



III SIMPOSIO DE HIGIENE INDUSTRIAL
Santander, 28 y 29 de octubre de 2024



INDUSTRIAL HYGIENE FROM A GENDER PERSPECTIVE

Chemicals management in workplaces and sex differences: why a differentiated approach?

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WHY A DIFFERENTIATED APPROACH?

Because, physiologically speaking, Men and Women are not the same.

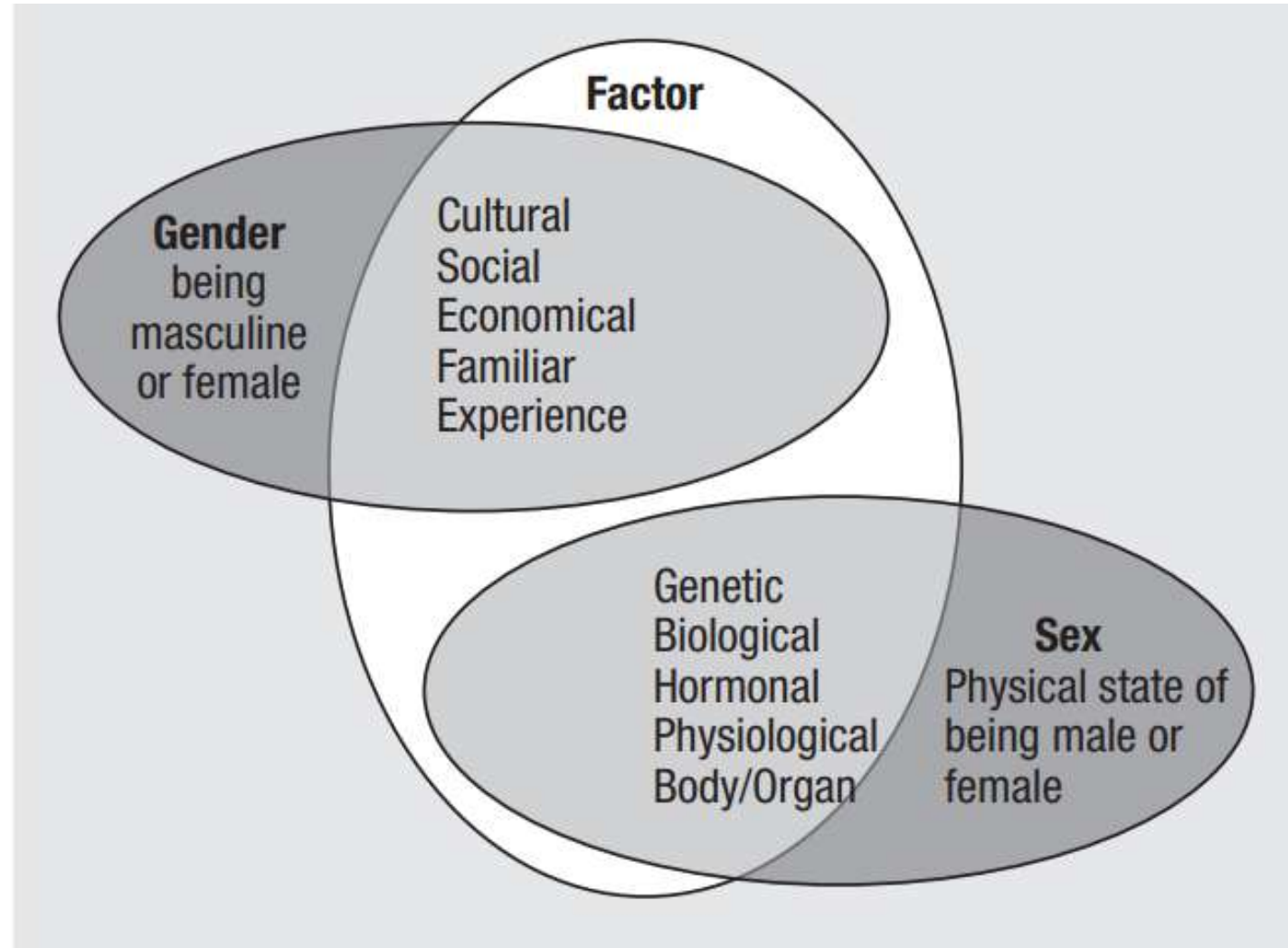
“Being male or female is an important fundamental variable that should be considered when designing and analyzing basic and clinical research.”

Institute of Medicine (IOM)(Wizemann and Pardue 2001)



DIFFERENCE OF SEX/GENDER

Factors influencing gender and sex differences in human health



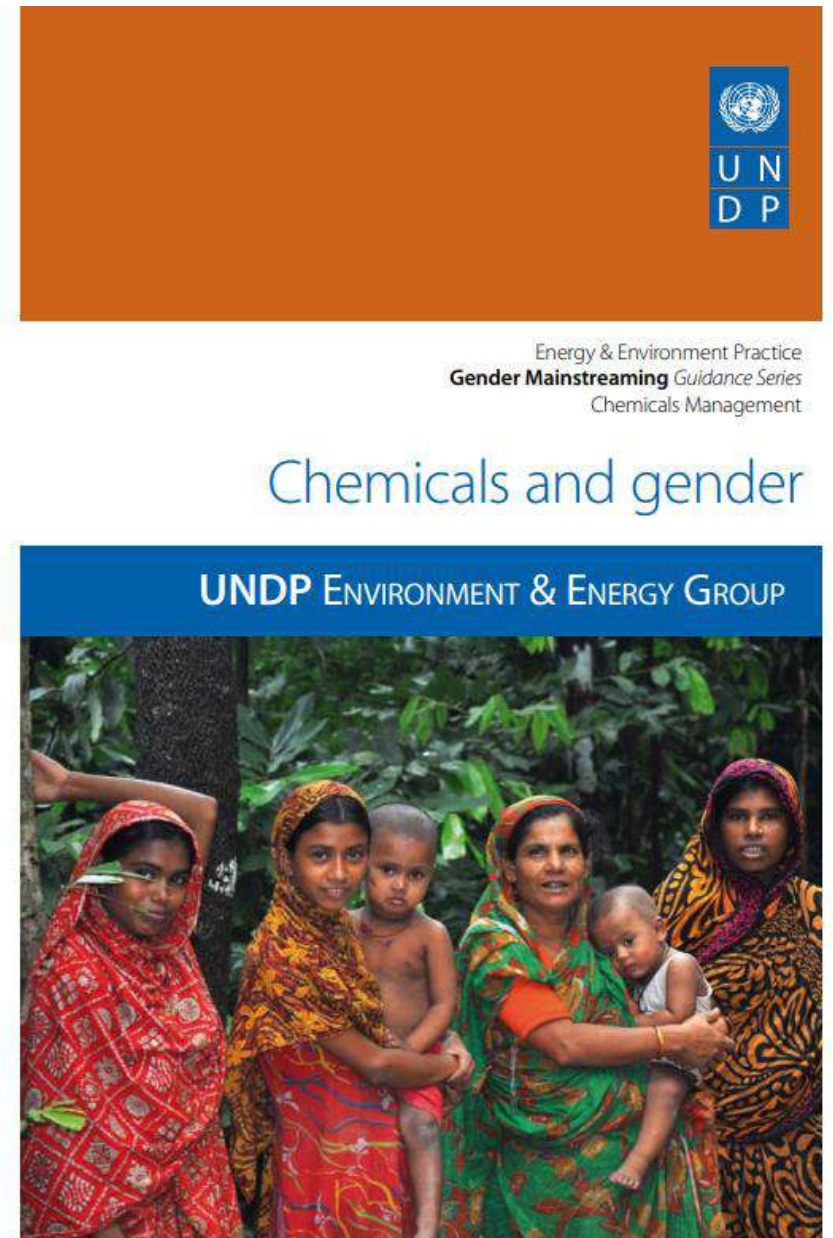
IN 2011 ALSO THE UNITED NATIONS FOCUSED THEIR ATTENTION TO THIS THEME

The attention was for environmental and work-related exposures.

The chemicals with higher evidences of effects on women were:

- METALS (LEAD, CADMIUM, NICKEL AND MERCURY IN PARTICULAR),
- ENDOCRINE INTERFERENCES
- PERSISTENT ORGANIC COMPOUNDS

BUT, ALSO, WITH EVIDENCE IN TERMS OF DIFFERENT CONDITIONS of exposure in daily life or occupational setting



Integrating gender medicine into the workplace health and safety policy in the scientific research institutions: a mandatory task

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The Law introduced the **gender issue in the risk assessment** in workplaces.

The European Parliament in December 2011 adopted a resolution on the mid-term review of the European Strategy 2007-2012 on health and Safety at work (Report 2011/2147(INI)) and emphasizes that women report a higher level of work related health problems than men, irrespective of the type of work. Hence measures of health and safety surely need a gender approach.

TOXYCOLOGY: Is there a difference in the response to a toxic substance based on sex?

In acute exposure to chemicals, under the same exposure conditions, between man and woman, it is correct to consider:

- the same amount of toxic in the same target organs
- That the toxic is absorbed in the same quantities
- That the toxic reached the same target organs
- That the toxic is able to produce the same health effects



there is great variability in relation to the chemical agent.
there are, however, in different cases, evidences of different
situations between man and woman



DIFFERENCES: WHY?

Are there sex and gender differences in acute exposure to chemicals in the same setting?

Tye E. Arbuckle*

Physiological differences

menses

pregnancy

Feeding time

menopause

body fat

Ventilation speed



VARIABLES CAUSING DIFFERENCES BETWEEN MEN AND WOMEN

Anatomical
differences

Mass of organs

Blood flow volume

discretionary
elements

diet

smoke

Use of drugs

Occupational
factors

Even in the same occupational activity, often, men and women lived different exposure conditions



DIFFERENCE IN THE TOXIC PROCESS

ABSORPTION



Few differences emerged in this phase [Ernstgard, 2003]

DISTRIBUTION



Women have got:

- ✗ a mean body weight < than men
- ✗ a higher fat portion
- ✗ a lower plasmatic volume
- ✗ a reduced blood flow to the organs

All these aspects are linked to the possibility and speed of distribution of toxics in the body [Gandhi, 2004; Dorman, 2004]

METABOLISM (examples)



1. Man and Woman have got different epatic metabolism of organic anions (there is a complex model of sex-specific expression of organic polypeptides transporting anions) [Rost, 2005]
2. Phase II of metabolism (glucuronization, acetylation, methylation or conjugation reactions) is generally faster in men than in women [Schwartz, 2003]

DIFFERENCES HIGHLIGHTED IN THE TOXIC PROCESS

EXCRETION AND ACCUMULATION



The higher rate of body fat in women, generally, allows a greater accumulation of lipophilic products [Valentin, 2001].

Women with a lack of Calcium (II) can accumulate some divalent compounds in the bones instead of calcium (II).

Men instead showed a higher rate of renal clearance, this means that women can retain a larger portion of contaminants, even if already metabolized [Kadiri, 2000]

WHERE THE CHEMICAL IS ABLE TO INTERACT WITH THE HORMONAL SYSTEM,
DIFFERENCES IN HEALTH EFFECTS MAY BECOME FURTHER EVIDENT

HYSTORIC EVIDENCES: THE LEAD

"Women are more vulnerable to lead toxicity than men"

("Dangerous Trade", sir Thomas Oliver, 1902)



"Neurotoxic exposure and effects: gender and sex matter!" Hänninen, Neurotoxicology 2011

...in our law: the biological exposure limit of lead for women in childbearing age is lower than the one for men, due to the higher vulnerability and this situation is underlined also with the new Dir (UE) 2024/869

INAIL

U. S. DEPARTMENT OF LABOR
BUREAU OF LABOR STATISTICS

ROYAL MEEKER, Commissioner

BULLETIN OF THE UNITED STATES } { No. 253
BUREAU OF LABOR STATISTICS }

INDUSTRIAL ACCIDENTS AND HYGIENE SERIES

WOMEN IN THE LEAD INDUSTRIES

ALICE HAMILTON, M. D.



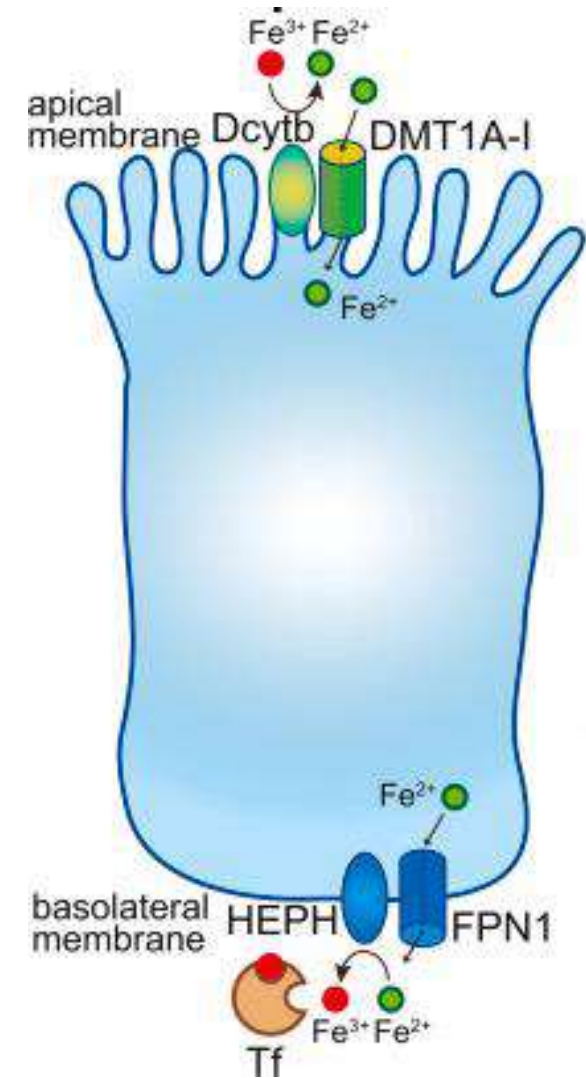
FEBRUARY, 1919

LITERATURE EVIDENCES: CADMIUM

The higher levels of cadmium in the tissues of women compared to men are widely documented

Linked to the greater uptake of cadmium from the intestinal tract of women, which increases when there is iron deficiency. (Vahter 2007, Gunshin 1997)

(DMT1 - transporter of divalent metals at the duodenal level, responsible for the absorption of iron, also has affinity for Cadmium)



EXAMPLE: REPROTOXIC SUBSTANCES

Considering reprotoxic chemicals with an armonized classification of danger (annex VI Reg CE 1272/2008), we found more than 300 substances or chemical compounds as reprotoxic of category 1.

Boric acid, borates and perborates

Organotin compounds

Glycol ethers

Triazole, imidazole and derivatives

Some epoxies

phthalates

Metals and some metallic compounds (Pb, Ni, Cd, Cr, Hg, Te, Co)

Organohalogenated compounds

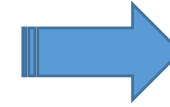
Alkylphenols (i.e BPA, BPS,...)

Some phytosanitary active ingredients or biocides

Othe compounds: CO, IPA, Ethylene oxide,...

PHTHALATES: EFFECTS ON HEALTH

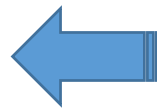
Antiandrogenic effects (they interfere with steroidogenesis)



They act as xenoestrogenic substances



Higher time to pregnancy, increased difficulty in conception, endometriosis



THE RESTRICTIONS

Reprotoxic substances were widely studied in the last years so numerous law restrictions were published in Europe:

For examples: about polyfluorinated compounds (PFAS), bisphenol A (BPA) or some phthalates (DEHP...), Mercury, Lead,...

The cosmetic use was banned for almost all these compounds, with really few exceptions.



EXAMPLE: SENSITIZER CHEMICALS

There's a first phase of contact with the toxic, with a sensitization of the body, while a second contact produce the adverse reaction

Health effects of sensitizer chemicals are on **respiratory function** and/or **skin**.

Causal factors could be:

Endogenous: like skin structure, physiology, genetic and hormonal status (here we talk about SEX difference)

Exogenous: ethnicity, sociocultural background, environmental exposures, lifestyle habits, occupational exposures (here we talk about GENDER difference)

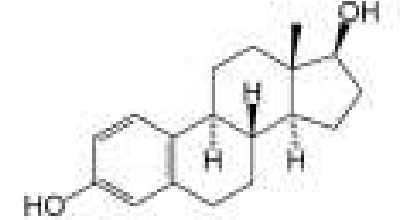


ASTHMA and SEXUAL HORMONES

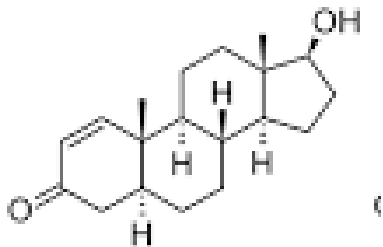
The link between the onset or severity of asthma and hormonal status is really interesting (the role of hormones in immunity homeostasis).

Asthma is prevalent in prepubertal males, but this prevalence reverses after puberty. Adult women tend to have more severe asthma and not responder to treatments.

Oral contraceptives reduce asthma exacerbation. More severe episodes or a new onset may occur during menopause.



17 - Beta Estradiolo



Testosterone

Estrogen and Progesterone directly modulate the pathways involved in the pathogenesis of asthma

While testosterone appears protective against inflammatory processes potentially involved in asthma (although some uncertainties are present)

- Gender difference, sex hormone, and immediate type hypersensitivity reactions. Chen et al, 2008 Allergy.

- Endogenous and exogenous sex steroid hormones in asthma and allergy in females: a systematic review and meta analysis. McCleary et al, 2018 J Allergy Clin Immunol

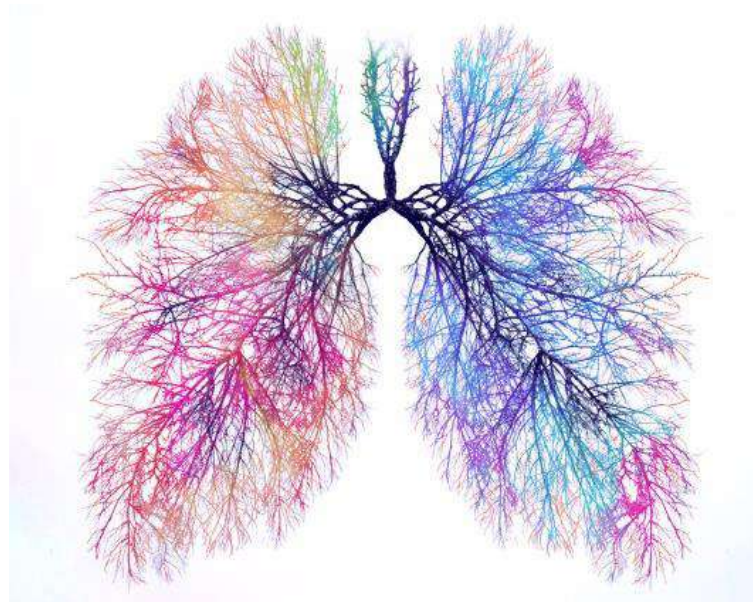
ANATOMIC DIFFERENCES: RESPIRATORY FUNCTION

Sex differences in lung architecture and respiratory function

MALES

Males have, in the prepubertal phase, a more likely dysaptic growth of the lung.

The bronchial tracts tend to grow later than the parenchymal growth, this generates a disproportion of the alveoli compared to the airways.



FEMALES

In girls, the bronchial tracts and lung parenchyma grow proportionally

- Sex difference in respiratory function. LoMauro et al, 2018. *Breath*
- Personalized treatment of Asthma: the importance of sex and gender differences. Jenkins et al. 2022 *J allergy Clin Immunol Pract*

After puberty, men develop larger airway diameters, greater lung volume and expiratory flow, and greater surface diffusion than girls. This contributes to an important extent in the observed sex difference effects.

RESEARCH ARTICLE



Prevalence and predictors of occupational asthma among workers in detergent and cleaning products industry and its impact on quality of life in El Asher Men Ramadan, Egypt

Amani Shawki Ahmed¹ · Dalia Anas Ibrahim² · Tarek Hamdy Hassan² · Wael Galal Abd-El-Azem¹

Workforce with average seniority of 36 years, 1 in 4 women, 76% non-smokers

Cleaning products may contain mixtures of chemical agents, including sensitizers (disinfectants, fragrances) often associated with respiratory irritants.

This study looked at the prevalence of occupational asthma in 780 workers. **35.4% of the workforce developed asthma.**

The main risk factors highlighted for the development of the pathology were:

Risk factors	OR	95% CI
Being women	1,39	1,09-1,96
Doing manual activity	3,07	1,72-5,46
Clinical history of atopy	1,60	1,09-2,33



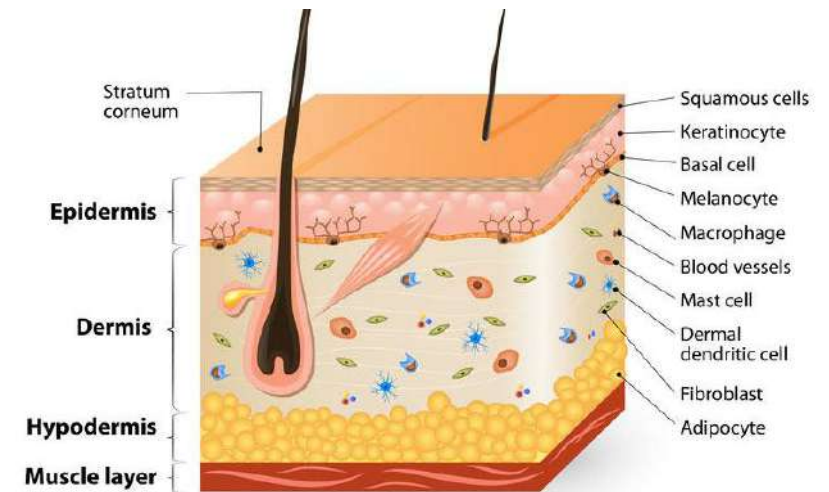
ANATOMICAL DIFFERENCES: THE SKIN

The biophysical properties of **human skin are influenced by steroid hormones**, and these determine sex-related variability, although some experimental results remain controversial.

Female skin is thinner than male skin, at any age (lower collagen content)

Other researchers have assessed how there is a different composition of proteins in the stratum corneum between men and women.

However, the consequences of these differences in terms of toxicant permeability remain largely unknown.



Male versus female skin: what dermatologists and cosmeticians should know. Rahrovan et al, 2018, Int J Women's Dermatol.

OCCUPATIONAL EXPOSURE

OR 2.2, CI 1.65-2.97

^{La} **Medicina del Lavoro**

Med Lav 2021; 112, 1: 34-43
DOI: 10.23749/mdl.v112i1.9794

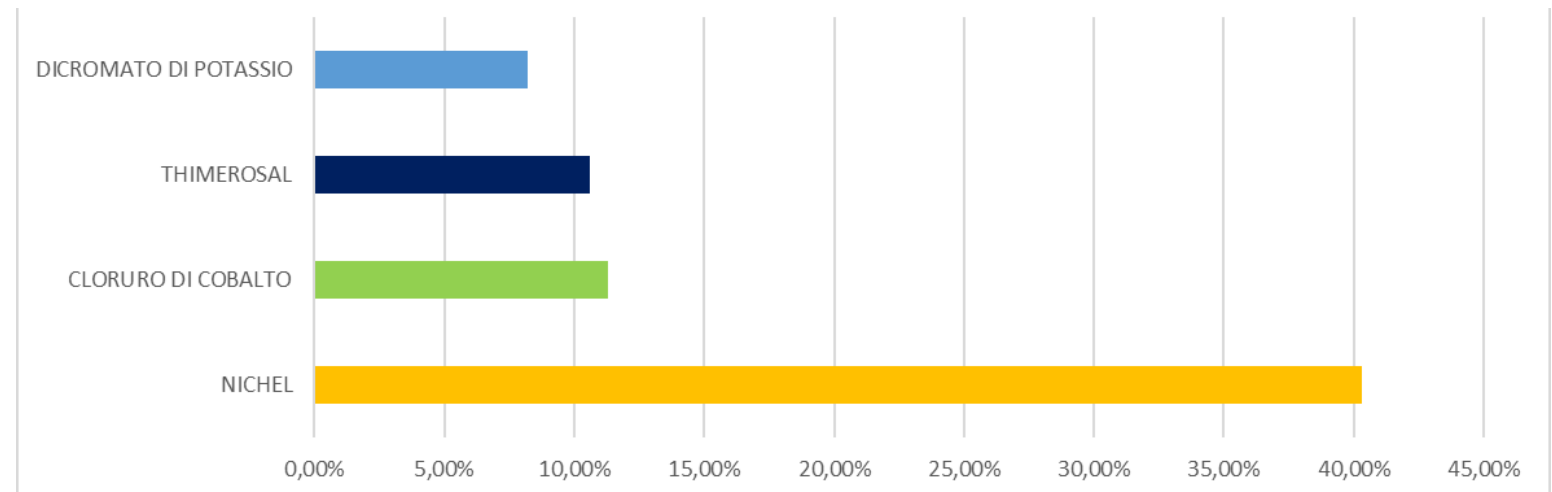
Occupational contact dermatitis in a gender perspective: North East Italian data 1996-2016

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Considering allergic contact dermatitis, it emerges that for women there is a higher prevalence rate in every job category than for men. Main work activities involved:

- 1- healthcare workers
- 2- restaurant workers
- 3- mechanical technicians
- 4- hairdresser



ALLERGIC CONTACT DERMATITIS: NICKEL

Contact allergy to nickel affects on average more than **20% of the female population** while only **4-5% of the male population**.

*Contact Dermatitis 2004; 50: 53-59
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CONTACT DERMATITIS

Review Article

The sex of the individual as a factor in allergic contact dermatitis

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Historically, women have higher nickel exposure through contact with jewellery, in particular earrings (remember that there is currently a REACH restriction in this sense precisely due to epidemiological evidence).

It was highlighted that 17% of the population who was "exposed" to nickel before the restrictive legislation developed an allergic reaction to the use of earrings containing nickel. While the awareness of girls who used earrings after the regulatory restriction was 3.9%.

Some authors suggested that exposure situations are the key for the observed gender differences, with higher rate of health effects in women



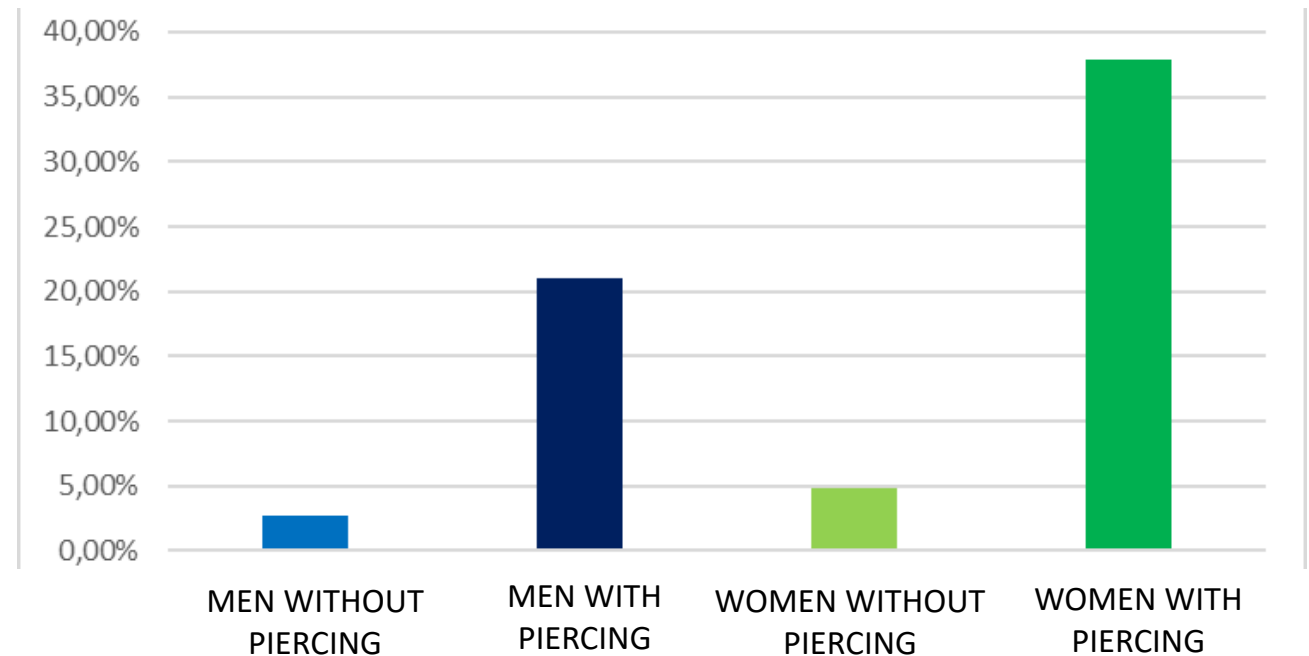
ALLERGIC CONTACT DERMATITIS: NICKEL

A Danish study in particular saw a reduction in awareness of nickel among the female population after the restrictions were issued.

from 24.8% to 9.2%

Piercing seems to be the element that influences nickel sensitization, rather than sex itself. But historically this involved the female population (gender difference)

NICKEL ALLERGY PREVALENCE



OCCUPATIONAL ALLERGIC CONTACT DERMATITIS

Women show a higher incidence of allergic contact dermatitis than men in the workplace

FACTORS INFLUENCING THIS RESULT:

- 1- contact with the chemical agent in the workplace
- 2- previous contact with the same sensitizing chemical agent in living environments
- 3- «wet» work and the use of detergents. In fact, water and detergents can make the skin barriers more "fragile" and therefore favor a clearer and/or faster adverse response.

Women tend to hold jobs in which "wet" work is present.

In Sweden, the activities that have the highest incidence of allergic contact dermatitis are hairdressers, machine fitters, cooks, dental assistants, mechanics, cleaners, kitchen assistants, nurses.

66.7% of cases involve women, largely because many of these businesses are female-dominated.

DAILY LIFE HABITS

It should also be considered that on average women deal with "wet" activities even in daily life.

It has been estimated that women who do not use a dishwasher and who have children under 4 years old show a prevalence of dermatitis 4 times higher than other women.



CONCLUSIONS

For numerous substances it is possible to highlight different health effects between men and women.

This is why risk management in the workplace must be organized considering also sex and gender differences.

Considerations on physiological differences (sex) must be appropriately conducted but associated with situations, in living and working environments, that can affect the diversification of effects (gender)



CONCLUSIONS: What can we hypothesize for the future?

Occupational exposure limit with different values for men and women? (for more chemicals?)

Greater and better involvement of Occupational physicians in risk assessment to facilitate the decision making for preventive gender-oriented activities?

More research studies to highlight the differences...

.....and much more!



**Thank you for your
attention**

