a. English Translation of the Study

Review article

The use of deodorants/antiperspirants does not constitute a risk factor for breast cancer.

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Summary: Based on the observation of a high incidence of breast cancer in the upper outer quadrant adjacent to the usual area of application of deodorants and/or antiperspirants, several scientific teams have advanced the hypothesis of a possible link between antiperspirants and breast cancer. The possibility of the involvement of parabens and aluminium salts, traditional components of a number of cosmetic products, has been advanced by the same teams.

In order to ascertain whether this hypothesis could or could not be confirmed, a Group of clinical experts in oncology was set up to search and analyse the literature data relating to the problem raised with the aim of answering three predefined questions:

- Does it exist experimental or biological arguments supporting a potential link between the use of deodorants/antiperspirants and breast cancer?
- Does the use of deodorants/antiperspirants have any effect on the increase in the risk of breast cancer?
- Could a causal relationship between the use of deodorants/antiperspirants and breast cancer be accepted?

The scientific data were searched systematically in the PubMed® database (http://www.ncbi.nlm.nih.gov/sites/entrez) using standardised search equations. Fifty-nine studies resulting from the literature search were reviewed and nineteen articles with various methodologies were selected for in-depth analysis.

In view of the fact that parabens are generally not present in deodorants/antiperspirants, the reflection group's search related purely to the question of aluminium salts. Among these nineteen articles, many are methodologically unsound, do not answer to the questions

posed or deal with the question of parabens and were therefore discarded by the reflection Group.
The expert group's conclusion coincides with those of the French, European and American health authorities. After analysis of the available literature on the subject, no scientific evidence to support the hypothesis was identified and no validated hypothesis appears likely to open the way to interesting avenues of research.

Key words: deodorants/antiperspirants, breast cancer, risk factor, parabens, aluminium

INTRODUCTION

Breast cancer is the most common malignant disease in women in the Western world [1], as in France for example, where it killed 11,000 people in 2005 [1bis]. Affecting nearly one woman in ten, predominantly after the menopause, the population concerned has a heightened awareness of the therapeutic, diagnostic, but also epidemiological advances that could optimise its prevention and management [2].
In terms of risk factors, it is now clearly established that a minority of cancers relating to a familial hereditary form usually occur at a younger age, one of the main risk factors moreover continuing to be oestrogens [3].
The progressive increase in the incidence of breast cancer in Western countries is primarily related to the ageing of the population and the endogenous or exogenous oestrogen impregnation [4]. The cause and effect relationships in these different contexts of hormonal impregnation have often been studied and there appears to be no association with excess mortality due to breast cancer, particularly in case of hormone replacement therapy [5].
Recent USA epidemiological data have shown that the incidence of breast cancer has remained stable in young women and decreased in 2003 and 2004 in women aged over 50 years without any obvious explanation yet being advanced. The main hypothesis that might explain this lower incidence is the reduced frequency with which hormone replacement therapy is administered at menopause, but other hypotheses are under study [6].
For several years numerous articles in the general press have reproduced a pathophysiological theory implicating the use of paraben-based or aluminium-based antiperspirants (despite the fact that most of these products do not contain parabens) as a factor that increases the risk of breast cancer occurring [7,8]. The anxiety generated by these scientific speculations regularly prompts a number of patients and women to consult their doctors about the safety of use of these products. As the doctor has to be the source of evidence-based information and must not bend to media pressure, it was therefore important to summarise the answers to be given following analysis of the scientific literature devoted to the subject.
Five experts met together over a period of 6 months for this purpose and present below the outcome of their investigations.

METHOD

The method of establishing conclusions about the use of deodorants/antiperspirants is based on an analysis of the literature data and the expertise of clinicians who manage patients suffering from breast cancer.

- Formulation of the questions by the experts at a meeting:
    - Does it exist experimental or biological arguments supporting a potential link between the use of deodorants/antiperspirants and breast cancer?
    - Does the use of deodorants/antiperspirants have any effect on the increase in the risk of breast cancer?
    - Could a causal relationship between the use of deodorants/antiperspirants and breast cancer be accepted?

- Data search: the scientific data were searched systematically in the PubMed® database using standardised search equations (Table 1). In addition, the research centre of one of the main manufacturers of antiperspirants provided supplementary biological, chemical and biochemical data about these products at the request of the experts.
- Data selection: meta-analyses and randomised trials were given priority by the experts.
- Analysis and methodological summary of the data by the clinicians in the course of 3 plenary sessions. Monitoring of the scientific data was instituted.
- Development of the argument by the clinicians. The data were graded and accompanied by levels of evidence of the literature (Table 2).
- Publication of a report on the expert committee's conclusions.

Table 1: Search method of the literature data

- Search equations (no time-limiting criterion)
    - **Number of articles obtained with the following key words on Pubmed:**
        - "breast cancer and risk factors" = 11,460
        - "breast cancer and risk factors and aluminium" = 3
        - "breast cancer and risk factors and parabens" = 1
        - "breast cancer and aluminium" = 52
        - "breast cancer and aluminium salts" = 3
        - "breast cancer and parabens" = 22

- Number of articles reviewed: **59**

- Number of articles selected for in-depth reading and/or analysis:
    - **19 articles selected by the reflection group from the whole of the available literature**
    - **8 excluded after in-depth reading and/or analysis**

- Evaluation grill of the articles selected (Table 3), indicating:
  - **the study title and type,**
  - **its level of evidence,**
  - **its grade,**
  - **the conclusion and remarks of the Group of experts.**

- Supplementary references [9,10] on the positions of:
  - **the AFSSAPS in France *[French Health Products Safety Agency]***
  - **the FDA and NCI in the United States**

Table 2: Levels of evidence and grades of recommendation according to ANAES [National Agency for Accreditation and Evaluation in Healthcare] 2000

Level of scientific evidence provided by the literature	Grade of recommendation
Level 1 Powerful randomised comparative trials Meta-analysis of randomised comparative trials Decision analysis based on well-conducted studies	**Grade A** Established scientific evidence
Level 2 Less powerful randomised comparative trials Well-conducted randomised comparative studies Cohort studies	**Grade B** Scientific presumption
Level 3 Case-control studies Comparative trials with historical series	**Grade C** Low level of scientific evidence
Level 4 Comparative studies involving major biases Retrospective studies Series of cases Descriptive epidemiological studies (cross-sectional, longitudinal)	

The observation:

Based on the observation of a high incidence of breast cancer in the upper outer quadrant adjacent to the usual area of application of deodorants and/or antiperspirants and of an increasingly more frequent use of deodorants and antiperspirants [11], several scientific teams have sought to establish a possible link between antiperspirants and breast cancer, advancing the possible role of parabens (p-hydroxybenzoic acid esters) and aluminium salts.
Parabens, in particular, are postulated because of their possible oestrogenic role in cell growth *in vitro* (MCF7 and ZR-75-1) and *in vivo,* promoting the growth of uterine cells in rats.
Regarding aluminium salts, they are evoked by several authors as potential metalloestrogens though this hypothesis is not verified, and even so, the possibility for

aluminium salts to bind to skin estrogen receptors is in no case correlated to a possible transcutaneous passage. Indeed, while absorption via the skin certainly occurs, it is slow, and the relationship between shaving (whether electric or otherwise) and cutaneous penetration has also been mentioned in the literature.

Definition of deodorants and antiperspirants:

- The aluminium salt-based *antiperspirant* combats the flow of perspiration and the breakdown of sweat (bacteria) [11,12].
- The bactericide-based (ethanol, triclosan, etc.) *deodorant* combats offensive odours [12].
- Parabens are generally not present in deodorants/antiperspirants, which may be explained by the fact that, as bactericides, deodorants/antiperspirants are self-preservative and therefore do not need the addition of preservatives such as parabens.

ARTICLES SELECTED AND LEVELS OF EVIDENCE:

Articles selected: *Fifty-nine studies resulting from the literature search were reviewed and nineteen articles analysed in detail.*

Several types and methods of study are represented among these 19 articles:

- 1 case-control,
- 2 retrospective,
- 1 case report,
- 8 experimental,
- 7 articles in general reviews.

In view of the fact that parabens are generally not present in deodorants/antiperspirants, the members of the reflection group wished their report to relate purely to the question of aluminium salts and in the end excluded articles about parabens.

A total of 8 articles from among the 19 selected were excluded after a detailed reading either because they did not provide a response to one of the 3 questions posed by the experts, or because they did not concern aluminium.

ANALYSIS, INTERPRETATION AND DISCUSSION

LITERATURE RESPONSES TO THE QUESTIONS ASKED BY THE EXPERTS

There are no prospective studies in the data selected by the authors and few retrospective studies, some of which involve only one or a limited number of case controls (Table 3).
The articles considered to be excluded after detailed analysis (8 studies) and listed in table 3 out of the total of 19 articles selected initially will not be examined further.

Table 3: 19 articles selected by the reflection Group from the whole of the literature available.

Methodology	Study	Conclusion/remarks	Level	Grade
Case-control				
Epidemiological N=1606	Mirick DK, Davis S, Thomas DB. Antiperspirant use and the risk of breast cancer. *J Natl Cancer Inst* 2002 Oct 16; 94(20): 1578-80 [13]	Absence of link between use of antiperspirants and breast cancer. Only study designed with a control group.	**3**	**B**
Retrospective				
Cohort study: women having survived breast cancer N=437	McGrath KG. An earlier age of breast cancer diagnosis related to more frequent use of antiperspirants/deodorants and underarm shaving. *Eur J Cancer Prev* 2003 Dec; 12(6): 479-85 [7]	Supports a link between use of deodorant/antiperspirant and breast cancer *Bias:* absence of control arm *Observation*: younger women use more deodorants/antiperspirants.	**4**	**C**
Cohort study: women with a breast implant N = 3486	McLaughlin JK, Lipworth L, Fryzek JP, Ye W, Tarone RE, Nyren O. Long-term cancer risk among Swedish women with cosmetic breast implants: an update of a nationwide study. *J Natl Cancer Inst* 2006 Apr 19; 98(8): 557-60 [14]	Excluded*, contains no data on aluminium, The study concludes there is an increased risk of lung cancer in women with a breast implant. *Bias*: larger number of smokers in this population, absence of control arm.		
Case report				
Study of an isolated case N=1	Guillard O, Fauconneau B, Olichon D, Dedieu G, Deloncle R. Hyperaluminemia in a woman using an aluminum-containing antiperspirant for 4 years. *Am J Med* 2004 Dec 15; 117(12): 956-9 [15]	Suspected transcutaneous passage of aluminium without any evidence of its origin. No link mentioned between the presence of aluminium and breast cancer. *Observation:* aluminium levels in the blood and urine decrease on discontinuation of the use of antiperspirant. Study of dermal absorption of aluminium performed for the AFSSAPS by the same author.	**4**	**C**
Laboratory				
Study of dermal absorption N=2	Flarend R, Bin T, Elmore D, Hem SL. A preliminary study of the dermal absorption of aluminium from antiperspirants using aluminium-26. *Food Chem Toxicol* 2001 Feb; 39(2): 163-8 [16]	The study shows passage into the blood following application of a high dose of aluminium under occlusion. *Bias*: dosage outside normal conditions of use, other potential sources of aluminium.		
Study by chromatography and spectrometry on samples of human breast cancer tumours.	Darbre PD, Aljarrah A, Miller W R, Coldham N G, Sauer M J and Pope GS, « Concentration of parabens in human breast cancer tumours ». J. Appl. Toxicol. 24, 5-13 (2004) [17]	Excluded*, contains no data on aluminium, relates to parabens Demonstration that parabens can be found intact in human breast tissue.		

N=20				
Adhesive tape sampling technique	Quatrale RP, Thomas EL, Birnbaum JE. The site of antiperspirant action by aluminum salts in the eccrine sweat glands of the axilla. J Soc Cosmet Chem 1985; 36(6): 435-40 [18]	Excluded*, studies the site of action of three aluminium salts used in antiperspirants		

Methodology	Study	Conclusion/remarks	Level	Grade
Experimental				
Study on samples of human breast cancer cells	Darbre PD. Aluminium, antiperspirants and breast cancer. *J Inorg Biochem* 2005 Sep; 99(9): 1912-9 [8]	Possible interference between aluminium and oestrogen receptors of MCF7 cells. No causal relationship with deodorants/antiperspirants		
Study in mice and rats	Hart MM, Adamson RH. Antitumor activity and toxicity of salts of inorganic group IIIa metals: aluminum, gallium, indium, and thallium. *Proc Natl Acad Sci U S A* 1971 Jul; 68(7): 1623-6 [19]	Excluded*, concerns a possible antitumour action of metal salts Tests of doses of metal salts to evaluate their antitumour activity on different solid tumours.		
Study on the MCF-7 human breast tumour cell line	Martin MB, Reiter R, Pham T, Avellanet YR, Camara J, Lahm M, *et al*. Estrogen-like activity of metals in MCF-7 breast cancer cells. *Endocrinology* 2003 Jun;144(6):2425-36 [20]	Excluded*, contains no data on aluminium Treatment of cells with different metals not including aluminium.		
Comparative study in mice N=600	Oneda S, Takasaki T, Kuriwaki K, Ohi Y, Umekita Y, Hatanaka S, *et al*. Chronic Toxicity and tumorigenicity study of aluminum potassium sulfate in B6C3F1 Mice. *In Vivo* 1994 May-Jun; 8(3): 271-8 [21]	Excluded*, concerns the oral absorption of aluminium Study of the tumorigenic potential of aluminium potassium sulphate added to the feed in mice. Puts into perspective the article by Pennington in mice [28].		
Study in mice and rats N=334	Schroeder HA and Mitchener M. Life-term studies in rats: effects of aluminium, barium, beryllium, and tungsten. *J Nutr* 1975 Apr; 105(4): 421-7 [22]	Excluded*, concerns the oral absorption of metals Studies the consequences of the introduction of aluminium, barium, beryllium and tungsten into the drinking water of rats.		
General reviews				
	Darbre PD. Underarm cosmetics and breast cancer. *J Appl Toxicol* 2003 Mar-Apr; 23(2): 89-95 [23]	In support of a link between use of deodorant/antiperspirant and breast cancer. Absence of scientific evidence.	**4**	**C**
	Darbre PD. Metalloestrogens: an emerging class of inorganic xenoestrogens with potential to add to the oestrogenic burden of the human breast. *J Appl Toxicol* 2006 May-Jun; 26(3): 191-7 [24]	No analysis or scientific evidence of the effect of aluminium; this is only mentioned in conclusion. Analysis of articles about the effect of different metals.	**4**	**C**

	Gikas PD, Mansfield L, Mokbel K. Do underarm cosmetics cause breast cancer?. *Int J Fertil Womens Med* 2007 Sep-Oct; 49(5): 212-4 [25]	No arguments in support of penetration and accumulation of aluminium salts in breast tissue in vivo. The article by Mirick DK is referenced [13].	**4**	**B**
	Höltze E. Topical pharmacological treatment. *Curr Probl Dermatol* 2002; 30: 30-43 [26	Deals with the subject of the local treatment of hyperhydrosis and antiperspirants. *Observation:* provides no new information.	**4**	**C**
	Höltze E. Antiperspirants. In: Gabard B (Ed). *Dermatopharmacology of Topical Preparations*. Berlin: Springer-Verlag, 2000; 401-16 [27]	Mechanism of action of antiperspirants and aluminium salts. *Observation:* provides no new information.	**4**	**C**
	Pennington JA, Schoen SA. Estimates of dietary exposure to aluminium. *Food Addit Contam* 1995 Jan-Feb; 12(1): 119-28 [28]	Concerns the oral absorption of aluminium and the effects of the passage of aluminium into the general circulation.	**4**	**C**
	Harvey PW, Everett DJ. Significance of the detection of esters of p-hydroxybenzoic acid (parabens) in human breast tumours. *J Appl Toxicol* 2004 Jan-Feb; 24(1): 1-4 [29]	Excluded*, relates to parabens Studies the link between parabens, oestrogenic effects and breast cancer. Complementary article to that by Darbre, 2004 [17].		

*Excluded: article (or study) initially selected but excluded following analysis as not answering one of the 3 questions asked or containing no data on aluminium.

What about the role of parabens? The hypothesis of the role played locally by parabens in the increased risk of breast cancer is no longer topical and the articles relating to this question were excluded by the experts after reading and/or in-depth analysis (Table 3). In fact, parabens are generally not present in deodorants/antiperspirants and the question of a possible link between the onset of breast cancer and the presence of parabens in deodorants/antiperspirants will not be considered in the analysis conducted here by the reflection Group.

What about the level of evidence of the selected studies? The level of evidence of these studies is poor overall since all are of level 4, except for the study by Mirick, the only one to be able to claim a level 3 [13]. They usually present unverified hypotheses relating to the role played by parabens and/or aluminium salts, traditional ingredients of deodorants/ antiperspirants. None of them consider confounding factors, currently known risk factors for breast cancer or determining biological factors, such as hormone receptors.

Overall, the methodologies of these studies fail to identify a risk factor and their results are contradictory. The only one that is methodologically rigorous, the case control study by Mirick relating to 813 patients and 793 control subjects, provides no conclusive evidence in favour of an increased risk associated with the use of antiperspirants and deodorants [13]. The results of this study alone therefore reinforce the lack of evidence.

Are there arguments to support a possible increase in the risk of breast cancer in women using deodorants/antiperspirants? Several studies have attempted to provide an answer to this question.

In 2003, the retrospective study by McGrath (level 4, grade C) [7] included 437 women who had survived breast cancer, divided into 4 groups according to the frequency of use of

deodorants/antiperspirants and shaving practices. The age on diagnosis of the cancer appeared to be less than 22 years in the most frequent users of deodorants (at least twice a week) and those who shaved most often (at least 3 times a week). The absence of a control arm composed of healthy women constitutes a major bias, which precludes an affirmative response to the initial question with any degree of certainty, particularly without an analysis of the other risk factors of breast cancer. The only assertion confirmed by the study is that younger women use more deodorants.
Conversely, the study by Mirick published in 2002 in the Journal of the National Cancer Institute [13] is a methodologically sound case control study (level 2 grade B). A large population of 1,600 women (813 breast cancers, 793 healthy controls) was included, 90% of whom used antiperspirants. None of the habits studied (regular use of antiperspirant or deodorant, use of these products combined with shaving the armpits with a razor, application of these products within an hour of shaving) had any effect on the risk of breast cancer (OR odds ratio: 0.9 (0.7 to 1.1), p=0.23 regular use of antiperspirant; OR: 1.2 (0.9 to 1.5), p=0.19 regular use of deodorant; OR: 0.9 (0.7 to 1.1), p=0.40 antiperspirant applied within one hour of shaving; OR: 1.2 (0.9 to 1.5), p=0.16 deodorant applied within one hour of shaving). The results of this one study conducted according to a strict methodology therefore contradict the hypothesis of a link between the use of antiperspirants and breast cancer.

Can a causal relationship be established between the use of deodorants/ antiperspirants and the occurrence of breast cancer? Based on the observation of a high incidence of breast cancer in the upper outer quadrant adjacent to the usual area of application of deodorants/antiperspirants [11], the known toxicity of aluminium and its presence in these hygiene products, Darbre conducted an experimental study (level 4 grade C) to investigate the possible link between aluminium and breast cancer [8]. This biological study published in 2005 and supporting the presence of a risk was conducted on MCF7 human breast cancer cell lines. It revealed no causal relationship between deodorant/antiperspirant and breast cancer and simply showed a mechanism of interference between aluminium and the oestrogen receptors of MCF7 cells. The author therefore added aluminium to the list of metallo-oestrogens, metal ions interfering with the action of oestrogens.
De facto, conversely to what Darbre tried to demonstrate, it is well established that the binding of aluminiun salts to the oestrogen receptor without subsequent induction of cell proliferation, is a property of oestrogen receptor antagonists, as attested by the great success of products such as Tamoxifen in the treatment of breast cancer. Furthermore, it would have been interesting to investigate the potential effect of aluminium on tissues other than the breast and the possible role of other risk factors of breast cancer in the course of this study, but the author failed to do so. Lastly, it is important to note that concepts of hormonal tumour receptors and use of antiperspirants are lacking in the study.
In 2006, the results of a new study conducted by Darbre showed the functional role of the combined interactions of metallo-oestrogens present in our environment (aluminium in cosmetic products, cadmium in food and tobacco, etc.) with environmental oestrogens, pharmacological oestrogens, phyto-oestrogens and physiological oestrogens in the incidence of breast cancer [24]. This study therefore appears to support the idea of a multiplicity of risks rather than a possible single risk related to aluminium in hygiene products.
Two other studies among the 19 studies selected investigate the dermal absorption of aluminium, but without providing any information about the supposed link between aluminium and breast cancer [15,8].

The first, published by Flarend in 2001, is an experimental study of dermal absorption (level 4, grade B) which showed the passage into the blood of a large concentration of aluminium from a high dose applied occlusively beneath the arm in a man and a woman, conditions which differ from those of a standard application of deodorant/antiperspirant [16]. This study also pointed out that there are other potential sources of absorption of aluminium, in particular dietary.
The second, published by Guillard in 2004 (level 4 grade C), showed the probable transcutaneous passage of aluminium into the blood [15]. The circumstances of the study and the absence of obvious exposure of the subject to anything other than repeated deodorant/antiperspirant application for 4 years suggest that the latter product could have been the main source of aluminium, although there are many other sources not mentioned here. However, this is a single study relating to a single case control subject. No link is mentioned between the presence of aluminium in the blood and urine and breast cancer in either of these studies.

What about the role of the aluminium?
The hypothesis of the role played locally by aluminium salts in the increased risk of breast cancer and the possible causal relationship is not confirmed by any studies.
As regards a possible systemic action of aluminium salts, only the study by Guillard tends to show very slow systemic passage, but as has been seen previously this is a study of a single case control under unrepresentative conditions of actual life (shaving 3 times a week) and relatively unsound from a methodological viewpoint [15]. Even though the number of subjects included remains limited and the operating conditions not particularly optimal, the studies of the penetration of aluminium salts through the skin [15,16], and more specifically the changes in the blood concentrations of aluminium salts after discontinuation of the use of antiperspirant products, may raise the question, but do not constitute proof as such.
At the present time therefore there is no scientific evidence to support a causal relationship between the use of deodorants/antiperspirants and the risk of breast cancer.

Criteria of causation. The nine criteria established by Sir Austin Bradford Hill (Table 4) represent a proven method of establishing a causal link between a potential agent and a disease. Used for smoking and lung cancer, these criteria can be applied today to the surmised causal relationship between deodorants/antiperspirants and breast cancer [30,31,32].

Table 4: Bradford Hill's criteria [after 30,31,32].

Bradford Hill's criteria	**Hypothesis of a causal relationship between deodorants/antiperspirants and breast cancer.**
1. Strength of association. The stronger the relationship between an independent variable and a dependent variable, the less chance this relationship has of being due to another variable.	NO: The only methodologically rigorous study concluded that there was no relationship between the use of antiperspirants and breast cancer [13].
2. Temporal relationship. The cause must logically precede the effect in time.	NO: The increased sales of deodorants/antiperspirants in the USA since the 1970s (figure 1 [33-34]) has coincided with a stable incidence of breast cancer in women under 50 years of age and a drop in incidence in over-50-year-olds in 2003-2004 (figure 2 [6]).
3. Consistency. Repeated observation of the association by different people, in different places, in different circumstances and at different times increases the likelihood of the causal relationship.	NO: 19 articles relating to the initial hypothesis were selected from the Pubmed database. Only 11 were retained following review or detailed analysis.
4. Coherence. The association must be compatible with existing theory and knowledge.	NO: Literature searches and analysis by the group of experts failed to identify a scientific substratum validating some of the hypotheses advanced, or even raising any doubt as to a potential toxic effect of the aluminium contained in deodorants/antiperspirants.
5. Theoretical probability. It is easier to accept a causal relationship when there is a rational and theoretical basis for such a conclusion.	NO: Transcutaneous passage of aluminium has not been established with certainty and sources of aluminium are not confined to the salts contained in deodorants/antiperspirants.
6. Specificity. Ideally the effect has a single cause.	NO: there are a number of currently recognised risk factors for breast cancer [35].
7. Dose-response relationship. There should be a direct relationship between the risk factor (independent variable) and the status of the population with respect to the disease (dependent variable).	Not studied: the only rigorous study failed to establish a relationship between the use of deodorants/antiperspirants and breast cancer [13].
8. Experimental evidence. Any research associated with and based on experiments makes the causal relationship more likely.	NO: Of the 5 experimental studies selected initially, 4 were excluded following a review or detailed analysis [24,25,27,29]; the fifth provides no evidence in favour of a causal relationship [8].
9. Analogy. Sometimes a phenomenon commonly accepted in one field can be applied to another field.	Lack of obvious analogy.

A review of these criteria and analysis of the selected articles show that not all of the criteria are fulfilled in respect of the question that concerns us.

Therefore, regardless of the approach adopted, the conclusion coincides with that of the French and American health authorities.

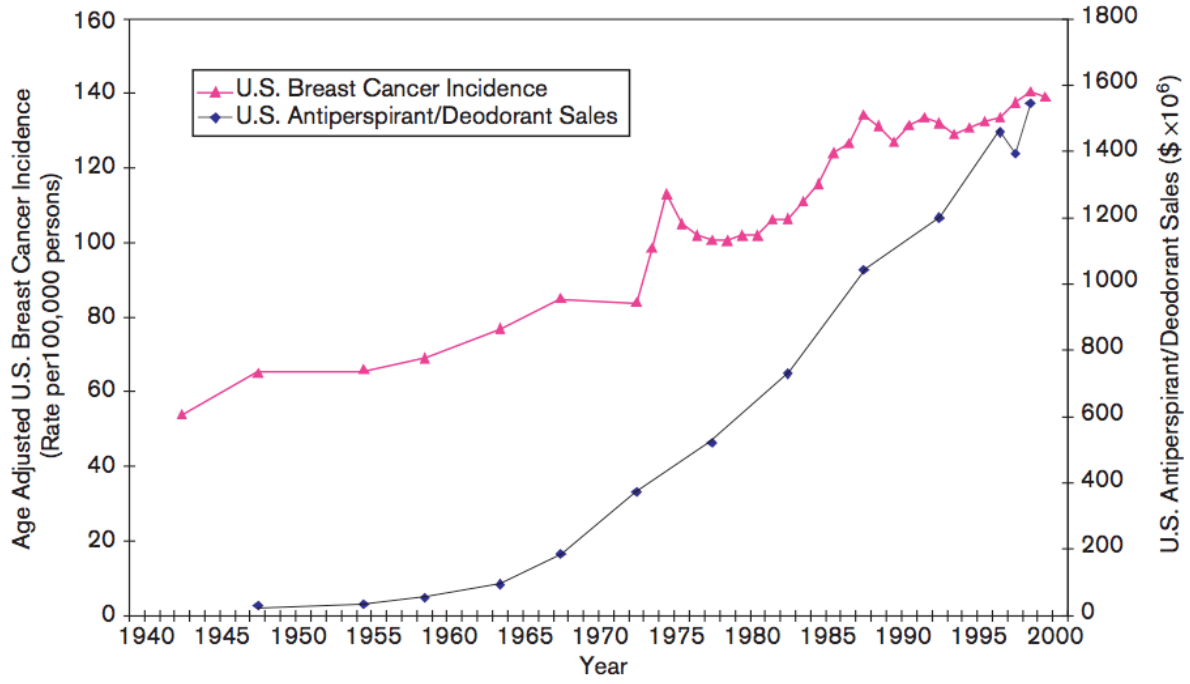
Despite an in-depth expert study of all the data available from these different health authorities, the harmfulness of aluminium present in antiperspirants has not been confirmed, thus prompting the experts to decide in favour of the safety of cosmetic products containing aluminium [9,12].

RELEVANCE OF THE HYPOTHESES PROPOSED IN THE LITERATURE

The literature that attempts to associate the use of deodorant/antiperspirant products containing aluminium salts with an increased risk of breast cancer overall is open to a fair degree of criticism, both methodologically and scientifically.

In the article by McGrath, two curves are intended to show that since 1940 the evolution of breast cancer incidence has paralleled that of the sale of antiperspirant and deodorant products (Figure 1) [7]. To grant credence to this hypothesis would be to ignore all the other markets that have grown over the same period: household apparatuses, cars, computers, foreign travel, etc.

Figure 1: Incidence of breast cancer in the USA and sale of deodorants/antiperspirants



(Roush et al., 1987 [33] ; SEER Incidence public-Use Database, 2001 [36]. ; US Cosmetic and Toiletries Market, 2001 [34]) [7]

Figure 2: Change in annual incidence of breast cancer in women between 1975 and 2004

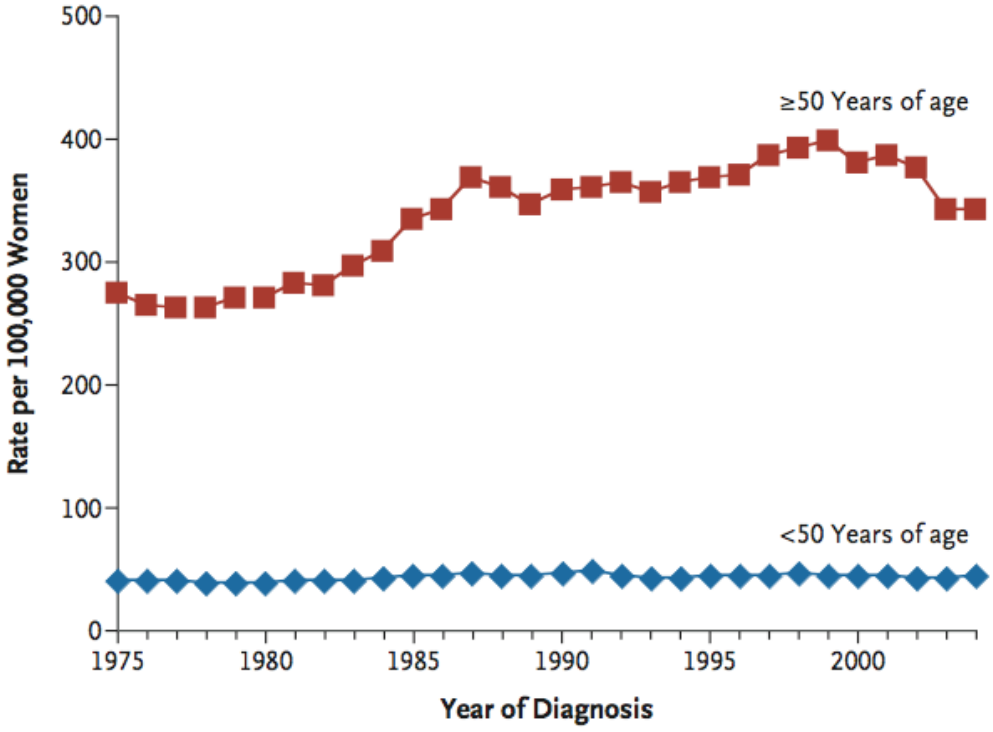
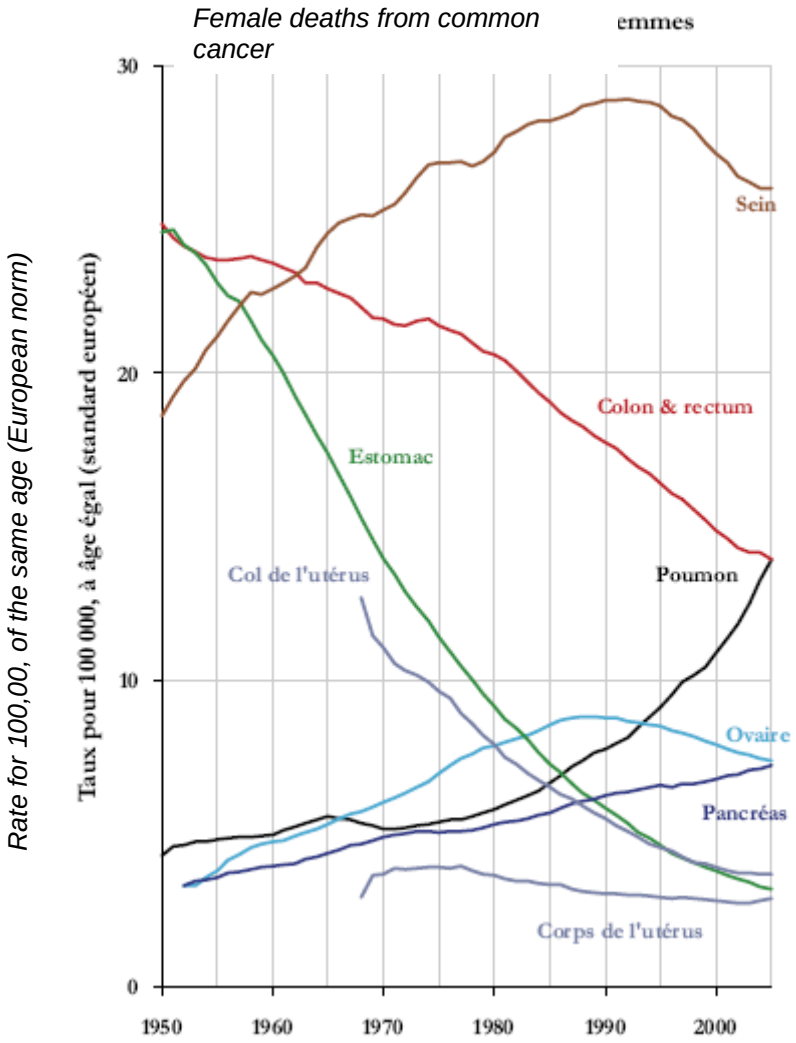


Figure 1. Annual Incidence of Female Breast Cancer (1975–2004).
Data are from nine of the NCI's SEER registries. SEER sites include San Francisco, Connecticut, Detroit (metropolitan area), Hawaii, Iowa, New Mexico, Seattle–Puget Sound, Utah, and Atlanta (metropolitan area).

Recent epidemiological data further contradict this hypothesis: despite the constant increase in sales of deodorants/antiperspirants from the 1970s to 2000, the incidence of breast cancer has remained stable in young women, who are extensive users of these products. In women over 50 years old, the incidence decreased by 8.6% between 2001 and 2004 (95% CI: 6.8-10.4) (Figure 2) [6]. Although the use of deodorants/antiperspirants has certainly been less widespread in over 50-year-olds, some of them may have been using deodorants/antiperspirants for thirty years as they could have started in the 1970s at the age of twenty.

At the same time, while mortalities caused by breast cancer rose by 50% in France between 1950 and 1992, they have been going down ever since (figure 3) [1bis]. Among the deaths from breast cancer attributable to proven risk factors among human beings, only the proportion attributable to HRT (1,100 deaths in 2000) should go down along with the reduction in prescriptions.

Figure 3: Female deaths by cancer in France between 1950 and 2005 [1bis].



More seriously, based on a possible cause and effect relationship between the frequent localisation of breast cancer in the upper outer quadrant and the proximity to the usual area of application of deodorants/antiperspirants [11], Darbre postulates the involvement of aluminium [8], a component in hygiene products and a metal salt known for its toxicity to cell DNA. Aluminium, according to the author, is apparently capable of acting via an oestrogenic effect. Such hypotheses may be interesting, but none of these studies provides scientific evidence to verify them. Starting from unverified hypotheses and extrapolating from these to obtain a final conclusion by qualifying one's own observations is far from a strict scientific procedure. And without scientific evidence, no conclusion can be anything but wrong. As regards the oestrogenic effect proposed by the same author, this is weak for parabens and non-existent in the case of aluminium salts. It is important to remember that there are a number of sources of aluminium in our environment (diet, etc.) other than deodorants/antiperspirants. If this effect exists, it is less than 1.20 and therefore cannot be considered a risk factor [13].

Even in the event of transcutaneous passage, the responsibility of aluminium cannot be confirmed by the sole case-control studied (a single subject who, moreover, did not develop cancer) [15].

The literature search and the analysis by the group of experts failed to identify a scientific substratum to validate some of the hypotheses advanced or even to raise any doubt as to a potential toxic effect of the aluminium contained in deodorants/antiperspirants.

SUMMARY OF RISK FACTORS OF BREAST CANCER

Table 5 lists the currently recognised risk factors of breast cancer, together with an estimate of their relative risk.

Table 5: Summary of the recognised risk factors relative to the development of breast cancer in women [35].

Risk factor	**Estimate of relative risk** (High risk/ Low risk)
Recognised risk factors (relative risk greater than 4.0)	
Age	**The risk increases more than 4-fold** (> 50 years/< 50 years)
Family history	
Relative with bilateral breast cancer before the menopause	**The risk increases more than 4-fold** (yes/no)
2 first-degree relatives suffering any form of breast cancer	**The risk increases more than 4-fold** (yes/no)
Country of birth	**The risk increases more than 4-fold** (North America, Northern Europe/Asia, Africa)
Benign proliferative breast disease	
Atypical hyperplasia	**The risk increases more than 4-fold** (yes/no)
Lobular carcinoma in situ	**The risk increases more than 4-fold** (yes/no)
Presence of atypical epithelial cells in nipple aspirate fluid	**The risk increases more than 4-fold** (yes/no fluid produced)
Mutations of the BRCA1 or BRCA2 gene, breast cancer at a young age	**The risk increases more than 4-fold** (yes/no)
Recognised risk factors (relative risk of 2.1 to 4.0)	
Chest irradiation (ionising radiation)	**The risk increases 2- to 4-fold if exposure occurred between puberty and the childbirth period** (high/minimal)
Family history	
1 first-degree relative suffering any form of breast cancer	**The risk increases 2- to 4-fold** (yes/no)
Dense breast tissue on mammographic screening	**The risk increases 3- to 4-fold** (>75%/fatty tissue)
Benign proliferative breast disease confirmed by biopsy	**The risk increases 2- to 4-fold** (yes/no)
Presence of non-atypical hyperplastic epithelial cells in nipple aspirate fluid	**The risk increases 2- to 4-fold** (yes/no fluid produced)
Recognised risk factors (relative risk of 1.1 to 2.0)	
Age at first full-term pregnancy	**The risk increases 1.1- to 3-fold** (> 30 years/< 20 years)
Bilateral oophorectomy before the age of 40 years	**The risk increases 1.1- to 3-fold** (no/yes)
Previous history of primary ovarian or endometrial cancer	**The risk increases 1.1- to 2-fold** (no/yes)
Socio-economic situation (income, education)	**Increase of 1.1- to 3-fold** (well off/disadvantaged)
Marital status	**The risk increases 1.1- to 2-fold** (never married/already married)
Place of residence	**The risk increases 1.1- to 2-fold** (urban environment/rural environment)
Race/ethnic origin, breast cancer < 45 years	**The risk increases 1.1- to 2-fold** (person of white/hispanic race, Asian person)
Race/ethnic origin, breast cancer < 40 years	**The risk increases 1.1- to 2-fold** (person of black/hispanic race, Asian person)
Religion	**The risk increases 1.1- to 2-fold** (Jew/Seventh-day Adventist, Mormon)
Age at menopause	**The risk increases 1.1- to 2-fold** (55/45)
Age at onset of first menstrual period	**The risk increases 1.1- to 2-fold**
Parity	**The data in the event of multiparity are not conclusive**

Adapted from Health Canada. Canadian breast cancer initiative. Report 2001.

In terms of lifestyle and environmental risk factors, studies are often difficult to conduct and the scientific evidence complicated to establish. This is the case with studies concerning deodorants/antiperspirants and the risk of breast cancer. Their unsound methodology, the absence of a control group, the small sample sizes, the problems relating to stability and the transposition of cell models to live patients render their conclusions unreliable.
Certain questions and observations also appear to have been overlooked by the authors of these studies. Thus, if the link between the use of deodorants/antiperspirants and breast cancer is a genuine one, how can the non-bilaterality of breast cancers be explained? Or the lack of increase in breast cancer in men? Or the fact that breast cancers are not all hormone-dependent? And the fact that breast cancer is not the only cancer that can be hormone-dependent? It might be therefore, as Lorette claims, that the greater frequency of breast cancer in the upper outer quadrant of the breasts is simply related to the presence of a greater quantity of breast tissue in this quadrant [11].

In the absence of scientific evidence identified by the work group, it seems reasonable to agree with the approaches of the French Health Products Safety Agency (AFSSAPS) [9], the European health authorities and the Food & Drug Administration (FDA) [10], according to which there is at present no obvious evidence that a constituent in deodorants/antiperspirant can induce breast cancer.

CONCLUSION

Use of deodorants/antiperspirants and increased incidence of breast cancer: are we on the wrong track?

No prospective epidemiological study to date has demonstrated this hypothesis, but the anxiety generated by these pseudo-scientific speculations regularly prompts a number of patients and women to raise the question of the safety of use of these products with their doctor.
Despite a reassuring response published recently by the AFSSAPS on the use of antiperspirants, our expert group wished to make a detailed analysis of the pathophysiological hypothesis and the epidemiological data in order to respond scientifically and methodologically to patients' anxiety.
After analysing the available literature on the subject, no scientific evidence to support the hypothesis has been identified. Furthermore, after elimination of off-subject studies, studies which appear methodologically unsound or relating to parabens – substances which are generally not used in the composition of deodorants/antiperspirants – there remains no validated hypothesis likely to open the way to interesting avenues of research.
In conclusion, it can be said that this question does not constitute a public health problem and that it therefore appears unnecessary to continue research on the subject.
Taking into account the high prevalence of breast cancer, particularly in France [37], it seems essential, rather than alarm women with groundless assumptions, to heighten their awareness of the importance of prevention and the value of screening by relaying to them the information campaigns set up by the authorities, hospitals and patient associations to combat this scourge better.

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