ENDOMETRIOSE ET ENVIRONNEMENT

P. MADELENAT, A. LE TOHIC, L. FRIEDERICH, V. KAHN

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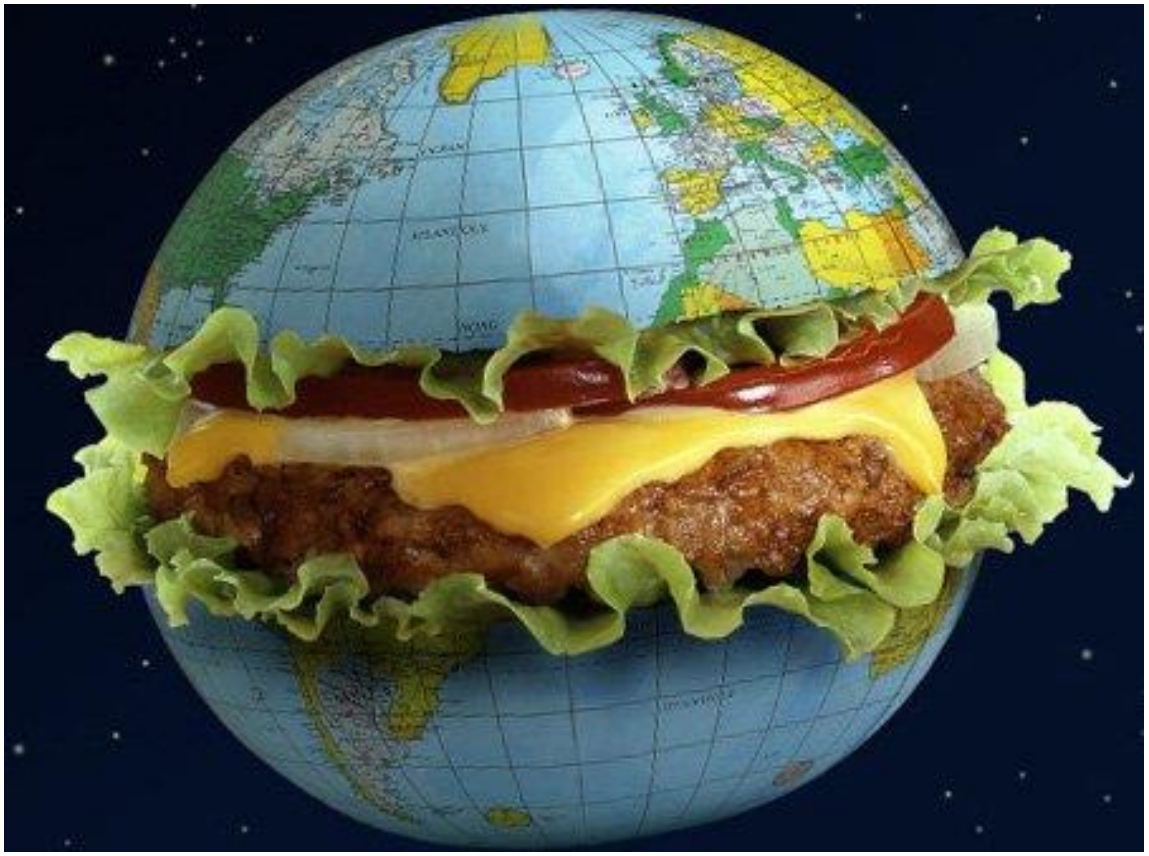
ENDOMETRIOSE: UNE CAUSALITE ALIMENTAIRE ?



« Mal bouffe »: mythe ou réalité ?

DIET AND ENDOMETRIOSIS RISK: A LITERATURE REVIEW

Main findings for effects of specific foods on endometriosis-associated pathological processes

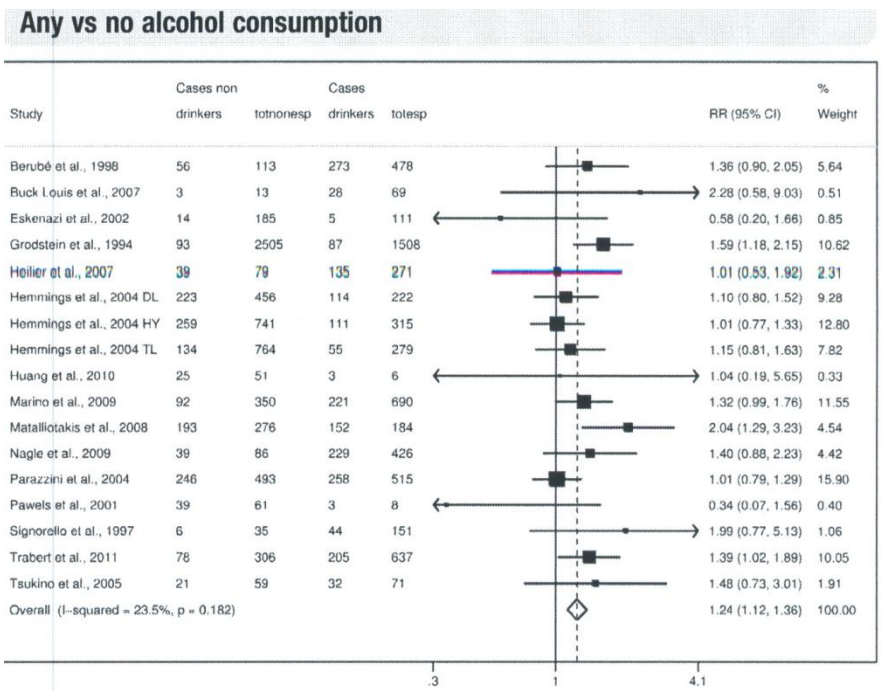
	Food	*Effect on the disease*		*Processes potentially involved*
+	Vegetables	Debated	↓	Supply or regenerating DNA methyl groups in critical genes (Riscuta and Dumitrescu, 2012)
	Fruits	Debated		Polychlorinated biphenyl containers interfering with hormonal pathways (Grassi et al., 2010; Craig et al., 2011; Buck Louis et al., 2012)
	Carrots, β-carotene and vitamin A	Debated		Production of ROS and cell proliferation (Mier-Cabrera et al., 2009; Traber and Stevens, 2011)
	Vitamins C and E	Debated		Production of ROS and cell proliferation (Ngô et al., 2009; Traber and Stevens, 2011)
	Folates	No effec reported		—
	Total fat	Debated		Increased plasma concentration of oestradiol and oestrogen-mediated disease maintenance (Bulun et al., 2012; Fung et al., 2012)
−	Red meat: ham, saturated fat	Debated	↑	Increased plasma concentration of oestradiol and oestrogen-mediated disease maintenance (Bulun et al., 2012; Fung et al., 2012)
	Butter	Debated		Oestrogen-mediated disease maintenance (Pape-Zambito et al., 2010; Bulun et al., 2012)
	Olive oil, monounsaturated fats	Debated		ROS scavengers (Psaltopoulou et al., 2011)
+	Fish, omega-3 polyunsaturated fatty acids	Debated	↓	Production of prostaglandin E_2 and cytokines (Calder, 2003)
−	*Trans* fat	Debated	↑	Increased concentrations of inflammatory markers (Mozaffarian, 2006)
	Milk, vitamin D	Debated		Effect on the immune system (Correale et al., 2009; Chambers and Hawrylowicz, 2011; Kriegel et al., 2011)
	Fibres	Debated		Decrease bioavailable oestrogens (Kaneda et al., 1997)
	Refined and whole cereal carbohydrates	Debated		Endometrial cell proliferation through insulin and insulin-like growth factor-1 receptors (Friberg et al., 2011)
	Soy phyto-oestrogens	Debated		Anti-oestrogenic effect (Yavuz et al., 2007; Chen et al., 2011)
−	Coffee	Debated	↑	Changes in availability of various hormones (Ferrini and Barrett-Connor, 1996; Lucero et al., 2001; Homan et al., 2007)

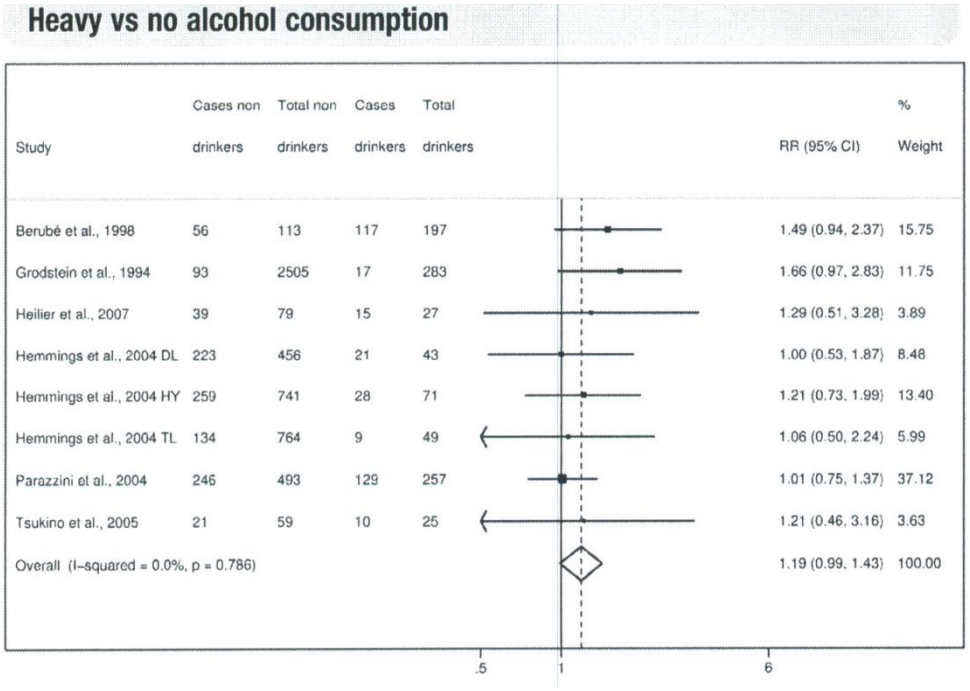
Arrows indicate risk direction.
ROS = reactive oxygen species.

Fabio Parazzini [a], Paola Viganò [b,*], Massimo Candiani [c], Luigi Fedele [a]

Reproductive BioMedicine Online (2013) **26**, 323–336

A METAANALYSIS ON ALCOHOL CONSUMPTION AND RISK OF ENDOMETRIOSIS





The present metaanalysis provides evidence for an association between alcohol consumption and endometriosis risk.

Fabio Parazzini, MD; Sonia Cipriani, ScD; Francesca Bravi, PhD; Claudio Pelucchi, ScD; Francesca Chiaffarino, ScD; Elena Ricci, PhD; Paola Viganò, MD

American Journal of Obstetrics & Gynecology AUGUST 2013

ELSEVIER MASSON

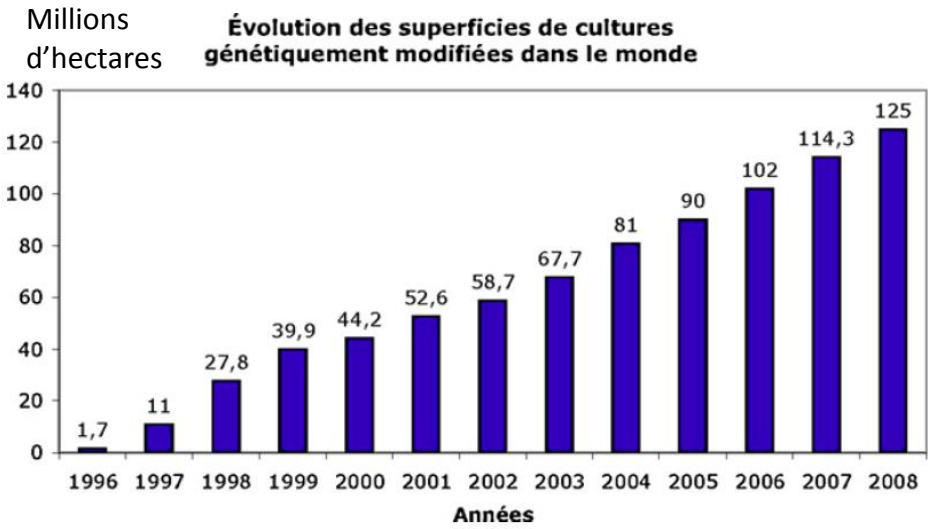
Lien hypothétique entre l'endométriose et l'accumulation de xénobiotiques associés aux aliments génétiquement modifiés

Hypothetical link between endometriosis and xenobiotics-associated genetically modified food

K. Paris [a], A. Aris [a,*,b]

Une nouvelle alimentation, fruit de la biotechnologie moderne, et sa face cachée:

Les xénobiotiques



- Phthalates
- Biphenyl polychlorés (BPC)
- Dioxines
- Bisphenol A (BPA)

MODES D' ACTION SUPPOSES:

Perturbateurs endocriniens, toxines immunitaires, agents pro oxydants

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Phthalates and risk of endometriosis

Kristen Upson [a,b,*], Sheela Sathyanarayana [c,d,e], Anneclaire J. De Roos [a,b], Mary Lou Thompson [f], Delia Scholes [a,g], Russell Dills [c,h], Victoria L. Holt [a,b]

Surgically-confirmed cases (n=92) diagnosed between 1996 and 2001 and population-based controls (n=195).
A strong inverse association between urinary mono (2 ethyl 5 hexyl) phthalate (MEHP) concentration and endometriosis risk. An inverse association between endometriosis and urinary concentrations of other di-2-ethylhexyl phthalate (DEHP) metabolites (mono-(2-ethyl-5-hydroxyheryl) phthalate (MEHHP), mono-(2-ethyl-5-oxoheryl) phthalate (MEOHP) and ∑DEHP, however, the confidence intervals include the null. **INCREASED ENDOMETRIOSIS RISK WITH GREATER URINARY CONCENTRATIONS OF MONO-BENZYL PHTHALATE (MBzP) AND MONO-ETHYL PHTALATE (MEP) ALTHOUGH THE ASSOCIATIONS WERE NOT STATISTICALLY SIGNIFICANT.**

Laboratory measurement of urinary phthalate metabolite concentrations and distribution by case status, Group Health, 1996–2001.

Phthalate metabolite	LOQ (ng/mL)	Study samples (n=287) Measured ≥LOQ n (%)	Cases (n=92) Median (IQR)	Controls (n=195) Median (IQR)
MEHP	0.4	240 (83.6)	2.2 (0.6–4.6)	3.4 (1.0–11.1)
MEHHP	0.2	285 (99.3)	14.8 (5.3–31.0)	18.8 (6.3–56.5)
MEOHP	0.2	287 (100.0)	8.1 (3.5–18.0)	10.8 (3.5–29.1)
MECPP	0.3	286 (99.7)	14.4 (5.9–32.5)	18.0 (5.8–51.9)
MBzP	0.5	266 (92.7)	4.5 (2.2–9.9)	5.0 (2.0–11.5)
MEP	0.8	284 (99.0)	61.9 (23.5–155.9)	43.9 (16.8–144.4)
MiBP	0.2	270 (94.1)	1.3 (0.6–2.7)	1.5 (0.7–3.1)
MnBP	0.3	284 (99.0)	9.8 (5.0–20.9)	10.0 (4.9–23.5)

Environmental Research 126 (2013) 91–97

Possible role of phthalate in the pathogenesis of endometriosis: *in vitro*, animal, and human data

Table 1. Clinical characteristics and urinary levels of phthalate metabolites of patients and controls

	Control group (n = 33)	Endometriosis group (n = 55)	P-value	P-value adjusted[a]	Odds ratio (95% CI)[a]
Age[b]	32.6 ± 1.4	29.9 ± 0.6	0.080[c]		
No. of deliveries[b]	0.7 ± 0.2	0.3 ± 0.1	0.055[d]		
Body mass index[b] (kg/m^2)	21.0 ± 0.9	21.0 ± 3.4	0.779[d]		
Creatinine-adjusted urine levels($\mu g/g$ creatinine)					
MEHHP	12.9 ± 1.4	18.2 ± 1.7	0.021[d]		
MEOHP	10.3 ± 0.9	13.4 ± 1.1	0.050[d]		
MnBP	32.4 ± 3.1	41.7 ± 6.2	0.474[d]		
MBzP	7.3 ± 1.9	5.8 ± 1.0	0.966[d]		
MECPP	19.0 ± 1.7	23.8 ± 1.9	0.061[d]		

- **Objective**: to compare the urinary levels of several phthalate metabolites between women with and without endometriosis.
- **Design**: prospective case-control study for human sample analyses.
- **Main outcome measures**: urinary concentrations of several phthalate metabolites were compared between women with and without endometriosis.
- **Resultats**: the urinary concentration of mono (2-ethyl-5-hydroxyhexyl) phthalate (mEHHP), mono (2-ethyl-5-oxohexyl) phthalate (mEOHP), mono (2-ethyl-5-carboxyphentyl) phthalate (mECPP) were significantly higher in women with endometriosis compared with controls.
- **Conclusion**: these findings strongly suggest that exposure to phthalate may lead to establishment of endometriosis by enhancing invasive and proliferative activities of endometrial cells.

J Clin Endocrinol Metab. Doi: 10.1210/jc.2015-2478
Sung Hoonkim et al

INCREASED PLASMA LEVELS OF PHTHALATE ESTERS IN WOMEN WITH ADVANCED-STAGE ENDOMETRIOSIS: A PROSPECTIVE CASE-CONTROL STUDY

The plasma concentrations of phthalate esters are elevated in women with advanced-stage endometriosis. The concentrations of **monoethylhexyl phthalate** are significantly higher in those with advanced-stage endometriosis.

Clinical characteristics and the plasma levels of phthalate esters in patients with endometriosis and controls.

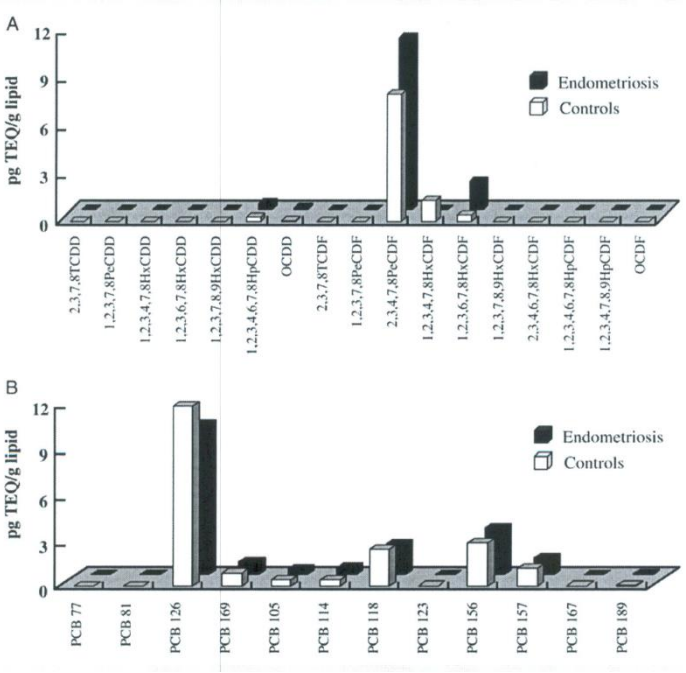
Characteristic	Control group (n = 169)	Endometriosis group (n = 97)	*P* value[a]	OR[b] (95% CI)/ *P* value[b]	OR[c] (95% CI)/ *P* value[c]
Age (y)[d]	34.9 ± 0.5	34.8 ± 0.7	.804		
No. of deliveries[d]	0.9 ± 0.1	0.6 ± 0.1	.031	0.819 (0.609–1.101)/.186	0.827 (0.615–1.112)/.208
BMI[d] (kg/m^2)	22.7 ± 0.3	21.4 ± 0.3	.001	0.890 (0.816–0.971)/.009	0.887 (0.811–0.969)/.008
MEHP[d] (ng/mL)	12.4 ± 1.1	17.4 ± 1.5	<.001	1.020 (1.003–1.038)/.020	
DEHP[d] (ng/mL)	92.5 ± 31.1	179.7 ± 32.5	.010		1.001 (1.000–1.002)/.161

KIM SH et al

Fertility and Sterility® Vol. 95, No. 1, January 2011

human reproduction ORIGINAL ARTICLE *Gynaecology*

Dioxins in ascites and serum of women with endometriosis: a pilot study



Distribution pattern of dioxins (**A**) and dioxin-like PCBs (**B**) in ascites.

Lipid-adjusted levels of dioxin-like PCBs, PCDDs and PCDFs in serum and ascites.

	Serum levels			Ascites levels		
	EM (n = 10)	Control (n = 7)	P-value	EM (n = 10)	Control (n = 7)	P-value
PCDFs (10)	7.5 ± 2.6 (51/100)[a]	6.9 ± 2.3 (37/70)	0.61[b]	11.8 ± 10.4 (10/100)	10.6 ± 12.5 (6/70)	0.84[b]
PCDDs (7)	8.6 ± 3.2 (64/70)	7.4 ± 2.7 (34/49)	0.43[b]	0.5 ± 0.5 (15/70)	0.3 ± 0.4 (10/49)	0.89[c]
Total (PCDDs + PCDFs) (17)	16.1 ± 5.6 (115/170)	14.3 ± 3.1 (71/119)	0.51[b]	12.2 ± 10.5 (25/170)	10.8 ± 12.3 (16/119)	0.89[c]
Total non-ortho Co-PCBs (4)	4.1 ± 1.6 (31/40)	4.7 ± 3.2 (23/28)	0.81[c]	11.3 ± 3.9 (27/40)	12.1 ± 7.5 (20/28)	0.81[c]
Total mono-ortho Co-PCBs (8)	3.2 ± 0.6 (80/80)	3.1 ± 1.4 (56/56)	0.74[b]	7.4 ± 2.9 (80/80)	7.4 ± 2.5 (56/56)	0.86[b]
Total Co-PCBs (12)	7.2 ± 1.8 (111/120)	7.5 ± 3.9 (79/84)	0.54[c]	18.7 ± 5.3 (107/120)	19.3 ± 9.7 (76/84)	0.74[c]

CONCLUSIONS: This is the first report suggesting that higher concentrations of dioxins (PCDDs and PCDFs) in peritoneal fluid are linked to endometriosis. More detail and epidemiological research is warranted to further explore this link.

L.Y. Cai[1], S. Izumi[1,*], T. Suzuki[1], K. Goya[1], E. Nakamura[1], T. Sugiyama[1], and H. Kobayashi[2]

Human Reproduction, Vol.26, No.1 pp. 117–126, 2011

Présence de Dioxine dans les Tissus Adipeux

Increased levels of dioxin-like substances in adipose tissue in patients with deep infiltrating endometriosis

Study question: are the levels of biologically active and the most toxic dioxin-like substances in adipose tissue of patients with deep infiltrating endometriosis (DIE) higher than in a control group without endometriosis?

What is know already: some studies have investigated the levels of dioxin-like substances, in serum samples, in patients with endometriosis with inconsistent results.

Study design: the study group (DIE group) consisted of 30 patients undergoing laparoscopic surgery because of DIE. The non endometriosis control group (control group) included the next consecutive patient undergoing laparoscopic surgery in our center due to adnexal benign gynecological disease.

Methods: dioxin-like substances were analyzed in adipose tissue in DIE patients and controls.

Table III Toxic equivalence (TEQ) of the dioxins and furans analyzed in adipose tissue samples in the two groups and odds ratios (OR) and 95% CIs for the relationship between each dioxin or furan and deep infiltrating endometriosis (DIE).

	TEQ pg/g lipid Median (interquartile range)		OR (95% CI)	P*
	DIE group ($n = 30$)	Control group ($n = 30$)		
Dioxins				
2,3,7,8-TCDD	0.70 (0.53, 0.76)	0.40 (0.32, 0.64)	1.41 (1.12–2.10)	<0.01
1,2,3,7,8-PeCDD	2.41 (2.12, 2.89)	1.67 (1.11, 2.53)	1.82 (1.36–7.14)	<0.01
2,3,4,7,8-PeCDF	1.55 (1.28, 1.85)	1.18 (0.84, 1.56)	2.13 (1.97–6.42)	<0.01

Results: both dioxins and PCBs were significantly higher in patients with DIE in comparison with the control group (P<0,05). Mainly due to the significantly higher values TCDD1. Our resultats suggest a potential role of dioxin-like substances in the pathogenesis of DIE.

M.A. Martínez-Zamora[1], L. Mattioli[2], J. Parera[2], E. Abad[2], J.L. Coloma[1], B. van Babel[3], M.T. Galceran[4], J. Balasch[1], and F. Carmona[1,*]

Human Reproduction, Vol.30, No.5 pp. 1059–1068, 2015

Organochlorine pesticides and risk of endometriosis: findings from a population-based case-control study.

Objective: endometriosis risk in relation to environmental exposure to OCPs.

Methods: data from the women's risk of endometriosis (WREN) study.
OCP concentrations were measured in sera from surgically confirmed endometriosis cases (n=248) first diagnosed between 1996 and 2001 and from population-based controls (n=538).

Pesticide (pg/g serum)	Measured ≥ LOD [*n* (%)]	Measured < LOD [*n* (%)]	Interference [*n* (%)]	Cases (*n* = 248) [median (IQR)]	Controls (*n* = 538) [median (IQR)]
β-HCH	709 (90.2)	30 (3.8)	47 (6.0)	51.91 (29.19, 80.79)	43.06 (26.99, 74.03)
Mirex[a]	300 (38.2)	453 (57.6)	33 (4.2)	< 10.00 (< 10.00, 15.61)	< 10.00 (< 10.00, 13.11)

Results: our data suggested increased endometriosis risk associated with serum concentrations of ß-hexachlorocyclohexane (HCH) and mirex.

Conclusion: extensive past use of environmentally persistent OCPs in the United States or present use in other countries may affect the health of reproductive-age women.

Upson K, De Roos AJ, Thompson ML, Sathyanarayana S, Scholes D, Barr DB, Holt VL.
PMID: 24192044 (PubMed-indexed for MEDLINE) PMCID: PMC3855515 Free PMC Article

Endocrine toxicants including 2, 3, 7, 8- Terachlorodibenzo-P-Dioxin (TCDD) and Dioxin-like chemicals and endometriosis: is there a link?

SUMMARY OF EPIDEMIOLOGICAL STUDIES

	Authors	Cases vs. controls	Study design	Exposure	Tissue	Outcome
+	Gerhard and Runnebaum, 1992	28/441	Case control	PCB congeners, heavy metals, and chlorinated pesticides	S	Positive association for PCB (138, 153, and 180).
-	Boyd et al., 1995	15/15	Case control	Dioxins and furans	S	No relationship
	Mayani et al., 1997	44/35	Case control	Dioxin	B	Authors report a positive association for TCDD exposure; 8 of cases 44 (18%) had detectable levels of TCDD compared to 1 of controls 35 (3%). However, CI includes unity and thus it is concluded that this study fails to demonstrate a positive association.
-	Lebel et al., 1998	86/70	Case control	PCB congeners, and chlorinated pesticides	P	No statistically significant relationship between exposure and endometriosis.
+	Eskenazi et al., 2001	82/307	Nested case control	Dioxin	S	The authors report a nonsignificant doubling of risk in women with TCDD serum levels > 100 ppt.
-	Pauwels et al., 2001	42/29	Case control	Dioxin-like activity determined by CALUX assay and PCB (118, 138, 153, 180) by GC/MS.	S	This study found that a statistically significant relationship between dioxin exposure and endometriosis in infertile women did not exist.
-	De Felip et al., 2004	23/17	Case control	Dioxin-like PCB in serum	S	No statistically significant relationship between dioxins and endometriosis.
+	Propora et al., 2006	—	Case control	PCB congener-specific analysis	S	Higher levels of PCBs were found in serum of women with endometriosis vs. controls, odds ratio for upper tertile 4.0, CI 95% 1.3–13; $p = .0003$
+	Heilier et al., 2005	50/21	Case control	Dioxins, dibenofurans and dioxin-like PCB	S	An increased risk was found for peritoneal endometriosis (OR, 1.9; 95% CI, 0.9–3.8) for total TEQ levels and for dioxins alone (OR, 3.2; 95% CI, 1.0–9.9).

Warren G. Foster

Journal of Toxicology and Environmental Health, Part B, 11: 177-187, 2008

Contents lists available at ScienceDirect

Reproductive Toxicology

journal homepage: www.elsevier.com/locate/reprotox

Trace elements and endometriosis: The ENDO Study

Anna Z. Pollack[a,*], Germaine M. Buck Louis[a], Zhen Chen[a], C. Matthew Peterson[b], Rajeshwari Sundaram[a], Mary S. Croughan[c], Liping Sun[a], Mary L. Hediger[a], Joseph B. Stanford[d], Michael W. Varner[e], Christopher D. Palmer[f], Amy J. Steuerwald[f], Patrick J. Parsons[f]

473 women aged 18-44 years were recruited into an operative cohort, along with 131 similarly aged women recruited into a population cohort. Endometriosis was defined as surgically visualized disease in the operative ochort, and magnetic resonance imaging diagnosed disease in the population cohort. No association was observed between any element and endometriosis in the population cohort. **In the operative cohort, blood cadmium was associated with a reduced odds of diagnosis, while urinary chromium and copper reflected an increased odds.**

Simultaneous modeling of significant metals and odds of an endometriosis diagnosis in the operative cohort, ENDO Study.

Metals	Adjusted[a] OR (95% CI)	Adjusted[b] OR (95% CI)
Blood Cadmium (μg/L)		
<0.21	Reference	Reference
0.21–0.36	0.75 (0.46, 1.24)	0.78 (0.47, 1.29)
≥0.37	0.52 (0.29, 0.93)	0.52 (0.29, 0.94)
Urine (μg/L) Chromium		
<0.47	Reference	Reference
0.47–1.30	2.32 (1.42, 3.79)	2.34 (1.43, 3.86)
>1.31	0.99 (0.59, 1.66)	0.97 (0.57, 1.63)
Copper		
<7.08	Reference	Reference
7.08–13.80	0.96 (0.53, 1.74)	0.97 (0.53, 1.77)
≥13.81	1.15 (0.73, 1.80)	1.12 (0.71, 1.78)

Copper, ceruloplasmin and oxidative stress in patients with advanced-stage endometriosis

AIM: to compare patients with advanced stage endometriosis with control patients without endometriosis with respect to serum Copper (Cu) and Ceruloplasmin (Cp) levels and oxidative stress markers.

Patients and methods: 72 women who underwent laparoscopy or laparotomy. Propsective clinical study. Control patients (n=41) without endometriosis and study group (n=31) with stage III/IV (advanced stage) endometriosis. Correlations between Cu, Cp and oxidative stress markers were determined.

	Endometriosis	Control
Cu: cuivre	↗	
Cp: ceruplasmin	↗	
TAS: total ant. Oxydant status		↘
TOS: total oxydant status		↘
OSI oxydative stress index	↗	
PON1 panaoxonase	↗	
MDA: mulondialdelyde	→	

Parameters	Advanced-stage endometriosis (n = 31) (mean ± SD)	Controls (n = 41) (mean ± SD)	*p* value
TAS (mmol Trolox Equivalent/L)	1.01 ± 0.10	1.15 ± 0.17	< 0.001
TOS (μmol H_2O_2 Equiv/L)	25.40 ± 9.35	15.98 ± 6.97	< 0.001
OSI (H_2O_2/Trolox)	25.07 ± 9.21	14.05 ± 6.69	< 0.001
PON-1 (u/l)	73.38 ± 44.34	98.47 ± 44.46	0.020
MDA (mmol/L)	220.87 ± 41.84	205.49 ± 43.57	0.136
Cu (μg/ml)	1088.00 ± 273.58	811.20 ± 265.77	< 0.001
Cp (mg/dl)	38.41 ± 9.58	26.50 ± 8.63	< 0.001

Turgut A, Ozler A, Goruk NY, Tunc SY, Evliyaoglu O, Gül T. Eur Rev Med Pharmacol Sci 2013. Jun; 17 (11): 1472-8.

STRESS OXYDATIF ET ENDOMETRIOSE

Low-density lipoproteins oxidation and endometriosis.
Polak G et al.
Mediators inflamm 2013; 2013:624540

Increased levels of oxidative stress markers in the peritoneal fluid of women with endometriosis
Polak G et al.
Eur J Obstet Gynecol Reprod Biol 2013 Jun; 168 (2): 187-90.

Oxidative cell injury as a predictor of endometriosis progression
Carvalho et al
Reprod Sci 2013. Jun; 20(6): 688-98.

Serum markers of oxidative stress and endometriosis
Rosa e Silva JC et al
Clin Exp Obstet Gynecol 2014; 41 (4): 371-4

Oxidative Cell Injury as a Predictor of Endometriosis Progression

Background: these is increasing evidence that oxidative stress is one of the key factors for progression of endometriosis. We measured 6 different biomarkers of oxidative stress targeting protein, lipid, and DNA to quantify the severity and progression of endometriosis.

Methods: 44 patients were allocated to 3 groups: stage I / II (n=14), stage III/IV (n=16), and a control group (n=14). The levels of biomarkers were accessed in peritoneal fluid and tissue.

Results: significantly higher levels of 8-OHdG and PC were seen in patients with endometriosis. OGGI expression was found to be significantly lower in patients with endometriosis; ROS, TAC, and LPO were similar in stages I/II, stages III/IV and control group.

Table 1. Summary of Oxidative Cell Injury Biomarkers Measured in Control; Minimal and Mild Endometriosis (Stage I/II); and in Moderate and Severe Endometriosis (Stage III/IV).[3]

Factor	Control (n = 14)	Stage I/II (n = 14)	Stage III/IV (n = 16)	P value
8-OhdG, %	2.38 (0.38, 3.29)	13.2 (9.43, 14.21)	17.68 (15.47, 29.44)	<.001
OGG1, %	15.68 (14.5, 21.23)	9.16 (4.76, 13.08)	4.25 (3.02, 7.88)	.001
PC, nmol/mL	1.56 (1.26, 2.5)	3.29 (2.84, 4.54)	3.52 (2.13, 4.06)	.033
TAC, µmol Trolox	1110 (910, 1250)	1030 (940, 1250)	1200 (1060, 1250)	.84
ROS, RLU	17475 (9638, 22514)	4719 (0, 11780)	2401.5 (0, 13914)	.24
LPO, µmol MDA/L	1.53 (1.25, 1.64)	1.02 (1, 1.03)	3.02 (1.87, 3.04)	.09

Conclusions: In this cohort, higher DNA damage and lower DNA repair activity was related to endometriosis progression. Oxidative stress as a biomarker of cell injury can be used as a reliable quantitative test of endometriosis severity

Luiz Fernando Pina Carvalho et al
Reproductive Sciences 20(6) 688-698

Increased levels of oxidative stress markers in the peritoneal fluid of women with endometriosis

Objective: to evaluate 8-hydroxy-2-deoxyguanosine (8-OHdG) and 8-isoprostane levels in the peritoneal fluid (PF) of women with endometriosis.

Study design: one hundred and ten women with endometriosis and as reference groups, 119 patients with ovarian cysts. **Peritoneal fluid 8-OHdG and 8-isoprostane concentrations were evaluated.**

8-OHdG concentrations (ng/ml) in the peritoneal fluid of studied groups.

	Median	Minimum	Maximum	Lower quartile	Upper quartile
Serous cysts	2.4	0.2	21.4	1.7	3.4
Dermoid cysts	2.3	0.5	7.1	1.3	3.2
Endometriosis I rASRM	2.9	1.1	17.8	1.8	5.1
Endometriosis II rASRM	2.6	0.9	11.6	1.3	3.6
Endometriosis III rASRM	3.2	0.8	26.7	1.8	5.8
Endometriosis IV rASRM	4.6	2.2	85.8	3.1	14.3
Endometriosis	3.2	0.8	85.8	2.2	5.3

8-Isoprostane concentrations (ng/ml) in the peritoneal fluid of studied groups.

	Median	Minimum	Maximum	Lower quartile	Upper quartile
Serous cysts	8.5	1.6	262.5	5.6	17.8
Dermoid cysts	12.5	1.6	156.2	5.6	27.2
Endometriosis I rASRM	19.8	3.9	109.3	7.6	31.2
Endometriosis II rASRM	19.7	4.8	211	10.5	48.9
Endometriosis III rASRM	24.6	5.8	173.2	17.8	56.2
Endometriosis IV rASRM	25.7	6.5	447.8	13.1	65.5
Endometriosis	23.2	3.9	447.8	12.3	58.1

Results: 8-OHdG and 8-isoprostane levels in peritoneal fluid were significantly higher in patients with endometriosis compared with the reference groups.

Conclusions: endometriosis induces greater oxidative stress and frequent DNA mutations in peritoneal fluid. The most severe oxidative stress occurs with more advanced stages of the disease.

Grzegorz et al
European Journal of Obstetrics & Gynecology and Reprodutive Biology 168 (2013) 187-190

Stress oxidatif, endométriome et cortex

Oxidative stress status in normal ovarian cortex surrounding ovarian endometriosis

The percentage of immunostained nuclear surface for 8-hydroxydeoxyguanosine.

	Endometriosis	Dermoid	Serous
Age (y)[a]	29.0 (22–34)	27.0 (16–34)	28.0 (25–30)
Normal ovarian cortex (%)[b]	35.4 ± 6.1[c] (11)	2.5 ± 1.2 (7)	2.8 ± 2.5 (5)
Surrounding cyst			
Epithelial cells (%)[b]	47.6 ± 6.3[c] (47)	1.1 ± 0.3 (24)	17.2 ± 3.7[d] (11)
Non epithelial cells (%)[b]	38.1 ± 7.1[c] (47)	0.4 ± 0.2 (24)	9.1 ± 2.6 (11)

Sachiko Matsuzaki et al
Fertility and Sterility Vol 93, N°7, May 1, 2010

Increased levels of oxidative and carbonyl stress markers in normal ovarian cortex surrounding endometriotic cysts.

Table 1. Immunohystochemistry data of MG-AGE, 8-OHdG and FOXO3A staining in ovarian tissue with dermoid cysts ($n = 35$), endometriotic cysts ($n = 32$) and follicular cysts ($n = 37$).

	FOXO3A (mean score ± std. dev.)	8-OHdG (mean score ± std. dev.)	MG-AGE (mean score ± std. dev.)
Endometriotic cyst	15.90 ± 0.28**[A]	13.33 ± 2.07**[A]	12.58 ± 4.34*[a]
Follicular cyst	9.04 ± 0.29**[B]	2.67 ± 2.67**[B]	11.31 ± 2.95*[b]
Dermoid cyst	2.02 ± 0.18**[C]	4.33 ± 2.58**[B]	10.56 ± 4.03*[b]

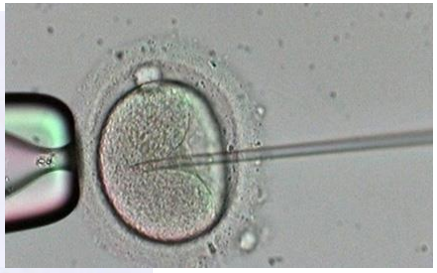
G. Di Emidio et al
Gynecol Endocrinol 2014, 30 (11) 808-812

ENDOMETRIOSE ET FIV: STRESS OXIDATIF

Fertil Steril. 2014 Jul;102(1):151-159.e5. doi: 10.1016/j.fertnstert.2014.03.053. Epub 2014 May 10.

Dynamics of nitric oxide, altered follicular microenvironment, and oocyte quality in women with endometriosis.

Goud PT[1], Goud AP[2], Joshi N[3], Puscheck E[3], Diamond MP[4], Abu-Soud HM[3].



CONCLUSION(S): Increased protein nitration, GC apoptosis, resistance to IVM, and oocyte aging indicate the involvement of **oxidative** dysregulation of NO in the pathophysiology of altered follicular milieu and poor oocyte quality in women with **endometriosis**.

Clin Exp Obstet Gynecol. 2013;40(3):372-6.

The expression and role of oxidative stress markers in the serum and follicular fluid of patients with endometriosis.

Liu F[1], He L, Liu Y, Shi Y, Du H.

CONCLUSION: Patients with **endometriosis** have increased **oxidative stress**, as well as lower mature oocyte rates and fertilization rates. Nevertheless, there is no evidence that the **oxidative stress** status is directly related to the outcome of IVF treatment.

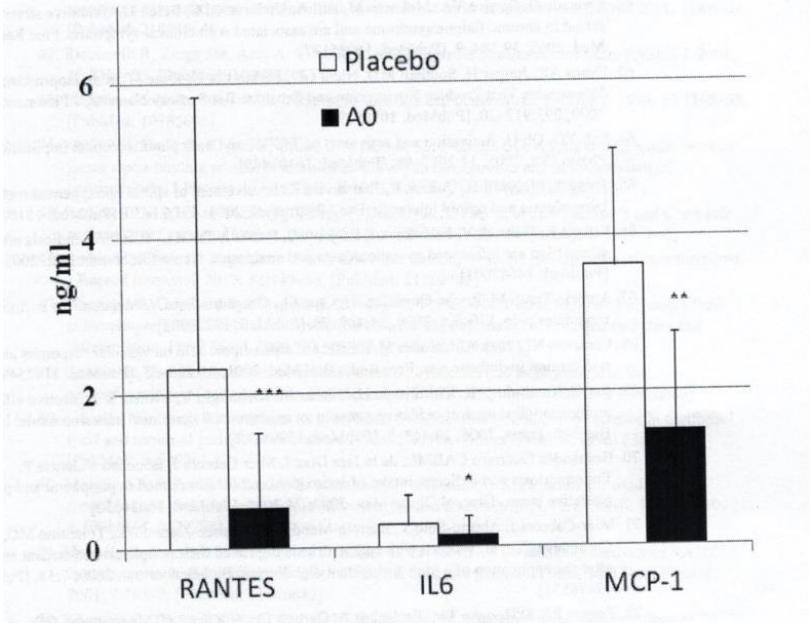
Reprod Toxicol. 2013 Dec;42:116-24. doi: 10.1016/j.reprotox.2013.08.005. Epub 2013 Aug 29.

Markers of oxidative stress in follicular fluid of women with endometriosis and tubal infertility undergoing IVF.

Singh AK[1], Chattopadhyay R, Chakravarty B, Chaudhury K.

Increased levels of ROS, NO, LPO, cadmium and lead were observed in women who did not become pregnant compared to women who did. Intrafollicular zinc levels were higher in women with **endometriosis** who subsequently became pregnant following IVF.

Antioxidant supplementation reduces endometriosis related pelvic pain in humans



Effect of Antioxidant supplementation on "Everyday pain"

Group:	Antioxidants	Placebo
Decreased pain	18 (43%)[a]	0 (0%)
No change	22 (52%)	11 (100%)
Increased pain	2 (5%)	0 (0%)
No pain at baseline	4	2
Total	46	13

Nalini Santanam et al
Transl Res 2013 March; 161 (3): 189-195

A pilot study to search possible mechanisms of ultralong gonadotropin-releasing hormone agonist therapy in IVF-ET patients with endometriosis

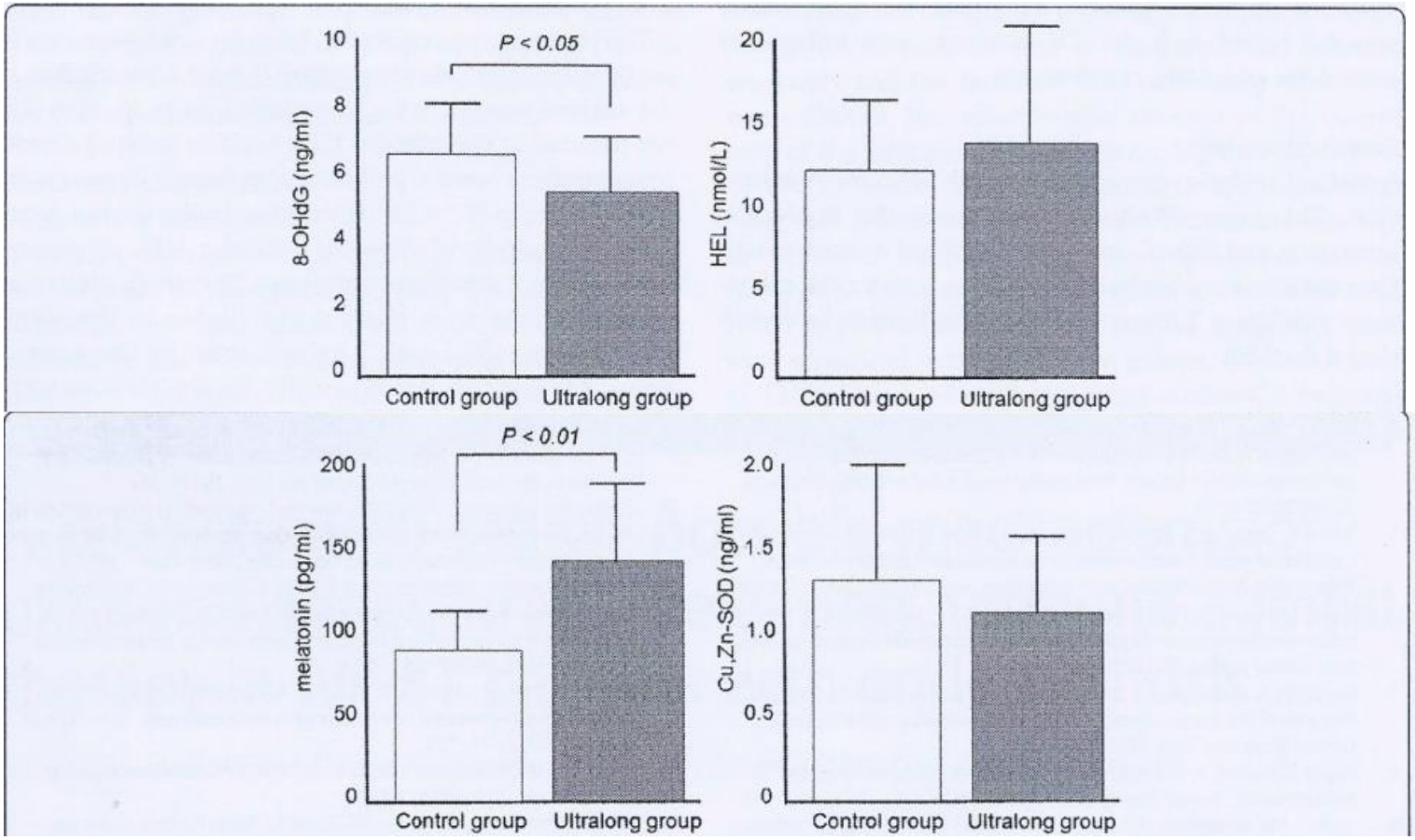


Figure 3 Concentrations of antioxidants in follicular fluids. Twenty-three infertile women with Stage III or IV endometriosis were recruited for this study. Eleven patients received three courses of GnRHa (1.8 mg s.c. every 28 days), followed by a standard controlled ovarian hyperstimulation (COH) for IVF-ET (ultralong group). Twelve patients received a standard COH with mid-luteal phase GnRHa down-regulation (control group). The levels of Cu,Zu-superoxide dismutase (Cu,Zn-SOD) and melatonin, as antioxidants, were measured in the follicular fluid obtained at the time of oocyte retrieval. Values are mean ± SD. Statistical analysis was employed with the Mann–Whitney U-test using the Bonferroni correction.

Hiroshi Tamura et al
Journal of ovarian research 2014, 7:100

Air Pollution Exposures During Adulthood and Risk of Endometriosis in the Nurses' Health Study II

Shruthi Mahalingaiah,[1] Jaime E. Hart,[2,3] Francine Laden,[2,3,4] Ann Aschengrau,[5] and Stacey A. Missmer[2,4,6]

Background: particulate matter and proximity to large roadways contribute to the development and severity of endometriosis.

Objective: the association of air pollution exposures during adulthood, including distance to road, particulate matter < 2,5µm, between 2,5 and 10µm, and < 10µm, and timing of exposure Nurses Health Study II.

Results: 84,060 women, 2,486 incident cases of surgically confirmed endometriosis over 710,230 person-years of follow-up.

Conclusions: traffic and air pollution exposures during adulthood were not associated with incident endometriosis in this cohort of women.

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CONCLUSION
POLLUTION MONDIALE: UNE NOUVELLE ERE
L' ANTHROPOCENE

Perturbateurs endocriniens environnementaux :

Quels risques pour la santé humaine ? »