Persistent Toxic Substances and Public Health in Spain

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In Spain, there are substantial gaps in available information about contamination of food, humans, and the environment by persistent toxic substances (PTSs), although studies have shown detectable concentrations of DDE, PCBs, hexachlorobenzene, or hexachlorocyclohexane in 80–100% of the population. Spain will soon try to implement the Stockholm treaty on persistent organic pollutants (POPs). A country that ratifies the treaty is required to develop a National Implementation Plan (NIP). Such NIPs should provide for studies of factors that influence body concentrations of PTSs in the population, and thus ultimately reduce PTS data gaps. Spain’s PTS-related problems are similar to those of many other countries. Elucidation of their causes, consequences, and possible solutions will be of benefit beyond national boundaries.

Key words: persistent toxic substances; persistent organic pollutants; organochlorines; food; environment/chemistry; public policy.

INT J OCCUP ENVIRON HEALTH 2003;9:112–117

Persistent toxic substances (PTSs) are present in a wide variety of the foods we eat daily, and virtually all inhabitants of the earth now store them in fatty tissues.1,5 The contamination of the general population by PTSs is relevant from a public health perspective. It is also important for environmental, food, industrial and economic policies.

The term PTS is used by various authors6-11 and organizations—prominently, the United Nations Environment Programme (UNEP) in its “Regionally Based Assessment of Persistent Toxic Substances.”12 This worldwide program considers the 12 persistent organic pollutants (POPs) currently included in the Stockholm Convention as well as several other toxic substances with similar characteristics of persistence. The so-called “dirty dozen” Stockholm POPs are eight pesticides (DDT, aldrin, chlordane, dieldrin, endrin, heptachlor, mirex, and toxaphene), two types of industrial chemicals (hexachlorobenzene [HCB] and the polychlorinated biphenyls [PCBs]) and two byproducts (dioxins and furans).13 The term PTS hence includes all chemicals currently on the UNEP POPs list, and it is used in this article unless we refer exclusively to the 12 Stockholm POPs.

Like other countries in Europe and other parts of the world, Spain lacks population-based indicators of the impact that environmental processes have on human health, in spite of the fact that the Spanish government also has a legal obligation to assess the risks of adverse health effects associated with exposures to environmental agents such as PTSs. Both in Spain and elsewhere in Europe, several government levels (municipal, regional, federal) have roles waiting to be fulfilled in the monitoring of biological levels of PTSs in humans; this is necessary to perform the governments’ mission to protect the public health.14,15 The scarcity of environmental health information systems is in sharp contrast to the abundance of economic indicators; it is a flaw in post-industrial democracies; and it hampers the development of sound environmental and public health policies.

Information gaps relative to PTSs appear to follow a fourthfold downward gradient: first, large data gaps exist for PTS contamination of the environment, i.e., in soils and waters (many areas of Europe even lack systematic surveys); second, large gaps exist, too, for human food and animal feed contamination (municipal and regional public health systems seldom have comprehensive, continuous surveillance programs in operation, and the capacity to detect accidental contaminations is weak in many areas); third, few countries regularly conduct population-wide, representative surveys of concentrations of PTSs and other environmental chemical agents in the general healthy population; and fourth, very few studies are devoted to PTS health effects on humans.16
While a number of studies of environmental contamination by PTSs have been conducted in Spain, their review is beyond the scope of the present paper.

**Contamination of Food in Spain**

With these caveats in mind, it is nonetheless possible to state that in Spain food contamination by PTSs is significant. A few examples follow. One study showed that 96% and 74% of pasteurized milk samples had residues of hexachlorocyclohexane (HCH) and DDT analogs, respectively; concentrations were in the range of 0.002–0.756 and of 0.002–0.538 ppm, respectively.17 Another study found that 100% of the lamb and pork samples analyzed had HCH and hexachlorobenzene (HCB) residues, while 83% of the lamb samples contained 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane (DDT) analogs (range: 0.008–0.091 ppm).18 A further study observed that 50% of fish-based meals contained residues of polychlorinated biphenyls (PCBs) (mean: 96.3 ppm).19 PCB congeners 138, 153, and 180, have also been detected in other types of food.19,20 Of 160 food samples from the Basque Country, in northern Spain, 21% had DDE residues (found principally in eggs, fish, dairy products, and meat), 17% contained γ-HCH (lindane) residues (eggs, cereals, meat, dairy products, bread), and 15% contained HCB (eggs, meat and dairy products).21 Spanish butter samples had significantly higher levels than did samples from other European countries of γ-HCH, β-HCH, HCB and p,p’DDE, (1,1-dichloro-2,2-bis(p-chlorophenyl)ethane).22 In a different study, based on butter samples from 23 countries, Spain had the highest levels of HCH isomers, along with China and India.23

**European Concerns about PTS Residues in Food**

Certainly, the problem of contamination of food by PTSs is not unique to Spain. The European Commission has identified food safety as one of its top priorities. The *White Paper on Food Safety*24 set out the plans for a proactive new food policy: modernizing legislation into a coherent and transparent set of rules, reinforcing controls from the farm to the table, and increasing the capability of the scientific advice system, so as to guarantee a high level of human health and consumer protection. The strategic priorities of the White Paper are: first, to create a European Food Safety Authority; second, to consistently implement a farm-to-table approach in food legislation; third, to establish the principle that feed and food operators have primary responsibility for food safety; fourth, that member states need to ensure surveillance and control of these operators; and finally, that the Commission shall test the member states’ control capacities and capabilities through audits and inspections.

A compilation of European Union (EU) dioxin exposure and health data25 shows concentrations of dioxins in foodstuffs for EU member states. The most comprehensive data sets seem to be available for Finland, Germany, The Netherlands, Sweden, Spain, and the United Kingdom. Estimates of average total dietary exposures to PCDD/PCDFs for consumers vary from 69 pg I-TEQ/day in The Netherlands to 210 pg I-TEQ/day in Spain. These estimates do not include dioxin-like PCBs, or the highly prevalent, non-dioxin-like, non-coplanar PCBs.26

**Human PTS Contamination**

In Spain, the scarcity of information about the concentrations that PTSs have in humans is well illustrated by the fact that a representative study of a general healthy population living in a wide geographic area has never been conducted. The apparent exception is the studies developed in the town of Flix and in four non-contaminated surrounding villages.27-29 However, this small area, located to the south of Barcelona, is home to a factory that currently produces HCB, and which for many years manufactured DDT and other PTSs. Hence, this population cannot be deemed representative of most other populations in Spain.

Longitudinal population studies of PTS concentrations in humans (i.e., studies that measure PTS internal concentrations in representative samples of a human population at regular time intervals) are important for monitoring and control purposes.26,30 Only one such longitudinal study is available in Spain: it was carried out in the town of Mataró (north of Barcelona) in order to analyze the impact of the opening of an incineration plant.31-35 One of the interesting findings was that over the four-year period of the study concentrations of dioxins and furans increased by approximately 40–45% in the entire population of Mataró (Table 1). Serum concentrations of PCBs 138, 153, and 180 increased 6.6%. The most likely explanation for the unexpected increase is background food contamination. Concentrations of dioxins and furans in the study area were approximately 25% higher than values in other developed countries.31-33

Though these studies must be viewed with caution because, as mentioned, they were generally conducted in special population groups, the available studies suggest that around 80–100% of the Spanish population may have detectable body concentrations of DDE, PCBs, HCB or lindane.26-28,34 Thus, in a study of newborns in Flix, HCB and PCBs were detected and quantifiable in 100% of cord blood samples.28 In another study, women from Málaga had significantly higher levels of p,p’DDE than did women from four other European cities.35 Our PANKRAS II Study included 144 patients with exocrine pancreatic cancer from the Mediterranean coast of Spain.36 Table 2 shows that serum concentrations of DDE and PCBs in these patients were over two times and over three times higher, respectively, than those found in pancreatic cancer cases from the San Francisco Bay area; the
The serum concentration of HCB was over 66 times higher in the Spanish cases (more than 6,000% increase over concentrations in U.S. cases).26,36,37

In addition to DDE, DDT is still commonly detected in Spaniards (again, as in other population groups throughout the world).1-12 It is currently unknown whether such detection is solely the result of relatively high past exposures or whether some amount of human exposure to DDT—albeit minor—is still ongoing in Spain. To properly address the issue it would be necessary to integrate information about the human metabolic half-life of DDT, source strength, ecologic half-life, food habits, and occupational exposures; no such analysis is yet available.

Clearly, in Spain temporal trends of PTS contamination in humans are impossible to assess, because of the limited number of studies, the small number of subjects analyzed, their lack of representativeness, and inappropriate reporting of methods in some studies.26

A great deal of information is also lacking about past uses and effects of PTSs in Spain. For example, a systematic review of the historical uses of DDT is not available. Yet, for public health and environmental professionals a review addressing the following questions would be important:

- Does the p,p’DDT currently detected in individuals, human food, and animal feed come from old exposures, recent exposures or both? If human exposure is still ongoing through the diet, is it only from imported food or also from illegal uses in home agriculture?
- When did marketing and widespread availability of DDT begin in Spain? What were the economic conditions that favored its use? What was the time and space diffusion of the extensive use of DDT in agriculture?
- How much DDT was produced in Spain? How much was exported and imported?
- When was it first detected in Spaniards? How did trends evolve across geographic areas and social groups?
- When was it first detected in human food and animal feed? How did trends evolve?
- What acute and chronic effects did DDT have and is DDE having on human health, agriculture, wildlife, and the environment in Spain?

The rationale behind several of these questions similarly applies to other PTSs and to other European countries, many of which lack comprehensive reviews or databases with the corresponding information, particularly in Eastern Europe.26

### TABLE 1. Changes in Blood Concentrations of Selected Organochlorine Compounds among Inhabitants of the City of Mataró (Barcelona, Spain), 1995-1999

<table>
<thead>
<tr>
<th>Compound</th>
<th>Group A* (n = 57)</th>
<th>Group B† (n = 75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCDD/PCDF</td>
<td>19.4 pg I-TEQ</td>
<td>+44.5</td>
</tr>
<tr>
<td>PCB 28</td>
<td>0.02 µg/L</td>
<td>–60.0</td>
</tr>
<tr>
<td>PCB 52</td>
<td>0.01 µg/L</td>
<td>0.0</td>
</tr>
<tr>
<td>PCB 101</td>
<td>0.02 µg/L</td>
<td>–33.3</td>
</tr>
<tr>
<td>PCB 138</td>
<td>0.50 µg/L</td>
<td>–2.0</td>
</tr>
<tr>
<td>PCB 153</td>
<td>0.78 µg/L</td>
<td>+9.9</td>
</tr>
<tr>
<td>PCB 180</td>
<td>0.66 µg/L</td>
<td>+8.2</td>
</tr>
</tbody>
</table>

*Inhabitants of Mataró living nearer a newly opened incineration plant.
†Inhabitants of Mataró living about 4 km away from the plant.

### TABLE 2. Serum Concentrations of p,p’DDE, Hexachlorobenzene and PCBs among Patients with Exocrine Pancreatic Cancer in Spain and in San Francisco

<table>
<thead>
<tr>
<th>Compound/Study</th>
<th>No. of Cases</th>
<th>Mean Serum Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>p,p’DDE—Spain</td>
<td>144</td>
<td>4,156 ng/g lipid</td>
</tr>
<tr>
<td>p,p’DDE—San Francisco</td>
<td>108</td>
<td>2,054 ng/g lipid</td>
</tr>
<tr>
<td>Total PCBs—Spain</td>
<td>51</td>
<td>1,332 ng/g lipid</td>
</tr>
<tr>
<td>Total PCBs—San Francisco</td>
<td>108</td>
<td>433 ng/g lipid</td>
</tr>
<tr>
<td>Hexachlorobenzene—Spain</td>
<td>144</td>
<td>1,938 ng/g lipid</td>
</tr>
<tr>
<td>Hexachlorobenzene—San Francisco</td>
<td>108</td>
<td>28 ng/g lipid</td>
</tr>
<tr>
<td>Spain vs San Francisco</td>
<td></td>
<td>+102% 1,287 ng/g lipid</td>
</tr>
<tr>
<td>Spain vs San Francisco</td>
<td></td>
<td>+208% 329 ng/g lipid</td>
</tr>
<tr>
<td>Spain vs San Francisco</td>
<td></td>
<td>+6,821% 1,460 ng/g lipid</td>
</tr>
<tr>
<td>Spain vs San Francisco</td>
<td></td>
<td>+6,536% 22 ng/g lipid</td>
</tr>
</tbody>
</table>


**TABLE 3. Report on Human Exposure to Environmental Chemical Agents**

The overall purpose of the report would be to provide to citizens, social organizations, policymakers, and scientists population-based, valid information about body concentrations of environmental chemical agents (ECAs) in order to help prevent diseases that result from exposure to POPs, other PTS, and other ECAs.

The study could be done in any relevant socio-geographic setting: local (e.g., city), national, regional (e.g., the Mediterranean region), the European Union, the whole European continent.

The specific uses of the report would be:

1. To determine whether selected ECAs are entering the bodies of citizens and what levels of these chemicals are present in blood, fat tissues, or urine.
2. For chemicals with a known toxicity level, to measure the prevalence of people in the population who have increased levels of ECAs.
3. To assess the effectiveness of societal efforts to reduce the exposures of citizens to specific ECAs.
4. To establish reference ranges that help determine whether a person has an unusually high concentration of an ECA.
5. To track over time trends in levels of exposure of the population to ECAs.
6. To determine whether levels of ECAs are higher in children, the elderly, women of childbearing age, workers at risk, people of lower income, or other population groups.
7. To set priorities for research on the ecologic and human health effects of ECAs.

The primary focus of the report could be the 12 POPs included in the Stockholm treaty. It could also study other POPs, other PTSs, and other ECAs.

It is important that the individuals studied constitute a representative sample of the general population. If this is not possible, then one could attempt to study large groups as similar as possible to the general healthy population, and measure accurately their characteristics (e.g., age, gender, occupation, or education).

Data collection should focus on body (blood, fat, urine) concentrations of ECAs. In addition, if possible, efforts should be made to collect data that will enable explaining the observed concentrations (e.g., individuals could be interviewed about their dietary habits, occupations, other lifestyle and environmental factors). In some countries it may be possible or preferable to integrate the Report within an ongoing National Health Interview Survey or related studies.

*Modified from Centers for Disease Control and Prevention, National Center for Environmental Health. National Report on Human Exposure to Environmental Chemicals.33

**PTS Effects in Humans**

The potential low-dose, indirect, and long-term effects of PTSs include endocrine disruption, cancer promotion, and various neurologic and immunologic effects.14,16,17,26-30,34-41 These effects may result—perhaps, in some yet undefined, more susceptible groups—in a variety of clinical problems such as infertility, congenital defects, learning disabilities, tremors, diabetes, or cancer.14,16,26-34-41 Yet, crucial questions remain unsolved, including the potential magnitudes of individual lifetime cumulative risks associated with low and intermediate levels of exposure, or the population-attributable risks of PTSs. It is worth noting that even if individual risks were low, the population impact of exposure to PTSs could be significant (i.e., the burden of disease could be high), since the latter is essentially the product of the individual risk and the number of exposed individuals. No estimate of the burden of disease that PTSs might cause in Spain is currently available.

Extremely few studies have evaluated the effects of PTSs on human health in Spain. One study showed that airborne exposure to HCB in the Flix population was insufficient to trigger a significant alteration of the heme biosynthesis pathway.32 In another study in the same village, thyroid cancer, soft-tissue sarcomas, and brain cancer were associated with organochlorine compound mixtures with a high HCB content.43 Another study showed that the exposure to HCB did not affect the general health status of this population, but it was associated with specific health effects in the more highly exposed subjects.44 Finally, a study of babies from Flix suggested that HCB reduces intrauterine physical growth.45 A study of babies born in Granada (south of Spain), suggested that exposure to pesticides in farm work was associated with cryptorchidism.46

Other results from our group suggest that p,p’DDT, p,p’DDE, and some of the highly prevalent hexa- and hepta-chlorinated PCBs (such as congeners 138, 153, 180) may play a role in the pathogenesis of exocrine pancreatic cancer through modulation of K-ras activation.36 Specifically, as compared with cases in the lower tertile of PTS exposure, cases in the upper tertile of exposure had five- to 18-fold increased risks of a K-ras mutated tumor. These findings provided the first link between K-ras mutations—the most common oncogene mutation in human cancer—and an environmental compound among humans living in normal conditions.

The mentioned study36 is just an example of the potential for studies of gene-environment interactions
to yield information about mechanisms of carcinogenesis. However, there is still comparatively little research that integrates the environmental, clinical, and genetic dimensions of PTS effects on human health. Assessing the clinical, epidemiologic, ecologic, and social relevance of the more subtle, indirect, and long-term effects of PTSs will continue to pose difficult challenges during the next decade.

Beyond Stockholm: The National Implementation Plan

Like many other countries, Spain will soon try to implement the Stockholm treaty on POPs. This constitutes a new opportunity to develop more efficient policies to control POPs, other PTSs, and other environmental chemical agents present in food, humans, and the environment. Each party to the Stockholm Convention is required to develop a National Implementation Plan (NIP) describing how it will meet the obligations set by the Convention. Within two years from the treaty’s entry into force governments must develop NIPs that set priorities for initiating future activities to protect human health and the environment from POPs. Theoretically, the NIP will supply a framework for a country to develop and implement, in a systematic and participatory way, priority policy and regulatory reform, capacity building, and investment programs. Developed countries will have to provide funds and technical assistance to less developed nations, so that the latter can take effective measures. The Stockholm Convention is likely to add more PTSs to the current list of 12 POPs, and some countries are already working on this wider scale.

However, as discussed, there are large data gaps relative to POPs and other PTSs, particularly with respect to human concentrations and effects. Thus, it is our view that national plans to implement the Stockholm treaty should include provisions to reduce PTS data gaps and, specifically, should launch systematic studies of factors that influence body concentrations of POPs and other PTSs in the general population (Table 3). Such studies could be based on initiatives such as the U.S. National Report on Human Exposure to Environmental Chemicals. Sharing expertise in this and other areas could be mutually beneficial for many countries. Analyses of the common causes and consequences of human exposures to PTSs, and of possible solutions, are also of interest beyond national boundaries.

The authors thank Estefanía Blount, Ferran Ballester, Nicolás Olea, Joan Albaigés, Mary Wolff, Benedetto Terracini, and Joan Grimalt for scientific advice. Technical assistance provided by David J. MacFarlane, Olga Juan, and Puri Barbas is also gratefully acknowledged.

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