, and the risk of pancreatic cancer is not described, nor can it suggest an association related to geographical distribution and gender, since the data are scarce.

Many factors are difficult to interpret in the analysis of this relationship because of the small number of cases in prospective studies leading to weak statistical power. In addition, difficulties in classification of different levels of exposure, the over-employment, the cumulative effect of prior occupational exposures and problems related to the diagnosis of the disease, make the analysis difficult since in the latter case, the disease usually occurs in the elderly and immunohistological confirmation usually cannot be performed.

Although epidemiological evidence cannot be conclusive, research is needed to find quality information on the observed associations and to find exhibitions that remain unevaluated, considering that several studies point to the possibility of existence of risk workers exposed to solvents and chemicals, and to seek some kind of effective diagnostic screening test.

Of particular interest is the study of gene-environment interactions, thus identifying an area with strong development potential in the field of research related to genes associated with pancreatic cancer as K-ras, the tumor suppressor genes such as p53, and polymorphisms of genes involved in DNA repair are other sources of study.

As prevention is important to emphasize on the safety and health general recommendations at work, which allow to control certain risk factors for different illnesses that may also be involved in the onset of pancreatic cancer. Also, eating habits and consumption of fruits and vegetables, in which protective factors are present through mechanisms of inhibition of chemical carcinogenesis, may also be recommended. This would be indicated by promoting consumption by advising a proper diet for workers, by accompanying information campaigns and by smoking cessation, as one of the factors that seem to have more to do with the onset of disease¹⁰.

CONCLUSIONS

The literature review on pancreatic cancer and occupational exposure to chlorinated hydrocarbons suggests that some exposures have been associated with excess risk for pancreatic cancer, but very few have been firmly established as associated factors due to

the fact that most studies have been found to have a weak or moderate effect in connection with the limited number of participants. The scarcity of studies on this and other factors such as clinical aggressiveness of pancreatic cancer limited the selection of cases and obtaining quality information on occupational exposures, which makes it particularly difficult to perform case-control studies. As a result, there is no conclusive data to establish relationships so far.

Furthermore, studies investigating the association by type of occupation do not usually specify agents to which the worker is exposed, and we were looking for concrete exposure to organochlorines.

It seems important to highlight the need to increase the number of these studies, emphasizing the need to clearly identify the compounds used in each exposure in order to avoid using the same or find other similar compounds, but with less risk. Future epidemiological investigations would be necessary also because the results could serve as a warning to countries that continue to use OC for agriculture and vector control.

It seems especially important to study the possible association of gene-environment interactions in search of more conclusive results of the association between K-ras, tumor suppressor genes such as p53, polymorphisms of genes involved in DNA repair and other sources of study in this field that advance the field of prevention of occupational hazards and allow more specific conclusions to be reached, that could lead to the prevention of this disease.

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