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Evidence synthesis related to occupational risks in pregnant workers (period 2000-2010)

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Evidence synthesis related to occupational risks in pregnant workers. Analysis period 2000-2010

Systematic review is a tool used by the research community to study a certain topic in a reliable manner. A systematic review summarises the results of available carefully designed healthcare studies and provides a high level of evidence on the effectiveness of healthcare interventions.[1].

To carry out a systematic review, it is first necessary to establish a protocol for researching and reviewing the documentation. Secondly, a clearly defined, focused question must be formulated according to the PICO[2] method (**P**opulation, **I**ntervention/Exposure, **C**omparison, and **O**utcome). Third, criteria must be developed for including and excluding studies. Then, the documentation must be obtained to carry out a critical evaluation of its utility and validity. Finally, a report is drafted explaining the previous steps, results, and conclusions that have been reached through the review process in order to answer the review question.

1. Background

Article 26 of the Act on Prevention of Occupational Risks relating to maternity protection, as amended by Organic Law 7/2007, requires employers to assess the work place where a woman worker performs her job during pregnancy or breastfeeding. In this way, the Act includes a series of mechanisms to ensure that working conditions do not pose a risk to the woman worker, the embryo, or the newborn.

In 2008, Spain recorded 519,779 births[3]. 333,815 of these newborns were born to women with employment contracts at the time of delivery. This represents 64.2% of 2008 births. That same year, 359,160 maternity leave requests were handled[4].

Since 2008, women at risk during pregnancy may apply for maternity risk allowance. Specifically, in 2009, 14,488 allowances were registered[5].

In addition, according to data from the National Health Survey of 2006, 320,500 women consulted a midwife during the month prior to the survey. Of those, 183,000 had an employment contract at the time of the visit.

All these data show, in a more or less detailed way, the population covered by this systematic review and the interest that exists regarding it.

[1] Iberoamerican Cochrane Centre.
[2] PICO Method: Sackett DL, Straus S, Richardson S, Rosenberg W, Haynes B. *Evidence based medicine: how to practice and teach EBM* (2nd ed.). London: Churchill Livingston.
[3] Source: National Institute of Statistics.
[4] Source: Social Security Treasury Office.
[5] Source: Social Security Treasury Office.

2. Purpose of the review

Present the scientific evidence for damages to the health of pregnant workers arising from occupational risks, gathered in the period 2000 – 2010.

3. Research strategy and question

The research in this systematic review answers the following question:

Do pregnant workers or the foetus or infant suffer more damage from the risks to which they are exposed in the workplace?

In this case, the question is framed in the workplace.
Population: working women between 16 and 65 years of age.
Intervention/Exposure: occupational risks for pregnant workers.
Comparison: non-pregnant women workers of the same age.
Outcome: damage to the health of the woman and foetus.

The research procedure consisted of three steps:

a. Search for reviews in the database.
b. Selection of material corresponding to the question.
c. Independent consideration of systematic reviews by the two authors of the report.

During the search for reviews, the databases used were:

a. Medline
b. Cochrane
c. Library catalogue of the National Institute for Safety and Health at Work

a. **Medline Database**:

The keywords used to find documentation in Medline were the following: occupation, occupation*[6], work*, woman, women, risk, risks, pregnant and pregnancy. Table 1 details the specific search and results produced on 8 February 2010.

The search results were the following: 2,360 documents, of which, 374 were reviews and 320 were free texts. Of these 374 reviews, 200 were produced after 1999. The work was based on material produced after this date.

b. Cochrane Database:

Five searches were carried out among the titles and abstracts of the reviews.

The first search used the terms: *pregnancy* and *work*. 37 documents were found, but none responded to the question.

The second search used the following terms: *pregnancy* and *risk*. 59 documents were found, but none responded to the question.

The third, fourth, and fifth searches were meant to find evidence on biological risks and pregnancy. The terms *pregnancy* and *virus*; *pregnancy* and *bacteria*; and *pregnancy* and *Toxoplasma* were used. A total of 105 reviews were found, of which five responded to the question.

c. Library Catalogue National Institute of Safety and Health at Work:

Eight documents were found, of which three responded to the review question.

Below are listed the titles and abstracts of the systematic reviews found. Only those reviews that responded to the question at hand were selected: Do pregnant workers or the foetus or infant suffer more damage from the risks to which they are exposed in the workplace?

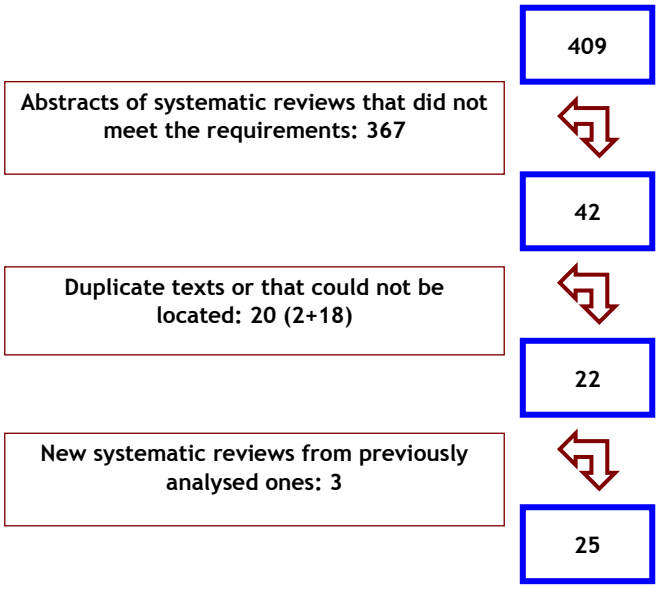
Subsequently, documents were requested from the libraries of various organisations: National Institute of Safety and Health at Work (INSHT, its acronlym in Spanish), the Institute of Documentary Studies on Science and Technology (IEDCYT, its acronym in Spanish; formerly CINDOC), the Universidad Autónoma de Barcelona-UAB, etc.

[6] *: Used in the search as the root of the word. The search engine will recognise all words starting with this root.

Table 1: Documents selected in the procedure

Database	Number of reviews		
	1st step	2nd step	3rd step
Medline	200	34	34
Cochrane	201	5	5
INSHT Catalogue	8	3	1
Derived			3
Total	409	42	**43**

Figure 1: Screening phases for systematic reviews



It is important to indicate that this systematic review poses a very broad question, intended to address, in general terms, the risks to which pregnant workers are exposed. This means that not all articles referring to each specific risk will be reviewed. It is likely that if each specific risk were to be individually analysed with concrete questions, the number of articles would have been even greater. In this case, several systematic reviews would have been needed, one for each potential risk. In this document, the reader will find scientific evidence for a large number of risks and damages that may affect the pregnant worker.

4. Data collection and analysis

The systematic reviews that met the previous requirements were analysed. From each systematic review, the corresponding scientific articles were extracted. Where available, full texts were read; otherwise, abstracts were used. In order to use the most complete and updated data, only the most recent articles and reviews from the same authors on the same subject were included in the bibliography of reviews (third step of Table 2).

The bibliography is available in the last section of this chapter.

In the first section of the bibliography are listed the reviews that were compiled and included in this review. In the second section are listed the reviews that were excluded from this review as they were not found. In the third section are listed the articles analysed stemming from the reviews from which conclusions were drawn. Lastly, in the fourth section, additional references are included to help delve into the description of this systematic review.

5. Results

Authors' note:

It is important to emphasise that, although each reference discussed makes special mention of the findings based on their statistical significance and the measures of association used (Relative Risk [RR], Odds Ratio [OR], Standardised Morbidity/Mortality Ratio [SMR], among others), the confidence interval (CI) of these measures will indicate the true measure of the strength of association and accuracy of the finding.

Moreover, this review does not go into a detailed analysis of the methodology followed in each of the referenced studies, nor does it attempt to judge whether the type of study selected by the various authors was the best suited to answer the research questions formulated, nor will it refute the conclusions of these studies, based on possible random or systematic errors which may have arisen in the design or execution of the various studies.

Finally, the authors of this review have deemed it appropriate to provide a brief reminder of the epidemiological criteria supporting a causal relationship. Generally, the conclusions derived from research investigations end up being abstract statistical terms that, by themselves and in isolation, do not guarantee a cause-effect relationship between two variables. In the biomedical sciences, the most commonly accepted

criteria for causality are those postulated by the epidemiologist Bradford Hill[7] in 1965. Below, the most relevant are listed to guide a good critical reading of the material presented here.

- **Strength of Association:** strong associations are more likely to be causal than weak ones. In practical terms, this means that a causal association is intense when the risk factor is associated with a high relative risk (RR).
- **Temporality:** although at times it is difficult to establish the cause, it should precede the effect, for which it is fundamental to choose a study design that closely follows or reconstructs the sequence.
- **Biological Gradient:** the higher the dose of exposure to the causal factor, the greater the risk of disease. The demonstration of the dose-response relationship has significant implications. On the one hand, it is good evidence of a true causal relationship between the exposure to a particular agent and an effect on health and, on the other hand, it can determine at which exposure levels it is unlikely or even impossible for this health effect to take place.
- **Consistency:** the results of a study and the magnitude of the strength of association linking an outcome with a possible risk factor should remain constant and be reproducible by other researchers analysing the same association. However, the lack of consistency does not exclude the causal association, as different levels of exposure and other conditions may reduce the effect of the causal factor in some studies.
- **Biological Plausibility:** the suggested causal relationship should be in line with the accepted scientific principles of the time; in other words, we believe more in a causal relationship if we know its pathogenic mechanism.
- **Experimental Evidence:** it is not always possible to carry out true experiments or clinical trials, but these are the strongest tests of causality.

The reader must thus have criteria to discriminate between that which is statistically significant from that which is epidemiologically relevant to properly interpret the results described in detail below.

[7] Bradford Hill A. *The Environment and Disease: Association or Causation? Proceedings of the Royal Society of Medicine*. 1965; 58: 295-300.

Below are the results of this systematic review, which discusses the primary risks faced by pregnant workers, grouped by occupation, agent, or labour-related factor.
These results are presented according to the following structure:

5.1 Economic Sector and Occupation Studies	
	Services sector
	Industrial sector
	Agriculture sector
5.2 Chemical risks	
	Lead and lead compounds
	Ethylene Oxide
	Nitrous oxide
	Anaesthetics
	Tetrachloroethylene
	Solvents
	Organic solvents
	Antineoplastic drugs
	Antibiotics
	Pesticides
	Dyes, lacquers and paints
	Congenital malformations
5.3 Ergonomic risks	
	Movements and postures
	Manual handling of loads
	Physical fatigue
5.4. Psychosocial risks	
	Work Demands
	Work Schedule: Workday Duration, Shift Work...
5.5. Physical risks	
	Non-Ionizing radiation
	Ionizing radiation
5.6. Biological risks	
	Cytomegalovirus (CMV)
	Hepatitis B and C
	Herpes simplex virus (HSV)
	Human Immunodeficiency Virus (HIV)
	Measles
	Parvovirus
	Rubella
	Varicella zoster virus (VZV)
	Tuberculosis
	Toxoplasmosis

5.1 Economic Sector and Occupation Studies

Service Sector

Within the Service sector, occupations belonging to the healthcare industry have been the subject of numerous studies.

Healthcare and Veterinary Activities:

A study published in 1993 in Atlanta analysed the histories of pregnant nurses between 1968 and 1980. The study was composed of 4,915 case babies with congenital defects and 3,027 control babies. The authors estimated the excess risk associated with the sector by calculating the Odds Ratio (OR) as a measure of the strength of association. The results detected an excess risk for certain congenital defects such as: genital system defects (OR: 1.61; CI 95%: 1.03-2.53), urinary system defects (OR: 3.43; CI 95%: 1.41-8.34), anencephaly or spina bifida (OR: 2.00; CI 95%: 1.01-4.30) and coarctation of the aorta (OR: 2.06; CI 95%: 1.10-3.82). (Matte TD, Mulinare J, Ericsson JD, 1993).

Female medical residents have also been the subject of analysis. This is the case of a historical cohort study published in 1989, which compares 67 pregnancies in practicing physicians with 201 pregnancies in nonphysicians. All the women in the study were cared for during pregnancy and delivery by the same obstetricians. The study concludes that practicing physicians are at higher risk for preterm delivery (RR: 4.0; CI 95%: 1.58-10.1). (Miller NH, Katz VL, Cefalo RC, 1989).

One year later, another prospective study with similar characteristics was published. The study sample was made up of 92 medical residents and 144 wives of medical residents. There was no significant difference in terms of premature births, spontaneous abortions, or presence of congenital abnormalities in infants. (Osborn LM, Harris DL, Reading JC, Prather MB, 1990).

The exposure of dental assistants to nitrous oxide was the subject of a study to determine its effect on spontaneous abortions. In 1987, questionnaires were sent to 7,000 to 7,000 dental assistants aged 18-39 years who were registered in California in 1987. 69% (4,856 persons) responded to the questionnaires. Analysis was based on the answers of 1,465 pregnant women who at the time of conception were working full-time. Women were asked how many hours per week they worked with nitrous oxide during their pregnancy and whether the excess gas was scavenged. The conclusion reached by this study was that dental assistants who worked with nitrous oxide for three or more hours per week in offices without gas scavenging equipment had more than twice the risk of spontaneous abortion around the 20th week of pregnancy; (RR: 2.6; CI 95%: 1.3-5.0, adjusted for age, smoking, and number of amalgams prepared per

week). This increased risk was not observed among those who worked in offices with gas scavenging equipment, which highlights the importance of the use of this equipment. (Rowland AS, Baird DD, Shore DL, Weinberg CR, Savitz DA, Wilcox AJ, 1995).

In order to gain a detailed understanding of the reproductive risks to which women veterinarians are exposed, a survey was carried out of all women graduates of a US veterinary school (n=537) and law school (comparison group, n=794). Pregnancies completed after the second year of professional school and from 1966 to 1986 were analysed. The authors observed that the risk of birth defects was four times higher in the children of veterinarians (RR: 4.2; CI 95%: 1.2-15.1), and this, according to the study's authors, should be considered as a hypothesis that would need to be corroborated in other studies. (Schenker MB, Samuels SJ, Green RS, Wiggins P, 1990).

***Other Activities in Service Sector*:**

The relationship between maternal exposure in various occupations during pregnancy and the occurrence of cleft palate was studied based on a sample of 851 women (100 mothers of babies with oral clefts and 751 control mothers) who worked during the first trimester of pregnancy. All the women were part of a multicentre European study that registered 6 congenital malformations between 1989 and 1992. Information about the mothers' occupational histories was obtained from interviews. The results obtained showed a statistically significant association between oral clefts and occupational exposures in service occupations such as beauticians/hairdressers (OR: 5.1; CI 95%: 1.0-2.6) and housekeepers (OR: 2.8; CI 95%: 1.1-7.2). (Lorente C, Cordier S, Bergeret A, De Walle HE, Goujard J, Aymé S, et ál., 2000).

In 2002, a study was published that aimed to investigate reproductive outcomes such as low birth weight, preterm births and post-term births among women working in research laboratories while pregnant. The sample was composed of 249 pregnant workers in research laboratories, selected from a list of Swedish laboratory staff, and a control group of 613 pregnant women who did not perform laboratory tasks. Information about exposure to various laboratory agents was obtained from a questionnaire. The results of the study indicated an increased risk of preterm births associated with working with solvents (OR: 3.4; CI 95%: 1.0-11.9) and of postterm births associated with working with bacteria (OR: 2.7; CI 95%: 1.0-7.4). (Wennborg H, Bonde JP, Stenbeck M, Olsen J, 2002)

Industrial Sector

Members of the *Institut de Recherche en Santé et en Sécurité du Travail du Québec* (IRSST, Canada) carried out a study on the risk of congenital defects in offspring. The sample was composed of 47,913 pregnant women, who at the time of conception were employed for 15 hours a week or more. Congenital defects were classified according to three types: chromosomal (group A), developmental (group B) and musculoskeletal (group C). The study concluded that children born to workers involved in leather and footwear manufacturing presented a greater risk of musculoskeletal defects (SMR: 2.13, p <0.05). (McDonald AD, McDonald JC, Armstrong B, Cherry N, Côté R, Lavoie J, et ál., 1988).

A study published in 1997, the aim of which is to investigate the relations between congenital malformations and maternal occupation during pregnancy, makes reference to several industrial occupations. The data of this study are derived from the *Florence Eurocat* registry surveillance programme. The sample includes cases with isolated conditions, including chromosomal anomalies (n=1,351), cases with multiple anomalies registered during the 1980-1991 period (n=440), and a control group (n=3,223) of newborns with no congenital malformations recognised at birth. The results indicated a statistically significant association between oral clefts and mothers involved in leather and footwear manufacturing (OR: 3.9; CI 99%: 1.5-9.8). This risk consistently increased when considering cases with isolated cleft palate separately (OR: 5.4; CI 95%: 1.8-13.4). Moreover, a significant association was identified between multiple anomalies in offspring and textile dye workers (OR: 1.9; CI 99%: 1.0-3.8). (Bianchi F, Cianciulli D, Pierini A, Seniori Costantini A, 1997).

Members of the Department of Preventive Medicine and Public Health, University of Valencia, assessed the relation between maternal occupation in the leather industry and several groups of congenital malformations (nervous system, cardiovascular, oral clefts, hypospadias/epispadias, musculoskeletal, and unspecified anomalies) in offspring. The data originated from a case-control study in eight public hospitals in Comunidad Valenciana during 1993-1994 (n cases=261 and n controls=261). The conclusions presented in this study were that the children of mothers working in the leather industry had an increased risk of oral clefts (OR: 6.18; CI 95%: 1.48-25.69). (García AM, Fletcher T, 1998).

Between 1982 and 1984, the cases of 56,067 women, treated for a spontaneous abortion in 11 Montreal hospitals covering 90% of such admissions, were studied. These women were interviewed in detail regarding their occupational, social, and personal characteristics in their most recent and past pregnancies (104,649 pregnancies in all). These data were analysed in relation to four main adverse outcomes: spontaneous abortion, stillbirth (without defect), congenital malformation, and low birth weight (less than or equal to 2,500 g). In their conclusions, the authors indicate that the offspring of women working in the manufacture of metal

and electrical goods were at greater risk of congenital defects (SMR: 1.14, p <0.05). (McDonald AD, McDonald JC, Armstrong B, Cherry N, Delorme C, D-Nolin A, et ál., 1987).

An epidemiological study was conducted in Beijing (China) to assess the association between petrochemical exposure and spontaneous abortion. 2,853 married women were selected, of 20-44 years of age, who had never smoked and who had been pregnant at least once. According to their employment record, about 57% of these women workers reported occupational exposure to petrochemicals during the first trimester of their pregnancy. Information on reproductive history, pregnancy outcomes, employment history, occupational exposure, smoking habits, alcohol consumption, indoor air pollution, and demographic variables, was collected from a questionnaire administered to this group of women and their husbands. In comparing the exposed and non-exposed group, a significantly greater risk of spontaneous abortion was observed among women with exposure to petrochemicals (OR: 2.7; CI 95%: 1.8-3.9). This risk increased slightly when the analysis was performed based on the information obtained from women' interview responses and after excluding 452 women who provided inconsistent reports between recalled exposure and work history (OR: 2.9; CI 95%: 2.0-4.4). Specifically, the risk of spontaneous abortion by exposure to chemical products was: benzene (OR: 2.5; CI 95%: 1.7-3.7), gasoline (OR: 1.8; CI 95%: 1.1-2.9) and hydrogen sulphide (OR: 2.3; CI 95%: 1.2-4.4). (Xu X, Cho Si, Sammel M, You L, Cui S, Huang Y, et ál., 1998).

Agriculture Sector

Many studies have attempted to understand the risks faced by women in agricultural activities, arriving at very diverse conclusions.

For example, in a study conducted in the Netherlands, the association between the occupation of mothers and spina bifida in offspring was examined. Children with spina bifida came from nine different hospitals throughout the country (n=353). The referent group comprised population-based referents who were randomly drawn from municipal birth registries (n=1,329). All children were born between 1980 and 1992. Data was collected from postal questionnaires for both parents with questions about occupational title, daily occupational activities, and potential counfounders. The authors found that the offspring of women in agricultural activities were at greater risk of spina bifida (OR: 5.6; CI 95%: 1.8-17.8). (Blatter BM, Roeleveld N, Zielhuis GA, Mullaart RA, Gabreëls FJ, 1996).

One year after the previous study -1997-, another study was published that was also carried out in the Netherlands, whose aim was to improve the ability to detect if spina bifida was due to a genetic risk factor or to teratogenic exposure. The sample was made up of 210 spina bifida patients who were classified into two relatively homogeneous groups, based on information on appearance and functional aspects of the lesion abstracted from medical records of the patients; and of a referent group of 671 children. The conclusions of this study regarding maternal occupational exposure indicated that offspring of women in agricultural

activities were at greater risk for spina bifida (OR: 14.3; CI 95%: 2.9-77.7). (Blatter BM, Lafeber AB, Peters PW, Roeleveld N, Verbeek AL, Gabreëls FJ, 1997).

In Spain, specifically in the Comunidad Valenciana, a case-control study was conducted to assess the relationship between occupational exposure to pesticides as a result of agricultural work and the prevalence of congenital malformations. A total of 261 cases and 261 controls were selected from children born in 1993 and 1994 in 8 public hospitals. The cases were children diagnosed during their first year of life with selected abnormalities (nervous system, cardiovascular, oral clefts, hypospadias/epispadias, musculoskeletal, and unspecified anomalies). Information on occupational exposures and potential confounders was collected from the parents. The conclusion of this study was that children whose mothers were involved in agricultural activities during the month prior to conception and during the first trimester of pregnancy presented a greater risk for nervous system abnormalities, oral clefts, and multiple anomalies (OR: 3.16; CI 95%: 1.11-9.01). For the authors of the study, the results obtained justify greater attention to agricultural work and exposure to pesticides. (García AM, Fletcher T, Benavides FG, Orts E, 1999).

The study carried out by members of the *Institut de Recherche en Santé et en Sécurité du Travail du Québec* (IRSST, Canada) mentioned above in the chapter on industrial occupations, also analysed the risk of congenital defects in offspring of women working in agriculture. The results of this study in regards to these workers were that their offspring were at greater risk for developmental defects (SRM: 4.54, p <0.01). (McDonald AD, McDonald JC, Armstrong B, Cherry N, Côté R, Lavoie J, et ál., 1988).

A retrospective cohort study was carried out in the state of Washington whose objective was to examine the association between maternal occupational exposure to agricultural chemical products and the risk of limb abnormalities among their offspring. To carry out the study, birth records for the years 1980 through 1993 were consulted. The exposed group, made up of 4,466 births to mothers employed in agriculture, was compared to two reference groups: the first, 23,512 births in which neither parent worked in agriculture (non-agricultural group) and the second, 5,994 births in which only the father worked in agriculture (paternal agriculture group). The outcome of interest was limb abnormalities (syndactyly, polydactyly, adactyly, and other limb reductions). The results of this study confirm the hypothesis that maternal occupational exposure to agricultural chemicals may increase the risk of giving birth to a child with limb abnormalities.
It was observed that there are significant differences between the group of exposed mothers and the non-agricultural group, with an elevated risk of abnormalities observed in the exposed group (OR: 2.6; CI 95%: 1.1-5.8). Nevertheless, the differences between the group of exposed mothers and the paternal agriculture group was not statistically significant (OR: 2.6; CI 95%: 0.7-9.5). (Engel LS, O'Meara ES, Schwartz SM, 2000).

In order to assess the risks of parental exposure to agricultural work, a case-control study was carried out in three Mexican states. The sample was made up of 151 cases of anencephaly of more than 20 weeks'

gestation, selected between March 2000 and February 2001 from among the records of the Epidemiological Surveillance System of Neural Tube Defects in Mexico. The controls, born alive without congenital malformations (n=151), were selected from the same maternity services as those of the cases. Information was obtained from both parents by means of a general questionnaire, a food frequency questionnaire, and a specific questionnaire on occupational exposure to pesticides. The conclusion reached by the authors of this study was that children of mothers who worked in agriculture during the three months before and one month after the last menstrual period had a greater risk of anencephaly (OR: 4.57; CI 95%: 1.05-19.96). (Lacasaña M, Vázquez-Grameix H, Borja-Aburto VH, Blanco-Muñoz J, Romieu I, Aguilar-Garduño C, et ál., 2006).

A case-control study was carried out in Denmark to observe the relationship between occupational exposure to pesticides and urogenital malformations in sons. The sample included individuals born between 1983 and 1992. It was made up of 6,177 cases of cryptorchidism and 1,345 cases of hypospadias whose parents worked in the farming or gardening industry, and of 23,273 controls. The results of the study indicated an increased risk of cryptorchidism, but not hypospadias, among sons of women working in gardening (OR: 1.67; CI 95%: 1.14-2.47). The risks were not increased in sons of men working in farming or gardening. (Weidner IS, Møller H, Jensen TK, Skakkebaek NE, 1998).

Table 2: Area of Risk: Occupations

Sector of activity	Occupation or activity	Damages or alterations in pregnant workers the risk of which is increased or may be increased	Foetal damages or alterations the risk of which is increased or may be increased
Service Sector	Nurses		Suffer at least one congenital disorder, damages in the reproductive system, urinary system disorders, anencephaly or spina bifida and aortic stenosis
	Women medical residents		Preterm birth
	Women research laboratory workers		Preterm birth
	Women working in laboratories where activities related to bacteria are carried out		Preterm birth
	Women clinical assistants		Spontaneous abortion
	Women veterinarians		Birth disorders
	Women hairdressers		Cleft palate
	Women domestic workers		Cleft palate
Industry Sector	Leather and footwear manufacturing		Cleft palate and musculoskeletal disorders
	Textile dyeing		Multiple malformations
	Metal or electrical products manufacturing		Congenital disorders
	Petrochemical industry		Spontaneous abortion
Agriculture Sector	Women farmers		Spina bifida, nervous system disorders, cleft palate, defects in development, anomalies of the limbs (syndactyly, polydactyly, adactyly and other types of limb shortening) and anencephaly
	Women gardeners		Cryptorchidism

5.2 Chemical Risks

Women workers may be exposed to a large variety of chemical compounds in their workplace. When the exposure involves pregnant workers, the embryos may also suffer adverse effects. This section will analyse the chemicals, in each case presenting them as they appear in the articles reviewed: by chemical families or by the effect produced.

Lead and Lead Compounds

In a study published in 2000 carried out on the European population, occupational exposure to various compounds was analysed. Specifically, 851 pregnant women in the first trimester of pregnancy were studied. From this group, 100 women gave birth to children with oral clefts. The exposure to lead compounds during this first trimester of pregnancy indicated an increased risk of oral clefts in their offspring (OR: 4.0; CI 95%: 1.3-12.2). (Lorente C, Cordier S, Bergeret A, De Walle HE, Goujard J, Aymé S, Knill-Jones R, Calzolari E, Bianchi F, 2000).

Another study conducted in Norway investigated the consequences of the exposure of women workers to lead and the effects on their offspring. All births in Norway from 1970 to 1993 with possible maternal or paternal occupational lead exposure were recorded. This group was compared to mothers and fathers with offspring born in the same period but not exposed to lead. The results of the study indicate that the offspring of women workers exposed to lead have an increased risk of low birth weight (RR: 1.34; CI 95%: 1.12-1.60) and neural tube abnormalities (RR: 2.87; CI 95%: 1.05-6.38). However, offspring of lead-exposed fathers had where not at greater risk of damage. (Irgens A, Krüger K, Skorve AH, Irgens LM, 1998).

Ethylene Oxide

In 1987, a sample of 7,000 laboratory professionals registered in California was analysed by means of a questionnaire, of which 1,320 were pregnant women aged between 18-39 who indicated exposure to ethylene oxide. These workers had conceived while working full-time in dental clinics. It was found that, after adjusting for age, the number of mercury amalgams prepared, and nitrous oxide to which they were exposed, the relative risk of spontaneous abortion, preterm birth, or postterm birth was 2.5 (CI 95%: 1.0-6.1). Specifically, the RR of spontaneous abortion was 2.5 (CI 95%: 1.0-6.3). (Rowland AS, Baird DD, Shore DI, Darden B, Wilcox AJ, 1996).

Nitrous Oxide

In 1987, a sample of 7,000 dental assistants registered in California was analysed by means of a questionnaire, of which 1,465 were pregnant women aged 18-39 who indicated exposure to nitrous oxide. These workers had conceived while working three or more hours per week in dental clinics with gas

scavenging equipment. It was found that, after adjusting for age, number of amalgams prepared per week, and smoking, the relative risk of spontaneous abortion around the 20th week of pregnancy was 2.6 (CI 95%: 1.3-5.0). However, this risk did not exist in clinics with gas scavenging equipment. (Rowland AS, Baird DD, Shore DL, Weinberg CR, Savitz DA, Wilcox AJ, 1995).

Anaesthetics

In 1997, a meta-analysis was published on the period 1984-1992. The aim was to assess the risk of spontaneous abortion in women exposed to anaesthetic gases in their workplace. By grouping the six most rigorous studies, an overall relative risk of 1.9 (CI 95%: 1.72-2.09) was observed in pregnant workers exposed to anaesthetic gases. (Boivin JF, 1997).

Tetrachloroethylene

In Jerusalem, a study was conducted on a cohort of mothers aged between 21 and 33 and having worked in dry cleaning between 1964 and 1976. The newborns of pregnant workers exposed to tetrachloroethylene presented a relative risk of 3.4 (CI 95%: 1.3-9.2, p=0.01) of schizophrenia relative to the control population. (Perrin MC, Opler MG, Harlap S, Harkavy-Friedman J, Kleinhaus K, Nahon D, et ál., 2007).

Solvents

There is a wide range of solvents used in industry. This section describes the studies carried out on pregnant workers exposed to solvents.

In a study conducted in France, the risk of congenital malformations due to exposure to solvents before or during pregnancy was assessed. 325 cases of newborns presenting malformations and 325 controls in 15 maternity hospitals were analysed. The mothers of newborns with oral clefts had been exposed more often to solvents at work during pregnancy, and worked primarily as cleaners (OR: 7.9; CI 90%: 1.8-44.9). Furthermore, exposure to solvents was also associated with digestive anomalies in offspring (OR: 11.9; CI 90%: 2.0-149). (Cordier S, Ha MC, Ayme S, Goujard J, 1992).

Between 1989 and 1992, another multicentre European case-control study was carried out. The study investigated the relationship between occupational exposures during pregnancy and the risk of oral clefts in offspring. The sample consisted of 851 working women (100 mothers of infants with oral clefts and 751 control mothers) who worked during the first trimester of pregnancy. 6 congenital malformations were registered. Information about the mothers' occupational histories was obtained from interviews. The results obtained showed a statistically significant association between oral clefts and maternal occupational exposure to aliphatic acids (OR: 6.0; CI 95%: 1.5-22.8) (Lorente C, Cordier S, Bergeret A, De Walle HE, Goujard J, Aymé S, et ál., 2000).

Organic Solvents

Exposure to organic solvents is common among dry cleaners, hairdressers, chemists, artists, and biologists, among others. A large number of articles have shown an association between maternal exposure during pregnancy to organic solvents and neurobehavioral impairments in their progeny. (Julvez J, Grandjean P, 2009).

A large number of articles showing a link between exposure to organic solvents and congenital malformations in newborns are referred to below.

In Toronto, Ontario, a study was carried out on 125 pregnant workers exposed to organic solvents during the first trimester of pregnancy, between 1987 and 1996. Each woman exposed to organic solvents was matched to a control that was not exposed to any teratogenic compounds. The measures were adjusted for age, gravidity, and smoking and drinking status. The offspring of women workers who had been exposed to organic solvents and had symptoms associated with their exposure had thirteen times the risk of congenital malformations, RR: 13.0 (CI 95%: 1.8-99.5). (Khattak S, K-Moghtader G, McMartin K, Barrera M, Kennedy D, Koren G, 1999).

The meta-analysis published in 1998 in Canada is another study that links exposure to organic solvents and congenital malformations. A total of 7,036 patients with major malformations from a group of five studies were analysed. The risk that offspring from pregnant mothers exposed to organic solvents during the first trimester of pregnancy or in the first 20 weeks would present congenital malformations was determined. The relative risk was 1.64 (CI 95%: 1.16-2.30). It was also indicated that many cases arose primarily among mothers who were laboratory technicians. (McMartin KI, Chu M, Kopecky E, Einarson TR, Koren G, 1998).

In Finland, maternal exposure to organic solvents and its consequences in offspring was also studied. Specifically, 406 cases of congenital cardiovascular malformations were studied (patent ductus arteriosus, transposition of the great arteries, tetralogy of Fallot) compared to 756 controls born in the country within the same time period. For each solvent, cases were grouped into a different number. The cases were babies born between 1982 and 1983 diagnosed with congenital cardiovascular malformations. Women workers exposed to lacquers and paints during the first trimester of pregnancy were at greater risk of giving birth to offspring with ventricular septal abnormalities or abnormalities in other areas of the heart (OR: 2.9; CI 95%: 1.2-7.5). Exposures to plastic raw materials, disinfectants, pesticides, microwaves or video display terminals were also analysed. In this case, these agents were not identified as risk factors for congenital cardiovascular malformations. (Tikkanen J, Heinonen, 1992).

Also in relation to this cohort, for those newborns with ventricular septal defect, the exposure of women workers to organic solvents during pregnancy was evaluated, finding an adjusted OR of 1.8 (CI 95%: 1.0-3.4). On the other hand, it was observed that occupational exposure to anaesthetic gases, disinfectants, pesticides, wood preservatives, or video display terminals were not factors associated with the risk of ventricular septal defect. (Tikkanen J, Heinonen, 1991).

Another study exploring the link between exposure during pregnancy to organic solvents and the risk of suffering cleft lip was carried out in the Rhône-Alps region in France from 1985 to 1989. For each newborn with cleft lip, two controls without congenital malformations among infants born in the same month were selected. Exposures during the two first months of pregnancy were analysed. The Odds Ratio of the newborns with cleft lip whose mothers had been exposed to organic solvents was 1.62 (CI 95%: 1.04-2.52). Furthermore, an association was detected between the exposure to halogenated aliphatic solvents and congenital oral malformations (OR: 4.4; CI 95%: 1.41-16.15). (Laumon B, Martin JL, Collet P, Bertucat I, Verney MP, Robert E, 1996).

In Montreal, Canada, 301 cases of women workers who had given birth to an infant with a congenital malformation were studied between 1982 and 1984. They were matched with 301 controls. All the mothers were employed 30 or more hours a week until at least the thirteenth week of pregnancy. In analysing the compounds to which they were exposed, aromatic solvents, specifically toluene, clearly demonstrated increased rates of congenital malformations, in a ratio of 18:8. Of these malformations, those of the urinary tract group were the most prevalent with a ratio of 9:0. (McDonald JC, Lavoie J, Côté R, McDonald AD, 1987).

A case-control study carried out in Finland analysed the incidence of spontaneous abortions and congenital malformations among women working in laboratories. The relationship between these abortions and malformations as a function of the chemical product to which they were exposed was investigated. In this way, 535 women, 206 of which were cases and 329 of which were controls, were evaluated to study spontaneous abortions. Products such as toluene, xylene, and formalin to which the workers were exposed three or more times a week were measured. Significant associations with spontaneous abortion were found for exposure to toluene (OR: 4.7; CI 95%: 1.4-15,9), xylene (OR 3.1; CI 95%: 1.3-7.5) and formalin (OR: 3.5; CI 95%: 1.1-11.2). In the case of this study of congenital malformations, the sample was of 141 women (36 cases and 105 controls). No association with congenital malformation was found with these chemicals. (Taskinen H, Kyyrönen P, Hemminki K, Hoikkala M, Lajunen K, Lindbohm ML, 1994).

In a case-control multicentre study in six regions in Europe, 984 cases of congenital malformations were studied, compared to 1,134 controls matched for place and date of birth. Among other agents, exposure to glycol ethers was evaluated during pregnancy. The overall Odds Ratio of congenital malformation associated

with glycol ether exposure by the mother was 1.44 (CI 95%: 1.10-1.90). Specifically, the malformations most strongly associated with this exposure were: neural tube abnormalities (OR: 1.94; CI 95%: 1.16-3.24), multiple anomalies (OR: 2.00; CI 95%: 1.24-3.23) and cleft lip (OR: 2.03; CI 95%: 1.11-3.73). In this last subgroup, risk tended to increase with the level of exposure. (Cordier S, Bergeret A, Goujard J, et ál., 1997).

In Finland, the exposure to solvents among dry cleaner and laundry workers was studied. Specifically, cases of women exposed during the first trimester of pregnancy were analysed. In the study period, 247 spontaneous abortions and 33 cases of births with congenital malformations were recorded. Each case of spontaneous abortion was matched with three controls and each case of congenital malformation was matched with five controls, in both cases, born on the same dates. In this study, a statistically significant association was detected between maternal exposure to tetrachloroethylene and spontaneous abortion (OR: 3.6; CI 95%: 1.3-11.2). (Kyyrönen P, Taskinen H, Lindbohm M-L, Hemminki K, Heinonen OP, 1989).

A prospective cohort study in three districts of Brittany (France) was carried out beginning in 2002 and concluding in 2005. During this time, 3,421 pregnant women were recruited before 19 weeks of pregnancy. From this group, 3,005 women workers exposed to solvents were studied. Logistic regressions were used to adjust for potential confounders. The workers most affected by exposure to solvents, by exposure as well as dose, were nurses, nurses' aides, hairdressers, and chemists/biologists. Notably, a statistically significant association was observed between exposure to solvents and congenital malformations in offspring. In the comparison between the group exposed to solvents and the non-exposed groups, the Odds Ratio was 2.48 (CI 95%: 1.4-4.4), and in the comparison between the highest level of exposure to no exposure, the Odds Ratio increased to 3.48 (CI 95%: 1.4-8.4). The most common malformations in newborns were oral, urinary, and male genital malformations. (Garlantézec R, Monfort C, Rouget F, Cordier S, 2009).

In France, a case-control study was published in 2006 assessing the relationship between maternal occupational exposure to mixtures of organic solvents during pregnancy and the risk of oral defects in offspring. 164 cases of cleft lip with or without cleft palate, 76 cases of cleft palate, and 236 controls were analysed. In the control group, 39% of the women who reported working during pregnancy were exposed to at least one type of organic solvent. The mothers who were exposed to solvents during the start of their pregnancy had an increased risk of giving birth to children with cleft lip. Specifically, and by agent, the strength of association was the following: oxygenated solvents (OR: 1.8; CI 95%: 1.1-2.9); chlorinated solvents (OR: 9.4; CI 95%: 2.5-35.3) and petroleum derivatives (OR: 3.6; CI 95%: 1.5-8.8). The risk of congenital oral defects increased linearly with the level of exposure to oxygenated solvent (Aliphatic alcohols, glycol ethers, and other oxygenated solvents such as esters, ketones, and aliphatic aldehydes) to which the mother was exposed. (Chevrier C, Dananché B, Bahuau M, Nelva A, Herman C, Francannet C, Robert-Gnansia E, Cordier S, 2006).

Antineoplastic Drugs (Cancer Chemotherapy Drugs)

Members of the *Institut de Recherche en Santé et en Sécurité du Travail du Québec* (IRSST, Canada) carried out a study on the risk of congenital abnormalities in offspring. The sample was composed of 47,913 pregnant women employed for 15 hours a week or more at time of conception. Congenital defects were classified according to three types: chromosomal (group A), developmental (group B) and musculoskeletal (group C). 60 occupations were examined. Regarding doctors and nurses in the sample who administered antineoplastic drugs in the first trimester of pregnancy, eight types of congenital defects were observed in newborns. The results must therefore be considered with caution due to the small sample size. The authors concluded that there was an increased risk that offspring would present all types of anomalies (SMR: 4.05, p <0.05). (McDonald AD, McDonald JC, Armstrong B, Cherry N, Côté R, Lavoie J, et ál., 1988).

In Finland a case-control study was carried out examining the relation between foetal loss and occupational exposure to antineoplastic drugs in nurses. Nurses from 17 Finnish hospitals who were pregnant between 1973 and 1980 were studied. Each nurse who had suffered a spontaneous abortion was matched with three control nurses who had given birth. A statistically significant association was observed between spontaneous abortions and occupational exposure to antineoplastic drugs during the first trimester of pregnancy, OR: 2.30 (CI 95%: 1.20-4.39). Specifically, associations between spontaneous abortion and cyclophosphamide, doxorubicin, and vincristine were detected, though the independent effect of each individual drug could not be specifically identified, since many nurses reported handling more than one of these agents. (Selevan SG, Lindbohm ML, Hornung RW, Hemminki K, 1985).

In France, a survey was conducted to understand the relation between ectopic pregnancy and maternal occupational exposure to chemicals. Two groups of workers were analysed to compare results: operating-theatre staff and nurses from other departments. The researchers asked pregnant workers about potential exposure to anaesthetic gases, formol, ionising radiation, and antineoplastic drugs during the first trimester of pregnancy. Of 734 pregnancies, fifteen (2%) were ectopic. A statistically significant association was observed between ectopic pregnancy and occupational exposure to antineoplastic drugs, the woman's age, and the number of previous pregnancies. No other relationship was observed with other types of occupational exposures. (Saurel-Cubizolles MJ, Job-Spira N, Estryn-Behar M, 1993).

In 1999, a study investigated spontaneous abortion caused by exposure to chemical agents. Specifically, the study analysed the differences between spontaneous abortions in women workers exposed to antineoplastic agents and those who were not exposed to such drugs. Women workers were studied along with male workers exposed to these agents whose partners had become pregnant. The subject group of this systematic review is the first group, though we will discuss both results of this article by origin. In total, 7,094 pregnancies in 2,976 pharmacy and nursing staff were analysed. After controlling for the effect of factors

such as age during pregnancy, prior gravidity, maternal smoking during pregnancy, and occurrence of a spontaneous abortion in a prior pregnancy, it was observed that maternal exposure to antineoplastic drugs during pregnancy increased the risk of spontaneous abortion (OR: 1.5; CI 95%: 1.2-1.8) and the combined risk of spontaneous abortion and stillbirth (OR: 1.4; CI 95%: 1.2-1.7). However, no association was seen between exposure and the risk of stillbirth alone. The sample made up of partners of exposed male workers was too small and, therefore, no final conclusions could be drawn. (Valanis B, Vollmer Wm, Steele P, 1999).

Antibiotics

In Denmark, in 1985, a national case-control study was carried out to assess the risk of spontaneous abortion among female pharmacy assistants. The cohort was made up of 4,939 women who were members of the Danish Association of Pharmaceutical Technicians between 1979 and 1984, under the age of 40. 93% responded to questionnaires regarding chemical and drug exposure. The internal control group was made up of pharmacy assistants who worked in administration and customer service. Among the results obtained, a strong association (three times greater) was observed between the handling of antibiotics during pregnancy and the risk of spontaneous abortion, OR: 3.2 (CI 95%: 1.7-6.1). (Schaumburg I, Olsen J, 1990).

Pesticides

The exposure of mothers to organophosphate pesticides is associated to neurobehavioral changes in infants. (Julvez J, Grandjean P, 2009).

In Norway, a study was carried out on malformations in newborns registered in the Medical Birth Registry of Norway. Specifically, 4,565 cases of births between 1967 and 1991 to parents who worked in the Agriculture Sector between 1969 and 1989 were analysed. The control group was made up of non-farming parents of boys and girls born in the same years in agricultural municipalities: 61,351 births. The main hypothesis was that parental exposure to pesticides was associated with abnormalities of the central nervous system, orofacial clefts, male genital abnormalities, and limb reduction defects. Among the results, it was seen that newborns of mothers exposed to pesticides in orchards or greenhouses were at greater risk of spina bifida (OR: 2.76; CI 95%: 1.07-7.13) and hydrocephaly (OR: 3.49; CI 95%: 1.34-9.09). On the other hand, exposure to pesticides, in particular in grain farming, was also associated to upper and lower limb reduction defects (OR: 2.50; CI 95%: 1.06-5.90). (Kristensen P, Irgens LM, Andersen A, Bye AS, Sundheim L, 1997).

The Baltimore-Washington Infant Study was carried out between 1987 and 1989. A case-control study design was used to learn about congenital heart abnormalities in live born infants between 1981 and 1989. Parents were interviewed about a wide range of environmental exposures that may have occurred during and before the pregnancy. Analysis of the data revealed an association between maternal exposure to any pesticide during the first trimester of pregnancy with transposition of the great arteries in their infants (OR: 2.0; CI 95%: 1.2-3.3). No other significant association between pesticide exposure and cardiac abnormalities was

observed. When analysed by type of pesticide, it was found that herbicides in particular were nearly three times as risky, OR: 2.8 (CI 95%: 1.3-7.2), and that rodenticidal chemicals were nearly five times as risky, OR: 4.7 (CI 95%: 1.4-12.1), which are quite different from the result for insecticides, OR: 1.5 (CI 95%: 0.9-2.6). (Loffredo CA, Silbergeld EK, Ferencz C, Zhang J, 2001).

On the other hand, there are studies, such as the one cited below, which conclude that there is no relationship between maternal exposure to pesticides and congenital malformations affecting the upper and lower limbs of infants. In this article, it is specifically important to highlight that the researchers did identify cases of limb reduction, but as the authors themselves explain, the absence of an adequate classification of pathologies and types of pesticides made it impossible to establish a clear link between these two factors. (Lin S, Marshall EG, Davidson GK, 1994).

In 2001, a study was published on the health of farming families in Ontario farms that explored the association of pesticide exposure prior to conception and the risk of spontaneous abortion. A total of 2,110 women provided information on 3,936 pregnancies, including 395 spontaneous abortions. In order to explore critical windows of exposure and target sites for toxicity, the research team examined exposure separately for preconception (three months before and up to month of conception) and post conception (first trimester) windows and the times at which the spontaneous abortions occurred, i.e.: less than twelve weeks (early spontaneous abortion) and between weeks 12 and 19 (late spontaneous abortion). Increases in risk of early abortions were observed for preconception exposures to phenoxy acetic acid herbicides (OR: 1.5; CI 95%: 1.1-2.1), triazines (OR: 1.4; CI 95%: 1.0-2.0) and any herbicide (OR: 1.4; CI 95%: 1.1-1.9). For late abortions, the results were as follows: glyphosate (OR: 1.7; CI 95%: 1.0-2.9), thiocarbamates (OR: 1.8; CI 95%: 1.1-3.0); and the miscellaneous class of pesticides (OR: 1.5; CI 95%: 1.0-2.4) was associated with elevated risks of spontaneous abortions. Older maternal age (> 34 years of age) was the strongest risk factor for spontaneous abortions. In this group of workers, exposure to pesticide mixtures had the most impact. Another relevant contribution of the study was that it showed the importance of knowing the timing of exposure and when the spontaneous abortion took place in order to describe the reproductive toxicity of pesticides. (Arbuckle TE, Lin Z, Mery LS, 2001).

In Bogotá (Colombia) a study was carried out on a sample of 8,867 persons (5,916 women and 2,951 men) working in the floriculture industry and who had been exposed to 127 different types of pesticides for at least six months. The prevalence rates for abortion, prematurity, stillbirths, and malformations were studied among those women workers and male workers' wives who had been exposed to pesticides. The research team concluded that there was a moderate increase in risk of spontaneous abortion in women exposed to pesticides, OR: 2.2 (CI 95%: 1.8-2.7). (Restrepo M, Muñoz N, Day NE, Parra JE, de Romero L, Nguyen-Dinh X, 1990).

Between 1989 and 1992, a multicentre European case-control study was carried out. The study investigated the relationship between occupational exposures during pregnancy and the risk of oral clefts in offspring. The sample consisted of 851 working women (100 mothers of newborns with oral clefts and 751 control mothers), who worked during the first trimester of pregnancy. 6 congenital malformations were registered. Information about the mothers' occupational histories was obtained from interviews. The results obtained showed a statistically significant association between oral clefts and occupational exposures to biocides (OR: 2.5; CI 95%: 1.0-6.0). (Lorente C, Cordier S, Bergeret A, De Walle HE, Goujard J, Aymé S, et ál., 2000).

In this systematic review, articles were found regarding organochloride compounds, among which DDT (dichlorodiphenyltrichloroethane) and DDE (dichlorodiphenyldichloroethylene).

In 2008, a study was published examining exposure to organochloride compounds in pregnant women in relation to the length of time that it took them to become pregnant. The sample consisted of 402 pregnant farm workers who were exposed to various types of organochloride compounds. The concentration of pesticides in their blood was measured. The authors concluded that there was no association between exposure to these pesticides and longer time to get pregnant (OR: 0.8; CI 95%: 0.6-1.0). (Harley KG, Marks AR, Bradman A, Barr DB, Eskenazi B, 2008).

Another study about this group of pesticides analysed the relation between women workers' exposure to DDT and the risk of spontaneous abortions. In this case, the women were textile workers. The study was a case-control study with participants selected from a longitudinal study on the reproductive effects of rotating shifts among Chinese women textile workers. The workers were married, aged 22-34, nulliparous without a history of spontaneous abortion or infertility, and planning pregnancy. 412 cases were analysed. The cases and controls were non-smokers and did not differ in age, body mass index (BMI), passive smoke exposure, or workplace exposures. Cases had significantly higher serum levels than the controls: p, p'-DDE (22 vs. 12 ng/g) and o, p'-DDE (0.09 vs. 0.05 ng/g). After adjustment for age and BMI, the authors associated the exposure of p, p'-DDE with a greater risk of spontaneous abortion (OR: 1.13; CI: 1.02-1.26). (Korrick SA, Chen C, Damokosh AI, Ni J, Liu X, Cho SI, et ál., 2001).

Another case-control study was conducted between October 1986 and September 1987 in 29 hospitals in Shanghai (China). During that time, 75,756 persons were born with birth weights greater than or equal to one kilogram. All perinatal deaths and newborns with birth defects were matched with an equal number of infants born alive and without birth defects. The study sample included 1,875 cases and the same number of controls. Among the cases, 1,013 were newborns with birth defects and 1,134 resulted in perinatal death (some, also, with birth defects). Regarding perinatal deaths, the research team referred to intrapartum foetal death, antepartum foetal death, and early neonatal death during the first week of life. Case and control working mothers were interviewed to determine their occupational exposure to various agents: radiation,

chemicals, noise, and pesticides, and the time at which they were exposed to these agents during pregnancy. Logistic regression analysis was performed, controlling for potential confounders. The team concluded that exposure by women workers to pesticides during the first trimester of pregnancy increased the risk of threatened abortion (OR: 3.9; CI 95%: 1.2-12.6). (Zhang J, Cai WW, Lee DJ, 1992).

Dyes, Lacquers, and Paints

Between 1982 and 1983 a study was carried out in Finland to understand the possible causes of congenital cardiovascular malformations. Among other substances, maternal exposure to dyes, lacquers, or paints was analysed. The sample consisted of 408 cases and 756 controls. The controls were offspring born in the same period as the cases. Interviews with mothers were conducted three months after delivery. The results regarding exposure to dyes, lacquers, and paints indicated a greater risk of conal septal abnormalities in infants, OR: 2.9 (CI 95%: 1.2-7.5). (Tikkanen J, Heinonen OP, 1990).

Congenital Malformations

Between 1982 and 1984, a case-control study was conducted in Montreal (Canada). Specifically, 301 cases of women workers who had given birth to an infant with a congenital malformation were matched with 301 controls of infants without congenital malformations. All case and control mothers had been working thirty or more hours a week until at least the thirteenth week of pregnancy. In a paired analysis, it was observed that case mothers had been more frequently exposed to chemicals than control mothers (63:47), and this was associated with an increased risk of congenital cardiovascular malformations (10:5) and other varied malformations (15:79). (McDonald JC, Lavoie J, Côté R, McDonald AD, 1987).

To evaluate the potential associations between cardiovascular malformations and maternal occupational exposure to various agents during the first trimester of pregnancy, a case-control study was carried out in Finland between 1982 and 1983. 406 cases of congenital cardiac malformations and 756 controls born in the country during the same time were studied. Overall maternal exposure to chemical products at the workplace was more prevalent among case women (35.8%) than among control women (26.2%, $p < 0.01$). The alterations that were observed in neonates were related to cardiac malformations, primarily ventricular septal abnormalities, patent ductus arteriosus, hypoplastic left heart syndrome, and other congenital cardiac malformations. (Tikkanen J, Heinonen OP, 1992).

In the case-control study mentioned in the section above, on pesticide exposure, a sample of infants born between October 1986 and September 1987 in 29 hospitals in Shanghai (China) was analysed. During that time, 75,756 persons were born with birth weights greater than or equal to one kilogram. All perinatal deaths and newborns with birth defects were matched with an equal number of infants born alive and without birth defects. The study sample included 1,875 cases and the same number of controls. Among the cases, 1,013 were newborns with birth defects and 1,134 resulted in perinatal death (some, also, with birth defects). In the

case of perinatal death, the research team referred to antepartum foetal death, death during delivery, and early neonatal death during the first week of life. Case and control working mothers were interviewed to determine their occupational exposure to various agents: radiation, chemicals, noise, and pesticides, and the time at which they were exposed to these agents during pregnancy. Logistic regression analysis was performed, controlling for potential confounders. It was concluded that chemical exposure before pregnancy increased the risk for antepartum foetal death (OR: 2.9; CI 95%: 1.6-5.1) and birth defects (OR: 1.7; CI 95%: 1.2-2.5). Similarly, chemical exposure during the first trimester of pregnancy increased the risk of antepartum foetal death (OR: 3.5; CI 95%: 1.8-6.9), early neonatal death during the first week of life (OR: 2.2; CI 95%: 1.1-4.3), and birth defects (OR: 3.5; CI 95%: 2.1-5.9). (Zhang J, Cai WW, Lee DJ, 1992).

Table 3: Area of Risk: Chemical Risks

Specific risk	Activity, characteristics and moment of exposure	Damages or alterations in pregnant workers the risk of which is increased or may be increased	Foetal damages or alterations the risk of which is increased or may be increased
Lead and its compounds			Cleft palate, neural tube defects, low birth weight
Ethylene Oxide	Laboratories		Spontaneous abortion, preterm birth, post-term birth
Nitrous oxide			Spontaneous abortion
Anaesthetics	Health workers		Spontaneous abortion
Tetrachloroethylene			Schizophrenia, spontaneous abortion
Solvents			Congenital, digestive and oral malformations
Aliphatic acids			Cleft palate
Organic solvents			Congenital malformations, malformations of the heart (ventricular septal defects) and of the urinary tract
Toluene			Spontaneous abortion
Xylene			Spontaneous abortion
Formaldehyde			Spontaneous abortion
Glycol ethers			Congenital malformations, neural tube defects, multiple abnormalities, cleft lip
Oxygenated solvents (esters, ketones, aldehydes, …)			Congenital oral malformations
Chlorinated solvents			Congenital oral malformations
Petroleum products			Congenital oral malformations
Antitumor drugs	Health workers (Medicine, pharmacy, nursing)		Malformations, spontaneous abortion, foetal death, ectopic pregnancy
Antibiotic drugs	Pharmacists		Spontaneous abortion
Biocides	Exposure during the first trimester of pregnancy		Cleft palate

Specific risk	Activity, characteristics and moment of exposure	Damages or alterations in pregnant workers the risk of which is increased or may be increased	Foetal damages or alterations the risk of which is increased or may be increased
Pesticides	Women employed in orchards and greenhouses. Exposure during the first trimester of pregnancy		Spina bifida, hydrocephalus, shortening of upper and lower limbs
	Agricultural sector. Between week 12 and 19 of pregnancy		Late spontaneous abortion
	Floriculture sector. At least six months of exposure before pregnancy		Spontaneous abortion
Glyphosate	Exposure during the first trimester of pregnancy Agricultural sector. Between week 12 and 19 of pregnancy		Threatened abortion Late spontaneous abortion
Thiocarbamate	Agricultural sector. Between week 12 and 19 of pregnancy		Late spontaneous abortion
Dichlorodiphenyldichloroethylene (DDE)	Chinese textile industries. Exposure before pregnancy		Spontaneous abortion
Herbicides	Agricultural sector. First trimester of pregnancy		Cardiac abnormalities (Transposition of the great arteries in infants)
	Agricultural sector. Before conception and before the 12th week of pregnancy		Early abortion
Phenoxyacetic acid type herbicides	Agricultural sector. Before conception and before the 12th week of pregnancy		Early abortion
Triazine-type herbicides	Agricultural sector. Before conception and before the 12th week of pregnancy		Early abortion
Chemical substances against rodents	Agricultural sector. First trimester of pregnancy		Cardiac abnormalities (Transposition of the great arteries in infants)
Dyes, lacquers and paints			Conal septal defects

Specific risk	Activity, characteristics and moment of exposure	Damages or alterations in pregnant workers the risk of which is increased or may be increased	Foetal damages or alterations the risk of which is increased or may be increased
Undetermined chemical substances	Exposure before the 13th week of pregnancy		Congenital malformations of the heart
	Exposure during the first trimester of pregnancy		Ventricular septal malformations, persistent patent ductus arteriosus, hypoplastic left ventricle syndrome, other congenital malformations of the heart
	Exposure before pregnancy		Antepartum foetal death, congenital malformations
	Exposure during the first trimester of pregnancy		Antepartum foetal death, foetal death in the first week of life

5.3 Ergonomic Risks

The multiple ergonomic risks at the workplace may have harmful consequences for the health of the woman and her baby. Below are presented the results of the reviewed articles, classified in three major groups: work movements and postures, physical exertion, and physical fatigue.

Movements and Postures

In 2000, a meta-analysis was published aimed at evaluating the association between working conditions and adverse pregnancy outcomes. The analysis included 29 observational studies (160,988 women) evaluating the effect of one or more of the following work-related exposures on adverse pregnancy outcome: physically demanding work, prolonged standing, long work hours, shift work, and cumulative work fatigue score. Outcomes of interest were preterm birth, preeclampsia and small-for-gestational-age (SGA). The results obtained referring to movements and postures of pregnant workers indicated that prolonged standing was significantly associated with the risk of preterm birth (OR: 1.26; CI 95%: 1.13-1.40). (Mozurkewich EL, Luke B, Avni M, Wolf FM, 2000).

In 1995, a Danish study was published aimed at evaluating the influence of standing and walking at work in the second trimester of pregnancy on the risk of preterm delivery in a population with a low frequency of other workplace risks. From a prospective cohort established during 1989-1991, 4,259 women were selected who worked during the 16th week of pregnancy. The information collected at this time of the pregnancy included medical and obstetrical history, general lifestyle factors, and exposures at work. The researchers noted that many women were unable to separate periods of standing from periods of walking, so both exposures were studied as a combined measure. From this study, it was concluded that women who reported standing and walking for five or more hours each work day in the second trimester of pregnancy were at greater risk of preterm delivery than those who reported two hours or less on either of the exposures each day (OR: 3.3; CI 95%: 1.4-8.0). (Henriksen TB, Hedegaard M, Secher NJ, Wilcox AJ, 1995).

A case-control study across 16 European countries was carried out to analyse the relation between preterm birth and working conditions. The analysis included 5,145 preterm (cases) and 7,911 term births (controls) of which 2369 preterm and 4098 term births were to women employed during pregnancy. Analyses of working conditions were carried out for women working through at least the third month of pregnancy. The results of this study indicated that pregnant working women standing more than 6 hours a day are at greater risk of preterm birth (OR: 1.26; CI 95%: 1.1-1.5). (Saurel-Cubizolles MJ, Zeitlin J, Lelong N, Papiernik E, Di Renzo GC, Bréart G, 2004).

Between 1980 and 1982, a study was carried out in Connecticut (USA) to examine the association of the prolonged standing required by certain jobs with the rate of preterm births and low birth weight deliveries. The study sample was made up of 1,206 women. The study demonstrated that there was a significant association between standing on the job and preterm birth (OR: 2.72; CI 95%: 1.24-5.95). (Teitelman AM, Welch LS, Hellenbrand KG, Bracken MB, 1990).

A case control study was carried out in Quebec (Canada) to study the association of several risk factors with preterm birth. The sample was made up of 101 women in preterm labour and 202 matched pregnancies for gestational age, as controls. The study identified seven risk factors for preterm birth in an explanatory multivariate model among 117 variables: Body mass index (BMI) of less than 20 (OR: 3.96; CI 95%: 2.61-7.09), previous preterm labour (OR: 3.61: CI 95%: 1.12-11.65), previous low birth weight (OR: 2.24 CI 95%: 1.05-7.71), standing at work more than 2 hours (OR: 3.90; CI 95%: 1.53-9.91), abruptio placentae (OR: 5.88; CI 95%: 1.20-28.76), urinary tract infection (OR: 4.43; CI 95%: 1.47-13.34) and stress score greater than 5 (OR: 2.56; CI 95%: 1.20-5.54). It is of interest to mention that the most stressful events for this last parameter were related to family illness, mortality, violence, and financial distress. (Moutquin JM, 2003).

Another study was carried out in Quebec (Canada), i.e. the same city where the previous study was conducted, to assess the relation of some maternal job characteristics to the risks of delivering a small-for-gestational-age (SGA) or preterm infant. The sample was composed of 4,390 women who gave birth between January and October 1989. The results of the investigation indicated that the risk of having a small-for-gestational-age infant was increased among those women who worked at least 6 hours a day in a standing position (OR: 1.42; CI 95%: 1.02-1.95). Physical effort, lifting heavy objects, and long workhours were not related to either a small-for-gestational-age or a preterm infant. (Fortier I, Marcoux S, Brisson J, 1995).

One year later, in 1996, a study conducted in Mexico City was published that examined the effect of working conditions, occupational stress, and antenatal leave on the risk of small-for-gestational-age (SGA) and premature births. The study sample was made up of 2,663 women who had worked at least three months during pregnancy. Among all the cases studied, 288 preterm births and 261 SGA infants were identified. The study results indicate that standing more than 7 hours a day was linked to a greater risk of small-for-gestational age births (OR: 1.40; CI 95%: 1.03-1.91). (Cerón-Mireles P, Harlow SD, Sánchez-Carrillo CI, 1996).

In Guatemala a study was carried out to determine the effect of physical exertion by a mother on pregnancy outcomes. For this, various degrees of physical exertion were examined in 15,786 pregnant women. The results of this study, looking at small-for-gestational-age births (SGA), indicated that manual work, compared to office work, increases the risk for an SGA (OR: 1.32; CI 95%: 1.12-1.56). Regarding physical demands at

work, there was an increased risk of preterm births among women who worked in a standing position compared with those who worked in a sitting position (OR: 1.56; CI 95%: 1.04-2.60). (Launer LJ, Villar J, Kestler E, de Onis M, 1990).

A study was done in the state of New York to examine the association between two birth defects, neural tube defects and oral cleft defects, and maternal physical work demands during the periconceptional period. A case-control study was conducted by comparing exposure characteristics of 520 mothers of malformed infants by comparing characteristics of 520 mothers with 1,154 mothers of non-malformed infants. Then, case groups were further subdivided based on whether infants had additional defects. Occupational exposure information was collected from a questionnaire. The results of the investigation showed no general differences between both groups in most variables. However, those infants with cleft defects plus additional defects tended to be more associated with maternal jobs requiring standing for at least 75% of the work day (OR: 1.76; CI 95%: 1.02-3.21). (Lin S, Gensburg L, Marshall EG, Roth GB, Dlugosz L, 1998).

Another study also carried out in the United States aimed to examine the relation of physical exertion and the risk of spontaneous abortion in a prospective study of 5,144 pregnant women. Physical exertion was measured using the following parameters: time spent working, standing, and bending at work, hours between breaks, and hours spent doing housework or yard work; shift worked; number of times lifted weights and more than 15 pounds (6.8 kg) at work or at home; number of children under age five cared for at home. None of the exertion measures was appreciably associated with an increased risk of spontaneous abortion overall; additionally, combined physical activity at work and at home was not related to increased risk. However, for women who had already suffered two or more spontaneous abortions, standing at work more than 7 hours per day was associated with spontaneous abortion (OR: 4.3; CI 95%: 1.6-11.7). (Fenster L, Hubbard AE, Windham GC, Waller KO, Swan SH, 1997).

A study conducted in the Netherlands and published in 1993 analysed the influence of occupational physical activity on early pregnancy failure. The sample was composed of 24 cleaners, 36 kitchen staff, and 110 clerical workers from 39 Dutch hospitals. These women were enrolled before becoming pregnant between August 1987 and January 1989. Two fundamental factors were defined: one, the occupational energy expenditure defined by an intensity and fatigue score, studied individually and in combination with working hours and working speed; and the other, occupational biomechanical load, defined by a peak and chronic pressure score. It was observed that intensity and fatigue scores were not associated with the risk of spontaneous abortion. Nevertheless, work involving a high biomechanical load, in particular high peak pressure scores, showed an increased risk of spontaneous abortion (OR: 3.1; CI 95%: 1.1-8.9), especially bending movements (OR: 3.2; CI 95%: 1.3-9.8). (Florack E, Zielhius GA, Pelegrino JEMC et al., 1993).

Manual handling of loads

A study was carried out in Finland to investigate whether occupational exposure among physiotherapists is associated with spontaneous abortion or congenital malformation in offspring. The study was a retrospective case-control study, where pregnancy outcome data were collected from medical registers from 1973 to 1983. The final study sample for spontaneous abortion data was made up of 240 cases and 483 controls. While in the study on congenital malformations, there were 46 cases and 187 controls. The finding of interest from the ergonomic perspective was that heavy lifting (greater than 10 kg or transfer of patients more than 50 times a week) leads to an increase in risk of spontaneous abortion (OR: 3.8; CI 95%: 1.1-9.0; p <0.05). (Taskinen H, Kyyrönen P, Hemminki K, 1990).

A study was carried out among all parturients in Norway from 16 October 1989 to 26 November 1989 to analyse the association between working conditions and preeclampsia. The study sample included 5,388 women, of which 3,321 continued working beyond the third month of pregnancy. The study results demonstrated that preeclampsia was more frequent among those women whose jobs involved the lifting of heavy loads of 10-20 kg (OR: 1.8; CI 95%: 1.2-2.5). (Wergeland E, Strand K, 1997).

Based on the study mentioned above, carried out among all parturients in Norway from 16 October 1989 to 26 November 1989, analysis was performed to examine whether strenuous working conditions in pregnancy are associated with reduced birthweight. The study sample included 5,388 women, of which 3,321 continued working beyond the third month of pregnancy. The study results indicated that strenuous working conditions involving the lifting of heavy loads increased the risk of low birthweight among nulliparae, particularly in non-smokers (OR: 2.8; CI 95%: 1.2-6.5). (Wergeland E, Strand K, Børdahl PE, 1998).

Physical fatigue

In 2000, a meta-analysis was published (already mentioned above in the section on *Movements and Postures*) aimed at evaluating the association between working conditions and adverse pregnancy outcomes. The analysis included 29 observational studies (160,988 women) evaluating the effect of one or more of the following work-related exposures on adverse pregnancy outcome: physically demanding work, prolonged standing, long work hours, shift work, and cumulative work fatigue score. The outcomes of interest were preterm birth, preeclampsia and small-for-gestational-age (SGA). The results obtained referring to physical fatigue indicated that physically demanding work was significantly associated with preterm birth (OR: 1.22; CI 95%: 1.16-1.29), SGA (OR: 1.37; CI 95%: 1.30-1.44) and preeclampsia (OR: 1.60; CI 95%: 1.30-1.96). It was also observed that a high cumulative work fatigue score was associated with the risk of preterm birth (OR: 1.63; CI 95%: 1.33-1.98). (Mozurkewich EL, Luke B, Avni M, Wolf FM, 2000).

A study published in 2000 was carried out in Denmark, aimed at studying the relation between maternal physical strain and the risk of spontaneous abortion. This study's method differed from others, as it followed a

cohort of women who were planning their first pregnancy, rather than a typical retrospective study. The analysis included 181 pregnancies. Information was provided by women, who had to record their physical activity during early pregnancy in a structured diary. The results of this study indicated that women who reported physical strain higher than average at day 6 to 9 after the estimated date of ovulation had twice the risk of spontaneous abortion (OR: 2.5; CI 95%: 1.3-4.6). (Hjollund NH, Jensen TK, Bonde JP, Henriksen TB, Andersson AM, Kolstad HA, et ál., 2000).

In Italy, a case-control study was carried out to evaluate the impact of type of employment and level of physical activity at work on the risk of severe preeclampsia. The sample was composed of 160 cases, nulliparous pregnant women with preeclampsia, and 320 controls. Information was collected on the type of employment and level of physical activity through a questionnaire. The degree of physical activity at work was assessed by a four-level activity score based on type of work, physical intensity, posture at work, and weekly working hours. There was a significant linear trend relating the degree of physical activity at work to preeclampsia (p=0.002). Thus, it was determined that moderate/high physical activity at work was associated with a greater risk of preeclampsia compared to mild activity (OR: 2.08; CI 95%: 1.11-3.88). (Spinillo A, Capuzzo E, Colonna L, Piazzi G, Nicola S, Baltaro F, 1995).

Also in Italy, the impact of type of occupation and physical effort at work was evaluated on the risk of ultrasonographically confirmed foetal growth retardation (IUGR) among nulliparous women. Logistic regression analysis was used to compare the characteristics of work such as work posture, weekly working hours, and physical effort at work, in 349 patients with confirmed foetal growth retardation and 698 controls (with appropriate foetal growth). The authors concluded that the risk of foetal growth retardation was similar between unemployed and formally employed women at the beginning of pregnancy. However, manual workers were at a slightly greater risk of IUGR than women not formally employed (OR: 1.81; CI 95%: 1.15-2.85). The risk of IUGR was also greater among women reporting moderate-to-heavy as compared to light physical effort at work (OR: 2.46; CI 95%: 1.36-4.21). (Spinillo A, Capuzzo E, Baltaro F, Piazzi G, Nicola S, Iasci A, 1996).

At Southwest Texas State University (United States) a study was carried out to examine the relation of occupational physical activity and the risk of preterm birth among US Army active-duty primigravidas between 1981 and 1984. The sample was composed of 604 cases of preterm deliveries (≤ 37 weeks gestation) and 6,070 controls (term and post-term deliveries). It was observed that women in the highest physical activity levels had increased odds of preterm delivery. Specifically, the results obtained in this study for the risk of preterm delivery were as follows: women with high physical activity levels presented OR: 1.69 (CI 95%: 1.08-2.04) and those with very high physical activity levels, OR: 1.75 (CI 95%: 1.12-2.75). The authors concluded that due to missing data, the results should be interpreted with caution. (Ramírez G, Grimes RM, Annegers JF, Davis BR, Slater CH, 1990).

In 1990 another study in the United States, like the one above, sought to investigate whether work-related physical exertion increases a woman's risk of delivering prematurely (giving birth at least three weeks early) or of giving birth to a low birthweight infant (<2,500 g). The sample was composed of 773 women, included n the National Longitudinal Survey of Labor Market Experience, Youth Cohort (NLSY). The results of this study revealed that there was a greater rate of preterm deliveries and low birthweight babies among women in jobs characterised by high physical exertion (RR: 5.1; CI 95%: 1.5-17.7). For the authors, these findings support a policy of limiting work-related physical exertion during pregnancy. (Homer CJ, Beresford SA, James SA, Siegel E, Wilcox S, 1990).

In California (United States) a case-control study was carried out to examine the association of physical exertion and spontaneous abortion. The study sample was made up of 607 women whose pregnancies ended in spontaneous abortion, and by a control group of 1,287 women who gave birth in 1986 and 1987. Women were interviewed about the number of hours they spent doing heavy housework and caring for young children. Information was also collected regarding the work schedule of those women who were employed during their pregnancy (71% of each group), and on the number of hours they were standing, stooping, or bent, and the number of times per day they lifted weights of greater than 15 pounds (6.8 kg). The results indicated that standing more than 8 hours per day at work was the only variable associated with a greater risk of spontaneous abortion (OR: 1.6; CI 95%: 1.1-2.3). This association was evident only in cases of women with a history of spontaneous abortion (OR: 2.8; CI 95%: 1.4-5.9). This group of women also presented a greater risk of abortion in the second trimester of pregnancy (OR: 4.9; CI 95%: 1.0-12.2). The results of the study, in the authors' words, indicate that the specific type and context of physical exertion may be important in determining the risk of spontaneous abortion. (Eskenazi B, Fenster L, Wright S, English P, Windham GC, Swan SH, 1994).

A study was carried out in Finland to analyse the association of physical workload and structural malformations among offspring. The sample was composed of 1,475 mothers of infants with malformations and the same number of women with healthy children. The results of the study indicate that when analysis was limited to non-agricultural workers in the socioeconomic class of lower-level employees with administrative and clerical occupations and manual work, mothers with a moderate physical work load in the first trimester of pregnancy had a greater risk of central nervous system abnormalities (OR: 3.0; CI 95%: 1.6-5.5) and orofacial clefts (OR: 1.9; CI 95%: 1.1-3.0). If this load was in the third trimester of pregnancy, the probability that newborns were small-for-gestational-age increased (OR: 2.4; CI 95%: 1.3-4.6). Thus, in the cases of exposure to increased short-term physical load, an increased probability of central nervous system abnormalities was observed (OR: 1.6; CI 95%: 1.1-2.4) compared to workers who had only performed light physical activities. (Nurminen T, Lusa S, Ilmarinen J, Kurppa K, 1989).

Table 4: Area of risks: Ergonomic risks

Specific risk	Activity and characteristics of the exposure	Damages or alterations in pregnant workers the risk of which is increased or may be increased	Foetal damages or alterations the risk of which is increased or may be increased
Movements and postures	Prolonged standing (for 5 or more hours In a work day)		Preterm and small-for-gestational-age birth
	Bending movements		Spontaneous abortion
Manual handling of loads	Heavy lifting (10 kg or more)	Pre-eclampsia	Spontaneous abortion and low birth weight
Physical fatigue	High physical load	Pre-eclampsia	Preterm birth, spontaneous abortion and small-for-gestational-age birth

Reference time: from the 2nd trimester of pregnancy

5.4 Psychosocial Risks

Results relating to psychosocial risks from the reviewed articles are presented below, classified into two groups. The first concerns factors relating to work demands and, the second, factors related to working hours, a section that includes aspects such as workday duration, shift work, and alterations to these.

Work Demands

From 1983 to 1985, a study was carried out in Denmark to investigate whether increasing job stress (defined as increasing job demands and decreasing job control) increased the risk of adverse pregnancy outcomes. The population base included 214,108 commercial and clerical women workers working during the aforementioned period. Six case groups were selected: 1) 2,248 spontaneous abortions, 2) 209 stillbirths or deaths within the first year of life, 3) 661 infants with congenital malformations, 4) 593 preterm deliveries, 5) 587 infants with term low birth weights, and 6) 988 infants with light-for-date birth weights. The reference group was constituted by 2,252 pregnancies. When dichotomized scales on data concerning job demand and control were used, an increased risk of spontaneous abortion was observed (OR: 1.28; CI 95%: 1.05-1.57) and a lower term birthweight (OR: 1.46; CI 95%: 1.05-2.04) among women experiencing high job stress. For the other case groups, no significant differences were found. The authors of the study concluded that recall bias is one explanation for the results, and therefore recommend the results be interpreted with caution. (Brandt LP, Nielsen CV, 1992).

In 1997, a case-control study was published conducted in North Carolina (United States) to assess the relationship between occupational stress and preterm delivery. The study sample was made up of 421 cases, that is, 421 women who gave birth prematurely (prior to 37 weeks gestation) and a control group of 621 women delivering infants at term. The results of the investigation indicated that those women who worked for 30 or more weeks in a “high strain” job (i.e., high demand and low control), presented a greater risk of preterm delivery (OR: 1.4; CI 95%: 1.0-2.2). From these findings, the authors concluded that chronic exposure during pregnancy to work characterised by high demand and low control may be modestly associated with preterm delivery. (Brett Km, Strogatz DS, Savitz DA, 1997).

A study in Israel was carried out to assess the impact of workload on pregnancy among women physicians in public hospitals. Information regarding demographic data, perceived stress, and complications during pregnancy was collected through a questionnaire. The findings indicated significant differences in the rates of stillbirths (32/1000 births versus 3.7/1000, p <0.01) and premature delivery (12.4% versus 7.6%, p=0.0014) between women physicians and the general population. According to the study’s authors, these results suggest that working long hours in a stressful occupation, in this case a hospital, has an adverse effect on

pregnancy course and is associated with increased rates of stillbirth and premature delivery. (Pinhas-Hamiel O, Rotstein Z, Achiron A, Gabbay U, Achiron R, Barak Y, et ál., 1999).

In the United States, a case-control study was conducted to determine whether job stress during pregnancy resulted in an increased risk of preeclampsia. The sample was made up of 110 nulliparous women with preeclampsia and 115 controls (healthy nulliparous women). All the women in the sample gave birth between 1984 and 1987. Each women was assigned a stress score based on job title. Logistic regression analysis indicated that those women employed in high-stress jobs (high psychological demand and low job control) presented a risk of preeclampsia 3.1 times higher (CI 95%: 1.2-7.8) than her peers. Additionally, women with low-stress jobs presented an increased risk compared with nonworking women (OR: 2.0; CI 95%: 1.0-4.3). Furthermore, working women had 2.3 times the risk of developing preeclampsia compared with nonworking women (CI 95%: 1.2-4.6). In view of these results, the authors concluded that work-related psychosocial strain increased the risk of preeclampsia. (Klonoff-Cohen HS, Cross JL, Pieper CF, 1996).

Another case-control study focused on preeclampsia risk was conducted in Quebec (Canada), published in 1999. The aim of the study was to assess whether exposure to high job strain during the first 20 weeks of pregnancy increases the risk of preeclampsia and gestational hypertension. The sample was composed of a group of cases, 128 women with preeclampsia and 201 with gestational hypertension, and a control group (n=401). The women in the sample were primiparous women who had a paid occupation for at least one week during the first 20 weeks of their pregnancy and who delivered between 1984 and 1986. Based on job title, women were assigned to two exposure groups: 1) high job strain (high demand, low control) and 2) low job strain (low demand, high control). The study findings demonstrated that women exposed to high job strain were more likely to develop preeclampsia than women exposed to low job strain (OR: 2.1; CI 95%: 1.1-4.1). (Marcoux S, Bérubé S, Brisson C, Mondor M, 1999).

Another study was carried out to examine the association between work during pregnancy and pregnancy-induced hypertension in the United States. The study was a prospective cohort study with a sample of 717 women. The cases were classified into gestational hypertension (n=16) and preeclampsia (n=11). All cases of pregnancy-induced hypertension occurred among the 575 women who worked during the first trimester of pregnancy. In the findings, it was observed that among lower-status jobs, hypertension was associated with lower decision latitude, a stress factor, (OR: 2.4; CI 95%: 1.1-5.2) and low job complexity (OR: 2.1; CI 95%: 1.04-4.6). (Landsbergis PA, Hatch MC, 1996).

A study was carried out in Norway, already mentioned above in the section on *Ergonomic* risks, to analyse the association between working conditions and preeclampsia. The study sample included all parturients in Norway from 16 October 1989 to 26 November 1989. The study sample included 5,388 women, of which 3,321 continued working beyond the third month of pregnancy. The study results demonstrated that

preeclampsia was more frequent among those women whose jobs involved a hectic work pace (OR: 1.4; CI 95%: 1.0-2.0; p <0.05). (Wergeland E, Strand K, 1997).

Work Schedule: Workday Duration, Shift Work…

Shift work has been associated with many health complaints, for example, pregnancy loss. This risk was analysed in a study published in 1993 that aimed to analyse the association between shift work and pregnancy loss. For this, the work schedule during pregnancy of two groups of women was compared: the first, made up of 331 women who had pregnancy loss, and the second, made up of 993 pregnant women. The authors observed in this study that women with a fixed evening schedule had four times the risk of pregnancy loss than workers on a fixed day schedule (OR: 4.17; CI 95%: 2.19-7.92). Nevertheless, the differences with the group of workers on fixed night schedules were not statistically significant (OR: 2.68; CI 95%: 0.53-13.43). (Infante-Rivard C, David M, Gauthier R, Rivard GE, 1993).

In China a study was conducted in 1992 to investigate the association between shift work and low birthweight and preterm birth. The sample was made up of 845 women (887 live births) who worked in three modern textile mills in Anhui. About 72% of the women worked an 8-day cycle with shift changes every 2 days throughout pregnancy. In this study, it was observed that for rotating shift workers, there was a greater risk of preterm birth (OR: 2.0; CI 95%: 1.1-3.4) and low birthweight (OR: 2.1; CI 95%: 1.1.-4.1). (Xu X, Ding M, Li B, Christiani DC, 1994).

In the United States, a study was carried out to study the relationship of stress and working conditions with adverse reproductive outcomes. The sample was composed of a cohort of 584 female lawyers, aged 25 to 63. In this study it was observed that the number of weekly work hours in the first trimester of pregnancy was strongly associated with risk of spontaneous abortion (OR: 3.0; CI 95%: 1.4-6.6). (Schenker M, Eaton M, Green R, Samuels S, 1997).

Another study carried out in 1989 investigated the relation between irregular work hours, nitrous oxide (N_2O) exposure, and the risk of spontaneous abortion. A questionnaire was sent to 3,985 women born in 1940 or later, who were members of the Swedish Midwives Association. The questions related to exposure before and during all of their pregnancies, and also on work conditions such as occupation, extent of employment, workplace, work schedules, use of anaesthetics, and workload. The midwives on night shifts had an increased risk of late spontaneous abortions (after the 12^{th} week of pregnancy): OR 3.33 (CI 95%: 1.13-9.87). Nevertheless, no association was observed between the risk analysed and the use of nitrous oxide (>50% of the deliveries). According to the study's authors, the results support the hypothesis that night work increases the risk of spontaneous abortion. (Axelsson G, Ahlborg G Jr, Bodin L, 1996).

Based on the study mentioned previously, carried out in 3,985 female members of the Swedish Midwives Association, the authors published an article in 1999 analysing the relation between shift work and occupational nitrous oxide exposure in the second trimester of pregnancy and birth weight and gestational age at delivery. Models were used with allowance for dependence between births for the same woman and found that night work was associated with an increased risk of preterm birth (<37 weeks gestation), OR: 5.6 (CI 95%: 1.9-16.4). In addition, exposure to nitrous oxide use was associated with reduced birthweight, -77 g (CI 95%: -129 g - -24g), and with a greater risk that infants would be small-for-gestational-age (≤ tenth percentile of weight for gestational week), OR: 1.8 (CI 95%: 1.1-2.8). (Bodin L, Axelsson G, Ahlborg G Jr, 1999).

In 2005 a study was conducted in the United States between January 1995 and April 2000 to assess whether exposure to standing, lifting, night work, or long work hours during three periods of pregnancy are associated with an increased risk of preterm or small-for-gestational-age (SGA) birth. The study sample was made up of 1,908 women who provided information about physical exertion during pregnancy. No significant elevations in preterm delivery were observed among those women who lifted repeatedly or stood at least 30 hours per week; however, there was an increased risk among women who worked at night (RR during the first trimester: 1.5; (CI: 95%: 1.0-2.0). Regarding the risk of an SGA birth, none of the risk factors studied were found to be associated. (Pompeii LA, Savitz DA, Evenson KR, Rogers B, McMahon M, 2005).

In 2000, a meta-analysis was published aimed at evaluating the association between working conditions and adverse pregnancy outcomes. The analysis included 29 observational studies (160,988 women) evaluating the effect of one or more of the following work-related exposures on adverse pregnancy outcome: physically demanding work, prolonged standing, long work hours, shift work, and cumulative work fatigue score. The outcomes of interest were preterm birth, preeclampsia and small-for-gestational-age (SGA). The results obtained referring to work schedule indicated that shift work and night work were associated with the risk of preterm birth (OR: 1.24; CI 95%: 1.06-1.46). However, no significant association was observed between the risk of preterm birth and long work hours (OR: 1.03; CI 95%: 0.92-1.16). (Mozurkewich EL, Luke B, Avni M, Wolf FM, 2000).

A study was conducted to investigate the risks of physical activity at work for pregnancy. 1,327 mothers were interviewed from the Southampton Women's Survey (SWS) during their 34th week of pregnancy. Questions focused on activities (working hours, time spent standing/walking/kneeling/squatting/trunk bending, lifting, and night shifts) in jobs held at different weeks of their pregnancy (weeks 11, 19, and 34). Additionally, information about four possible birth outcomes was collected: preterm delivery, small-for-gestational-age (SGA), reduced abdominal circumference, and reduced head circumference. The rationale for studying this last parameter is that it has been demonstrated that small cranial circumference in newborns is related to arterial hypertension in childhood and in adulthood, glucose intolerance, and a high prevalence of mortality

due to cardiovascular disease. The results obtained in this study indicate that pregnant women with long work hours of 40 hours/week or more during weeks 11 and 19 of pregnancy had a greater risk, OR: 1.71 (CI 95%: 1.11-2.63) and OR: 1.72 (CI 95%: 1.11-2.65), respectively, of giving birth to offspring with reduced head circumference.
It was also observed that women who worked at 34 weeks of pregnancy had a greater risk (OR: 2.92; CI 95%: 1.27-6.70) of preterm delivery when performing work that entailed trunk bending in either a seated or standing position for at least one hour per day. (Bonzini M, Coggon D, Godfrey K, Inskip H, Crozier S, Palmer KT, 2009).

A case-control study across 16 European countries was carried out to analyse the relation between preterm birth and working conditions. The case group was composed of 5,145 preterm births and the control group was made up of 7,911 term births; of these, 2,369 women who had preterm births and 4,098 women who had term births worked during pregnancy. The analysis of working conditions focused on those women who worked at least through the third month of pregnancy. The results of this study indicated that the risk of preterm birth is greater among pregnant women who worked more than 42 hours per week (OR: 1.33; CI 95%: 1.1-1.6) and those with a low level of job satisfaction (OR: 1.27; CI 95%: 1.1-1.5). (Saurel-Cubizolles MJ, Zeitlin J, Lelong N, Papiernik E, Di Renzo GC, Bréart G, 2004).

In 1996, a study performed in Mexico City was published that examined the effect of working conditions, occupational stress, and antenatal leave on the risk of small-for-gestational-age (SGA) and premature births. The study sample was made up of 2,663 women who had worked at least three months during pregnancy. Among all the cases studied, there were 288 premature births and 261 SGA children. The study results indicate that working more than 50 hours a week (OR: 1.59; CI 95%: 1.14-2.22) and no antenatal leave (OR: 1.55; CI 95%: 1.12-2.14) were associated with an increased risk of small-for-gestational-age births. It was also observed that those women who did not take antenatal leave were much more likely to give birth prematurely (OR: 3.04; CI 95%: 2.31-3.99). (Cerón-Mireles P, Harlow SD, Sánchez-Carrillo CI, 1996).

In 1991, a study conducted in the United States was published with the aim of evaluating whether various work characteristics increased the risk of preterm delivery and foetal growth retardation (<2,500 g at term). Work characteristics studied were: number of hours worked per week, physical activities, and environmental conditions. The sample was made up of 2,711 women. The results indicated that those mothers who worked 40 or more hours per week were more likely to have a low birthweight delivery (OR: 1.7; CI 95%: 1.03-2.68). (Peoples-Sheps MD, Siegel E, Suchindran CM, Origasa H, Ware A, Barakat A, 1991).

A study was carried out among all parturients in Norway, as already mentioned in the section on *Ergonomic Risks*, from 16 October 1989 to 26 November 1989 to analyse the association between working conditions and preeclampsia. The study sample included 5,388 women, of which 3,321 continued working beyond the

third month of pregnancy. The study results demonstrated that preeclampsia was more frequent among those women who already had children if they performed shift work (OR: 2.0; CI 95%: 1.1-3.6). (Wergeland E, Strand K, 1997).

Table 5: Area of risk: Psychosocial risks

Specific risk	Activity and characteristics of the exposure	Damages or alterations in pregnant workers the risk of which is increased or may be increased	Foetal damages or alterations the risk of which is increased or may be increased
Workload	Increasingly demanding task and progressive loss of control over the activity	Pre-eclampsia	Spontaneous abortion and low birth weight
	Chronic exposure (30 weeks or more)		Preterm birth
	Long working hours in stressful occupations		Adverse effects during pregnancy and stillbirth
Working time	Fixed afternoon shift		Spontaneous abortion
	Night shift		Late spontaneous abortion and preterm birth
	Rotating shifts	Pre-eclampsia (in women with children)	Preterm birth and low birth weight
	Long working hours during the first trimester of pregnancy		Spontaneous abortion
	Long working hours (>40 hours/week)		Preterm birth, small-for-gestational-age birth and smaller head circumference

5.5 Physical Risks

The results obtained regarding physical risks from a review of the articles, corresponding to the search period 2000-2010, all refer to radiation risks, which are classified into two major groups: non-ionising and ionising.

Non-Ionising Radiation

In Finland, a case-control study was carried out to investigate whether occupational exposure among physiotherapists is associated with spontaneous abortion or congenital malformation in offspring. Data were collected from medical registers from 1973 to 1983. The final study sample for spontaneous abortion data was made up of 240 cases and 483 controls; while in the study on congenital malformations, there were 46 cases and 187 controls. Ultrasound is one of the most common forms of therapy used by the physiotherapists in the study and it was observed that handling ultrasound equipment for at least 20 hours per week increased the risk of spontaneous abortion in a significantly (OR: 3.4; CI 95%: 1.2-9.0). Handling equipment producing electric currents for at least five hours per week also increased this risk (OR: 2.0; CI 95%: 1.0-3.9). Regarding the risk of congenital malformations, it was observed that exposure for at least 5 hours per week to transcutaneous nerve stimulation therapies increased the risk of malformations (OR: 4.7; CI 95%: 1.2-18.7), although it is important to indicate that for this specific type of therapy, only four cases existed in the sample. Moreover, it was observed that handling shortwave equipment for 1-4 hours per week increased this risk of congenital malformations (OR: 2.7; CI 95%: 1.2-6.1), similarly to deep heat therapy for 1-4 hours/week (OR: 2.4; CI 95%: 1.0-5.3). (Taskinen H, Kyyrönen P, Hemminki K, 1990).

In 1993 a study was published carried out in the United States, also among physical therapists, with the aim of evaluating the impact of occupational use of microwave and shortwave diathermy at the time of conception. In 1989, questionnaires were mailed to 42,403 physical therapists to obtain information on occupational and reproductive histories. The study sample was finally composed of 1,753 case women who had suffered spontaneous abortions and a control group of 1,753 pregnant women. In the study, a pregnancy was considered exposed if the mother reported using these techniques at any point in the six months prior to the first trimester of pregnancy or during the first trimester. The results of this study revealed that pregnant women who reported exposure to microwaves had an increased risk of spontaneous abortion (OR: 1.28; CI 95%: 1.02-1.59). This risk increased with increasing level of exposure ($\chi^2 = 7.25$, $p < 0.005$) and specifically, the group with the greatest exposure (≥20 exposures/month) presented an OR of 1.59. The overall OR was slightly lower after it was controlled for prior foetal loss, OR: 1.26 (CI 95%: 1.00-1.59); but the exposure-response effect remained ($\chi^2 = 5.17$, $p< 0.01$). However, the study did not demonstrate that the use of shortwave diathermy increased the risk of spontaneous abortion (OR: 1.07; CI 95%: 0.91-1.24), with the OR in the highest exposure group being 0.87. (Ouellet-Hellstrom R, Stewart WF, 1993).

In Great Britain a study was conducted to develop a reliable method for collecting information on reproductive outcome in an occupational setting and to investigate the health of children born to medical radiographers. The sample was comprised of 6,730 members of the College of Radiographers, aged between 30 and 64 years and resident in Britain. Information was collected through a questionnaire. There was little difference between men and women in the frequency of adverse reproductive events reported, with the exception that male radiographers reported fewer medical terminations in their partners. The study observed that the rates of congenital malformations (RR: 1.0; CI 95%: 0.9-1.2), chromosomal anomalies (RR: 1.4; CI 95%: 0.8-2.3) and cancer (RR: 1.2; CI 95%: 0.7-2.0) among children in the study were as expected based on general population rates. There was also an increased risk of chromosomal anomalies other than Down's syndrome in the children of female radiographers (RR: 3.9; CI 95%: 1.3-9.0), although this result should be interpreted cautiously as only five cases were observed. The authors indicate that dose-response relations could not be examined, as long-term dose records of radiographers are not routinely kept in an accessible form. (Roman E, Doyle P, Ansell P, Bull D, Beral V, 1996).

Regarding electromagnetic radiation, there is little evidence regarding the relationship between exposure to this radiation by pregnant workers and congenital malformations in offspring.

In a study published in 1988, data from the Montreal survey on occupational factors in pregnancy were used to test the hypothesis that visual display units (VDUs) constituted a risk to reproduction. Use of a VDU was recorded in 4,712 current and 2,164 previous pregnancies of women in full-time employment at time of conception. The results of the study indicated that the risk of spontaneous abortion in current pregnancies was greater relative to all working women (RR: 1.19; CI 90%: 1.09-1.30). In an analysis by occupational title, eight categories were established according to use of VDUs and it was observed that the relative risk for spontaneous abortion was RR: 1.06 (CI 90%: 0.8-1.4) and for previous pregnancies, RR: 1.01 (CI 90%: 0.7-1.3). For the authors, this result suggests that the small excess of spontaneous abortions among individual women reporting the use of VDUs in current pregnancies may have been due to recall bias. No significant differences were found for the risk of stillbirth, preterm birth, and low birthweight. However, the risk of offspring presenting renal and urinary abnormalities was greater for current pregnancies, RR: 1.84 (CI 90%: 1.07-3.15), though not for previous pregnancies, RR: 1.66 (CI 90%: 0.82-3.25). The study's authors concluded that, there being no prior to reason to suspect a causal link with this type of defect, the interpretation remains open to question and in need of further investigation. (McDonald AD, McDonald JC, Armstrong B, Cherry N, Nolin AD, Robert D, 1988).

In 1991, a study conducted in the United States was published whose objective was to analyse the relation between spontaneous abortion and the use of video display terminals (VDTs), as previous investigations had reported inconsistent findings. Two cohorts of women were compared, one made up of female telephone operators who used VDTs at work, and the other made up of operators who did not use VDTs. Of a total of

2,430 women interviewed, there were 882 pregnancies that met the criteria for inclusion in the study. To perform the analysis, the number of hours worked with a VDT were determined and the electromagnetic fields were measured at VDT workstations, and at workstations without VDTs. It was observed that operators who used VDTs had a higher abdominal exposure to very-low-frequency (15 kHz) electromagnetic fields, and workstations without VDTs did not emit energy of this type. However, abdominal exposure to extremely-low-frequency fields (45-60 Hz) were similar for both operators who used VDTs and those who did not. The study's findings revealed that there was no excess risk of spontaneous abortion among women who used VDTs during the first trimester of pregnancy (OR: 0.93; CI 95%: 0.63-1.38), and no dose-response relation was apparent when examining the women's hours of VDT use per week: for 1-25 hours/week (OR: 1.04; CI 95%: 0.61-1.79); and for greater than 25 hours/week (OR: 1.00; CI 95%: 0.61-1.64). Therefore the authors concluded that the use of VDTs and exposure to accompanying electromagnetic fields were not associated with an increased risk of spontaneous abortion in this study. (Schnorr TM, Grajewski BA, Hornung RW, Thun MJ, Egeland GM, Murray WE et ál., 1991).

A study was carried out in Finland in order to examine whether work with a video display terminal (VDT) and exposure to associated magnetic fields are related to spontaneous abortion. The study sample was comprised of women employed as bank clerks and clerical workers in three companies in Finland. The data for the cases (191 women who had spontaneous abortions) and the controls (394 births) came from Finnish medical registers for the years 1975-1985. Information regarding VDT exposure came from the workers' own reports and information provided by the companies. The study found that the Odds Ratio for spontaneous abortion was not increased by working with VDTs (OR: 1.1; CI 95%: 0.7-1.6). However, the odds ratio for workers who had used a VDT with a high level of extremely low frequency magnetic fields (> 0.9 μT) was greater than those workers using terminals with low levels of these magnetic fields (<0.4 μT), OR: 3.4 (CI 95%: 1.4-8.6). For the authors, the results of this study suggest the need for future studies with precise assessment of exposure to magnetic fields, as the potential risk observed is only seen in a small group of equipment. (Lindbhom ML, Hietanen M, Kyyronen P, Sallmen M, von Nandelstadh P, Taskinen H, et ál., 1992).

In 2003, a study conducted in Quebec (Canada) was published analysing the relation between maternal occupational exposure to extremely low frequency magnetic fields (ELF-MF) during pregnancy and the risk of offspring developing childhood leukaemia. It consisted of a case-control study, with 491 children 0-9 years of age with lymphoblastic leukaemia diagnosed between 1980 and 1993, and 491 healthy children as controls. Mothers were interviewed to obtain detailed prenatal occupational history, and individual exposure to ELF-MF was estimated based on three exposure indicator levels: cumulative, average, and maximum. The results indicated an statistically significant increased risk of developing childhood leukaemia following occupational exposures ≥0.4 μT, (OR: 2.5; CI 95%: 1.2-5.0). The same authors of this study found that this limit is exceeded in several occupations such as in the case of electronics workers in an assembly plant (0.7 μT),

sewing machine operators in a textile factory (0.68 µT) and in footwear factories (0.66 µT). The association indicated was based on three factors: 1) proximity of electrical devices to the abdomen of pregnant women, 2) particular vulnerability during the foetal period to environmental contaminants and 3) considerable mean time of exposure from preconception until the end of pregnancy. According to the study authors, these results are compatible with the theory that children of women exposed to the highest occupational levels of ELF-MF during pregnancy have an increased risk of childhood leukaemia. (Infante-Rivard C, Deadman JE, 2003).

Ionising Radiation

In 1992, a case-control study was published that was conducted in 29 hospitals in Shanghai (China) between October 1986 and September 1987. During that time, 75,756 persons were born with birth weights greater than or equal to one kilogram. All perinatal deaths and newborns with birth defects were matched with an equal number of infants born alive and without birth defects. The study sample included 1,875 cases and the same number of controls. Among the cases, 1,013 were newborns with birth defects and 1,134 resulted in perinatal death (some, also, with birth defects). In the case of perinatal death, the research team referred to antepartum foetal death, death during delivery, and early neonatal death during the first week of life. Case and control working mothers were interviewed to determine their occupational exposure to various agents: radiation, chemicals, noise, and pesticides, and the time at which they were exposed to these agents during pregnancy. Logistic regression analysis was performed, controlling for potential confounders. It was concluded that exposure to ionising radiation during the first trimester of pregnancy increased the risk of spontaneous abortion (OR: 3.2; CI 95%: 1.4-7.6), and low birthweight for gestational age at the time of delivery (OR: 2.7; CI 95%: 1.1-6.3). (Zhang J, Cai WW, Lee DJ, 1992).

Here it is interesting to cite the principles set out in Article 10, "*Special protection during pregnancy and lactation*", of Royal Decree 783/2001 approving the Regulations on health protection against ionising radiation, since they are widely mentioned in the texts analysed in this systematic review:

"*1. The moment a pregnant woman informs the title-holder of the practice of her condition, the protection of the foetus must be comparable to that of the members of the public. To this end, the working conditions of the pregnant woman shall be such that the equivalent dose for the foetus be as low as is reasonably possible, in such a manner as to make it unlikely that this dose exceeds 1 mSv, at least from the moment she informs of her condition and until the end of the pregnancy.*

2. From the moment a woman, who is in the lactation period, informs of her condition to the title-holder of the practice, she shall not be assigned tasks that suppose a significant risk of radioactive contamination. In such cases adequate monitoring must be ensured in terms of possible radioactive contamination of her organism."

Pregnant women exposed to ionising radiation in their work are particularly vulnerable, and this risk is particularly significant in the area of health, where the number of women workers of childbearing age exposed to radiation of this type is high. For this reason, in 2002, the Spanish Nuclear Safety Council (CSN,

its acronym in Spanish) published a document drafted by a working group made up of its own staff as well as hospital staff, titled “La protección de las trabajadoras gestantes expuestas a radiaciones ionizantes en el ámbito hospitalario” (“The protection of pregnant workers exposed to ionising radiation in hospitals and clinics.”) The intent of this publication was to explain the risks associated with prenatal exposure to radiation of this type and restrictions on occupational activity for pregnant women in medical radioactive facilities, establishing directives for radiation dosage surveillance among pregnant women at work, as well as providing information to all those professionals who could be exposed to ionising radiation.

As the aforementioned document points out, the factors defining risk of exposure to ionising radiation are gestational age, absorbed dose, and the dose rate of exposure.

Below are summarised the various damages that may result from ionising radiation according to gestational development time of exposure as discussed in the CSN article. The results obtained experimentally in animal models establish that equivalent doses between 100-200 mSv in the pre-implantation phase (phase from conception to implantation, i.e., the first two weeks) are responsible for 1% to 2% of fatal cases, although it must be taken into account that the prevalence of spontaneous abortions in this phase, even without exposure to this radiation, is high –as high as 30% according to several authors.

In the organogenesis phase (between week 3 and 8 of development) malformation of organs developing at that time may result. Skeletal, ocular, and genital anomalies have been described, as well as growth retardation in experimental models performed in animals. The minimum required dose in these experiments to provoke an increase in malformations in animals is 500 mSv, from which the threshold dose (below which this does not occur) in humans is set at 100-200 mSv.

Between weeks 8 and 15 of development, the most significant damage observed is mental retardation, which could extend from a reduction in intelligence quotient (IQ) to severe mental retardation. The threshold dose below which mental retardation is not observed is 120-200 mSv.

In the period between weeks 16 and 25, the previously described effects have been seen, but the risk is significantly lower, and thus the threshold value for severe mental retardation is estimated at 500 mSv.

In the last trimester of pregnancy, no radiation-induced incidence of malformations or mental retardation is expected, although the probability of children under the age of five developing cancer slightly increases.

It has been demonstrated that deterministic effects, such as abortion, congenital malformations, or mental retardation, do not take place if the embryo receives doses under 100 mSv. It must be clear that these effects may occur due to other causes not related to ionising radiation, such as the mother’s age, consumption of medicines, alcohol or tobacco, family history, infections during pregnancy, pregnancy characteristics, labour…

On the other hand, regarding statistical effects, it is known that radiation is one of the many agents that can cause cancer, but this probability is depreciable at doses of 1 mSv.

To be able to apply the appropriate protective measures, it is essential that the pregnant worker inform the business owner of her condition as soon as possible, as established in the legislation, as this person is responsible for ensuring that working conditions are such that the equivalent dose to the foetus does not

exceed 1 mSv. In practice, this limit translates into an equivalent dose to the abdominal surface (lower trunk) of the woman of less than 2 mSv through to the end of the pregnancy. (Spanish Nuclear Safety Council Working Group, 2002).

In 1928, an international commission was established that was to become later the International Commission on Radiological Protection (ICRP). It is a body dedicated to establishing the philosophical bases of radiological protection, providing recommendations for the safe use of ionising radiation, promoting progress in the science of radiological protection and dealing with all situations in which humans may be exposed to this radiation. The ICRP drafts numerous documents to disseminate knowledge regarding ionising radiation, such as the Annals of the ICRP, annual reports, and independent documents of interest.

Specifically, Publication ICRP-84 (2001), "*Pregnancy and Medical Radiation*", discusses the issue of pregnancy and medical radiation from an overall, and not just occupational, standpoint, in order to present the various effects the foetus could suffer owing to irradiation of the uterus during pregnancy. Regarding effects on the central nervous system, it has been studied that in the period between weeks 8 and 25 of pregnancy, it is especially sensitive to radiation, specifically foetal doses greater than 100 mGy could result in a measurable decrease in IQ, and with a dose of 1 Gy, there is an increased probability of severe mental retardation. The sensitivity is, however, greatest between weeks 8 and 15, when foetal doses of 1 Gy could cause a decrease in 30 IQ points, as well as a 40% probability of having children with severe mental retardation. Regarding risks of leukaemia and childhood cancer, the ICRP document points out that a recent analysis of many of the epidemiological studies on prenatal X-ray exposure and childhood cancer establish a relative risk of 1.4 for foetal doses of 10 Gy. However, it also states that the best methodological studies suggest that the risk is probably lower. The conclusion presented is that, even if relative risk were of 1.4, the probability of childhood cancer due to uterine radiation would be very low (around 0.3-0.4%), as the natural incidence is of this same order (0.2-0.3%).

The document dedicates a chapter to controlling occupational ionising radiation exposure in pregnant workers. It establishes that, once the business owner is informed of a woman's condition, he/she must adopt the necessary measures to ensure that the additional dose received by the foetus is kept below 1 mGy during the entire pregnancy. This restriction does not imply that women in these jobs must abandon them during their pregnancy; it simply means that working conditions must be such that they guarantee their safety and that of their foetus. The recommended dose limit refers to the foetal dose and is not comparable to the dose measured with a personal dosimeter in women workers, as this could lead to overestimation of the foetal dose by 10 times or more.

Recommendations are summarised in the last chapter, where the importance of medical professionals knowing the effects of ionising radiation risks to the foetus in the various phases of pregnancy is strongly emphasised, among others. (ICRP, 2000).

Table 6: Area of Risk: Physical Risks

Specific risk	Activity, characteristics and moment of exposure	Damages or alterations in pregnant workers the risk of which is increased or may be increased	Foetal damages or alterations the risk of which is increased or may be increased
Non-ionizing radiation	Ultrasound		Spontaneous abortion
	ELF-EMR[8] (exposures ≥4μT)		Childhood acute leukemia
Ionizing radiation	During the first trimester of pregnancy		Spontaneous abortion and low birth weight
	Gestation period: 3rd-8th week. If the threshold dose is exceeded (100-200 mSV)		Malformations
	Gestation period: 8th–15th week. If the threshold dose is exceeded (120-200 mSV)		Lower IQ, severe mental retardation.
	Gestation period: 16th-25th week. If the threshold dose is exceeded (500 mSV)		Lower IQ, severe mental retardation.
	Third trimester of pregnancy		Cancer (before 5 years of age)

[8] *TN: Extremely Low Frequency Electromagnetic Radiation*

5.6 Biological Risks

One of the primary risk groups in the occupational environment is biological risk. The presence of biological agents in the workplace is a risk that needs to be identified in many businesses. There are certain occupations where the biological risk is more evident: healthcare, cleaners, food industry, etc.
The references discussed below exclusively cover those agents on which research studies published between 2000-2010 are based, and which meet the search criteria discussed above in the methodology. Therefore, the annotated list of agents below cannot be considered in any way exhaustive.

Cytomegalovirus (CMV)

Cytomegalovirus belongs to the viral group *Herpesviridae*. The most recognised effects in foetuses of exposed women are: hearing loss and congenital cytomegalovirus infection in newborns. Virus transmission after primary maternal infection occurs in 15% of cases and 5% of infected cases show symptoms. (Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchman SD, *Hospital Infection Control Practices Advisory Committee*,1998).

Cytomegalovirus is a major cause of central nervous system damage leading to sensorineural hearing loss, mental retardation, and cerebral palsy. The objective of this Italian study was to analyse the type of organ involvement and understand the histopathogenesis of damage in foetuses of women with a CMV-highly positive amniotic fluid. In the study, thirty four foetuses were analysed. Three foetuses died in utero naturally, and thirty one remaining pregnancies were effectively terminated at 20-21 weeks gestation. CMV antigens appeared in the following organs: placenta (100%), pancreas (100%), lung (87%), kidney (87%), liver (71%), brain (55%), and heart (44%). An inflammatory response was found in practically all cases, and the severity of the inflammatory response was directly correlated with the organ damage. Brain damage with necrosis was observed in 33% (9/27) of cases and mild leukoencephalopathy was seen in 22% (6/27) of foetuses studied. (Gabrielli L, Bonasoni MP, Lazzarotto T, Lega S, Santini D, Foschini MP et ál., 2009).

Hepatitis B and C

Hepatitis B Virus (HBV) has various routes of transmission. One of these is vertical transmission. Among the consequences of this transmission is the development of chronic Hepatitis in the newborn. Specifically, 90% of foetuses are HBeAg seropositive and between 0-25% of cases will be HBeAg seronegative. (Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchman SD, *Hospital Infection Control Practices Advisory Committee*, 1998).

Regarding Hepatitis C (HCV), this same group found that in materno-foetal transmission, between two and five percent of offspring will acquire Hepatitis. (Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchman SD, *Hospital Infection Control Practices Advisory Committee*, 1998).

In an Israeli study, the pregnant population between 1988 and 2007 was analysed. The aim was to examine the impact of maternal Hepatitis B and C virus on pregnancy outcome. Two groups were compared: HBsAg and/or anti-HCV seropositive women and all other women not affected by these viruses. Logistic regression models were used. 0.4% of women were identified as seropositive for Hepatitis (749 of 186,619 deliveries). Among infected mothers, there were higher rates of preterm deliveries (<37 weeks gestation; 11.5% vs. 7.9%, p <0.001), premature rupture of membranes (8.9% vs. 6.9%, p=0.026), placental abruption (1.5% vs. 0.7%, p=0.018), labour induction (33.9% vs. 28.1%, p <0.001) and Caesarean deliveries (19.0% vs. 13.2%, p <0.001). Additionally, higher rates of perinatal mortality (2.3% vs. 1.3%, p=0.016), congenital malformations (7.2% vs.. 5.1%, p=0.01) and low birthweight (<2500 kg; 10.4% vs. 7.8%, p=0.009) were noted in newborns of Hepatitis carriers compared with the control group. (Safir A, Levy A, Sikuler E, Sheiner E, 2010).

Herpes simplex virus (HSV)

Herpes simplex virus can produce spontaneous abortion, low birthweight, preterm birth, mucocutaneous lesions, encephalitis, and congenital malformations. (Davies JK, Gibbs RS, 2008).

It has been observed that the risk of HSV transmission through the birth canal is of between 33 and 50%, when the mother is infected. There is also a recurrent risk of 4%. (Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchman SD, *Hospital Infection Control Practices Advisory Committee*, 1998).

Herpes simplex virus causes a rare but devastating disease in newborns that could present varied symptoms: from skin and eye infection, to shock, organ failure, brain infection, and death. Newborn herpes infection is an uncommon complication of active genital herpes in the mother around the time of delivery or after direct contact with a herpes blister (“fever blister”, “cold sore”) of an infected caregiver.
Herpes simplex virus (HSV) is a rare but serious neonatal pathogen. The incidence of HSV infection varies from 1:3,500 to 1:5,000 live births in the United States (Sullivan-Bolyai J, Hull HF, Wilson C, Corey L, 1983; Gutierrez KM, Falkovitz Halpern MS, Maldonado Y, Arvin AM 1999), to 1:10,000 to 1:50,000 live births in the United Kingdom (Tookey P, Peckham CS, 1996) and Australia (Jones CA, Isaacs D, McIntyre P, Cunningham A, Garland S, 2006). Type 1 and 2 HSV can cause neonatal illness and the predominant type varies around the world (Garland S, Jones CA, 2001). The majority of newborns contract the infection via infection during delivery, between 5% and 10% are infected post-birth by a caregiver and close to 5% are infected in utero (Whitley RJ, 1993). Neonatal infection can produce localised skin, eye, or mouth infection, encephalitis, pneumonia, or disseminated disease (Whitley RJ, 1993).

The highest frequency for neonatal illness due to HSV occurs among the offspring of women who acquired their first genital HSV infection without seroconversion completion before labour (Brown ZA, Selke S, Zeh J, Kopelman J, Maslow A, Ashley RL, et ál., 1997). The use of foetal-scalp electrodes is an additional risk factor for neonatal HSV infection (Whitley RJ, 1993). The diagnosis for neonatal HSV infection is difficult as more than 70% of women with genital herpes are unaware of their infection (Brown ZA, Benedetti J, Ashley R, Burchett S, Selke S, Berry S, et ál., 1991). As such, there is often a significant delay between the appearance of symptoms in the newborn and the commencement of antiviral treatment. (Jones Ch, Walker K, Badawi, N, 2009).

Human Immunodeficiency Virus (HIV)

Vertical transmission of *HIV* represents the most common means by which children acquire *HIV*. This transmission may take place in utero, intrapartum, or through breast milk transmission after birth. Hundreds of thousands of children are infected in this way each year, and most of them live in developing countries. Some significant progress has been made in preventing mother-to-child transmission when the newborn is still in utero or intrapartum. (Horvath T, Madi BC, Iuppa IM, Kennedy GE, Rutherford G, Read JS, 2009).

Other sources estimate the risk of perinatal transmission of *HIV* between 9% and 30% in mothers carrying the virus. It is estimated that the newborn will develop AIDS, after this primary infection, by age 2-3. (Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchman SD, *Hospital Infection Control Practices Advisory Committee*, 1998).

It is estimated that 1,200 children under the age of fifteen contract *HIV* every day (420,000 new infections per year) (UNAIDS, 2008). The majority of children with *HIV* acquire the infection through mother-to-child transmission in utero, around labour and in delivery, or through breastfeeding after birth (Read JS, 2005a). Children born to mothers with HIV have high rates of mortality, independently of their own infection state (Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F, *Ghent International AIDS Society (IAS) Working Group on HIV Infection in Women and Children*, 2004).

In a grouped analysis of randomised trials from sub-Saharan Africa, children born to mothers in advanced stages of *HIV* infection were at considerably greater risk of death compared to those of mothers with early *HIV* infection (independently of the *HIV* infection state of the child), and this association was even stronger for uninfected children. (Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F, *Ghent International AIDS Society (IAS) Working Group on HIV Infection in Women and Children*,2004). In addition, the time of acquiring *HIV* infection was associated with mortality, as children who were infected prior to their fourth week of life had an increased risk of death during the first 12-24 months of life following infection than those who acquired the infection after the fourth week of life (through breastfeeding). (Horvath T, Madi BC, Iuppa IM, Kennedy GE, Rutherford G, Read JS, 2009).

Measles

Measles is an infectious and exanthematous disease caused by a paramyxovirus of the genus *Morbilivirus*. The World Health Organisation describes 23 genotypes, grouped into eight distinct serotypes. The symptoms include exanthema in the form of a red blotchy rash, fever, and general weakness. The complications that could result from this infection are: blindness, pneumonia, encephalitis, and death.

The samples that appear in the studies in this systematic review regarding congenital measles are very small. One of the possible causes is the high immunisation rate among mothers in the countries were the studies have been conducted, due to the implementation of specific vaccines several years ago. In the reviewed articles regarding vertical transmission of measles from mother-to-child, the consequences in offspring depend particularly upon the time of transmission.

In Atlanta, a study was conducted to describe the effects of measles in pregnancy. 58 cases of pregnant women with measles were identified from several hospitals. 60% of them were hospitalised for measles, 26% were diagnosed with pneumonia, and 3% died of measles complications. Excluding three induced abortions, 31% of pregnancies ended prematurely: five were spontaneous abortions and thirteen were preterm deliveries. Of these 18 cases, all but two, terminated within fourteen days of rash onset. Two term infants were born with minor congenital anomalies, but their mothers had measles late in the third trimester. No newborns were diagnosed with congenital measles. The research team concluded, after analysing the cases, that the incidence of death and other complications from measles among pregnant women is higher than that for age-comparable, non-pregnant women. Measles in pregnancy may lead to high rates of foetal loss and prematurity, especially in the first two weeks after the onset of rash. (Eberhart-Phillips JE, Frederick PD, Baron RC, Mascola L, 1993).

In another study conducted in Japan from late 2000 to early 2001, eight cases of pregnancyal measles were described. The idea was to describe in detailed form the clinical course of the disease and the effects on the mother and foetus. Three of the four cases before 24 weeks of pregnancy ended in spontaneous abortion or stillbirth. In these cases, pregnancy termination was sudden. In contrast, the four pregnancies where measles infection took place after 25 weeks of pregnancy ended with half of the children born healthy and the other half presenting congenital measles.
No maternal death took place and the complications among mothers were two cases of pneumonia and one hemorrhagic shock case. The study's authors conclude that gestational measles pose a potential risk to the foetus and is one of the serious complications that can occur during pregnancy. (Chiba ME, Saito M, Suzuki N, Honda Y, Yaegashi N, 2003).

In this review, we present a third study carried out in Houston, where twelve pregnant women and one parturient were hospitalised with measles. Seven of the mothers presented pneumonia; another seven, hepatitis; four, premature labour; one, spontaneous abortion; and one died. The foetuses of the four most severe cases of the thirteen women, who presented measles complicated with pneumonia, suffered abortion of prematurity. The research team associated the gravity of the mothers to more serious consequences in pregnancy outcome. The clinical course of disease in pregnant women suggests that pregnancy is associated with more serious complications for patients. (Atmar RL, Englund JA, Hammill H, 1992).

Parvovirus

Parvovirus B19 is a virus in the family *Parvoviridae*. Infection may be asymptomatic in mothers, and still produce foetal loss. The consequences for foetuses are caused by an increased production of red blood cells and an inability of the immune system to control infection. This causes erythroblastosis that can cause spontaneous abortion or non-immune hydrops fetalis. Prevalence studies indicate that between 25-75% of pregnant women are seropositive. The rate of vertical transmission is about 30% and the incidence of foetal loss varies, according to studies, from 1.7% to 9%. In general, infection during pregnancy leads to the birth of a healthy child. Increased mortality corresponds to those cases where the mother was infected in the first trimester of pregnancy. Maternal antibodies transmitted to the foetus are insufficient to eliminate the virus, which continues replicating for weeks, leading to foetal loss at approximately 4-6 weeks after maternal infection, generally in the third or fourth month of pregnancy. Infection in the second trimester is associated predominantly with hydrops fetalis; aplasia of reticulocytes provokes severe anaemia with cardiac failure, generalised oedema, and potentially death, occurring late following maternal infection (up to 12 weeks). (García AM, Lozano MC, Fernández C, 2001).

Transplacental transmission of parvovirus B19 to the foetus is an important cause of intrauterine death, abortion, stillbirth, and non-immune hydrops fetalis. These adverse outcomes can occur after symptomatic and asymptomatic maternal infection. Only rare cases of congenital malformations and foetal disease in live-born infants have been associated with B19 virus infection. (Eis-Hübinger AM, Dieck D, Schild R, Hansmann M, Schneweis KE,1998).

The estimated risk of foetal infection by *Parvovirus* B19 with maximum adverse outcomes is estimated between 3% and 9%. (Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchman SD, *Hospital Infection Control Practices Advisory Committee*, 1998)

In an Italian study, five cases of intrauterine foetal death were analysed. In four of the cases, foetal death occurred in the absence of previous symptoms in the mother. In the fifth case, the patient was hospitalised following an ultrasound diagnosis of foetal hydrops and foetal death took place five days later. Three of the cases occurred in the second trimester, and the other two, in the third trimester. Foetal infection presented in

those corresponding to the second trimester and one from the third trimester. In the last case, foetal death was characterised by placental involvement. (Silingardi E, Santunione AL, Rivasi F, Gasser B, Zago S, Garagnani L, 2009).

Rubella

Rubella is a disease caused by a virus from the genus Rubivirus of the family *Togaviridae*. The disease is contagious and typically causes a scarletiniform rash, cervical lymphadenopathy, and mild constitutional symptoms, but in older children and adults, especially women, it may be more severe, with joint involvement and purpuric rash. (Edlich RF, Winters KL, Long WB, Gubler KD, 2005).

50% of cases are asymptomatic. If the infection occurs in the first trimester of pregnancy, the virus can pass transplacentally, infecting the foetus and producing severe anomalies (abortions, deafness, cataracts, mental retardation,…) These symptoms are described as congenital rubella syndrome (CRS). (Santos-Sancho JM, Gil-Prieto R, Álvaro-Meca A, Gil-de Miguel A, 2010).

Infection during the first 12 weeks of pregnancy results in congenital infection and/or miscarriage in 80-90% of cases. Congenital rubella syndrome (CRS) involves multiple organ systems and has a long period of active infection and virus shedding in the postnatal period. (Edlich RF, Winters KL, Long WB, Gubler KD, 2005).

It is estimated that each year, there are 100,000 cases worldwide. (Robertson SE, Featherstone DA, Gacic-Dobo M, Hersh BS, 2003).

Congenital rubella syndrome occurs in 45% to 50% overall. 90% of cases occur between the first and twelfth week of pregnancy. (Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchman SD, *Hospital Infection Control Practices Advisory Committee*, 1998).

Rubella virus can affect the foetus at any point during gestation, but adverse effects are rarely noted after the 16th week of pregnancy. The most common abnormalities in congenital rubella syndrome include hearing loss, mental retardation, cardiac malformations, and eye abnormalities. Other typical manifestations include diabetes mellitus, thyroid disease, glaucoma, and other delayed manifestations. (Freij BJ, South MA, Sever JL, 1988).

Varicella-zoster virus (VZV)

Varicella is a common, highly contagious infection, caused by varicella-zoster virus (VZV) (Brunei PA, 1987). It is typically an early childhood disease with 90% of cases occurring in children of 1-14 years of age (Preblud SR, Orenstein WA, Bart KJ, 1984). The disease is more serious in newborns (Gershon AA, 1975; Meyers JD,

1974), adults (Preblud SR, 1981) and immuno-compromised individuals (Feldhoff CM, Balfour HH Jr, Simmons RL, Najarian JS, Mauer SM, 1981; Feldman S, Hughes WT, Daniel CB, 1975).
Varicella is generally self-limiting in small children and is manifested by fever, mild constitutional symptoms, and vesicular skin rash. Complications from varicella vary and may occur in 5% to 10% of all patients. These are more common in newborns, adults, and immuno-compromised individuals (Preblud SR, Orenstein WA, Bart KJ, 1984; Rotbart HA, Levin MJ, Hayward AR, 1993). These adverse effects primarily affect the skin, nervous system, and respiratory system (Drwal-Klein LA, O'Donovan CA, 1993; Mouzard A, 1998). The most frequent complication is secondary bacterial infection of cutaneous lesions (Mouzard A, 1998; Preblud SR, Orenstein WA, Bart KJ, 1984). In the case of neurological damage, the most frequent types are: cerebellar ataxia and encephalitis; in the respiratory system: pneumonia and upper respiratory tract infections (particularly otitis media). (Klassen TP, Hartling L, Wiebe N, Belseck EM, 2008).

When varicella is contracted by a pregnant woman, the effects on the foetus could include congenital malformations of various organs (skin, limb, central nervous system, etc.) and development of varicella. Affected foetuses number about 25%. 0-4% of cases develop congenital syndrome. (Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchman SD, *Hospital Infection Control Practices Advisory Committee*, 1998).

Varicella virus in pregnancy can cause significant morbidity for the pregnant woman and congenital varicella syndrome. The incidence of this syndrome as a result of varicella contraction by the mother during the first two trimesters of pregnancy is less than 1% across multiple cohort studies. In contrast, infection in the third trimester is not associated with this syndrome. In this case, the newborn could develop herpes zoster during the first two years of life. Varicella infection just before or after delivery presents a high risk for disseminated varicella in the infant. (Smith CK, Arvin AM, 2009).

During pregnancy, varicella may have serious consequences for pregnant women and for the foetus. Specifically, pregnant women who contract varicella are at increased risk of pneumonia. Between the 5th and 24th weeks of pregnancy, the foetus may be affected by congenital varicella syndrome. In the last few weeks of pregnancy and shortly after delivery, the virus can cause chickenpox in the newborn. The consequences may be lethal for the newborn in the case of infection during the five days before and two days following delivery. In this case, disseminated neonatal varicella is expected. (Wutzler P, Sauerbrei A, 2007).

Other authors expand the timeframe of acquisition of congenital varicella syndrome (CVS) for the foetus to the first two trimesters. Following infection, in the first 20 weeks, the incidence of this syndrome is estimated to be about 2%. In the literature to date, nearly one hundred infants born with signs of CVS have been reported. The symptoms consist of skin lesions (76%), neurologic abnormalities (60%), eye diseases (51%),

and skeletal anomalies (49%). 30% of infants born with these lesions died in the first months of life. (Sauerbrei A, Wutzler P, 2000).

Tuberculosis

Tuberculosis is an infectious disease caused by various species of the genus *Mycobacterium*. The most common species causing tuberculosis is *Mycobacterium tuberculosis* or Koch's bacillus, although other species of the same genus exist that also cause the disease in immuno-compromised patients.

Tuberculosis contracted by a pregnant woman could cause hepatomegaly, pulmonary abnormalities, and CNS abnormalities in the foetus. (Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchman SD, *Hospital Infection Control Practices Advisory Committee*, 1998).

In a transverse retrospective study carried out in Taiwan, authors aimed to determine whether tuberculosis in pregnant women was responsible for certain adverse pregnancy outcomes: low birthweight or preterm birth. Between 2001 and 2003, 761 women gave birth who had received medication treatment for tuberculosis during their pregnancy. The control group was made up of 3,805 unaffected women in the same period. Logistic regression analyses were performed to analyse the data.
Mothers diagnosed with tuberculosis during pregnancy were at much greater risk of having a low birthweight baby: 8.5% versus 6.4% (p: 0.033) and preterm births who were small-for-gestational-age: 19.7% versus 16.7% (p: 0.048). There were no significant differences among the two groups in the case of preterm births. The adjusted odds ratio of having low birthweight offspring was 1.35 (CI 95%: 1.01-1.81) and for preterm births small-for-gestational age was 1.22 (CI 95%: 1.00-1.49) compared with the control group. (Lin HC, Lin HC, Chen SF, 2010).

A Swedish study analysed the risk of contracting tuberculosis in relation to birth weight and ponderal index. To do so, twins born in Sweden between 1926 and 1958 were analysed using a cohort design. The sample included 21,596 infants. Using a cohort design, the risk of contracting tuberculosis was 11% lower for every 500 g more of birthweight (p: 0.05), and 8% lower for every 0.2 of ponderal index (p: 0.08). This association was stronger in male individuals (87% risk reduction, p: 0.02). (Villamor E, Iliadou A, Cnattingius S, 2010).

Toxoplasmosis

Toxoplasmosis is a generally asymptomatic parasitic disease. It is caused by the protozoan *Toxoplasma gondii*. This agent may be transmitted to the mother orally, in undercooked meat or in contaminated food and drink. However, infection in pregnant women may cause congenital infection in offspring, which could result in mental retardation and blindness in the newborn. The risk of congenital toxoplasmosis is related to the gestational timeframe (Dunn D, Wallon M, Peyron F, Petersen E, Peckham CS, Gilbert RE, 1999). The risk of transmission to the foetus is highest in the third trimester, but the disease is more serious if acquired in the

first trimester (Hohlfeld P, Daffos F, Thulliez P, Aufrant C, Couvreur J, Mac Aleese J et al, 1989; Peyron F, Wallon M, Liou C, Garner P, 2008).

Toxoplasma can cause fatal consequences for the foetus. Foetal consequences include: hearing loss, mental and psychomotor retardation, haematological abnormalities, hepatosplenomegaly and death. (Montoya JG, Remington JS, 2008).

The majority of newborns with congenital toxoplasmosis do not tend to present specific symptoms at birth, as these appear between the third week and third month of life. Symptoms could include chorio-retinitis, hydrocephaly, intracranial calcifications, pneumonia, lymphadenopathy, hepatosplenomegaly, thrombocytopenia,… If diagnosis and treatment is not provided quickly, encephalitis and systemic toxoplasmosis could ensue quickly and fatally.

For this reason, children affected by gestational toxoplasma infection must be examined, for clinical sequelae, during the first year of life. (Di Carlo P, Mazzola A, Romano A, Schimmenti MG, Colicchia P, Bellipanni P, Titone L, 2005).

In Palermo (Italy) retrospectively analysed pregnancy management of 54 women with Toxoplasma gondii (TG) and prospectively enrolled their infants to compare prenatal management with postnatal clinical outcome. The prospective study involved a 48-month follow-up (1999-2004). Infection was dated to the first trimester for 45% of cases (24), to the second trimester for 33% of cases (18) and to the third trimester for 22% of cases (12). The rate of maternal-foetal transmission was 17.2%. Prenatal diagnosis from amniotic fluid was performed in 25/54 pregnant subjects and showed positive results in six cases. Despite diagnosis of *Toxoplasma* infection, nine women were not treated and only two presenting positive amniocentesis received treatment. In ten of 55 cases, enrolled infants were infected and half of them were preterm and/or small-for-gestational-age babies at birth. None showed signs of toxoplasmosis at birth, but four had abnormalities during the follow-up period. Nine of ten infected children were born to mothers who had undergone neither amniocentesis nor combined therapy. (Di Carlo P, Mazzola A, Romano A, Schimmenti MG, Colicchia P, Bellipanni P, Titone L, 2005).

Table 7: Risk Area: Biological risks

Specific risk	Activity, characteristics and moment of exposure	Damages or alterations in pregnant workers the risk of which is increased or may be increased	Foetal damages or alterations the risk of which is increased or may be increased
Cytomegalovirus (CMV)			Sensorineural hearing loss, congenital syndrome in infants, mental retardation, cerebral palsy, abortion by CMV-infected foetal organs
Hepatitis B		Hepatitis	Chronic Hepatitis, preterm birth, premature rupture of membranes, placental abruption, labour induction, caesarean sections, higher rates of perinatal death, congenital malformations, low birth weight
Hepatitis C		Hepatitis	Chronic Hepatitis, preterm birth, premature rupture of membranes, placental abruption, labour induction, caesarean sections, higher rates of perinatal death, congenital malformations, low birth weight
Herpes simplex virus (HSV)			Spontaneous abortion, low birth weight, preterm birth, mucocutaneous lesions (skin, eyes and mouth), sespis, encephalitis, shock, organ failure, congenital malformations, pneumonitis, death. Herpetic infection
Human Immunodeficiency Virus (HIV)			AIDS, death
Measles		Measles (redness, fever and weakness), pneumonia, hepatitis and death	Spontaneous Abortion, preterm birth, congenital measles, blindness, encephalitis
Parvovirus			Erythroblastosis, spontaneous abortion, non-immune hydrops foetalis, severe anemia, heart failure, generalised oedema, intrauterine death

Specific risk	Activity, characteristics and moment of exposure	Damages or alterations in pregnant workers the risk of which is increased or may be increased	Foetal damages or alterations the risk of which is increased or may be increased
Rubella		Scarlatiniform rash, cervical lymphadenopathy, limb involvement, purpuric rash	Congenital rubella syndrome (abortion, hearing loss, cataracts, mental retardation, heart malformations, diabetes mellitus, thyroid disease, glaucoma)
Varicella-zoster virus		Varicella (fever, itchy vesicular rash, cerebellar ataxia, encephalitis, pneumonia and infections of the upper respiratory tract, secondary bacterial infection of skin lesions)	Congenital malformations (skin, limbs, central nervous system), congenital varicella syndrome (skin lesions, neurological involvement, eye diseases, bone abnormalities), herpes zoster, varicella (fever, itchy vesicular rash, cerebellar ataxia, encephalitis, pneumonia and infections of the upper respiratory tract, secondary bacterial infection of skin lesions), death
Tuberculosis		Tuberculosis	Hepatomegaly, lung disease, central nervous system disease, low birth weight, preterm birth for gestational age
Toxoplasmosis			Hearing loss, mental illness, psychomotor retardation, blood disorders, hepatosplenomegaly, chorioretinitis, hydrocephalus, cerebritis and intracranial calcifications , pneumonitis, lymphadenopathy, thrombocytopenia, fatal systemic toxoplasmosis, death

6. Conclusions

All sectors considered, healthcare activities in the services sector were the most studied, with congenital abnormalities (urogenital, neurologic, and cardiovascular), risk of preterm birth, and spontaneous abortion being the most prevalent outcomes of interest.
As for other service sector activities, researchers have also shown an interest in the association of various foetal malformations in hairdressers and housekeepers' offspring.
Leather and footwear manufacturing stands out among the industrial branches that were examined by the studies reviewed. The results of the articles examined indicate an increased risk that the offspring of workers in this industry present oral clefts and musculoskeletal disorders.
Certain studies focused on other industries, such as textile dyeing, the manufacture of metallic or electrical products, and the petrochemical industry, have revealed the association between these activities and the increased risk of congenital abnormalities or spontaneous abortions.
In addition, there are numerous references studying the risks to which agricultural workers may be exposed during pregnancy. Specifically, the articles analysed indicate a possible association between this activity and certain malformations in offspring.

In parallel, the analysis of the evidence found within this systematic review has demonstrated the association between the exposure to physical, chemical, and biological agents, and occupational conditions, etc., with the occurrence of damages to the health of the pregnant worker and her offspring.

The risk of spontaneous abortion increases with exposure to ethylene oxide, nitrous oxide, anaesthetics, antibiotics, and pesticides. It is also associated with moderate-to-high workloads and elevated stress levels.
The onset of preterm labour is associated with exposure to ethylene oxide. It is also associated with prolonged standing for a significant part of the workday, heavy lifting, long workdays, remaining on rotating shifts or night shifts, moderate or high physical exertion, and high stress levels.
Preeclampsia is associated with lifting, rotating shifts or night shifts, moderate or high physical exertion, and high stress levels.
The birth of small-for-gestational-age infants is associated with lead exposure. It is also associated with prolonged standing for a significant part of the workday, rotating shifts, moderate or high physical exertion, long workdays, and high stress levels.
Various exposure types have been associated with congenital malformations: exposure to organic solvents increases the occurrence of oral clefts, cardiovascular malformations and urinary tract abnormalities in newborns; the birth of newborns with oral clefs is associated with exposure to lead and biocides; pesticides have generally been associated with various genetic abnormalities and, specifically, organophosphate pesticides are associated with the occurrence of spina bifida and hydrocephalus in newborns.

Antineoplastic drugs should have special consideration, as they increase the occurrence of ectopic pregnancies, and are associated with various congenital malformations in the foetus and foetal death.

The effect of ionising radiation on the foetus is a long-standing fact established well before the search period. Nevertheless, and despite the existence of universally accepted evidence, several studies have focused in the last decade on exposure to these physical agents and the appearance of congenital malformations and mental retardation in infants.

Concerning contact with certain infectious microorganisms, there is also consolidated evidence of their effects on the foetus, strongly proven in a multitude of studies prior to this review. However, references have been found that insist on the significant effects some maternal infections have on the foetus.

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