

The impact of chronic exposure on the Dokkarat district population of Fez city to endocrine disrupting chemicals

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Received xxNov 2016,

Revised xxDec 2016,

Accepted xxDec 2016

Abstract

In Morocco, the industrial revolution and agricultural activities are contributing to the increase of water pollution, leading to possibility to the appearance of serious diseases of endocrine origin. The objective of this study is to focus on the impact of industrial pollution in the Dokkarat district of the Fez city on the appearance of some endocrine diseases in the adjacent population and equally important on the waters upstream from Oued Fez. The results of the diagnosis show that the Dokkarat district includes several modern tanneries and other food industries that use chemicals identified as toxically. The physicochemical and bacteriological characterization of Oued Fez water downstream from the industries diagnosed, displays that they are slightly basic, carrying a high bacterial load, a mineral and organic load in the surface water quality standards, a metallic charge at the limit of the standards with the exception of arsenic. The statistical analysis of the survey data recorded the presence of six endocrine diseases (diabetes, neurological disorders, hormonal imbalance, obesity, and thyroid and growth disorders) and a strong correlation between ages, years of experience, length of exposure and occurrence of endocrine pathological signs.

Keywords: Endocrine disrupters; endocrine diseases; chemicals investigation, , characterization; surface water.

1. Introduction

The development of industrial, artisanal activities and the excessive use of water and chemicals during the manufacture of finished products is a threat to water quality since these effluents do not meet the surface water quality standards [1], which could affect human health by causing serious diseases of endocrine origin (diabetes, thyroid, hyperthyroidism, hypothyroidism, obesity, gonads ...,) [2,3]. Indeed, these products interfere with our endocrine system and act at very low doses [4]. In this case, the scientific community has accumulated evidence of the link between these chronic diseases and the environment, air pollution, water, soil, how we produce, living and working conditions. Similarly, a recent report by the United Nations Environment Program (UNEP) indicates that more than eight per cent of deaths worldwide in 2011 are related to the increasing use of chemicals particularly in the countries of the South [5]. The World Health Organization (WHO) appreciates that chemical-related deaths amount to five million deaths per year, or 8% of global mortality. The annual health costs of endocrine disruptors alone would amount to € 157 billion in the European Union (1.2% of GDP) [6]. In the Fez-Meknes region, the annual incidence rate of the population affected by diabetes increased from 3.44% in 2010 to 2016, of which 1.66% is related to the population of Fez city [7]. Previous work has exhibited that between 2011 and 2012, the mortality rate due to endocrine diseases has been increased from 4.4% to 7.6% [8]. In 2014, France was the first country in Europe to adopt a strategy for the sustainability of support for research on endocrine disruptors, continuation of population and environmental monitoring, implementation of an expertise program on substances, consideration of endocrine disruptors in regulation and public information [9]. It is, therefore, essential to make a hypothesis on the interactions between both diseases of endocrine origin in the population exposed to endocrine disrupting chemicals and water pollution in order to understand the stakes involved. Our project consists of studying the impact of certain chemicals responsible for endocrine diseases in the population adjacent to the estimated polluting industries of the Dokkarat industrial district of Fez city. For this reason, we accomplished an in-depth diagnosis in consultation with the organizations concerned to:

- Realize the activities of this neighborhood, the exposure of the population to these products, the sources of the latter, their mode of use and rejection, etc.
- To assess the water quality of the neighboring Oued by measuring the microbiological and physicochemical parameters likely to be elements among endocrine disruptors and the different ways of its exploitation.
- Evaluate the effects of such exposures through a cross-sectional epidemiological study.

The organizations that participated in the diagnosis were Autonomous Water and Electricity Distribution Authority of Fez (RADEEF), Sanitation Facility Network System Service -Fez (SRES), Prefectural Epidemiology Unit-Fez (CPE), Regional and Epidemiological Department of Health Watch - Fez (DREVS), Chamber of Commerce, Industry and Service of Fez city (CCIS) and High Commission for Planning of the Fez-Meknes Region (HCP). The descriptive analysis of the survey data was conducted using SPSS software.

2. Methods

In order to defeat the risks linked to the exposure of the population to the toxic chemicals responsible for endocrine diseases among the population of a neighborhood in the Fez city, which is supposed to be the most polluted by industrial activities as well as the pollution generated by, we carried out an assessment of the polluting load of the Oued surrounding these industries and a cross-sectional epidemiological study by conducting a simple descriptive and analytical home-based survey of a well-defined population for three months.

2.1. Environmental study of oued water near the Dokkarat district

In the environmental study, we evaluated the pollutant loading of the Oued Fez upstream water by a physico-chemical, metallic and microbiological characterization in order to trace the various products potentially used in the industries, identified by the survey area of study.

2.2.1. Area of study

Oued Fez, representing the main collector that receives several effluents, is a river flowing in the heart of the medina, hides under the houses and flows peacefully from one end to the other of the medina of Fez. The catchment area of Oued Fez lies between the parallels $33^{\circ} 30'$ and $34^{\circ} 08'N$ and between the meridians $4^{\circ} 54'$ and $5^{\circ} 09'W$. It is composed of several sub-basins of different sizes and morphologies: Oued Boufekrane (52.40 km^2), Oued El Mehraz (52.40 km^2), Oued El Himmer (80.74 km^2), Oued Chkou (428.08 km^2) and Oued El Malleh, downstream of the catchment area (34.03 km^2) [10]. The Water samples were taken from the Oued Fez upstream.

2.2.2. Sampling and sample

The Sampling was achieved out seasonally during the year of 2016 by the composite method while taking into account the various activities identified in the area study (domestic, industrial and agricultural wastewater). The Water samples were collected using sterile vials. Additionally, they were then stored in a cooler at $4^{\circ}C$ during transport to the laboratory and then analyzed 24 hours. In this respect, for each sample, water temperature, electrical conductivity and pH were measured in situ. The water samples and their methods of analysis are those recommended by AFNOR enacted by Rodier [11].

2.2.3. Fed water analysis

Physico-chemical analysis includes: pH, conductivity, temperature, chemical oxygen demand (COD), biological oxygen demand (BOD5), Nitrates, Total Kjeldahl Nitrogen (TKN), suspended matter (SM) and heavy metals ML (Cr, Zn, Cd, As, Ni, Pb). The nitrate and nitrite ions were assayed by molecular absorption spectrometry (JP.SELECTA.sa.a). The heavy metals were analyzed by Inductive Coupled Plasma Spectrometry ICP-AES (Ultima 2_jobin yvon). The bacteriological analysis concerns the determination of total germs, fecal coliforms, total coliforms, staphylococci, streptococci and Escherichia-Coli.

2.2. Cross-sectional epidemiological study of the Dokkarat neighborhood population

This is a simple cross-sectional epidemiological survey with both a descriptive and analytical focus on a well-defined population.

2.2.1. Location

Dokkarat district of Fez city, whose population is most affected by industrial pollution, delimited by the Geographic Information System GIS (Fig1). Population adjacent to the estimated polluting industries of the Dokkarat district of Fez city the recruitment involved women, men, adolescents and the elderly.

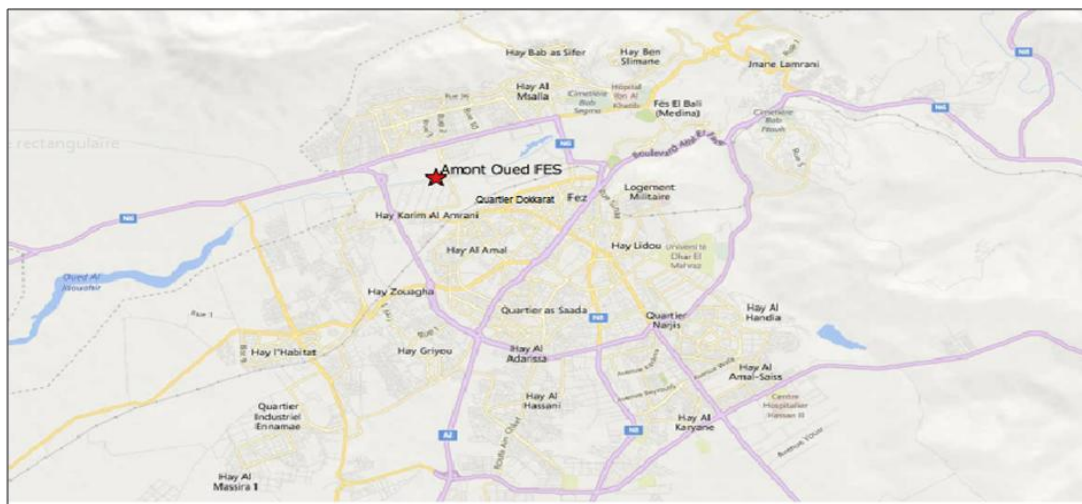


Figure 1. Overview of the study area. Sampling locations are indicated with ()



2.2.2. Inclusion and exclusion criteria

2.2.2.1 Inclusion criteria

- Age between 15 and over.

- Consent to participate in the study.

2.2.2.2. Exclusion criteria

- Persons with cognitive impairment.
- Pregnant or nursing women

- Those present who refused to participate in the study.

2.2.3. Sample size

Based on a representative sample of the population, distributed over the area of study. The sample size (N1) is calculated from the number (N) for large populations. The outcomes of the diagnosis allowed us to determine the number of people to be interviewed in the Dokkarat neighborhood, representing the sample size of 350 (N) which was rounded off by 380 (N1).

2.2.4. Data collection

It was conducted using an established questionnaire that included socio-demographic data (age, sex, place of residence, marital status, level of education, occupation, monthly household income, number of people living under the same roof, number of children of the respondent ...) and data on:

- Occupation and job description, number of years of experience,
- Consumption of tobacco and alcohol,
- The duration of exposure to chemicals and non-occupational exposure
- The mode of exploitation of the waters of the neighboring Oued
- The most frequent endocrine diseases (diabetes, endocrine obesity, thyroid ...) and the personal family history of endocrine diseases.

2.2.5. Statistical analysis

The data from the questionnaires have been processed, coded, captured and statistically validated by the SPSS (Statistical Package for Social Sciences) software since the data are constituted by a set of individuals for which we have several variables structured in groups. Our study is composed of two types of quantitative variables, the age, place of habitat, type of population and Duration of exposure, years of experience, endocrine diseases,

3 Results and discussion

3.1. Description of the population studied

The results of the diagnosis show that Fez city is the 2nd largest city in Morocco with a population of 1 112072 inhabitants according to the census of the year 2014 by the high commissioner of plan [12]. Further, it is affected by diabetes as well as major endocrine disease, its annual incidence rate in the Fez-Meknes region increased between 2010 and 2016 from 4.07% to 7.51% and in Fez city, is high from 2.24% to 3.9% [13]. The city is known for its modernization of the artisanal sector such as tanneries, dinandies, pottery, etc., agricultural and industrial development (oil and textile industries, food industries, etc.) pesticides and toxic chemicals (Cr, Ni, Pb, Cd, Zn, As, S, Cyanides...) and excessive water consumption. Consequently, wastewater from these industries is discharged into watercourses without prior treatment, which generates a significant polluting load of the latter. The Dokkarat district includes 33 industries including 14 tanneries, 8 oil mills, 1 food products, 1 chemical parachemistry and 7 milling plants [14].

3.2. Environmental study of the waters of Oued Fez

To better understand the effect of water pollution by industrial discharges from the Dokkarat district on the adjacent population, we carried out an evaluation of the surrounding Oued quality by a physicochemical, metallic and microbiological characterization.

3.2.1. Physicochemical and metallic characterization

The average values of the results obtained seasonally from the physicochemical and metallic characterization of the water upstream of Oued Fez, are shown respectively in **Table s 1** and **2** and are compared with those of the surface water quality standards.

Table 1. Physicochemical characterization of water upstream of Oued Fez

Physico-chemical parameters	T (°C)	pH	Conductivity ($\mu\text{S. cm}^{-1}$)	TKN (mg.L^{-1})	Nitrates (mg.L^{-1})	Suspended Matter (mg.L^{-1})	BOD5 (mg.L^{-1})	COD (mg.L^{-1})
Value	25.5	8	796	1.18	27.06	1023	12	41
Surface Water Standards [15]	25-30	6.5-8.5	750-1300	1_2	25-50	(1000-2000)	(10-25)	(40-80)
Quality	Middl e	Good	Good	Middle	Middle	Bad		

The analysis of the results obtained records that the water of the Oued Fez upstream is slightly neutral to alkaline. Its temperature belongs to the middle to excellent class [15]; its nitrogen load is generally good and meets the standards for surface water quality. But the suspended matter (MES) and organic load (COD / BOD5 > 2.5) of this water, they exceed the standards. For the metal parameters, we find that Cr, Pb and As exceed surface water quality standards; which classifies this water among those of poor to very poor quality according to the grid of Moroccan norms especially during the summer season [15]. Several studies show that many metals used in industrial processes arrive in the human environment through air emissions, water as well as solid waste, such as eg arsenic, cadmium, chromium, copper, manganese, mercury, nickel, selenium or organic zinc [16, 17], as the Lead, Arsenic are regarded as among the endocrine disruptors, and the first causes metabolic, neurological and disruptions thyroid function [18] and the second is a potent endocrine disruptor [19].

Table 2. Metallic characterization of water upstream of Oued Fez

Metallic Parameters	Nickel ($\mu\text{g.L}^{-1}$)	Chrome ($\mu\text{g.L}^{-1}$)	Lead ($\mu\text{g.L}^{-1}$)	Cadmium ($\mu\text{g.L}^{-1}$)	Arsenic ($\mu\text{g.L}^{-1}$)	Zinc (mg.L^{-1})
Value	12.6	51	55	4.62	53	3.1
Surface water quality [15]	<20	>50	>50	3-5	>50	3-5
Quality	Good	Very Bad	Very Bad	Middle	Very Bad	Middle

3.2.2. Bacteriological characterization

The average of the results obtained from the bacteriological characterization of the water upstream of Oued Fez, are shown respectively in **Table 3**:

Table 3. Bacteriological characterization of water upstream of Oued Fez

Parameters	Total germs	Total coliforms	Fecal coliforms	Staphylococci	Streptococci	Escherichia- Coli
Value (UFC/100mL)	12000	25000	22000	2500	3000	30000
Surface water quality [15]	-----	>50000	>20000	-----	1000-10000	-----

The outcomes of the bacteriological characterization marked high concentrations of total coliforms, fecal and *Escherichia coli*; indicating a medium to large bacterial contamination of human and / or animal origin and various industrial activities. According to the Moroccan classification of surface waters, the values found (>20.000 Unit Forming Colonies / 1mL) classify this water of poor bacteriological quality. As a result, the waters upstream of Oued Fez near the Dokkarat district could cause adverse effects on the life and health of the adjacent population. Compared to the results of the environmental study of Oued Fez water upstream, it is shown that they are slightly basic, carrying a high bacterial load, a mineral and organic charge in the surface water quality standards a metallic charge at the limit of the standards with the exception of arsenic, chrome and Lead. In this case, these results are probably due to domestic, industrial, artisanal or agricultural waste dumps of the neighborhood and to solid waste deposited randomly in the Oued rich in heavy metals. Previous studies have shown, according to the General Insurance Scheme, that metals such as cadmium and arsenic disrupt the glucose-lipid metabolism which are considered as obesogenic and diabetogenic pollutants to characterize the pathophysiological effects of these substances [20, 21, 22]. To confirm the results of the environmental study established between the use of endocrine disrupting chemicals and the appearance of signs of endocrine origin, we carried a cross-sectional epidemiological study.

3.3. Transverse epidemiological study of the Dokkarat district population

The average of positive responses to the population of the district Dokkarat, which we investigated for endocrine diseases, is 51%. Thus, respondents in this neighborhood suffer from the most frequent endocrine diseases: diabetes, obesity, thyroid, growth disorders, neurological disorders, hormonal imbalance.

3.3.1. Sociodemographic data

The results of the socio-demographic data of the surveyed population reveal that:

- The age of the respondents varies between 21 and 65,

- 33.5% of respondents were aged 41-50 and 26.5% were over 50 years of age,
- 33% have experiences of more than 20 years and 62.5% work from 4 to 8 hours,
- 25% of the population work more than 8 hours and 62.5% are exposed to chemicals more than 8h / day,
- 45.5% of surveyed habitats are slums. We only record those people who are most affected by endocrine diseases.

3.3.2. Endocrine diseases reported in the area of study

The statistical analysis on endocrine diseases of the district Dokkarat is presented in the **Table 4**. Overall, the endocrine diseases that have been recorded with the population of the area of study are divided into 25.9% of diabetes, 21.7% of neurological disorders, 20.8% of hormonal imbalance, 16.4% of obesity, 9.1% thyroid and less than 5% growth disorders. It should be noted that endocrine diseases affecting almost 25% of the target population have diabetes, hormonal imbalance and neurological disorders. In this respect, this could be explained by age, nutrition, exposure of the population to chemicals in their occupational practice, and environmental factors such as consumption or exploitation of polluted water, use of cosmetic products, hygiene measures, etc. Similar studies in 2008 suggest that the evolution of our environment and our lifestyles seem to contribute significantly to the prevalence of obesity and diabetes pathologies [23, 24]. Moreover, in France and according to the figures of the General Insurance Scheme for Long-Term Disorders, the rate of diabetes is directly related to obesity [25]. Furthermore, In Europe, obesity is responsible for over 80% of type 2 diabetes [26].

Table 4. The positive rate responses on endocrine diseases in the area of study (%)

Endocrine diseases	Diabete	Obesity	Thyroid	Neurological disorders	Hormonal imbalance	Growth disorders
The rate (%)	25.9	16.4	9.1	21.7	20.8	4.7

3.3.3. Age groups

The results of the effect of age on the appearance of endocrine diseases studied are listed in the **Table 5**. The factor of age is an important one unquestionably linked to exposure to endocrine diseases. For this reason, the analysis of the results showing some endocrine diseases according to the age groups of the population under study denotes that:

- Hormonal imbalance and thyroid disease affect almost all age groups with about 30%, with the exception of the 31-40 age group, which is to a lesser degree 17%,
- Diabetes appears in 38%, 40% and 42% respectively of the population over 31-40 years, 15-20 years and >50 years of age and less than 14% in the population below that age,
- Obesity reaches 40% of the population with the 41-50 age group and about 23% for the other age groups,
- The Neurological disorders are 33% in adults (21-30 years) and in the Middle Ages (41-50 years) and less than 21% in other age groups.

Then, these results permit us to observe that almost the majority of the endocrine diseases appear in the population from 40 years. This could be explained by the onset of aging of the population, as reported in the report of the Canada Health Committee [27]. Studies have highlighted the prevalence of endocrine disease in the elderly from 74 to 90% [28]. Similarly, other studies show that obesity favors the development of diabetes when the age of the population advances [29, 30]. Hence, these results display the influence of age on the appearance and occurrence of the endocrine diseases studied.

Table 5. The effect of age on the occurrence of endocrine diseases studied in the area of study

Endocrine diseases	Age group	The rate (%)
Diabete	15-20 years	38
Neurological disorders, Hormonal imbalance	21_30 years	33
Obesity, Thyroid	31-40 years	40
Diabete, Obesity	41_50 years	40
Diabete	>50 years	42
Hormonal imbalance, thyroid	All age group	30

3.3.4. Type of population

The results of the type of population effect on the occurrence of endocrine diseases are listed in the **Table 6**. The representation of the gender of the population investigated according to the type of endocrine diseases enabled us to observe that these diseases are very encountered in humans with a rate of between 60 and 80% with the exception of growth disorders that occur in women with 50%. The analysis of the outcomes of the genome of the population could probably be explained by the fact that men are the most exposed to chemical substances in their professional circles. These results corroborate a similar study in Belgium [31, 32].

Table 6. The effect of type of population on the occurrence of endocrine diseases in the area of study

Endocrine diseases	Type of population (%)			
	Men	Women	Children	Elderly
Obesity	69	12	4	4
Diabete	67	18	5	11
Neurological disorders	64	8	7	13
Thyroid	70	13	2	2
Hormonal imbalance	73	7	10	5

3.3.5. Duration of exposure

The results of the population type effect on the occurrence of endocrine diseases studied are listed in the **Table 7**. The analysis of the consequences of the exposure duration effect on the occurrence of the endocrine diseases studied displays that for a working time of between 4 and 8 hours per day, 70% of respondents suffering and being obese, about 65% presenting a hormonal imbalance, 55% having neurological disorders, 43% being diabetic and 30% suffering from the thyroid. For people who work more than 8 hours, 35% are obese or 37% are diabetic, 58% endure thyroid and 39% suffering the neurological disorders. These results demonstrate the effect of exposure to chemicals without safety measures, especially as the majority of the population works either in tanneries, textile industries or foodstuffs. Previous studies show that there is a link between exposure to chemicals and the prevalence of certain diseases of endocrine origin such as obesity and type 2 diabetes²³. Similarly, 11.6% of workers in Belgium are exposed one quarter of their working time to endocrine disrupting chemicals [33], 17% of European workers claim to handle hazardous substances and 14% breathe more toxic fumes of 25% of their working time [34].

Table 7. The effect of duration of exposure on the occurrence of endocrine diseases in the area of study

Endocrine diseases	Duration of exposure (%)	
	4 and 8 hour/day	> 8 hour/day
Obesity	70	35

Diabete	43	37
Neurological disorders	55	39
Thyroid	30	58
Hormonal imbalance	65	23

3.3.6. Years of experience

The results of years of experience effect on the occurrence of endocrine diseases studied are listed in the **Table 8**. The examination of results on the effect of years of experience on the occurrence of some endocrine diseases in the target population reveals that after 10 years of work in a chemical industry the risk of these diseases is major. Indeed, 50% of the population questioned, suffers from growth disorders after 10 years of work and for a one-year exposure period, between 20 and 36% require one of the endocrine diseases (diabetes, obesity, hormonal imbalance, neurological disorders). We also noticed that between 24% of the population suffer from growth disorders. These results is proved the results obtained by the cumulative effect of the substances recognized as endocrine disrupters in the adipose tissues of the human body and cocktail effect due to the accumulation of one or more products, having biological properties that may interact together. The more additive and synergistic their interactions, the greater the risk of adverse effect. Others are eliminated more or less rapidly by metabolism. However, as the exposure is continuous, our organism is permanently impregnated by a mixture of low doses of these products [32]. Thus, several studies have been carried out to identify endocrine disrupting chemicals and to demonstrate their effects during short and long-term exposure [35, 36]. On the other hand, less than 18% of the population not exposed to chemicals protests the existence of diabetes, obesity, hormonal imbalance or neurological. which leads us to the assumption that it might be a correlation between epidemiological findings concerning diseases of endocrine origins and environmental results as Chromium, Lead and Arsenic are considered among the endocrine disrupters identified by scientific several communities.

Table 8. The effect of years of experience on the occurrence of endocrine diseases in the area of study

Endocrine diseases	Years of experience (%)	
	1-10 year	>10 years
Obesity	28	32
Diabete	30	21
Neurological disorders	25	27
Thyroid	33	36
Hormonal imbalance	22	28
Growth disorders	24	50

4. Conclusion

The study carried out on the impact of certain toxic chemicals responsible for endocrine diseases in the population adjacent to the estimated polluting industries of the Dokkarat industrial district of Fez city was achieved by carrying out an assessment of the polluting load of Oued water near the district studied following a diagnosis and a cross-sectional epidemiological survey of 380 people from the target population So, the results obtained relate the following conclusions:

- The Dokkarat district comprises 14 modern tanneries, 8 textile industries, 8 oil mills and food production plants using chemicals.

- The population of the Dokkarat district is exposed to the chemicals used in the above-mentioned industries, which can spread in water, soil and air and exploits the water of the Oued Fez upstream for irrigation, washing of utensils, swimming of their children, washing of vegetables **Table** (carrots, turnips, radishes ...).
- The results of the physicochemical and bacteriological study of the water upstream from Oued Fez located downstream of the industries diagnosed show that they are slightly basic, carry a high bacterial load, a mineral and organic load in the quality standards of surface water, a metallic charge at the limit of standards with the exception of arsenic, Lead and chrome. Consequently, the latter can act even at very low doses due to chronic exposure and daily water consumption.
- The cross-sectional descriptive epidemiological study displayed the presence of 6 types of endocrine diseases in the target population divided into 25.9%, 21.7%, 20.8%, 16.4%, 9.1% and 5% respectively of diabetes, neurological disorders, hormonal imbalance, obesity, thyroid and growth disorders that are marked in men more than women and children. Approximately 40% of the population over the age of 30 years suffers from one of these diseases except neurological disorders, which occur at an age of less than 30 years. Most of these diseases are claimed in the surveyed population for an exposure of more than 4h /day and for a working period of more than one year, with the exception of 50% of the population affected by growth disorders after 10 years exercises. Hence, the greater the duration of exposure, the greater the risk of occurrence of endocrine disease.

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