

Growing Burden of Diabetes in Sub-Saharan Africa: Contribution of Pesticides ?

Colette Sylvie Azandjeme^{1,2}, Michèle Bouchard³, Benjamin Fayomi⁴, Francois Djrolo⁴, Dismand Houinato^{4,5} and Hélène Delisle^{1*}

¹TRANSNUT, WHO Collaborating Centre on Nutrition Changes and Development, Department of Nutrition, Faculty of Medicine, University of Montreal, PO Box 6128, Downtown Station, Montreal (Qc) Canada H3C 3J7; ²Regional Institute for Public Health, University of Abomey-Calavi, 01 BP 918 Cotonou, Benin, Canada; ³Department of Environmental and Occupational Health, Chair in Toxicological Risk Assessment, University of Montréal, PO Box 6128, Downtown Station, Montreal (Qc) Canada H3C 3J7; ⁴Faculty of Health Sciences, University of Abomey-Calavi, 01 BP 188 Cotonou, Bénin, Canada; ⁵Benin Republic National Program of Non Communicable Diseases, Canada

Abstract: The diabetes burden is growing in Sub-Saharan Africa (SSA). The low overall access to health care has been documented to contribute to the high diabetes-related mortality. Due to economic, demographic, epidemiological and nutrition transitions in SSA, the growing prevalence of diabetes appears to be related to obesogenic lifestyles and the inter-generational impact of malnutrition in women of childbearing age. Both overnutrition and undernutrition have been associated with the development of diabetes and other chronic diseases. Africans are also suspected of being genetically predisposed to diabetes. According to existing data in developed countries, exposure to pesticides, particularly organochlorines and metabolites, is associated with a higher risk of developing type 2 diabetes and its comorbidities. In African countries, pesticide exposure levels often appear much higher than in developed countries. Furthermore, undernutrition, which is still highly prevalent in SSA, could increase susceptibility to the adverse effects of organic pollutants. Therefore, the growing and inadequate use of pesticides may well represent an additional risk factor for diabetes in SSA. Additionally, high exposure to pesticides in African infants *in utero* and during the perinatal period may increase the intergenerational risk of developing diabetes in SSA.

Keywords: Pesticides, africa, diabetes, developmental origins, nutrition.

INTRODUCTION

Diabetes is a public health problem in Sub-Saharan Africa (SSA); the prevalence is growing and mortality is high. In most cases, the disease is diagnosed late and often at the stage of crippling complications. The diabetes burden in SSA occurs in a context of poverty where access to health care is limited [1]. Diabetes is also an economic burden for SSA [2]. According to the International Diabetes Federation (IDF) projections, SSA is the region where diabetes prevalence will have the greatest increase by 2030 [1-3]. In SSA, diabetes is implicated in the double nutritional burden issue, with concurrent nutrition-related non-communicable diseases (NCDs) and malnutrition in the same populations. However, limited attention has been given so far to NCDs such as diabetes, cardiovascular disease and cancers. The meagre health resources are rather focused on malnutrition and communicable diseases such as malaria, tuberculosis and Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome (HIV/AIDS) [4]. Hopefully, a shift of health priorities will result from the impetus given by the High Level Meet-

ing of the United Nations for the prevention and control of NCDs [5].

In SSA, there is a trend for an increasing use of pesticides in agriculture and in other fields, for instance to fight against malaria. Low level of education, greed and corruption that often affect low-income countries, coupled with little concern for health, lead to suboptimal management and inadequate use of pesticides. Therefore, populations and their environment are at high risk of contamination [6, 7]. Current data support an association between exposure to certain environmental pollutants and diabetes. Could the high levels of pesticides exposure contribute to the ever increasing prevalence of diabetes in African populations? The aim of this review is to examine various factors that might influence the burden of diabetes in SSA and highlight the potential contribution of pesticides.

GENERAL METHODOLOGY FOR THIS REVIEW

In this review, we expose the features of diabetes prevalence and its contributing factors in SSA. We also examine the level of exposure to pesticides of African populations on the basis of available data. A summary of the existing evidence for the association between pesticide exposure and diabetes is then summarized to assess the potential contribution of pesticides to the rapid progression of diabetes in SSA.

*Address correspondence to this author at the TRANSNUT, WHO Collaborating Centre on Nutrition Changes and Development, Department of Nutrition, Faculty of Medicine, University of Montreal, PO Box 6128, Downtown Station, Montreal (Qc) Canada H3C 3J7; Tel: 1 514 343-6111 Extension 25219; Fax: + 1 514 343-7395; E-mail: helene.delisle@umontreal.ca

Databases such as Pubmed, Medline, Embase, Cab abstract, Cinhal, Toxline and 'Banque de Données en Santé Publique' (BDSP) were explored. Relevant publications cited by other authors were found using Web of Science. Additional information was sought on the official websites of governments, scientific associations and regulatory bodies. The main keywords used were: diabetes, pesticides, Africa*. The words organochlorin*, organophosphor*, pyrethrin*, carbamat*, Pollutants and POPs (Persistent organic pollutants) were also used as substitutes for "pesticides". Similarly, "health" and "disease" also replaced "diabetes".

Relevant documents of the last 20 years were given priority but less recent papers were also used as appropriate. Article selection focused on diabetes and the factors that explain its increasing prevalence. The retained articles focused on pesticide levels in biological tissues and environment, and health effects. Publications on the relationship between pesticide exposure and diabetes were exploited.

EPIDEMIOLOGY OF DIABETES IN SSA

In SSA, the three classical types of diabetes are observed: type I diabetes, type II diabetes and gestational diabetes [8, 9]. In addition, intermediate forms between type I and type II have been described such as type 1B diabetes [10-20], malnutrition related diabetes and fibro-calculeous pancreatic diabetes [12, 21-25]. These atypical forms of diabetes observed specifically in SSA are not formally recognized due to lack of evidence to clarify their pathogenesis. They are therefore not taken into account in official classifications of the World Health Organisation (WHO) and the International Federation of Diabetes (IDF) although recent studies confirm their presence in SSA [16].

The estimated prevalence of diabetes among African adults aged 20 to 79 years increased from nearly null to the epidemic stage within a generation [26]. Epidemiological data on diabetes in SSA are few and inconsistent due to the variability in data collection methodology and definition criteria. The existing prevalence data come primarily from STEPwise (STEPS) surveys as recommended by WHO for chronic diseases monitoring [27, 28], hospital studies [29, 30] and a few population based studies [31-33]. From 3% over the last ten years, the prevalence of type II diabetes rose to 4.5% in 2011 and will reach 4.9% by 2030 according to the IDF [1, 34, 35]. The prevalence varies from 1 to 12% depending on the country [36]. Although the observed prevalence in SSA is low compared to other continents, the growth rate of 90% by 2030 is the highest in world. Type I diabetes and gestational diabetes also increase rapidly but the increase is lower than in developed countries [1]. The prevalence rates of type I diabetes and gestational diabetes were respectively estimated at 4-12 for 100 000 and 0- 9% in 2011 [36]. According to IFD 5th atlas, 36.1 thousands of African children under 14 years old were affected with type 1 diabetes and 5.9 thousands were detected every year. These prevalence figures could be underestimated due to lack of detection and high mortality associated with poor access to treatment, particularly for type 1 diabetes [37-40].

The burden of diabetes in SSA is also characterized by the high rate of complications, as these are generally the mode of detection of the disease. Indeed, SSA has the

highest estimated proportion of undiagnosed diabetes (78%) while the overall worldwide rate is estimated at 50% [1-3]. Microvascular complications are the most common. Retinopathy affects 15-55% of patients and kidney complications 5-28% in the first year of diagnosis. Peripheral neuropathy accounts for approximately 10-36% of complications [26, 41-43]. In SSA, 6.1% of deaths are attributable to diabetes and two-thirds of affected subjects die of cardiovascular complications [1, 44]. The high complication and death rates of diabetes are due to late diagnosis and poor access to healthcare, but the determining factors of the rapid increase in the prevalence of the diseases need to be better understood. Ketoacidosis is the most frequent complication observed in Type 1 diabetes [39].

FACTORS ASSOCIATED WITH INCREASED PREVALENCE OF DIABETES IN SSA

Transitional Context and Intergenerational Impact of 'Dysnutrition'

In SSA, economic transition and increasing urbanization lead to a demographic transition characterized by aging of the population due to improved life expectancy. This translates into a widening of the upper part of the age pyramid. It is estimated that SSA's urban population will have increased by 98% in 2050 [45]. This rise in the urban population will contribute to the increase in the number of persons living with diabetes in the order of two-fifths [26]. Indeed, changes from traditional to urban lifestyles and eating patterns foster obesity and the development of diabetes as a consequence. Living in an urban area has been shown to be conducive to the adoption of an obesogenic lifestyle characterized by a high caloric diet rich in sugar and fat as well as by sedentary behaviors [46]. Thus, economic, demographic and nutrition transitions appear to usher the emergence of new epidemiological paradigms such as obesity, diabetes and cardiovascular disease [46-48]. While diabetes is usually more prevalent in urban areas [32], an increasing trend is also observed in rural areas [49]. Diabetes has been documented to occur more frequently in individuals of lower than higher socio-economic status, but this varies according to the context. At least in developed countries, it has been reported that food choices of the poor and food insecure are oriented primarily towards energy-dense foods but low in micronutrients [50-52]. This adaptation strategy might contribute to explain the obesity of poverty paradox [53-55]. Hence, obesity is a threat at both ends of the socioeconomic spectrum. This pattern may explain the observed increase in obesity in SSA [56-59], while underweight also prevails. Hence both forms of 'dysnutrition' [60], that is, undernutrition and overnutrition, coexist.

While it is generally stated that 80% of persons with diabetes are obese, less than half the individuals with diabetes in SSA are obese [30]. Obesity is far more common in women than men [44, 58]. This can be explained by the fact that in several African cultures, overweight and obesity are regarded as socially desirable. A beauty feature in women, overweight is a sign of wealth in their spouses [61-63]. Meanwhile, 27-51% of women of childbearing age in SSA are undernourished and 21% of newborns have a low birth weight [64]. According to the established theory on the de-

velopmental origins of chronic diseases, children with low birth weight are more likely to develop chronic diseases later in life when exposed to an obesogenic environment [65-71].

Type 1 diabetes seems to be more prevalent in girls and is usually associated with undernutrition or low socioeconomic status as reported in several countries [15, 40, 72]. Type 1 diabetes is also consistently associated with environmental factors that interact with gene susceptibility [15].

Diabetes and Infections in SSA

Some infectious diseases such as tuberculosis and HIV are suspected to contribute to the development of diabetes. Current data show that tuberculosis is associated with diabetes [73, 74] and increases the risk of metabolic syndrome and cardiovascular diseases [75-77]. However, the relationship between the two diseases seems to be bidirectional [78]. Additionally, some drugs such as Isoniazid used in the treatment of tuberculosis could lead to hyperglycemia [75]. Antiretroviral drugs for HIV such as Zidovudine and Stavudine are also associated with an increased risk of developing diabetes by promoting dyslipidemia and insulin resistance [77-79]. Since tuberculosis and HIV infections are highly prevalent in SSA and since medicines are becoming more accessible, these diseases may be involved in the increasing prevalence of diabetes. This was suggested in a recent study showing a concomitant increase in the prevalence of diabetes, tuberculosis and HIV [80].

In summary, diabetes in SSA has been associated with factors related to demographic and nutrition transitions, with the intergenerational effect of undernutrition, as well as with some infectious diseases, particularly in genetically predisposed individuals. Data on Africans are scarce [81], but several studies in African-Americans have revealed a genetic predisposition to diabetes among people of African descent [82]. The weakness of African healthcare systems for the screening and prevention of diabetes is another factor. Environmental pollutants such as pesticides could also be an additional factor related to the burden of diabetes in SSA, as summarized by (Fig. 1).

EXPOSURE TO PESTICIDES AND DIABETES IN SSA

Factors that contribute to pesticide exposure in African populations are reviewed first. We then discuss the potential contribution of pesticides to diabetes risk, particularly in SSA.

Level of Exposure to Pesticides in SSA

Pesticide Utilization

Economic challenges, the need to reduce postharvest food losses, and the fight against human disease vectors foster the increasing use of pesticides in SSA. Pesticides represent one group of chemical pollutants within the larger family of environmental pollutants. According to the nomenclature used in this review, the major groups of pesticides are insecticides, herbicides, fungicides, rodenticides [83]. A subgroup of insecticides, that of organochlorines, organophosphates, carbamates and pyrethroids, is in general of more concern because they are documented as being the most harmful. Other chemical pollutants have also been associated with the development of diabetes, such as polychlorinated biphenyls (PCBs) and dioxins, but the present review focuses on pesticides as these are an issue in SSA.

Existing data provided by governmental agencies show that the amounts of pesticides used in SSA for crop protection and public health purposes have increased considerably over the years [7], although the amounts of pesticides officially available in SSA seem to be low (3% of world consumption) compared to other continents [84]. Persistent pesticides such as organochlorines are usually intended for cotton production for export. Pyrethroids are used for production and preservation of certain foods and also for public health purposes. Unfortunately, it is not uncommon to observe that dangerous pesticides are used in food production, processing and preservation. Numerous pesticides are also used by individuals for domestic purposes, and these are not registered in national reports.

Inadequate Management and Practices

Pesticides are often used inappropriately, with increased risk of human exposure. Persistent and harmful pesticides

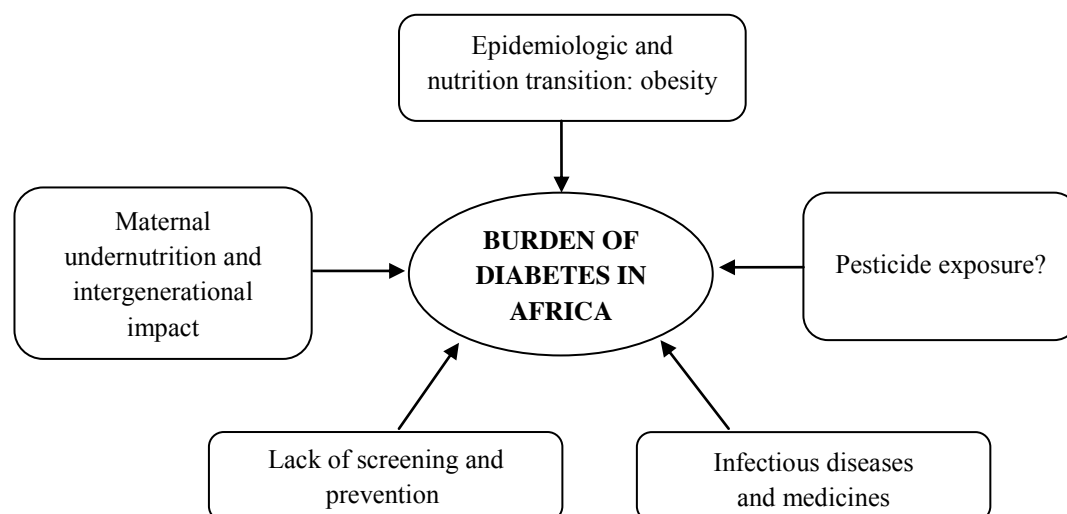


Fig. (1). Contributing factors to the burden of diabetes in SSA.

such as DDT (dichlorodiphenyltrichloroethane) are still being imported in SSA and might contribute to increased release in the environment and exposure of individuals [6, 7]. Even if they are excluded from the official lists of authorized chemicals in many countries in line with Stockholm and Rotterdam conventions [85-87], some of these harmful pesticides are still available on the informal market. Pesticides are sold in local shops, often near food products and restaurants, with high risk of contamination [88, 89]. Unfortunately, very little information is available on the nature of active ingredients, on the instructions to users and on the toxicity of pesticides imported fraudulently. Furthermore, since 2006, WHO has authorized DDT utilization in SSA to control malaria, despite its high persistence, because this chemical is still considered safe when sprayed into human and animal habitats according to guidelines [90]. However, these pesticides once sprayed on the walls are inhaled and absorbed by the exposed individuals even if the doses are extremely low.

Similarly, long-lasting bed nets that release pyrethroids slowly and gradually expose African people for many years to such pesticides. It is now suspected that long term exposure to low doses of these pesticides may contribute to their bioaccumulation in the human body and contribute to various chronic diseases including diabetes [91, 92].

Large amounts of obsolete pesticides are not destroyed and are often stored in inappropriate places. Containers are damaged over time and pesticides migrate into the environment, as observed in Ethiopia, Benin and elsewhere [93, 94]. Fortunately, a strategy for the destruction of obsolete stocks is underway in these countries. Empty pesticide containers and contaminated materials are often discarded in the environment or reutilized for various household needs [94]. The inadequate management of pesticide wastes is a common source of contamination of the environment as observed in Tanzania [95], and it is often responsible for fatal acute poisoning [96, 97]. Several cases of acute poisoning reported in African countries have been attributed to organochlorine or organophosphate pesticides, including more recently Endosulfan, which is now banned [96-98]. Protective equipments for pesticide users are not often available [94] and the instructions for individual and collective protection given to farmers are not followed for a variety of reasons [99, 100]. Despite the efforts of several institutions to provide coaching and training, the majority of pesticide users are still not well trained. Even when trained, due to the low levels of education, farmers may not be able to read or understand pictograms and instructions on containers [94, 100]. The inadequate protection was reflected in the high concentrations of pesticides on the pesticide users' skin, in a Gambian study [101]. Other inappropriate uses of pesticides have been observed, such as the utilization of pesticides in preparation of baits for fishing and hunting [95], overdosage during spraying, the cultivation of crops near pesticide-treated cotton fields and pesticide use for the preservation of food crops. These practices fueled by the pursuit of profit and poor education lead to significant contamination of the environment and individuals [102, 103].

Pesticide Levels in the Environment and Biological Fluids

High levels of the most persistent pesticides were detected in water, soil, air, plants, fish and other animals in

SSA countries [104-110]. Persistent organochlorine pesticides (POCs) were also found in dairy products and various other foods [95, 99, 111-116]. The concentrations of POCs found in food and drinking water were often higher than regulated maximum residue levels (MRLs) [110, 117], although the levels of organophosphates and pyrethroids found in food samples in Cameroon and Nigeria were reportedly lower than the prescribed limits [118, 119]. The wide variation may be ascribed to different analytical methods which could vary from spectrophotometric assays to chromatographic techniques.

Available human biomonitoring data are quite limited. Blood levels of various pesticides among exposed farmers were shown to be beyond acceptable limits [120-123]. Pesticide levels found in breast milk of African women farmers in Ghana, Kenya and South Africa exceeded the tolerable daily limit for infants [120, 124-128]. High concentrations of organochlorine pesticides may well have adverse effects on infant growth and development, thereby contributing to chronic diseases in adulthood [128]. Furthermore, African children usually accompany their parents in fields treated with pesticides and frequently work in these fields [94]. In a Kenyan study, children aged 0-14 years were found to be the first victims of acute poisoning, representing 40% of cases of pesticide poisoning identified in a hospital.

Available data on concentrations of organochlorine pesticides in human blood and other body fluids in SSA and non African countries are summarized in (Tables 1 to 4). The data show that pesticide concentrations in Africans were similar or higher than those observed in developed countries. For example, in a comparative study, pesticide concentrations in Tanzania were nine times higher than in Belgium [129]. Similarly, in Gambia, Ghana, Côte d'Ivoire and Tunisia, pesticide concentrations were approximately the same or higher than those in developed countries [130-134]. This high exposure in SSA may partly explain the occurrence of some cancers, reproductive disorders, respiratory diseases and metabolic disturbances leading to cardiovascular diseases. It thus appears relevant to ask the question whether pesticide exposure plays a role in the development of diabetes in SSA.

Pesticide Exposure and Risk of Diabetes

Scientific evidence on the relationship between diabetes and exposure to persistent organic pollutants including pesticides is now increasingly available [141-143]. Data linking diabetes and pesticide exposure primarily refer to type II diabetes. The relationship between persistent organic pollutants and diabetes was first suspected half a century ago [144]. This was further evidenced when symptoms were observed in veterans of the Vietnam War exposed to the defoliant herbicide known as 'Orange Agent'. Subsequent studies reported that one metabolite of that herbicide, 2,3,7,8-tetrachlorodibenzo-p-dioxine (TCDD), caused deleterious effects including diabetes. Available studies on the effects of organochlorine pesticide exposure showed a consistent association with diabetes [145-150]. A similar risk was found associated with other types of pesticides. For professional users, the risk of diabetes was twice as high when they were exposed to DDT [151]. The risk increased respectively by

Table 1. Blood Concentrations of DDT and its Metabolites in African and Non-African Countries.

Countries, Years	Authors (Reference)	N	p,p'-DDE	p,p'-DDD	p,p'-DDT	ΣDDTs
Ghana, 2001	N'tow [106]	20	380 ± 120	NA	NA	NA
Ghana, 2008	N'tow [120]	115	7.1± 1.2	<LOQ	0.5±0.1	9.1± 1.3
Gambia, 2002	Manirakiza [130]	100	M: 4020±3960 F: 3520±2720	M:560±700 F: 160±160	M: 1160±840 F: 900±920	M: 7920±5240 F: 5920±2640
Tanzania, 2006	Weiss [129]	46	M : 18.63 ±12.1 ^a F : 12.77 ± 9.7	NA	NA	NA
Tunisia, 2010	Ennaceur [132]	82	1.69±10,7 ^b	0.42±9.9	0.91±11.9	4.33±13.2
Tunisia, 2007	Ennaceur [131]	113	168.8±158	19.9±14.4	24.3±18.8	213.1±160
Belgium, 2006	Weiss [129]	42	M : 2.15 ±0.19 ^a F : 1.15 ± 0.9	NA	NA	NA
Sweden, 2007	Rignell-Hydbom [135]	543	C: 240 (93-970)* T: 140 (49-500)	NA	NA	NA
Sweden, 2009	Rignell-Hydbom [136]	742	C: 4.11±4.46 ^b T: 3.76±3.55	NA	NA	NA
USA, 2007	Cox [137]	1303	9 (1.98-228.2)**	NA	3.22(2-71.9)	NA
Finland, 2011	Airaiksen [138]	1988	610±12	NA	NA	NA
Corea, 2010	Son [139]	80	C: 652.3±646.7 T : 376.0±290.7	C: 6.6±3.6 T: 5.7±3.7	C: 34.2±21.3 T: 23.8±12.1	NA
Belgium, 2011	Dirinck [140]	144	205 (30.2–1073.2)**	NA	NA	NA

Mean values ± % relative standard deviation are expressed in ng/g of total serum lipid weight; ^aNon adjusted values in µg/kg on this row; ^bNon adjusted values in µg/L on this row; * Median (95th CI); **Median (Range); M = Male and F = Female; C= Cases and T = Controls; NA: Not available; LOQ: limit of quantification.

Table 2. Blood Concentrations of other Organochlorine Pesticides in African and Non-African Countries.

Countries, Year	Authors (Reference)	N	βHCH	HCB	Aldrin	Dieldrin	Endrin	Heptachlore	ΣEndosulfan	Trans-nonachlore
Ghana, 2001	N'tow [106]	20	NA	30 ± 10	NA	NA	NA	NA	NA	NA
Gambia, 2002	Manirakiza [130]	100	M: 220±340 F: 240±440	M:540±620 F: 260 ±300	M:320±240 F:260±260	M:440±640 F:80±100	M:1740±2300 F:260±180	M: 360±300 F: 220±240	M:2471±1307 F:872±749	NA
Tanzania, 2006	Weiss [129]	46	NA	NA	NA	0.5±0.07 ^a	NA	NA	NA	NA
Ghana, 2008	N'tow [120]	115	0,2±0,1	5,3±1,9	NA	127±27,2	NA	NA	NA	NA
Tunisia, 2010	Ennaceur [132]	82	0.30±19.6 ^b	0.42±15.4	NA	NA	NA	NA	NA	NA
Tunisia, 2007	Ennaceur [131]	87	26.4±34.7	49.1±29.6	NA	NA	NA	NA	NA	NA
Belgium, 2006	Weiss [129]	42	NA	NA	NA	0.02±0.01 ^a	NA	NA	NA	NA
USA, 2007	Cox [137]	1303	1.70 (1-13.68)*	1,34(1-3.92)	NA	1,50(1-9)	NA	NA	NA	1.52(1-17.6)

Table 2. Contd.....

Countries, Year	Authors (Reference)	N	β HCH	HCB	Aldrin	Dieldrin	Endrin	Heptachlore	Σ Endosulfan	Trans-nonachlore
Sweden, 2009	Rignell-Hydbom [136]	742	C: 240 (93-970)* T: 140 (40-500)	NA	NA	NA	NA	NA	NA	NA
Korea, 2010	Son [139]	80	C: 57.9 \pm 24.5 T: 44.0 \pm 28.3	C: 24.2 \pm 13.0 T: 18.3 \pm 9.5	NA	NA	NA	C: 11.2 \pm 6.4 T: 7.9 \pm 7.1	NA	C: 31.3 \pm 28.1 T: 20.2 \pm 17.4
Finland, 2011	Airaiksen [138]	1988	NA	NA	NA	NA	NA	NA	NA	32 \pm 0.40
Belgium, 2011	Dirinck [140]	144	19 (2–200)**	NA	NA	NA	NA	NA	NA	NA

Mean values \pm % relative standard deviations are expressed in ng/g of total serum lipid weight. Values on the same row are expressed in: ^a μ g/kg, ^b μ g/L; M = Male and F = Female; Values on the same row are: *mean (95th CI), **median (25th -75th); C= case, T = Control

Table 3. Concentrations of DDT and its Metabolites in Breast Milk in African Countries.

Countries, Year	Authors (Reference)	N	p,p'-DDE	p,p'-DDD	p,p'-DDT	Σ DDTs
Kenya, 1998	Kinyamu [127]	216	306 \pm 41	29 \pm 10	152 \pm 26	473 \pm 59
Ghana, 2001	N'tow [106]	20	490 \pm 230	NA	NA	NA
Zimbabwe, 2002	Chikuni [125]	116	735.6-13784.4*	2.4-156.8	268.4-2636	1303.6 - 16838.6
Tunisia, 2007	Ennaceur [131]	87	2421 \pm 1370	279 \pm 1510	1015 \pm 1570	3863 \pm 1200
Ghana, 2008	N'tow [120]	115	44.8 \pm 4.2	8.0 \pm 1.0	31.4 \pm 4.5	78.3 \pm 7.0
South Africa, 2008	Okonkwo [124]	30	1.13-850*	LOD - 480	LOD - 730	NA
Ivory Coast, 2009	Alle [133]	40	NA	NA	NA	61(LOD-68.4)**
Tunisia, 2010	Hassine [134]	36	508,7 \pm 570.1	218.1 \pm 363.5	437.2 \pm 519,9	1163.9 \pm 1005

Values are expressed in ng/g of breast milk lipid weight, as mean \pm % relative standard deviation; Values on the same row are expressed as: *Range; ** Mean (95th CI); * Range of region's means. LOD: Limit of Detection.

Table 4. Concentrations of other Organochlorine Pesticides in Breast Milk in African Countries.

Countries Year	Authors (Reference)	N	β HCH	Lindane	Σ HCH	HCB	Dieldrine	Heptachlore Epoxide	Endosulfan
Kenya, 1998	Kinyamu [127]	216	83 \pm 26	18 \pm 5	NA	NA	19 \pm 3	NA	NA
Ghana, 2001	N'tow [106]	20	NA	NA	NA	40 \pm 20	NA	NA	NA
Zimbabwe, 2002	Chikuni [125]	28	45.7-952*	5.1-514	6.6-1887	NA	NA	NA	NA
Tunisia, 2007	Ennaceur [131]	87	50 \pm 2210	NA	67 \pm 2090	260 \pm 1710	59 \pm 1920	NA	NA
Ghana, 2008	N'tow [120]	115	14 \pm 2.3	NA	46.4 \pm 5.5	4.9 \pm 0.3	112.8 \pm 24.8	NA	NA
Ivory Coast, 2009	Alle [133]	40	NA	5 (LOD-68)*	19 (LOD-24.6)	NA	43 (LOD-20.4)	6 (LOD-11.4)	2 (LOD-4.4)
Tunisia, 2010	Hassine [134]	36	39,7 \pm 43	36,5 \pm 32	76,2 \pm 62,28	286,8 \pm 272,6	9,1 \pm 13,9	NA	NA

Values are expressed in ng/g of lipid weight, as mean \pm %RSD relative standard deviation. Values on the same row are expressed as: *Mean (Range); * Range of region's means; LOD: Limit of Detection.

51%, 63% and 94% for aldrin, chlordane and heptachlor when exposed for 100 days or longer [152]. In subjects who consumed contaminated fish in polluted rivers, the risk of diabetes increased by 2.37 times or more [153, 154]. In the general population, studies conducted in Sweden, Korea, USA and other countries showed that the risk of diabetes was also strongly associated with exposure to organochlorine pesticides [138, 139, 143, 155-157]. Moreover, quite low levels of exposure were found to be associated with diabetes [139, 157-159]. In subjects who did not develop diabetes, exposure to organochlorine pesticides was associated with metabolic disturbances such as overall or abdominal obesity, dyslipidemia, insulin resistance and the metabolic syndrome, which are well known risk factor for type II diabetes. These metabolic effects were also observed in subjects who developed diabetes [91, 140, 156-158, 160-164]. Such metabolic dysfunctions may not only lead to diabetes but also to hypertension and cardiovascular diseases [165, 166].

Although the mechanisms linking pesticide exposure to diabetes are not fully elucidated, it is known that organochlorine pesticides, at low doses, act as endocrine disruptors over time [139, 157, 167]. Persistent organochlorine pesticides and their metabolites accumulate in adipose tissue and are gradually released into the bloodstream where they mimic or block cellular receptors and hormones. They reduce insulin sensitivity by mimicking estrogen receptors present in insulin-sensitive tissues and β cells of the pancreas [168]. In addition, most individuals are generally exposed simultaneously to various pesticides. This multiple exposure may increase the risk of developing diabetes because the effects of these pesticides may be additive or synergistic, and sometimes conflicting. These findings were confirmed by *in vitro* and animal studies showing that pesticides were related to disturbances in carbohydrate and lipid metabolism [169, 170-171]. The pesticides alter adipocyte differentiation, the functioning of mitochondria and Langherhans β cells, inducing insulin resistance [160, 172, 173]. Although the causal mechanism is not yet identified, there are several lines of evidence for a relationship between pesticide exposure, particularly organochlorines, and diabetes. Few studies have focused on organophosphates, carbamates and herbicides, and available data show inconsistent associations with diabetes [152, 160].

A recent review has confirmed the strong positive association of pesticides, particularly organochlorines pesticides, with diabetes although more experimental data are needed to establish the causality [174]. For pyrethroids, data are also scanty but frequent and regular exposure to low doses of these pesticides seems to induce abnormal glucose tolerance [175]. Organophosphates are also associated with glucose intolerance and insulin resistance [174, 176]. For rodenticides, some studies showed an association between exposure to Vacor and type 1 diabetes [177-182]. Very little data currently exist on fungicides [183]. Even if they are scarce, organic pollutants are consistently linked to type 1 diabetes through exacerbating autoimmunity [141, 184-186].

In summary, exposure to pesticides such as organochlorines may increase the risk of diabetes. Although there are no published studies on the relationship between diabetes and pesticides in SSA, there is every reason to believe that this

association observed elsewhere also holds in SSA where inappropriate use of pesticides has been widely documented.

DOES EXPOSURE TO PESTICIDES CONTRIBUTE TO THE INCREASED RISK OF DIABETES IN SSA?

The particularly rapid progression of diabetes in SSA when compared to other regions of the world could plausibly be associated with greater exposure to pesticides and other persistent organic pollutants (see Tables 1 to 6), in addition to other known risk factors such as nutrition and demographic transitions, malnutrition in early life, obesity and genetic predisposition. More importantly, all these factors predisposing to an increased risk of diabetes may have an intergenerational impact through epigenetic phenomena and birth defects [187].

Contamination of mothers during pregnancy entails children's exposure to pesticides and their metabolites very early in life through the placenta [188]. Moreover, children's exposure may continue through breastfeeding, complementary feeding and interaction with the environment. This early exposure during perinatal and infant periods may increase the risk of obesity [189] and early diabetes [141].

On the one hand, the nutrition transition, which entails a shift from traditional diets to a more westernized diet, is an important contributor to chronic disease development. On the other hand, fetal programming resulting from maternal malnutrition as well as early childhood malnutrition in combination with the effect of pesticide exposure [188] may contribute to early onset of diabetes and the rapid progression of the disease in SSA [189, 190]. The effect of chemical pollutant exposure during the prenatal and perinatal periods has been found to be detrimental to the offspring of exposed mothers [191-193]. Exposition to chemical pollutants early in life is considered as a risk factor for obesity [187, 194] and for diabetes through their abnormal programming effects as endocrine disruptors [195-197]. During pregnancy, pesticides interfere with pregnancy hormones and increase the risk of gestational diabetes. Indeed, several studies have shown that women exposed to pesticides or other pollutants tend to develop gestational diabetes and their offspring to develop early obesity and diabetes [194, 195, 198, 199]. Children are also considered more vulnerable to pesticides than adults because there are still in the growing process [182]. They are at greater risk of exposure of their digestive tract than adults through contaminated food and various objects in their environment that they put in their mouth. They are also more likely to be exposed to pesticides in play grounds [200]. In addition, it is currently hypothesized that exposure early in life to neurotoxicant pesticides such as organophosphates could later contribute to subconscious preference for high fat diets that promote obesity and diabetes [201]. In short, the evidence for the contribution of pesticides to the developmental origins of chronic diseases such as diabetes is increasing due to the detrimental effects of these endocrine disruptors on the development and functioning of the organs during prenatal and perinatal life [195]. Under the unfavorable nutritional and environmental conditions commonly observed in SSA, it can be contented that the risk is higher than that reported in developed countries. An increasing burden of diabetes in SSA could be the result

of adverse developmental effects of pollutants, combined with those of malnutrition, as suggested by Heindel and al [175].

It is possible that the use of pesticides in SSA could be associated with lower micronutrient content or bioavailability in food, thereby contributing to malnutrition which may itself increase the vulnerability to pollutants [189]. Although controversial, several authors argue that food derived from organic agriculture contain higher amounts of some micronutrients such as vitamin C, iron, magnesium, phosphorus, polyphenols such as flavonol, and carotenoids such as lycopene, than foods derived from conventional agriculture with the use of pesticides [202]. While it has not yet been proven that organic foods have positive effects on health, foods from conventional agriculture contain secondary pesticide metabolites that may delay growth or else reduce the bioavailability of micronutrients [203]. Some authors contend that variations in food levels of certain antioxidants and minerals are ascribable to differences in methods of fertilization, protection and conservation [202, 204-206].

The African genotype appears prone to diabetes [207-209]. Additionally, gene variants that modulate insulin action (but not insulin secretion) are affected by obesity and hence type 2 diabetes susceptibility is increased [208, 209]. This risk may be exacerbated by pesticides and other environmental pollutants [210]. Exposure to pesticides during the perinatal period may exacerbate epigenetic changes that cause metabolic disturbances (obesity and insulin resistance), which might in turn lead to diabetes later in life [182, 211]. While these factors exist in other countries, they are not as critical as in SSA. Developing countries such as India and China roughly had a similar burden of diabetes as SSA [212, 213]. However, despite major prevention and management of diabetes in these countries, the progression of diabetes barely slowed because of the strong genetic predisposition, levels of pesticide exposure and susceptibility to these environmental insults [214].

CONCLUSION

In addition to transitional factors inducing obesogenic lifestyles, we must now consider malnutrition and exposure to environmental pollutants as factors that might impact on future generations' health and increase the burden of diabetes in SSA. The protection of mothers and children should be a key strategy to halt the progression of diabetes in this continent. The promotion of sustainable food production systems in a healthier environment may contribute to a lower risk for developing diabetes. The use of biological pesticides should be given more emphasis. The reduction of maternal and child malnutrition as well as the promotion of healthy lifestyles could also foster a better future for next generations. More research is needed in SSA on the environmental risk factors for chronic disease. In order to contribute to generating evidence, an original study was recently launched in West Africa to explore the relationship between exposure to organochlorine pesticides and the risk of type II diabetes.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

Funding provided by the Canadian International Development Agency (CIDA)

ACS, MB and HD have contributed to the design, performance, analysis, and writing of the work. The other authors have contributed by editing the work.

ABBREVIATIONS

AIDS	=	Acquired Immunodeficiency Syndrome
BDSF	=	Banque de données de Santé Publique
DDT	=	Dichlorodiphenyltrichloroethane
IDF	=	International Diabetes Federation
HIV	=	Human Immunodeficiency Virus
MRL	=	Maximum Residue Limit
NCDs	=	Non communicable Diseases
ng/g	=	nanogram per gram
POCs	=	Pesticides Organochlorine
POPs	=	Persistent organic Pollutants
SSA	=	Sub-saharan Africa
STEPS	=	STEPwise approach to surveillance
TCDD	=	Tétrachlorodibenzo-p-dioxine
USA	=	United State of America
WHO	=	World Health Organisation

REFERENCES

- [1] International Diabetes Federation. IDF Diabetes Atlas, 5th edn. Brussels, Belgium: International Diabetes Federation, 2011 [cited 21 May 2012]. Available from: <http://www.idf.org/diabetesatlas>.
- [2] Kirigia JM, Sambo HB, Sambo LG, Barry SP. Economic burden of diabetes mellitus in the WHO African region. *BMC Int Health Hum Rights* 2009; 9(6): 1-12.
- [3] Whiting DR, Guariguata L, Weil C, Shaw J. IDF Diabetes Atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Res Clin Pract* 2011; 94(3): 311-21.
- [4] Global status report on noncommunicable diseases 2010. World Health Organization 2011 [cited 25 May 2012]. Available from: http://www.who.int/nmh/publications/ncd_report2010/fr/index.html.
- [5] Political declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases. United Nations. 2011 [cited 15 June 2012]. Available from: http://www.who.int/nmh/events/un_ncd_summit2011/en/index.html.
- [6] Williamson S. The dependency syndrome: pesticide use by African smallholders: a report for PAN UK's pesticides poverty and livelihoods project. Pesticide Action Network UK (PAN UK): London, U.K.: 2003.
- [7] Williamson S. Pesticide provision in liberalised Africa: out of control? *Agricultural Research and Extension Network* 2003. 15 July 2012, 126: Available from: http://www.odi.org.uk/work/projects/agren/papers/agrenpaper_126.pdf.
- [8] IDF Clinical Guidelines Task Force. Global guideline for Type 2 diabetes. Brussels. 2005 [cited 25 May 2012]. Available from: <http://www.idf.org/webdata/docs/IDF%20GGT2D.pdf>.
- [9] Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation. 2006 [cited 15 November 2011]. Available from: <http://www.who.int/diabetes/publications/en/>

- [10] Joffe BI, Seftel HC. Diabetes mellitus in the black communities of southern Africa. *J Intern Med* 1994; 235(2): 137-142.
- [11] Joffe BI, Panz VR, Wing JR, Raal FJ, Seftel HC. Pathogenesis of non-insulin-dependent diabetes mellitus in the black population of southern Africa. *Lancet* 1992; 340(8817): 460-462.
- [12] Papoz L, Delcourt C, Ponton Sanchez A, *et al.* Clinical classification of diabetes in tropical west Africa. *Diabetes Res Clin Pract* 1998; 39(3): 219-227.
- [13] Sobngwi E, Mauvais Jarvis F, Vexiau P, Mbanya JC, Gautier JF. Diabetes in Africans. Part 1: epidemiology and clinical specificities. *Diabetes Metab* 2001; 27(6): 628-634.
- [14] Sobngwi E, Choukem SP, Agbalika F, *et al.* Ketosis-prone type 2 diabetes mellitus and human herpesvirus 8 infection in sub-saharan africans. *JAMA* 2008; 299(23): 2770-6.
- [15] Osei K, Schuster DP, Amoah AG, Owusu SK. Diabetes in Africa. Pathogenesis of type 1 and type 2 diabetes mellitus in sub-Saharan Africa: implications for transitional populations. *J Cardiovasc Risk* 2003; 10(2): 85-96.
- [16] Mauvais-Jarvis F, Sobngwi E, Porcher R, *et al.* Ketosis-prone type 2 diabetes in patients of sub-Saharan African origin: clinical pathophysiology and natural history of beta-cell dysfunction and insulin resistance. *Diabetes* 2004; 53(3): 645-653.
- [17] Choukem SP, Sobngwi E, Fetita LS, *et al.* Multitissue insulin resistance despite near-normoglycemic remission in Africans with ketosis-prone diabetes. *Diabetes Care* 2008; 31(12): 2332-2337.
- [18] Sobngwi E, Mauvais Jarvis F, Vexiau P, Mbanya JC, Gautier JF. Diabetes in Africans. Part 2: Ketosis-prone atypical diabetes mellitus. *Diabetes Metab* 2002; 28(1): 5-12.
- [19] Gill GV, Mbanya JC, Ramaiya KL, Tesfaye S. A sub-Saharan African perspective of diabetes. *Diabetologia* 2009; 52(1): 8-16.
- [20] Kalk WJ, Joffe BI, Sumner AE. The waist circumference of risk in black South african men is lower than in men of European ancestry. *Metab Syndr Relat Disord* 2011; 9(6): 491-495.
- [21] Ntyonga pono PM, Mistoul I, Mikala-Moutsinga H, Ndong-Nguema JB, Lawson-Nzanga N, Mabamba C. La pancréatite chronique calcifiante une cause majeure de diabète chez l'homme gabonais. *Médecine d'Afrique Noire* 1996; 43(3):144-147.
- [22] Djrolo F, Hougbe H, Avode G, *et al.* Le diabète lie a la malnutrition (diabète tropical) A propos d'un cas observé en Médecine Interne à Cotonou. *Médecine d'Afrique Noire* 1998; 45(8/9):538-542.
- [23] Ranivontsoarivony M, Noronavalona A, Raharison N, Rajaona HR. Le manioc est-il un facteur diabétogène ? A propos d'un cas de diabète sucré chez un gros mangeur de manioc cru. *Bull Soc Pathol Exot* 2001; 94(4): 312-314.
- [24] Alemu S, Dessie A, Seid E, *et al.* Insulin-requiring diabetes in rural Ethiopia: should we reopen the case for malnutrition-related diabetes. *Diabetologia* 2009; 52(9): 1842-1845.
- [25] Raherison R, Rakotomalala P, Rabarijaona L. Un cas de diabète sucré lié à la malnutrition (vu dans le service d'endocrinologie du CHU Joseph Rasetta Befelatànana d'Antananarivo). *e-Santé Revue électronique en sciences de la santé*. 25 May 2010, 1: Available from: <http://www.revue-esante.info/document.php?id=575>.
- [26] Mbanya JC, Motala AA, Sobngwi E, Assah FK, Enoru ST. Diabetes in sub-Saharan Africa. *Lancet* 2010; 375(9733): 2254-2266.
- [27] Houinato D, Segnon-Agueh J, Djrolo F, Djigbenoude O. Rapport final de l'enquête STEPS au Benin. Programme National de Lutte contre les Maladies Non Transmissibles et Organisation Mondiale de la santé [cited 04 October 2010]: Available from: http://www.who.int/chp/steps/2008_STEPS_Report_Benin.pdf.
- [28] Muyer MT, Muls E, Mapatano MA, *et al.* Estimating prevalence of diabetes in a Congolese town was feasible. *J Clin Epidemiol* 2011; 64(2): 172-181.
- [29] Monteiro B, Gninafon M., Amoussou KJ. Contribution à l'étude épidémiologique du diabète sucré de l'adulte au centre national hospitalier et universitaire de Cotonou (C.N.H.U) - Bénin. *Médecine d'Afrique noire* 1991; 38(4): 263-269.
- [30] Oga AS, Tebi A, Aka J, *et al.* Diabetes in Ivory Coast: special epidemiological features. *Med Trop* 2006; 66(3): 241-246.
- [31] Djrolo F. P105 Prévalence du diabète sucré dans une population urbaine en milieu africain à Cotonou – Bénin. *Diabetes Metab*. 2009; 35, Supplement 1(0): A53.
- [32] Balde NM, Diallo I, Balde MD, *et al.* Diabetes and impaired fasting glucose in rural and urban populations in Futa Jallon (Guinea): prevalence and associated risk factors. *Diabetes Metab* 2007; 33(2): 114-120.
- [33] Christensen DL, Friis H, Mwaniki DL, *et al.* Prevalence of glucose intolerance and associated risk factors in rural and urban populations of different ethnic groups in Kenya. *Diabetes Res Clin Pract* 2009; 84(3): 303-310.
- [34] Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract* 2010; 87(1): 4-14.
- [35] Sicree RS, J., Zimmet, P. Baker. The Global Burden: Diabetes and Impaired Glucose Tolerance. IDF Diabetes Atlas fourth edition 2010 [cited 04 October 2010]: Available from: http://www.idf.org/sites/default/files/The_Global_Burden.pdf.
- [36] Hall V, Thomsen RW, Henriksen O, Lohse N. Diabetes in Sub Saharan Africa 1999-2011: epidemiology and public health implications. A systematic review. *BMC Public Health* 2011; 11: 564.
- [37] Gill GV, Huddle KR, Rolfe M. Mortality and outcome of insulin-dependent diabetes in Soweto, South Africa. *Diabet Med* 1995; 12(6): 546-550.
- [38] Gill GV, Huddle KR, Monkoe G. Long-term (20 years) outcome and mortality of Type 1 diabetic patients in Soweto, South Africa. *Diabet Med* 2005; 22(12): 1642-1646.
- [39] Majaliwa ES, Munubhi E, Ramaiya K, *et al.* Survey on acute and chronic complications in children and adolescents with type 1 diabetes at Muhimbili National Hospital in Dar es Salaam, Tanzania. *Diabetes Care* 2007; 30(9): 2187-2192.
- [40] Majaliwa ES, Elusiyan BE, Adesiyun OO, *et al.* Type 1 diabetes mellitus in the African population: epidemiology and management challenges. *Acta Biomed* 2008; 79(3): 255-259.
- [41] Sobngwi E, Ndour-Mbaye M, Boateng KA, *et al.* Type 2 diabetes control and complications in specialised diabetes care centres of six sub-Saharan African countries: the Diabcare Africa study. *Diabetes Res Clin Pract* 2012; 95(1): 30-36.
- [42] Mbanya JC, Sobngwi E. Diabetes in Africa. Diabetes microvascular and macrovascular disease in Africa. *J Cardiovasc Risk* 2003; 10(2): 97-102.
- [43] Kengne AP, Amoah AG, Mbanya JC. Cardiovascular complications of diabetes mellitus in sub-Saharan Africa. *Circulation* 2005; 112(23): 3592-3601.
- [44] Danquah I, Bedu-Addo G, Terpe KJ, *et al.* Diabetes mellitus type 2 in urban Ghana: characteristics and associated factors. *BMC Public Health* 2012; 12(1): 210.
- [45] United Nations. World Urbanization Prospects, the 2011 Revision: Highlights. New York: United Nations, Department of Economic and Social Affairs, Population Division; 2012 [cited 14 July 2012]; 1-50]. Available from: <http://esa.un.org/unpd/wup/Documentation/highlights.htm>.
- [46] Delisle H, Ntandou-Bouzitou G, Agueh V, Sodjinou R, Fayomi B. Urbanisation, nutrition transition and cardiometabolic risk: the Benin study. *Br J Nutr* 2012; 107(10): 1534-1544.
- [47] Popkin BM, Adair LS, Ng SW. Global nutrition transition and the pandemic of obesity in developing countries. *Nutr Rev* 2012; 70(1): 3-21.
- [48] Popkin BM. Understanding the nutrition transition. *Urban Health Newsl* 1996; 30: 3-19.
- [49] Napoli N, Mottini G, Arigliani M, *et al.* Unexpectedly high rates of obesity and dysglycemia among villagers in Cameroon. *Diabetes Metab Res Rev* 2010; 26(1): 10-2.
- [50] Mendoza JA, Drewnowski A, Cheadle A, Christakis DA. Dietary energy density is associated with selected predictors of obesity in U.S. Children. *J Nutr* 2006; 136(5): 1318-1322.
- [51] Aggarwal A, Monsivais P, Cook AJ, Drewnowski A. Does diet cost mediate the relation between socioeconomic position and diet quality? *Eur J Clin Nutr* 2011; 65(9): 1059-1066.
- [52] Martin SS. From Poverty to Obesity: Exploration of the Food Choice Constraint Model and the Impact of an Energy-Dense Food Tax. *Am Econ* 2005; 49(2): 78-86.
- [53] Martin-Prevel Y, Maire B, Depeulch F. Nutrition, urbanisation et pauvreté en Afrique sub-saharienne. *Med Trop (Mars)* 2000; 60: 179-91.
- [54] Deleuze G, Fayomi B, Delisle H. Child malnutrition and maternal overweight in same households in poor urban areas of Benin. *Sante* 2005; 15(4): 263-270.
- [55] Sodjinou R, Agueh V, Fayomi B, Delisle H. Dietary patterns of urban adults in Benin: relationship with overall diet quality and

- socio-demographic characteristics. *Eur J Clin Nutr* 2009; 63(2): 222-228.
- [56] Sodjinou R, Agueh V, Fayomi B, Delisle H. Obesity and cardiometabolic risk factors in urban adults of Benin: relationship with socio-economic status, urbanisation, and lifestyle patterns. *BMC Public Health* 2008; 8: 84.
- [57] Sossa C, Delisle H, Agueh V, Makoutode M, Fayomi B. Four-Year Trends in Cardiometabolic Risk Factors according to Baseline Abdominal Obesity Status in West-African Adults. *The Benin Study. J Obes* 740854. doi: 10.1155/2012/740854. Epub 2012 Feb 12.
- [58] Zeba AN, Delisle HF, Renier G, Savadogo B, Baya B. The double burden of malnutrition and cardiometabolic risk widens the gender and socio-economic health gap: a study among adults in Burkina Faso (West Africa). *Public Health Nutr* 2012; 15(12): 2210-2219.
- [59] Ntandou G, Delisle H, Agueh V, Fayomi B. Abdominal obesity explains the positive rural-urban gradient in the prevalence of the metabolic syndrome in Benin, West Africa. *Nutr Res* 2009; 29(3): 180-189.
- [60] Delisle H, Receveur O. Malnutrition in developing countries. *CMAJ* 2007; 176(1): 65.
- [61] Mvo Z, Dick J, Steyn J. Perceptions of overweight African women about acceptable body size of women and children. *Curatationis* 1999; 22(2): 27-31.
- [62] Holdsworth M, Gartner A, Landais E, Maire B, Delpeuch F. Perceptions of healthy and desirable body size in urban Senegalese women. *Int J Obes Relat Metab Disord* 2004; 28(12): 1561-1568.
- [63] Puoane T, Tsolekile L, Steyn N. Perceptions about body image and sizes among Black African girls living in Cape Town. *Ethn Dis* 2010; 20(1): 29-34.
- [64] Blössner M, De Onis M. Malnutrition: quantifying the health impact at national and local levels. *World Health Organization (WHO Environmental Burden of Disease Series N°12): Geneva* 2005.
- [65] Barker DJ. The developmental origins of chronic adult disease. *Acta Paediatr Suppl* 2004; 93(446): 26-33.
- [66] Gluckman PD, Hanson MA, Beedle AS. Early life events and their consequences for later disease: a life history and evolutionary perspective. *Am J Hum Biol* 2007; 19(1): 1-19.
- [67] Gluckman PD, Hanson MA. Developmental plasticity and human disease: research directions. *J Intern Med* 2007; 261(5): 461-471.
- [68] Gluckman PD, Hanson MA, Low FM. The role of developmental plasticity and epigenetics in human health. *Birth Defects Res C Embryo Today* 2011; 93(1): 12-18.
- [69] Gluckman PD, Hanson MA, Pinal C. The developmental origins of adult disease. *Matern Child Nutr* 2005; 1(3): 130-141.
- [70] Gluckman PD, Hanson MA, Mitchell MD. Developmental origins of health and disease: reducing the burden of chronic disease in the next generation. *Genome Med* 2010; 2(2): 14.
- [71] Delisle H. Foetal programming of nutrition-related chronic diseases. *Sante* 2002; 12(1): 56-63.
- [72] Motala AA, Omar MA, Pirie FJ. Diabetes in Africa. Epidemiology of type 1 and type 2 diabetes in Africa. *J Cardiovasc Risk* 2003; 10(2): 77-83.
- [73] Touré NO, Dia Kane Y, Diatta A, et al. Tuberculose et diabète. *Rev Mal Respir* 2007; 24 (7): 869-875.
- [74] Balde NM, Camara A, Camara LM, Diallo MM, Kake A, Bah Sow OY. Associated tuberculosis and diabetes in Conakry, Guinea: prevalence and clinical characteristics. *Int J Tuberc Lung Dis* 2006; 10(9): 1036-1040.
- [75] Sidibe AT, Dembele M, Diarra AS, et al. Tuberculose pulmonaire chez le sujet diabétique en médecine interne de l'hôpital du point G, Bamako – mali. *Mali Médical* 2005; 1&2: 45-47.
- [76] Young F, Critchley JA, Johnstone LK, Unwin NC. A review of comorbidity between infectious and chronic disease in Sub Saharan Africa: TB and diabetes mellitus, HIV and metabolic syndrome, and the impact of globalization. *Global Health* 2009; 5(9): 1-9.
- [77] Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. *PLoS Med* 2008; 5(7): 1091-10101.
- [78] Jeon CY, Harries AD, Baker MA, et al. Bi-directional screening for tuberculosis and diabetes: a systematic review. *Trop Med Int Health* 2010; 15(11): 1300-1314.
- [79] Van VM, Schellekens O, Reiss P, Hamers R, Rinke de Wit T. Diabetes and HIV/AIDS in sub-Saharan Africa: the need for sustainable healthcare systems. *Diabetes Voice* 2008; 52(3).
- [80] Goldhaber-Fiebert JD, Jeon CY, Cohen T, Murray MB. Diabetes mellitus and tuberculosis in countries with high tuberculosis burdens: individual risks and social determinants. *Int J Epidemiol* 2011; 40(2): 417-428.
- [81] Hult M, Tornhammar P, Ueda P, et al. Hypertension, diabetes and overweight: looming legacies of the Biafran famine. *PLoS ONE* [2962634] 22 October 2010; Available from: <http://www.plosone.org/article/info:doi/10.1371/journal.pone.0013582>.
- [82] Cheng CY, Reich D, Haiman CA, et al. African ancestry and its correlation to type 2 diabetes in African Americans: a genetic admixture analysis in three U.S. population cohorts. *PLoS ONE* [3306373] 13 February 2013; Available from: <http://www.hindawi.com/journals/jobes/2013/396416/>.
- [83] World Health Organization. The WHO recommended classification of pesticides by hazard and guidelines to classification 2009. Geneva [cited 27 December 2010]; Available from: http://www.who.int/ipcs/publications/pesticides_hazard/en/.
- [84] Zhang W, Jiang F, Ou J. Global pesticide consumption and pollution: with China as a focus. *Proceedings of the International Academy of Ecology and Environmental Sciences* 2011; 1(2): 125-144.
- [85] Programme des Nation-Unies pour l'Environnement. Convention de Rotterdam sur la procédure de consentement préalable en connaissance de cause applicable à certains produits chimiques et pesticides dangereux qui font l'objet d'un commerce international. [cited 09 January 2011]; Available from: <http://www.admin.ch/ch/f/ff/2000/5655.pdf>.
- [86] United Nations Environment Programme. Stockholm Convention on Persistent Organic Pollutants (POPs) : text and annexes. Geneva, Switzerland [cited 24 July 2013]. Available from: http://www.pops.int/documents/convtext/convtext_en.pdf.
- [87] Ministère de l'Environnement et de la Protection de la nature. Plan national de mise en oeuvre de la convention de Stockholm: polluants organiques persistants. Bénin [cited 02 May 2011]; Available from: http://chm.pops.int/Portals/0/docs/from_old_website/documents/implementation/nips/submissions/PNM-BENIN%20VERSION-FINALE.pdf.
- [88] Wandiga SO. Use and distribution of organochlorine pesticides. The future in Africa. *Pure Appl Chem* 2001; 73 (7): 1147-55.
- [89] Thiam A, Sagna MB. Monitoring des pesticides au niveau des communautés à la base: Rapport régional Afrique. Pesticide Action Network Africa 2009. [cited 05 August 2012] Available from: http://pan-afrique.org/index2.php?option=com_docman&task=doc_view&gid=29&Itemid=85.
- [90] The use of DDT in malaria vector control: WHO Position Statement. World Health Organization-Global Malaria Programme 2011 [cited 03 August 2013]; Available from: http://whqlibdoc.who.int/hq/2011/WHO_HTM_GMP_2011_eng.pdf.
- [91] Lee D-H, Steffes MW, Sjodin A, Jones RS, Needham LL, Jacobs DR, Jr. Low dose organochlorine pesticides and polychlorinated biphenyls predict obesity, dyslipidemia, and insulin resistance among people free of diabetes. *PLoS ONE* [PMC3027626] 26 January 2011; Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3027626/pdf/pone.0015977.pdf>.
- [92] Lee DH, Jacobs, D. R. Jr., Porta, M. Could low-level background exposure to persistent organic pollutants contribute to the social burden of type 2 diabetes? *J Epidemiol Community Health* 2006; 60(12): 1006-1008.
- [93] Haylamicheal ID, Dalvie MA. Disposal of obsolete pesticides, the case of Ethiopia. *Environment International* 2009; 35(3): 667-673.
- [94] Hinson AV, Dedjan H, Fayomi BE. Biomarkers, clinical and behavioural indicators of pesticide exposure at community level. *Afr Newslett on Occup Health and Safety* 2007; 17: 14-16.
- [95] Ngowi AV, Mbise TJ, Ijani AS, London L, Ajayi OC. Pesticides use by smallholder farmers in vegetable production in Northern Tanzania. *Crop Prot* 2007; 26(11): 1617-1624.
- [96] Pesticide Action Network United Kingdom. Living with poison – pesticides in West African cotton growing. *Pesticides News*. 3 May 2011, 74; Available from: <http://www.pan-uk.org/pestnews/Contents/pn74.html>.
- [97] Watts M. Time to act on endosulfan. *Pesticide News* 2008; 81: 1-3.
- [98] Rosendahl I, Laabs V, Atcha-Ahowe C, James B, Amelung W. Insecticide dissipation from soil and plant surfaces in tropical horticulture of southern Benin, West Africa. *J Environ Monit* 2009; 11(6): 1157-1164.

- [99] Matthews G, Wiles T, Baleguel P. A survey of pesticide application in Cameroon. *Crop Protection* 2003; 22(5): 707-14.
- [100] Maumbe BM, Swinton SM. Hidden health costs of pesticide use in Zimbabwe's smallholder cotton growers. *Social Science & Medicine* 2003; 57(9): 1559-1571.
- [101] Kuye RA, Donham KJ, Marquez SP, *et al.* Pesticide handling and exposures among cotton farmers in the gambia. *J Agromedicine* 2007; 12(3): 57-69.
- [102] Akogbeto MC, Djouaka R, Noukpo H. Use of agricultural insecticides in Benin. *Bull Soc Pathol Exot* 2005; 98(5): 400-405.
- [103] Akogbeto MC, Djouaka RF, Kinde-Gazard DA. Screening of pesticide residues in soil and water samples from agricultural settings. *Malar J* 2006; 5: 22.
- [104] Manirakiza P, Akinbamijo O, Covaci A, Pitonzo R, Schepens P. Assessment of organochlorine pesticide residues in West African city farms: Banjul and Dakar case study. *Arch Environ Contam Toxicol* 2003; 44(2): 171-179.
- [105] Manirakiza P, Covaci A, Nizigiymana L, Ntakimazi G, Schepens P. Persistent chlorinated pesticides and polychlorinated biphenyls in selected fish species from Lake Tanganyika, Burundi, Africa. *Environ Pollut* 2002; 117(3): 447-455.
- [106] Ntow WJ. Organochlorine pesticides in water, sediment, crops, and human fluids in a farming community in Ghana. *Arch Environ Contam Toxicol* 2001; 40(4): 557-563.
- [107] Asante KA, Ntow W. J. Status of Environmental Contamination in Ghana, the Perspective of a Research Scientist Interdisciplinary Studies on Environmental Chemistry-Environmental Research in Asia 2009; 2: 253-260.
- [108] Pazou EY, Boko M, Van Gestel CA, *et al.* Organochlorine and organophosphorous pesticide residues in the Oueme River catchment in the Republic of Benin. *Environ Int* 2006; 32(5): 616-623.
- [109] van Wyk E, Bouwman H, van der Bank H, Verdoorn GH, Hofmann D. Persistent organochlorine pesticides detected in blood and tissue samples of vultures from different localities in South Africa. *Comp Biochem Physiol C Toxicol Pharmacol* 2001; 129(3): 243-264.
- [110] Ize-Iyamu OK, Asia IO, Egwakhide PA. Concentrations of residues from organochlorine pesticide in water and fish from some rivers in Edo State Nigeria. *International Journal of Physical Sciences* 2007; 2(9): 237-241.
- [111] Pazou EY, Laleye P, Boko M, *et al.* Contamination of fish by organochlorine pesticide residues in the Oueme River catchment in the Republic of Benin. *Environ Int* 2006; 32(5): 594-599.
- [112] Okoumassoun LE, Brochu C, Deblois C, *et al.* Vitellogenin in tilapia male fishes exposed to organochlorine pesticides in Oueme River in Republic of Benin. *Sci Total Environ* 2002; 299(1-3): 163-172.
- [113] Assogba-Komlan F, Anihouvi P, Achigan E, *et al.* Pratiques culturales et teneur en éléments anti nutritionnels (nitrates et pesticides) du Solanum macrocarpum au sud du Bénin. *African Journal of Food, Agriculture, Nutrition and Development*. 03 April 2011; 7(4): Available from: http://www.ajfand.net/Issue15/PDFs/3%20Assogba-IPGR2_3.pdf.
- [114] Darko G, Acquah SO. Levels of organochlorine pesticide residues in dairy products in Kumasi, Ghana. *Chemosphere* 2008; 71(2): 294-298.
- [115] Kahunyo JM, Frosliè A, Maitai CK. Organochlorine pesticide residues in chicken eggs: a survey. *J Toxicol Environ Health* 1988; 24(4): 543-550.
- [116] Kahunyo JM, Maitai CK, Frosliè A. Organochlorine pesticide residues in chicken fat: a survey. *Poult Sci* 1986; 65(6): 1084-9.
- [117] Mawussi G, Sanda K, Merlina G, Pinelli E. Assessment of average exposure to organochlorine pesticides in southern Togo from water, maize (*Zea mays*) and cowpea (*Vigna unguiculata*). *Food Addit Contam Part A Chem Anal Control Expo Risk Assess* 2009; 26(3): 348-354.
- [118] Gimou MM, Charrondière UR, Leblanc JC, Pouillot R. Dietary exposure to pesticide residues in Yaounde: the Cameroonian total diet study. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess* 2008; 25(4): 458-471.
- [119] Adeyeye A, Osibanjo O. Residues of organochlorine pesticides in fruits, vegetables and tubers from Nigerian markets. *Sci Total Environ* 1999; 231(2-3): 227-233.
- [120] Ntow WJ, Tagoe LM, Drechsel P, Kelderman P, Gijzen HJ, Nyarko E. Accumulation of persistent organochlorine contaminants in milk and serum of farmers from Ghana. *Environ Res* 2008; 106(1): 17-26.
- [121] Guardino X, Serra C, Obiols J, *et al.* Determination of DDT and related compounds in blood samples from agricultural workers. *J Chromatogr A* 1996; 719(1): 141-147.
- [122] Dalvie MA, Africa A, Solomons A, London L, Brouwer D, Kromhout H. Pesticide exposure and blood endosulfan levels after first season spray amongst farm workers in the Western Cape, South Africa. *J Environ Sci Health B* 2009; 44(3): 271-277.
- [123] Kanja LW, Skaare JU, Ojwang SB, Maitai CK. A comparison of organochlorine pesticide residues in maternal adipose tissue, maternal blood, cord blood, and human milk from mother/infant pairs. *Arch Environ Contam Toxicol* 1992; 22(1): 21-24.
- [124] Okonkwo JO, Mutshatshi TN, Botha B, Agyei N. DDT, DDE and DDD in human milk from South Africa. *Bul Environ Contam Toxicol* 2008; 81(4): 348-354.
- [125] Chikuni O, Nhachi CF, Polder A, Bergan S, Nafstad I, Skaare JU. Effects of DDT on paracetamol half-life in highly exposed mothers in Zimbabwe. *Toxicol Lett* 2002; 134(1-3): 147-53.
- [126] Kanja L, Skare JU, Nafstad I, Maitai CK, Lokken P. Organochlorine pesticides in human milk from different areas of Kenya 1983-1985. *J Toxicol Environ Health* 1986; 19(4): 449-464.
- [127] Kinyamu JK, Kanja LW, Skaare JU, Maitho TE. Levels of Organochlorine Pesticides Residues in Milk of Urban Mothers in Kenya. *Bul Environ Contam Toxicol* 1998; 60(5): 732-738.
- [128] Bezek S, Ujhazy E, Mach M, Navarova J, Dubovicky M. Developmental origin of chronic diseases: toxicological implication. *Interdiscip Toxicol* 2008; 1(1): 29-31.
- [129] Weiss J, Bauer O, Blüthgen A, *et al.* Distribution of persistent organochlorine contaminants in infertile patients from Tanzania and Germany. *J Assist Reprod Genet* 2006; 23(9): 393-9.
- [130] Manirakiza P, Akimbamijo O, Covaci A, *et al.* Persistent chlorinated pesticides in fish and cattle fat and their implications for human serum concentrations from the Sene-Gambian region. *J Environ Monit* 2002; 4(4): 609-617.
- [131] Ennaceur S, Gandoura N, Driss MR. Organochlorine pesticide residues in human milk of mothers living in northern Tunisia. *Bul Environ Contam Toxicol* 2007; 78(5): 325-329.
- [132] Ennaceur S, Driss MR. Serum organochlorine pesticide and polychlorinated biphenyl levels measured in delivering women from different locations in Tunisia. *Int J Environ Anal Chem* 2010; 90(10): 821-828.
- [133] Alle A, Dembelle A, Yao B, Ado G. Distribution of Organochlorine Pesticides in Human Breast Milk and Adipose Tissue from Two Locations in Côte d'Ivoire. *AJAS* 2009; 2: 456-463.
- [134] Hassine SB, Ameer WB, Gandoura N, Driss MR. Determination of chlorinated pesticides, polychlorinated biphenyls, and polybrominated diphenyl ethers in human milk from Bizerte (Tunisia) in 2010. *Chemosphere* 2012; 89(4): 369-377.
- [135] Rignell-Hydbom A, Rylander, L., Hagmar, L. Exposure to persistent organochlorine pollutants and type 2 diabetes mellitus. *Hum Exp Toxicol* 2007; 26(5): 447-452.
- [136] Rignell-Hydbom A, Lidfeldt J, Kiviranta H, *et al.* Exposure to p,p'-DDE: a risk factor for type 2 diabetes. *PLoS ONE [PMC2759028]* 19 October 2009; Available from: <http://www.plosone.org/article/info:doi/10.1371/journal.pone.0007503>.
- [137] Cox S, Niskar AS, Narayan KM, Marcus M. Prevalence of self-reported diabetes and exposure to organochlorine pesticides among Mexican Americans: Hispanic health and nutrition examination survey, 1982-1984. *Environ Health Perspect* 2007; 115(12): 1747-1752.
- [138] Airaksinen R, Rantakokko P, Eriksson JG, Blomstedt P, Kajantie E, Kiviranta H. Association between type 2 diabetes and exposure to persistent organic pollutants. *Diabetes Care* 2011; 34(9): 1972-1979.
- [139] Son HK, Kim SA, Kang JH, *et al.* Strong associations between low-dose organochlorine pesticides and type 2 diabetes in Korea. *Environ Int* 2010; 36(5): 410-414.
- [140] Dirinck E, Jorens PG, Covaci A, *et al.* Obesity and persistent organic pollutants: possible obesogenic effect of organochlorine pesticides and polychlorinated biphenyls. *Obesity* 2011; 19(4): 709-714.
- [141] Thayer KA, Heindel JJ, Bucher JR, Gallo MA. Role of environmental chemicals in diabetes and obesity: a national

- toxicology program workshop review. *Environ Health Perspect* 2012; 120(6): 779-789.
- [142] Cicolella A, Nalbone, G., Laot-Cabon, S. Évaluation du lien entre environnement chimique, obesite et diabete (Projet ECOD). France [cited 23 August 2012]: Available from: http://reseau-environnement-sante.fr/wp-content/uploads/2012/03/Rapport_ECOD_VF1.pdf.
- [143] Porta M, Lee, D-H. Review of the science linking chemical exposures to the human risk of obesity and diabetes. United Kingdom [cited 21 June 2012]: Available from: http://www.chemtrust.org.uk/Obesity_and_Diabetes_publications.php.
- [144] Rausch F, Ladwig W. [Clinical course of a rescued case of E 605 poisoning; development of diabetes mellitus]. *Arztl Wochensh* 1954; 9(44): 1053-1057.
- [145] Henriksen GL, Ketchum NS, Michalek JE, Swaby JA. Serum dioxin and diabetes mellitus in veterans of Operation Ranch Hand. *Epidemiology* 1997; 8(3): 252-258.
- [146] Kang HK, Dalager NA, Needham LL, *et al.* Health status of Army Chemical Corps Vietnam veterans who sprayed defoliant in Vietnam. *Am J Ind Med* 2006; 49(11): 875-884.
- [147] Kim JS, Lim HS, Cho SI, Cheong HK, Lim MK. Impact of Agent Orange exposure among Korean Vietnam veterans. *Ind Health* 2003; 41(3): 149-157.
- [148] Longnecker MP, Michalek JE. Serum dioxin level in relation to diabetes mellitus among Air Force veterans with background levels of exposure. *Epidemiology* 2000; 11(1): 44-48.
- [149] Steenland K, Calvert G, Ketchum N, Michalek J. Dioxin and diabetes mellitus: an analysis of the combined NIOSH and Ranch Hand data. *Occup Environ Med* 2001; 58(10): 641-648.
- [150] The Department of Veterans Affairs. Disease associated with exposure to certain herbicide agents: type 2 diabetes. Final rule. *Fed Regist* 2001; 66(89): 23166-263169.
- [151] Beard J, Sladden T, Morgan G, Berry G, Brooks L, McMichael A. Health impacts of pesticide exposure in a cohort of outdoor workers. *Environ Health Perspect* 2003; 111(5): 724-730. [Environmental health perspectives].
- [152] Montgomery MP, Kamel F, Saldana TM, Alavanja MC, Sandler DP. Incident diabetes and pesticide exposure among licensed pesticide applicators: Agricultural Health Study, 1993-2003. *Am J Epidemiol* 2008; 167(10): 1235-1246.
- [153] Turyk M, Anderson H, Knobeloch L, Imm P, Persky V. Organochlorine exposure and incidence of diabetes in a cohort of Great Lakes sport fish consumers. *Environ Health Perspect* 2009; 117(7): 1076-82.
- [154] Rylander L, Rignell-Hydbom A, Hagmar L. A cross-sectional study of the association between persistent organochlorine pollutants and diabetes. *Environ Health* 2005; 4: 28.
- [155] Lee DH, Lee I-K, Song K, *et al.* A strong dose-response relation between serum concentrations of persistent organic pollutants and diabetes: results from the National Health and Examination Survey 1999-2002. *Diabetes Care* 2006; 29(7): 1638-1644.
- [156] Lee D, Lee I, Jin S, Steffes M, Jacobs DR, Jr. Association between serum concentrations of persistent organic pollutants and insulin resistance among nondiabetic adults: results from the national health and nutrition examination survey 1999-2002. *Diabetes Care* 2007; 30(3): 622-628.
- [157] Lee DH, Steffes MW, Sjodin A, *et al.* Low Dose of Some Persistent Organic Pollutants Predicts Type 2 Diabetes: A Nested Case-Control Study. *Environ Health Perspect* 2010; 118(9): 1235-1242.
- [158] Lim S, Cho YM, Park KS, Lee HK. Persistent organic pollutants, mitochondrial dysfunction, and metabolic syndrome. *Ann N Y Acad Sci* 2010; 1201: 166-176.
- [159] Lim JS, Son HK, Park SK, Jacobs DR, Jr., Lee DH. Inverse associations between long-term weight change and serum concentrations of persistent organic pollutants. *Int J Obes (Lond)* 2010; 35(5): 744-747.
- [160] Lim S, Ahn SY, Song IC, *et al.* Chronic exposure to the herbicide, atrazine, causes mitochondrial dysfunction and insulin resistance. *PLoS ONE* [Internet]. 13 April 2009; 4(4). Available from: <http://www.plosone.org/article/info:doi/10.1371/journal.pone.0005186>.
- [161] Park SK, Son HK, Lee SK, *et al.* Relationship between serum concentrations of organochlorine pesticides and metabolic syndrome among non-diabetic adults. *J Prev Med Public Health* 2010; 43(1): 1-8.
- [162] Lee D-H, Lind L, Jacobs DR, Jr., Salihovic S, Bavel Bv, Lind PM. Associations of persistent organic pollutants with abdominal obesity in the elderly: the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study. *Environ Int* 2012; 40: 170-178.
- [163] Lee DH. Persistent organic pollutants and obesity-related metabolic dysfunction: focusing on type 2 diabetes. *Epidemiology & Health* 2012; 34: 1-3.
- [164] Uemura H, Arisawa K, Hiyoshi M, *et al.* Prevalence of metabolic syndrome associated with body burden levels of dioxin and related compounds among Japan's general population. *Environ Health Perspect* 2009; 117(4): 568-573.
- [165] Ha MH, Lee, D. H., Jacobs, D. R. Association between serum concentrations of persistent organic pollutants and self-reported cardiovascular disease prevalence: results from the National Health and Nutrition Examination Survey, 1999-2002. *Environ Health Perspect* 2007; 115(8): 1204-1209.
- [166] Ha MH, Lee DH, Son HK, Park SK, Jacobs DR, Jr. Association between serum concentrations of persistent organic pollutants and prevalence of newly diagnosed hypertension: results from the National Health and Nutrition Examination Survey 1999-2002. *J Hum Hypertens* 2009; 23(4): 274-86.
- [167] Kortenkamp A, Martin O, Faust M, Evans R, McKinlay R, Orton F, *et al.* State of the art assessment of endocrine disruptors. European Commission [cited 23 August 2012]: Available from: http://ec.europa.eu/environment/chemicals/endocrine/documents/studies_en.htm.
- [168] Alonso-Magdalena P, Quesada I, Nadal A. Endocrine disruptors in the etiology of type 2 diabetes mellitus. *Nat Rev Endocrinol* 2011; 7(6): 346-353.
- [169] Latini G, Marcovecchio ML, Del Vecchio A, Gallo F, Bertino E, Chiarelli F. Influence of environment on insulin sensitivity. *Environ Int* 2009; 35(6): 987-993.
- [170] Karami Mohajeri S, Abdollahi M. Toxic influence of organophosphate, carbamate, and organochlorine pesticides on cellular metabolism of lipids, proteins, and carbohydrates: a systematic review. *Hum Exp Toxicol* 2011; 30(9): 1119-40.
- [171] Ukropec J, Radikova Z, Huckova M, *et al.* High prevalence of prediabetes and diabetes in a population exposed to high levels of an organochlorine cocktail. *Diabetologia* 2010; 53(5): 899-906.
- [172] Ruzzin J, Petersen R, Meugnier E, *et al.* Persistent organic pollutant exposure leads to insulin resistance syndrome. *Environ Health Perspect* 2010; 118(4): 465-471.
- [173] Sargis RM, Johnson DN, Choudhury RA, Brady MJ. Environmental endocrine disruptors promote adipogenesis in the 3T3-L1 cell line through glucocorticoid receptor activation. *Obesity (Silver Spring)* 2010; 18(7): 1283-1288.
- [174] Taylor KW, Novak RF, Anderson HA, *et al.* Evaluation of the Association between Persistent Organic Pollutants (POPs) and Diabetes in Epidemiological Studies: A National Toxicology Program Workshop Review. *Environ Health Perspect* 2013; 121(7): 774-783.
- [175] Wang J, Zhu Y, Cai X, Yu J, Yang X, Cheng J. Abnormal glucose regulation in pyrethroid pesticide factory workers. *Chemosphere* 2011; 82(7): 1080-1082.
- [176] Slotkin TA. Does early-life exposure to organophosphate insecticides lead to prediabetes and obesity? *Reprod Toxicol* 2011; 31(3): 297-301.
- [177] Miller LV, Stokes JD, Silpipat C. Diabetes mellitus and autonomic dysfunction after vacor rodenticide ingestion. *Diabetes Care* 1978; 1(2): 73-76.
- [178] Peters KS, Tong TG, Kutz K, Benowitz NL. Diabetes mellitus and orthostatic hypotension resulting from ingestion of Vacor rat poison: endocrine and autonomic function studies. *West J Med* 1981; 134(1): 65-68.
- [179] Ferner RE. Drug-induced diabetes. *Baillieres Clin Endocrinol Metab* 1992; 6(4): 849-866.
- [180] Kim JM, Lee TH, Lee MC, *et al.* Endoneurial microangiopathy of sural nerve in experimental vacor-induced diabetes. *Ultrastruct Pathol* 2002; 26(6): 393-401.
- [181] Gallanosa AG, Spyker DA, Currow RT. Diabetes mellitus associated with autonomic and peripheral neuropathy after Vacor rodenticide poisoning: a review. *Clin Toxicol* 1981; 18(4): 441-449.

- [182] Karam JH, Lewitt PA, Young CW, *et al.* Insulinopenic diabetes after rodenticide (Vacor) ingestion: a unique model of acquired diabetes in man. *Diabetes* 1980; 29(12): 971-978.
- [183] Kjaerstad MB, Taxvig C, Nellemann C, Vinggaard AM, Andersen HR. Endocrine disrupting effects in vitro of conazole antifungals used as pesticides and pharmaceuticals. *Reprod Toxicol* 2010; 30(4): 573-582.
- [184] Howard SG, Lee DH. What is the role of human contamination by environmental chemicals in the development of type 1 diabetes. *J Epidemiol Community Health* 2012; 66(6): 479-81.
- [185] Forlenza GP, Rewers M. The epidemic of type 1 diabetes: what is it telling us. *Curr Opin Endocrinol Diabetes Obes* 2011; 18(4): 248-251.
- [186] Myers MA, Mackay IR, Zimmet PZ. Toxic type 1 diabetes. *Rev Endocr Metab Disord* 2003; 4(3): 225-31.
- [187] Snijder CA, Roeleveld N, Te Velde E, *et al.* Occupational exposure to chemicals and fetal growth: the Generation R Study. *Hum Reprod* 2012; 27(3): 910-920.
- [188] La Merrill M, Birnbaum LS. Childhood obesity and environmental chemicals. *Mt Sinai J Med* 2011; 78(1): 22-48.
- [189] Gladen BC, Ragan NB, Rogan WJ. Pubertal growth and development and prenatal and lactational exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene. *J Pediatr* 2000; 136(4): 490-496.
- [190] Neel BA, Sargis RM. The paradox of progress: Environmental disruption of metabolism and the diabetes epidemic. *Diabetes* 2011; 60(7): 1838-1848.
- [191] Zidenberg-Cherr S, Neyman MR, Fechner K, *et al.* Nutrition may influence toxicant susceptibility of children and elderl. *Calif Agric* 2000; 54(5): 19-25.
- [192] Saldana TM, Basso O, Hoppin JA, *et al.* Pesticide exposure and self-reported gestational diabetes mellitus in the Agricultural Health Study. *Diabetes Care* 2007; 30(3): 529-534.
- [193] Saldana TM, Basso O, Hoppin JA, *et al.* Pesticide Use And Gestational Diabetes Mellitus Among Wives Of Farmers In The Agricultural Health Study. *Am J Epidemiol* 2006; 163(11 Suppl): S77.
- [194] Janesick A, Blumberg, B. Endocrine disrupting chemicals and the developmental programming of adipogenesis and obesity. *Birth Defects Res C Embryo Today* 2011; 93(1): 34-50.
- [195] Verhulst SL, Nelen V, Hond ED, *et al.* Intrauterine exposure to environmental pollutants and body mass index during the first 3 years of life. *Environ Health Perspect* 2009; 117(1): 122-126.
- [196] Newbold RR, Padilla-Banks E, Snyder RJ, Jefferson WN. Perinatal exposure to environmental estrogens and the development of obesity. *Mol Nutr Food Res* 2007; 51(7): 912-917.
- [197] Newbold RR. Developmental exposure to endocrine-disrupting chemicals programs for reproductive tract alterations and obesity later in life. *Am J Clin Nutr* 2011; 94(S6): 1939S-42S.
- [198] Newbold RR. Impact of environmental endocrine disrupting chemicals on the development of obesity. *Hormones (Athens)* 2010; 9(3): 206-217.
- [199] Spencer SJ. Early life programming of obesity: the impact of the perinatal environment on the development of obesity and metabolic dysfunction in the offspring. *Curr Diabetes Rev* 2012; 8(1): 55-68.
- [200] Howard SG, Heindel JJ, Thayer KA, Porta M. Environmental pollutants and beta cell function: Relevance for type 1 and gestational diabetes. *Diabetologia* 2011; 54(12): 3168-3169.
- [201] Reigart JR, Roberts JR. Pesticide in children. *Pediatr Clin North Am* 2001; 48(5): 1185-1198.
- [202] Heindel JJ, vom Saal FS. Role of nutrition and environmental endocrine disrupting chemicals during the perinatal period on the aetiology of obesity. *Mol Cell Endocrinol* 2009; 304(1-2): 90-96.
- [203] Gyorene KG, Varga A, Lugasi A. A comparison of chemical composition and nutritional value of organically and conventionally grown plant derived foods]. *Orv Hetil* 2006; 147(43): 2081-2090.
- [204] Worthington V. Effect of agricultural methods on nutritional quality: a comparison of organic with conventional crops. *Altern Ther Health Med* 1998; 4(1): 58-69.
- [205] Dangour AD, Dodhia SK, Hayter A, Allen E, Lock K, Uauy R. Nutritional quality of organic foods: a systematic review. *Am J Clin Nutr* 2009; 90(3): 680-685.
- [206] Bourn D, Prescott J. A comparison of the nutritional value, sensory qualities, and food safety of organically and conventionally produced foods. *Crit Rev Food Sci Nutr* 2002; 42(1): 1-34.
- [207] McCormack S, Grant SF. Genetics of obesity and type 2 diabetes in African Americans. *J Obes* 2013; 2013: 396416.
- [208] Cauchi S, Nead KT, Choquet H, *et al.* The genetic susceptibility to type 2 diabetes may be modulated by obesity status: implications for association studies. *BMC Med Genet* 2008; 9: 45.
- [209] Choquet H, Meyre D. Genetics of Obesity: What have we Learned? *Curr Genomics* 2011; 12(3): 169-179.
- [210] Dangour AD, Lock K, Hayter A, Aikenhead A, Allen E, Uauy R. Nutrition-related health effects of organic foods: a systematic review. *Am J Clin Nutr* 2010; 92(1): 203-210.
- [211] Kim KY, Kim DS, Lee SK, *et al.* Association of low-dose exposure to persistent organic pollutants with global DNA hypomethylation in healthy Koreans. *Environ Health Perspect* 2010; 118(3): 370-374.
- [212] Rezg R, Mornagui B, Benahmed M, *et al.* Malathion exposure modulates hypothalamic gene expression and induces dyslipidemia in Wistar rats. *Food Chem Toxicol* 2010; 48(6): 1473-1477.
- [213] Qu W, Suri RP, Bi X, Sheng G, Fu J. Exposure of young mothers and newborns to organochlorine pesticides (OCPs) in Guangzhou, China. *Sci Total Environ* 2010; 408(16): 3133-3138.
- [214] Ramachandran A. Epidemiology of diabetes in India--three decades of research. *J Assoc Physicians India* 2005; 53: 34-38.