TIH

Toxicology and Industrial Health
27(3) 257–263

DOI: 10.1177/0748233710386409
tih.sagepub.com
SAGE

Thyroid functions in paints production workers and the mechanism of oxidative-antioxidants status

Amal Saad-Hussein[1], Hanaa Hamdy[2], Hisham M Aziz[1] and Heba Mahdy-Abdallah[1]

Abstract

Assessment of occupational exposure to paints production chemicals mainly organic solvents in production of thyroid dysfunction and the mechanism of oxidative-antioxidant imbalance. Triiodothyronine (T_3), thyroxine (T_4), malondialdehyde (MDA), nitric oxide (NO) and total antioxidants was measured in 36 workers and 40 controls. T_3 and T_4 were elevated in 18.8% and 44.4% of the workers, respectively. T_3, T_4, MDA and NO levels were significantly higher in workers compared to controls. Total antioxidants was significantly lower in workers than in controls. T_3 and T_4 were significantly correlated with duration of exposure, while, total antioxidants was inversely correlated. In workers, T_3 was significantly correlated with MDA and inversely correlated with total antioxidants levels. MDA and NO were significantly higher in workers with abnormal T_4 than normal workers. Workers exposed to organic solvents proved to be at risk for hyperthyroidism. Oxidative-antioxidant imbalance was found to have a significant role in development of hyperthyroidism with increasing duration of exposure.

Keywords

Organic solvents, thyroid hormones, oxidative stress biomarkers, total antioxidants, paints production workers

Introduction

Literatures on thyroid disrupting effects due to environmental chemical contaminants are rapidly increasing. In vivo and in vitro studies revealed a multiple potential mechanisms of actions on thyroid disruption. Persistent chemicals such as polychlorinated biphenyls are more likely to cause thyroid disruption than rapidly metabolized ones as such as phthalates (Boas et al., 2006).

Broadly defined, thyroid disrupting chemicals are xenobiotics that alter the structure or the function of thyroid gland, alter regulatory enzymes associated with thyroid hormones (TH) homeostasis or change circulating or tissue concentrations of TH (Crofton et al., 2005).

Thyroid disruption may be caused by a variety of mechanisms, as different chemicals may interfere with the hypothalamic-pituitary-thyroid axis at different levels. Environmental chemicals may interfere with thyroid homeostasis through many mechanisms of action at the receptor level or at the peripheral level. At the receptor level, environmental chemicals may interfere with thyroid homeostasis in binding to transport proteins, in cellular uptake mechanisms or in modifying the metabolism of thyroid hormones. Also, peripheral metabolism of the TH can be affected through effects on iodothyronine deiodinases or hepatic enzymes (Morreale et al., 2004). Several environmental chemicals have a high degree of structural resemblance to the TH, thyroxine (T4) and

[1] Department of Environmental and Occupational Medicine, National Research Center, Cairo, Egypt
[2] Department of Hormone Researches, National Research Center, Cairo, Egypt

Corresponding author:
Amal Saad-Hussein, Department of Environmental and Occupational Medicine, National Research Center, El-Behoos Street, Dokki, Cairo 12311, Egypt
Email: amel_h@hotmail.com

triiodothyronine (T3), and therefore interfere with binding of TH to receptors (TR) or transport proteins. This in turn, may lead to sub-clinical hypothyroidism, which in adults is often diagnosed only by chance because of subtle symptoms (Boas et al., 2006). In addition, several recent studies show that TR may be unintended targets of chemicals manufactured for industrial purposes to which humans are routinely exposed. Polychlorinated biphenyls, polybrominated diphenyl ethers, bisphenol A (BPA), and specific halogenated derivatives and metabolites of these compounds have been shown to bind to TR and perhaps have selective effects on TR functions (Thomas, 2007).

Moreover, TH disruption is thought to be caused through increased T4 metabolism by uridine diphosphate glucuronyl transferases (UDPGTs), blocking TH signaling through TR, and induction of mitochondrial membrane permeability transition (Kashiwagi et al., 2009).

Alteration of the redox potential is known to accompany a variety of pathological states in different cell types and tissues (Samiec et al., 1998). The close relationship between free-radicals formation and the adverse health effects from some occupational exposures has been demonstrated by several epidemiological surveys and experimental studies (Castro et al., 1995; Cavalieri and Rogan, 1995).

Many agents may induce oxidative stress, and the cellular defense mechanisms may be grouped in two categories: enzymatic (i.e. superoxide dismutase, catalase, thioredoxin) and non-enzymatic (i.e. glutathione [GSH]) scavengers. Healthy organism supports a balance between oxidants and antioxidants. The term 'oxidative stress' expresses the status of disturbance of this balance, with predominance of the former (McCord, 1993).

Workers involved in the manufacture of paint products are potentially exposed to a variety of chemicals, such as pigments and extenders, organic solvents, film-forming components and additives. Additionally, paints contain many other toxic chemicals; such as red lead pigment, isocyanates, cadmium, copper oxide, arsenic, cobalt, chromium and volatile organic compounds (Green, 1993).

There is a concern that specific effects of occupational exposure to environmental pollutants on the thyroid function is still limited, further researches are needed to obtain accurate information to be used in establishing guidelines for the protection of health.

Thus, this research aimed to study the role of occupational exposure to a common used environmental toxin, mainly organic solvents, in the development of thyroid endocrinal disturbance among population at risk; such as paints manufacture workers. Additionally, it assessed the mechanism of oxidative-antioxidant imbalance produced secondary to occupational exposure to organic solvent in the production of thyroid functions disturbance in the exposed workers.

Subjects and methods

The present work was a cross-sectional comparative study conducted in new paints production industrial company located in 3rd Industrial Zone Sadat City in Egypt. This company is concerned with the manufacture of car paints, nitrocellulose, putty filler and thinner. Steps of production are assembling materials, mixing, dispersing, thinning and adjusting, filling, handling of materials and laboratory work.

All the workers employed for more than 5 years in the production department were included in the present study as an exposed group (36 male workers). They were exposed to mixture of the chemicals used in production of paints, mainly the organic solvents benzene and toluene. Suitable protective equipments were available, but the workers neglect wearing them. A comparative group of 40 clerk males were selected as control group from National Research Centre. The control subjects were those who never previously worked in painting jobs or were never occupationally exposed to the chemicals used in paints production. The two groups were matched for age, socioeconomic status and special habits.

After verbal consent from each subject, all the subjects completed an investigator-administered questionnaire to assess their general health, smoking habit, current and previous occupational exposures, possible symptoms of thyroid gland dysfunction (both hypo- or hyperthyroid state), use of any medication and the previous medical and family history for chronic health problems.

Both the exposed and the control groups were subjected to clinical examination. Local examination of the thyroid gland and signs of thyroid gland dysfunction were probably investigated.

Random blood samples were collected from all the included subjects by sterile disposable syringes. Quantitative measurements of plasma total 3,5,3′ Triiodothyronine (T3) and L-Thyroxin (T4) were carried out using enzyme immunoassay kit that was purchased

Table 1. Comparison of thyroid hormones, oxidative stress biomarkers and total antioxidants between the two examined groups

	Controls (40)		Workers (36)		Independent *t*-test	
	Mean	SD	Mean	SD	*t*-test	*p* value
T_3 (ng/mL)	1.0	0.05	2.1	0.24	4.275	<0.0001
T_4 (μg/dL)	77.7	1.95	122.5	11.50	3.837	<0.0001
MDA (nmol/mL)	7.0	0.41	18.9	2.48	4.742	<0.0001
NO (μmol/mL)	14.7	0.31	151.3	30.62	4.462	<0.0001
TAC (mmol/L)	2.3	0.05	1.6	0.11	6.616	<0.0001

MDA: malondialdehyde, NO: nitric oxide, T_3: triiodothyronine, T_4: thyroxine, TAC: total antioxidant capacity.

from International Immuno Diagnostics Co., USA (Gamma Trade company), using the methods described by Larsen (1972) and Wisdom (1976), respectively. T3 > 2.0 (ng/mL) is considered abnormal T3 and T4 > 100 (μg/dL) is considered abnormal T4.

Quantitative determination of plasma malondialdehyde (MDA) was carried out colorimetrically using kit purchased from Biodiagnostic Co., Egypt, according to method described by Martinez et al. (2002). Calorimetric method was performed for determination of the plasma total antioxidant using kit purchased from Biodiagnostic Co., according to method described by Koracevic et al. (2001).

Plasma nitrate concentration as a stable end product of nitric oxide was estimated by the Griess reaction after quantitative conversation of nitrate to nitrite by nitrate reductase according to the method of Moshage et al. (1995), using kit purchased from R&D system GmbH (Germany).

Statistical analysis

Statistical analyses were carried out using 'Statistical Package for Social Science' (SPSS) Inc., Chicago, Illinois, USA (Version 14.0). The quantitative results were expressed as means ± standard deviation (SD) and qualitative results as number (No.) and percent (%). Independent *t*-test and Pearson's chi-square were used for comparison between the two groups. Pearson's correlation coefficient as well as partial correlation coefficient were also calculated to evaluate relationships. The difference was considered significant at a level of $p \leq 0.05$.

Results

Statistical analysis revealed that there was no significant difference between the exposed workers and their controls according to their age (31.1 ± 6.5 and 30.2 ± 5.5, respectively). About one third of the workers and the controls were smokers (33.3% and 30%, respectively), without significant difference. The duration of occupational exposure of the workers was in the range 5−16 years (8.4 ±2.7 years).

Table 2. Correlation coefficient between SI of the exposed workers and their levels of thyroid hormones, oxidative stress biomarkers and total antioxidants

	Exposed group SI	
	r	*p* value
T_3 (ng/mL)	0.9	<0.0001
T_4 (μg/dL)	0.03	NS
MDA (nmol/mL)	0.6	<0.0005
NO (μmol/mL)	0.4	0.01
TAC (mmol/L)	−0.7	<0.0001

MDA: malondialdehyde, NO: nitric oxide, SI: smoking index, T_3: triiodothyronine, T_4: thyroxine, TAC: total antioxidant capacity.

Table 1 shows that the levels of T3, T4, MDA and nitric oxide (NO) were significantly higher in the workers compared to their controls. While, total antioxidants was significantly lower in the workers than in the controls.

There were symptoms suggestive of hyperthyroidism in six exposed workers (16.67%) in the form of tachycardia, excessive sweating, palpitation and irritability. However, these symptoms were not detected in the control group. Also, 18.8% of the workers had elevated T_3 and 44.4% had elevated T_4.

In the exposed workers, Table 2 shows that the levels of T3, MDA and NO were significantly correlated with the smoking index (SI), and there was an inversely significant correlation between total antioxidants and SI.

Table 3. Relationships between the thyroid hormones (T_3 and T_4) in the workers and the levels of oxidative stress biomarkers and total antioxidants; after adjustment for SI

	Exposed group			
	T_3		T_4	
Controlled for SI	*r*	*p* Value	*r*	*p* Value
MDA (nmol/mL)	0.5	<0.01	0.3	NS
NO (μmol/mL)	0.3	NS	0.3	NS
TAC (mmol/L)	−0.6	<0.0005	-0.2	NS

MDA: malondialdehyde, NO: nitric oxide, SI: smoking index, T_3: triiodothyronine, T_4: thyroxine, TAC: total antioxidant capacity.

Table 4. Comparison of the levels of oxidative stress biomarkers and total antioxidants between the workers with normal T_4 and elevated T_4

	Normal T_4 (20)		Abnormal elevated T_4 (16)		Independent t-test	
In workers	Mean	SD	Mean	SD	t-test	*p* value
MDA (nmol/mL)	12.7	1.60	25.8	4.40	2.812	<0.01
NO (μmol/mL)	65.7	13.46	261.3	56.11	3.391	<0.005
TAC (mmol/L)	1.7	0.14	1.4	0.17	1.033	NS

MDA: malondialdehyde, NO: nitric oxide, T_3: triiodothyronine, T_4: thyroxine, TAC: total antioxidant capacity.

On controlling for SI, Table 3 shows that T_3 in the exposed group was significantly correlated with MDA and inversely correlated with total antioxidants. While, there was no significant relations between T_3 and NO, as well as between T_4 and the levels of MDA, NO and total antioxidants. In the control group after controlling for SI, there was no significant relationship between the thyroid hormones (T_3 and T_4) and the levels of MDA, NO and total antioxidants.

Table 4 shows that there were significant elevations of the oxidative biomarkers (MDA and NO) in the workers with abnormal elevated T_4 compared with those with normal T_4. While, there was no significant difference between the two sub-groups according to total antioxidants.

Table 5 shows that after controlling for SI, the duration of exposure was significantly correlated with age and thyroid hormones (T_3 and T_4) of the workers and inversely significantly correlated with their total antioxidants.

Table 5. Correlation coefficient of the duration of exposure of the workers and the levels of thyroid hormones, oxidative stress biomarkers and total antioxidants, after adjustment for SI

	Duration of exposure	
Controlled for SI	r	*p* value
Age	0.9	<0.0001
T_3 (ng/mL)	0.4	0.05
T_4 (μg/dL)	0.5	<0.01
MDA (nmol/mL)	0.3	NS
NO (μmol/mL)	0.2	NS
TAC (mmol/L)	−0.3	0.05

MDA: malondialdehyde, NO: nitric oxide, SI: smoking index, T_3: triiodothyronine, T_4: thyroxine, TAC: total antioxidant capacity.

Discussion

There are growing evidences that environmental chemical contaminations can disrupt endocrine systems Crofton (2008). Several groups of chemicals have potential for thyroid disruption. There are substantial evidences that polychlorinated biphenyls, dioxins and furans cause hypothyroidism in exposed animals and that environmental contaminations affect human thyroid homeostasis. Even small changes in thyroid homeostasis may adversely affect human health.

In the present study, although the two groups were matched for age and smoking habits, there were symptoms suggestive of hyrerthyroidism in six paints production workers (16.67%); in the form of

tachycardia, excessive sweating, palpitation and irritability, but, none of those symptoms were found in their controls. Moreover, the current study also revealed that 18.8% of the exposed workers had elevated T_3, and 44.4% had elevated T_4. These results are to be supported by Crofton et al. (2005), they stated that endocrine disruption from environmental contaminants has been linked to a broad spectrum of adverse outcomes. They found that potential additive or synergistic effects of mixtures of thyroid-disrupting chemicals will affect serum T_4 concentrations in a dose-additive manner.

Paints contain many toxic chemicals such as red lead pigment, isocyanates, cadmium, copper oxide, arsenic, cobalt, chromium and volatile organic compounds, which are particularly hazardous and can lead to varying conditions of ill-health (Green, 1993). Prescott et al (1992) proved that occupational exposure to cobalt blue dyes increases the levels of serum T_4, unaltered serum thyroid stimulating hormone (TSH) and marginally reduced T_3. Moreover, Uzma et al. (2008) proved that organic solvent, especially benzene, cause hematological and thyroid dysfunctions.

BPA is used to manufacture polycarbonate and numerous plastic products including adhesives and powder paints. BPA is rapidly glucuronidated in rats and humans (Boas et al., 2006). Rats exposed to BPA exhibited increased weight of the thyroid but without histopathological changes (Tan et al., 2003). No significant effects on TH levels were found in either polecats (Nieminen et al., 2002a) or field voles (Nieminen et al., 2002b) after BPA exposure. However, a positive correlation between increasing BPA and activity of the hepatic enzymes uridinediphosphate-glucuronosyltransferase (UDPGT) was found – UDPGT catalyzes the conjugation of various substances to glucuronic acid and an increase in activity may lead to faster metabolism of TH (Iwamuro et al., 2003). BPA fed to pregnant rats was associated with significant increase of total T_4 at postnatal day 15 in the pups (Zoeller et al., 2005). But, BPA acts as an antagonist to T_3 (Moriyama et al., 2002).

The present results demonstrate a significant effect of the industrial exposures in paints manufacturing on thyroid hormone metabolism, as serum levels of T_3 and T_4 in the workers were significantly elevated compared to their controls.

Contradictorily, Zaidi et al. (2004) found that the percentage of hypothyroidism was higher in spray painters using solvent-based paints (28%) compared to their controls (8.5%). They considered that as an indication of interference of the chemicals with the thyroid hormones. They added that interference of solvent-based chemicals with the uptake of iodine by thyroid gland and further prevention of organification of absorbed iodine with thyroid-binding globulins (TBGs) and the release of thyroid hormones are some of the possible causes of thyroid dysfunction among spray painters (Zaidi et al., 2004). Several studies proved that oxidative stress state is provoked by the effect of reactive metabolites formed at biotransformation of different xenobiotics in the organism. In healthy organism, a balance between oxidative stress and antioxidants levels is rapidly supported (McCord, 1993). Oxidative-antioxidant unbalance could be attributed to environmental exposures to oxidative stressor chemicals. Oxidative stress biomarker MDA was found to be significantly increased in shoemakers exposed to organic solvents, while, the antioxidant enzymes (SOD and GR) were significantly decreased (Hussein et al., 2008).

In the current study, paints production workers were also exposed to organic solvents as well as many oxidative stressor chemicals. The present results revealed that the levels of the oxidative stress biomarkers (MDA and NO) were significantly increased in the paints manufacturing workers compared to their controls. While, total antioxidants was significantly lower in the workers than in the controls. This was considered to be an imbalance between oxidative-antioxidant status in the exposed workers compared to their controls, and this could be contributed to their occupational exposure to oxidative stressor chemicals, such as organic solvents.

Hyperthyroidism has been associated with alteration in the activities of antioxidant enzymes. It is reported that SOD activity was increased in the cardiac muscle and liver in hyperthyroid rats (Asayama et al., 1989). Also, the increase of SOD have been shown in the blood of patients with hyperthyroidism. On the contrary, some investigators found decreased SOD activity in the blood samples of patients with hyperthyroidism (Fernandez et al., 1988). Cetinkaya et al. (2005) found that sub-clinical hyperthyroidism gives rise to oxidative stress, as the high levels of free radicals inside the cells increase the MDA levels and the organism defends itself against the effects of oxidative stress by the significant increase in SOD activity as a protection mechanism.

In the present study, smoking index of the workers was found to have a significant role in the increasing of the levels of the oxidative biomarkers (MDA and

NO) and in the decreasing of the levels of total antioxidants, as well as in increasing of the levels of T_3. After controlling of the confounding effect of SI in the exposed workers, the current results revealed that T_3 was significantly correlated with MDA and inversely significantly correlated with total antioxidants. Additionally, there were significant elevations in oxidative stress biomarkers (MDA and NO) in the workers with abnormally elevated T_4 compared to those with normal T_4. Thus, our results coincided with the results of Cetinkaya et al. (2005).

Exposure to environmental pollution proved to have significant oxidative stress. Thus, the present findings may add another mechanism to the variety of mechanisms mentioned by Morreale and his colleagues (2004) in the explanations of thyroid disruption causes by environmental chemicals exposures.

In our opinion, this elevation in oxidative stress biomarkers and the oxidative-antioxidant imbalance in the paints production workers could lead to the development of hyperthyroidism and not the opposite (hyperthyroidism in the workers produced secondary to occupational exposures lead to oxidative stress). But, the end results are the same. Oxidative stress and hyperthyroidism considered as a health problem in paints manufacturing workers.

Moreover, the risk of development of thyroid cancer was increasing. In a study done to explore thyroid cancer risk in the Swedish population, it was concluded that exposure to organic solvents, used mainly in shoe and leather industry, seemed to be associated with excess thyroid cancer among the exposed women (Lope et al., 2009). Thus, further studies are needed, especially after the present results.

In the current study, the duration of employment of the exposed workers was significantly correlated with the levels of T_3 and T_4 and was inversely correlated with their total antioxidants. Unexpected, there was no relationship between the duration of employment and the levels of MDA and NO. The significant correlation between the duration of employment and the age of the workers may explain this discrepancy, as Chehade et al. (1999) proved that old age played a significant role in blunting the effect of altered thyroid function on the levels of MDA in experimental animals with induction of hypothyroidism or hyperthyroidism.

In conclusion, occupational exposure to indoor pollutants in paints production industry is considered a risk factor for development of hyperthyroidism. This hyperthyroidism could be attributed to oxidative-antioxidants imbalance produced secondary to occupational exposure to oxidative stressor chemicals, mainly organic solvents. Oxidative stress could play an important role in the progression of thyroid dysfunction in workers occupationally exposed to organic solvents. This progression could be aggravated by the lower levels of their antioxidants status.

Thus, dietary corrections or antioxidant supplementations could be an additional protective measure besides, personal protective equipment and indoor environmental monitoring, to control the released pollutants. Also we recommend further studies for workers employed for a longer duration of exposure, to support the present findings, as our studied workers were employed for less than 12 years.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not for-profit sectors.

References

Asayama K, Dobashi K, Hayashibe H, and Kato K (1989) Effects of beta-adrenergic blockers with different ancillary properties on lipid peroxidation in hyperthyroid rat cardiac muscle. *Endocrinologia Japonica* 36(5): 687–694.

Boas M, Feldt-Rasmussen U, Skakkebaek NE, and Main KM (2006) Environmental chemicals and thyroid function. *European Journal of Endocrinology* 154(5): 599–611. Review.

Castro GD, Stamato CJ, and Castro JA (1995) Proline interaction with trichloromethyl and trichloromethyl peroxyl free radicals in a model system: studies about the nature of the reaction products formed. *Drug Metabolism Review* 27: 257–275.

Cavalieri EL, Rogan EG (1995) Central role of radical cation in metabolic activation of polycyclic aromatic hydrocarbons. *Xenobiotica* 25: 677–688.

Cetinkaya A, Kurutas EB, Buyukbese MA, Kantarceken B, and Bulbuloglu E (2005) Levels of malondialdehyde and superoxide dismutase in subclinical hyperthyroidism. *Mediators of Inflammation* 1: 57–59.

Chehade J, Kim J, Pinnas JL, and Mooradian AD (1999) Age related changes in the thyroid hormone effects on malondialdeyde modified proteins in rat heart. *Society for Experimental Biology and Medicine* 222: 59–64.

Crofton KM (2008) Thyroid disrupting chemicals: mechanisms and mixtures. *International Journal of Andrology* 31(2): 209–223.

Crofton KM, Craft ES, Hedge JM, et al. (2005) Thyroid-hormone-disrupting chemicals: evidence for

dose-dependent additively or synergism. *Environmental Health Perspectives* 113(11): 1549–1554.

Fernandez V, Llesuy S, Solari L, et al. (1988) Chemical illuminescent and respiratory responses related to thyroid hormone-induced liver oxidative stress. *Free Radical Respiratory Communication* 5(2): 77–84.

Green DH (1993) Zinc: environmental constraints and opportunities for a base metal, conference. Hobart: Australian Institute of Mining and Metallurgy.

Hussein ASA, Abdalla MSH, Hussein JS, Shousha WGH, and Mohamed AH (2008) Antioxidants in shoe-makers exposed to organic solvents. *Journal of Applied Sciences Research* 4(9): 1107–1117.

Iwamuro S, Sakakibara M, Terao M, et al. (2003) Teratogenic and anti-metamorphic effects of bisphenol A on embryonic and larval Xenopus laevis. *General and Comparative Endocrinology* 133: 189–198.

Kashiwagi K, Furuno N, Kitamura S, et al. (2009) Disruption of thyroid hormone function by environmental pollutants. *Journal of Health Science* 55(2): 147–160.

Koracevic D, Koracevic G, Djordjevic V, Andrejevic S, and Cosic V (2001) Method for the measurement of antioxidant activity in human fluids. *Journal of Clinical Pathology* 54: 356–361.

Larsen PR (1972) Triiodothyronine: review of recent studies of its physiology and patho-physiology in man. *Metabolism* 21: 1073–1092.

Lope V, Perez-Gḿez B, Aragonés N, et al. (2009) Occupational exposure to chemicals and risk of thyroid cancer in Sweden. *International Archives of Occupational and Environmental Health* 82(2): 267–274.

Martinez R, Quintana K, Navarro R, et al. (2002) Pro-oxidation and antioxidant potential of catechol estrogens against ferryl-myoglobin-induced oxidative stress. *Biochimica et Biophysica Acta* 1583: 167–175.

McCord JM (1993) Human disease, free radicals, and the oxidant/antioxidant balance. *Clinical Biochemistry* 26: 351–357.

Moriyama K, TagamiT, Akamizu T, et al. (2002) Thyroid hormone action is disrupted by bisphenol A as an antagonist. *Journal of Clinical Endocrinology and Metabolism* 87: 5185–5190.

Morreale G, Obregon MJ, and Escobar F (2004) Role of thyroid hormone during early brain development. *European Journal of Endocrinology* 151: 5–37.

Moshage H, Rok B, and Huizenga JR (1995) Method of nitric acid measurement. *Clinical Chemistry* 41: 892–896.

Nieminen P, Lindstrom-Seppa P, Juntunen M, et al. (2002) In vivo effects of bisphenol A on the polecat (Mustela putorius). *Journal of Toxicology and Environmental Health A* 65: 933–945.

Nieminen P, Lindstrom-Seppa P, Mustonen AM, Mussalo-Rauhamaa H, and Kukkonen JV (2002) Bisphenol A affects endocrine physiology and biotransformation enzyme activities of the field vole (Microtus agrestis). *General and Comparative Endocrinology* 126: 183–189.

Prescott E, Netterstrm̊ B, Faber J, Hegedüs L, Suadicani P, and Christensen JM (1992) Effect of occupational exposure to cobalt blue dyes on the thyroid volume and function of female plate painters. *Scandinavian Journal of Work Environment and Health* 18(2): 101–104.

Samiec PS, Drews-Botsch C, Flagg EW, Kurts JC, Stenberg P Jr, Reed RL, et al. (1998) Glutathione in human plasma: decline in association with aging, age-related macular degeneration, and diabetes. *Free Radical Biology and Medicine* 24: 699–704.

Tan BL, Kassim NM, and Mohd MA (2003) Assessment of pubertal development in juvenile male rats after sub-acute exposure to bisphenol A and nonylphenol. *Toxicology Letters* 143: 261–270.

Thomas RZ (2007) Environmental chemicals impacting the thyroid: targets and consequence. *Thyroid* 17(9): 811–817.

Uzma N, Salar BMKM, Kumar BS, Aziz N, David MA, and Reddy VD (2008) Impact of organic solvents and environmental pollutants on the physiological function in petrol fillin workers. *International Journal of Environmental Research and Public Health* 5: 139–146.

Wisdom GB (1976) Enzyme-immunoassay. *Clinical Chemistry* 22: 1243–1255.

Zaidi SA, Sunil Kumar DD, and Tiwari RR (2004) Assessment of health risk among spray painters with special reference to reproductive and endocrine functions. Ann Rep / ZDI/6/ Plenary Address p 5.

Zoeller RT, Bansal R, and Parris C (2005) Bisphenol-A, an environmental contaminant that acts as a thyroid hormone receptor antagonist in vitro, increases serum thyroxin, and alters RC3/neurogranin expression in the developing rat brain. *Endocrinology* 146: 607–612.