Woman and work: risk assessment

Alessandra Di Marzio[1]
Claudia Di Pastena[1]
Federica Sinibaldi[1]
Carmina Sacco[2]
Roberto Massimi[2]
Serafino Ricci[3]
Pasquale Ricci[3]
Teodorico Casale[2]
Benedetta Pimpinella[2]
Francesco Tomei[2]
Gianfranco Tomei[4]

[1] Department of Anatomy, Histology, Legal Medicine and Orthopaedics, OU of Occupational Medicine, "Sapienza" University of Rome, Italy
[2] Spin-off of "Sapienza", University of Rome, Italy
[3] Department of Anatomy, Histology, Legal Medicine and Orthopaedics, OU of Legal Medicine, "Sapienza" University of Rome, Italy
[4] Department of Psychiatric and Psycological Science, "Sapienza" University of Rome, Italy

Corresponding Author:
Francesco Tomei
Spin-off of "Sapienza" University of Rome
Viale Regina Elena 336
00161 Rome, Italy
E-mail: francesco.tomei@uniroma1.it

Abstract

The working environments have undergone profound changes over the years, introducing more and more the presence of women.
The Employer is required to carry out the assessment of the risks present in the company and to put in place protective measures towards workers. As part of the assessment, he must identify and assess regularly all the risks and dangers deriving from the activities usually carried out by the pregnant or puerperium or breastfeeding workers up to seven months after delivery.
The risk assessment must first focus on the identification of all work prohibited during pregnancy and up to seven months after delivery and must not neglect any other residual risk factors for pregnancy such as time, type of shifts, posture... For each of them optimal strategies must be developed, aimed to prevent and reduce any damage to the workers themselves.
There are also examples of risks present in some of the most common work activities carried out by female workers.

KEY WORDS: risk, risk assessment, work, working mother.

Introduction

In the previous monography we have seen how the working environments have undergone profound changes over the years, introducing more and more the presence of women. We have also found that in Italy the phenomenon of female employment, in proportion to the male counterpart, continues to grow over the years; therefore, the need to pay more and more attention to the protection of women's health, understood not only as a worker but also as a working mother, seems fundamental.

Assessment of specific risk and health protection

Article 28 of Legislative Decree 81/08 (1) states that the Employer is required to carry out the assessment of the risks present in the company and to put in place protective measures towards workers. As part of the assessment, he must identify and assess regularly all the risks and dangers deriving from the activities usually carried out by the pregnant or puerperium or breastfeeding workers up to seven months after delivery. This is in line with the general principles of European legislation regarding the protection of health in the workplace.
The specific rules aimed at protecting maternity apply to workers as defined by art. 2 paragraph 1 letter "e" of Legislative Decree 151/01 (2): "For workers, unless otherwise specified, we mean employees, including those with an apprenticeship contract, public administrations, private employers as well as workers of cooperatives".
The evaluation, carried out with extreme care and attention, must first consider the health of women and children, and must bring out the necessary measures to be implemented for the purposes of protection and prevention in the company. There are often fundamental changes such as changes in working time and working conditions or moving to a different job from the usual and certainly not at risk. The assessment must be carried out by the Employer in collaboration

with the company figures provided for by Legislative Decree 81/08 (1), in particular the Head of the Prevention and Protection Service and the Occupational Physician who plays a role of primary importance in the identification of the tasks considered as prejudicial and in the development of the consequent protective measures to be adopted. The Employer must then obligatorily inform the workers (they are not excluded the working mothers about their specific risks) and their Safety Representatives about both the results obtained, and the preventive and protective decisions to be implemented, as established by the article 36 of Legislative Decree 81/08 (1). The violation of the law is specifically sanctioned by art. 55 paragraph 5 letter c. When a worker informs the Employer that she is pregnant (it is advisable to do as soon as she is aware of it), the preventive assessment will allow to carry out the individualized risk assessment and, at the same time, to implement the appropriate protection measures (revision of the contents of the task, elimination of everything that could represent a risk, change of job, request to the Provincial Service of the Provincial Directorate of the Work of interdiction of the employee if is not possible to assign the worker, in any way, to activities not at risk and possible appointment of a substitute).

In fact, taking action as soon as possible on the elimination of risks is very important and avoids damages that could be irreparable, especially during the first delicate stages of gestation, where even minimal risks could lead to the onset of abortions or serious malformations.

The risk assessment must first focus on the identification of all work prohibited during pregnancy and up to seven months after delivery and must not neglect any other residual risk factors for pregnancy such as time, type of shifts , posture, etc.

For each of them optimal strategies must be developed, aimed to prevent and reduce any damage to the workers themselves.

Then the Employer will have to identify other tasks, compatible with the state of pregnancy and with the entire post-partum period, and assign the employee.

Finally, if the shift is not feasible, for organizational reasons or for lack of activities considered not detrimental to the well-being and health of the working mother and future baby, the Employer must start the procedure of early interdiction with the Provincial Service of the Provincial Labor Directorate.

It is a good rule for the Employer to plan in advance each of these operations, defining the procedures and establishing which are the company subjects involved (Responsible for the Prevention and Protection Service, Occupational Physician, Workers' Safety Representatives) and continuous, subsequently, to constantly monitor the condition of their own company; so they are able to intervene with absolute immediacy if there are any changes that require a reevaluation of the risks (already examined or of any new onset).

Summarizing the Employer must:

1. Evaluate and define the activities prohibited to the pregnant worker, using if necessary the collaboration of the classic company figures (Head of the Prevention and Protection Service, Occupational Physician, Representative of Workers for Safety)
2. Constantly update the Risk Assessment Document, listing the operations at risk and the activities not carried out by pregnant women and specifying for each one the prevention and protection measures that it intends to adopt:
   - modification of working conditions (including any changes in working hours, shifts, ...)
   - placement of the worker to another job not at risk
   - request for the issue of early termination of work for pregnant workers at the Provincial Service of the Provincial Labor Directorate
3. Provide information to all workers of child-bearing age of the results of the risk assessment carried out and of the importance of promptly communication of the state of pregnancy as soon as they are aware of it.

In Figure 1 there is a simplified outline of the main steps taken by the worker and the employer.

Analysis of some tasks

The following are examples of risks present in some of the most common work activities carried out by female workers (Tabella 1).

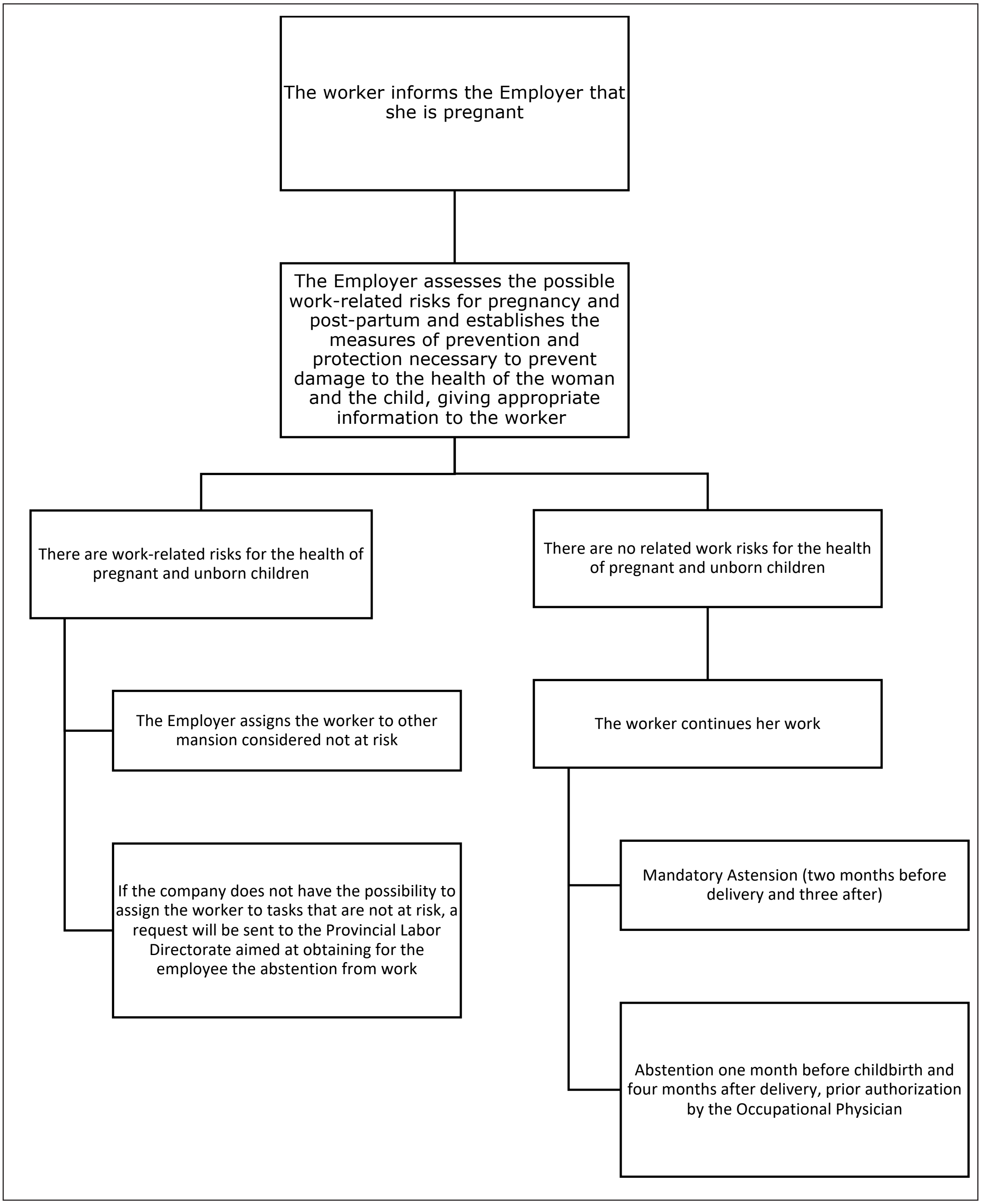

Figure 1 - Main steps taken by the worker and the employer.

Table 1. Examplesor risks present in work activities.

Working Activity	Risk Factors	Legislative Decree 151/01 (2)
Hairdresser Beautician	Incongruous Posture and/or prolonged standing posture Biological risk (blood, secretions, etc.) Chemical risk (toxic, irritant products)	**Ann. A letter G** → works that involve a station standing for more than half the time or that force a particularly fatiguing position, during gestation and until the end of the period of interdiction from work. **Ann. C** → Biological agents of risk groups 2 to 4 pursuant to art. 75. **Ann. A letter C** → those exposed to silicosis and asbestosis, as well as to other occupational diseases referred to in annexes 4 and 5 to Presidential Decree 1124/65 and subsequent amendments and additions (s.a.a.): during gestation and up to 7 months after birth. **Ann. C letter A point 3 a) e b)** → Chemical agents. a) substances labeled R 40; R 45; R 46 and R 47 pursuant to the directive n. 67/548 / EEC, ... b) chemical agents listed in Annex VIII of the Legislative Decree 19 September 1994, n. 626, and s.a.a.
Administrative employee	Prolonged standing posture Incongruous Posture	**Ann. A letters F e G** → F) heavy labor: during gestation and until the end of the period of interdiction from work; G) works that involve a station standing for more half of the time or obliging one position particularly fatiguing, during gestation and up at the end of the period of interdiction from work. **Art. 17 paragraph 1** → 1. The ban is anticipated at three months from the presumed date of delivery when the workers are employed in jobs that, in relation to the advanced state of pregnancy, are to be considered burdensome or prejudicial.
Cleaning company	Chemical, physical, biological risks Hard works Prolonged standing posture Incongruous postures Use of stairs	**Ann. A letter C** → C) those exposed to silicosis and asbestosis, as well as to other occupational diseases referred to in annexes 4 and 5 to Presidential Decree 1124/65 and s.a.a.: during gestation and up to 7 months after birth. **Att. C letter A point 3 a) e b)** → 3. Chemical agents. a) substances labeled R 40; R 45; R 46 and R 47 pursuant to the directive n. 67/548 / EEC, ... b) chemical agents listed in Annex VIII of the Legislative Decree 19 September 1994, n. 626, and s.a.a. **Att. C letter A point 1 c), g)** →1. Physical agents, when they are considered as agents that cause lesions of the fetus and / or risk causing the placental detachment, in particular: c) noise g) movements and positions of work, movements, both inside both outside the establishment, effort mental and physical and other physical discomfort related to the activity carried out by the workers referred to in art. 1. **Att. C** → Biological agents. Biological agents of risk groups 2 to 4 pursuant to art. 75.

to be continued

Continue from **Table 1.**

		Att. A letters F e G → F) heavy labor: during gestation and until the end of the period of interdiction from work G) works that involve a station standing for more half of the time or obliging one position particularly fatiguing, during gestation and up at the end of the period of interdiction from work. **Att. A letter E→** E) work on ladders and mobile and fixed scaffolding: during gestation and until the end of period of interdiction from work. **Ann. C letter A point 1 e) e f) →** 1. Physical agents e) non-ionizing radiation f) thermal stresses. **Art. 7 paragraph 4 →** 4. he worker is also moved to other tasks in cases where ... they ascertain that working or environmental conditions are detrimental to women's health.
Ironing or packaging of clothes or tissues	Microclimate and heat Chemical risk Heavy work, prolonged standing posture, incongruous postures Manual handling of loads	**Ann. A letter C →** C) those exposed to silicosis and asbestosis, as well as to other occupational diseases referred to in annexes 4 and 5 to Presidential Decree 1124/65 and s.a.a .: during gestation and up to 7 months after birth. **Ann. C letter A point 3 a) e b) →** 3. Chemical agents. a) substances labeled R 40; R 45; R 46 and R 47 pursuant to the directive n. 67/548 / EEC, ... b) chemical agents listed in Annex VIII of the Legislative Decree 19 September 1994, n. 626, and s.a.a. **Ann. A letter G →** G) works that involve a standing station for more than half the time or that force a particularly fatiguing position, during gestation and until the end of the period of interdiction from work. **Ann. A letter F →** F) heavy labor: during gestation and until the end of the period of interdiction from work. **Ann. C letter A point 1 b) →** b) manual handling of heavy loads involving risks, especially lumbar spine.
Ecological operator	Manual handling of loads Driving vehicles Biological risk Heavy work, prolonged standing position Noise	**Ann. A letter F →** F) heavy labor: during gestation and until the end of the period of interdiction from work. **Ann. C letter A point 1 b) →** b) manual handling of heavy loads involving risks, especially lumbar spine. **Ann. A letter O →** O) work on board ships, planes, trains, buses and any other means of communication in motion: during gestation and until the end of the period of interdiction from work. **Ann. C →** 2. Biological agents. Biological agents of risk groups 2 to 4 pursuant to art. 75. **Ann. A letter G →** G) works that involve a standing station for more than half the time or that force a particularly fatiguing position, during gestation and until the end of the period of interdiction from work.

to be continued

Continue from **Table 1.**

		Ann. C letter A point 1c) → A.1. Physical agents. c) noise; ...
Cashier, Saleswoman, Counters (gastronomy department)	Fixed and prolonged standing posture Movements repetitive upper limbs Stress and fatigue Thermal stresses (low temperatures)	**Ann. A letter G →** G) works that involve a standing station for more than half the time or that force a particularly fatiguing position, during gestation and until the end of the period of interdiction from work. **Ann. C letter A point 1 g) →** A. Agents. g) movements and positions of work, movements, both inside both outside the establishment, effort mental and physical and other physical discomfort related to the activity carried out by the workers referred to in art. 1. **Art. 7 paragraph 4 →** 4. The worker is also moved to other tasks in cases where ... they ascertain that the working or environmental conditions are detrimental to the health of the woman.
Driver or activity on means of transport	Vibrations Posture incongruous, obliged and fatiguing	**Ann. A letter O →** O) work on board ships, planes, trains, buses and any other moving vehicle: during gestation and until the end of the period of prohibition from work. **Ann. A letter G →** G) works that involve a standing station for more than half the time or that force a particularly fatiguing position, during gestation and until the end of the period of interdiction from work.
Cook	Heavy work, prolonged standing posture, incongruous postures Manual handling of loads Microclimate Chemical risk	**Ann. A letter F →** F) heavy labor: during gestation and until the end of the period of interdiction from work. **Ann. A letter G →** G) works that involve a standing station for more than half the time or that force a particularly fatiguing position, during gestation and until the end of the period of interdiction from work. **Ann. C letter A point 1 b) →** b) manual handling of heavy loads involving risks, especially lumbar spine. **Ann. C letter A point 1 e) e f) →** 1. A Physical agents e) non-ionizing radiation f) thermal stresses. **Art. 7 paragraph 4 →** 4. the worker is also moved to other tasks in cases where ... they ascertain that working or environmental conditions are detrimental to women's health. **Ann. A letter C →** C) those exposed to silicosis and asbestosis, as well as to other occupational diseases referred to in annexes 4 and 5 to Presidential Decree 1124/65 and s.a.a .: during gestation and up to 7 months after birth. **Ann. C letter A point 3 a) e b) →** 3. Chemical agents. a) substances labeled R 40; R 45; R 46 and R 47 pursuant to the directive n. 67/548 / EEC, ... b) chemical agents listed in Annex VIII of the Legislative Decree 19 September 1994, n. 626, and s.a.a.
		Ann. A letter F → F) heavy labor: during gestation and until the end of the period of interdiction from work.

to be continued

Continue from **Table 1.**

Teachers of kindergarten, primary school, support teachers, nursery schools	Fatigue, prolonged standing posture, incongruous postures, risk of violent reactions (support teachers) Manual handling of loads Biological risk	**Ann. A letter G →** G) works that involve a standing station for more than half the time or that force a particularly fatiguing position, during gestation and until the end of the period of interdiction from work. **Ann. A letter L →** L) the assistance and care of the sick in sanatoriums and departments for infectious diseases and for nervous and mental illnesses: during gestation and for 7 months after childbirth. **Ann. C letter A point 1 b) →** b) manual handling of heavy loads involving risks, especially lumbar spine. **Ann. C** → 2. Biological agents. Biological agents of risk groups 2 to 4 pursuant to art. 75.
Health sector	Fatigue, prolonged standing posture, incongruous postures Manual handling of loads Biological risk Chemical risk, (anesthetic gases, drugs, cleaning products, for sterilization) Risk of sudden and violent reactions from patients Non-ionizing radiation Ionizing radiation	**Ann. A letter F →** F) heavy labor: during gestation and until the end of the period of interdiction from work. **Ann. A letter G →** G) works that involve a standing station for more than half the time or that force a particularly fatiguing position, during gestation and until the end of the period of interdiction from work. **Ann. C letter A point 1 b) →** b) manual handling of heavy loads involving risks, especially lumbar spine. **Ann. C** → 2. Biological agents. Biological agents of risk groups 2 to 4 pursuant to art. 75. **Ann. A letter C →** C) those exposed to silicosis and asbestosis, as well as to other occupational diseases referred to in annexes 4 and 5 to Presidential Decree 1124/65 and s.a.a .: during gestation and up to 7 months after birth. **Ann. C letter A point 3 a) e b) →** 3. Chemical agents. a) substances labeled R 40; R 45; R 46 and R 47 pursuant to the directive n. 67/548 / EEC, ... b) chemical agents listed in Annex VIII of the Legislative Decree 19 September 1994, n. 626, and s.a.a. **Ann. A letter L →** L) he assistance and care of the sick in sanatoriums and departments for infectious diseases and for nervous and mental illnesses: during gestation and for 7 months after childbirth. **Ann. C letter A point 1 e) →** A. Agents. e) non-ionizing radiation. **Ann. A letter C →** C) those exposed to silicosis and asbestosis, as well as other occupational diseases referred to in annexes 4 and 5 to the Presidential Decree. 1124/65, and s.a.a .: during gestation and up to 7 months after delivery.

to be continued

Continue from **Table 1.**

		Art.8 → 8.1. Women, during pregnancy, cannot carry out activities in classified areas or, in any case, be engaged in activities that could expose the unborn child to a dose that exceeds one millisievert during the period of pregnancy. **Ann. A letter D →** D) work involving exposure to ionizing radiation: during gestation and for 7 months after delivery.

References

1. Decreto Legislativo 9 aprile 2008, n.81. Testo unico sulla salute e sicurezza sul lavoro. Available from: http://www.lavoro.gov.it/documenti-e-norme/studi-e-statistiche/Documents/Testo%20Unico%20sulla%20Salute%20e%20Sicurezza%20sul%20Lavoro/Testo-Unico-81-08-Edizione-Giugno%202016.pdf
2. Decreto legislativo 151/2001. "Testo Unico disposizioni in materia di tutela e sostegno della maternità e della paternità". Available from: http://www.camera.it/parlam/leggi/deleghe/01151dl.htm

Sentinel lymph-node biopsy in breast cancer

Walter Antonelli

Division of Surgery, Hospital of Macerata, Italy

Corresponding Author:
Walter Antonelli
Division of Surgery, Hospital of Macerata
Via Santa Lucia 2
62100 Macerata, Italy
E-mail: w.antonelli@libero.it

Abstract

Sentinel lymph-node biopsy is an innovative method for axillary staging in breast cancer patients, based on the concept that information about the status of the entire lymphatic drainage from a tumour site could be obtained by identification and sampling of a "sentinel node".
The aim of the study was to evaluate the impact of sentinel lymph-node biopsy in the management of patients with early invasive breast carcinoma.
Three hundred and forty-one patients with primary invasive breast carcinoma measuring less than 2 cm (less than 3 cm from January 2012) and clinically negative axillary nodes were recruited into the study.
Sentinel lymph-nodes were positive for metastases in 108/841 cases (31.7%). Micrometastases were found in 22 patients and isolated tumour cells in 1 case. The mean number of sentinel lymph-nodes removed was 1.8 per patient. The sentinel lymph-node was the only positive node in 57 of 108 patients (52.8%). The percentage of axillary recurrence in sentinel lymph-node-negative patients was 0%. The accuracy of sentinel lymph-node biopsy for axillary staging has been confirmed in many studies. Axillary recurrences after sentinel lymph-node biopsy range from 0 to 1.6% in many series, while axillary recurrence after axillary lymph-node dissection is about 0-3%. In our experience we observed no axillary recurrences in 283 patients with sentinel lymph-node biopsy alone, with a median follow-up of 33 months, confirming the accuracy of the procedure, and sentinel lymph-node negative patients with sentinel lymph-node biopsy alone are no more at risk for axillary recurrences than those undergoing axillary lymph-node dissection.

KEY WORDS: breast cancer, radionuclide imaging, sentinel lymph-node biopsy.

Introduction

Axillary lymph-node dissection (ALND) has been the surgical standard treatment of the axilla for breast cancer patients for decades.
It provides staging information as well as reducing axillary recurrence. The mammographic screening programs led to an increase in the number of women diagnosed with small primary breast cancer with axillary lymph-nodes free of metastases (1).
Sentinel lymph-node biopsy (SLNB) is an innovative method for axillary staging in breast cancer patients, based on the concept that information about the status of the entire lymphatic drainage from a tumour site could be obtained by identification and sampling of a "sentinel node"(2). The technique of SLNB is simple and concerns the identification and subsequent removal of the initial lymph-nodes upon which primary tumour drains. Histopathological evaluation of these nodes identify patients who are likely to be node negative, avoiding ALND and associated major problems such as pain, restriction of arm motion, neurovascular injury or chronic lymphoedemam (1-3). In the present study, we report our prospective experience from a community-based Breast Cancer Unit. We adopted SLNB as standard procedure for all patients presenting with early invasive breast cancer.
The aim of the study was to evaluate the impact of SLNB in the management of all women with early invasive breast carcinoma.

Materials and methods

Between March 2006 and October 2014, 341 patients presenting at our Institution with primary invasive breast carcinoma measuring less than 2 cm (less than 3 cm from January 2012) and clinically negative axillary nodes were entered into the study. Patients who had previous excision of the primary tumour or multicentric lesions were excluded. All patients were informed of the aims of the procedure and signed a consent form at the time of admission. The diagnosis of invasive breast carcinoma was performed by fine needle or core needle biopsy prior to surgery in all cases. The median follow-up was 53 months with a maximum time of 94 months and a minimum follow-up time of 23 months.

Table 1 - Characteristics of the 341 study patients.

Age	53,45
Range	27-83
Sex	
F	341
T (clinical)	
1	284
2	57
Surgical Procedure	
Quadrantectomy	341

Patients characteristics are summarized in Table 1.
The combined technique using radioactive tracer was performed to identify SLNB.
A detailed report of both methods used to identify the SLN is entirely described in a previous trial performed by the Authors (4). In short, on the day before surgery the radioactive tracer was injected peritumour by nuclear medicine physician if cancer was palpable.
Ultrasound or mammographic localization was used for not palpable lesions. Colloidal particles of human albumin (Nanocoll, Sorin Biomedica, Saluggia, Italy) labeled with 300 mCi of 99" Technetium were used as radioactive tracer. A two projection lymphoscintigram was used to identify any "hot spot" in the draining basin and skin marks were placed to facilitate axillary incision. Following removal of each node, the gamma probe was placed back into the wound to identify additional sentinel nodes. Suspicious palpable nodes detected during the procedure were excised also. All removed nodes were submitted for definitive histologic evaluation. Complete axillary dissection was performed whereas sentinel nodes contained metastases.
Histological examination of sentinel node was made on a few sections of the specimen such as lymph-nodes of a typical axillary dissection. The number of sections was increased, so that it was possible a complete examination of the whole sentinel node to detect micrometastases. Here is described the technique used at our Institution. First, the SLN is sliced at 2 mm intervals perpendicular to long axis. One routine haematoxylin-eosin (H&E) stained section is examined; if negative, serial level slices are performed through each block (two sections for each level, with aspacing of 50 micro between the following levels). One segment for each level is stained with H&E and one is for an additional immuno-histochemical analysis with keratins to compare cluster of histologically suspected cells. This approach offers a good sensitivity for detection of micrometastases and isolated tumoral cells with reasonable costs.
Recently there is a trend toward examining the entire lymph-node at 0.25 mm intervals with keratin, to be sure to detect ITC (isolated tumoral cells). This procedure has the highest rate of specificity (100%), but some controversy exists to accept it as standard protocol because the clinical significance of these occult metastases will be determined by long-term follow-up. For this reason the above mentioned method is not usually employed by the Authors.

Results

The SLNB was identified in 331 of 341 cases, calculating an identification rate of 97% with a false negative rate of 0%. More frequent histotype was ductal cancer (260 cases); a lymphovascular invasion was found in 128 patients, while neural invasion in 61. Positiveness for ER was frequent, 288 on 332 tested histological specimen; a similar report was recorded for PgR (283 positive cases). HER2/neu overexpression showed the following profile: 180 patients were negative, 30 patients had a 1+ positivity, 23 expressed a 2+ positivity and 35 patients had an intense and complete expression (3+). More histological findings are enlisted in Table 2.
SLNs were positive for metastases in 108 of 341 cases (31.7); micrometastases were found in 22 patients and isolated tumoral cells in 1 case. The mean number of SLNs removed was 1.8 per patients. See Table 2 for further nodes characteristics.
The SLN was the only positive no de in 57 of 108 patients (52.8%). The percentage of axillary recurrence in SLN negative patients was 0%.In our experience after the first 3 years in which SLNB was per-formed with an admission of 2-3days, starting from 2003 sentinel biopsy is carried out in Day-Surgery regimen.

Discussion

It has been well accepted that the node that receives drainage directly from the primary tumour "sentinel node" - is the first to be involved when lymphatic dissemination occurs (5). SLNB is a minimally invasive surgical procedure that can be easily carried out by experienced surgeons working in experienced teams, after a learning curve of about 20-30 cases and by maintaining experience by performing at least six procedures a month (6, 7). If general recommendations regarding the learning curve and the technique are followed, the procedure can be carried out easily by the sentinel node team that include breast surgeon, nuclear medicine physician and pathologist. The accuracy of SLNB for axillary staging has been confirmed in many studies; a review of 2160 patients with breast cancer showed that the radioactive tracer method was able to detect the sentinel lymph-node in 93.6% of cases (range 88-100%),with a predicted negative value of 96.6% (range 88-100%), an accuracy of 96.8% (range 96-100%), and a false negative rate of 3.8% (range 0-15%). An important data emerging from the review is that the higher the number of evaluated cas-

Table 2 - Tumour characteristics in 341 patients undergoing.

Histotype	
Ductal	260
Lobular	25
Ductal and lobular	17
Others	39
Grading	
G1	31
G2	197
G3	113
Lynphovascular Invasion (LVI)	
Yes	128
No	209
Not specified	4
Neural Invasion	
Yes	61
No	275
Not specified	5
ER	
Positive	288
Negative	44
Not tested	9
PgR	
Positive	283
Negative	49
Not tested	9
Ki-67	
Positive	161
Negative	2
Not tested	178
HER2/new/overexpression	
0	180
1+	30
2+	23
3+	35

es, the higher is the accuracy and the lower is the rate of false negative. The learning curve is about 20-30 patients (8). A review of 1219 patients operated for breast carcinoma in the same period proved that blue dyeing was successful to localize sentinel lymph-nodes in 83% of cases (range 66-97%). Predicted negative value was 95% (range of 81-100%), while the accuracy was 93% (ranging from 81 to 100%) and the false negative rate was 7.5% (range of 5-12%) (9, 10). In a previous study performed on 102 patients comparing both methods, the Authors reported that the lymphoscintigraphy had a higher rate of identification of lymphnodes than the patent blue method (97 *vs* 73%); the false negative rates were respectively 0 and 8%; the predicted negative values were 100 and 92% and the accuracy was 100 and 92% (11, 12).

About 30-40% of patients with early breast cancer have positive axillary lymph-nodes, the remaining 60-70% of patients are lymph-node negative and may therefore be overtreated with ALND, with the disadvantage of early and late complications as seroma, pain, limited arm motion, numbness or lymphoedema of the arms (8). Axillary recurrences after SLNB range between 0 and 1.6% in many series (Table 3), while axillary recurrence after ALND is about 0-3% (13).

In our experience we observed no axillary recurrence in 233 patients with SLNB alone with a median follow-up of 53 months confirming the accuracy of SLNB and SLN negative patients with SLNB alone are not at risk for axillary recurrences more than ALND (14, 15).

Anyway the complete knowledge of long-term outcomes of SLNB without ALND must be evaluated with prospective randomised studies (16-18). To date there are many trials that are evaluating the recurrence and the survival after SLNB: the European ALMANAC (Axillary Lymphatic Mapping Against Nodal Axillary Clearance) (19), the American NSABP-32 (National Surgical Adjuvant Bowel and Breast Project) (20) and the trial of European Institute of Oncology (EIO). The latter, per- formed by Veronesi et al, showed that there are no differences in term of axillary recurrence between patients undergoing SLNB and ALND (15).The other two studies are in the recruitment phase. What has not confidently been determined is the real benefit of further ALND in case of positive SLN. Other studies are currently investigating the need of completion ALND in patients with positive SLNs. The EORTC 10981 AMAROS (After Mapping of Axilla Radiotherapy or Surgery) trial is comparing axillary radiotherapy versus completion ALND in patients with a tumourpositive SLN and hopes to find comparable loco-regional control with less morbidity in the patients treated with ax-

Table 3 - Nodes characteristics in 341 patients undergoing sentinel.

Sentinel Node	
N0	233
N+	108
Average number of sentinel node per patient	1,8
Number of sections of sentinel node analysed	
Average	27,1
Range	4-72
Micrometastases	22
Isolated tumour cells	1

illary radiotherapy (21). The ACSOG Z0011 (American College of Surgeons Oncology Group) trial is randomizing patients with a tumour positive SLNB to ALND and noALND; both groups of patients receive systemic therapy and breast irradiation. Objective of this study is to look for differences in survival, local control and morbidity between two groups (22).

Nevertheless the results of prospective randomised trials in terms of some technical aspects and long term results are not available, we believe that in the hands of an experienced team of professionals (Nuclear Medicine, Surgery and Pathology), SLNB without ALND in negative SLN breast cancer appears to be a safe and reliable procedure to determine nodal status and ensure loco-regional control of the neoplastic disease, as now well reported in the Annual S. Antonio Breast Cancer Symposium 2011 (23).

References

1. Reitsamer R, Peintinger F, Prokop E, et al. 200 sentinel lymph-node biopsies without axillary lymph-node dissection - no axillaiy recurrences after a 3-year follow-up. Br J Surg. 2004;90:1551-1554.
2. Van dervegt B, Doting MHE, Jager PL, et al. Axillary recurrence after sentinel lymph node biopsy. EJSO. 2004; 30:715-720.
3. Bonnema J, van de Velde CJH. Sentinel lymph node biopsy in breast cancer. Ann Oncol. 2002;13:1531-1537.
4. Marrazzo A, Taormina P, Noto A, et al. Localization of the sentinel node in breast cancer: prospective comparison of vital staining and radioactive tracing methods. Chir Ital. 2004;56:621-627.
5. Kapteijn BAE, Nieweg OE, PeterseJL, et al. Identification and biopsy of the sentinel node in breast cancer. Eur J Surg Oncol. 1998;24:427-430.
6. Cox CE, Salud CJ, Cantor A, et al. Learning curves for breast cancer sentinel lymph node mapping based on surgical volume analysis. J Am Coll Surg 2001;193:593-600.
7. McMasters KM, Wong SL, Chao C, et al. Defining the optimal surgeon experience for breast cancer sentinel lymph node biopsy: a model for implementation of new surgical techniques. Ann Surg. 2001;234:292-299.
8. Kuehn T, Klauss W, Darsow M, et al. Long-term morbidity following axillary dissection in breast cancer patients - clinical assessment, significance for life quality and the impact of demographic, oncologic and therapeutic factors. Breast
9. Giuliano AE, Haigh Pl, Brennan MB, et al. Prospective obsen/ational study of sentinel lymphadenectomy without further axillary dissection in patients with sentinel node-negative breast cancer. J Clin Oncol. 2000;18:2553-2559.
10. Schrenk P, Hatzl-Griesenhofer M, Shamiyeh A, Waynad W. Follow-up sentinel node negative breast cancer patients without axillary lymph node dissection. J Surg Oncol. 2001;77:165-170.
11. Hansen NM, Grube BJ, Giuliano AE. The time has come to change the algorhitm for the surgical management of early breast cancer. Arch Surg. 2002;137:1131-1135.
12. Chung MA, Steinhoff MM, Cady B. Clinical axillary recurrence in breast cancer patients after a negative sentinel node biopsy. Am J Surg. 2002;184:310-314.
13. Recht A, Houlihan MJ. Axillary lymphnodes and breast cancer: a review. Cancer. 1995;76:1491-1512.
14. Reitsamer R, Peintinger F, Prokop E, et al. Sentinel lymph node biopsy alone without axillary lymph node dissection follow up of sentinel lymph node negative breast cancer patients. EJSO. 2003;29:221-223.
15. Veronesi U, Paganelli G, Viale C, et al. A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. N Engl J Med. 2003;349:546-553.
16. Fenaroli P, Merson M, Giuliano L, et al. Population-based sentinel lymph node biopsy in early invasive breast cancer. EJSO. 2004;30:618-623.
17. Ponzone P, Biglia N, Maggiorotto F, et al. Sentinel node dissection as definitive treatment for node negative breast cancer patients. EJSO. 2003;29:703-706.
18. Badgwell BD, Povoski SP, Abdessalam SF, et al. Patterns of recurrence after sentinel lymph node biopsy for breast cancer. Ann Surg Oncol. 2003;10:376-380.
19. Mansel RE, Goyal A. European studies on breast lymphatic mapping. Semin Oncol. 2004;31:304-310.
20. Wilke LG, Giuliano A. Sentinel lymph node biopsy in patients with early-stage breast cancer: status of the National Clinical Trials. Surg Clin North Am. 2003;83(4):901-910.
21. Cataliotti L, Christiaens MR, Nieweg OE. After mapping of the axilla: radiotherapy or surgery? EORTC protocol 10981. European Organization for Research and Treatment of Cancer. Available from: http://www.eortc.be/services/doc/10981-Protocol-Version5.pdf
22. Ross M. Sentinel node dissection in early-stage breast cancer: ongoing prospective randomized trials in the USA. Ann Surg Oncol. 2001;8:77-81.
23. Barranger E, Delpech Y, Coutant C. San Antonio Breast Cancer Symposium 2011 (SABCS): what place will remain to the axillary dissection? Gynecol Obstet Fertil. 2012; 40(4):201-203.

An interesting case of "simulation-based learning" applied to health organization

Giusi Piccinno[1]
Gianmarco Troiano[2]
Nicola Nante[2]
Filomena Autieri[1]
Fabrizio Niccolini[1]
Luca Lavazza[3]

[1] Hygiene and Health organization, Hospital "Careggi", Florence, Italy
[2] Post Graduate School of Public Health, University of Siena, Italy
[3] Health Director, Hospital Careggi, Florence, Italy

Corresponding Author:
Gianmarco Troiano
Post Graduate School of Public Health
University of Siena
Via Aldo Moro 2
53100 Siena, Italy
E-mail: gianmarco.troiano@student.unisi.it

Abstract

Simulation is a technique for practice and learning that can be applied to many different disciplines and types of trainees: we decided to use it in order to improve the management of emergencies and maxi-emergencies in Careggi Teaching Hospital (Florence, Italy). From 2014 we organized each month a Security Day, with simulations about an emergency plan or procedure. 30 Security Days have been organized with a consequent growing knowledge of plans and procedures. From the beginning of 2017, 42 informative meetings were organized and attended by about 600 professionals. 10 simulations of "interruption of power supply" were also organized: the status of emergency lamps, equipment, batteries were tested. The monthly checks carried out on the telephone numbers (of the health and technical operation centers) have shown a progressive reduction of the criticalities. Finally, the participation in the periodic meetings of the Maxi-emergencies Regional Coordination allowed a comparison with the other structures creating interesting work ideas also in order to uniform the attitudes within the Tuscany Region. Simulation-based learning represents a valid tool to improve the Hospital Organization: it is an useful tool to develop health professionals' skills and knowledge, whilst protecting patients from unnecessary risks.

KEY WORDS: emergency, health organization, simulations.

Letter to Editor

Simulation is a technique for practice and learning that can be applied to many different disciplines and types of trainees. It is a technique (not a technology) to replace and amplify real experiences with guided ones, often "immersive" in nature, that evoke or replicate substantial aspects of the real world in a fully interactive fashion. "Immersive" here implies that participants are immersed in a task or setting as if it were the real world (1, 2).

In Careggi Teaching Hospital (Florence, Italy) we tried to use the simulation as a method to improve the Hospital Organization, and in particular to improve the management of emergencies and maxi-emergencies based on the already present procedures.

Careggi Teaching Hospital has 5450 employees, but the entire population attending the hospital is higher, including 2400 students, 650 residents and about 400 attendants, volunteers, trainees etc; if we consider also the number of patients, of their accompanists and visitors, we are in presence of a community close to 10,000 persons. For this reason, the management of internal emergencies (3) and of the resources in presence of an external unexpected event should take into account the above-mentioned peculiarities.

In October 2012, a working group was created to revise the Hospital Emergency Procedures. In November 2013, a project for the implementation and revision of these procedures began, also with the aim to improve the collaboration with other Services (Ambulances, Firemen, Civil protection, etc.).

One of the first interventions was represented by the update of the hospital intranet website with the creation of a folder containing all the procedures (periodically revised).

From January 2017 the Emergency Coordination Unit organized some meetings (of almost 30-40 minutes) in order to inform all the professionals (including the workers of the external companies that work in the hospital) about the procedures and about the correct use of the hospital intranet website.

Each month a Security Day was organized, with simulations about an emergency plan or procedure. Simulations were carried out with the participation of "simulants". The date and the type of each simulation was decided by the Health Director. The day of simulation participants was involved in simulants' preparation and, when everything was ready, the alarm call was activated, launching the simulation. At the end of each simulation a debriefing was organized with representatives of each involved category (nurses, doctors, etc.), registering all the critical issues and trying to identify strategies to improve and resolve the problems. With the help of photographers were realized some short movies (of almost 20-30 minutes) used to review some of the courses with the involved professionals.

Simulations of “interruption of the supply of electricity” were also organized monthly, following the same steps of the above mentioned emergency simulation. In these simulations, settled in hospital wards, real patients were involved.

From the beginning of 2017, 42 informative meetings were organized and attended by about 500 professionals. Professionals showed a big interest and some professionals directly contacted the Health Direction to organize further meetings and to suggest simulations in the structures where they work.

30 Security Days have been organized with as many simulations on plans and emergency procedures. From the debriefings, a growing knowledge of plans and procedures has emerged, and professionals demonstrated to be more aware of how it is necessary to test the response to a maxi-emergency.

10 simulations of “interruption of power supply” were organized; the status of equipment, buffer batteries, emergency lamps, presence of privileged or ordinary lines, were also tested. In addition a census of the devices without backup batteries was done.

The monthly checks carried out on the telephone numbers (of the health and technical operation centers) have shown a progressive reduction of the criticalities; all professionals answer the phone calls in an appropriate manner knowing the reason for the call.

Finally, the participation in the periodic meetings of the Maxi-emergencies Regional Coordination allowed a comparison with the other structures creating interesting work ideas also in order to uniform the attitudes within the Tuscany Region.

Concluding, simulation-based learning can be the answer to develop health professionals’ knowledge, skills, and attitudes, whilst protecting patients from unnecessary risks. Simulation-based training has opened up a new educational application in medicine and could be used also to improve the Hospital Organization (4, 5). We encourage other colleagues and other facilities to invest further resources for this kind of training because unexpected events, due to their rarity, are often very difficult to manage and to control and may create important damages.

References

1. Gaba DM. Human work environment and simulators. In: Miller RD, ed. Anaesthesia. 5th Ed. Churchill Livingstone. 1999:18-26.
2. Gaba DM. The future of simulation in health care. Qual Saf Health Care. 2004;13(1):2-10.
3. Montella G, Raiola V, Nante N. Il triage nelle maxi emergenze. Mondo Sanitario. 2009;(4):1-7.
4. Lateef F. Simulation-based learning. Just like the real thing. J Emerg Trauma Shock. 2010;3(4):348-352.
5. Fierro Perez EG, Gentile AM, Nante N. Il fattore umano nel modello organizzativo. Mondo Sanitario. 2010;11:15-20.

Effects of atmospheric nickel on LH blood levels

Alessandra Di Marzio[1]
Andrea Ianne[1]
Carmina Sacco[2]
Anastasia Suppi[2]
Serafino Ricci[3]
Lidia Ricci[3]
Nadia Nardone[2]
Roberto Giubilati[2]
Francesco Tomei[2]
Gianfranco Tomei[4]

[1] Department of Anatomy, Histology, Legal Medicine and Orthopaedics, OU of Occupational Medicine, "Sapienza" University of Rome, Italy
[2] Spin-off of "Sapienza", University of Rome, Italy
[3] Department of Anatomy, Histology, Legal Medicine and Orthopaedics, OU of Legal Medicine, "Sapienza" University of Rome, Italy
[4] Department of Psychiatric and Psycological Science, "Sapienza" University of Rome, Italy

Corresponding Author:
Francesco Tomei
Spin-off of "Sapienza" University of Rome
Viale Regina Elena 336
00161 Rome, Italy
E-mail: francesco.tomei@uniroma1.it

Abstract

***Introduction*: The nickel (Ni) present in urban air pollutant interferes with the functioning of the endocrine system altering the production the release, the transport the metabolism and the mechanism of activity.**
The purpose of the study is to verify whether occupational exposure to low of nickel (Ni) present in urban air may affect the LH values in outdoor workers performing different tasks of a large Italian city.
***Materials and methods*: 164 subjects of both sexes were included in the study. We assessed the dosage of urinary nickel LH blood. We used statistical methods for description for comparison between medium (T test, Mann- Whitney U test and ANOVA) and for correlation (Pearson test and Multiple Linear Regression).**
***Results*: Urinary nickel is associated with female sex for all the statistical test adopted.**
***Discussion*: It can be assumed that occupational exposure to low doses of nickel present in pollution affects urban LH levels in female outdoor workers exposed.**

KEY WORDS: air pollution, LH, nickel, occupational exposure, work.

Introduction

Numerous studies in the literature link the environmental and occupational exposure to nickel compounds and nickel metal with increased serum levels in subjects exposed.
Metallic nickel is present in more than 3000 different alloys used in the manufacture of kitchen utensils, batteries, coins, car parts, it is contained in cigarettes, in paint, in solvents and in some pesticides. The mining and manufacturing industries are responsible, for the emission nickel in the biosphere. The extraction and the refining of nickel, waste incineration, steel production and burning release the Ni in the atmosphere.
The nickel is also present in the oil and coal from which is released into the atmosphere through the combustion and is used as a catalyst to produce light fuel (petrol, diesel, kerosene). The gradual increasing use of catalytic converters instead of fuels containing lead has led to the use of Ni as catalyst component. Nickel is also used as an additive in unleaded gasoline to increase octane (1).
Nickel is an immunotoxic, neurotoxic, genotoxic, hepatotoxic and nephrotoxic metal. In vitro the Ni produces chromosome aberrations and sister chromatid exchanges in human lymphocytes (2).
In laboratory animals the inhalation of dust of Ni causes disorders of hematopoiesis, the gradual emergence of pneumosclerosi, marked vasoconstrictor action on the coronary vessels, hyperglycemia, degenerative changes of the testale, epididymis and sperm cells, alternations of the dopaminergic system, of the growth hormone and interference with reproduction-related hypothalamic hormones LH, FSH, and testosterone (3).
The main toxic effects of this metal are allergenic and irritant (for example, the DAC) but some compounds ok nickel may have more serious effect on the respiratory or reproductive systems (4, 5).
Outdoor workers such as policemen are daily exposed to a large number of pollutants from urban traffic and to many psychosocial stress factors. In the literature, these stressors have been associated with abnormalities of fan plasma levels of androstenedione, testosterone, FSH and LH, but to date studies on the effects

of Ni on plasma LH are rather weak (6, 7).

A growing number of studies suggests the correlation between the chemicals in the environment resulting from the traffic and the interference on both male and female reproductive system (8, 9).

IARC estimates that nickel a possible human carcinogen (IARC Class 2B) in numerous scientific articles the metal is considered responsible endocrine and reproductive abnormalities (10-15).

In this regard the study of Kochman (16) and the study of Kozlowski (17) testify to the significant and direct correlation between the nickel and the alterations of sex hormones, in particular LH.

This study is to evaluate the existence of the correlation between the levels of Ni in the air caused b urban and alterations in plasma LH in the policeman of a large Italian city assigned to different types of outdoor tasks.

Materials and methods

Study population

The study was conducted on 164 outdoor workers, 52 females and 112 males, all employees in the Municipal Police of a large Italian city and assigned to different types of outdoor tasks, divided as follows: 87 traffic policemen, 59 drivers and/or 2nd in patrol, 8 assigned to other outdoor job. All subjects included in the study are in the program of health promotion in the workplace. All 164 workers have lived and worked in the same urban area for at least five years.

This program is conducted in accordance with the current legislation and aims to investigate the health of individuals occupationally exposed to urban pollutants.

Employees with the role of traffic policemen were assigned to the control of vehicular traffic in the streets and in the areas of high and medium traffic, to the monitoring of traffic at intersections, in parking areas and others. Workers with the role of drivers and/or 2nd in patrol were assigned to traffic control and specific interventions in case of accidents and other activities including drivers and/or 2nd in patrol. Workers with other outdoor activities were assigned to different roles, including support to social outcasts activities in the construction field, in the Judicial Police, Environmental Police, etc.

Most of these activities were outdoor, only drivers were in cars for at least 80% of their working time (8 hours a day, 5 days a week).

Each worker completed, in the presence of a doctors clinical medical history questionnaire to be included in the search. The questionnaire included information about age, area of residence in the last five years and proximate and remote physiological (exposure to cigarette smoke) and clinical history. As for the smoking status, reference was made to the World Health Organization (WHO) so we considered smokers all subjects who had or claimed to have smoked at least 100 cigarettes in their lives or have stopped smoking less than six months before or subjects who declared themselves smokers (18).

To avoid the influence of confounding factors we excluded from the study workers who reported exposure to solvents, paints and pesticides in their leisure activities, subjects using drugs and habitual drinkers of alcohol (consumption of alcohol exceeding 2 Alcoholic Unit per day for men, where 1 Alcoholic Unit corresponds to approximately 12 grams of ethanol) (19).

Each subject underwent a biological monitoring (evaluation of urinary Ni) and dosage of LH; subjects with urinary nickel values below the limit of detection were excluded from the study.

For statistical analysis were considered the following factors: sex, smoking, habit, task, age and seniority.

Each subject agreed to make their personal information available, being aware that such data would be classified as "sensitive information". They also agreed that they would be treated anonymously and collectively, would be examined with scientific methods and analyzed for scientific purposes according to the principles of the Helsinki Declaration.

Environmental monitoring

We performed eight individual air samples on a group of traffic policemen selected from 8 workplaces considered representative of the topographic distribution of all workers, as well as four air samples of four drivers of the cars in which there were 2 agents per shift. In this way the results were representative of the colleagues in the same.

All subjects were asked to abstain from smoking during the sampling. The individual air samples were collected by means of the Dorr- Oliver cyclone with a cutpoint for the particles having diameter of 5 microns. Each cyclone was attached to a pump for the air sampling; the pump was calibrated to a flow rate of 1.7.1 of air per minute, following the method 7521 suggested NIOSH (20). Each cyclone was fitted with a cassette holding a 37 mm polyvinyl chloride (PVC) membrane filter. The cyclone and the tapes were attached to the shirt collar in the breathing zone of the subject; the pump was placed in a padded envelope. Each worker wore the air sampler during his entire shift (seven hours). After the sampling, the cyclone was carefully disassembled. The filter membranes containing the collected particulates were analysed to detect the Ni according to the method 7251 indicated by NIOSH. The samples of the particulates were analysed through the Graphite Furnace Atomic Absorption Spectrometry (Perkin-Elmer, mod. HGA-2100). The detection of the method was 1 microg/l. For each individual air sampling, the time-weighted averge (TWA) level of exposure to Ni for seven hours was obtained. The American Conference of Governmental Industrial Hygienists (21) proposed a TLV-TWA 1.5 mg/m^3 limit for workers occupationally exposed to Ni.

Nickel and urinary LH

The measurement of the urinary nickel appears more appropriate for the evaluation of occupational expo-

sure to this metal, since there is a good correlation between the concentration of nickel in the air and those present in the urine of exposed subjects (22).
The dosage of urinary nickel and the LH were carried out on 164 workers.
Each worker underwent the urine and blood sample tests after four continuous working days, at the end of his shift. Each worker was asked not to eat such food as cocoa, chocolate, soya beans, oatmeal, nuts and seeds, fresh or dried legumes during the four days before the examination.
The urine samples were transported within an appropriate thermal bag at a temperature of +4°C and then stored in the chiller at -20°C until analysis. The determination of urinary creatinine was carried out for all the samples by the Jaffè method.
The determination of urinary Ni was attained by subjecting the samples to complexation with ammonium pyrrolidinedithiocrabamate (APDC) and graphite furnace atomic absorption. The lower limit of the method (LOD) for the urinary nickel was 1.0 mg/g of urinary creatinine.
In order to consider the dilution of the concentration of nickel in the different samples we divided nickel (g/L) by urinary creatinine (g/L) and expressed the urinary concentration of nickel in terms of g/g urinary creatinine.
For the LH plasma a 10 ml venous blood sample was taken from each worker in the morning 6.45/9.30. The blood samples were stored at work in a refrigerator at +4°C until they were transferred (in a suitable container and at the same temperature) to the laboratory where they were centrifuged and subsequently stored at 20°C until they were analysed (within 3 days). In the lab the dosage of LH was measured by the method of radioimmunoassay (radioimmunoassay - RIA). Normal levels of LH were considered routinely taken in the laboratory: 71.1 mIU/ml.

Statistical Analysis

The results were analysed and compared, in accordance with the nature of the individual variables. The t-test for independent samples, the Mann- Whitney U test for two modes variables (sex, smoking status), the ANOVA test and the Kruskal Wallis test for variables with more than two ways (age, seniority service and task) were performed on the total sample. The Pearson correlation coefficient (two-tailed p) between the parameters was evaluated in both the total sample and after stratification by sex, smoking status and job. Even the multiple linear regression was performed after taking into account the main confounding factors on the total sample and subcategories.

Results

Characteristics of the sample studied

The final sample consists of 164 subjects, 112 men and 52 women; 64 smokers and 100 non-smokers; 87 traffic policemen, 59 drivers and 8 employees. The characteristics of the sample are shown in Table 1.
Through the t-test for independent samples and the Mann-Whitney test no significant differences were found between the values of urinary Ni and the habit of cigarette smoking.
Also no significant differences were found between the various outdoor duties in relation to the average values and to the distribution by age and smoking habits. These results of timed by means of t-test, ANOVA and Mann- Whitney test, are reported in Table 2.
No subject reported suffering or having suffered from some diseases related to the reproductive system.

Environmental monitoring of Nickel: film badge

The values of individual exposures to Ni pollution are found in Table 3. All subjects reported they had not smoked during the sampling. No sample exceeded the average value of 1.5 mg/m^3 ACGIH proposed for those occupationally exposed.

Urinary Nickel and LH

All values of urinary creatinine were within the normal range (0.3 to 3.0 g/L) recommended by the World Health Organization (23).
The concentration values of Ni and urinary LH are expressed in terms of mean, median, standard deviation and range (min-max) and are shown in Table 1.

Table 1 - Features of the studied population.

Mean (s.d)	4.2 (0.5)
Median	2.8
Range	0-53
Urinary nicked (ng/g creatinine)	
Mean	5,08 (4,6)
Median	3,5
Range	1-30
Nicked: individual air samplings (ng/m^3)	Traffic policemen (N=8)
Mean (s.d)	152.8 (112.8)
Median	65.1
Range	15.3-350

Table 2 - Results of Independent sample T test, Univariate Anova test, Mann-Whitney U test.

	Dependent variable: LH			Dependent variable: Urinary Ni		
	Independent Sample T test (p)	Univariate Anova test (p)	Mann-Whitney U test (p)	Independent Sample T test (p)	Univariate Anova test (p)	Mann-Whitney U test (p)
Gender	0.00		0.00	0.56		0.099
Smoke	0.504		0.092	0.074		0.036
Age		0.000			0.42	
Job		0.975			0.505	

Table 3 - Multiple linear regression on the 12 individual air samplings.

	Total sample			Traffic policemen			Drivers		
	Beta	**t**	**p**	**Beta**	**t**	**p**	**Beta**	**t**	**p**
Air Ni	0.79	23.43	0.00*	0.89	23.7	0.00*	0.81	3.72	0.00*
Age	-0.03	-0.17	0.67	-0.02	0.45	0.77	-0.05	-1.32	0.74
Length of service	0.02	-0.33	0.75	0.07	0.51	0.48	-0.06	-0.23	0.62
Smoke	0.04	-0.35	0.48	0.05	-0.44	0.59	0.21	0.65	0.41

Dependent variable: Urinary Ni; *Statistically significant.

The statistical tests of correlation taken into account (Pearson test and multiple linear regression) indicate some significance between the values of Ni and those of urinary LH plasma exclusively in female workers as expression in Tables 4 and 5. There is no other significance.

Table 4 - Person's correlation coefficient between LH and Urinary Ni in the total sample and after the stratification by gender, smoking habit and job.

Sample	Results
Total sample (n.164) p:0.719	r: 0.030
Non-smokers (n.100) p:0.429	r:-0.083
Smokers (n.64) p:0.293	r:-0.183
Men (n.112) p:0.293	r:-0.105
Women (52) p:0.929	r: -0.013
Traffic policemen (87) p:0.423	r:-0.086
Drivers (n.59) p:0.386	r:0.125
Other duties (n.8) p:0.666	r:-0.501

Discussions

Endocrine disruptors are defined as those exogenous agents that interfere with the production, the release, the transport, the metabolism, the binding, the action or elimination of hormones naturally present in the body and are responsible for the maintaining of homeostasis and regulation of developmental processes. Previous studies in literature have shown that various toxic substances arising from urban pollution are endocrine disruptors, although it is not entirely clear which components are responsible for such effects (24-28).

It has however been demonstrated that the toxicity of PM 2.5 depends, at least in part on specific chemicals that are adherent to it and that the metals are often implicated as causative agents (23, 29).

Most of the studies on the toxicity of metals on the reproductive system are derived from experimental animal studies, which are generally performed with high doses of exposure and/or short-term exposures, thereby providing patterns that can be applied to the most common situations of human exposure. Moreover the fertility and the endocrine system in humans can differ from that of other mammals, as well as the susceptibility to different metals. We believe epidemiological studies are needed to validate the effect identified in experimental models. The data on the toxicity of metals on the reproductive system at the moment are rather poor and usually limited to non-occupationally

Table 5 - Multiple linear regression in total sample and subcategories.

Sample	Independent Variables	Beta	t	p
Total Sample	Age	0.006	0.071	0.943
	Urinary Ni	0.30	0.363	0.717
Smokers	Age	0.375	2.652	0.011
	Urinary Ni	-0.087	-0.617	0.540
Non-smokers	Age	0.069	0.696	0.488
	Urinary Ni	-0.099	-0.991	0.324
Men	Age	0.023	0.217	0.829
	Urinary Ni	-0.083	-0.792	0.431
Woman	Age	-0.010	-0.073	0.942
	Urinary Ni	0.181	1.308	0.197
Traffic Policemen	Age	-0.164	-1.552	0.124
	Urinary Ni	-0.086	-0.810	0.420
Drivers	Age			
	Urinary Ni			
Other duties	Age	0.241	0.136	0.701
	Urinary Ni	0.114	0.289	0.792

exposed subjects or people resident near areas with high levels of pollution or subjects exposed to metals through consumption of contaminated food and water (30-33).

These data concerning the toxicity of the metals on the human endocrine system are limited only to some metal ions, especially those of lead. The effects on the endocrine system of other metals nickel in this case are very few and usually limited to subjects with occupational exposures to high concentrations, for example the workers employed in mines, refineries, electrical installations and foundries (34, 35).

Specifically Kozlowski (17), in his work shows the relationship between changes in the release of luteinizing hormone and exposure to metal nickel; similarly Kochman (16) demonstrated *in vivo* the ability some heavy metals have to affect sex hormones just as the nickel.

The present study is the first research focused on the exposure to occupational Ni in outdoor workers exposed to environmental low pollutants and their effects on the levels of plasma LH. Our study was conducted in one of the largest cities of central Italy where about 2.8 million inhabitants with a density of vehicles of about 1.5 per square kilometres.

In the city fixed station for monitoring the pollutants show that the average annual values of Ni in urban air have had a slight decline, from 4.9 in 2008 to 4.4 ng/m^3. These values indicate that the urban pollution from Ni on the particulate matter in suspension (PTS) in the city object of study can be considered at low doses.

The results of the individual dosimetry are in agreement with the data obtained in fixed station. Even if on average higher than the levels in fixed stations the samples did not exceed the limit value of 1.5 mg/m^3 established by ACGIH for persons occupationally exposed to Ni. The occupational exposure of the outdoor workers we studied much lower than the exposure of indoor industrial workers (limit values ACGIH 2014). The mean values of Ni that we had with the individual dosimetry are still higher than the estimated annul target value for the general population (20 ng/m^3), proposed by ARPA Lazio by legislative decree 152 of 03/08/2007 following the European Directive 2004/107/EC. The results of our study show that in the female group of workers we studied when the levels of urinary nickel increase the levels of LH increase too. The statistical tests used do not show, however, statistically significant correlation between other confounding factors such as age and the smoking status and the plasma levels of LH. The fact that that nickel is not a cumulative toxic may explain why in our research it does not change with age and smoke (27); as to smoking habits the data on the effects of nickel in cigarettes on health are rather controversial, actually it seems that the main source of exposure for outdoor occupationally expose smokers is the nickel in the air (36, 37).

In this study we evaluate the possible correlation between exposure to low doses of nickel present in the urban environment and LH levels in outdoor workers, using the results of the individual dosimetries and the biological monitoring of urinary nickel.

The results showed the existence of a significant association between occupational exposure to low doses of environmental nickel and increase in LH levels in female works. These results should lead to examine a larger of people and to deepen the study of the effects of nickel on the working populations exposed to urban pollutants. Elevated LH may in fact be related to various diseases and disorders of the human reproductive system.

Therefore, preventive measures should be taken to protect the health not only of outdoor workers but also to all exposed workers. The LH could be used as early biomarker, valid for the group, to be used in subjects exposed to low doses of nickel before the appearance of out of range values.

References

1. ARPA Lazio. Regional Agency for the environmental Protection. Quarto rapporto sulla qualità delle acque superficiali e sotterranee della Provincia di Roma. 2007. Available from: http://www.arpalazio.it
2. Lippmann M, Ito K, Hwang JS, et al. Cardiovascular effects of nickel in ambient air. Environ Health Perspect. 2006;114:1662-1669.
3. Massoni F, Ricci P, Simeone C, Ricci S. Cardiac death in aortic valve sclerosis and coronary artery disease. An autopsy report. Acta Medica Mediterranea. 2014;30:77-80.
4. Barnes CS, Alexis NE, Bernstein JA, et al. Climate Change and Our Environment: The Effect on Respiratory and Allergic Disease. J Allergy Clin Immunol Pract. 20131:137-141.
5. Hystad P, Demers PA, Johnson KC, et al. Long-term Residential Exposure to Air Pollution and Lung Cancer Risk. Epidemiology. 2013;24:762-772.
6. Caciari T, Casale T, Ciarrocca M, et al. Correlation between total blood lead values and peripheral blood counts in workers occupationally exposed to urban stressors. J Environ Sci Health A Tox Hazard Subst Environ Eng. 2013;48:1457-1469.
7. Ricci S, Massoni F, Di Meo M, et al. Correlation among measures of stress, indicators of biohumoral nature and medico-legal considerations. Riv Psichiatr. 2013;48:113-120.
8. Pérez-Cadahìa B, Laffon B, Porta M, et al. Relationship between blood concentrations of heavy metals and cytogenetic and endocrine parameters among subjects involved in cleaning coastal areas affected by the “Prestige” tanker oil spill. Chemosphere. 2008;71:447-455.
9. Gil F, Hernandez AF, Marquez C, et al. Biomonitorization of cadmium, chromium, manganese, nickel and lead in whole blood, urine, axillary hair and saliva in an occupationally exposed population. Science of the Total Environment. 2009;409(6):1172-1180.
10. IARC Monographs. Arsenic, metals, fibres and dusts. Volume 100C. A review of human carcinogens. 2012. Available from: http://monographs.iarc.fr/ENG/Monographs/vol100C/mono100C.pdf
11. Chen YW, Yang CY, Huang CF, et al. Heavy metals, islet function and diabetes development. Islets. 2009;1:169-176.
12. Krockova JZ, Massànyi P, Sirotkin AV, et al. Nickel induced structural and functional alterations in mouse Leydig cells in vitro. J Trace Elem Med Biol. 2011;25:14-18.
13. Fu Y, Tian W, Pratt EB, et al. Down-regulation of ZnT8 expression in INS-1 rat pancreatic beta cells reduces insulin content and glucose- inducible insulin secretion. PLoS One. 2009;4:e5679.
14. Apostoli P, Catalani S. Metal ions affecting reproduction and development. Met Ions Life Sci. 2011;8:263-303.
15. Tomei F, Rosati MV, Baccolo TP, et al. Plasma concentration of adrenocorticotropic hormone in traffic policemen. Journal of Occupational Health. 2003;45:242-247.
16. Kochman K, Gajewska A, Kozlowski H, et al. Increased LH and FSH release from the anterior pituitary of ovariectomized rat, in vivo, by copper- nickel- and zinc-LHRH complexes. J Inorg Biochem. 1992;48:41-46.
17. Kozlowski H, Masiukiewicz E, Potargowicz E, et al. Ovulation-inducing activity of luliberin (LHRH) complexed by copper (II), nickel (II), and zinc (II) ions. J Inorg Biochem. 1990;40:121-125.
18. Shiels MS, Rohrmann S, Menke A, et al. Association of cigarette smoking, alcohol consumption, and physical activity with sex steroid hormone levels in US men. Cancer Causes Control. 2009;20:877-886.
19. Saunders J B, Aasland OG, Babor TF, et al. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption-II. Addiction. 1993;88: 791-804.
20. Environmental Protection Agency (EPA). Methods for the Chemical Analysis of Water and Wastes. Publication Offices of the Center for Environmental Research Information, Cincinnati, OHIO. 1983. Available from: https://www.wbdg.org/FFC/EPA/EPACRIT/epa600_4_79_020.pdf
21. American Conference of Governmental Industrial Hygienists – ACGIH. Documentation ofthe threshold limit values and biological exposure indices. 7th ed. Cincinnati, OH. 2012.
22. Campurra G. Appendice 1, agenti chimici. In Manuale medicina del lavoro; Ipsoa Indicitalia Eds. Italy. 2010;868-869.
23. World Health Organization Regional Office for Europe Copenhagen. Air quality guidelines for Europe, 2nd Edition. WHO Regional Publications, European Series, No. 91. 2000. Available from: http://apps.who.int/iris/bitstream/handle/10665/107335/E71922.pdf;jsessionid=FEEB60562D1B927E713DC431DB3C7B07?sequence=1
24. Ciarrocca M, Capozzella A, Tomei F, et al. Exposure to cadmium in male urban and rural workers and effects on FSH, LH and testosterone. Chemosphere. 2013;90:2077-2084.
25. Ciarrocca M, Caciari T, Ponticiello BG, et al. Follicle-stimulating hormone levels in female workers exposed to urban pollutants. Int J Environ Health Res. 2011;28:1-11.
26. Tomao E, Tomei G, Rosati MV, et al. Luteinizing hormone (LH) levels in male workers exposed to urban stressors. Sci Total Environ. 2009;407:4591-4595.
27. Tomei F, Rosati MV, Ciarrocca M, et al. Urban pollution and nickel concentration in serum. Int J Environ Health Res. 2004;14:65-74.
28. Vitarelli A, Martino F, Capotosto L, et al. Early myocardial deformation changes in hypercholesterolemic and obese children and adolescents: a 2D and 3D speckle tracking echocardiography study. Medicine (Baltimore). 2014; 93:e71.
29. Xu X, Rao X, Wang TY, et al. Effect of co-exposure to nickel and particulate matter on insulin resistance and mitochondrial dysfunction in a mouse model. Part Fibre Toxicol. 2012;9:40.
30. Castanho A, Artaxo P. Wintertime and summertime Sao Paulo aerosol source apportionment study. Atmos Environ. 2001;35:4889-4902.
31. Singh M, Jaques PA, Sioutas C. Size distribution and diurnal characteristics of particle-bound metals in source and receptor sites of the Los Angeles Basin. Atmos Environ. 2002;36:1675-1689.
32. Wang G, Huang L, Gao S, Wang L. Characterization of water-soluble species of PM 10 and PM2.5 aerosols in urban area in Najing. China. Atmos Environ. 2002;36:1299-1307.
33. Morales GJ, Morton-Bermea O, et al. Assessment of Atmospheric Metal Pollution in the Urban Area of Mexico City, Using Ficus benjamina as Biomonitor. Bull Environ

Contam Toxicol. 2011;86:495-500.
34. Stridsklev IC, Schaller KH, Langard S. Monitoring of chromium and nickel in biological fluids of grinders grinding stainless steel. Int Arch Occup Environ Health. 2007;80:450-454.
35. Kozo Y, Yasushi J, Yukihiro K, et al. Urinary elimination of nickel and cobalt in relation to airborne nickel and cobalt exposures in a battery plant. Int Arch Occup Environ Health. 2007;80:527-531.
36. Stojanovic D, Nikic D, Lazarevic K. The level of nickel in smoker's blood and urine. Cent Eur J Public Health. 2004;12:187-189.
37. Torjussen W, Zachariasen H, Andersen I. Cigarette smoking and nickel exposure. J Environ Monit. 2003;5:198-201.